CATALYTIC TRANSFORMATIONS *VIA* METALLOCARBENES

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CONTENTS

1.1. Carbenes

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ABBREVIATIONS

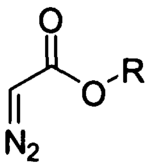
Ac	acetyl
acac	acetyl acetonate
AcOH	acetic acid
aq.	aqueous
ar	generic aromatic group
ax	axial
Bn	benzyl
BNP	1,1'-bi-2-naphtholphosphate
BPTV	*N*-benzene-fused phthaloyl group
Brsm	based on recovered starting material
Bu^n	*n*-butyl, C_4H_9-
Bu^t	*tert*-butyl
Bz	benzoyl
cap	caprolactamate
cat.	catalyst
CI	chemical ionisation
COSY	correlation spectroscopy
Cy	cyclohexyl
Δ	heat
d	day(s)
DCM	dichloromethane
DDBPN	6,6'-didodecyl-1,1'-bi-2-naphtholphosphate
DEM	diethyl maleate
DEF	diethyl fumarate
DMAD	dimethyl acetylenedicarboxylate
DOSP	*N*-(4-dodecylbenzenesulphonyl)prolinate
dr	diastereomeric ratio
ee	enantiomeric excess
EI	electron impact
equiv.	equivalent(s)
ES	electrospray
Et	ethyl

EDA	ethyl diazoacetate
FI	field ionisation
GC	gas chromatography
h	hour(s)
hv	light
HRMS	high-resolution mass spectrometry
Im	imidazole
IR	infra-red (spectroscopy)
lit.	literature
M	molar concentration ($moldm^{-3}$)
m	medium
m-	*meta-*
Me	methyl
Mes	mesityl
min.	minute(s)
m.p.	melting point
MS	mass spectrometry
NMR	nuclear magnetic resonance
NOE	nuclear overhauser effect
o-	*ortho-*
p-	*para-*
pfb	perfluorobutyrate
Ph	phenyl
PNB	*para*-nitrobenzyl
ppm	parts per million
Pr^i	isopropyl
PTTL	*N*-phthaloyl-*tert*-leucinate
py	pyridine
quat.	quarternary
R	generic alkyl group
RCM	ring closing metathesis
rearr.	rearrangement(s)
R_f	retention factor
Rh(II)	generic rhodium(II) catalyst
rt	room temperature

s	strong
sat.	saturated
soln.	solution
T	temperature
TBS	*tert*-butyl dimethylsilyl
tfa	trifluoroacetate
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
Tol	*para*-tolyl
Tr	trityl
TS	transition state
TMP	5,10,15,20-tetramesityl porphyrin
Tol	*para*-tolyl
TPP	5,10,15,20-tetraphenyl porphyrin
TTP	5,10,15,20-tetra-*p*-tolyl porphyrin
w	weak

STRUCTURES OF DIAZO COMPOUNDS

α-Diazoacetates



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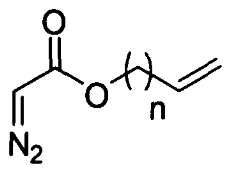

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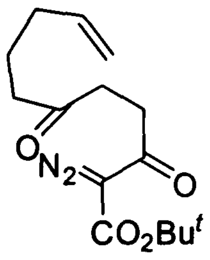
Carbonyl Ylide precursors



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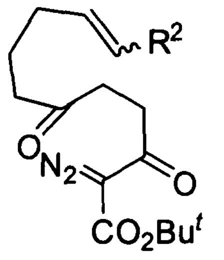

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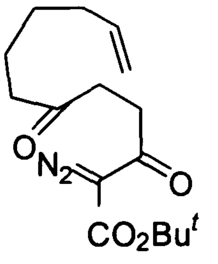

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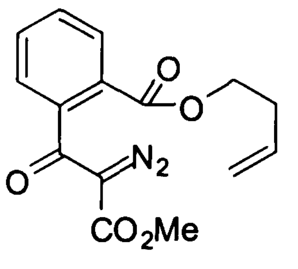

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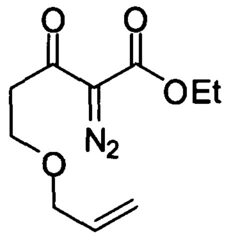
Oxonium Ylide precursors



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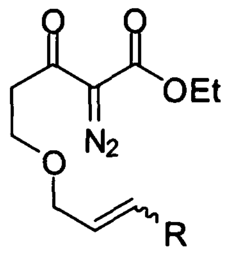

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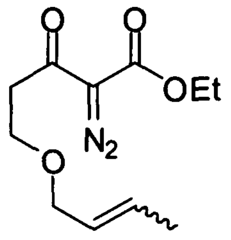

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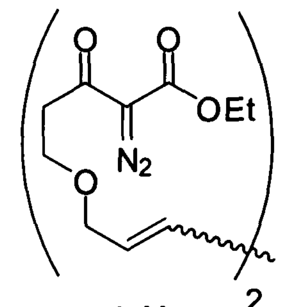

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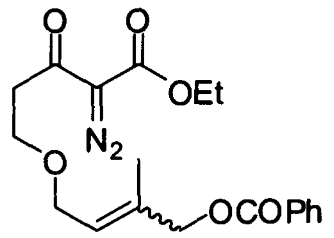

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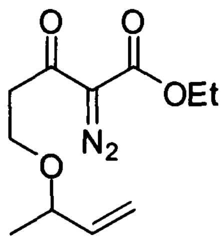

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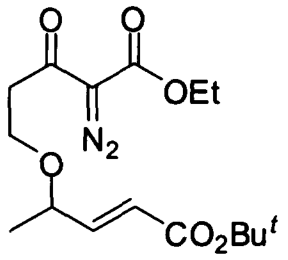

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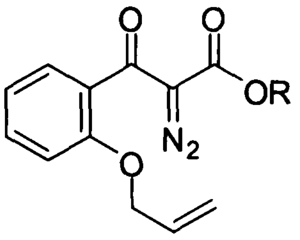
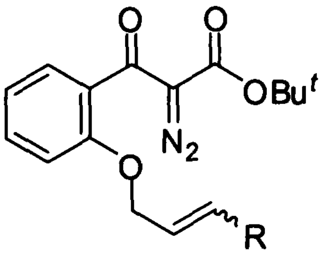


4.34a, R = Bu^t
4.34b, R = Et



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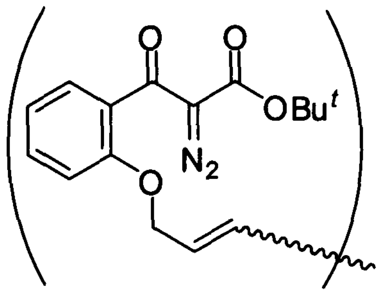

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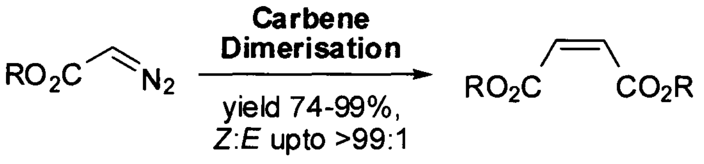
ABSTRACT

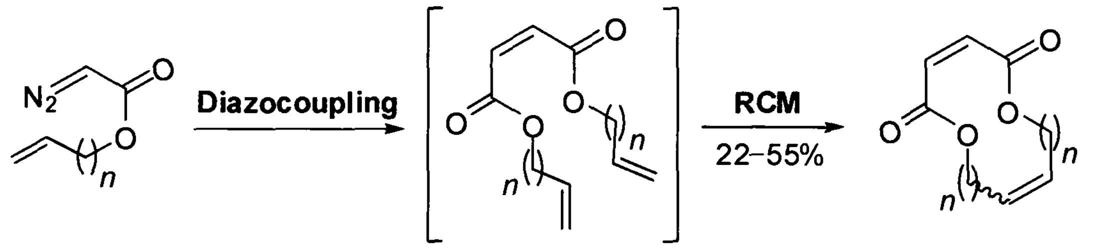
Catalytic Transformations *via* Metallocarbenes

Deepshikha Angrish — *Degree of Doctor of Philosophy*
St. Cross College — *Hilary 2007*

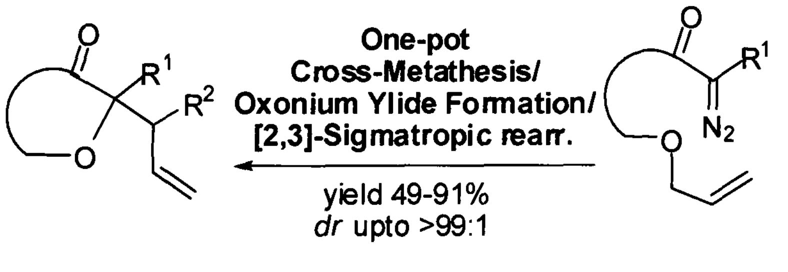
This thesis describes a new catalytic activity of a commonly used metathesis catalyst and demonstrates the viability of directly coupling two powerful C-C bond forming strategies: cross-metathesis and ylide transformations, both proceeding *via* metal-catalysed carbene transfer. Catalytic C-C bond formation reactions are highly significant; my studies focus on such transformations involving metallocarbenes. Grubbs' 2nd generation Ru catalyst is the most commonly used catalyst in olefin metathesis to generate thermodynamically preferred *trans*-olefins. During the course of my studies, I established that Grubbs 2nd generation catalyst (0.5 mol%) can also dimerise diazoacetates to give *cis*-enediesters (maleates) in good to excellent yields (74–99%) with high stereoselectivity (*Z*:*E* >95:5). The reaction between two different diazoacetates, catalysed by Grubbs catalyst gave access to unsymmetrical *cis*-enediesters with high stereoselectivity (*Z*:*E* >95:5, generally 99:1).

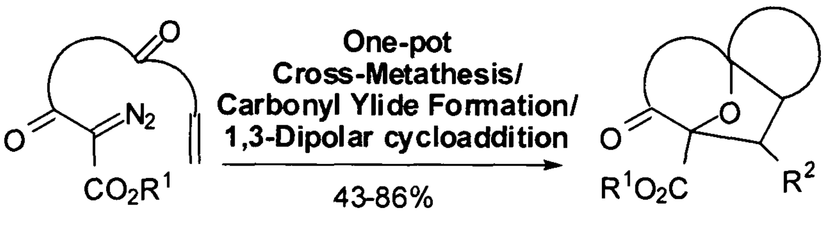


The catalyst was found to retain its alkene metathetical activity during diazo coupling; building on this latter observation a novel route to access dienyl dilactones by *head*-to-*head* dimerisation of unsaturated diazoacetates was developed.



Cross-metathesis was found to be chemoselective in the presence of diazo functionality (when flanked by two carbonyl groups), allowing the functionalisation of tethered olefin. The elaborated diazocarbonyl olefins were subjected to $Rh_2(OAc)_4$ catalysed ylide formation and subsequent transformations. Significantly, one-pot cross-metathesis/ylide transformations (1,3-dipolar cycloaddition and [2,3]-simgatropic rearrangement) also proved to be viable, establishing that the spent Ru catalyst following metathesis does not affect the subsequent Rh(II)-catalysed transformation.





CHAPTER 1

INTRODUCTION

INTRODUCTION

This thesis is concerned with the formation of metallocarbenes from α-diazocarbonyl compounds in presence of transition metal complexes and their subsequent transformations: dimerisation, formation of carbonyl/ oxonium ylides and 1,3-dipolar cycloadditions/ [2,3]-sigmatropic rearrangements of these ylides respectively. Therefore, this introduction will cover: the carbenes in general (their structure, reactivity and methods of generation) (Section 1.1), transformations involving α-diazocarbonyl compounds (Section 1.2), use of rhodium catalysts for diazo-decomposition (Section 1.3) and the summaries of the reactions of metallocarbenes (Section 1.4) are provided to place the reactions discussed in my research in perspective.

1.1. Carbenes

1.1.1. Structure and Reactivity

Carbenes are highly reactive, neutral intermediates, represented by R_2C:,[1,2,3] and are capable of undergoing a number of synthetically useful transformations. They are sp^2 hybridised, with two bonding electrons (both in sp^2 hybrid orbitals) and two non-bonding electrons. The non-bonding electrons can have parallel or antiparallel spins, thus giving rise to two spin states, namely *singlet* and *triplet* (Figure1.1).

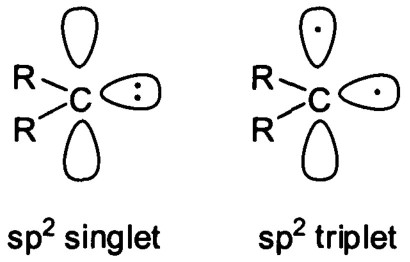


Figure 1.1. Spin states in carbenes.

The *singlet* carbene has the spins of the two non-bonding electrons paired in the sp^2 orbital with a vacant *p*-orbital, giving it a spin multiplicity = 1. However, in *triplet* carbenes, the two non-bonding electrons have parallel spins, each present in a sp^2 and a *p*-orbital, thus having spin multiplicity = 3. In general, triplet is the ground state (energy difference between the singlet and

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[1] M. Jones, R. A. Moss, *Carbenes*, Wiley, New York, **1973–1975**.

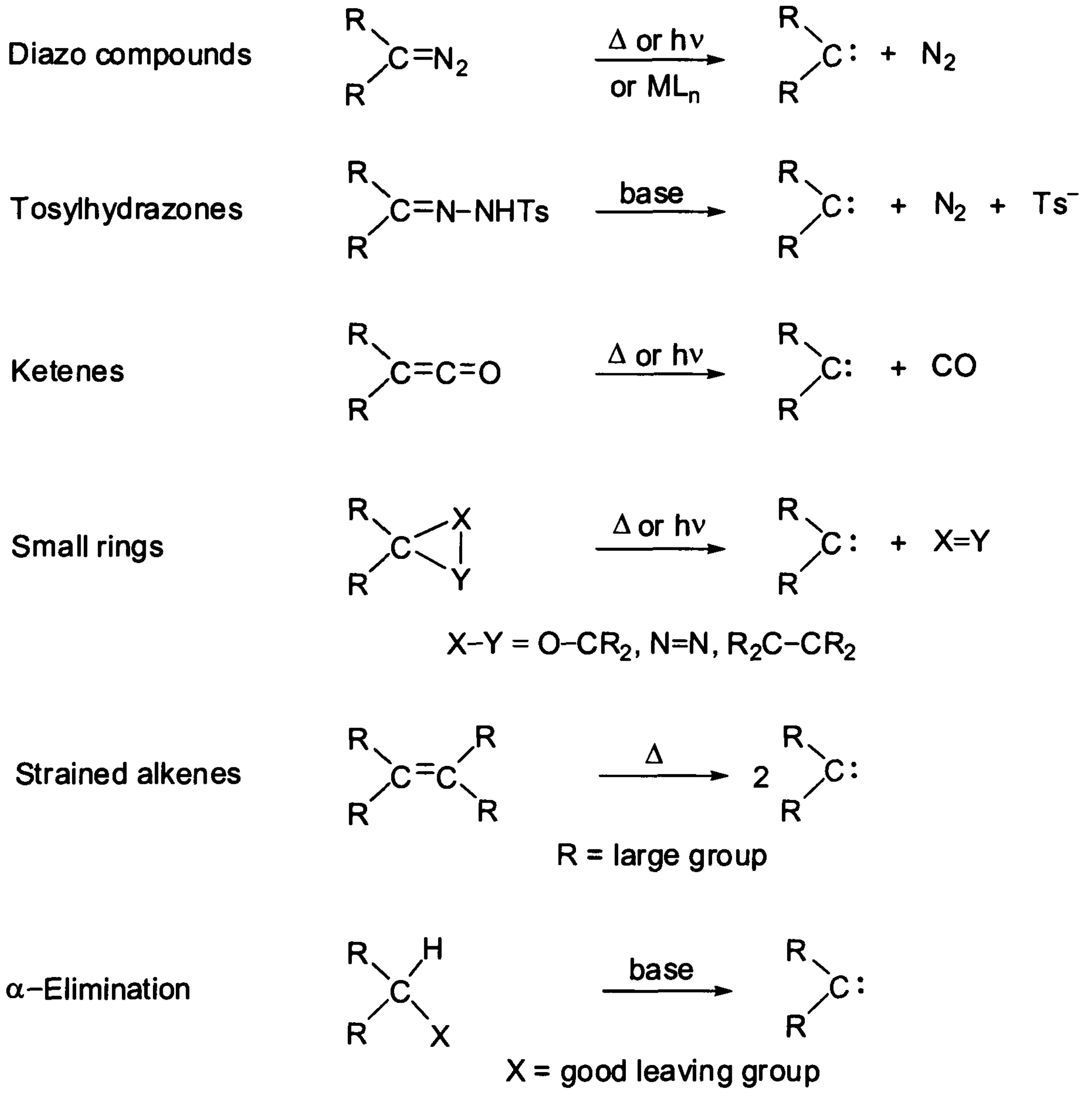
[2] D. Bethell, *Adv. Phys. Org. Chem.* **1969**, *7*, 153–209.

[3] J. March, *Advanced Organic Chemistry: Reactions, Mechanisms and Structure*, John Wiley & Sons, Singapore, **2000**, pp. 195–202.

the triplet states estimated to be 32–42 $kJmol^{-1}$ for H_2C:).[4,5,6] The nature of the substituent attached can alter the ground state, e.g. when R is a good π-donor, then the ground state changes from triplet to singlet, due to electron donation to the vacant *p*-orbital, thus stabilising the singlet state through dipolar resonance structures.

Carbenes are electron deficient intermediates, as the carbon atom has only six electrons in the valance shell and, hence are electrophilic in their reactions. The more electron withdrawing the substituents, the more electrophilic is the carbene. However, with strong π-donor substituents (such as amino groups), carbenes can be nucleophilic in their reactions.

1.1.2. Methods of Generation of Carbenes



Scheme I.1. Methods for generation of carbenes.

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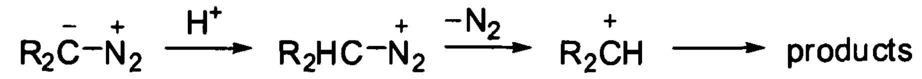
[4] M. J. S. Dewar, R. C. Haddon, P. K. Weiner, *J. Am. Chem. Soc.* **1974**, *96*, 253–255.
[5] R. R. Lucchese, H. F. Schaefer, *J. Am. Chem. Soc.* **1977**, *99*, 6765–6766.
[6] R. K. Lengel, R. N. Zare, *J. Am. Chem. Soc.* **1978**, *100*, 7495–7599.

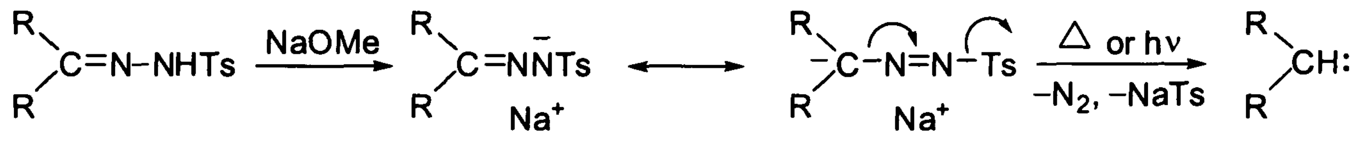
Carbenes are generated under thermal, photochemical, or under milder conditions by transition metal catalysis. The methods of generating carbenes are based on elimination[7] or fragmentation[8,9] reactions, usually involving the formation of thermodynamically stable by-products (Scheme 1.1). Diazo compounds are the most commonly used carbene precursors. The stability of diazo compounds depends upon the nature of the substituents attached to the diazo carbon. The decomposition of diazo compounds can be carried out thermally or photochemically.[8,9] They can also be decomposed by acids, by C-protonation followed by loss of nitrogen (Scheme 1.2).



$$R_2\overset{-}{C}-\overset{+}{N}_2 \xrightarrow{H^+} R_2HC-\overset{+}{N}_2 \xrightarrow{-N_2} R_2\overset{+}{C}H \longrightarrow \text{products}$$

Scheme 1.2. Acid catalysed decomposition of diazo compounds.

Carbenes can also be generated from tosylhydrazones in presence of a base (such as NaH or NaOMe), which removes the acidic NH proton to give the isolatable sodium salt of tosylhydrazone. This, upon heating or irradiation, decomposes to give the carbene with loss of sodium 4-toluenesulfonate (NaTs) and nitrogen (Scheme 1.3).



Scheme 1.3. Carbenes from tosylhydrazones, Bamford-Stevens reaction.[10]

However, the mildest method involves the use of transition metal catalysts. In presence of a transition metal catalyst, diazo compounds decompose to generate carbenes bound to the metal, referred to as metallocarbenes.[11,12,13,14]

1.2. Transformations involving α-Diazocarbonyl Compounds

As mentioned above, α-diazocarbonyl compounds are sources of carbenes. The decomposition of diazo compounds to generate carbene intermediates can be accomplished by a

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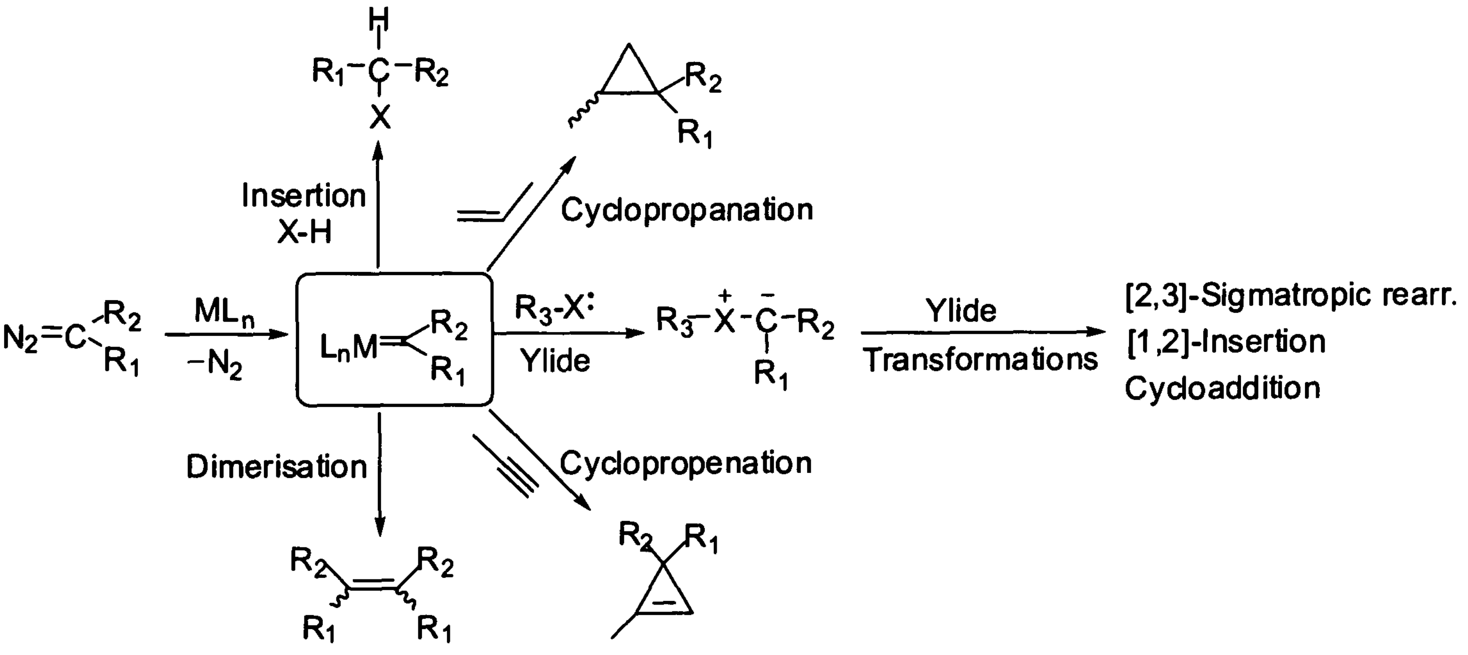
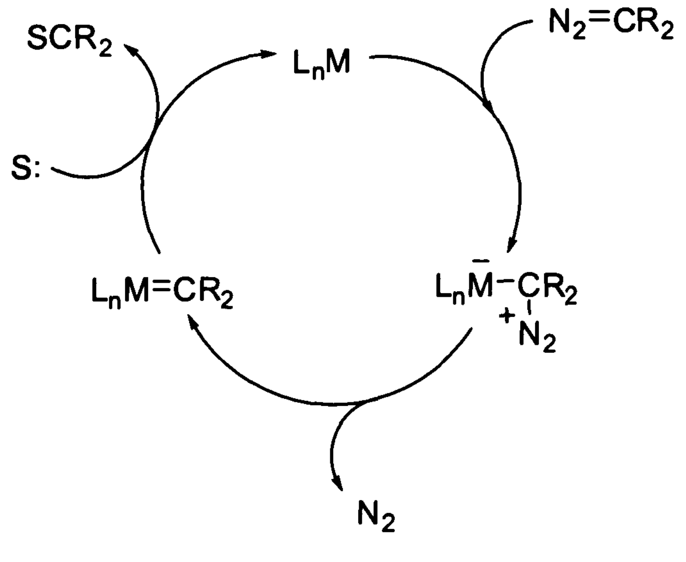
[7] W. Kirmse, *Angew. Chem. Int. Ed. Engl.* **1965**, *4*, 1–10.
[8] M. Regitz, G. Maas, *Diazo Compounds*, Academic Press, New York, **1986**, pp. 170–184.
[9] M. T. H. Liu, *Chem. Soc. Rev.* **1982**, *11*, 127–140.
[10] W. R. Bamford, T. S. Stevens, *J. Chem. Soc.* **1952**, 4735–4740.
[11] T. Ye, M. A. McKervey, *Chem. Rev.* **1994**, *94*, 1091–1160.
[12] A. Padwa, M. D. Weingarten, *Chem. Rev.* **1996**, *96*, 223–270.
[13] M. P. Doyle, D. C. Forbes, *Chem. Rev.* **1998**, *98*, 911–936.
[14] G. Mehta, S. Muthusamy, *Tetrahedron* **2002**, *58*, 9477–9504.

number of transition metal catalysts to give metal bound carbenoids. The conditions required for this are generally mild, and the reactivity of the carbene is influenced by the bound metal catalyst: the carbenoid reacts as an electrophilic carbene, with the degree of electrophilicity dependent on the metal complex employed. The metallocarbenes are capable of undergoing a number of synthetically useful transformations, such as carbene dimerisation, cyclopropanation, cyclopropenation, X–H insertion (X = C, O, N), ylide formation and its subsequent transformations (such as [2,3]-sigmatropic rearrangement, [1,2]-Stevens rearrangement and carbonyl ylide cycloadditions) (Scheme 1.4). Dimerisation and ylide transformations will be discussed further in later sections.



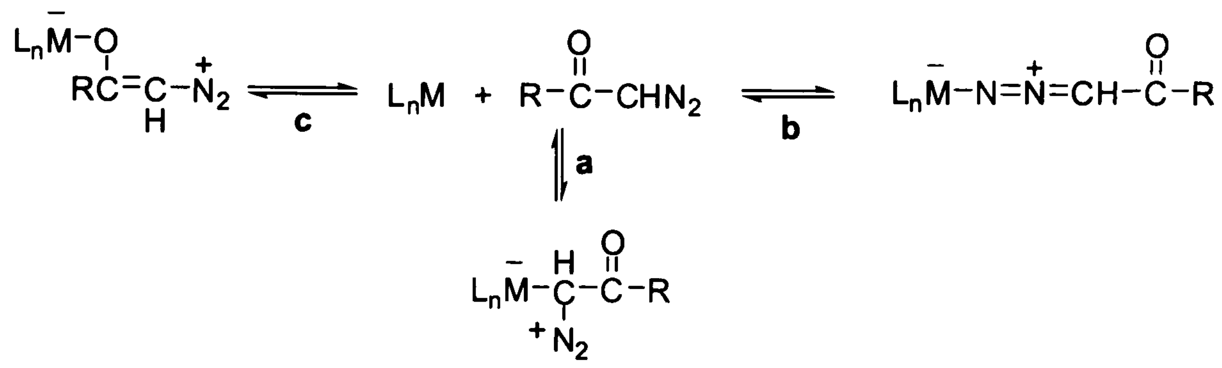
Scheme 1.4. Carbene transformations of diazo compounds.

The general accepted mechanism for the catalytic decomposition of diazo compounds is described in Scheme 1.5.



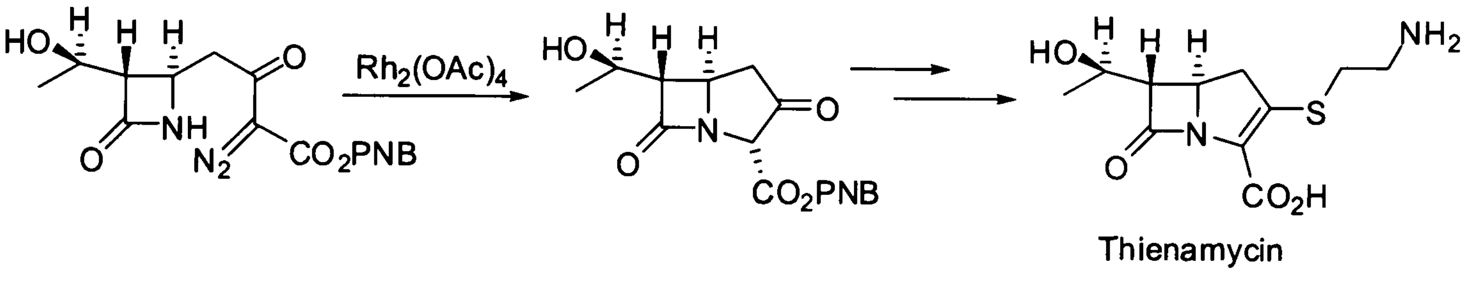
Scheme 1.5. General mechanism for diazo decomposition.

The addition of diazo compound to the metal complex, followed by the loss of nitrogen gives the metal bound carbene (metallocarbene). Transfer of the electrophilic carbene to the electron rich substrate(s), regenerates the catalytically active metal complex ML_n, thus completing the catalytic cycle. α-Diazocarbonyl compounds have three basic sites for potential coordination to the metal complex, namely from carbon (a), nitrogen (b) and oxygen (c) (Scheme 1.6).



Scheme 1.6. Possible coordination sites for transition metal catalyst.

Although association from nitrogen and oxygen can occur, metallocarbenes are generally derived from association with carbon (Scheme 1.6, a). Commonly-used transition metals for carbene transformations are those of copper(I)[15] and rhodium(II).[16] The use of ruthenium, osmium, iron, platinum, nickel and chromium complexes has also been explored.[17] One of the most significant carbene reactions is the dirhodium(II) tetraacetate catalysed intramolecular insertion into the N–H bond of a β-lactam, developed by Merck in the synthesis of the antibiotic thienamycin (Scheme 1.7).[18,19]



Scheme 1.7. Merck synthesis of thienamycin.

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[15] W. Kirmse, *Angew. Chem. Int. Ed.* **2003**, *42*, 1088–1093.

[16] a) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*, John Wiley & Sons, New York, **1998**, pp 397–416; b) M. P. Doyle, M. Protopopova, *Tetrahedron* **1998**, *54*, 7919–7946.

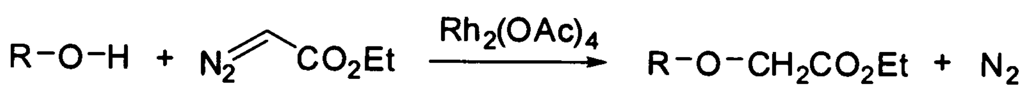
[17] G. Maas, *Chem. Soc. Rev.* **2004**, *33*, 183–190.

[18] D. G. Melillo, I. Shinkai, T. Liu, K. Ryan, M. Sletzinger, *Tetrahedron Lett.* **1980**, *21*, 2783–2786.

[19] T. N. Salzmann, R. W. Ratcliffe, B. G. Christensen, F. A. Bouffard, *J. Am. Chem. Soc.* **1980**, *102*, 6161–6163.

1.3. Rhodium Catalysts in Diazo Decomposition

Dirhodium(II) catalysts are the most effective, versatile and the widely-used metal complexes for decomposition of diazo compounds. The wide variety of bridging ligands provides a control of reactivity and selectivity during the process. The most commonly used rhodium complex, dirhodium(II) tetraacetate $Rh_2(OAc)_4$ (Figure 1.2), was first introduced as a catalyst for carbene transformations by Teyssie and co-workers in 1973 for the insertion of ethyl diazoacetate (EDA) into the O–H bond of alcohols, water and weak acids (Scheme 1.8).[20]



Scheme 1.8. O–H insertion of diazoacetate.

$Rh_2(OAc)_4$ has an octahedral geometry with a D_{4h} symmetry; there are four bridging acetate ligands and one vacant axial coordination site per Rh(II).[21]

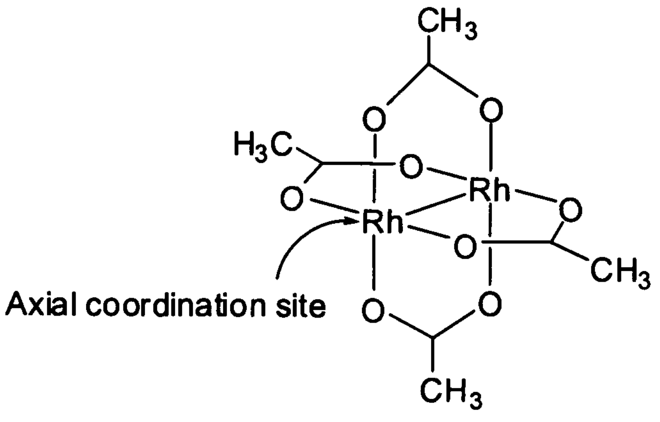


Figure 1.2. Dirhodium(II) tetraacetate.

Replacing the acetate ligand with other carboxylates changes the physical and the chemical properties of the dirhodium(II) carboxylate according to the characteristics of the ligands. $Rh_2(OAc)_4$ is prepared by reaction of $RhCl_3.xH_2O$[22] with acetic acid and acetic anhydride at reflux. The other tetracarboxylate complexes (such as dirhodium trifluouroacetate,[23] butyrate,[24] perfluorobutyrate[25]) are prepared from $Rh_2(OAc)_4$ by refluxing with an excess of the corresponding acid and its anhydride.[26] Ligand exchange is also accomplished from $Rh_2(OAc)_4$ in refluxing chlorobenzene by using an excess of the corresponding carboxylic acid (Scheme 1.9).

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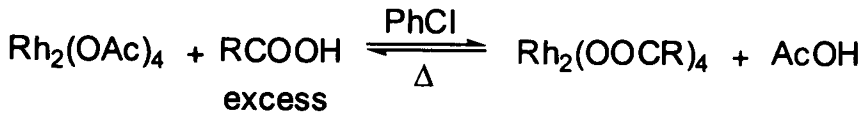
[20] R. Paulissenen, H. Reimlinger, E. Hayez, A. J. Hubert, P. Teyssie, *Tetrahedron Lett.* **1973**, *14*, 2233–2236.
[21] E. B. Boyar, S. D. Robinson, *Coord. Chem. Rev.* **1983**, *50*, 109–208.
[22] G. A. Rempel, P. Legzdins, H. Smith, G. Wilkinson, *Inorg. Synth.* **1972**, *13*, 90–91.
[23] R. S. Drago, J. R. Long, R. Cosmano, *Inorg. Chem.* **1982**, *21*, 2196–2202.
[24] R. S. Drago, J. R. Long, R. Cosmano, *Inorg. Chem.* **1981**, *20*, 2920–2927.
[25] M. P. Doyle, M. S. Shanklin, *Organometallics* **1994**, *13*, 1081-1088.
[26] T. R. Felthouse, *Prog. Inorg. Chem.* **1982**, *29*, 73–166.

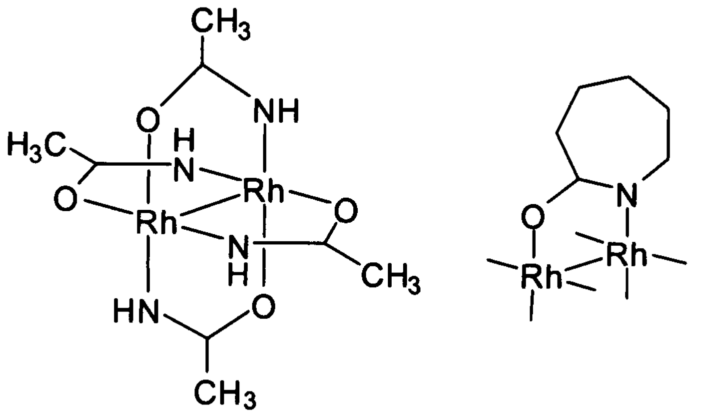
Co-distillation of chlorobenzene-acetic acid is often used to remove acetic acid to drive the reaction to completion.[27]



$$\underset{}{Rh_2(OAc)_4} + \underset{\text{excess}}{RCOOH} \underset{\Delta}{\overset{PhCl}{\rightleftharpoons}} Rh_2(OOCR)_4 + AcOH$$

Scheme I.9. Rh(II) Carboxylates by ligand exchange.

Dirhodium(II) carboxamidates are another class of rhodium(II) complexes used in diazo transformations. The simplest one in this class being rhodium(II) acetamidate, $Rh_2(CH_3CONH)_4$, (Figure 1.3) in which each rhodium is bonded to two oxygen and two nitrogen atoms, which are oriented in a *cis*-geometry.[28]



Rh(II) acetamidate Rh(II) caprolactamate

Figure. 1.3. Rhodium(II) carboxamidates.

Rhodium carboxamidates are also prepared from $Rh_2(OAc)_4$ in refluxing chlorobenzene by using an excess of the carboxamide, using a Soxhlet extractor containing sodium carbonate to trap the acetic acid, to drive the ligand exchange to completion.[29]

Chiral rhodium(II) catalysts (Figure 1.4) have also been developed in diazo chemistry to effect enantioselective transformations. Chiral carboxylate ligands have been independently reported by Brunner (**1.01**),[30] McKervey (**1,02**),[31] and Hashimoto/ Ikegami (**1.03**)[32] for intermolecular cyclopropanation and C–H insertion, but their enantioselectivities in intermolecular reactions with simple alkenes have been marginal.

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[27] H. J. Callot, C. Piechocki, *Tetrahedron Lett.* **1980**, *21*, 3489–3492.

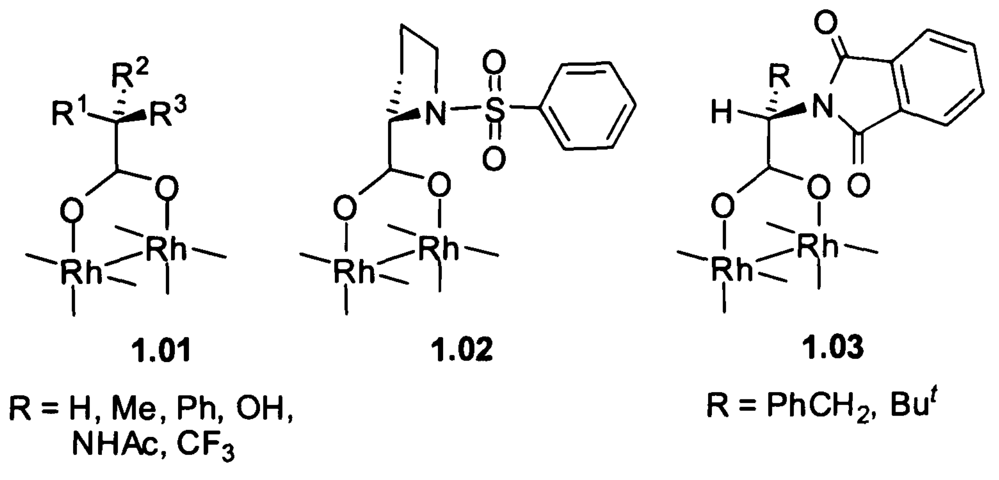
[28] M. Q. Ahsan, I. Bernal, J. L. Bear, *Inorg. Chem.* **1986**, *25*, 260–265.

[29] M. P. Doyle, L. J. Westrum, W. N. E. Wolthuis, M. M. See, W. P. Boone, V. Bagheri, M. M. Pearson, *J. Am. Chem. Soc.* **1993**, *115*, 958–964.

[30] H. Brunner, H. Kluschanzoff, K. Wutz, *Bull. Chem. Soc. Belg.* **1989**, *98*, 63–72.

[31] M. Kennedy, M. A. McKervey, A. R. Maguire, G. H. P. Roos, *J. Chem. Soc., Chem. Commun.* **1990**, 361–362.

[32] S. Hashimoto, N. Watanabe, S. Ikegami, *Tetrahedron Lett.* **1994**, *31*, 5173–5174.



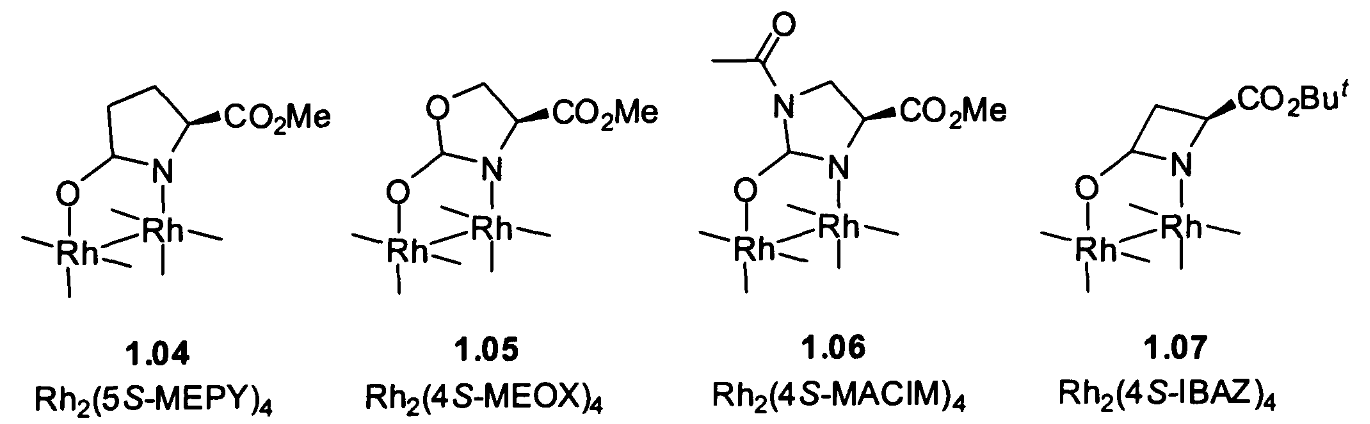
1.01
R = H, Me, Ph, OH, NHAc, CF_3

1.02

1.03
R = $PhCH_2$, Bu^t

Figure 1.4. Chiral rhodium(II) carboxylates.

Chiral rhodium(II) carboxamidates based on enantiomerically pure α-substituted carboxamides have also been developed by Doyle and co-workers.[33] These are based on 2-oxopyrrolidine (**1.04**),[34,35] 2-oxazolidinone (**1.05**),[36] *N*-acylimidazolidin-2-one (**1.06**),[37,38] and 2-azetidinone (**1.07**)[39] (Figure 1.5). Apart from chiral carboxylates and carboxamidates, rhodium(II) catalysts with chiral binaphthyl phosphates,[40,41,42] have also been studied in enantioselective diazo transformations.



1.04
$Rh_2(5S\text{-MEPY})_4$

1.05
$Rh_2(4S\text{-MEOX})_4$

1.06
$Rh_2(4S\text{-MACIM})_4$

1.07
$Rh_2(4S\text{-IBAZ})_4$

Figure 1.5. Chiral rhodium carboxamidates.

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[33] M. P. Doyle, *Russ. Chem. Bull.* **1994**, *43*, 1770–1782.

[34] M. P. Doyle, W. R. Winchester, J. A. A. Hoorn, V. Lynch, S. H. Simonsen, R. Ghosh, *J. Am. Chem. Soc.* **1993**, *115*, 9968-9978.

[35] M. P. Doyle, W. R. Winchester, S. H. Simonsen, R. Ghosh, *Inorg. Chim. Acta* **1994**, *220*, 193–199.

[36] M. P. Doyle, W. R. Winchester, M. N. Protopopova, P. Müller, G. Bernardinelli, D. Ene, S. Motallebi, *Helv. Chim. Acta* **1993**, *76*, 2227–2235.

[37] M. P. Doyle, et al. *J. Am. Chem. Soc.* **1995**, *117*, 5763–5775.

[38] M. P. Doyle, Q. -L. Zhou, C. E. Raab, G. H. P. Roos, S. H. Simonsen, V. Lynch, *Inorg. Chem.* **1996**, *35*, 6064–6073.

[39] M. P. Doyle, Q.-L. Zhou, S. H. Simonsen, V. Lynch, *Synlett* **1996**, 697–698.

[40] N. McCarthy, M. A. McKervey, T. Ye, M. MnCann, E. Murphy, M. P. Doyle, *Tetrahedron Lett.* **1992**, *33*, 5983–5986.

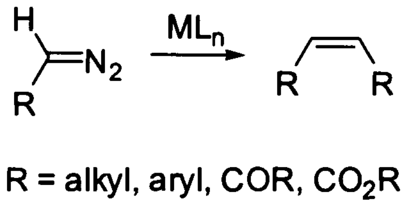
[41] M. C. Pirrung, J. Zhang, *Tetrahedron Lett.* **1992**, *33*, 5987-5890.

[42] D. M. Hodgson, P. A. Stupple, C. Johnstone, *Chem. Commun.* **1999**, 2185–2186.

1.4. Reactions of Metallocarbenes

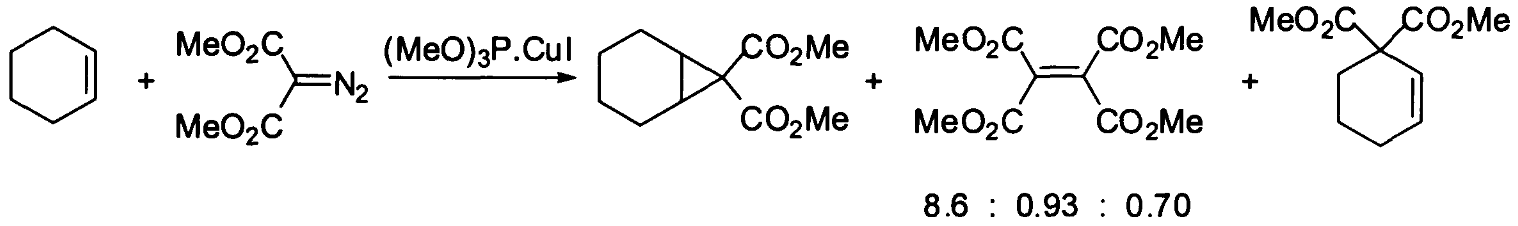
1.4.1. Carbene Dimerisation

The formation of alkenes from carbene dimerisation is often regarded as an unwanted side reaction during transformations involving diazo compounds. However, dimerisation has also been shown to be an efficient and synthetically useful transformation. Initially, copper salts [CuO, $CuBr_2$ or $Cu(ClO_4)_2$] were used for the diazo coupling to give thermodynamically less stable *cis*-olefins, with poor stereoselectivity (Scheme 1.10).[43,44]



Scheme 1.10. Homocoupling of diazo compounds.

An interesting example of copper catalysed carbene dimerisation is the formation of tetramethoxycarbonylethylene (by carbene dimerisation) as a by-product during the reaction of cyclohexene with dimethyl diazomalonate (Scheme 1.11).[44,45]



Scheme 1.11. Tetrasubstituted olefin from diazo coupling.

Raney nickel has also been found to decompose methyl diazoacetate quantitatively to a 93:7 mixture of dimethyl maleate and dimethyl fumarate.[46] Though a number of other transition metal catalysts have been reported to effect the diazo coupling, so far, Ru based catalysts have been the most successful in achieving highest levels of selectivity. Porphyrin based [Ru(2,6-Cl_2TPP)(CO)] **1.08** also catalyses the inter and intramolecular coupling of diazoacetates highly stereoselectively (Scheme 1.12).[47]

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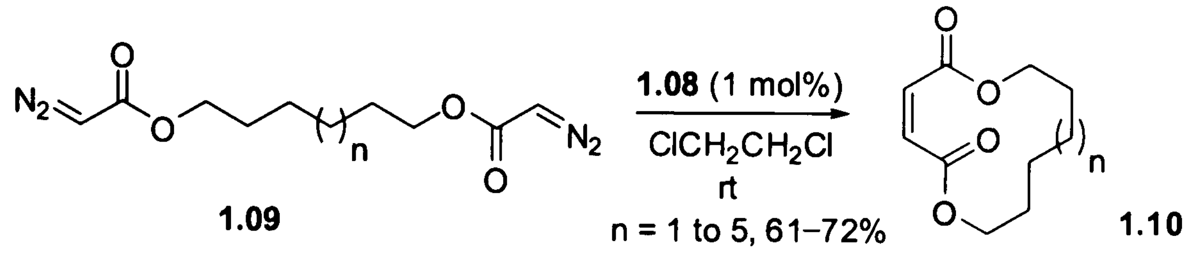
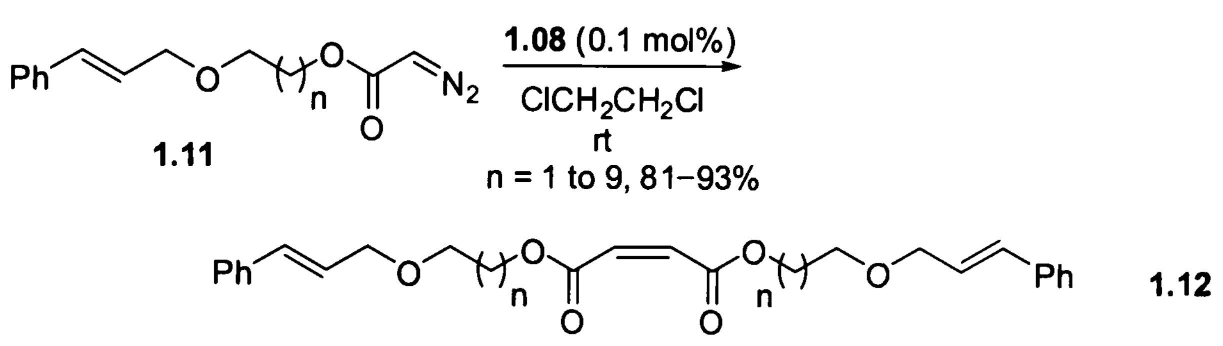
[43] T. Oshima, T. Nagai, *Tetrahedron Lett.* **1980**, *21*, 1251–1254.
[44] D. S. Wulfman, B. W. Peace, R. S. McDaniel, *Tetrahedron* **1976**, *32*, 1251–1255.
[45] B. W. Peace, D. S. Wulfman, *Tetrahedron Lett.* **1971**, *41*, 3799–3802.
[46] H. Bock, H. P. Wolf, *Angew. Chem. Int. Ed. Engl.* **1985**, *23*, 418–419.
[47] G. -Y. Li, C. -M. Che, *Org. Lett.* **2004**, *6*, 1621–1623.



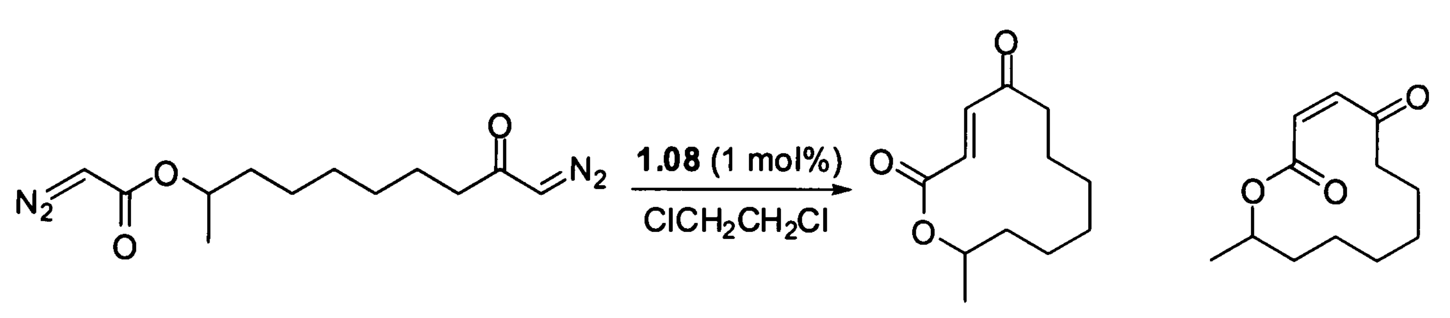
Scheme 1.12. Intramolecular diazo coupling.

Interestingly, with unsaturated diazoacetates **1.11**, neither the *trans* isomer nor the intramolecular cyclopropanation was observed using the same catalyst (Scheme 1.13).



Scheme 1.13. Intermolecular diazo coupling.

Catalytic carbene dimerisation has been successfully employed for the synthesis of patulolide A **1.14a** and patulolide B **1.14b** (the biologically active macrocyclic lactones, isolated from *penicillium utricae* mutants).[48] Doyle and co-workers first demonstrated this by intramolecular coupling of diazoketoester **1.13**, catalysed by $Rh_2(OAc)_4$, however this gave a 1:1 mixture of *trans* and *cis*-isomers in modest 30% yield.[49] The use of porphyrin based [Ru(2,6-Cl_2TPP)(CO)] **1.08** gave the *cis*-isomer, patulolide B with high stereoselectivity (*cis*:*trans* >40:1) and good yield (67%) (Scheme 1.14).[47]



1.13 **1.14a** Patulolides A **1.14b** Patulolides B

Scheme 1.14. Diazo coupling toward biologically active lactones.

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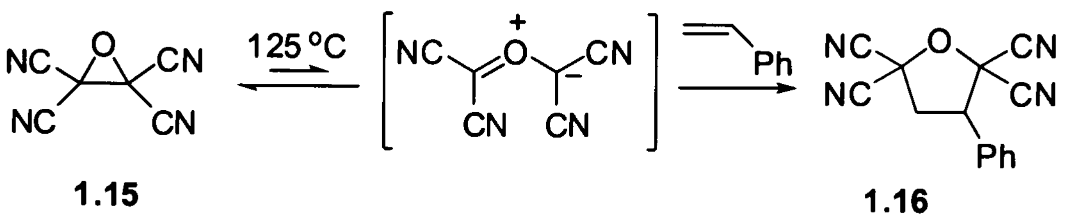
[48] J. Sekiguchi, H. Kuroda, Y. Yamada, H. Okada, *Tetrahedron Lett.* **1985**, *26*, 2341–2342.

[49] M. P. Doyle, W. Hu, L. M. Phillips, *Org. Lett.* **2000**, *2*, 1777–1779.

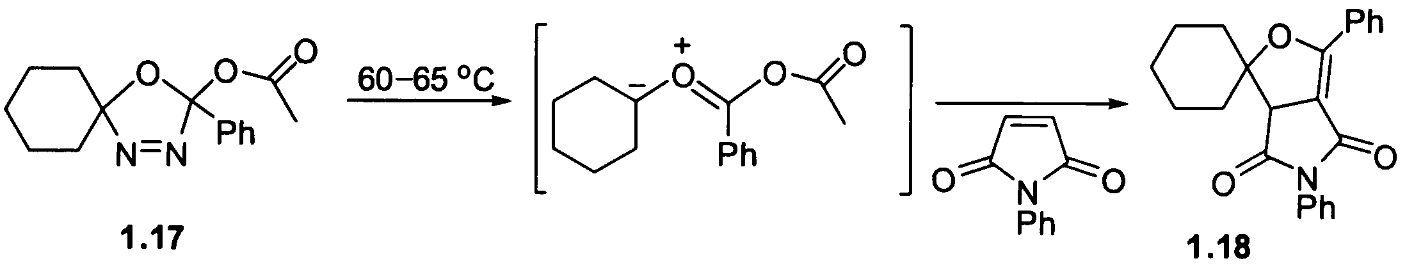
1.4.2. Tandem Carbonyl Ylide Formation-Cycloaddition

Carbonyl ylides are reactive intermediates, which can be prepared in several ways: a) by electrocyclic ring opening of epoxides bearing electron withdrawing substituents under thermal or photochemical conditions.[50] The small equilibrium contribution of the transient ylide is capable of undergoing 1,3-dipolar cycloaddition with a dipolarophile. Linn and Benson,[51,52] demonstrated the ability of tetracyanoethylene oxide **1.15** to add to olefins, acetylenes, and even to benzene, at elevated temperatures, forming reduced furan derivatives (Scheme 1.15).



Scheme 1.15. Carbonyl ylides from epoxides.

b) thermal extrusion of nitrogen from 1,3,4-dioxadiazolines in the presence of a dipolarophile (e.g. *N*-phenyl maleimide) can also effect cycloaddition of the transient carbonyl ylide (Scheme 1.16).[53]



Scheme 1.16. Carbonyl ylides from dioxadiazolines.

c) the simplest approach for the generation of carbonyl ylides involves the interaction of a metallocarbene (from diazo compound) with carbonyl oxygen (Scheme 1.17).[54] This can be achieved by transition metal catalysed decomposition of α-diazo compounds in the presence of a carbonyl group, present in the same molecule or added externally. The ylide can subsequently undergo 1,3-dipolar cycloaddition to a π-bond to give a furan or reduced furan derivative. Such a cascade process is of interest because it allows rapid generation of molecular complexity.

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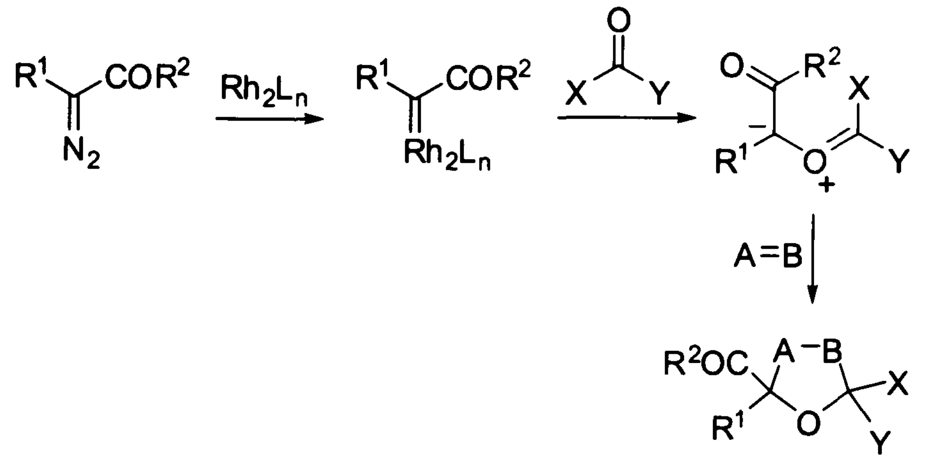
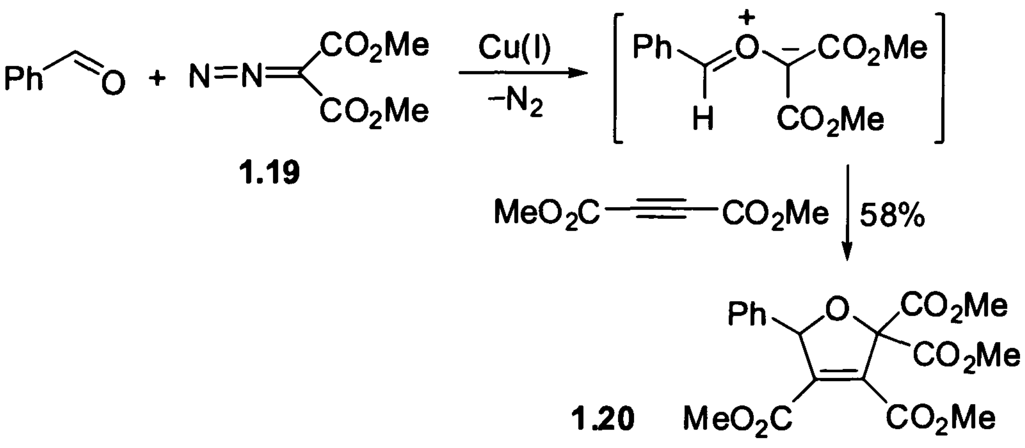
[50] R. Huisgen, *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 572–585.
[51] W. J. Linn, *J. Am. Chem. Soc.* **1965**, *87*, 3665–3672.
[52] W. J. Linn, R. E. Benson, *J. Am. Chem. Soc.* **1965**, *87*, 3657–3665.
[53] N. Shimizu, P. D. Bartlett, *J. Am. Chem. Soc.* **1978**, *100*, 4260–4267.
[54] M. P. Doyle, *Acc. Chem. Res.* **1986**, *19*, 348–356.



Scheme 1.17. Rh(II) catalysed carbonyl ylide formation-cycloaddition.

1.4.2a. Intermolecular Carbonyl Ylide Formation

The bimolecular reaction between a metallocarbene and a carbonyl compound was first studied by Huisgen and de March.[55,56] They found that a carbonyl ylide could be generated by the Cu(I) catalysed decomposition of dimethyl diazomalonate **1.19** in the presence of benzaldehyde. The carbonyl ylide formed underwent cycloaddition either with benzaldehyde or an alternative dipolarophile (such as dimethyl acetylenedicarboxylate, DMAD) to give a dioxolane or a furan derivative, respectively (Scheme 1.18).



Scheme 1.18. Intermolecular carbonyl ylide formation-cycloaddition.

Doyle and co-workers also studied the intermolecular formation of carbonyl ylides derived from diazoacetates and aromatic aldehydes, which subsequently underwent cycloaddition with a suitable dipolarophile.[57] These investigations highlight the potential problem of forming isomeric carbonyl ylides (Scheme 1.19). The *trans*-stereochemistry observed in the cycloadduct **1.21**

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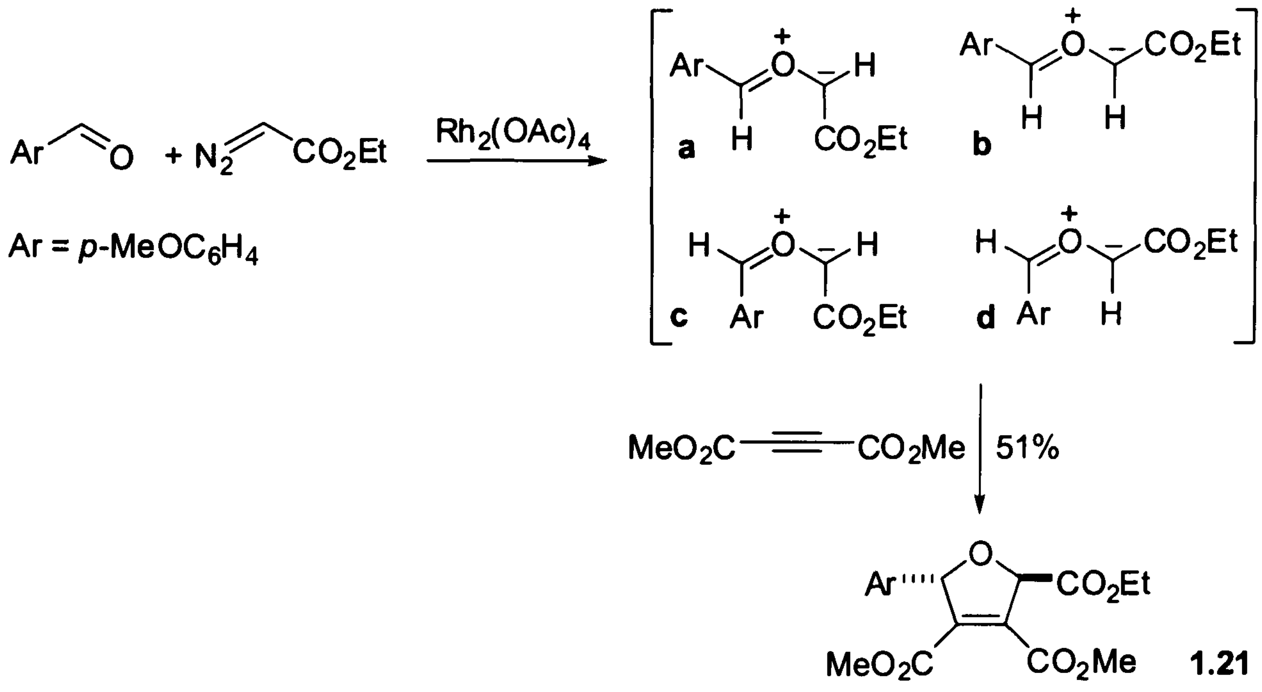
[55] R. Huisgen, P. de March, *J. Am. Chem. Soc.* **1982**, *104*, 4953–4954.

[56] P. de March, R. Huisgen, *J. Am. Chem. Soc.* **1982**, *104*, 4952–4953.

[57] M. P. Doyle, D. C. Forbes, M. N. Protopopova, S. A. Stanley, M. M. Vasbinder, K. R. Xavier, *J. Org. Chem.* **1997**, *62*, 7210–7215.

suggests that the cycloaddition proceeds *via* either carbonyl ylide **a** or **d**. On the basis of the molecular modelling studies, **a** was predicted to be the product forming ylide.

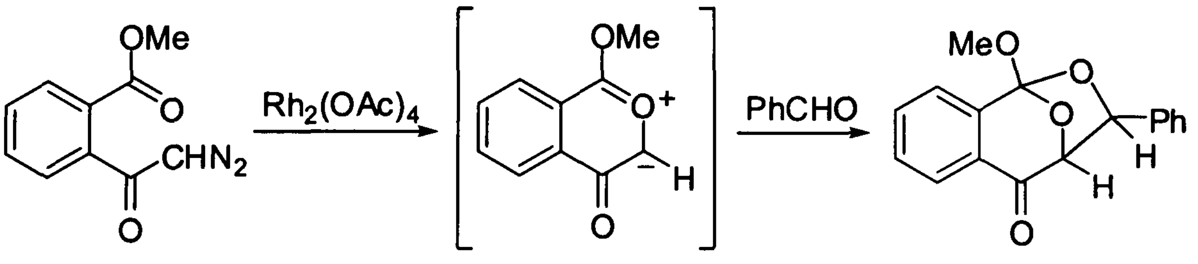


1.21

Scheme 1.19. Intermolecular carbonyl ylides formation-cycloaddition.

1.4.2b. Intramolecular Carbonyl Ylide Formation

The geometry of the carbonyl ylide could be controlled if the carbonyl group is tethered to the diazo functionality. If the tether is of appropriate length, the constraints associated with it will allow the formation of single cyclic ylide. Ibata and co-workers[58,59] demonstrated the utility of this process in rhodium(II) catalysed decomposition of *o*-(alkoxycarbonyl)-α-diazoacetophenone **1.22** to give a carbonyl ylide which was rapidly trapped by a number of dipolarophiles (such as benzaldehyde, DMAD, *N*-phenyl maleimide) (Scheme 1.20).



1.22 **1.23**

Scheme 1.20. Intramolecular carbonyl ylide formation-intermolecular cycloaddition.

Work in the Hodgson group involving carbonyl ylide cycloaddition reactions has been directed toward concise syntheses of four of the nemorensic acid family, for which the key step involved

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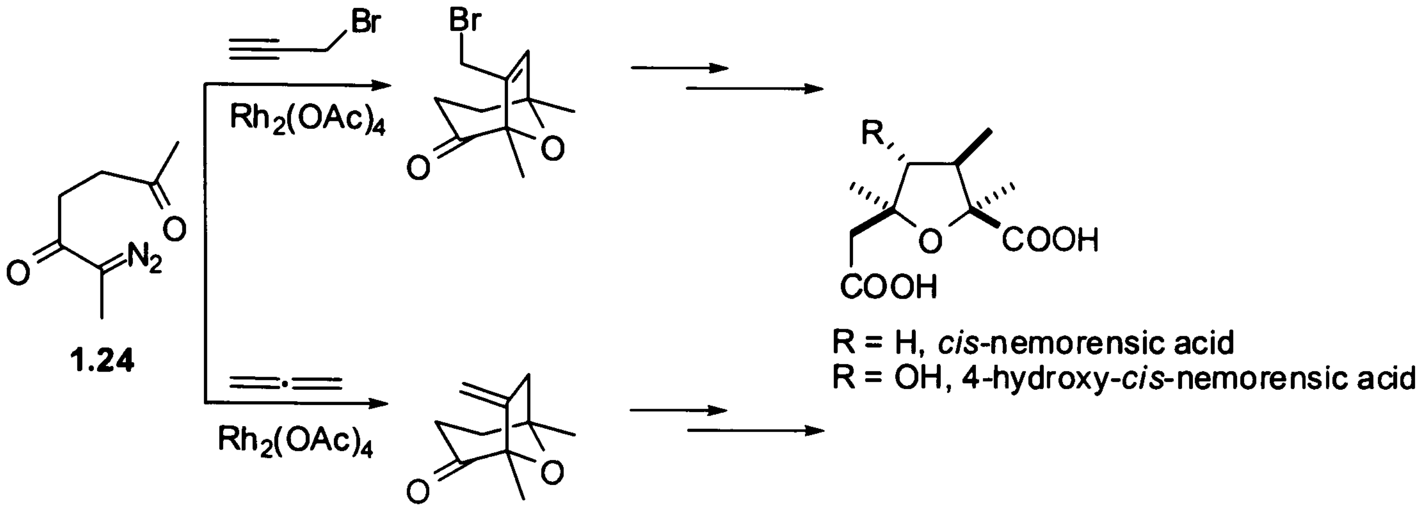
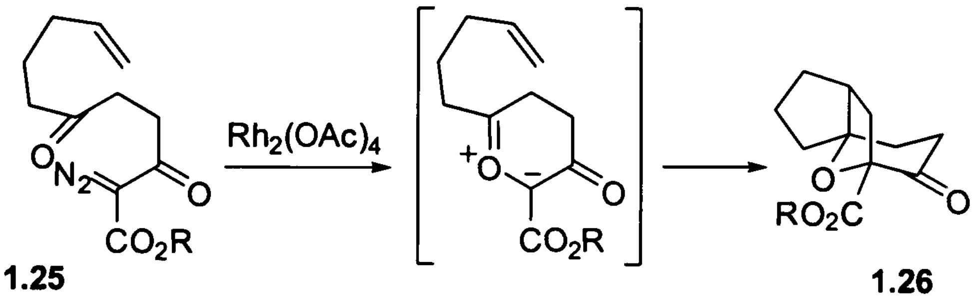
[58] K. Ueda, T. Ibata, M. Takebayashi, *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3582–3585.
[59] T. Ibata, J. Toyoda, M. Sawada, T. J. Tanaka, *J. Chem. Soc., Chem. Commun.* **1986**, 1266–1267.

the regioselective cycloaddition of a cyclic carbonyl ylide derived from α-diazodiketone **1.24** with propargyl bromide or allene (Scheme 1.21).[60,61,62]



Scheme 1.21. Intermolecular carbonyl ylide cycloaddition in total synthesis.

This tandem carbonyl ylide formation-cycloaddition methodology was further elaborated by the intramolecular trapping of carbonyl ylides with an alkene and alkyne dipolarophiles. This represents an effective method for synthesis of complex oxapolycycles (Scheme 1.22).[63]



Scheme 1.22. Intramolecular carbonyl ylide cycloaddition.

Closely related system (Scheme 1.22, CO_2R = H) has also been shown to undergo intramolecular carbonyl ylide cycloaddition.[64] The carbonyl group of an ester can complicate ylide formation compared to the carbonyl group of a ketone. This has been found by Padwa with α-diazoketoester **1.27**, where the principal product was hydroxyketone **1.28**, presumed to be derived from O–H insertion into water (Scheme 1.23).[65]

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[60] D. M. Hodgson, T. D. Avery, A. C. Donohue, *Org. Lett.* **2002**, *4*, 1809–1811.

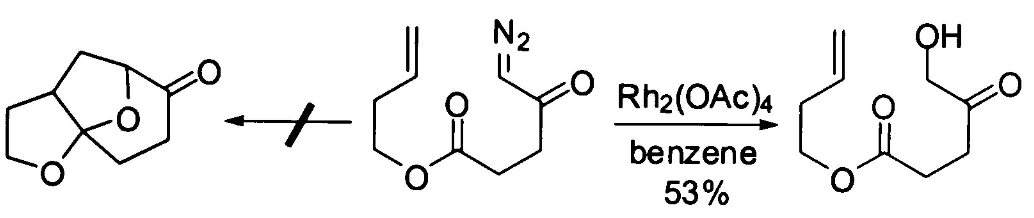
[61] D. M. Hodgson, F. Le Strat, *Chem. Commun.* **2004**, 822–823.

[62] D. M. Hodgson, F. Le Strat, T. D. Avery, A. C. Donohue, T. Brückl, *J. Org. Chem.* **2004**, *69*, 8796–8803.

[63] D. M. Hodgson, P. A. Stupple, F. Y. T. M. Pierard, A. H. Labande, C. Johnstone, *Chem. Eur. J.* **2001**, *7*, 4465–4476.

[64] A. Padwa, S. F. Hornbuckle, G. E. Fryxell, Z. J. Zhang, *J. Org. Chem.* **1992**, *57*, 5747–5757.

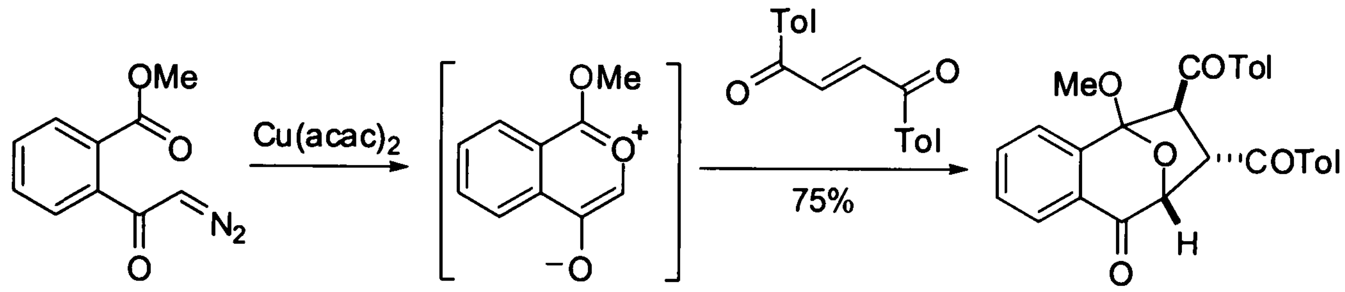
[65] A. Padwa, S. F. Hornbuckle, G. E. Fryxell, P. D. Stull, *J. Org. Chem.* **1989**, *54*, 817–824.



1.27 **1.28**

Scheme 1.23. O–H Insertion of α-diazoketoester.

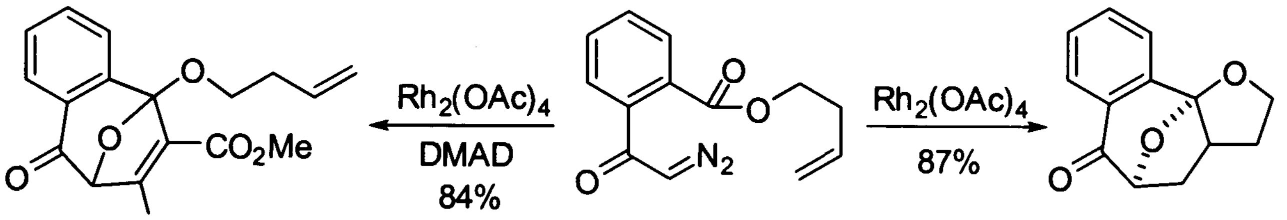
However, Ibata and co-workers[66,67,68] demonstrated that the carbonyl ylides derived from ester functionality could be generated from copper catalysed decomposition of benzofused α-diazo ketoester **1.29** and trapped by various dipolarophiles (Scheme 1.24).



1.29 **1.30**

Scheme 1.24. Intermolecular cycloaddition of an α-diazoketoester.

Such benzofused carbonyl ylides which are aromatic carbonyl ylides (also called oxidopyryliums) could also be trapped intramolecularly to furnish polycyclic cycloadducts (Scheme 1.25).



1.33 **1.31** **1.32**

DMAD = $MeO_2C{\equiv}CO_2Me$

Scheme 1.25. Inter-/ intramolecular cycloaddition of aromatic carbonyl ylides.

However, such cyclic carbonyl ylides can undergo competing intermolecular cycloaddition in presence of a dipolarophile stronger than that tethered to the substrate. For example, in presence

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[66] T. Ibata, J. Toyoda, *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2489–2493.

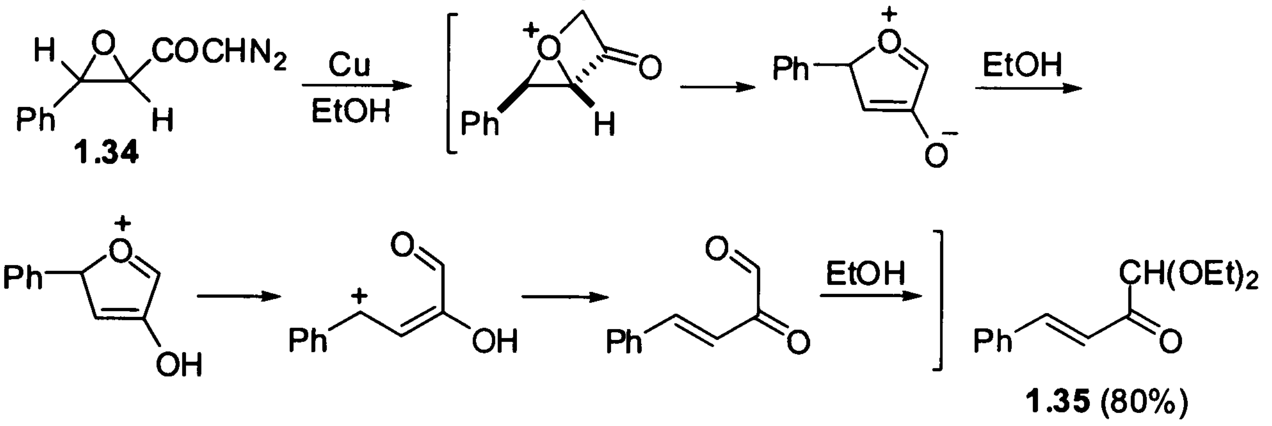
[67] T. Ibata, J. Toyoda, M. Sawada, *J. Chem. Soc., Chem. Commun.* **1986**, 1266–1267.

[68] K. Ueda, T. Ibata, M. Takebayashi, *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2779–2782.

of DMAD, the intramolecular cycloaddition of **1.31** is completely suppressed and only the cycloadduct **1.33** derived from intermolecular cycloaddition is observed.[69]

1.4.3. Oxonium Ylide Formation-Rearrangement

Oxonium ylides are reactive intermediates in which a positively charged oxygen atom is connected to a carbon possessing an unshared pair of electrons. Such ylides can be generated by two different approaches. One route involves either the deprotonation[70] or desilylation[71] of appropriate oxonium ions. Although these methods do yield products from oxonium ylide rearrangement, competitive alkylation results in lower yields. An alternative approach involves the interaction of a metal carbenoid with an unshared pair of electrons from an oxygen atom.[72] One of the earliest examples of intramolecular oxonium ylide formation involved reaction of an α,β-epoxy diazomethyl ketone **1.34** with Cu powder in refluxing EtOH, producing unsaturated oxoacetals **1.35** (Scheme 1.26).[73]



Scheme 1.26. Oxonium ylide from α,β-epoxy diazomethyl ketone.

The synthetic utility of tandem oxonium ylide formation and rearrangement was established in studies from Pirrung[74] and Johnson.[75] They explored the intramolecular generation of unsaturated oxonium ylides *via* Rh(II) and Cu(II) carbenoids and their subsequent [2,3]-sigmatropic rearrangement (Scheme 1.27). Treatment of an α-diazoketone or an α-diazo-β-ketoester bearing a tethered allylic ether with cat. $Rh_2(OAc)_4$ afforded cyclic ethers arising from [2,3]-sigmatropic

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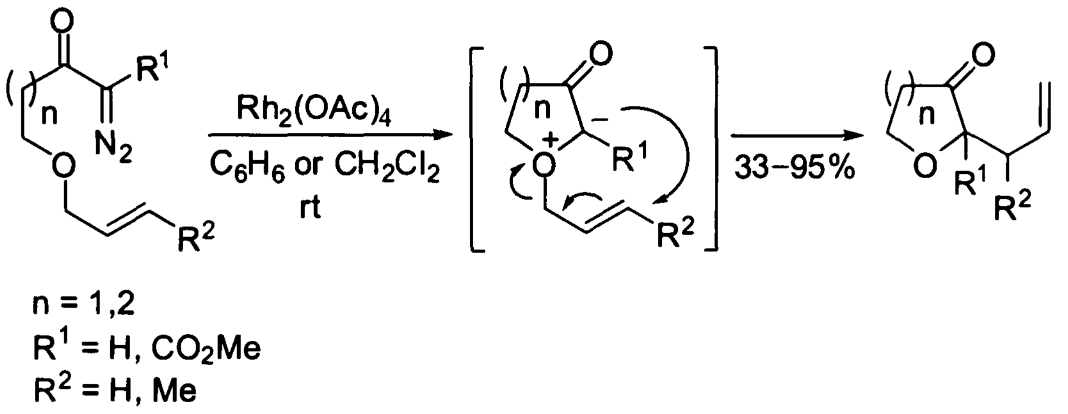
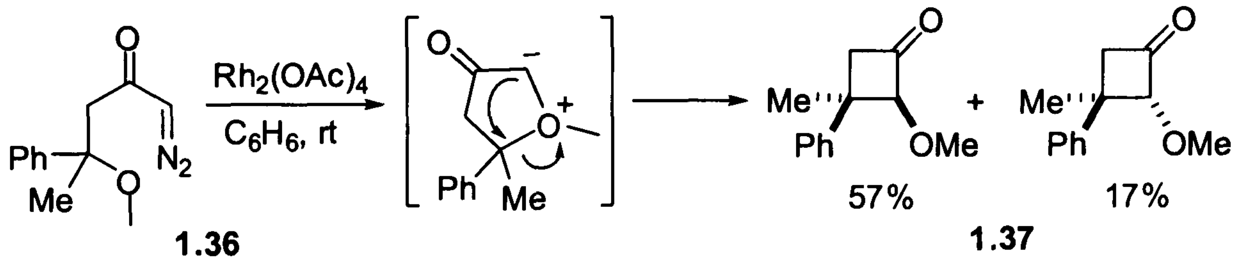
[69] A. Padwa, S. P. Carter, H. Nimmesgern, P. D. Stull, *J. Am. Chem. Soc.* **1988**, *110*, 2894–2900.
[70] G. A. Olah, H. Doggerweiler, J. D. Felberg, *J. Org. Chem.* **1984**, *49*, 2112–2116.
[71] G. A. Olah, H. Doggerweiler, J. D. Felberg, *J. Org. Chem.* **1985**, *50*, 4847–4851.
[72] J. S. Clark, *Nitrogen, Oxygen and Sulfur Ylide Chemistry*, Oxford University Press, Oxford, **2002**.
[73] L. Thijis, B. Zwanenburg, *Tetrahedron* **1980**, *36*, 2145–2148.
[74] M. C. Pirrung, J. A. Werner, *J. Am. Chem. Soc.* **1986**, *108*, 6060–6062.
[75] E. J. Roskamp, C. R. Johnson, *J. Am. Chem. Soc.* **1986**, *108*, 6062–6063.

rearrangement of oxonium ylides. Dihydrofuranones (n = 1) were generally obtained in good yields (70–90%), whereas pyranones (n = 2) were obtained in moderate yields (< 55%).



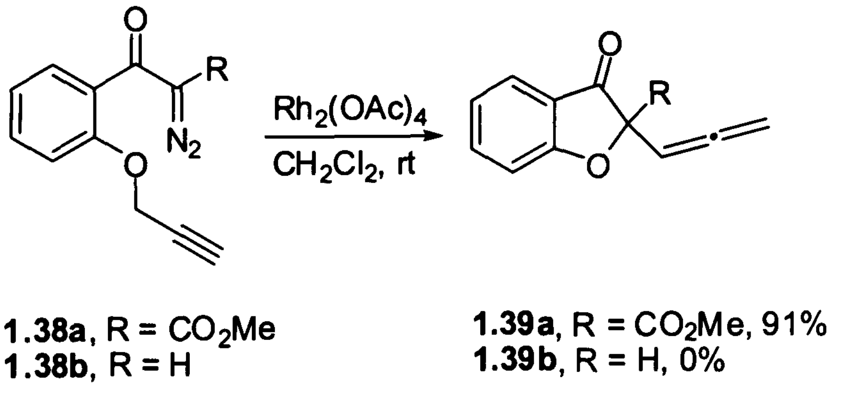
Scheme 1.27. Intramolecular oxonium ylide formation-rearrangement.

Johnson also examined [1,2]-rearrangement of the intramolecularly generated ylides.[75] Treatment of α-diazoketone **1.36** with $Rh_2(OAc)_4$ in benzene afforded diastereomeric mixture of cyclobutanones **1.37**, arising from [1,2]-rearrangement of the ylide (Scheme 1.28).



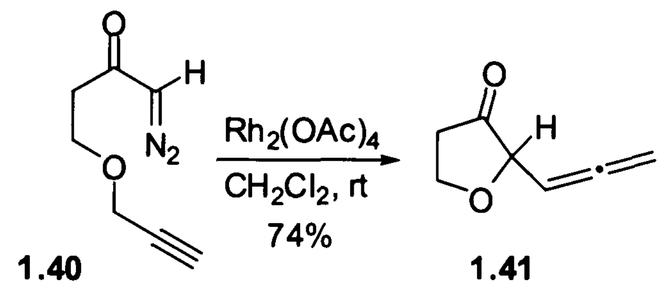
Scheme 1.28. [1,2]-Rearrangement of an oxonium ylide.[75]

The [2,3]-sigmatropic rearrangements of oxonium ylides have also been extended to propargylic ether tethers in α-diazo-β-ketoesters. Pirrung established the viability of the process, by treating an α-diazo-β-ketoester **1.38a** with $Rh_2(OAc)_4$, which gave the allene **1.39a** *via* [2,3]-rearrangement of an intermediate ylide (Scheme 1.29). Interestingly, the corresponding α-diazoketone **1.38b** failed to undergo the reaction under similar conditions.[74]



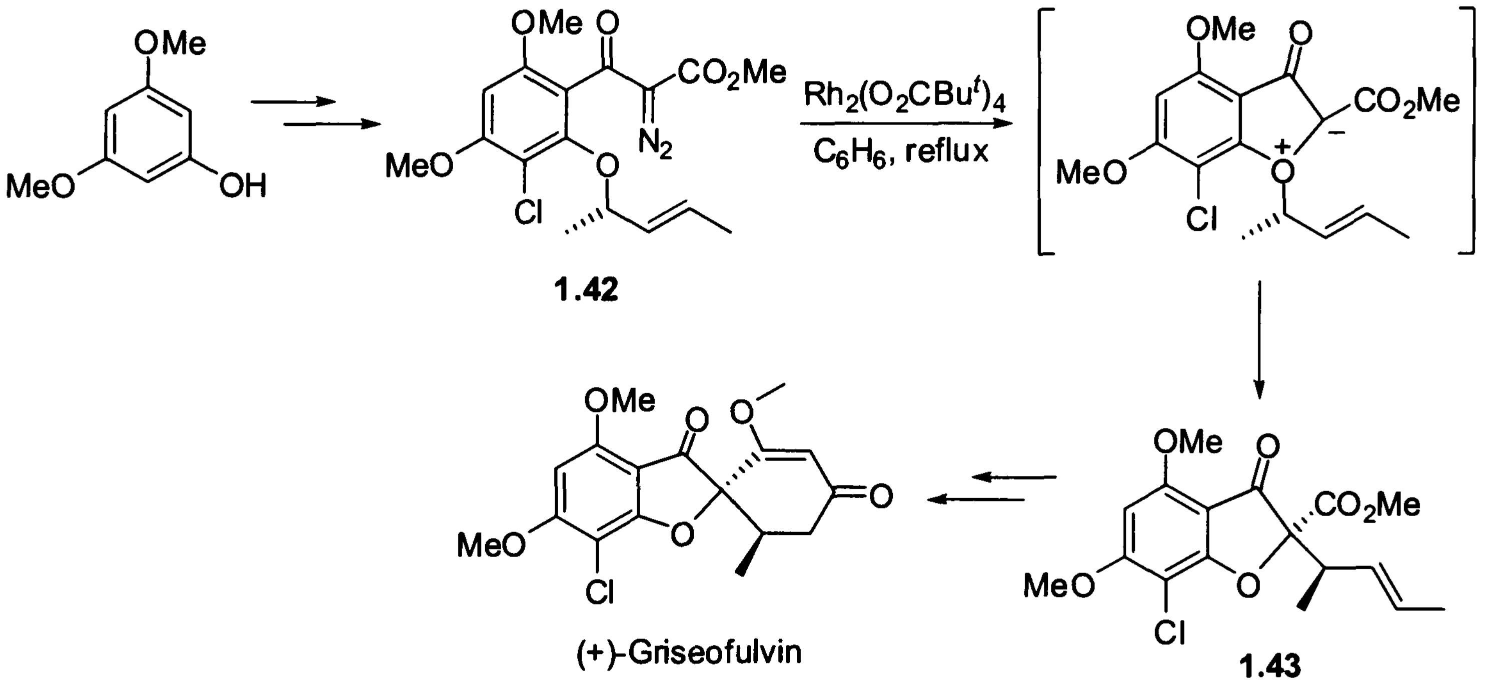
Scheme 1.29. Intramolecular oxonium ylide rearrangement of a propargylic ether.

However, the non aromatic α-diazoketone **1.40** containing propargylic ether functionality did undergo [2,3]-sigmatropic rearrangement in good yield (Scheme 1.30).[75]



Scheme 1.30. Intramolecular oxonium ylide rearrangement of a propargylic ether.

The above tandem chemistry has been applied by Pirrung *et al.* in the total synthesis of (+)-griseofulvin, an antifungal agent used in the treatment of dermatomycoses; the key step being the oxonium ylide formation-[2,3]-sigmatropic rearrangement.[76] These workers demonstrated that decomposition of α-diazo-β-ketoester **1.42**, with rhodium(II) pivalate provides the [2,3]-sigmatropic rearranged product **1.43** in 62% yield, as a single stereo and regioisomer (Scheme 1.31). Although the original stereogenic center is destroyed in the rearrangement, there is efficient chirality transfer (*via* [2,3]-sigmatropic rearrangement) during the process.



Scheme 1.31. Application of oxonium ylide rearrangement to (+)-griseofulvin.

Recently, Clark and co-workers reported a concise total synthesis of (±)-vigulariol, a marine natural product possessing *in vitro* cytotoxic activity against human-lung adenocarcinoma cells. The key ring expansion reaction involved [2,3]-sigmatropic rearrangement of oxonium ylide, derived from α-diazoketone **1.44**, in presence of copper(II) hexafluoroacetylacetonate, which gave

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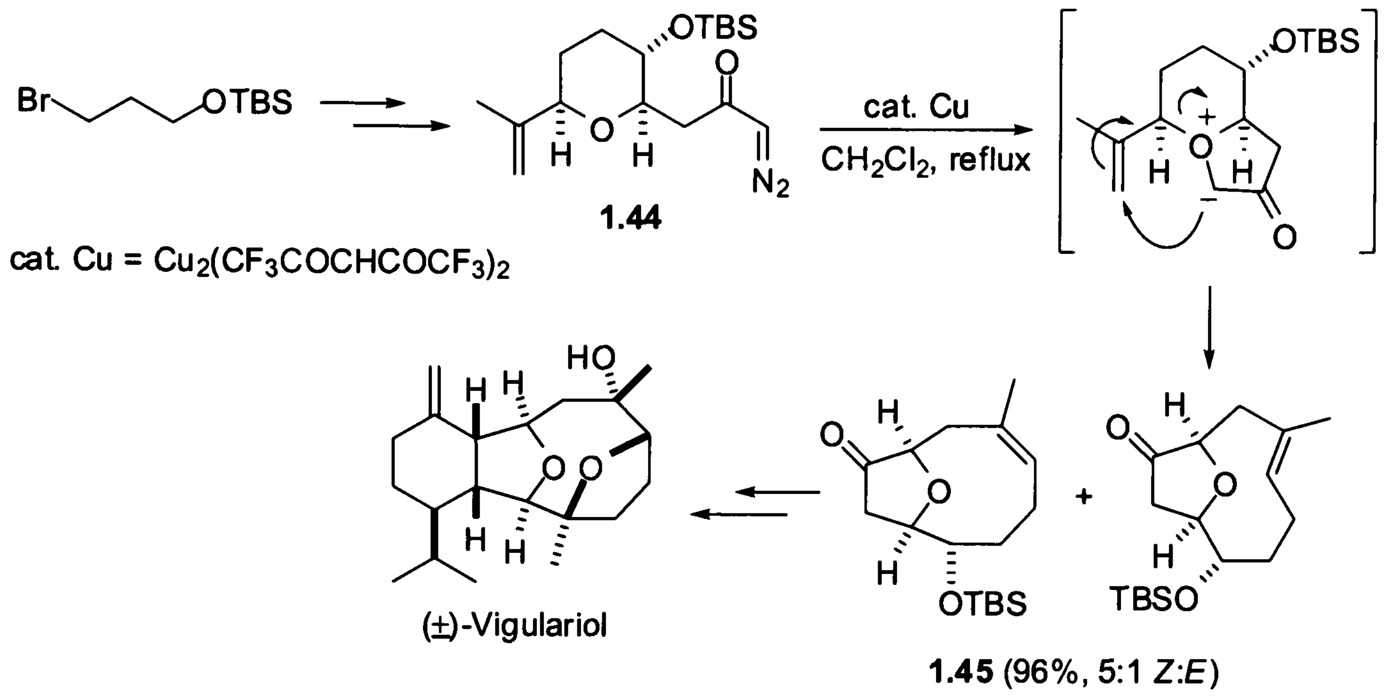
[76] M. P. Pirrung, W. L. Brown, S. Rege, P. Laughton, *J. Am. Chem. Soc.* **1991**, *113*, 8561–8562.

a 5:1 mixture of stereoisomers **1.45** in excellent yield (96%) (Scheme 1.32).[77] These examples demonstrate the power of the sigmatropic rearrangement of oxonium ylides in highly diastereo and enantioselective synthesis of natural products.



Scheme 1.32. [2,3]-Sigmatropic rearrangement of oxonium ylide in total synthesis.

Intermolecular formation and rearrangement of allylic oxonium ylides have also been attempted. However, this process potentially suffers from several disadvantages: first, that it is necessary to use a large excess of the allylic ether relative to the diazo compound, in order to minimise carbene dimerisation or further reaction of the diazo compound with the product. Also, in the presence of excess of an allylic ether, intermolecular cyclopropanation can compete with the ylide rearrangement. Doyle explored the synthetic utility of the intermolecular oxonium ylide formation-rearrangement using allylic ethers and simple α-diazoketones or acetates (Scheme 1.33).[78]

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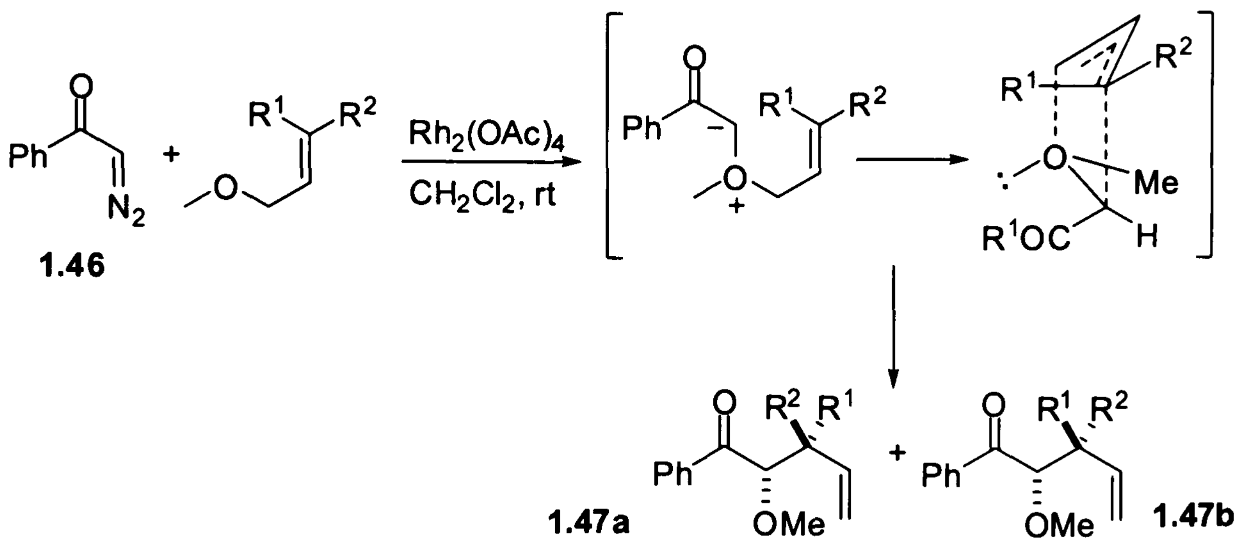
[77] J. S. Clark, S. T. Hayes, C. Wilson, L. Gobbi, *Angew. Chem. Int. Ed.* **2007**, *46*, 437–440.

[78] M. P. Doyle, V. Bagheri, N. K. Harn, *Tetrahedron Lett.* **1988**, *29*, 5119–5122.

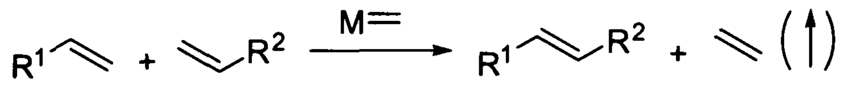


cis, R^1 = Ph, R^2 = H, 86%, 91:9
trans, R^1 = H, R^2 = Ph, 70%, 19:81

Scheme 1.33. Intermolecular oxonium ylide formation-rearrangement.

1.4.4. Olefin Metathesis

Transition metal catalysed olefin metathesis is another powerful approach for carbon-carbon bond formation involving metallocarbenes (Scheme 1.34).[79]



Scheme 1.34. Olefin metathesis.

This has been tremendously developed by Grubbs and Schrock, with the introduction of metal alkylidenes for the process (Figure 1.6). Grubbs developed ruthenium based catalyst **1.49**, known as Grubbs 1st generation catalyst[80], which, although, less reactive than Schrock's molybdenum based catalyst **1.48**,[81,82] has a greater functional group compatibility and is moisture and air stable, hence requiring simpler handling.

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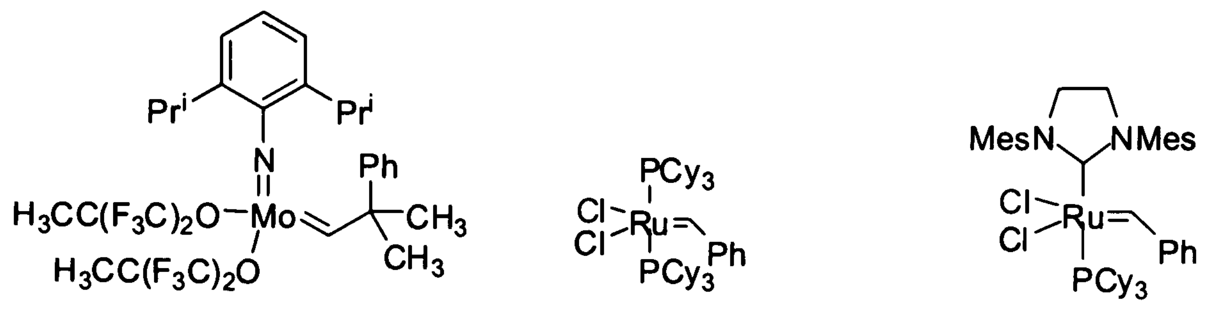
[79] a) J.-L. Herisson, Y. Chauvin. *Makromol. Chem.* **1971**, *141*, 161–176; b) Y. Chauvin, D. Commereuc, *J. Chem. Soc. Chem. Commun.* **1992**, 462–464.; c) R. H. Grubbs, *Handbook of Metathesis*, Wiley-VCH, Weinheim, **2003**.

[80] P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100–110.

[81] R. R. Schrock, J. S. Murdzek, G. C. Bazan, J. Robbins, M. DiMare, M. O'Regan, *J. Am. Chem. Soc.* **1990**, *112*, 3875–3886.

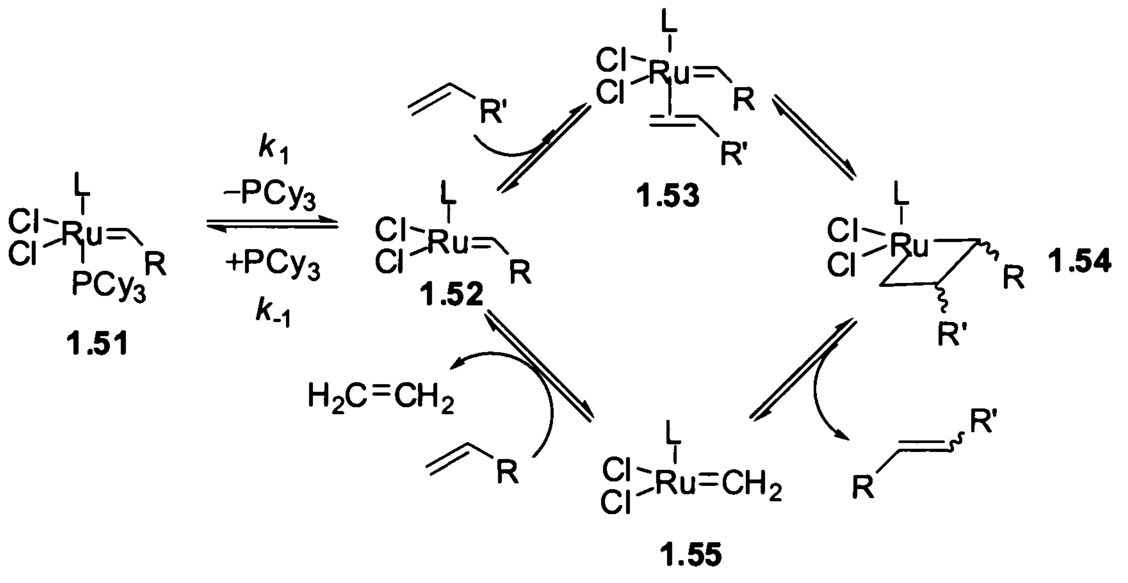
[82] G. C. Bazan, J. H. Oskam, H. N. Cho, L. Y. Park, R. R. Schrock, *J. Am. Chem. Soc.* **1991**, *113*, 6899–6907.



1.48 Schrock's cat. **1.49** Grubbs' 1^{st} generation cat. **1.50** Grubbs' 2^{nd} generation cat.

Figurel.6. Commonly used metathesis catalysts.

The general accepted mechanism of olefin metathesis promoted by Ru catalysts is depicted in Scheme 1.35.[83] The first step in the catalytic cycle is the catalyst initiation which involves phosphine dissociation to give a reactive 14-electron intermediate **1.52**.[84] The reaction of **1.52** with olefinic substrate generates the complex **1.53**.[85] The coupling of the olefin and alkylidene ligand within the coordination sphere of ruthenium produces the metallacyclobutane **1.54**. The metallacyclobutane can break productively to give the cross-metathesis product and methylidene **1.55** or collapse unproductively to give back the starting materials.



Scheme 1.35. General mechanism of olefin metathesis.

The overall catalyst activity during the process is governed by the rates of the following processes: (1) phosphine dissociation (k_1), (2) phosphine recombination (k_{-1}) and (3) olefin binding. High catalytic activity is observed when the initiation is faster (i.e. k_1 is large) and the 14-electron intermediate reacts rapidly with the olefin. In addition, the catalyst activity is also related

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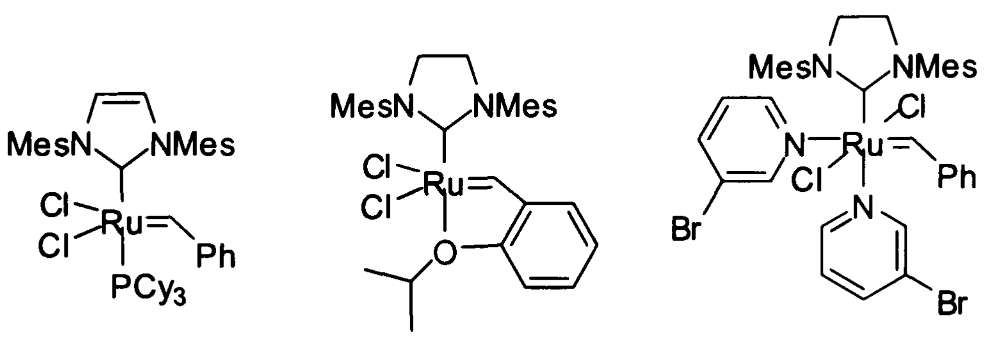
[83] M. S. Sanford, M. Ulmam, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 749–750.

[84] C. Hinderling, C. Adlhart, P. Chen, *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 2685–2689.

[85] J. A. Tallarico, P. J. Bonitatebus, M. L. Snapper, *J. Am. Chem. Soc.* **1997**, *119*, 7157–7158.

to the electron donating ability and the steric bulk of the phosphine ligand.[86] The *N*-heterocyclic carbenes (NHC)[87,88] are neutral ligands with higher basicity than the phosphine ligands. These are strong σ-donors and bind strongly to the metal centre; the NHC-Ru bonds are 20–40 kcal mol^{-1} stronger than PR_3-Ru bonds,[89] and hence facilitate phosphine dissociation.



1.56 **1.57** **1.58**

Figure 1.7. Other 2nd generation catalysts.

The NHC based Ru catalyst **1.50**, commonly called Grubbs 2nd generation catalyst[90] is a highly active metathesis catalyst, exhibiting excellent functional group compatibility. This was the first catalyst to enable the formation of tri-substituted olefins by cross-metathesis.[91] The processs is thermodynamically driven, and gives *E*-isomers predominantly in most cases.

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[86] T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18–29.

[87] W. A. Herrmann, C. Köcher, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2162–2187.

[88] D. Bourissou, O. Guerret, F. P. Gabbai, G. Bertrand, *Chem. Rev.* **2000**, *100*, 39–92.

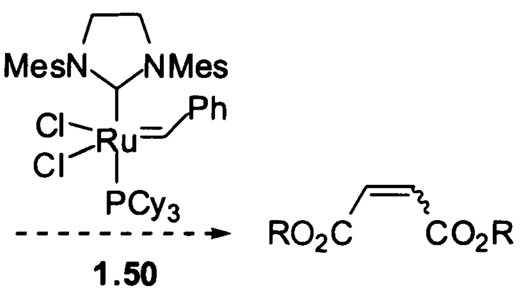
[89] J. Hunag, E. D. Stevens, S. P. Nolan, *J. Am. Chem. Soc.* **1999**, *121*, 2674–2678.

[90] M. Scholl, S. Ding, C. W. Lee and R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953–956.

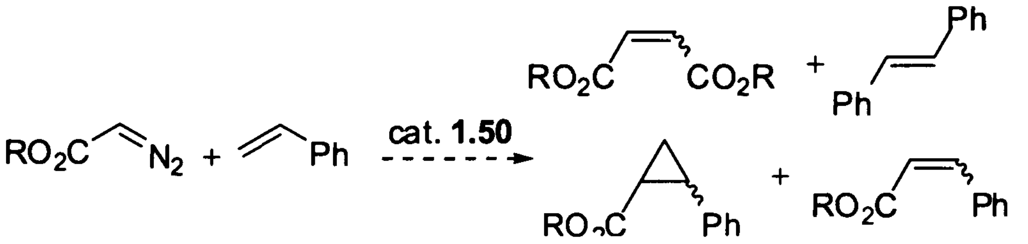
[91] A. K. Chatterjee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 1751–1753.

1.5. Aims of the Project

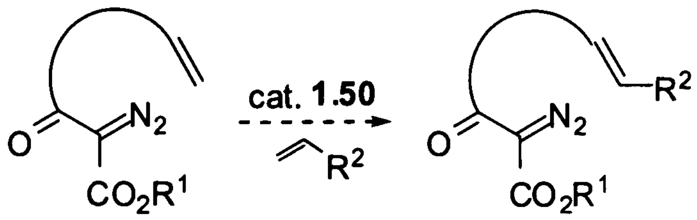
- Explore the non metathetical activity of Grubbs' 2nd generation catalyst (the most commonly used catalyst for olefin metathesis). To study if this catalyst (which is known to be synthesised from α-diazo compounds) could catalyse the coupling of α-diazoacetates, and, if so, with what stereoselectivity.



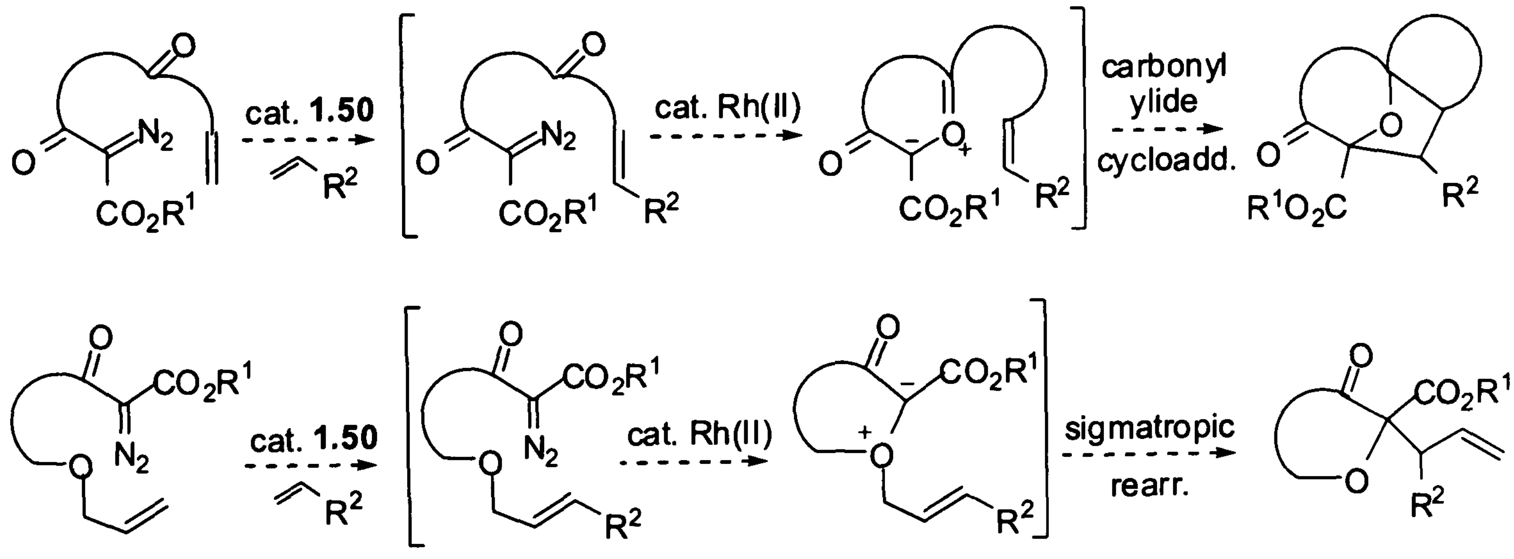
- If the catalyst is capable of catalysing the dimerisation of α-diazoacetates, will the metathetical activity of the catalyst be retained? If so, will it be able to catalyse two different carbene transformations (diazo coupling and metathesis) in the same flask?



- To study the behaviour of the Grubbs' 2nd generation catalyst toward more substituted α-diazo compounds.
- To examine if one can carry out chemoselective cross-metathesis in the presence of a stabilised α-diazo compound (e.g. an unsaturated α-diazo-β-ketoester), to functionalise an olefin tether in the substrate and use the diazo functionality for subsequent carbene transformation (such as intramolecular 1,3-dipolar carbonyl ylide cycloadditions, oxonium ylide rearrangements) for the construction of more complex oxapolycycles.



- To study if one can couple the two powerful carbene based transformations mentioned above (i.e. olefin metathesis and ylide transformations), catalysed by two different transition metal catalysts, in a one-flask operation and study the compatibility of these two catalysts in such sequential process.



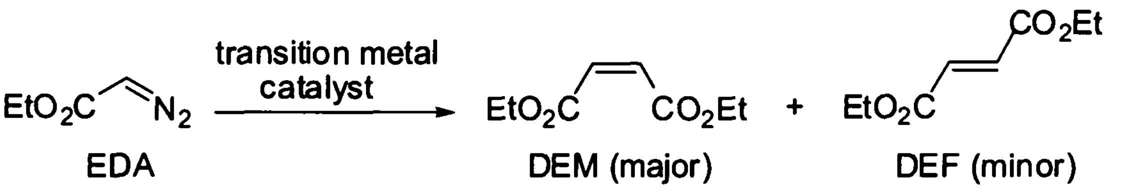
CHAPTER 2

INTERMOLECULAR COUPLING OF DIAZOACETATES

INTERMOLECULAR COUPLING OF DIAZOACETATES

2.1. Background

α-Diazo carbonyl compounds are a source of masked carbenes. When treated with transition metal catalysts they undergo a number of synthetically useful reactions *via* transient metallocarbenes, such as inter/intramolecular cyclopropanation, X-H insertion (X = C, O, N) and ylide generation.[1] These processes have been extensively developed into important stereo- and enantioselective transformations.[1,2] Transition metal catalysed dimerisation of α-diazocarbonyl compounds is the 'simplest' carbene-based reaction pathway, which has often been noted as an unwanted side reaction during the above processes. More recently however, catalysts have been developed for the stereoselective coupling of α-diazoacetates to generate *cis*-olefins with high stereoselectivity (Scheme 2.1),[3] and the process has seen application in target-oriented synthesis.[3,4,5]



Scheme 2.1. Transition metal catalysed homo-coupling of ethyl diazoacetate.

Porphyrin or phosphine based Ru and Os catalysts have been investigated for the stereoselective generation of *cis*-olefins from diazo compounds. Woo and Smith demonstrated the use of Os porphyrin complexes, such as $[(TTP)Os]_2$ and $[(TTP)Os(py)_2]$, in the stereoselective decomposition of ethyl diazoacetate (EDA), giving diethyl maleate (DEM) and diethyl fumarate (DEF) with ~26:1 selectivity.[6] The diazo coupling was shown to proceed by way of a metallo-ester carbene, $[(TTP)Os{=}CHCO_2Et)]$, which when independently prepared and treated with an excess of EDA gave similar olefin stereoselectivity (*Z*:*E* ~ 25:1). Subsequently, Collman showed that [Ru(TMP)] also reacts with EDA to give DEM and DEF in a 15:1 ratio (91% overall yield).[7] However, a similar rhodium(III) based complex [Rh(TTP)I] gave DEM in poor yield (36%). The

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[1] M. P. Doyle, M. A. McKevery, Y. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, John Wiley and Sons, New York, **1998**.

[2] a) D. M. Hodgson, F. Y. T. M. Pierard, P. A. Stupple, *Chem. Soc. Rev.* **2001**, *30*, 50–61; b) H. M. L. Davies, E. G. Antoulinakis, *Org. React.* **2001**, *57*, 1–326; c) D. M. Hodgson, P. A. Stupple, D. C. Forbes in *Rodd's Chemistry of Carbon Compounds, Topical Volume, Asymmetric Catalysis* (Ed.: M. Sainsbury), Elsevier, Oxford, **2001**, pp. 65–99.

[3] a) G. Maas, *Top. Curr. Chem.* **1987**, *137*, 75–253; b) Ref. 1, pp. 624–633.

[4] G. -Y. Li, C. -M. Che, *Org. Lett.* **2004**, *6*, 1621–1623.

[5] M. P. Doyle, W. Hu, I. M. Phillips, A. G. H. Wee, *Org. Lett.* **2000**, *2*, 1777–1779.

[6] L. K. Woo, D. A. Smith, *Organometallics* **1992**, *11*, 2344–2346.

[7] J. P. Collman, E. Rose, G. D. Venburg, *J. Chem. Soc., Chem. Commun.* **1993**, 934–935.

half-sandwich ruthenium(II) complex, $(PPh_3)_2ClRu(\eta^5\text{-}C_5H_5)$ was also found to dimerise EDA to DEM, quantitatively and with complete stereoselectivity (*Z*:*E*, >99:1);[8,9] this latter catalyst is also known to catalyse the intermolecular cyclopropanation of styrenes with EDA.[10,11] A simple ruthenium(II) phosphine complex, $Ru(PPh_3)_3Cl_2$, has also been used in the carbene dimerisation and the *Z*:*E* selectivity with this catalyst was found to be dependent on the reaction conditions employed (concentration, catalyst/diazo substrate, solvent).[12] More recently, $[Ru(2,6\text{-}Cl_2TPP)CO]$ complex has been used in the coupling of diazoacetates to give coupling products in 61–93% yield, with complete *cis*-selectivity.[4] Aside from these catalysts, transition metal complexes of nickel,[13] copper,[14] iridium,[15] tantalum,[16] chromium[17,18] and rhenium[19] have also been shown to effect the coupling of α-diazocarbonyl compounds.

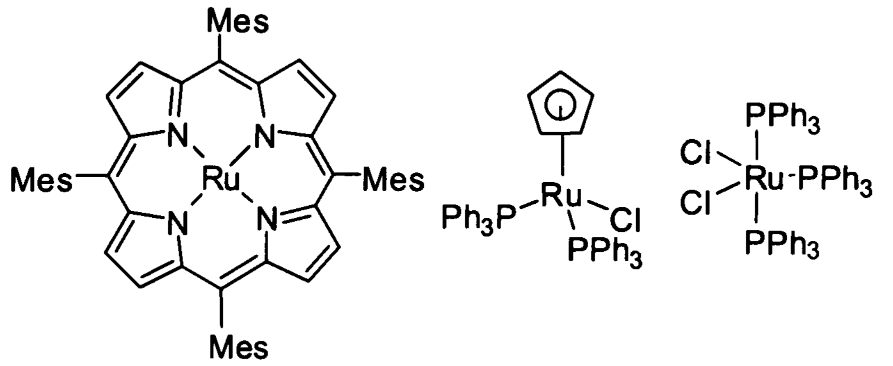

Figure 2.1. Commonly used transition metal catalysts for diazo coupling.

Olefin metathesis is another powerful olefin bond forming reaction proceeding *via* metallocarbenes.[20] The process has become synthetically significant following the development of highly active (pre)-catalysts, particularly Grubbs' 1st- and 2nd-generation ruthenium carbenes, **1.49**[21] and **1.50**,[22] respectively (Figure 2.2), which allow the chemistry to proceed under mild conditions, with high stereoselectivity and which also exhibit wide ranging functional group compatibility. I was interested in determining if such catalysts (which can be synthesised from α-

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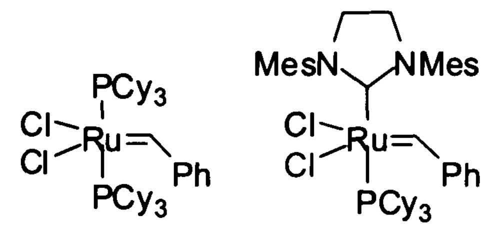
[8] W. Baratta, A. D. Zotto, P. Rigo, *Chem. Commun.* **1997**, 2163–2164.
[9] W. Baratta, A. D. Zotto, P. Rigo, *Organometallics* **1999**, *18*, 5091- 5096.
[10] W. Baratta, W. A. Herrmann, R. M. Kratzer, P. Rigo, *Organometallics* **2000**, *19*, 3664–3669.
[11] B. Çetinkaya, I. Özdemir, P. H. Dixneuf, *J. Organomet. Chem.* **1997**, *534*, 153–158.
[12] E. Graban, F. R. Lemke, *Organometallics* **2002**, *21*, 3823–3826.
[13] H. Bock, H. P. Wolf, *J. Chem. Soc., Chem. Commun.* **1990**, 690–692.
[14] T. Oshima, T. Nagai, *Tetrahedron Lett.* **1980**, *21*, 1251–1254.
[15] T. Kubo, S. Sakaguchi, Y. Ishii, *Chem. Commun.* **2000**, 625- 626.
[16] J. Goux, P. L. Gendre, P. Richard, C. Moïse, *J. Organomet. Chem.* **2006**, *691*, 3239–3244.
[17] J. Pfeiffer, K. H. Dötz, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2828–2830.
[18] D. Jan, F. Simal, A. Demonceau, A. F. Noels, K. A. Rufanov, N. A. Ustynyuk, D. N. Gourevitch, *Tetrahedron Lett.* **1999**, *40*, 5695–5699.
[19] Z. Zhu, J. H. Espenson, *J. Am. Chem. Soc.* **1996**, *118*, 9901–9907.
[20] R. H. Grubbs, *Handbook of Metathesis*, Wiley-VCH, Weinheim, **2003**.
[21] P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100–110.
[22] M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953–956.

diazo compounds),[21,23] could dimerise diazo compounds in a stereoselective manner and, if so, would the propensity to catalyse alkene metathesis be retained.

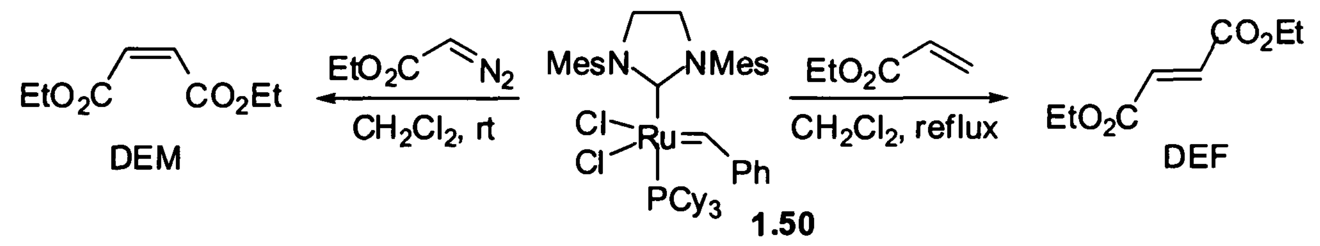


1.49 **1.50**

Figure 2.2. Carbene-based olefin metathesis catalysts.

2.2. Homo-coupling of α-Diazoacetates

In my initial studies, Grubbs' catalyst **1.50** (0.5 mol%) was found to catalyse the homo-coupling of EDA under mild conditions to give mainly DEM (Scheme 2.2).[24] In contrast, *trans*-2-ene-1,4-dicarbonyl compounds are known to be generated from α,β-unsaturated carbonyl compounds by olefin metathesis using catalyst **1.50** (5 mol%).[25]



Scheme 2.2. Diazo coupling and olefin metathesis[25] using catalyst **1.50**.

On comparing catalysts **1.49** and **1.50**, the 2nd generation catalyst **1.50** (0.5 mol%, 12–14 h, room temperature) was observed to be superior for the diazo coupling, with high control of stereoselectivity (95% isolated yield of DEM obtained, 98:2 *Z*:*E* stereoselectivity by GC-MS of the crude reaction mixture). In comparison, the 1st generation catalyst **1.49** (0.5 mol%, room temperature), although highly active (EDA was consumed within 1.5 h), gave only 73% isolated yield of DEM, with poor stereoselectivity (*Z*:*E*, 83:17). With reduced or higher loadings of catalyst **1.50** (0.1 or 5 mol%), the stereoselectivity during the carbene dimerisation was unaffected, but the latter reaction now took 72 h to reach completion (and the former had not completed by that time).

In order to examine the scope of catalyst **1.50** to catalyse the homo-coupling of diazoacetates to give *cis*-olefins, a range of diazoacetates **2.03** were studied. The diazoacetates **2.03** were straightforwardly prepared by esterification of glyoxylic acid chloride tosyl hydrazone

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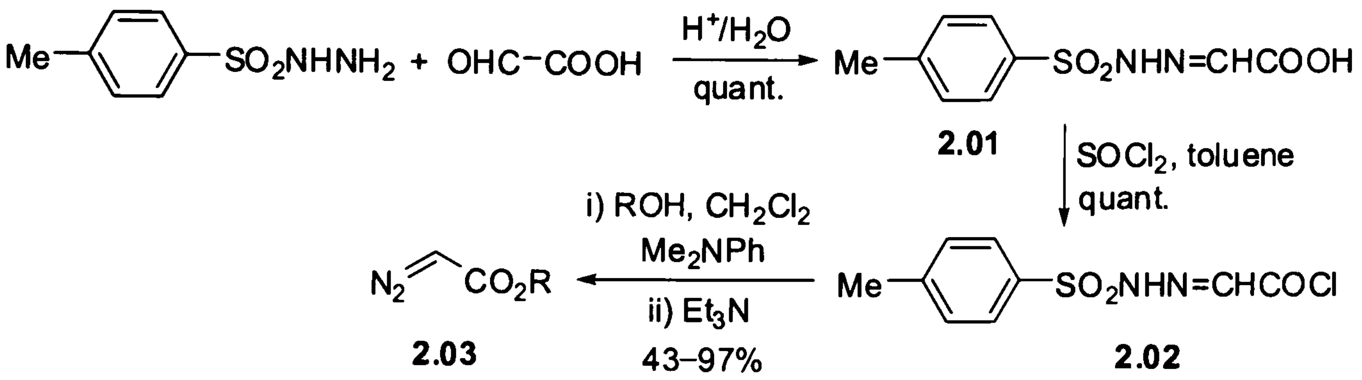
[23] P. Schwab, M. B. France, J. W. Ziller, R. H. Grubbs, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2039–2041.

[24] a) D. M. Hodgson, D. Angrish, *Chem. Commun.* **2005**, 4902–4904; b) D. M. Hodgson, D. Angrish, *Chem. Eur. J.* **2007**, *13*, 3470–3479.

[25] T. -L. Choi, C. W. Lee, A. K. Chatterjee, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 10417–10418.

2.02[26] with various alcohols using *N,N*-dimethylaniline, followed by base-induced diazo group generation (Scheme 2.3, Table 2.1).[27,28]



Scheme 2.3. Synthesis of α-diazoacetates **2.03**.

Entry	R		Yield (%)
1	*n*-Propyl	(**2.03b**)	68
2	*n*-Butyl	(**2.03c**)	89
3	*n*-Hexyl	(**2.03d**)	77
4	Benzyl	(**2.03e**)	90
5	Neopentyl	(**2.03f**)	76
6	Isopropyl	(**2.03g**)	43
7	Cyclohexyl	(**2.03h**)	84
8	2-Adamantyl	(**2.03i**)	77

Table 2.1. Synthesis of α-diazoacetates **2.03**.

In general α-diazoacetates **2.03** were obtained in good yields, (however, due to high volatility of the propyl diazoacetates, some was lost during concentration). With α-diazoacetates **2.03** in hand, we tested the generality of the dimerisation ability of catalyst **1.50**. Pleasingly, conversion to olefins **2.04** always occurred in high yields and with high stereoselectivity for *cis*-olefins, which were isolated as single (*Z*) isomers after chromatography (Scheme 2.4, Table 2.2). Typically, the unsaturated diesters **2.04** were formed with ≥94:6 *Z*:*E* stereoselectivity, although *n*-butyl diazoacetate reproducibly gave an anomalously low stereoselectivity (entry 3). Given the stereoselectivity observed for *n*-propyl and *n*-hexyl diazoacetate (95:5 and 94:6, respectively, entries 2 and 4), there is no obvious explanation for the reduced stereocontrol with *n*-butyl diazoacetate. No significant stereochemical dependence on ester group size was apparent,

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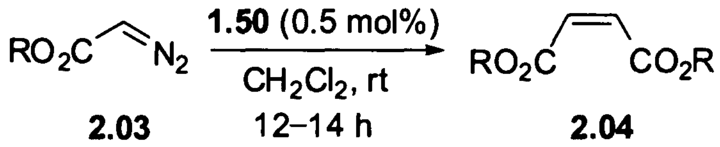
[26] C. J. Blankley, F. J. Saunter, H. O. House, *Org. Synth. Coll. Vol. V* **1973**, 258–263.
[27] E. J. Corey, A. G. Myers, *Tetrahedron Lett.* **1984**, *25*, 3559–3562.
[28] M. P. Doyle, I. M. Phillips, *Tetrahedron Lett.* **2001**, *42*, 3155–3158.

although intriguingly the most hindered ester examined (*tert*-butyl diazoacetate) gave the highest level of *cis*-selectivity (>99:1, entry 10).



Scheme 2.4. Maleates **2.04** from diazoacetates **2.03** using catalyst **1.50**.

Entry	R		Yield (%)	$Z{:}E^{a}$
1	Ethyl	(**2.03a**)	95 (**2.04a**)	98:2
2	*n*-Propyl	(**2.03b**)	84 (**2.04b**)	95:5
3	*n*-Butyl	(**2.03c**)	74 (**2.04c**)	86:14
4	*n*-Hexyl	(**2.03d**)	98^{b}(**2.04d**)	94:6
5	Benzyl	(**2.03e**)	79 (**2.04e**)	97:3
6	Neopentyl	(**2.03f**)	79 (**2.04f**)	97:3
7	Isopropyl	(**2.03g**)	95 (**2.04g**)	97:3
8	Cyclohexyl	(**2.03h**)	82 (**2.04h**)	95.5:4.5
9	2-Adamantyl	(**2.03i**)	75 (**2.04**)	95:5
10	*tert*-Butyl	(**2.03j**)	quant. (**2.04j**)	>99:1

a) Determined by GC-MS of crude; b) Chromatographically inseparable isomeric mixture.

Table 2.2. Maleates **2.04** from α-diazoacetates **2.03** using catalyst **1.50**.

Z/*E* Stereochemical assignments of the olefins were made by comparison with lit. data, or comparison with the commercial sample (**2.04a, c, d, h and j**), or by analogy (typically, δ_H for =CH 6.20–6.30 ppm for maleates and 6.60–6.85 for fumarates).

With $N_2CHSiMe_3$, no carbene dimerisation was observed using catalyst **1.50**, however Del Zotto reported the carbene dimerisation of $N_2CHSiMe_3$, using cyclopentadiene based, [RuCl(η^5-C_5H_5)(PPh_3)$_2$] catalyst, albeit with no selectivity (1:1 *cis*:*trans*).[29] The rate of $N_2CHSiMe_3$ dimerisation was found to be significantly slower with this latter catalyst, compared to EDA dimerisation.

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[29] A. D. Zotto, W. Baratta, G. Verardo, P. Rigo, *Eur. J. Org. Chem.* **2000**, 2795–2801.

2.3. Hetero-coupling of α-Diazoacetates

After establishing the ability of the catalyst **1.50** to catalyse the homo-coupling of α-diazoacetates, I was intrigued to see if the catalyst could induce hetero-coupling between two different α-diazoacetates to generate unsymmetrical *cis*-2-ene-1,4-diesters.[30] Unsymmetrical *cis*-2-ene-1,4-diesters are of interest as they have been used to modify poly vinylchloride to induce freeze resistance properties,[31] exhibit sex pheromone activity comparable to that of disparlure,[32] chiral unsymmetrical maleates can induce high asymmetric induction in Diels-Alder reactions,[33] and they also have found use in synthetic lubricating oil.[34] Related to this concept, the formation of unsymmetrical *cis*-2-ene-1,4-diones by hetero-coupling of two different α-diazoketones, has been previously examined by Del Zotto *et al.*:[29] symmetrical and unsymmetrical *cis*-enediones were formed in ratios close to those statistically expected (1:1:2).

A solution of α-diazoacetates (in 1:1 molar ratio) in CH_2Cl_2 was treated with 0.5 mol% of catalyst **1.50** at room temperature (Scheme 2.5, Table 2.3). After 12–16 h, the starting diazoacetates were completely consumed and the only products observed were symmetrical (**A-A**/ **B-B**) and unsymmetrical (**A-B**) maleates **2.05** arising from homo and hetero-coupling, respectively. The hetero-coupling proceeds highly stereoselectively to give predominantly maleates, and the proportion of fumarates never comprised more than 3% of the *Z*/*E* mixture. Due to the high reactivity of α-diazoacetates towards catalyst **1.50**, in most cases symmetrical (**A-A**/ **B-B**) and unsymmetrical (**A-B**) maleates **2.05** were formed in the molar ratio close to the statistically expected 1:1:2 (entries 6–12). However, during hetero-coupling between diazoacetates bearing significantly sterically different alkyl groups, unsymmetrical maleates were formed in higher than statistical ratios (entries 1–4). In several cases, the unsymmetrical maleates **2.05** were cleanly isolated by column chromatography (entries 2–6 and 9) from the mixture (of symmetrical and unsymmetrical maleates), thus providing a synthetic route to such unsymmetrical maleates.

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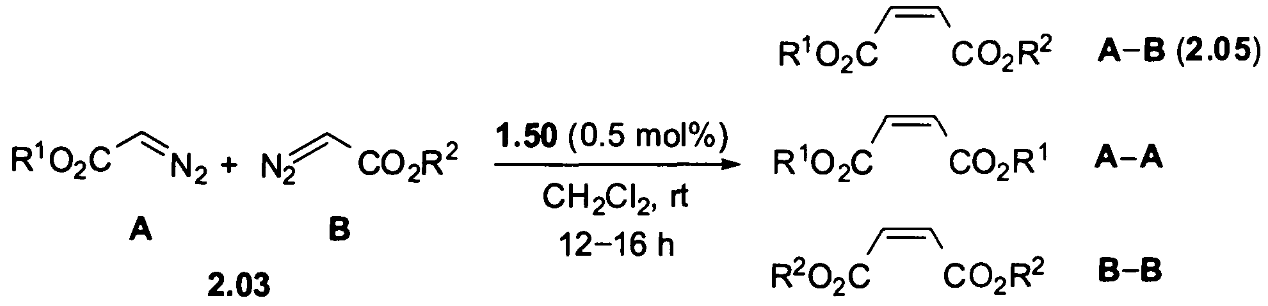
[30] D. M. Hodgson, D. Angrish, *J. Mol. Catal. A: Chem.* **2006**, *254*, 93–95.

[31] G. N. Ignatova, V. V. Puchkova, E. M. Moskovkina, N. I. Grishko, T. S. Balashova, T. N. Shlenskaya, *Plasticheskie Massy* **1970**, *1*, 17–20 [*Chem. Abstr.* **1970**, *72*, 99958].

[32] I. Oprean, F. Hodasan, H. Ciupe, G. Ileana, L. Dissescu, Patent RO 76–85618 [*Chem. Abstr.* **1983**, *98*, 160255].

[33] a) K. Maruoka, M. Akakura, S. Saito, T. Ooi, H. Yamamoto, *J. Am. Chem. Soc.* **1994**, *116*, 6153–6158; b) For an example of intramolecular Diels-Alder reaction of mixed maleates in the synthesis of drimane sesquiterpenes, see: J. F. He, Y. L. Wu, *Tetrahedron* **1988**, *44*, 1933–1940.

[34] P. S. Belov, V. A. Zavorotnyi, K. D. Korenev, V. L. Lashkhi, A. B. Vipper, F. N. Ermolov, V. V. Kulagin, O. N. Tsvetkov, Patent SU 77–2473216 [*Chem. Abstr.* **1980**, *92*, 180683].



Scheme 2.5. Unsymmetrical maleates **2.05** from hetero-coupling of α-diazoacetates **2.03**.

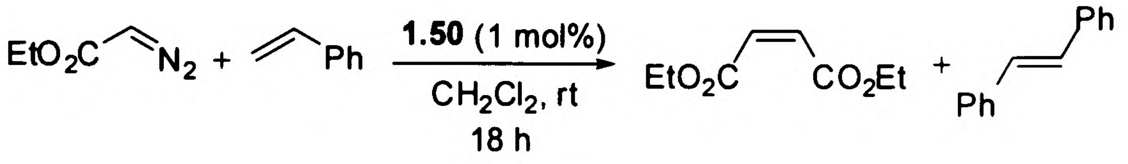
Entry	R^1 (**A**)	R^1 (**B**)	A–B : A–A : B–B[a]	*Z*:*E* (A–B)[b]
1	Ethyl	Benzyl	63 : 18 : 18	98:2 (**2.05a**)
2	Ethyl	Isopropyl	53[c] : 26 : 21	98:2 (**2.05b**)
3	Ethyl	Cyclohexyl	67[d] : 18 : 15	99:1 (**2.05c**)
4	Ethyl	*tert*-Butyl	55[e] : 28 : 17	>99:1 (**2.05d**)
5	Ethyl	2-Adamantyl	46[f] : 36 : 18	>99:1 (**2.05e**)
6	Cyclohexyl	Benzyl	52[g] : 24 : 24	>99:1 (**2.05f**)
7	Cyclohexyl	Isopropyl	52 : 24 : 24	>99:1 (**2.05g**)
8	Cyclohexyl	2-Adamantyl	48 : 33 : 19	>99:1 (**2.05h**)
9	*tert*-Butyl	Benzyl	50[h] : 25 : 25	97:3 (**2.05i**)
10	*tert*-Butyl	Isopropyl	50 : 25 : 25	>99:1 (**2.05j**)
11	*tert*-Butyl	Cyclohexyl	50 : 15 : 35	>99:1 (**2.05k**)
12	*tert*-Butyl	2-Adamantyl	50 : 25 : 25	97:3 (**2.05l**)

a) Determined by ^{1}H-NMR and/ or GC-MS of crude; b) Determined by GC-MS of crude; c) 42% Isolated; d) 57% Isolated; e) 42% Isolated; f) 44% Isolated; g) 50% Isolated; h) 45% Isolated.

Table 2.3. Unsymmetrical maleates **2.05** from α-diazoacetates **2.03** using catalyst **1.50**.

Alternative methods for the synthesis of such mixed systems typically involve a two stage procedure comprising alcohol-induced ring opening of maleic anhydride, followed by esterification of the half acid esters.[32a]

Z/*E* Stereochemical assignments of the olefins **2.05** were made by analogy to the symmetrical maleates **2.04** prepared earlier (typically, δ_H for =CH 6.20–6.30 ppm for maleates and 6.60–6.85 for fumarates).



Scheme 2.6. Homo-coupling of EDA and styrene using catalyst **1.50**.

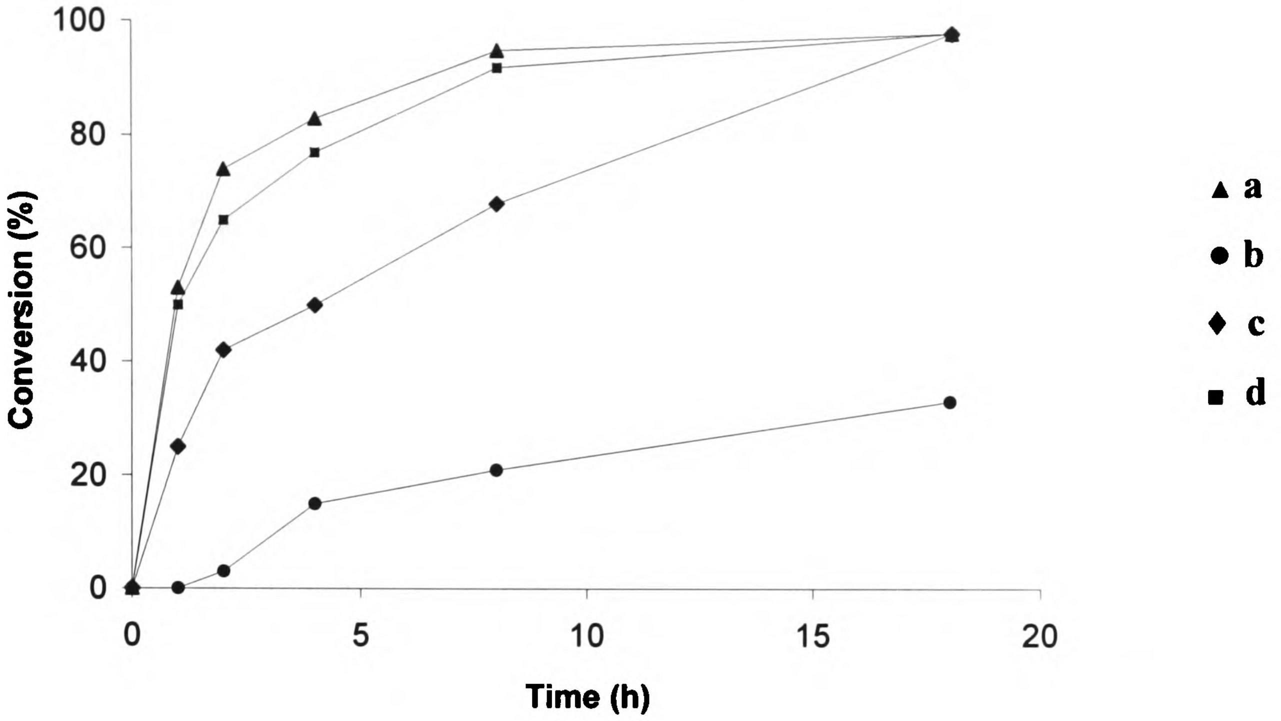


Figure 2.3. Conversion rates for homo-coupling of EDA (1 equiv.) and styrene (1 equiv.) by **1.50**: a) homo-coupling of EDA in the presence of styrene using **1.50** (1 mol%); b) metathesis of styrene in the presence of EDA using **1.50** (1 mol%); c) homo-metathesis of styrene in the absence of EDA using **1.50** (0.5 mol%); d) homo-coupling of EDA in the absence of styrene using **1.50** (0.5 mol%).

Having determined the ability of catalyst **1.50** to efficiently couple α-diazoacetates, it was of interest to study if the catalyst could catalyse carbene transfer from α-diazoesters to olefins. A 1:1 mixture of EDA and styrene (190 mM in CH_2Cl_2) was treated with catalyst **1.50** (1 mol%) at room temperature. After 18 h, the only products observed were DEM (98%, with traces of DEF, ≤2%) and *trans*-stilbene (~33%) arising from homo-coupling of EDA and homo-metathesis of styrene, respectively (Scheme 2.6). When the reaction mixture was concentrated at ~50 °C, prior to chromatography, the remaining styrene was converted to *trans*-stilbene (isolated in quantitative yield, along with 95% of DEM). The above studies suggested that a source of metathetically active catalyst was still present in the reaction mixture which catalysed the homo-metathesis of styrene. This was intriguing, implying that the catalyst is capable of catalysing two different carbene transformations in the same flask, without any cross-over.[35] Interestingly, no products

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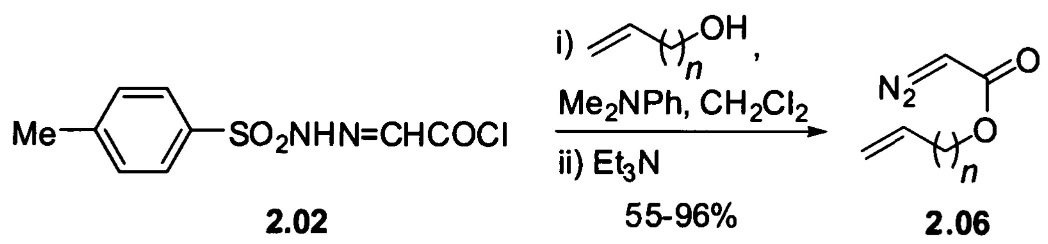
[35] For competitive cyclopropanation and cross-metathesis with EDA and alkenes using $Ru_2(OAc)_4$, see: a) A. F. Noels, A. Demonceau, E. Carlier, A. J. Hubert, R. L. Márquez-Silva, R. A. Sánchez-Delgado, *J. Chem. Soc., Chem. Commun.* **1988**, 783–784; b) A. F. Noels, A. Demonceau, D. Jan, *Russ. Chem. Bull.* **1999**, *48*, 1206–1211.

arising from the cyclopropanation of styrene by EDA were observed. With either slow (syringe pump) addition of EDA or using an increased amount of styrene (2 equiv.), again no cyclopropanation was observed. On ^{1}H-NMR monitoring of the reaction over 18 h, EDA was found to react relatively rapidly (50% consumed in 1 h, Figure 2.3, a) to give mainly DEM (95% isolated yield, *Z*:*E*, 98:2), whereas the metathesis of styrene proceeded more gradually to give *trans*-stilbene [Figure 2.3, b; in the absence of EDA, catalyst **1.50** (0.5 mol%) converts styrene quantitatively into *trans*-stilbene within 18 h at room temperature, Figure 2.3, c].

2.4. Intermolecular Coupling of Alkenyl Diazoacetates

In order to further examine the ability of catalyst **1.50** to catalyse both carbene dimerisation and alkene metathesis, I considered how the catalyst might behave if both diazo and olefin functionality were present in the same substrate. Representative unsaturated α-diazoacetates **2.06** were prepared following the procedure described above for the synthesis of α-diazoacetates **2.03** (*c.f.* Scheme 2.3, pp. 35), but using unsaturated alcohols (Scheme 2.7, Table 2.4).



Scheme 2.7. Synthesis of unsaturated α-diazoacetates **2.06** (n = 2–9).

Entry	n	Yield (%)
1	2 (**2.06a**)	55
2	3 (**2.06b**)	63
3	4 (**2.06c**)	90
4	5 (**2.06d**)	94
5	8 (**2.06e**)	96
6	9 (**2.06f**)	91

Table 2.4. Synthesis of unsaturated α-diazoacetates **2.06**.

With unsaturated α-diazoacetates **2.06**, the catalyst **1.50** could potentially induce: i) intra or intermolecular cyclopropanation[36,37,38] to give medium-sized cyclopropane-fused lactones, and/or

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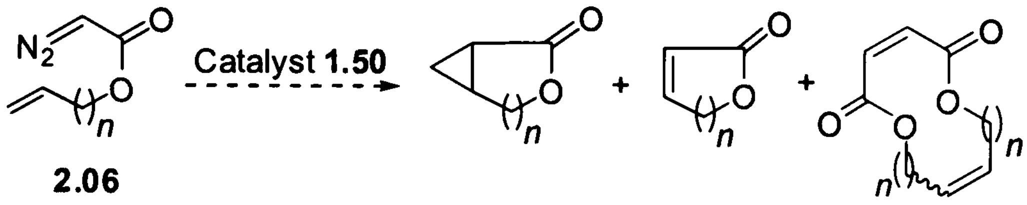
[36] B. G. Kim, M. L. Snapper, *J. Am. Chem. Soc.* **2006**, *128*, 52–53.

[37] B. P. Peppers, S. T. Diver, *J. Am. Chem. Soc.* **2004**, *126*, 9524–9525.

ii) hetero-coupling between diazo and olefin functionality[39] giving medium-sized unsaturated lactones, and/or iii) two independent carbene transformations in the same flask to give macrocyclic dilactones (Scheme 2.8).



Scheme 2.8. Possible carbene transformations of unsaturated diazoacetates **2.06.**

In the event, on mixing the unsaturated diazoacetates **2.06** with catalyst **1.50** (1 mol%) at room temperature, it was observed that maleate **2.07** formation was complete after 14–18 h in all cases, and ring-closing metathesis to generate macrocyclic dilactones **2.08** had proceeded to a variable extent depending on the ring size (**2.07**:**2.08** = 52:48 for 12-membered ring; 91:9 for 14-membered ring; 29:71 for 16-membered ring; and **2.08** not detected for 18–26-membered rings after this time). To expedite ring-closing metathesis an additional 1 mol% of catalyst **1.50** was added and the reaction was heated to reflux to give macrocyclic dienyl dilactones **2.08** (Scheme 2.9). As expected from above studies, only *Z* stereochemistry was seen at the 2-ene-1,4-dicarbonyl fragment, whereas *Z*:*E* mixtures (the ratios varied with the ring size, Scheme 2.9) were obtained during the ring-closing metathesis step. *Cis*-alkenes were preferentially formed for 12- and 14-membered dilactones, whereas *trans* stereochemistry was favoured for larger rings (16–26-membered). No products arising from hetero-coupling of the diazo and olefin functionality were observed.

Z/*E* Stereochemical assignments for the 1,2-dialkyl substituted olefin fragment were made from differences in the ^{13}C-NMR shifts of allylic carbons on the basis of gamma gauche steric effects,[40] and for 2-ene-1,4-diester fragment was done by analogy to the maleates synthesized above (typically, δ_H for =CH 6.20–6.30 ppm for maleates and 6.60–6.85 for fumarates).

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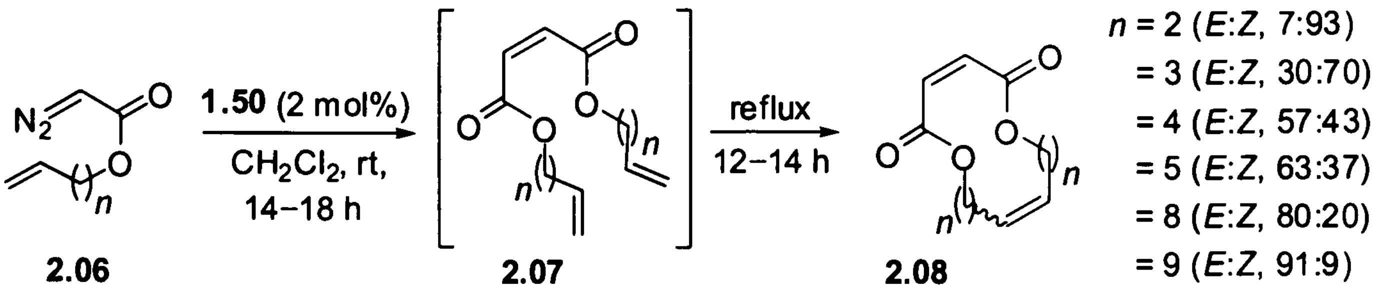
[38] G. Maas, *Chem. Soc. Rev.* **2004**, *33*, 183–190.

[39] F. Monnier, D. Castillo, S. Dérien, L. Toupet, P. H. Dixneuf, *Angew. Chem. Int. Ed.* **2003**, *42*, 5474–5477.

[40] H. Günther, *NMR Spectroscopy: Basic Principles, Concepts, and Applications in Chemistry, 2nd Edition*, John Wiley & Sons, Chichester, **1995**, pp. 501–504.



Scheme 2.9. Macrocyclic dilactones **2.08** from head-to-head carbene dimerisation.

Entry	n	Ring size	Conc. (mM)[a]	Yield (%)
1	2 (**2.06a**)	12	60–70	45 (**2.08a**)
2	3 (**2.06b**)	14	"	53 (**2.08b**)
3	4 (**2.06c**)	16	"	22 (**2.08c**)
4	5 (**2.06d**)	18	"	25 (**2.08d**)
5	8 (**2.06e**)	24	"	24 (**2.08e**)
6	9 (**2.06f**)	26	"	38 (**2.08f**)
7	4 (**2.06c**)	16	30	42 (**2.08c**)
8	5 (**2.06d**)	18	"	27 (**2.08d**)
9	8 (**2.06e**)	24	"	48 (**2.08e**)
10	9 (**2.06f**)	26	"	25 (**2.08f**)
11	2 (**2.06a**)	12	70→5[b]	49 (**2.08a**)
12	3 (**2.06b**)	14	"	38 (**2.08b**)
13	4 (**2.06c**)	16	"	43 (**2.08c**)
14	5 (**2.06d**)	18	"	42 (**2.08d**)
15	8 (**2.06e**)	24	"	26 (**2.08e**)
16	9 (**2.06f**)	26	"	55 (**2.08f**)

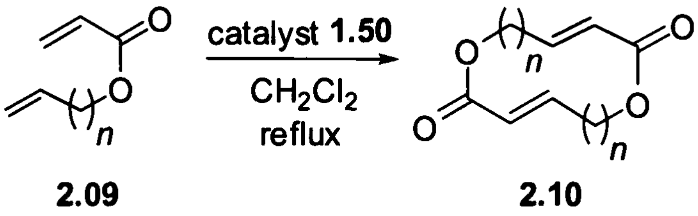
a) Based on **2.06**; b) $c = 70$ mM for intermolecular diazo coupling, then diluted to 5mM for intramolecular ring closing metathesis.

Table 2.5. Formation of macrocycles **2.08** from head-to-head carbene dimerisation.

At an initial substrate concentration of 60–70 mM, macrocycle formation was most effective to form 12- and 14-membered rings, 45–55% (Table 2.5, entries 1 and 2) *vs* larger rings, 20–38% (entries 3–6). Reducing the initial concentration (to 30 mM) led to a significant improvement only for 16- and 24-membered rings (entries 7 and 9) *vs* 18- and 26-membered rings (entries 8 and 10). Intermolecular carbene dimerisation was then attempted under the initial concentration conditions

(70 mM) but the (majority of the) intramolecular ring-closing metathesis under more dilute conditions (5 mM, based on **2.06**). On decreasing the concentration for the metathesis step, efficient macrocycle formation for 12, 16, 18 and 26-membered rings (entries 11, 13, 14 and 16) was observed compared to 14 and 24-membered rings (entries 12 and 15).

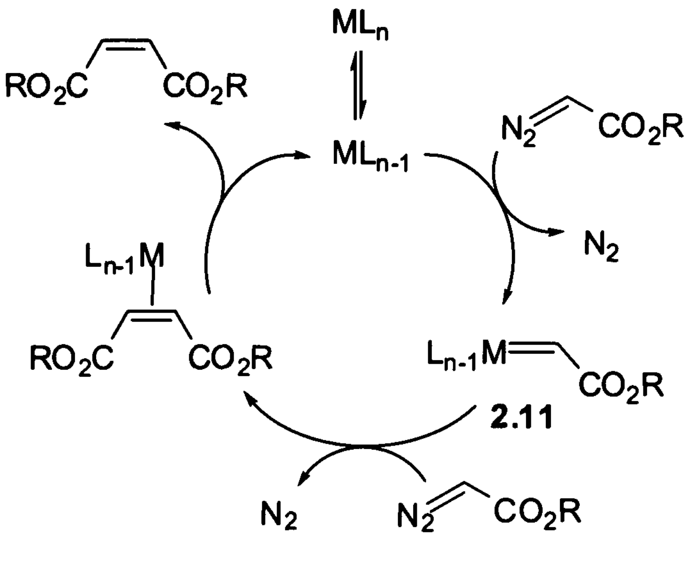
The above studies can be contrasted with those of Fürstner[41] and of Grubbs,[42] who previously obtained homo-dimeric lactones **2.10** by 'head-to-tail' dimerisation of unsaturated acrylates **4.09** (Scheme 2.10).



Scheme 2.10. Head-to-tail dimerisation of unsaturated acrylates **2.09**.

2.5. Mechanism and Selectivity in Carbene Dimerisation

The generally accepted reaction pathway for transition metal catalysed carbene dimerisation of diazoacetates, invokes initial attack of the diazoacetate at the metal centre to generate an ester carbene **2.11** (Scheme 2.11). Nucleophillic attack by diazoacetate on the ester carbene, followed by dissociation of maleate from the metal complex completes the catalytic cycle.[1]



Scheme 2.11. An outline reaction pathway for the metal catalysed homo-coupling of diazoacetates.

The origin of *cis*-selectivity during the (copper catalysed) coupling of α-diazo compounds has been rationalised by Nagai[14] and Wulfman[43] on the basis of steric and electronic effects. By analogy with these suggestions, nucleophilic attack of diazoacetate on the metallocarbene **2.12**

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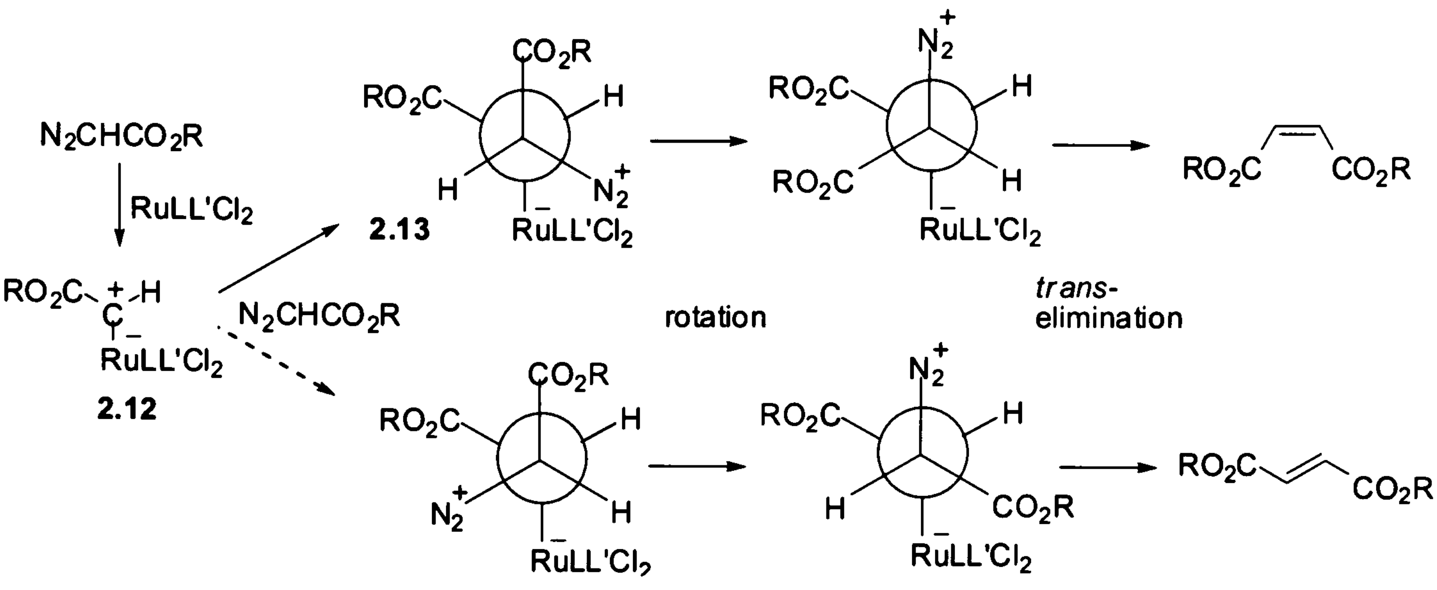
[41] A. Fürstner, O. R. Thiel, L. Ackermann, H. J. Schanz, S. P. Nolan, *J. Org. Chem.* **2000**, *65*, 2204–2207.

[42] C. W. Lee, R. H. Grubbs, *J. Org. Chem.* **2001**, *66*, 7155–7158.

[43] D. S. Wulfman, B. W. Peace, R. S. McDaniel, *Tetrahedron* **1976**, *32*, 1251–1255; see also: B. K. R. Shankar, H. Shechter, *Tetrahedron Lett.* **1982**, *23*, 2277–2280.

could preferentially proceed *via* an intermediate conformer **2.13**, where steric repulsions are minimised (H rather than N_2^+ placed in the most crowded position between ester and catalyst moieties), and the opposite charges (at diazonium and metal) stabilise each other (Scheme 2.12). Rotation and subsequent *trans*-elimination gives *cis*-olefin.



Scheme 2.12. Origin of *cis*-selectivity in dimerisation of α-diazoacetates.

The reaction pathway of dimerisation of EDA with Grubbs' catalysts was probed in more detail. When EDA was treated with PCy_3 (0.5 mol%), no DEM or DEF was observed. However, when catalyst **1.50** was subsequently added to this reaction mixture, carbene dimerisation started, but rather slowly (even after 40 h, 35% of unreacted EDA was still present) compared to when no additional phosphine was added (Figure 2.3, d). These observations suggest that phosphine dissociation is an important step in the carbene dimerisation pathway,[8,9,29] as it is in metathesis.[20] During my initial studies, I did not observe the formation of ethyl cinnamate in the reaction of EDA with Grubbs' catalyst **1.50**, leading to the suggestion that the diazo coupling might proceed *via* a bis-carbene.[24] However, when a solution of EDA (1.1 equiv.) in $CDCl_3$ was added slowly to a solution of catalyst **1.49**[44] (1 equiv.) in $CDCl_3$, formation of ethyl cinnamate[45] along with a phosphine complex was observed on following the reaction by ^{1}H NMR. On treating this mixture with excess of EDA, instant evolution of nitrogen and formation of DEM and DEF (*Z*:*E* ~ 83:17 by ^{1}H NMR) was observed in the same ratio as that obtained with catalyst **1.49**, when used catalytically. When the dimerisation of EDA with catalyst **1.49** (Ru=CH, δ_H = 19.76 ppm in $CDCl_3$) was studied at low temperature (−55 °C) in $CDCl_3$, the reaction was found to proceed *via* a new carbene (Ru=CH, δ_H = 19.56 ppm in $CDCl_3$). Based on the above observations, a catalytic

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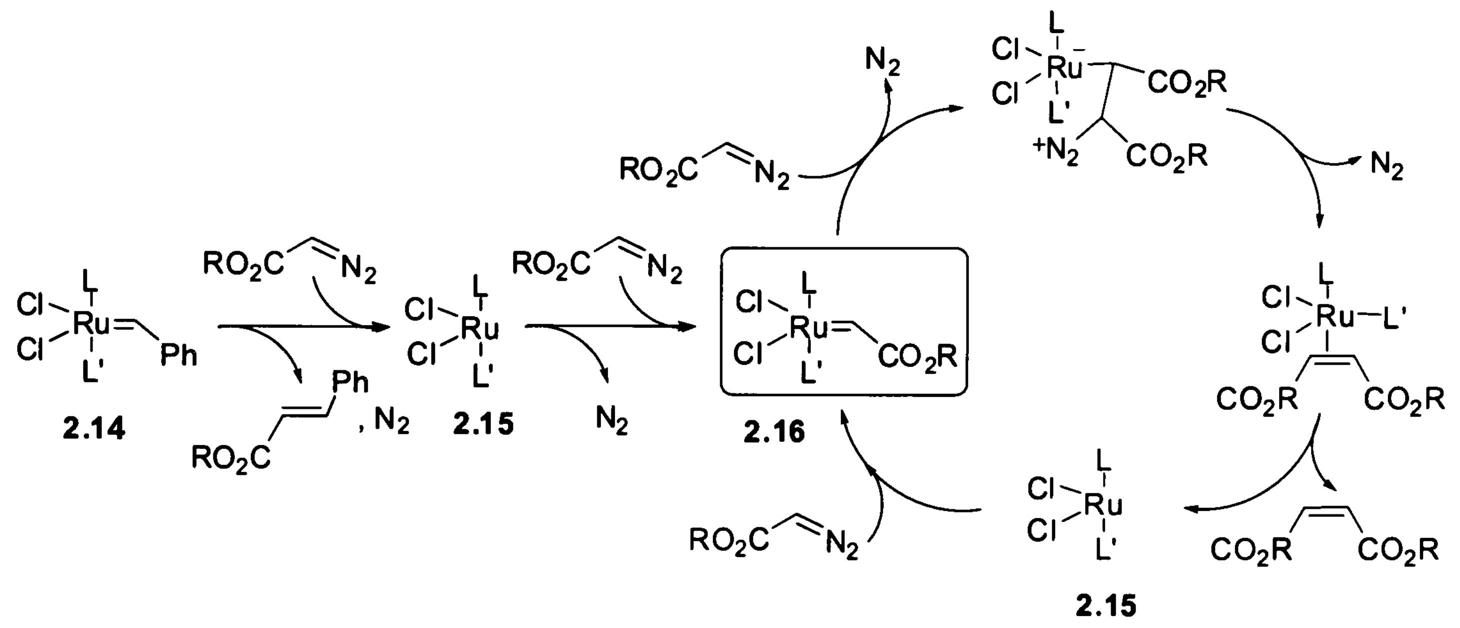
[44] The use of catalyst **1.49** leads to more readily interpretable spectra.

[45] ^3J(H,H) = 16 Hz for CH=CH; formation of the *E*-(rather than *Z*) alkene here (*cf.* the earlier preference for maleate, Scheme 2.12) may reflect the reversibility in the addition of EDA to the comparatively more stabilised metallocarbene **2.14**.

cycle can be proposed in order to rationalise the observations concerning diazo coupling and metathesis in one-pot (Scheme 2.13).



Scheme 2.13. Proposed catalytic cycle for diazo coupling using Ru carbenes **1.49** and **1.50**.

Initial attack of diazoacetate on the benzylidene (pre)-catalyst **2.14** generates carbene free Ru (II) complex **2.15** with the evolution of nitrogen and cinnamate. Further attack of diazoacetate on **2.15** generates an ester carbene **2.16**, which is suggested as the key intermediate catalysing the diazo coupling, similar to other ester carbenes proposed in the literature for this type of process.[4,6–9,29,46,47] Ru-ester carbenes (of the type $Cl_2(PR_3)_2Ru{=}CHCO_2R'$) are known to be unstable species (the stability of the which varies with alkyl groups), but they are reported to be very active initiators during olefin metathesis,[23,48,49] thus explaining the ability of carbene-based Grubbs' catalysts to catalyse diazo coupling and metathesis in same flask.[50]

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[46] E. Galardon, P. L. Maux, L. Toupet, G. Simonneaux, *Organometallics* **1998**, *17*, 565–569.

[47] H. M. Lee, C. Bianchini, G. Jia, P. Barbaro, *Organometallics* **1999**, *18*, 1961–1966.

[48] M. Ulman, T. R. Belderrain, R. H. Grubbs, *Tetrahedron Lett.* **2000**, *41*, 4689–4693.

[49] A. Demonceau, A. F. Noels, E. Saive, A. J. Hubert, *J. Mol. Catal.* **1992**, *76*, 123–132.

[50] For other examples of Grubbs' type catalysts playing a dual catalytic role (typically metathesis followed by ruthenium hydride chemistry), see: a) J. Louie, C. W. Bielawski, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 11312–11313; b) A. Fürstner, A. Leitner, *Angew. Chem. Int. Ed.* **2003**, *42*, 308–311; c) B. Schmidt, *Eur. J. Org. Chem.* **2004**, 1865–1880.

2.6. Conclusions

In summary, the ability of Grubbs' 2nd generation Ru carbene complex to catalyse the coupling of α-diazoacetates highly stereoselectively to give *cis*-olefins under mild conditions (room temperature, low catalyst loading) has been demonstrated. These studies together with those reported earlier by Grubbs and by Fürstner highlight the versatility of the catalyst for the synthesis of olefins with both *cis* and *trans* geometry from diazo coupling and cross-metathesis, respectively. In the presence of an additional alkene functionality, inter-/ intramolecular cyclopropanation is not observed but rather metathetical activity of the catalyst is retained, and has been exploited with unsaturated diazoacetates to generate dienyl dilactones by head-to-head diazo coupling followed by ring-closing metathesis.

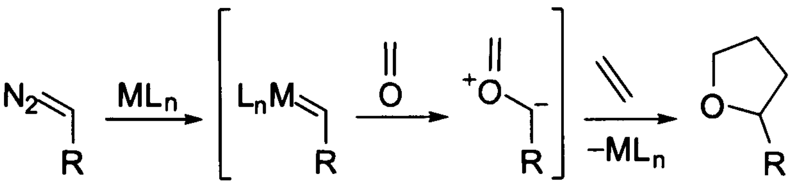
CHAPTER 3

INTRAMOLECULAR CARBONYL YLIDE CYCLOADDITIONS

INTRAMOLECULAR CARBONYL YLIDE CYCLOADDITIONS

3.1. Background

Carbonyl ylides **3.03**, generated from the interaction of a carbonyl functionality with metallocarbenes **3.02**, are capable of undergoing 1,3-dipolar cycloaddition with dipolarophiles to furnish substituted reduced furans **3.04** (Scheme 3.1).[1,2,3,4]



3.01 **3.02** **3.03** **3.04**

Scheme 3.1. Metal-catalysed 1,3-dipolar cycloaddition using diazo and carbonyl compounds.

Such cascade processes, catalysed by copper or rhodium complexes, originally developed by Ibata[5,6] and (especially) Padwa[7,8,9] for the synthesis of oxapolycycles, are of interest because of the opportunities for rapid generation of molecular complexity in a single operation.[10,11,12] Padwa reported that the rhodium catalysed decomposition of α-diazoketone **3.05** with rhodium(II) acetate [$Rh_2(OAc)_4$] or rhodium(II) caprolactamate [$Rh_2(cap)_4$], provides four different products: the carbonyl ylide derived cycloadducts **3.06a** and **3.06b**; and the cyclopropanation product **3.06c**[13] (Scheme 3.2). The major product isolated corresponded to the cycloadduct **3.06b** derived from the internal trapping of the carbonyl ylide intermediate. However, the use of fluorinated catalysts; rhodium(II) trifluoroacetate [$Rh_2(tfa)_4$] or rhodium(II) perfluorobutyrate [$Rh_2(pfb)_4$], caused a significant alteration in the product distribution, with cycloadduct **3.06a** as the major cycloadduct

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[1] M. C. McMills, D. Wright, in *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*, Vol. 59 (Ed.: A. Padwa, W. H. Pearson), John Wiley and Sons, New York, **2002**, pp. 253–314.

[2] J. S. Clark, *Nitrogen, Oxygen and Sulfur Ylide Chemistry*, Oxford University Press, Oxford, **2002**.

[3] G. Mehta, S. Muthusamy, *Tetrahedron* **2002**, *58*, 9477–9504.

[4] R. M. Savizky, D. J. Austin, in *Modern Rhodium-Catalyzed Organic Reactions*, (Ed.: P. A. Evans), Wiley VCH, Weinheim, **2005**, pp. 433–454.

[5] T. Ibata, J. Toyoda, *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2489–2493.

[6] T. Ibata, J. Toyoda, M. Sawada, T. Tanaka, *J. Chem. Soc., Chem. Commun.* **1986**, 1266–1267.

[7] A. Padwa, *Acc. Chem. Res.* **1991**, *24*, 22–28.

[8] A. Padwa, M. D. Weingarten, *Chem. Rev.* **1996**, *96*, 223–270.

[9] A. Padwa, J. Boonsombat, P. Rashatasakhon, J. Willis, *Org. Lett.* **2005**, *7*, 3725–3727.

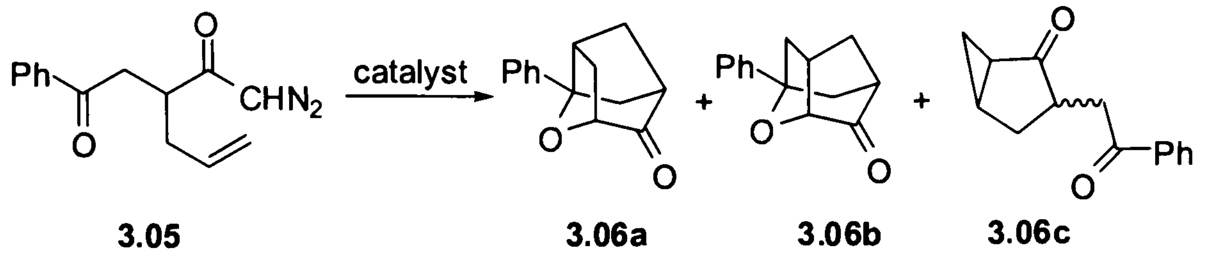
[10] D. M. Hodgson, T. Brückl, R. Glen, A. H. Labande, D. A. Selden, A. G. Dossetter, A. J. Redgrave, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5450–5454.

[11] S. Muthusamy, J. Krishnamurthi, M. Nethaji, *Chem. Commun.* **2005**, 3862–3864.

[12] X. Zhang, R. Y. Y. Ko, S. Li, R. Miao, P. Chiu, *Synlett* **2006**, 1197–1200.

[13] A. Padwa, D. J. Austin, S. F. Hornbuckle, *J. Org. Chem.* **1996**, *61*, 63–72.

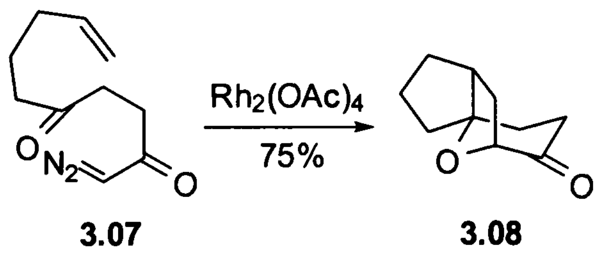
in both cases. Thus, the choice of the catalyst affects the regiochemistry of the cycloaddition and the relative proportions of cycloadducts **3.06a** and **3.06b**.



Catalyst	Relative Yield (%) a : b : c
$Rh_2(OAc)_4$	10 : 47 : 37
$Rh_2(cap)_4$	12 : 52 : 32
$Rh_2(pfb)_4$	33 : 12 : 42
$Rh_2(tfa)_4$	34 : 12 : 47

Scheme 3.2. Intramolecular cycloaddition and cyclopropanation of α-diazodiketone.

However, the treatment of α-diazoketone **3.07** with $Rh_2(OAc)_4$ proceeds smoothly to give only the oxapolycycle **3.08** in 75% yield (Scheme 3.3).[14] No intermolecular trapping is observed when the reaction of **3.07** is carried out with $Rh_2(OAc)_4$ in presence of an external dipolarophile such as dimethyl acetylenedicarboxylate (DMAD). The intramolecular cycloaddition with the tethered π-bond in the system is too rapid to allow the intermolecular trapping.



Scheme 3.3. Intramolecular cycloaddition of α-diazodiketone.

When α-diazoketone **3.09** (with a four methylene tether) is treated with $Rh_2(OAc)_4$, the cycloadduct **3.10** is formed in 60% yield; and in presence of DMAD, the intramolecular process is completely shut down. The only product observed is the one derived from intermolecular trapping of carbonyl ylide with DMAD (Scheme 3.4).

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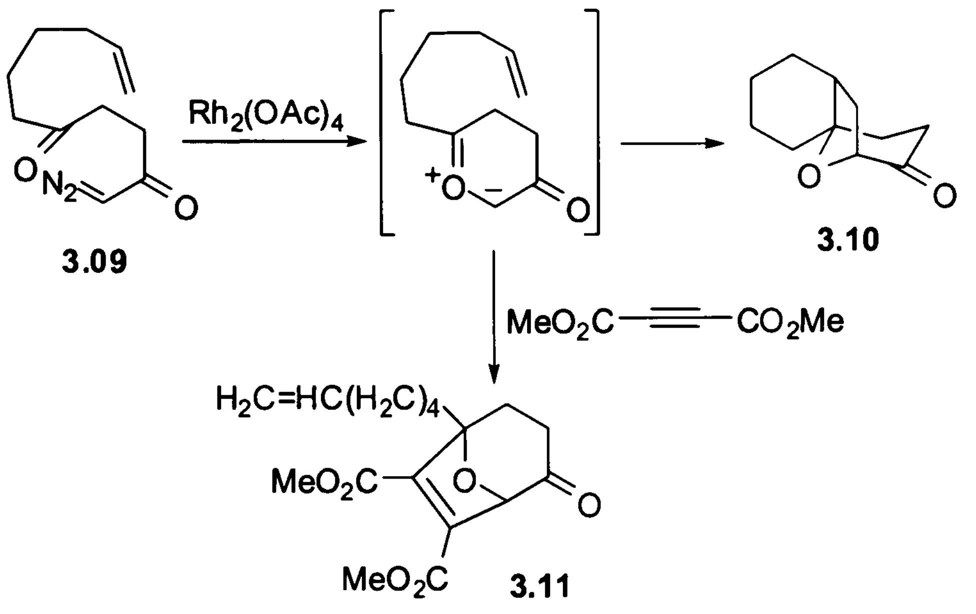
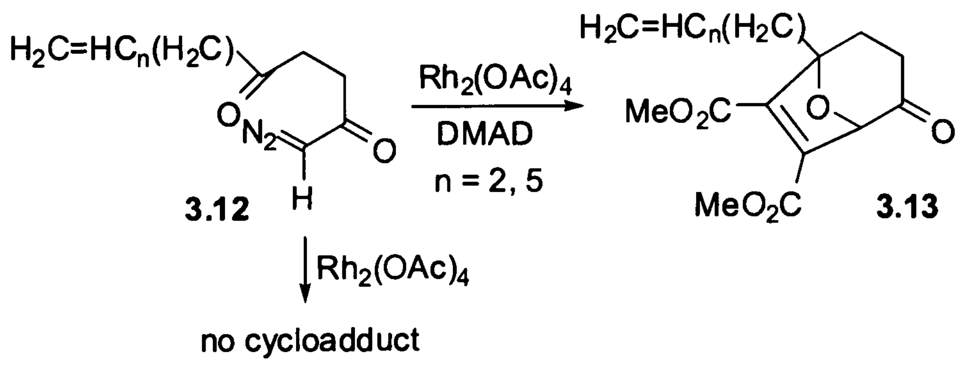
[14] A. Padwa, S. F. Hornbuckle, G. E. Fryxell, Z. J. Zhang, *J. Org. Chem.* **1992**, *57*, 5747–5757.



Scheme 3.4. Inter and intramolecular trapping of hexenyl tethered carbonyl ylide.

Treatment of the two or five methylene tethered diazo ketones **3.12** (n = 2, 5) affords no intramolecular cycloadduct. However, the reaction in presence of an excess of DMAD affords the intermolecular cycloadduct, confirming that although the dipole is formed in both cases, but the two carbon tether (leading to a strained tricyclic cyclobutane) or five carbon tether (leading to a seven membered ring) is ineffective in directing intramolecular cycloaddition (Scheme 3.5).



Scheme 3.5. Intermoleuclar trapping of carbonyl ylides.

Enantioselective intramolecular tandem carbonyl ylide formation-1,3 dipolar cycloaddition has also been examined. Hodgson *et al.* first reported the enantioselective intramolecular cycloaddition (Scheme 3.6).[15] Enantiomeric excess (*ee*) up to 52% was achieved using proline based catalyst Rh_2(*S*-DOSP)$_4$ **3.16** (Figure 3.1)[16] developed by Davies. The use of binaphthyl based Rh_2(*R*-BNP)$_4$ **3.17** (Figure 3.1) catalyst, developed by Pirrung[17] gave an improved asymmetric induction of 64%.

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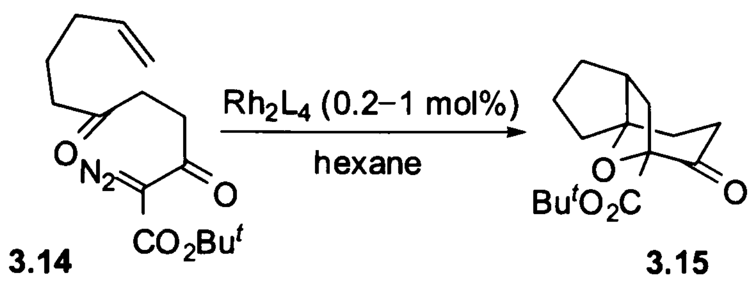
[15] D. M. Hodgson, P. A. Stupple, C. Johnstone, *Tetrahedron Lett.* **1997**, *38*, 6471–6472.

[16] H. M. L. Davies, P. R. Bruzinski, D. H. Lake, N. Kong, M. J. Fall, *J. Am. Chem. Soc.* **1996**, *118*, 6897–6907.

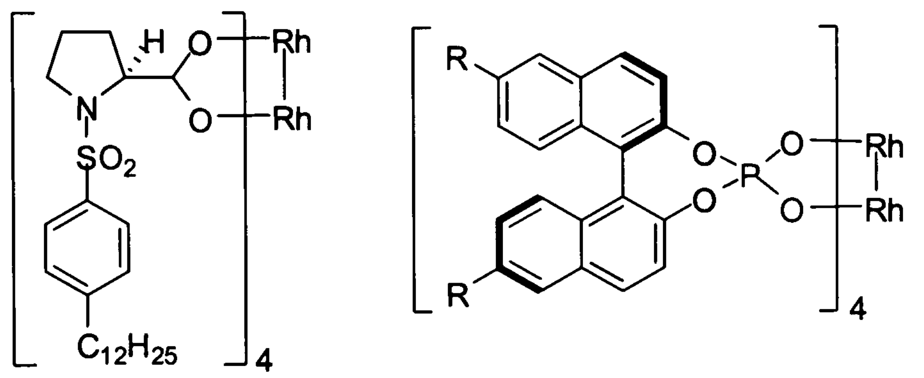
[17] M. C. Pirrung, J. Zhang, *Tetrahedron Lett.* **1992**, *33*, 5987–5990.



Catalyst	Temp.	Yield (%)	ee (%)
Rh_2(*S*-DOSP)$_4$	rt	77	52
Rh_2(*R*-BNP)$_4$	rt	65	64
Rh_2(*R*-DDBNP)$_4$	rt	76	81
Rh_2(*R*-DDBNP)$_4$	0 °C	81	88
Rh_2(*R*-DDBNP)$_4$	−15 °C	66	90

Scheme 3.6. Enantioselective intramolecular cycloddition.

Due to poor solubility of Rh_2(*R*-BNP)$_4$ in hexane (the solvent of choice for these reactions), it was envisaged that the performance of the catalyst could be improved by introducing solubilising groups. This led to the development of Rh_2(*R*-DDBNP)$_4$ **3.18** (Figure 3.1) containing hydrophobic dodecyl chains. With this latter catalyst, better yields and enantioselectivities were indeed observed; 81% *ee* at room temperature and 90% *ee* at −15 °C.[18,19]



3.16, Rh_2(*S*-DOSP)$_4$

3.17, R = H, Rh_2(*R*-BNP)$_4$
3.18, R = $C_{12}H_{25}$, Rh_2(*R*-DDBNP)$_4$

Figure 3.1. Chiral rhodium(II) catalysts.

Thus, intramolecular carbonyl ylide formation-1,3 dipolar cycloaddition allows a smooth conversion of an acyclic precursor with no stereocentres to a complex tricyclic core with three new stereocentres, under mild conditions and usually in good yields. With a tethered olefin, the dipolarophile could potentially be further elaborated by olefin metathesis,[20,21] another powerful and mild process for elaborating olefins for potential use in subsequent transformations. This could allow one to diversify the nature of the dipolarophile attached to the ylide and hence lead to the formation of more complex polycyclic systems. The aim of this part of the project was to couple two different carbene transformation reactions (olefin metathesis and intramolecular 1,3-dipolar cycloaddition), catalysed by two different transition metal catalysts in one-pot for diversity-oriented synthesis of complex oxapolycycles (Scheme 3.7).

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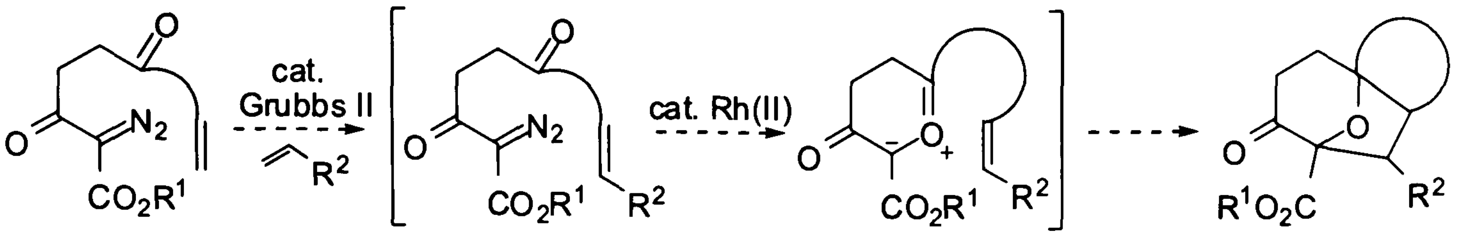
[18] D. M. Hodgson, P. A. Stupple, C. Johnstone, *Chem. Commun.* **1999**, 2185–2186.

[19] D. M. Hodgson, P. A. Stupple, F. Y. T. M. Pierard, A. H. Labande, C. Johnstone, *Chem. Eur. J.* **2001**, *7*, 4465–4476.

[20] R. H. Grubbs, *Handbook of Metathesis*, Wiley-VCH, Weinheim, **2003**.

[21] A. K. Chatterjee, T. -L. Choi, D. P. Sanders, R. H. Grubbs, *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370.



Scheme 3.7. Cross-metathesis and carbonyl ylide formation/ intramolecular cycloaddition strategy.

3.2. Cross-Metathesis of α-Diazo-β-ketoester 3.14

During my initial studies, I observed that Grubbs' 2nd generation catalyst **1.50**, the most commonly used catalyst for olefin metathesis, could also catalyse the coupling of α-diazoacetates under mild conditions to give *cis*-olefins (Scheme 2.4, pp. 36).[22,23] I was intrigued to further explore the reactivity of catalyst **1.50** with more substituted diazoesters. Ethyl α-diazopropanoate[24,25] was found to be stable to catalyst **1.50** in CH_2Cl_2 at room temperature but underwent decomposition at reflux. However, the more stabilised ethyl diazoacetoacetate,[26] an α-diazo-β-ketoester, was stable to catalyst **1.50**, not only at room temperature, but also under typical metathesis conditions (5 mol% **1.50**, CH_2Cl_2, reflux, 14–18 h). This suggested that the olefin metathesis might proceed in the presence of such dicarbonyl-stabilised diazo functionality. To test this concept, unsaturated 2-diazo-3,6-diketoester **3.14**,[18,19] capable of undergoing tandem carbonyl ylide formation-cycloaddition was selected. The diazoester was prepared following the lit. procedure,[18,19] starting from alkylation of 2,3-dihydrofuran with an alkenyl iodide, followed by hydrolysis/ oxidation with Jones' reagent[27] which in a single step gave the keto acid **3.19**, in 78% yield. *C*-Acylation of *mono*-ethyl malonate with carboxylic acid **3.19** following Masamune's procedure[28,29] gave the ketoester **3.20** in 59% yield. Finally, diazo transfer using *p*-acetamidobenzenesulfonyl azide,[26] gave cycloaddition precursor **3.14**, in 97% yield (Scheme 3.8).

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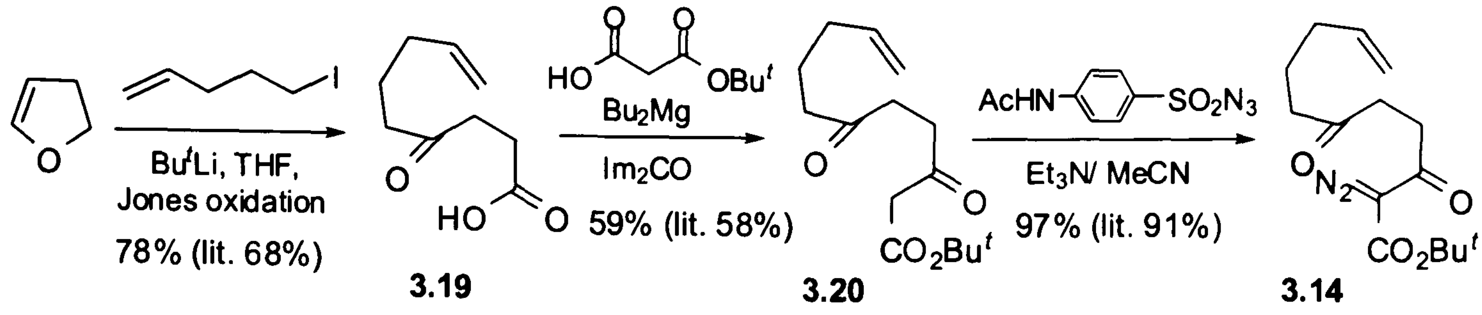
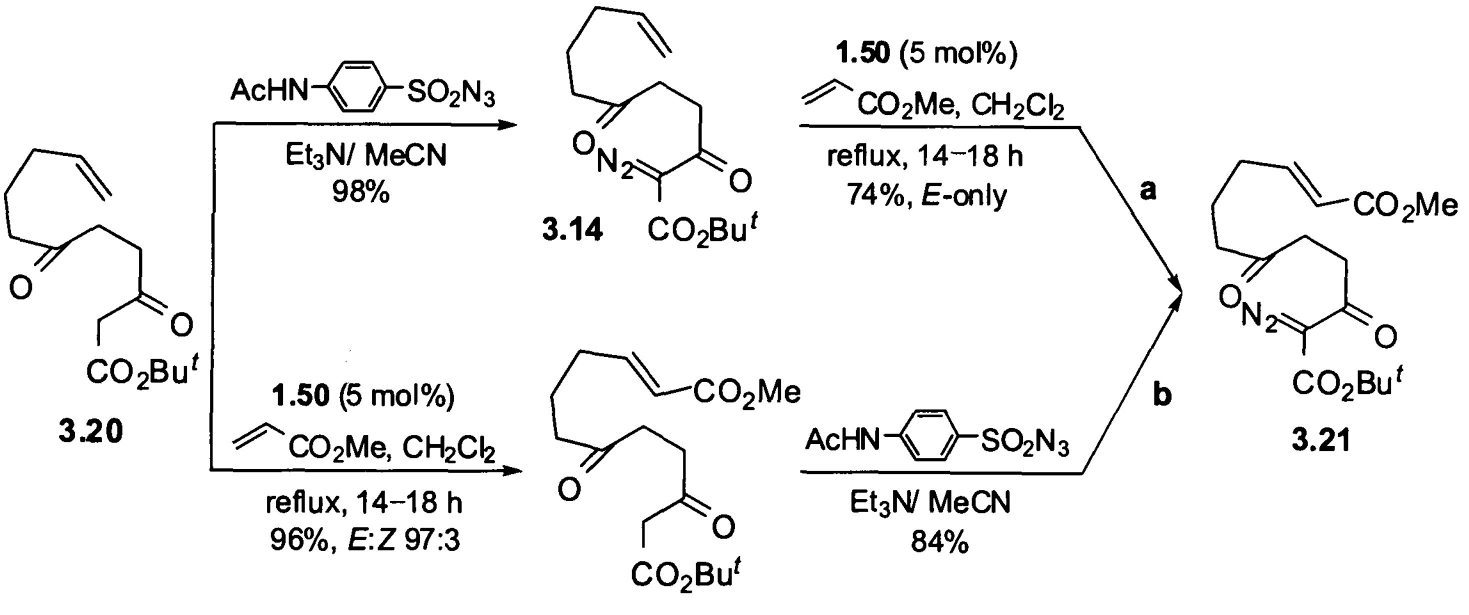
[22] D. M. Hodgson, D. Angrish, *Chem. Commun.* **2005**, 4902–4904.
[23] D. M. Hodgson, D. Angrish, *J. Mol. Catal. A: Chem.* **2006**, *254*, 93–95.
[24] M. Regitz, J. Hocker, A. Liedhegener, *Org. Synth. Coll. Vol. V* **1973**, 179–183.
[25] S. Bachmann, D. Fielenbach, K. A. Jørgensen, *Org. Biomol. Chem.* **2004**, *2*, 3044–3049.
[26] Y.-H. Lim, K. F. McGee, Jr., S. M. Sieburth, *J. Org. Chem.* **2002**, *67*, 6535–6538.
[27] M. A. Tschantz, L. E. Burgess, A. I. Meyers, *Org. Synth. Coll. Vol. IX* **1998**, 530–533.
[28] D. W. Brooks, L. D.-L. Lu, S. Masamune, *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 72–73.
[29] M. Ghosh, M. J. Miller, *Tetrahedron* **1996**, *52*, 4225–4238.



Scheme 3.8. Synthesis of 2-diazo-3,6-diketoester **3.14**.[18,19]

Labande[30] previously examined the cross-metathesis of 2-diazo-3,6-diketoester **3.14** with methyl acrylate, as the latter is known to undergo stereoselective cross-metathesis with terminal olefins,[20,31,32,33] and the resulting desired ester **3.21** was also known to undergo 1,3-dipolar cycloaddition.[34] In the event, cross-metathesis proceeded smoothly with 2-diazo-3,6-diketoester **3.14** and methyl acrylate (2.0 equiv.) using Grubbs' 2nd generation catalyst **1.50** (5 mol%, CH_2Cl_2, reflux, 16 h) to give the α,β-unsaturated ester **3.21** in good yield (74%) and complete with *E*-stereoselectivity. Importantly, retention of the diazo functionality was observed.



Scheme 3.9. Two way approach to the synthesis of diazoketoester **3.21**.

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[30] a) D. M. Hodgson, D. Angrish, A. H. Labande, *Chem. Commun.* **2006**, 627–628; b) D. M. Hodgson, D. Angrish, *Adv. Synth. Catal.* **2006**, *348*, 2509–2514.

[31] A. K. Chatterjee, J. P. Morgan, M. Scholl, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 3783–3784.

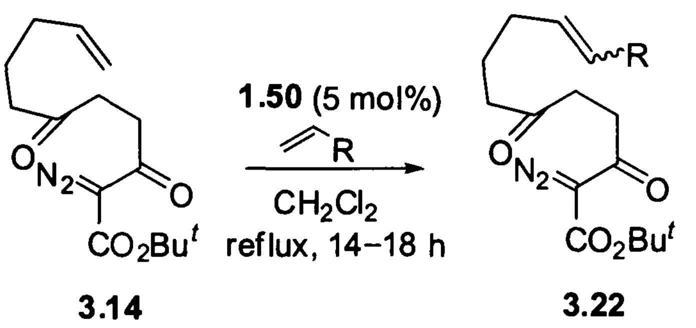
[32] J. P. Morgan, R. H. Grubbs, *Org. Lett.* **2000**, *2*, 3153–3155.

[33] T. -L. Choi, C. W. Lee, A. K. Chatterjee, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 10417–10418.

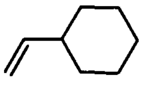
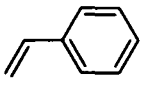
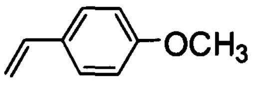
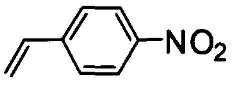
[34] D. M. Hodgson, A. H. Labande, F. Y. T. M. Pierard, M. Á. E. Castro, *J. Org. Chem* **2003**, *68*, 6153–6159.

3.21 Has previously also been prepared from **3.20** by cross-metathesis followed by diazo transfer (Scheme 3.9, b).[34] The advantage of carrying out diazo transfer prior to cross-metathesis lies in the fact that one would need to carry out the diazo transfer only once and the substrate **3.14** could be used to diversify the unsaturated diazoester by cross-metathesis.

I examined cross-metathesis of unsaturated 2-diazo-3,6-diketoester **3.14** with some terminal olefins (2.0 equiv.) using catalyst **1.50** (5 mol%) in CH_2Cl_2 (Scheme 3.10, Table 3.1). Modest yields were obtained, but with high stereoselectivity. Styrene and substituted styrenes gave only *E*-isomer selectively. Self metathesis of styrenes (giving crystalline *trans*-stillbenes) during the process resulted in lowering of the yield during cross-metathesis. Further addition of catalyst **1.50** or longer reaction times failed to drive the reaction to completion.



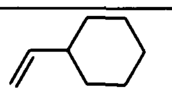
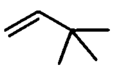
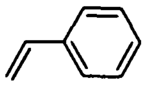
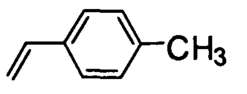
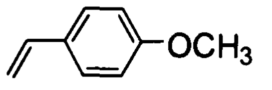
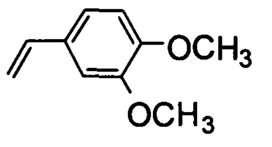
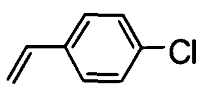
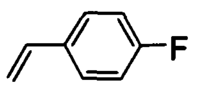
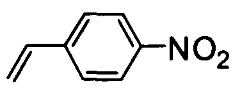
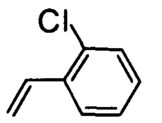
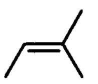
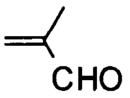
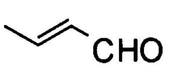
Scheme 3.10. Cross-metathesis using diazoester **3.14**.

Entry	Olefin	Equiv.	Time	Yield % (*E*:*Z*)[a]
1		2.0	18 h	49 (85:15)
2		2.0	14 h	49 (*E*-only)
3		2.0	17 h	37 (*E*-only)
4		2.0	15 h	60 (*E*-only)

a) Determined by ^{1}H-NMR.

Table 3.1. Cross-metathesis of diazoester **3.14** with terminal olefins.

Cross-metathesis of the diazoester **3.14** was then examined with an excess of styrene (10 equiv.) using catalyst **1.50** (5 mol%). Pleasingly, 81% (*E*-isomer only) of the desired olefin **3.22** was obtained. Subsequently, I studied the cross-metathesis of unsaturated 2-diazo-3,6-diketoester **3.14** with 4–10 equiv. of various olefins using catalyst **1.50** (5 mol%) in CH_2Cl_2 at reflux for 14–18 h; the substituted alkenes **3.22** were obtained in good to excellent yields and with high stereoselectivity (Table 3.2).

Entry	Olefin	Time (h)	Yield (%)	(*E*:*Z*)[a]
1		18	78 (**3.22a**)	85:15
2		18	74 (**3.22b**)	*E*-only
3		18	81 (**3.22c**)	*E*-only
4		18	69 (**3.22d**)	94:6
5		18–24	46[b] (**3.22e**)	*E*-only
6		18–30	36 (**3.22f**)	*E*-only
7		16	76 (**3.22g**)	*E*-only
8		18	76 (**3.22h**)	96:4
9		16	79 (**3.22i**)	*E*-only
10		18	89 (**3.22j**)	96:4
11		18	77 (**3.22k**)	–
12		18	83 (**3.22l**)	*E*-only
13		14	76 (**3.22m**)	*E*-only

a) Determined by ^{1}H NMR; b) 74% based on recovered diazoester **3.14**.

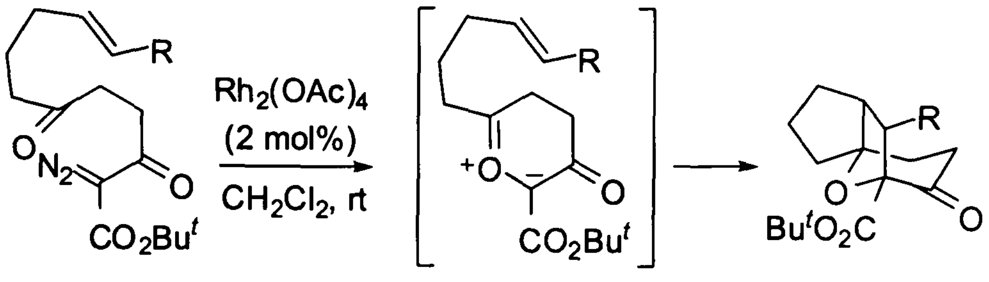
Table 3.2. Cross-metathesis of diazoester **3.14** with various olefins.

Vinylcyclohexane and sterically hindered 3,3-dimethyl-2-butene were efficient partners during the process, with the latter giving only the *E*-isomer (entries 1 and 2). Although styrene underwent cross-metathesis efficiently (entry 3), electron rich styrenes were reluctant partners in the process, as was evident from the drop in yields from 4-methylstyrene (entry 4) to 4-methoxystyrene (entry 5). 3,4-Dimethoxystyrene was even more sluggish towards cross-metathesis and yielded only 36% of the desired product (entry 6). Prolonged reaction times, further addition of catalyst or use of a large excess of methoxystyrenes (10–15 equiv.) failed to drive the reaction to completion. However, although the reaction was sluggish, only the *E*-isomer was obtained with methoxystyrenes. Electron withdrawing substituents, such as halides or nitro functionality, resulted in higher yields with complete *trans*-selectivity (entries 7–9). Even an *ortho* substituted styrene reacted efficiently to give the desired olefin **3.22j** in 89% yield, and with high *trans*-selectivity, *E*:*Z* 96:4 (entry 10). Furthermore, I examined α,β-unsaturated carbonyl compounds in cross-metathesis with α-diazo-β-ketoester **3.14** (entries 12 and 13). In these cases, cross-metathesis proceeded smoothly to give the desired product in good yields and complete *trans*-selectivity. Cross-metathesis with both amylene and methacrolein efficiently gave cycloaddition substrates **3.22k-l** bearing trisubstituted alkene dipolarophiles for subsequent Rh catalysed intramolecular cycloaddition (entries 11 and 12).

The stereochemical assignment of the *trans*-olefins **3.22** obtained from cross-metathesis was based upon the coupling constants (typically ^3J(H,H) = 15–16 Hz for CH=CH). The *E*:*Z* ratios were determined from ^{1}H NMR, by integration of the olefinic or the allylic protons of the major and minor isomers. However, for olefin **3.22l** (obtained by cross-metathesis with methacrolein) the stereochemical assignment was established by the NOE experiments, where the olefinic proton was established to be *cis* to the CHO group (see pp. 127). The *E* and *Z* isomers in all the above examples were inseparable and the isomeric mixtures were used as such in subsequent transformations.

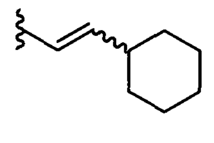
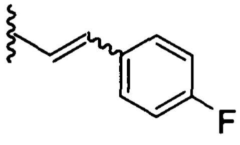
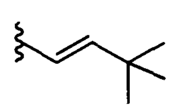
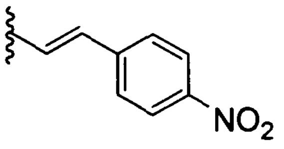
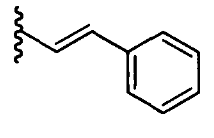
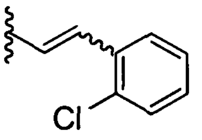
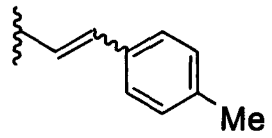
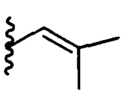
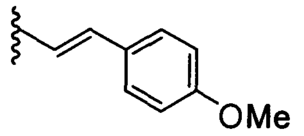
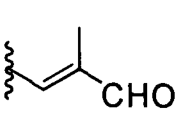
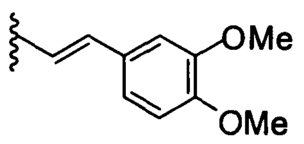
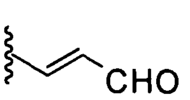
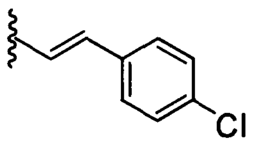
3.3. Tandem Carbonyl Ylide Formation/ Intramolecular Cycloaddition

With the above elaborated di/trisubstituted olefins **3.22** in hand, their propensity to undergo tandem carbonyl ylide formation-intramolecular cycloaddition was examined. In general, catalysis by $Rh_2(OAc)_4$ (2 mol%) in CH_2Cl_2 at room temperature for 3–4 h proceeded very efficiently to give the cycloadducts **3.23** in good to excellent yields (Scheme 3.11, Table 3.3).



3.22 **3.23**

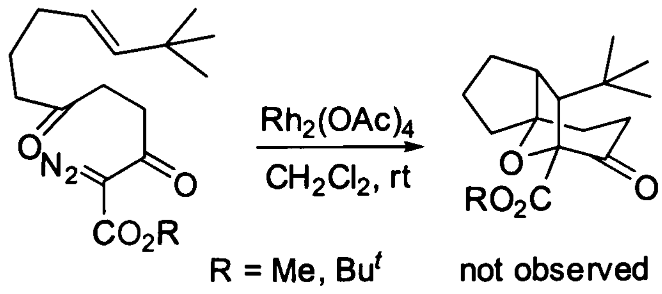
Scheme 3.11. Tandem intramolecular carbonyl ylide formation-cycloaddition.

Entry	Dipolarophile	Cycloaddition (%)	Entry	Dipolarophile	Cycloaddition (%)
1		78 **(3.23a)**	8		88 **(3.23h)**
2		–[a]	9		quant. **(3.23i)**
3		84 **(3.23c)**	10		78 **(3.23j)**
4		86 **(3.23d)**	11		74 **(3.23k)**
5		quant. **(3.23e)**	12		77[c] **(3.23l)**
6		–[b]	13		85[d] **(3.23m)**
7		82 **(3.23g)**			

a) No cycloadduct obtained; b) Not carried out; c) Isolated as ~ 1:1 mixture of **3.23l** with hydrate **3.24l**; d) Isolated as ~ 1:0.25 mixture of **3.23m** with hydrate **3.24m**.

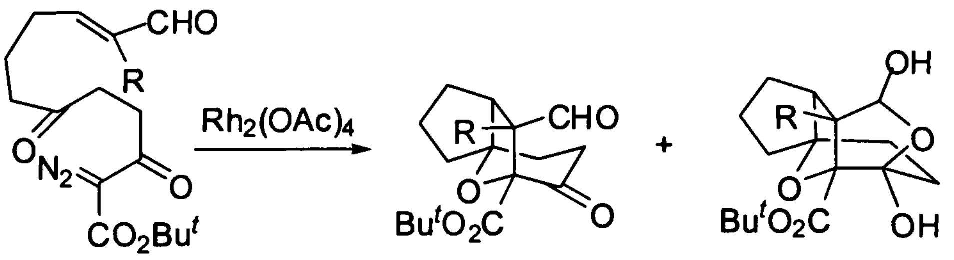
Table 3.3. Intramolecular carbonyl ylide formation-cycloaddition.

Aryl-substituted dipolarophiles underwent efficient cycloaddition with no observable influence of the electronic nature of the aromatic ring being evident (entries 3–10).[35] However, *tert*-butyl-substituted alkene **3.22b** (generated from cross-metathesis of **3.14** and 3,3-dimethyl-1-butene) failed to undergo cycloaddition, suggesting a limitation of the chemistry with hindered alkene dipolarophiles. Further evidence was obtained by the reaction of the methyl ester of α-diazo-β-ketoester **3.22b** (R = Bu^t → R = Me) [(*E*)-methyl 2-diazo-12,12-dimethyl-3,6-dioxotridec-10-enoate, **3.22n**], which also failed to undergo cycloaddition (Scheme 3.12).



Scheme 3.12. No cycloaddition with hindered dipolarophiles.

Trisubstituted olefins **3.22k-l** gave the corresponding cycloadducts **3.23k-l** efficiently (74% and 77% yields, respectively). Interestingly, the cycloadduct **3.23l** from methacrolein was isolated as a mixture with its cyclic hydrate **3.24l**. However, with crotonaldehyde, hydrate **3.24m** formation was observed to a lesser extent (Scheme 3.13).



3.22l (R = Me) **3.23l** (R = Me) 1 : 1 **3.24l** (R = Me)
3.22m (R = H) **3.23m** (R = H) 1 : 0.25 **3.24m** (R = H)

Scheme 3.13. Intramolecular cycloaddition with α,β-usaturated aldehyde dipolarophiles.

Single cycloadduct stereoisomers **3.23** were observed in all cases when starting with geometrically pure alkenes **3.22**. The stereochemistry of the cycloadducts was assigned on the basis that stereospecificity in this type of (intramolecular) cycloaddition with simple alkenes has been previously established (Scheme 3.14).[34] Epimers of the cycloadduct were obtained starting from the *cis* and *trans*-olefins.

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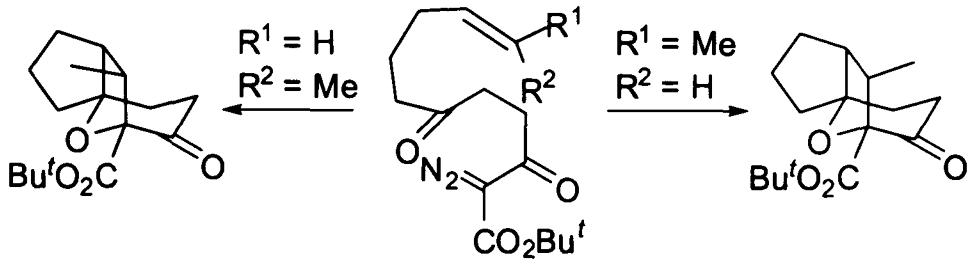
[35] D. M. Hodgson, R. Glen, G. H. Grant, A. J. Redgrave, *J. Org. Chem.* **2003**, *68*, 581–586.



Scheme 3.14. Stereospecificity in intramolecular cycloadditions.[34]

It was interesting to observe that the use of more polarised alkenes in the above studies did not lead to a loss of stereospecificity (e.g. by encroachment of a stepwise reaction process). Thus, these results expand the range of substituted alkene dipolarophiles that can be used in intramolecular cycloaddition chemistry.

3.4. One-Pot Cross-Metathesis/ Intramolecular Carbonyl Ylide Cycloaddition

In order to study the compatability of Rh(II) catalyst in presence of spent Ru catalyst (following metathesis) and hence see if the latter would affect the subsequent Rh-catalysed transformation,[36] the one-pot cross-metathesis/intramolecular carbonyl ylide cycloaddition cascade reaction was examined (Scheme 3.15). The one-pot cross-metathesis/carbonyl ylide cycloadditions were carried out using catalyst **1.50** (5 mol%) in CH_2Cl_2 at reflux for 14–18 h, followed by addition of $Rh_2(OAc)_4$ (2 mol%) after cooling to room temperature. The sequential process proceeded smoothly to yield the desired cycloadducts **3.23** in good to excellent yields, compared to the yields over 2-steps (Table 3.4). The one-pot protocol with vinylcyclohexane gave the cycloadduct **3.23a** in 63% yield, compared to 61% yield in 2-steps (entry 1). Again, no cycloadduct was observed for the dipolarophile bearing *tert*-butyl group (entry 2). Styrene and substituted styrenes were efficient in the one-pot procedure giving the cycloadducts in higher yields compared to the two-step procedure (entries 3, 4, 7–10). 4-Methoxystyrene, gave only 43% of the desired cycloadduct in one-pot (entry 5). The modest yield was evidently due to poor cross-metathesis (*c.f.* Table 3.2, entry 5, pp. 57).

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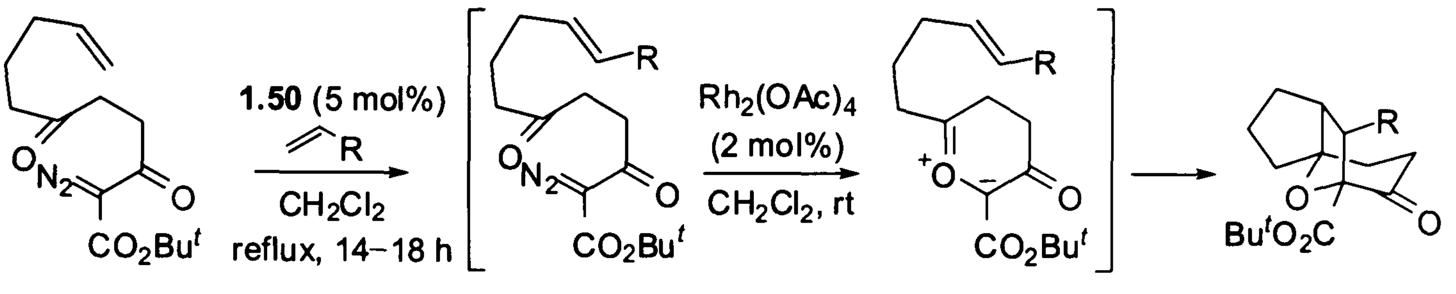
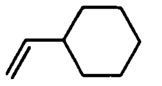
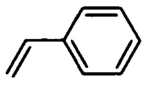
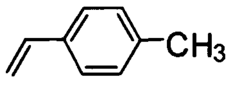
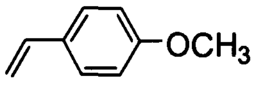
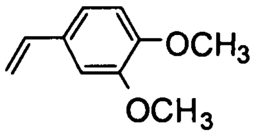
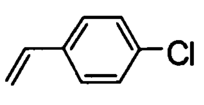
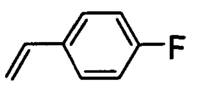
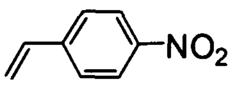
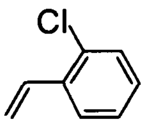
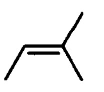
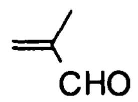
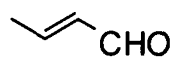
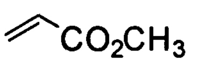
[36] For other one-pot processes involving alkene cross-metathesis, see: a) S. D. Goldberg, R. H. Grubbs, *Angew. Chem. Int. Ed.* **2002**, *41*, 807–810; b) B. M. Trost, J. L. Gunzner, O. Dirat, Y. H. Rhee, *J. Am. Chem. Soc.* **2002**, *124*, 10396–10415; c) J. Cossy, F. Bargiggia, S. BouzBouz, *Org. Lett.* **2003**, *5*, 459–462.



3.14 **3.22** **3.23**

Scheme 3.15. One-pot cross metathesis-carbonyl ylide cycloaddition.

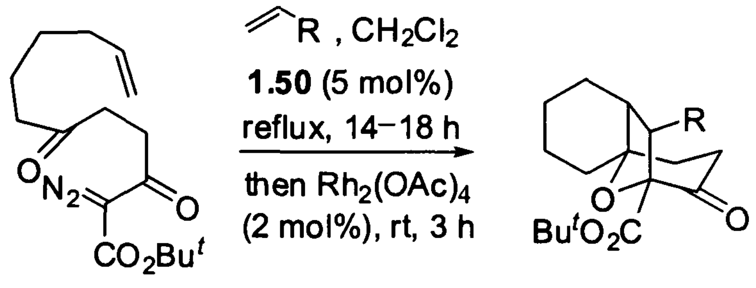
Entry	Olefin	Yield one-pot (%)	Yield over 2-steps (%)
1		63 (**3.23a**)	61
2		–[a]	–
3		73 (**3.23c**)	68
4		77 (**3.23d**)	59
5		43 (**3.23e**)	46
6		–[b]	–
7		68 (**3.23g**)	62
8		75 (**3.23h**)	67
9		76 (**3.23i**)	79
10		80 (**3.23j**)	69
11		79 (**3.23k**)	57
12		86[c] (**3.23l**)	64
13		70[d] (**3.23m**)	65
14		69 (**3.23n**)	66

a) No cycloadduct obtained; b) Not carried out; c) Isolated as 1:1 mixture of **3.23l** with hydrate **3.24l**; d) Isolated as 1:0.25 mixture of **3.23m** with hydrate **3.23m**.

Table 3.4. One-pot cross metathesis-carbonyl ylide cycloaddition.

Trisubstituted dipolarophiles underwent very efficient one-pot conversions to give the cycloadducts in very good yields (entries 11, 12). One-pot reactions of α,β-unsaturated carbonyl compounds also yielded the desired cycloadducts **3.23** in good to excellent yield (entries 12–14). Interestingly, no competing intermolecular 1,3-dipolar cycloaddition was observed with the excess of unreacted α,β-unsaturated carbonyl compounds present from the cross-metathesis reaction. With pleasing results from electron deficient olefins we tried a one-pot cross-metathesis/ cycloaddition with phenyl vinyl sulfone and were surprised that no cycloadduct was obtained. As cross-metathesis with vinyl sulphones is known[37,38] it is unclear if the interaction of the sulfone group with the rhodium catalyst interfered with the cycloaddition step.

One-pot protocol for the carbonyl ylide precursor containing a tethered hexenyl dipolarophile **3.25**[34] was also examined (Scheme 3.16). Cycloadducts **3.26** were obtained in satisfactory yields (Table 3.5) although the yields were lower compared to those obtained for carbonyl ylide precursors containing tethered pentenyl dipolarophiles **3.14** (*c.f.* Table 3.4, entries 1, 3 and 14, pp. 62).



3.25 **3.26**

Scheme 3.16. One-pot cross metathesis-cycloaddition for α-diazo-β-ketoester **3.25**.

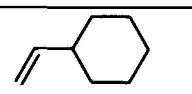
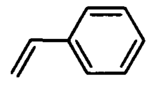
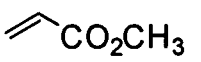
Entry	Olefin	Yield (%)
1		50 (**3.26a**)
2		66 (**3.26b**)
3		63 (**3.26c**)

Table 3.5. One-pot cross metathesis-cycloaddition for α-diazo-β-ketoester **3.25**.

Results from Padwa[14] and our group,[34] have established that there is an effect of tether length on the cycloaddition with α-diazo-β-ketone variant of **3.14** (i.e. CO_2Bu^t = H) reacting slowly, as the dipole in this case has been shown to trap intermolecularly if the reaction was carried out in the presence of DMAD (*c.f.* pp. 51). My results are thus in accordance with these above observations. Since hexenyl-tethered substrates possess slower rates of cycloaddition than the corresponding

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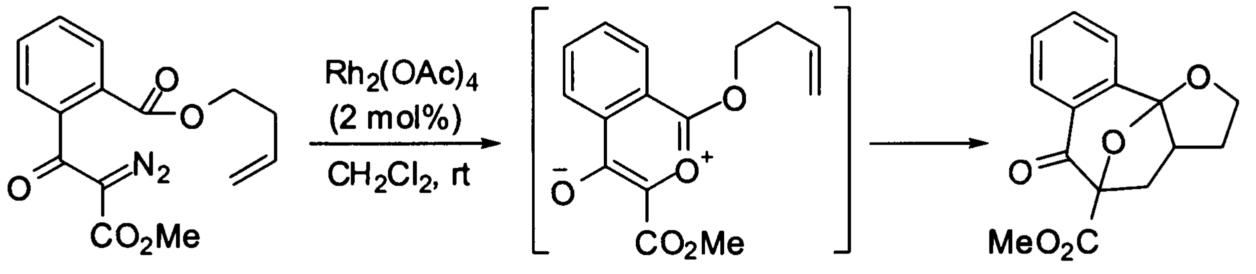
[37] K. Grela, M. Bieniek, *Tetrahedron Lett.* **2001**, *42*, 6425–6428.

[38] A. Michrowska, M. Bieniek, M. Kim, R. Klajn, K. Grela, *Tetrahedron* **2003**, *59*, 4525–4531.

pentenyl systems, it was interesting that no intermolecular trapping by excess methyl acrylate or fumarate (present from the cross-metathesis step) was observed in the one-pot synthesis of cycloadduct **3.26c**.

3.5. One-Pot Cross-Metathesis/ Oxidopyryliums Formation-Cycloaddition

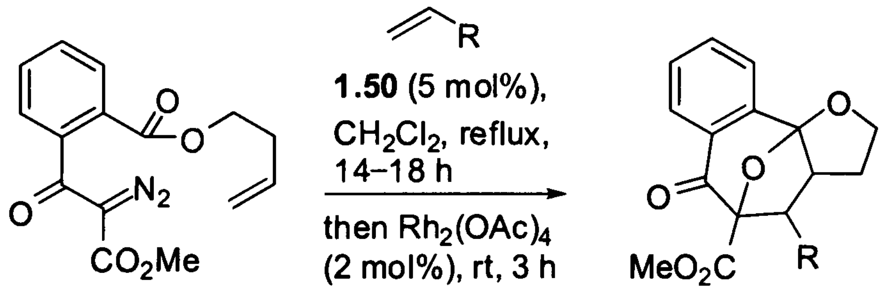
Oxidopyryliums (aromatic carbonyl ylides), derived from a carbenoid and an ester functionality are also known to undergo 1,3-dipolar cycloaddition to give tricyclic cycloadducts (Scheme 3.17).[39,40,41]



3.27 **3.28**

Scheme 3.17. Oxidopyrylium formation-cycloaddition.

I examined the one-pot cross-metathesis/ oxidopyrylium formation-cycloaddition chemistry with α-diazo-β-ketoester **3.27**,[42] and some olefins, to study the compatibility of Rh catalysed cycloaddition of ylide derived from an ester and a carbenoid, with the spent Ru catalyst present from cross-metathesis (Scheme 3.18, Table 3.6).



3.27 **3.29**

Scheme 3.18. One-pot cross-metathesis/ oxidopyrylium formation-cycloaddition.

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[39] A. Padwa, S. P. Carter, H. Nimmesgern, P. D. Stull, *J. Am. Chem. Soc.* **1988**, *110*, 2894–2900.

[40] H. Suga, K. Inoue, S. Inoue, A. Kakehi, *J. Am. Chem. Soc.* **2002**, *124*, 14836–14837.

[41] S. Kitagaki, M. Yasugahira, M. Anada, M. Nakajima, S. Hashimoto, *Tetrahedron Lett.* **2000**, *41*, 5931-5935.

[42] D. M. Hodgson, P. A. Stupple, C. Johnstone, *Arkivoc* **2003**, *7*, 49–58.

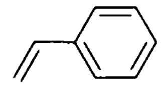
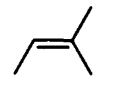
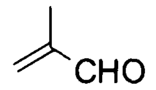
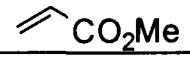
Entry	Olefin	Yield (%)
1		86 (**3.29a**)
2		83 (**3.29b**)
3		54 (**3.29c**)
4		68 (**3.29d**)

Table 3.6. One-pot cross metathesis oxidopyrylium formation-cycloaddition.

Pleasingly, the cascade reaction worked efficiently to give the tricyclic cycloadducts **3.29a-d** in good to excellent yields. Cross-metathesis with styrene generated the disubstituted cycloaddition precursor which subsequently gave the cycloadduct **3.29a** in 86% yield in one-pot (Table 3.6, entry 1). Amylene also worked well to give 83% of the desired cycloadduct **3.29b** (entry 2). α,β-Unsaturated carbonyls gave the cycloadducts **3.29** in moderate yield (entries 3 and 4). Traces of the cycloadduct (<1%) originating from the *cis*-olefin (from cross-metathesis) were also observed for styrene and ester substituted dipolarophiles. The oxidopyrylium formation-cycloaddition cascade was observed to be stereospecific; the *trans* arrangement of the olefin (from cross-metathesis) was preserved in the cycloadducts, as confirmed by NOE studies (see pp. 142–145).

3.6. Conclusions

In summary, above studies demonstrates that Grubbs' 2nd generation ruthenium carbene complex allows stereoselective cross-metathesis in the presence of diazo functionality (when the latter is flanked by two carbonyl groups). The spent ruthenium catalyst allows added $Rh_2(OAc)_4$ to catalyse carbonyl ylide cycloadditions, thus establishing the compatibility of these two late transition metal complexes sequentially catalysing different carbene transfer reactions. This demonstrates the viability of directly coupling two powerful transition metal-catalysed carbene transfer reactions in a one-flask operation for the rapid assembly of complex oxapolycycles.

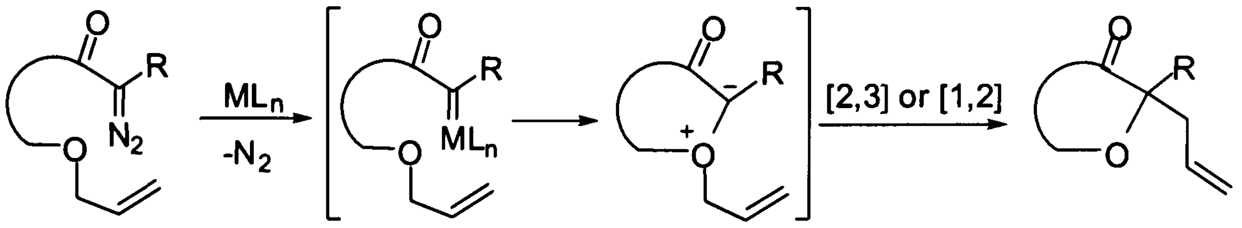
CHAPTER 4

INTRAMOLECULAR OXONIUM YLIDE REARRANGEMENTS

INTRAMOLECULAR OXONIUM YLIDE REARRANGEMENTS

4.1. Background

Oxonium ylides **4.03** can be generated by interaction between a metal carbenoid **4.02**, (usually derived from α-diazocarbonyl compounds) and a lone pair of electrons on an ethereal oxygen atom.[1] For tethered allylic systems, the ylide subsequently undergoes rearrangement to construct cyclic ethers or carbocycles (Scheme 4.1). The synthetic utility of sigmatropic rearrangements of oxonium ylides have been demonstrated in the synthesis of natural products.[2,3,4,5,6,7]



4.01 **4.02** **4.03** **4.04**

R = H, CO_2R', R' = alkyl group

Scheme 4.1. Intramolecular oxonium ylide formation-rearrangement.

Pirrung and Werner first reported rhodium(II) acetate catalysed intramolecular oxonium ylide generation and subsequent [2,3]-sigmatropic rearrangement (Scheme 4.2).[8] Roskamp and Johnson also independently reported the formation of reduced furanones by intramolecular oxonium ylide formation and subsequent [2,3]-sigmatropic rearrangement.[9]

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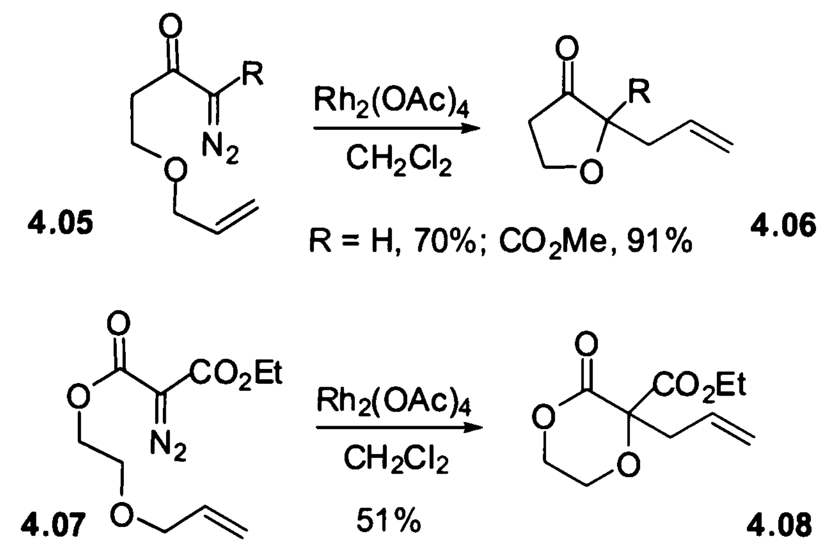
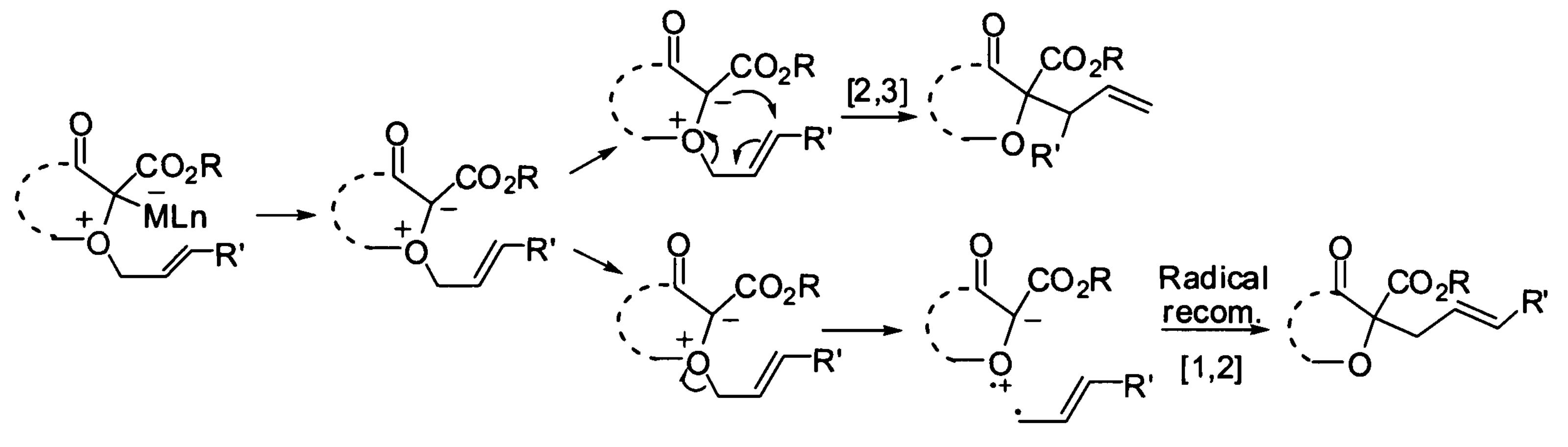
[1] J. S. Clark, *Nitrogen, Oxygen and Sulfur Ylide Chemistry*, Oxford University Press, Oxford, **2002**.
[2] M. C. Pirrung, W. L. Brown, S. Rege, P. Laughton, *J. Am. Chem. Soc.* **1991**, *113*, 8561–8562.
[3] J. S. Clark, G. A. Whitlock, *Tetrahedron Lett.* **1994**, *35*, 6381–6382.
[4] J. S. Clark, A. G. Dossetter, W. G. Whittingham, *Tetrahedron Lett.* **1996**, *37*, 5605–5608.
[5] J. S. Clark, T. C. Fessard, C. Wilson, *Org. Lett.* **2004**, *6*, 1773–1776.
[6] J. S. Clark, T. C. Fessard, G. A. Whitlock, *Tetrahedron* **2006**, *3762*, 73–78.
[7] J. S. Clark, S. T. Hayes, C. Wilson, L. Gobbi, *Angew. Chem. Int. Ed.* **2007**, *46*, 437–440.
[8] M. C. Pirrung, J. A. Werner, *J. Am. Chem.* Soc. **1986**, *108*, 6060–6062.
[9] E. J. Roskamp, C. R. Johnson, *J. Am. Chem.* Soc. **1986**, *108*, 6062–6063.



Scheme 4.2. Intramolecular Oxonium ylide formation-rearrangement.

The oxonium ylide intermediates can undergo [2,3] or [1,2]-sigmatropic rearrangement along with other competing reaction pathways (such as insertion, cyclopropanation and dimerisation).[10,11,12,13] The [2,3]-rearrangement is an energetically favourable pathway, proceeding *via* a pericyclic mechanism, whereas the [1,2]-rearrangement, proceeding *via* a radical dissociation-recombination, is less favoured (Scheme 4.3).[14,15,16]



Scheme 4.3. [2,3] *vs* [1,2]-Rearrangements of oxonium ylides.

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[10] N. McCarthy, M. A. McKervey, T. Ye, M. McCann, E. Murphy, M. P. Doyle, *Tetrahedron Lett.* **1992**, *33*, 5983–5986.

[11] J. S. Clark, S. A. Krowiak, *Tetrahedron Lett.* **1993**, *34*, 4385–4388.

[12] J. S. Clark, C. A. Baxter, J. L. Castro, *Synthesis* **2005**, *19*, 3398–3404.

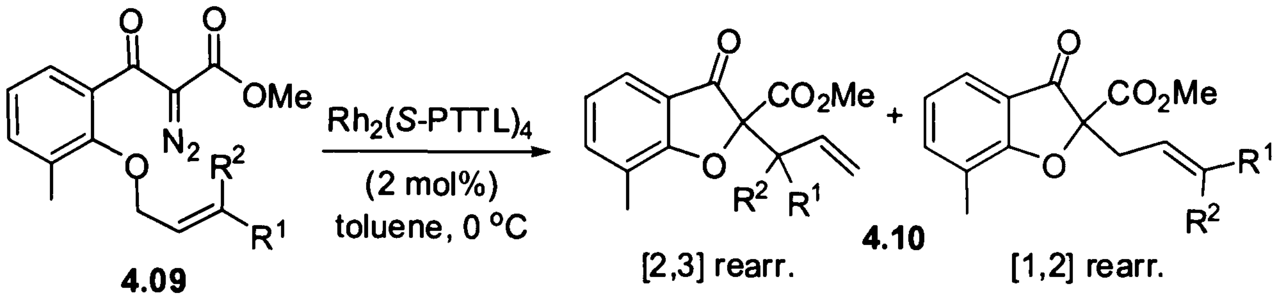
[13] S. Kitagaki, Y. Yanamoto, H. Tsutsui, M. Anada, M. Nakajima, S. Hashimoto, *Tetrahedron Lett.* **2001**, *42*, 6361–6364.

[14] W. Ando, T. Yagihara, S. Kondo, K. Nakayama, H. Yamato, S. Nakaido, T. Migita, *J. Org. Chem.* **1971**, *36*, 1732–1736.

[15] W. Ando, S. Kondo, K. Nakayama, K. Ichibori, H. Kohoda, H. Yamato, I. Imai, S. Nakaido, T. Migita, *J. Am. Chem. Soc.* **1972**, *94*, 3870–3876.

[16] T. H. Eberlein, F. G. West, R. W. Tester, *J. Org. Chem.* **1992**, *57*, 3479–3482.

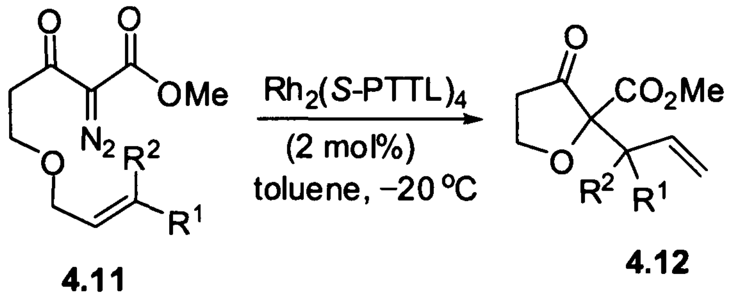
Hashimoto has shown that with an aromatic linked olefin tether, the putative oxonium ylide intermediate undergoes both [2,3] and [1,2]-rearrangements; the former being the major pathway, although with poor diastereoselectivity (Scheme 4.4).[13]



R^1	R^2	Yield (%)	dr	[2,3]:[1,2]
Me	H	63	60:40	92:8
H	Me	63	49:51	82:18
Me	Me	37	-	71:29

Scheme 4.4. Oxonium ylide rearrangement of aromatic diazoketoester **4.09**.

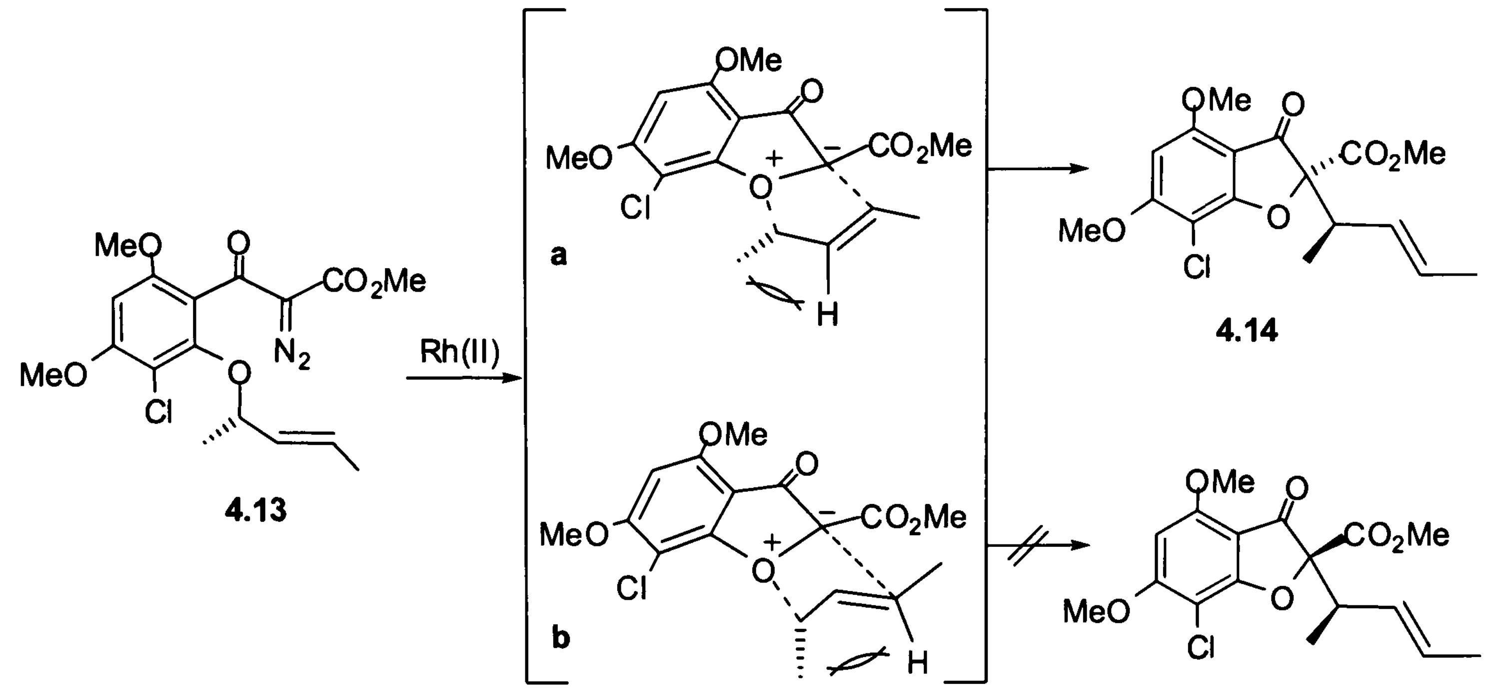
Hashimoto also demonstrated that aliphatic substrates display a complete preference for [2,3]-rearrangement (Scheme 4.5). This could be due to the absence of aromatic stabilisation of an oxonium radical (by the benzofused system, as in the previous case), which could have assisted radical formation, (*c.f.* Scheme 4.3, pp. 70) leading to the [1,2]-rearranged product.



R^1	R^2	Yield (%)	dr
Me	H	79	96:4
Me	Me	73	-

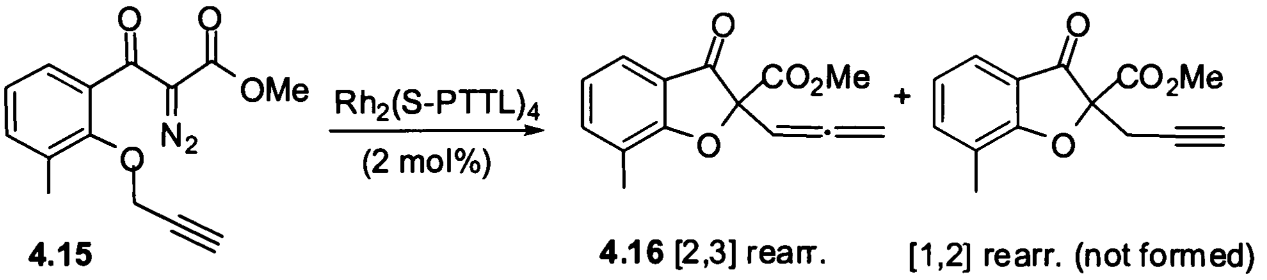
Scheme 4.5. Oxonium ylide rearrangement in non-aromatic substrate.

In contrast, in the total synthesis of (+)-griseofulvin by Pirrung and co-workers, where the key step involves the oxonium ylide formation-rearrangement on a benzofused system, the transformation was observed to be completely diastereoselective. Although, the original chiral centre was lost during the transformation, but efficient chirality transfer *via* highly stereoselective [2,3]-sigmatropic rearrangement was observed. (Scheme 4.6).[2] Although no explanation was offered to explain the complete selectivity, in this particular case it may be due to the presence of methyl group in an allylic position in a fixed geometry. If we consider that the product solely arises from pericyclic rearrangement, the complete diastereoselectivity could be explained on the basis of a transition state model, involving a five membered ring. In theory, two diastereomers can be accessed *via* two different transition states (TS), ***a*** and ***b***. However, due to 1,3-allylic strain, TS ***b*** may not be favoured, and so the reaction proceeds *via* TS ***a***, with less severe 1,2-allylic strain, giving rise to the single diastereomer observed.



Scheme 4.6. Oxonium ylide rearrangement in (+)-griseofulvin synthesis.

Complete selectivity for [2,3]- over [1,2]-rearrangement has also been observed with α-diazoketones.[8,9,17] Also, tethered propargylic ethers have been shown to have a strong preference for [2,3]- over [1,2]-rearrangement, as demonstrated by Hashimoto *et al.* (Scheme 4.7).[18]



Scheme 4.7. Oxonium ylide rearrangement of propargylic ethers.

In my studies below, I describe the olefin dependent selectivity for two different oxonium ylide rearrangements and the diastereoselectivity of the process during the one-pot cross-metathesis (to functionalise the olefin tether)/ tandem oxonium ylide formation-rearrangement.

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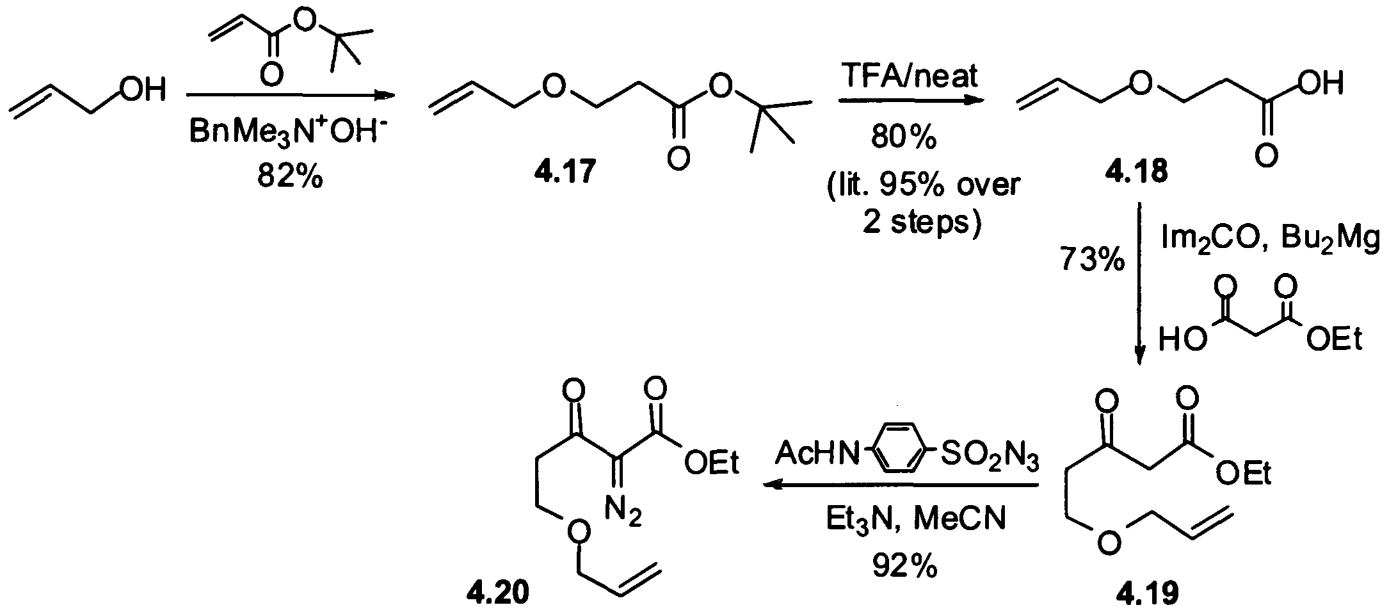
[17] J. S. Clark, M. Fretwell, G. A. Whitlock, C. J. Burns, D. N. A. Fox, *Tetrahedron Lett.* **1998**, *39*, 97–100.

[18] H. Tsutsui, M. Matsuura, K. Makino, S. Nakamura, M. Nakajima, S. Kitgaki, S. Hashimoto, *Isr. J. Chem.* **2001**, *41*, 283–295.

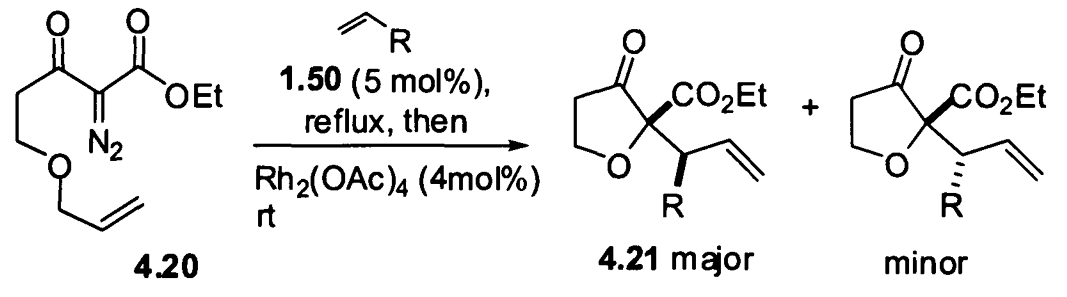
4.2. One-Pot Cross-Metathesis/ Oxonium Ylide Formation-Rearrangement

One-pot cross-metathesis/ oxonium ylide formation and subsequent rearrangement with diazoketoester **4.20**[13,19,20] was first examined. The substrate **4.20** was prepared following the lit. procedure (Scheme 4.8). Michael addition of allyl alcohol to *tert*-butyl acrylate gave the 1,4-adduct **4.17** in 82% yield, which was subsequently hydrolysed by neat TFA at reflux to give the corresponding carboxylic acid **4.18**[21], in 80% yield. *C*-Acylation of *mono*-ethyl malonate with carboxylic acid **4.18** following Masamune's method[22,23] gave the ketoester **4.19** in 73% yield. Finally, diazo transfer with *p*-acetamidobenzenesulfonyl azide[24] gave the desired α-diazo-β-ketoester **4.20**, in 92% yield.



Scheme 4.8. Synthesis of α-diazo-β-ketoester **4.20**.

With α-diazo-β-ketoester **4.20** in hand one-pot cross-metathesis/ oxonium ylide formation-rearrangement to generate dihydrofuranones **4.21** was examined (Scheme 4.9, Table 4.1).



Scheme 4.9. One-pot cross-metathesis/ oxonium ylide rearrangement of **4.20**.

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[19] N. McCarthy, M. A. McKervey, T. Ye, M. McCann, E. Murphy, M. P. Doyle, *Tetrahedron Lett.* **1992**, *33*, 5983–5986.

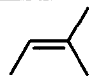
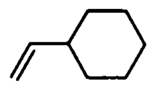
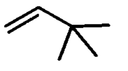
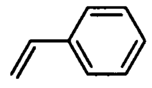
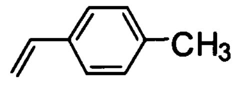
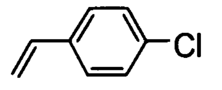
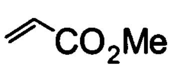
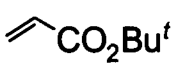
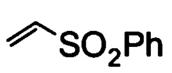
[20] N. Pierson, C. F. García, M. A. McKervey, *Tetrahedron Lett.* **1997**, *38*, 4705–4708.

[21] B. Simonot, G. Rousseau, *Synth. Commun.* **1993**, *23*, 549–560.

[22] D. W. Brooks, L. D. L. Lu, S. Masamune, *Angew. Chem. Int. Ed.* **1979**, *18*, 72–74.

[23] M. Ghosh, M. J. Miller, *Tetrahedron* **1996**, *52*, 4225–4238.

[24] Y.-H. Lim, K. F. McGee, S. McN. Sieburth, *J. Org. Chem.* **2002**, *67*, 6535–6538.

Entry	Olefin	Yield one-pot (%)	dr[a]
1		87 (**4.21a**)	-
2		79 (**4.21b**)	90:10
3		49 (**4.21c**)	94:6
4		66 (**4.21d**)	94:6
5		63 (**4.21e**)	98:2[b]
6		51 (**4.21f**)	93:7
7		81 (**4.21g**)	>99:1
8		82 (**4.21h**)	98:2
9		86 (**4.21i**)	84:16
10		18% of CM[c]	-
11		22% of CM[c]	-

a) Determined by ^{1}H NMR; b) Determined by GC-MS; c) Determined by crude ^{1}H-NMR.

Table 4.1. One-pot cross-metathesis/ oxonuim ylide rearrangement of **4.20**.

The one-pot cross-metathesis/ oxonium ylide formation-rearrangement was carried out using Grubbs' 2nd generation catalyst, **1.50** (5 mol%) with α-diazo-β-ketoester **4.20** and metathesis partner (5–10 equiv.) in CH_2Cl_2 at reflux for 14–20 h, followed by addition of $Rh_2(OAc)_4$ (4 mol%) at room temperature and the reaction left until completion (~12–14 h). As expected, in all cases [2,3]-sigmatropic rearrangement was the predominant pathway and only traces (<1%) of the [1,2]-rearrangement product were seen. This is also in accordance with the explanation above (pp. 71): as there is no aromatic ring to stabilise the O-radical cation, the energetically less favourable [1,2]-Stevens rearrangement is suppressed. Vinylcyclohexane worked quite efficiently in one-pot to give the dihydrofuranone in good yield (entry 2) and with high diastereoselectivity (90:10). With sterically hindered 3,3-dimethyl-1-butene, dihydrofuranone was obtained in modest (49%) yield, but with slightly higher diastereoselectivity (94:6) (entry 3), and no change in dr (93.5:6.5, with 54% isolated yield) was observed when the Rh catalysed step was carried out at reflux. Styrene and substituted styrenes gave dihydrofuranones in modest yields (51–66%), but with increased diastereoselectivities (entries 4–6). The modest yield for these examples in the one-pot procedure could be due to poor cross-metathesis of these olefins with α-diazo-β-ketoester **4.20** (see pp. 80). Ester functionality was then introduced by cross-metathesis, to study its effect on diastereoselectivity. Esters showed excellent diastereoselectivity and very good yields, during the process. No effect of sterics of the ester was observed, as a methyl ester gave >99:1 dr (entry 7) and a *tert*-butyl ester gave 98:2 dr (entry 8). With excellent diastereocontrol by ester groups it was speculated that this may be the case with other electron deficient olefins. So, other electron deficient α,β-unsaturated substrates were studied (entries 9–11). The reaction with methyl vinyl ketone gave the corresponding dihydrofuranone in 86% yield (entry 9), but with a comparatively poor dr (84:16) which, over time reduced to 54:46, and each diastereomer was found to exist in keto-enol forms ($d_{1(major)}$ 2:1 and $d_{2(minor)}$ 3:1). The change in dr of the product with time could be due to epimerisation *via* keto-enol tautomerisation. I then examined *N*,*N*-dimethylacrylamide and phenyl vinyl sulfone; however, these olefins were found to be sluggish towards cross-metathesis with α-diazo-β-ketoester **4.20**, and cross-metathesis proceeded only in 18% and 22% yields respectively (entries 10 and 11). So, these olefins were not studied in the one-pot methodology.

The relative stereochemistry of the major diastereomer **4.21** was supported by X-ray crystallography of dihydrofuranone **4.21f** (Figure 4.1), and the rest of the dihydrofuranone products were assigned by analogy. The dihydrofuranones **4.21** were obtained as mixtures of chromatographically inseparable diastereomers and diastereoselectivities were determined by ^{1}H-NMR or by GC-MS of the isolated products.

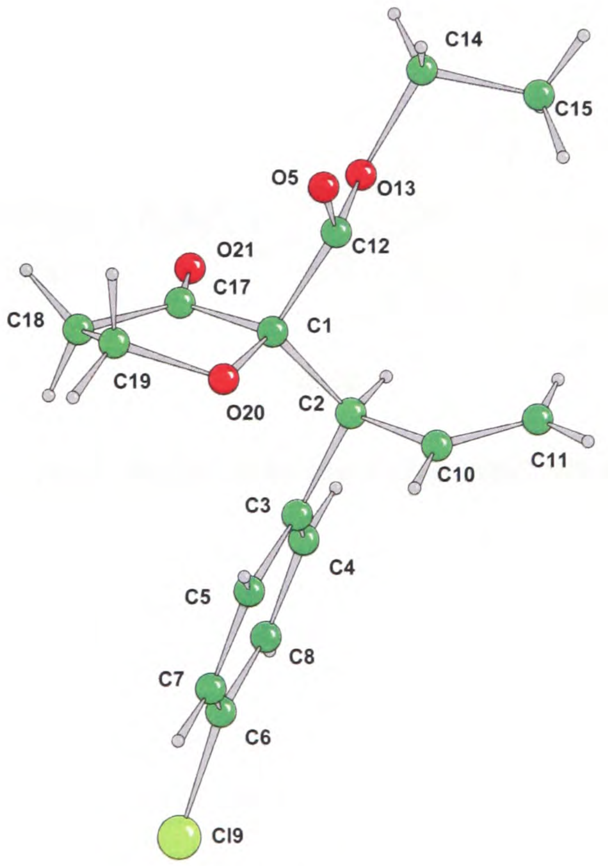
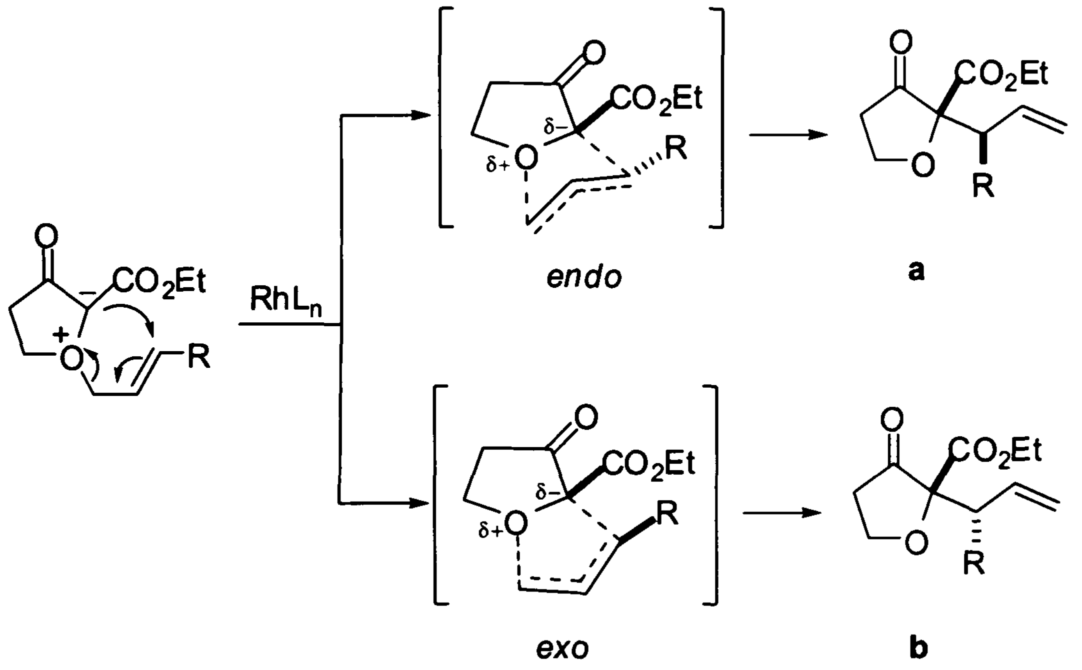


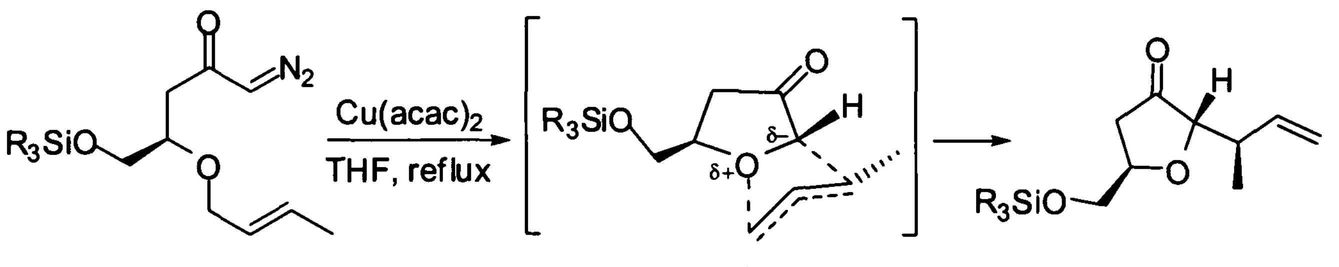
Figure 4.1. X-Ray crystal structure of dihydrofuranone **4.21f**.

[2,3]-Sigmatropic rearrangement of the putative oxonium ylide intermediate in the above chemistry can proceed through *exo* or *endo* transition states (TS). If rearrangement proceeds through an *endo*-TS, **a** will be obtained, however, if the rearrangement proceeds through an *exo*-TS, diastereomer **b** will be formed (Scheme 4.10).



Scheme 4.10. Oxonium ylide rearrangement *via exo*/*endo* TS.

The crystal structure obtained above suggests that the ylide rearrangement proceeds preferentially *via* an *endo*-TS. This is in accordance with results obtained by Clark (for oxonium ylide rearrangements of α-diazoketones **4.22**), who found ylide rearrangement proceeding *via* an *endo*-TS (Scheme 4.11).[5]

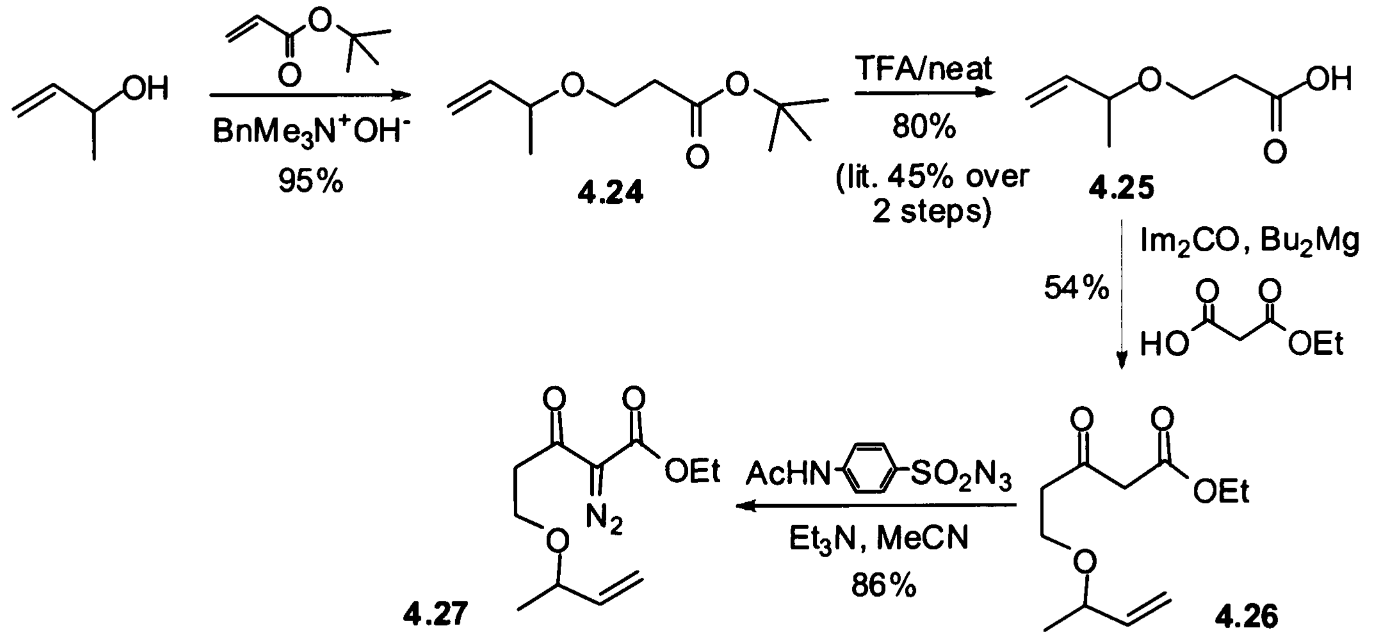


4.22 **4.23** (88%, dr >92:8)

Scheme 4.11. An oxonium ylide rearrangement *via* an *endo* TS.[5]

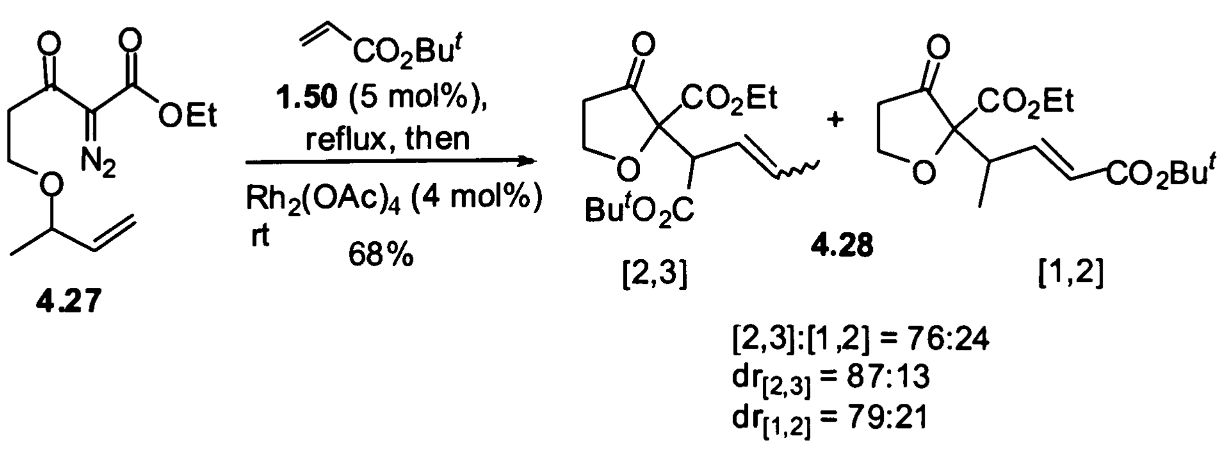
4.3. Effect of α-Methyl in the Rearrangement

In the total synthesis of (+)-griseofulvin by Pirrung *et al.*, the key step involving oxonium ylide formation/ [2,3]-rearrangement was observed to be completely diastereoselective, giving only a single isomer (Scheme 4.6, pp. 72).[2] The origin of the complete selectivity in the ylide rearrangement has not been explained. I was intrigued about studying the effect an α-methyl group would have on a non aromatic α-diazo-β-ketoester **4.20**. In order to investigate this, α-diazo-β-ketoester **4.27** was prepared following the procedure described above for the synthesis of α-diazo-β-ketoester **4.20** (*c.f.* Scheme 4.8, pp. 73), but using 3-buten-2-ol (Scheme 4.12).



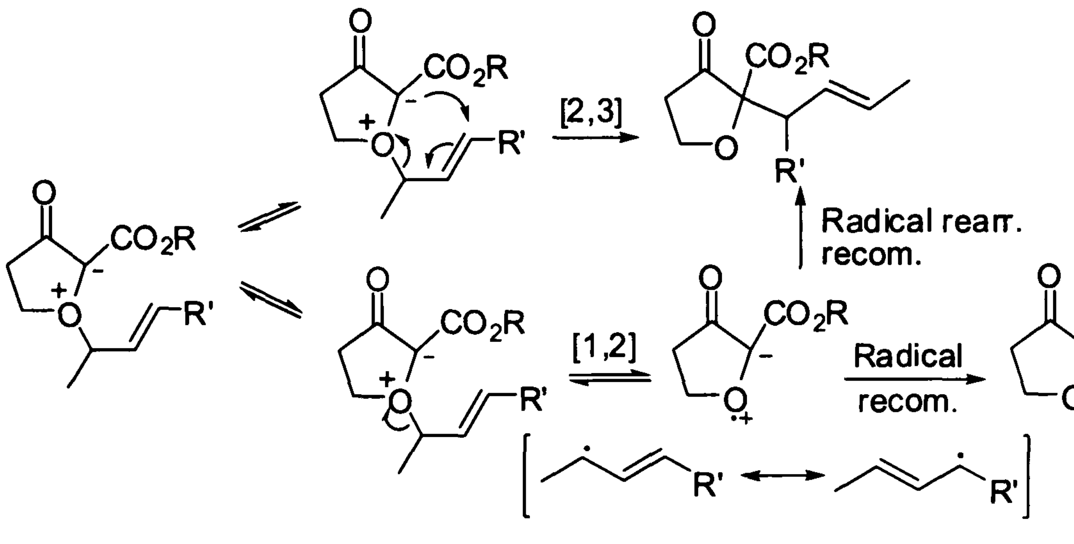
Scheme 4.12. Synthesis of α-diazo-β-ketoester **4.27**.

With the oxonium ylide precursor **4.27** in hand, one-pot cross-metathesis/ oxonium ylide rearrangement was examined, with *tert*-butyl acrylate (as esters gave the highest diastereoselectvity for α-diazo-β-ketoester **4.20**, (*c.f.* Table 4.1, pp. 74) (Scheme 4.13).



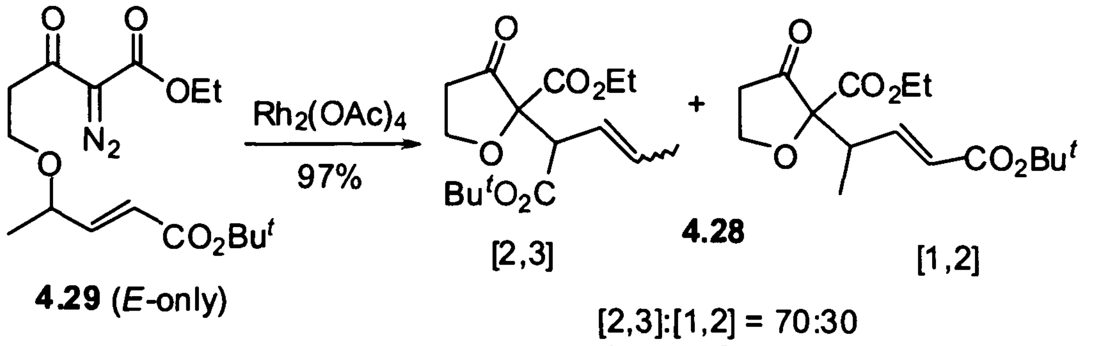
Scheme 4.13. One-pot cross-metathesis/ oxonium ylide rearrangement.

Surprisingly, the one-pot protocol gave the dihydrofuranone **4.28** in modest yield (68%), and as a mixture of isomers. The [2,3]:[1,2]-rearrangement products were formed in a ratio of 76:24, each as a mixture of diastereomers ($dr_{[2,3]}$ = 87:13 and $dr_{[1,2]}$ = 79:21). Formation of [1,2]-rearrangement products with this α-diazo-β-ketoester **4.27** suggests that the radical pathway is not completely shut down (as in the previous case, *c.f.* Scheme 4.3, pp. 70), possibly due to formation of a secondary allylic radical, which can either undergo recombination at the site of initial radical generation, to give the [1,2]-product, or recombine to give the 'formal' [2,3]-rearrangement product (Scheme 4.14). This explains the unexpected increase in the proportion of [1,2]-rearrangement product and the drop in diastereoselectivity during the process.



Scheme 4.14. Rearrangement *via* secondary allylic radical.

When geometrically pure *E*-olefin **4.29** (obtained by cross-metathesis of **4.27** with *tert*-butyl acrylate) was subjected to $Rh_2(OAc)_4$ catalysed oxonium ylide formation-rearrangement (Scheme 4.15), the product was obtained as an inseparable mixture of isomers in similar ratios to that obtained in from the one-pot operation (cross-metathesis/ oxonium ylide rearrangement) (*c.f.* Scheme 4.13, pp. 78). This indicates that the poor dr from the oxonium ylide is not due to poor stereoselectivity in the cross-metathesis reaction.



4.29 (*E*-only)

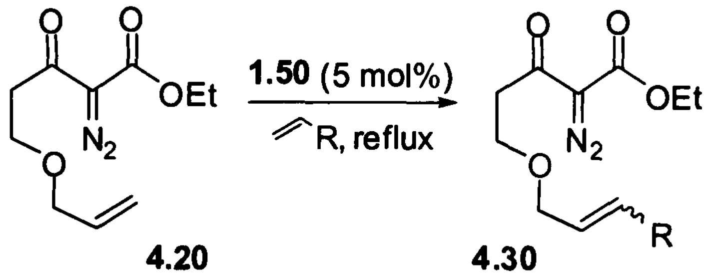
4.28

[2,3]:[1,2] = 70:30
$dr_{[2,3]}$ = 87:13
$dr_{[1,2]}$ = 78:22

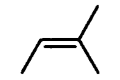
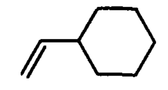
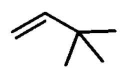
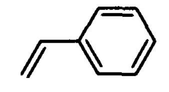
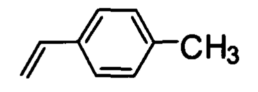
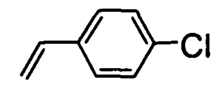
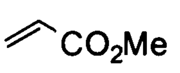
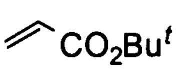
Scheme 4.15. Oxonium ylide formation-rearrangement of olefin **4.29**.

4.4. Cross-Metathesis of α-Diazo-β-ketoester 4.20

In order to study the origin of the diastereoselectivity during the ylide rearrangement, I examined the cross-metathesis of α-diazo-β-ketoester **4.20** (bearing a tethered allyl ether) with various olefins (4–10 equiv.), using catalyst **1.50** (5 mol%) in CH_2Cl_2 at reflux for 14–18 h. The substituted alkenes **4.30** were obtained in moderate to excellent yields and generally with high stereoselectivity (Scheme 4.16, Table 4.2).



Scheme 4.16. Cross-metathesis of α-diazo-β-ketoester **4.20**.

Entry	Olefin	Yield (%)	*E*:*Z*[a]	dr of [2,3]-rearr.[b]
1		82 (**4.30a**)	–	–
2		89 (**4.30b**)	90:10	90:10
3		50 (**4.30c**)	>99:1	94:6
4		47 (**4.30d**)	94:6	94:6
5		65 (**4.30e**)	98:2	98:2
6		54 (**4.30f**)	97:3	93:7
7		86 (**4.30g**)	95:5	>99:1
8		78 (**4.30h**)	>99:1	98:2
9		86 (**4.30i**)	98:2	84:16

a) Determined by ^{1}H-NMR; b) *c.f.* Table 4.1, pp. 74.

Table 4.2. Cross metathesis of α-diazo-β-ketoester **4.20**.

Cross-metathesis with amylene proceeded smoothly to give the trisubstituted allylic ether in excellent yield (entry 1). Vinylcyclohexane underwent efficient cross-metathesis, but the sterically hindered 3,3-dimethyl-1-butene, gave only 50% of the cross-metathesis product (entries 2 and 3), which is reflected in the poor yield during the one-pot process (*c.f.* Table 4.1, pp. 74). Styrene and substituted styrenes were found to be less efficient partners during cross metathesis with allyl ether tethered α-diazo-β-ketoester **4.20** (entries 4–6), compared to the α-diazo-β-ketoester **3.14** (precursor to tandem carbonyl ylide formation-1,3-dipolar cycloaddition, *c.f.* Table 3.2, pp. 57). However, the reaction proceeded with high stereoselectivity to give predominantly the *E*-isomer. α-β-Unsaturated carbonyl compounds were quite efficient partners and gave the disubstituted olefins with high stereoselectivity (entries 7–9).

The stereochemical assignment of the *trans*-olefins **4.30** obtained by cross-metathesis was based upon the coupling constants (typically, ^3J(H,H) = 15–16 Hz for CH=CH). The *E*:*Z* ratios were determined from ^{1}H NMR, by integration of the olefinic or the allylic protons of the major and minor isomers. The *E* and *Z* isomers in all the cases were inseparable and the isomeric mixtures were used as such in subsequent transformations. Interestingly, in most cases, the stereoselectivity during the cross-metathesis process was observed to be consistent with the diastereoselectivity observed during the ylide rearrangement, suggesting that ylide rearrangement proceeds only *via* a pericyclic pathway. However, some erosion of diastereoselectivity was observed starting from the olefins bearing *tert*-butyl and *p*-chlorophenyl groups (entries 3 and 6).

4.5. One-Pot Cross-Metathesis/ Oxonium Ylide Formation-Rearrangement of Diazoester 4.34

After examining the one-pot cross-metathesis/ oxonium ylide rearrangement, for allylic ether tethered α-diazo-β-ketoester **4.20** above, I was keen on examining the strategy for the benzofused variant **4.34**,[25] as the latter is known to undergo competitive [1,2]-Stevens rearrangement along with the [2,3]-sigmatropic rearrangement (with poor diastereoselectivity), even when starting from geometrically pure *cis* or *trans* olefins. The substrate **4.34** was prepared following a lit. procedure starting from commercially available salicylic acid (Scheme 4.17).[25] The allylation of salicylic acid with allyl bromide in presence of base gave allylated ester **4.31** quantitatively, which was hydrolysed by NaOH/ EtOH to give the corresponding carboxylic acid **4.32**[26] in 95% yield. *C*-Acylation of *mono-tert*-butyl malonate with carboxylic acid **4.32** following Masamune's method,[22,23] afforded ketoester **4.33a** in 55% yield. Diazo transfer using *p*-acetamidobenzenesulfonyl azide[24] gave the desired diazoketoester **4.34b**, in 73% yield.

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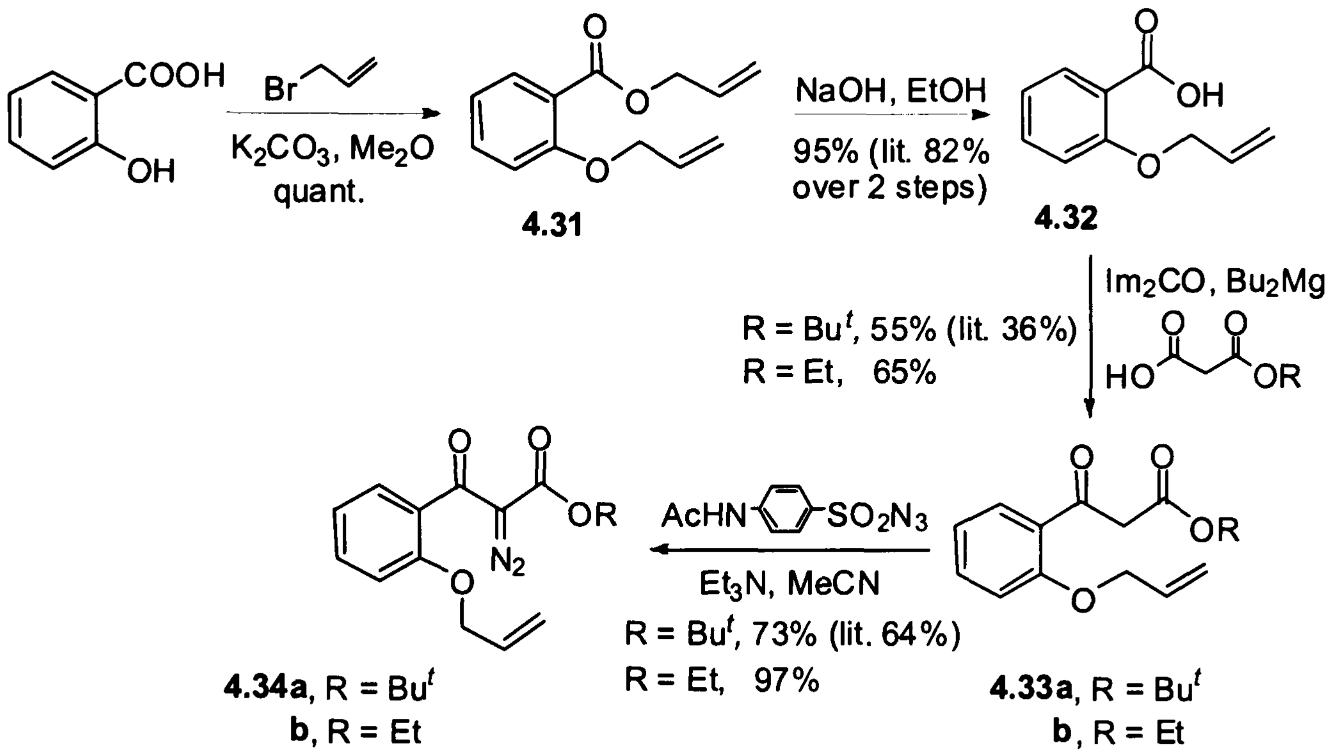
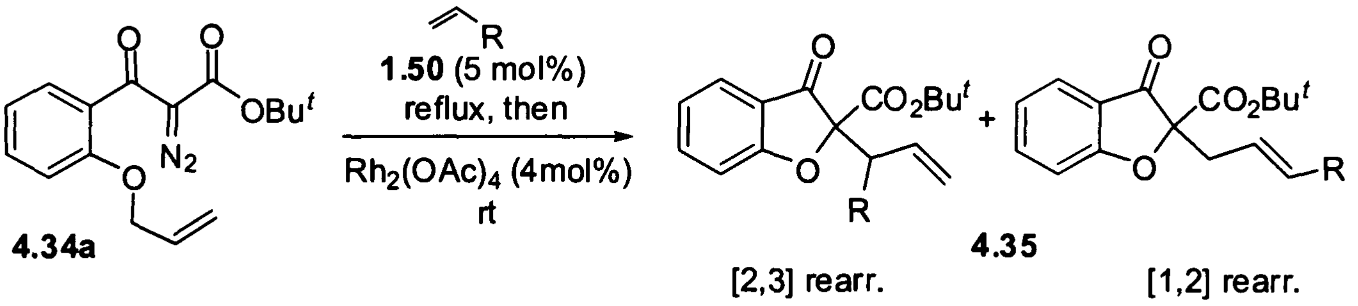
[25] D. M. Hodgson, M. Petroliagi, *Tetrahedron: Asymmetry* **2001**, *12*, 877–881.

[26] T. Ye, C. F. García, M. A. McKervey, *J. Chem. Soc., Perkin Trans. 1*, **1995**, 1373–1379.



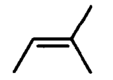
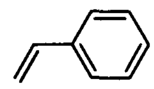
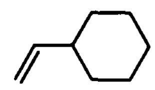
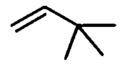
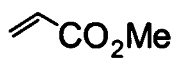
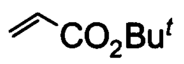
Scheme 4.17. Synthesis of α-diazo-β-ketoesters **4.34**.

With substrate **4.34a** in hand, the one-pot protocol involving cross-metathesis and oxonium ylide formation/ rearrangement was examined (Scheme 4.18, Table 4.3). The one-pot cross-metathesis/ oxonium ylide formation-rearrangement was carried out using Grubbs' 2nd generation catalyst **1.50** (5 mol%) in CH_2Cl_2 at reflux for 14–20 h, followed by addition of $Rh_2(OAc)_4$ (4 mol%) at room temperature (~12–14 h) or reflux (~6–8 h) and the reaction left until completion.



Scheme 4.18. One-pot cross metathesis-oxonium ylide rearrangement. of **4.34a**.

Amylene was first examined in the one-pot strategy. Cross-metathesis proceeded smoothly and the prenyl substituted diazoester after the ylide rearrangement gave a 75:25 mixture of [2,3]:[1,2]-rearrangement products (entry 1). Similar selectivity (79:21) was observed by Hashimoto, for a closely related substrate using chiral $Rh_2(S\text{-PTTL})_4$ catalyst in toluene at 0 °C (*c.f.* Scheme 4.4, $R^1 = R^2 =$ Me, pp. 71).[13] Styrene gave a disappointing ~1:1 mixture of [2,3] and [1,2]-rearrangement products, thus showing no selectivity towards the ylide rearrangement step, and also the dr of the [2,3] rearrangement product was ~1:1 (entry 2). Notably, the *trans*-geometry of the olefin was preserved in [1,2]-rearrangement. As mentioned earlier (pp. 71), the poor [2,3]:[1,2] rearrangement selectivity with the phenyl-substituted olefin could be due to the presence of fused aromatic ring system which could easily stabilise the O-radical cation; also, in this case, the allylic radical with tethered phenyl group could be further stabilised by radical delocalisation into the aromatic ring, hence allowing the less favourable pathway. As a result, no preference for either of the two competing rearrangements is observed (*c.f.* Scheme 4.14, pp. 78).

Entry	Olefin	Yield one-pot (%)	[2,3]:[1,2][a]	dr[a]
1		56 (**4.35a**)	75:25	–
2		72 (**4.35b**)	58:42	56:44
3	"	61[c] (**4.35b′**)	55:45	63:37
4		92 (**4.35c**)	96:4	55:45
5	"	91[b] (**4.35c**)	95:5	55:45
6	"	72[c] (**4.35c′**)	96:4	58:42
7		86 (**4.35d**)	97:3	69:31
8	 CO_2Me	79 (**4.35e**)	95:5	91:9
9	 CO_2Bu^t	83 (**4.35f**)	98:2	93:7

a) Determined by ^1H NMR; b) $Rh_2(OAc)_4$ catalysed step carried at reflux; c) $CO_2Bu^t = CO_2Et$ for **4.34**.

Table 4.3. One-pot cross metathesis-oxonium ylide rearrangement of **4.34**.

Surprisingly, introduction of alkyl groups (e.g. cyclohexyl and *tert*-butyl) on the olefin tether resulted in a very high selectivity for the [2,3]-rearrangement over the [1,2]-rearrangement >95:5 (entries 4–7). But, the diastereoselectivity of the [2,3]-rearrangement was disappointingly low, 55:45 (for cyclohexyl tether) and 69:31 (for *tert*-butyl tether). No appreciable change in the [2,3]:[1,2] or diastereoselectivity was observed when the Rh catalysed rearrangement was carried out at reflux (entry 5). I was then interested in studying if the steric demand of the *tert*-butyl ester present in substrate **4.34a** contributed to the lower diastereoselectivity. So, the ethyl ester variant **4.34b**[8,27] was prepared following the procedure described above (Scheme 4.17, pp. 81) and examined in the one-pot strategy with styrene and vinylcyclohexane (Table 4.3, entries 3 and 6). A slight (but not significant) increase in the dr was observed for both the cross-metathesis partners, but the [2,3]:[1,2]-rearrangement selectivity was found to be unaffected.

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[27] G. K. Murphy, F. G. West, *Org. Lett.* **2006**, *8*, 4359–4361.

The effect of electronics in olefin tether on the ylide rearrangement was then probed, by introducing ester groups (entries 8 and 9). Pleasingly, the introduction of the ester group, resulted in very high selectivity (>95:5) for [2,3]-rearrangement over the [1,2] (like the alkyl groups); also, a remarkable increase in diastereoselectivity was observed (91:9 and 93:7 for methyl and *tert*-butyl ester, respectively). However, no effect due to steric differences in the ester group was observed: the *tert*-butyl ester was found to be as efficient in the selectivity as the methyl ester. Thus, the ester group attached to the olefin, allows the diastereoselective synthesis of benzofuranones **4.35** by [2,3]-sigmatropic rearrangement with high selectivity.

The stereochemistry of the major diastereomer in these [2,3]-sigmatropic rearrangements was assigned by the X-ray crystallography of benzofuranone **4.35f** (Figure 4.2), the rest being assigned by analogy. The benzofuranones **4.35** were obtained as mixtures of chromatographically inseparable diastereomers and diastereoselectivities were determined by ^{1}H-NMR of the isolated products. The sense of stereoinduction is the same as observed earlier (i.e. rearrangement proceeds predominantly *via* an *endo* TS, pp. 76).

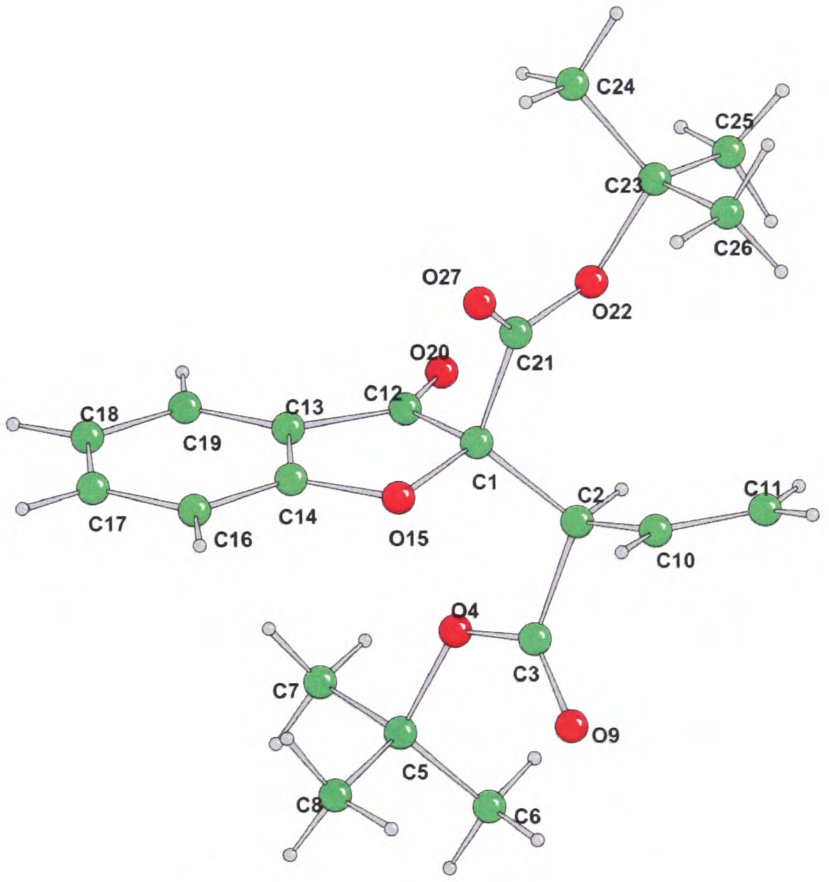
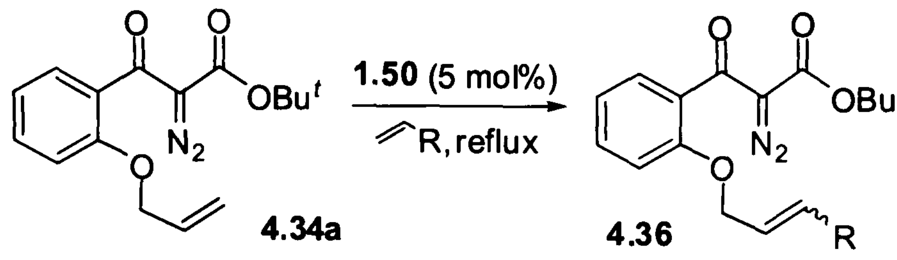


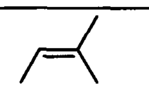
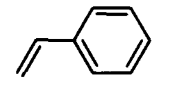
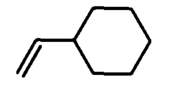
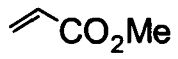
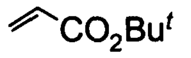
Figure 4.2. X-Ray crystal structure of benzofuranone **4.35f**.

4.6. Cross-Metathesis of α-Diazo-β-ketoester 4.34a

I further wanted to investigate if the origin of the diastereoselectivity in the rearrangement of the benzofused oxonium ylide is related to the stereoselectivity during the cross-metathesis (as in the case with non-aromatic substrate, pp. 79–80).



Scheme 4.19. Cross metathesis of α-diazo-β-ketoester **4.34a**.

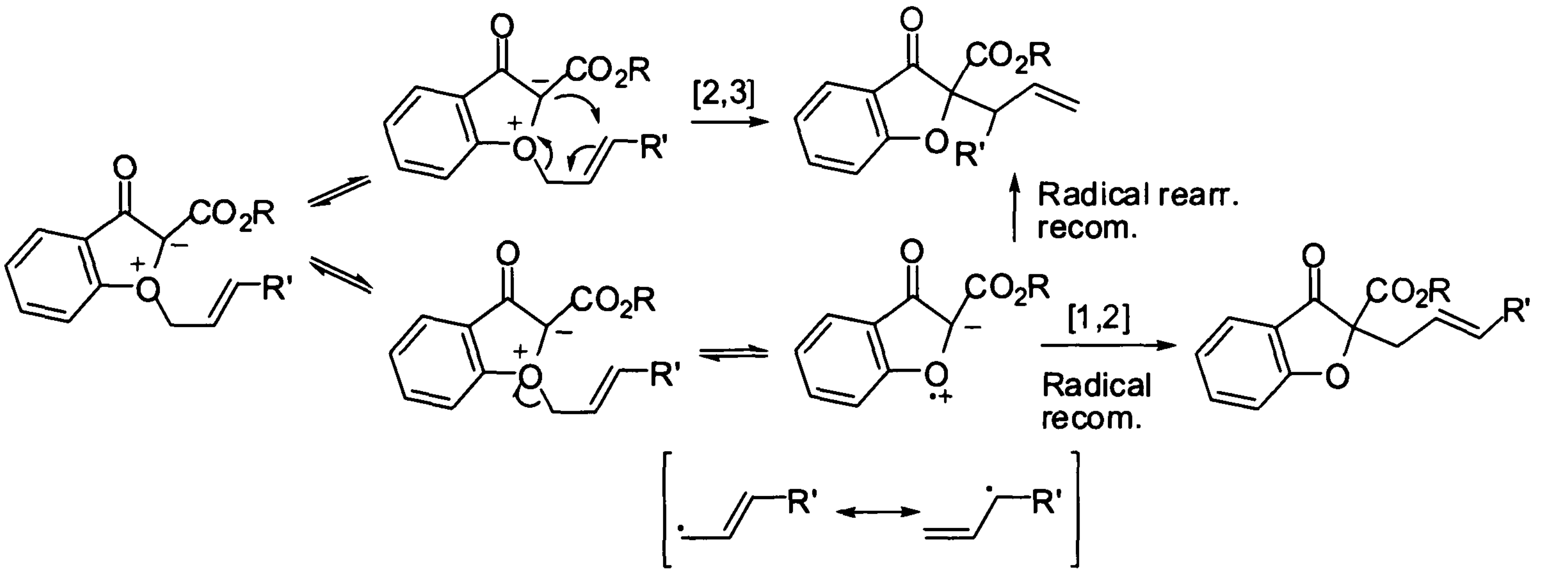
Entry	Olefin	Yield (%)	E:Z^a	dr of [2,3]-rearr.^{b}
1		81 (**4.36a**)	–	75:25
2		80 (**4.36b**)	97:3	58:42
3		88 (**4.36c**)	92:8	55:45
4		74 (**4.36d**)	97:3	69:31
5		90 (**4.36e**)	98:2	91:9
6		89 (**4.36f**)	98:2	93:7

a) Determined by ^{1}H NMR.; b) *c.f.* Table 4.3, pp. 82.

Table 4.4. Cross metathesis of α-diazo-β-ketoester **4.34a**.

So, the cross-metathesis of the diazoketoester **4.34a** with various olefins (5–10 equiv.) using catalyst **1.50** (5 mol%) in CH_2Cl_2 at reflux for 14–18 h (Scheme 4.19) was examined. The results are shown in Table 4.4. In general, cross-metathesis proceeded smoothly to give the desired functionalised α-diazo-β-ketoesters **4.36** in good to excellent yields and with high stereoselectivity. Notably, cross-metathesis with styrene (entry 2) was found to be much more efficient with this benzofused α-diazo-β-ketoester **4.34a**; in the case with the non aromatic substrate **4.20** (*c.f.* Table 4.2, entry 4, pp. 80) only 47% of the desired cross-metathesis product **4.30** was obtained. Interestingly, with this benzofused α-diazo-β-ketoester **4.34a**, the diastereoselectivity observed during the ylide rearrangement does not corelate with the stereoselectivity observed during cross-metathesis.

The observed increase in selectivity for [2,3]-sigmatropic rearrangement (over [1,2]-Stevens rearrangement) but with poor diastereoselectivity, for cyclohexyl and *tert*-butyl bearing olefin tethers (Table 4.4, entries 2 and 3) suggests that the [2,3]-rearrangement product is being formed not only from the pericyclic pathway, but also from the radical rearrangement/ recombination pathway (if the rearranged product was obtained only from pericyclic pathway, some corelation of diastereoselectivity (during sigmatropic rearrangement) and *E*/*Z* stereoselectivity (during cross-metathesis) should have been observed) (Scheme 4.20).

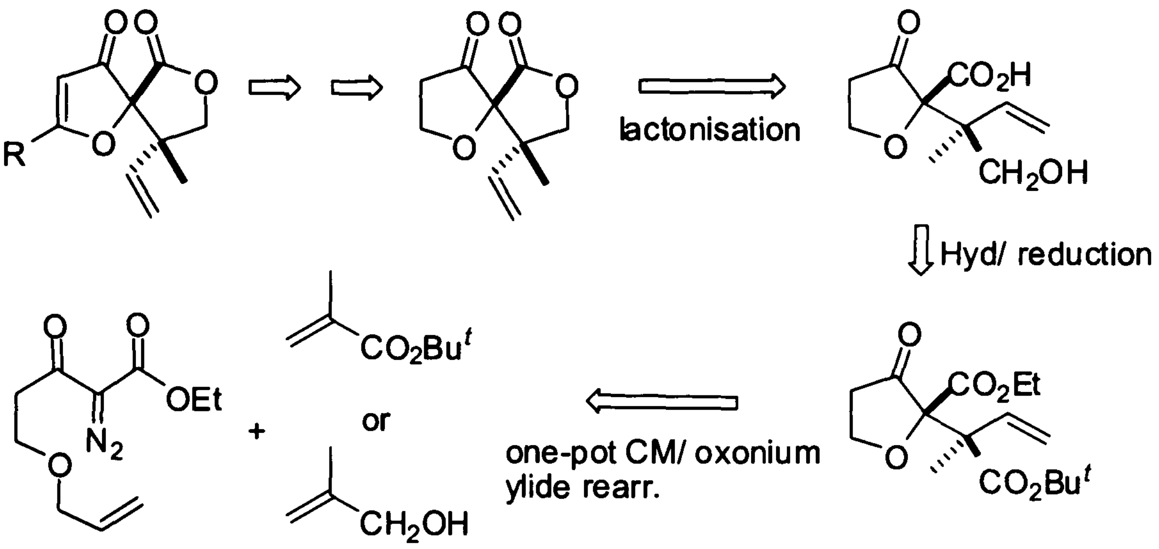


Scheme 4.20. Rearrangement of benzofused oxonium ylides.

However, with an ester group attached to the olefin, [2,3]-rearrangement was observed to be the predominant pathway and a marked increase in diastereoselectivity was also observed, suggesting that the putative allylic radical (bearing an ester functionality) intermediate formation is somehow being suppressed, so the ylide preferentially undergoes reaction *via* the pericyclic pathway (contrast entries 4 and 5).

4.7. Application of One-pot Cross-Metathesis/ Oxonium Ylide Rearrangement towards the Hyperolactone skeleton.

From my earlier studies it was established that one-pot cross-metathesis/ oxonium ylide rearrangement with α-diazo-β-ketoester **4.20** proceeds highly diastereoselectively, which was observed to be due to high stereoselectivity during cross-metathesis. I was curious to determine if an unsymmetrical trisubstituted olefin could be installed in α-diazo-β-ketoester **4.20** by cross-metathesis to allow potential application of the one-pot cross-metathesis/ ylide rearrangement strategy to the synthesis of hyperolactone motif (Scheme 4.21).[28] The hyperolactones are spirolactones, belonging to a class of novel metabolites found in *Hypericum chinese* L.[29] Although little is known about the biological activity of these compounds, their resemblance to known antiviral agents makes them interesting targets.



Scheme 4.21. Retrosynthetic route to hyperolactone motif.

Cross-metathesis of α-diazo-β-ketoester **4.20** with methacrylates were first attempted (Table 4.5, entries 1–4).[30,31,32] Unfortunately, no desired cross-metathesis product was observed, and only the dimer from homo-metathesis of α-diazo-β-ketoester **4.20** was formed. Using an excess of methacrylate or 0.5 equiv., had no effect on the process and only homo-metathesis was observed. Changing the sterics of the ester also had no effect on cross-metathesis. Methallyl alcohol was then examined for cross-metathesis. In this case only the starting materials were recovered; no homo-dimer of α-diazo-β-ketoester **4.20** was also seen (entry 5). Protecting the OH group as a trityl ether had no effect on the process; only the starting material **4.20** and dimer of α-diazo-β-ketoester **4.20** were obtained (entry 6). However, with benzoyl protected methallyl alcohol, 7% of

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[28] W. Schühly, S. L. Crockett, W. M. F. Fabian, *Chirality* **2005**, *17*, 250–256.

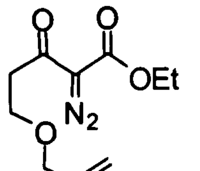
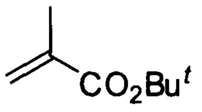
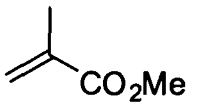
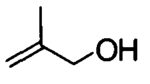
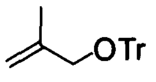
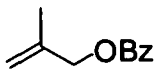
[29] Y. Aramaki, K. Chiba, M. Tada, *Phytochemistry* **1995**, *38*, 1419–1421.

[30] J. A. Marshall, J. J. Sabatini, *Org. Lett.* **2005**, *7*, 4819–4822.

[31] J. P. Morgan, C. Morrill, R. H. Grubbs, *Org. Lett.* **2002**, *4*, 67–70.

[32] A. K. Chatterjee, in *Handbook of Metathesis*, ed. Grubbs, R. H., Wiley-VCH, Weinheim, **2003**, pp. 246–295.

the desired cross-metathesis product (13% brsm) was obtained, with modest *E*:*Z* ~ 77:23 selectivity (entry 7). This selectivity is similar to that observed in lit.[32] for the cross metathesis of benzoyl protected methallyl alcohol with terminal olefins. This last result provided some encouragement, and I looked at various ways to reduce the dimerisation of the diazoester and hence improve cross-metathesis.[33,34]

Entry	Diazoester	Olefin (equiv.)	CM % (*E*:*Z*)	Diazo dimer (%)
1	 **4.20**	 (10)	n.o.	50
2		(0.5)	n.o.	31
3		 (5.0)	n.o.	22/ decomp^n
4		(10.0)	n.o.	
5		 (5.0)	n.o.	n.o.
6		 (5.0)	n.o.	n.d.
7		 (3.0)	7 (77:23) 13 (brsm)	38

n.o. = not observed; n.d. = exact % not determined by column chrotography.

Table 4.5. Cross-metathesis of α-diazo-β-ketoester **4.20** with gem disubstituted olefins.

For this, crotyl substituted α-diazo-β-ketoester **4.40**[13] was first examined. α-Diazo-β-ketoester **4.40** was prepared following the protocol described above for the synthesis of α-diazo-β-ketoester **4.20** (*c.f.* Scheme 4.8, pp. 73), but using crotyl alcohol (Scheme 4.22). However, in this case, *tert*-butyl ester **4.37** was hydrolysed by 2M NaOH at reflux for 12–14 h (hydrolysis of the *tert*-butyl ester with neat TFA gave a mixture of uncharacterised products, and with 1:1 TFA/CH_2Cl_2, the reaction did not go to completion even after 12 h at 70 °C) to give the corresponding carboxylic acid **4.38** in 65% yield, as a 95:5 mixture (by ^{1}H–NMR) of the desired carboxylic acid **4.38** and acrylic acid (obtained by retro Michael addition, followed by hydrolysis), and this mixture was used as such for further elaboration.

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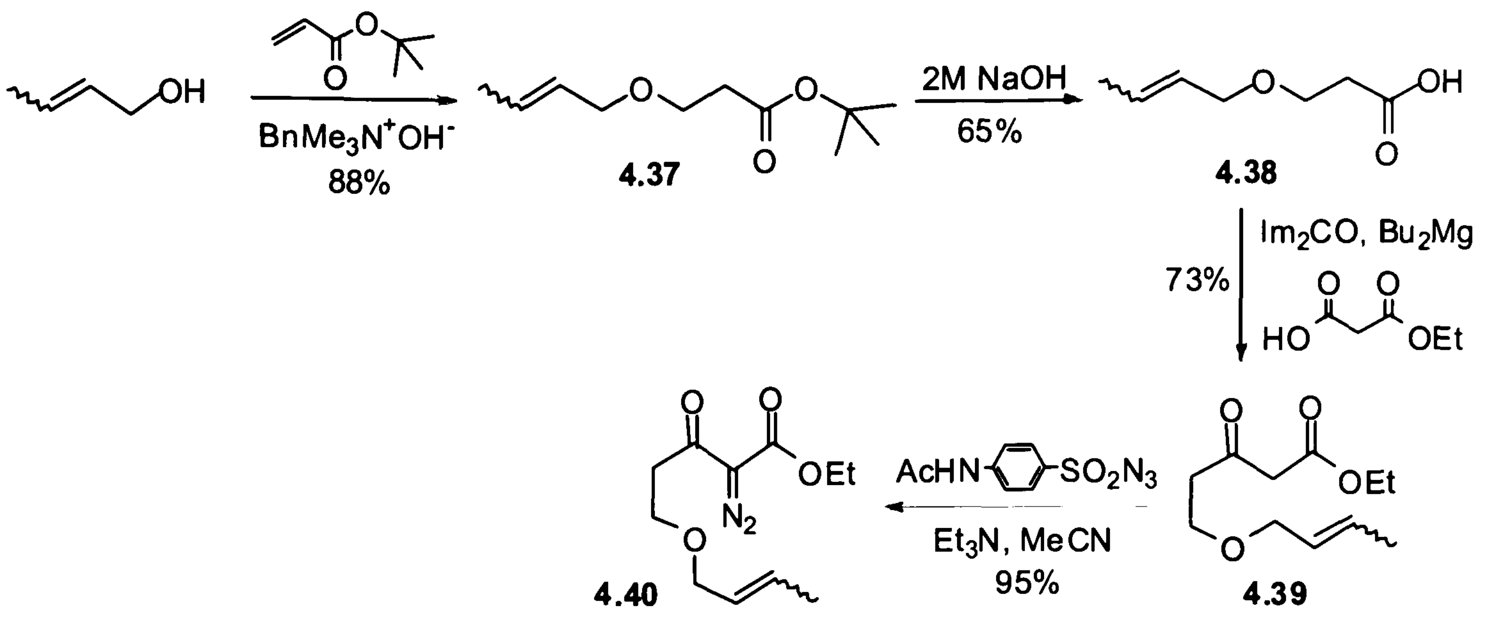
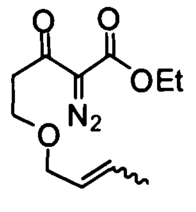
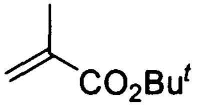
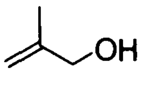
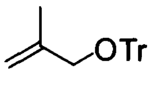
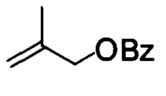
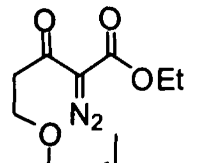
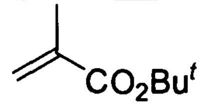
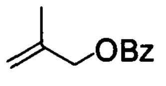
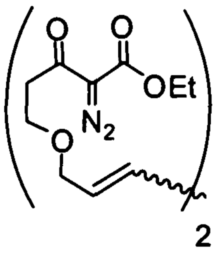
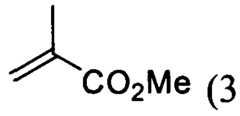
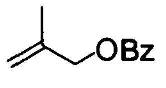
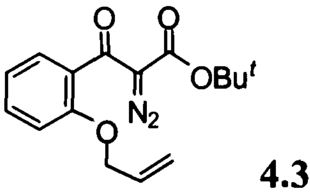
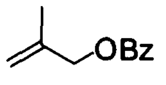
[33] G. Malaisé, W. Bonrath, M. Breuninger, T. Netscher, *Helv. Chim. Acta* **2006**, *89*, 797–812.

[34] D. J. O'Leary, H. E. Blackwell, R. A. Washenfelder, R. H. Grubbs, *Tetrhedron Lett.* **1998**, *39*, 7427–7430.



Scheme 4.22. Synthesis of α-diazo-β-ketoester **4.40**.

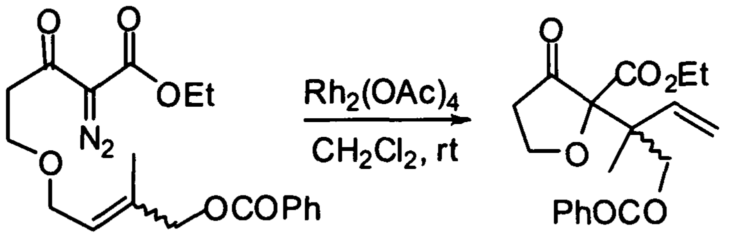
The crotyl substituted diazoester **4.40** was subjected to cross-metathesis with benzoyl protected methallyl alcohol. As expected, the dimerisation of diazoester **4.40** was reduced and the yield of cross-metathesis increased to 12.5% (19% brsm, Table 4.6, entry 4). Further, cross-metathesis of prenyl substituted diazoester **4.30a** (prepared by cross-metathesis of α-diazo-β-ketoester **4.20** with amylene) was attempted with benzoyl protected 2-methyl allyl alcohol. This was found to be reluctant towards cross-metathesis giving only 4.4% (11% brsm) of the desired cross-metathesis product (entry 6). A two step strategy for cross-metathesis of the terminal olefin was then attempted: dimer **4.41** of α-diazo-β-ketoester **4.20** was used for cross-metathesis with methyl methacrylate and benzoyl protected methallyl alcohol. However, this was again found to be reluctant towards metathesis, giving <9% of the desired product (entries 7 and 8). Looking back in the lit. it was found that it is challenging to generate unsymmetrical trisubstituted allyl ethers by cross-metathesis, and only a few reports of such processes are known.[30,32,33] It is not clear if it the allylic oxygen interferes with the catalyst, as metathesis proceeds efficiently with other terminal olefins (as demonstrated above), but not with unsymmetrical gem disubstituted ones. I also examined the cross-metathesis of benzofused α-diazo-β-ketoester **4.34** with benzoyl protected methallyl alcohol (entry 9), this gave 20% of the desired product (obtained as an inseparable mixture with the starting diazo compound **4.34**).

Entry	Diazoester	Olefin (equiv.)	CM % (*E*:*Z*)	Diazo dimer (%)
1	 **4.40**	 (3.0)	n.o.	n.d.
2		 (0.5)	n.o.	n.d.
3		 (3.0)	n.o.	26
4		 (3.0)	12.5 (73:27) 19 (brsm)	22
5	 **4.30a**	 (10)	n.o.	decomp^n
6		 (3.0)	4.4 (75:25) 11 (brsm)	n.o.
7	 **4.41**	 (3.0)	n.o.	35
8		 (3.0)	<9	n.o.
9	 **4.34**	 (3.0)	20 (80:20) 52 (brsm)	28

n.o. = not observed; n.d. = exact % not determined by column chrotography.

Table 4.6. Cross-metathesis to generate unsymmetrical tribsubstituted allylic ether.

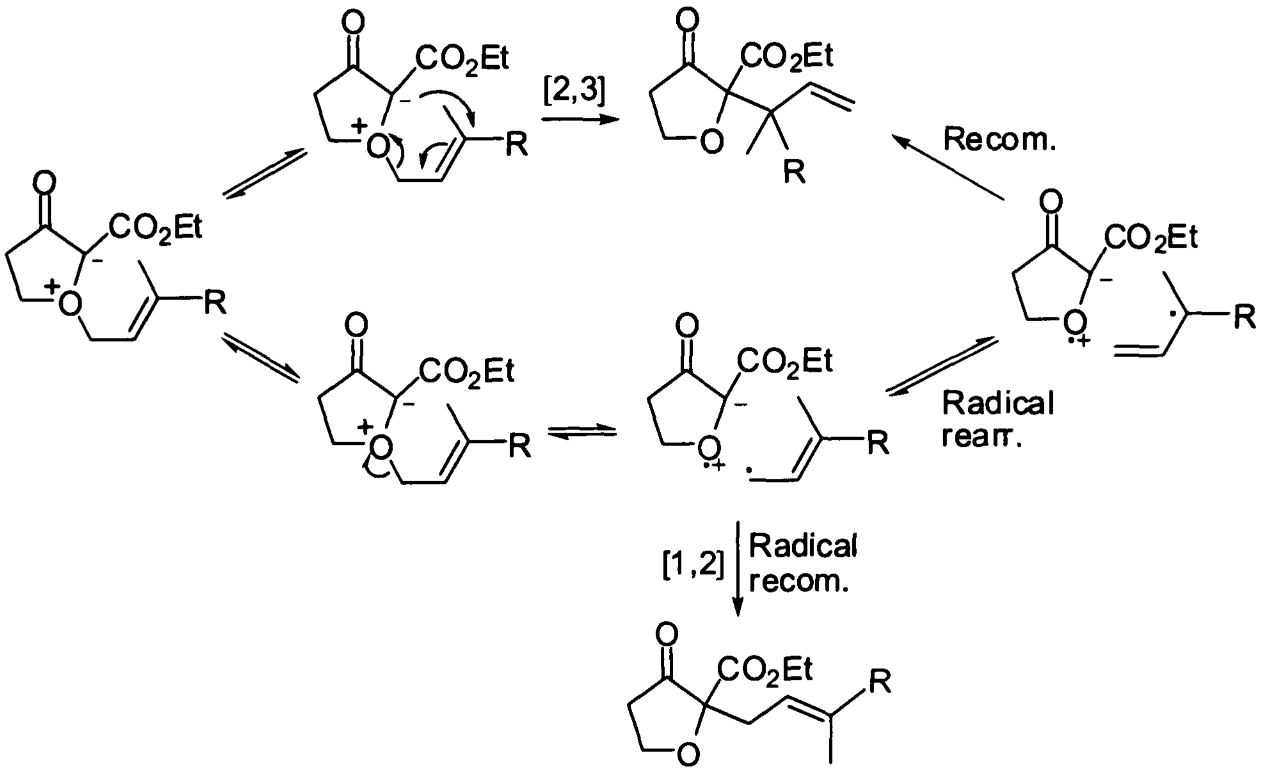
I was keen on studying if the stereoselectivity observed during cross-metathesis of diazoesters with benzoyl protected methallyl alcohol translates to diastereoselectivity during [2,3]-rearrangement process. So, we subjected the trisubstituted diazoester **4.42** to $Rh_2(OAc)_4$ catalysed oxonium ylide formation-rearrangement. The reaction proceeded efficiently to give the dihydrofuranone **4.43** in 85% yield (Scheme 4.23).



4.42 (*E*:*Z* ~ 3:1) **4.43** (85%, dr ~ 2:1)

Scheme 4.23. Oxonium ylide rearrangement of trisubstituted allylic ethers.

Interestingly, the diastereoselectivity (~2:1) was not observed to correlate with the stereoselectivity observed during metathesis (~3:1), possibly suggesting that [2,3]-rearrangement product is obtained not only from the pericyclic process, but also from the radical rearrangement-recombination pathway *via* a stabilised tertiary radical, which is favoured over the primary radical (which gives the [1,2]-rearrangement product) (Scheme 4.24). However, an encroachment of an *exo* selective [2,3]-rearrangement pathway cannot be ruled out at this time.



Scheme 4.24. Radical rearrangement in oxonium ylides.

4.8. Conclusions

In summary, these studies probe into the effect of electronics and the sterics during the oxonium ylide formation-rearrangement. The ylide rearrangement has been shown to proceed with high selectivity for the α-diazo-β-ketoester **4.20**; for the α-diazo-β-ketoester **4.34**, the selectivity could be enhanced with the introduction of suitable olefin substituents by cross-metathesis. The X-ray crystal structures of **4.21f** and **4.35f** suggests that the ylide rearrangement preferentially proceeds *via* an *endo* transition state. The success of one-pot cross-metathesis oxonium ylide formation-rearrangement further delineates the scope of two different carbene transformations occurring in a one flask operation.

CHAPTER 5

EXPERIMENTAL

5.1. General Remarks

Flash chromatography was performed on Kieselgel 60. Solvents were removed using a Buchi rotatory evaporator under reduced pressure.

Thin layer chromatography was carried out on aluminium backed plates pre-coated with silica (0.2 mm, 60 F_{254}, Merck), which were developed using standard visualising techniques: UV fluorescence (254 nm) and potassium permanganate solution with heating.

Infrared Spectra were recorded as thin films on NaCl discs on a Bruker Tensor 27 FT-IR spectrophotometer. The peaks are quoted as ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m) and weak (w). Only selected absorbances are reported.

^1H and ^{13}C -NMR Spectra were recorded in $CDCl_3$ using Brüker DPX200 (200 MHz), AV400 (400 MHz) or AV500 (500 MHz) spectrometers. Chemical shifts (δ) are reported in ppm relative to residual $CHCl_3$ (^1H NMR 7.26), or $CDCl_3$ (^{13}C NMR 77.4). The multiplicity of each signal is designated by the following abbreviations: s, singlet; d, doublet; dd, doublet of doublets; t, triplet. Coupling constants (*J*) are reported in Hz. For ^{13}C NMR spectra, due to long relaxation times N_2CHCO_2 and N_2CH were observed as broad signals only in concentrated samples.

Mass Spectra were obtained by the EPSRC National Mass Spectrometry Service at the University of Swansea, on a Micromass Quattro II low resolution triple quadrupole mass spectrometer using ES. GC-MS were obtained on a Micromass GCT using CI.

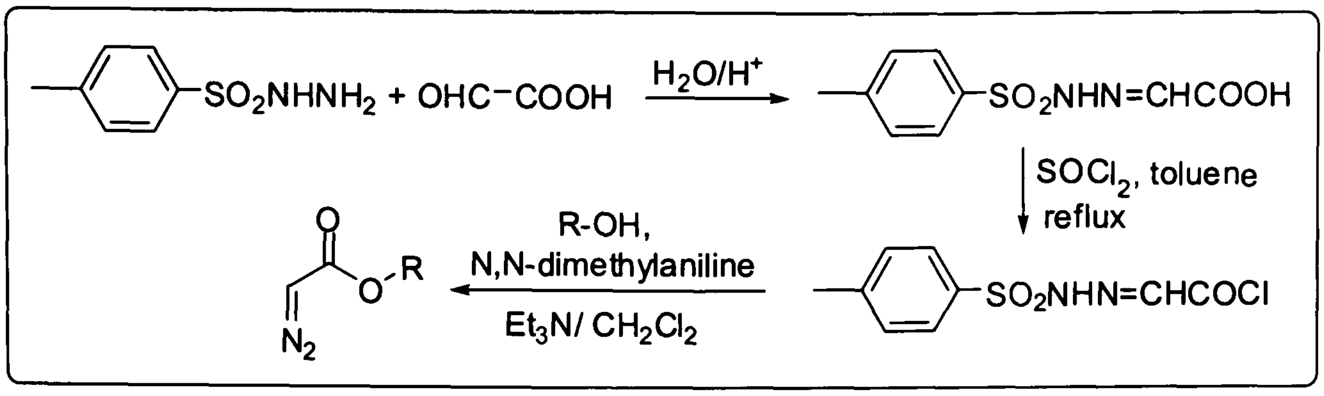
Accurate masses were obtained by the National Mass Spectrometry Service at the University of Swansea, on a Finnigan MAT 900 XLT high resolution double focusing mass spectrometer with tandem ion trap.

All reactions were performed in flame-dried glassware under an atmosphere of nitrogen. Starting materials were obtained commercially and used without further purification, unless otherwise stated. Solvents were dried before use. Et_2O, DCM, THF and MeCN were degassed and dried over alumina under argon.[1] Petrol refers to petroleum spirit (b.p. 30–40 °C).

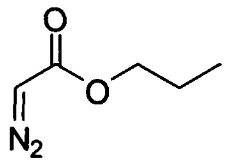
---

[1] A. B. Pangborn, M. A. Giaedello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* **1996**, *15*, 1518–1520.

5.2. Synthesis of a-Diazoacetates



n-Propyl diazoacetate, 2.03b[2]



***Typical procedure*:** A solution of glyoxylic acid chloride *p*-toluenesulfonylhydrazone **2.02**[3] (2.20 g, 8.46 mmol) in CH_2Cl_2 (10 mL) was added to an ice cooled solution of *n*-propanol (450 μL, 6.03 mmol) in CH_2Cl_2 (10 mL). *N,N*-dimethyl aniline (1.60 mL, 12.6 mmol) was added and the mixture stirred for 30 min. at 0 °C, followed by the addition of freshly distilled Et_3N (4.50 mL, 32.3 mmol). The resulting mixture was stirred for 30 min at 0 °C and 1 h at room temperature, followed by the addition of water (15 mL). The mixture was concentrated under reduced pressure. Saturated aq. citric acid (25 mL) was added and the aq. layer extracted with 10% EtOAc in hexane (3 × 30 mL). The combined organics were washed with sat. aq. citric acid (3 × 30 mL), dried (Na_2SO_4), concentrated under reduced pressure and purified by flash chromatography (5% Et_2O in petrol) to afford the diazoacetate **2.03b** (524 mg, 68%) as a yellow oil.

$\boldsymbol{R_f}$ = 0.51 (30% Et_2O in petrol); **IR** (neat): 2972s, 2113s, 1694s, 1462m, 1401s, 1361s; δ_H (400 MHz, $CDCl_3$) = 4.74 (br s, 1H, CHN_2), 4.13 (t, 2H, J = 6.7, OCH_2), 1.72–1.63 (m, 2H, OCH_2CH_2), 0.95 (t, 3H, J = 7.4, CH_3); δ_C (100 MHz, $CDCl_3$) = 166.9 (CO_2), 66.4 (OCH_2), 46.1 (CHN_2), 22.2 (OCH_2CH_2), 10.3 (CH_3); ***m/z*** (FI): 128 (M^+, 100%), 129 ($M + H^+$, 5), 198 (75); HRMS: M^+ found 128.0581, $C_5H_8N_2O_2$ requires 128.0586.

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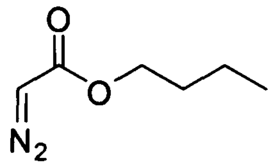
[2] M. Regitz, J. Hocker, A. Liedhegener, *Org. Prep. Proced.* **1969**, *1*, 99–104.

[3] a) E. J. Corey, A. G. Myers, *Tetrahedron Lett.* **1984**, *25*, 3559–3562; b) M. P. Doyle, I. M. Phillips, *Tertahedron Lett.* **2001**, *42*, 3155–3158.

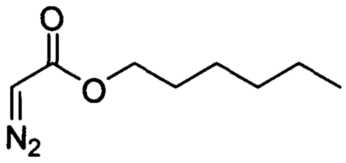
n-Butyl diazoacetate, 2.03c[2]



2.03c was prepared following the typical procedure using *n*-butanol (440 μL, 4.81 mmol). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the diazoacetate **2.03c** (611 mg, 89%) as a yellow oil.

R*f** = 0.47 (30% Et_2O in petrol); **IR** (neat): 2962m, 2112s, 1694s, 1398m, 1364m; **δ_H** (400 MHz, $CDCl_3$) = 4.74 (br s, 1H, CHN_2), 4.16 (t, 2H, J = 6.7, OCH_2), 1.66–1.59 (m, 2H, OCH_2CH_2), 1.43–1.34 (m, 2H, CH_3CH_2), 0.94 (t, 3H, J = 7.4, CH_3); **δ_C** (100 MHz, $CDCl_3$) = 166.9 (CO_2), 64.7 (OCH_2), 46.2 (CHN_2), 30.8 (OCH_2CH_2), 19.1 (CH_3CH_2), 13.7 (CH_3); ***m/z (FI): 142 (M^+, 100%), 143 ($M + H^+$, 3); HRMS: M^+ found 142.0737, $C_6H_{10}N_2O_2$ requires 142.0742.

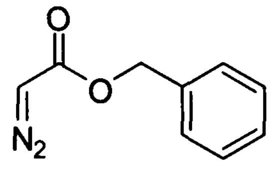
n-Hexyl diazoacetate, 2.03d



2.03d was prepared following the typical procedure using *n*-hexanol (0.80 mL, 6.37 mmol). The residue was purified by flash chromatography (5% Et_2O in petrol) to afford the diazoacetate **2.03d** (830 mg, 77%) as a yellow oil.

R*f** = 0.52 (30% Et_2O in petrol); **IR** (neat): 2958s, 2111s, 1698s, 1468m, 1398s, 1361s; **δ_H** (400 MHz, $CDCl_3$) = 4.74 (br s, 1H, CHN_2), 4.16 (t, 2H, J = 6.7, OCH_2), 1.67–1.59 (m, 2H, OCH_2CH_2), 1.38–1.25 (m, 6H, 3 × CH_2), 0.91–0.88 (m, 3H, CH_3); **δ_C** (100 MHz, $CDCl_3$) = 166.9 (CO_2), 65.0 (OCH_2), 46.1 (CHN_2), 31.4, 28.7, 25.5 and 22.5 (4 × CH_2), 13.9 (CH_3); ***m/z (FI): 170 (M^+, 100%), 171 ($M + H^+$, 15); HRMS: M^+ found 170.1053, $C_8H_{14}N_2O_2$ requires 170.1055.

Benzyl diazoacetate, 2.03e[4]



2.03e was prepared following the typical procedure using benzyl alcohol (0.65 mL, 6.29 mmol). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the diazoacetate **2.03e** (1.00 g, 90%) as a yellow oil.

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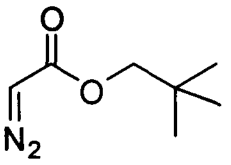
[4] M. Schroen, S. Bräse, *Tetrahedron* **2005**, *61*, 12186–12192.

R*$_f$** = 0.45 (30% Et_2O in petrol); **IR** (neat): 2113s, 1694s, 1498w, 1391s cm^{-1}; **δ_H** (400 MHz, $CDCl_3$) = 7.42–7.30 (m, 5H, Ar), 5.22 (s, 2H, CH_2), 4.80 (br s, 1H, CHN_2); **δ_C** (100 MHz, $CDCl_3$) = 166.7 (CO_2), 135.8 (Ar, quat.), 128.6, 128.3 and 128.2 (3 × Ar), 66.5 (CH_2), 46.4 (CHN_2); ***m/z (FI): 131 (15%), 176 (M^+, 100), 177 (M + H^+, 12); HRMS: M^+ found 176.0591, $C_9H_8N_2O_2$ requires 176.0586.

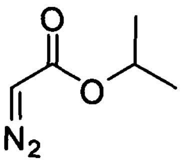
Neopentyl diazoacetate, 2.03f[5]



2.03f was prepared following the typical procedure using neopentanol (1.00 mL, 9.29 mmol). The residue was purified by flash chromatography (5% Et_2O in petrol) to afford the diazoester **2.03f** (1.10 g, 76%) as a yellow oil.

R*$_f$** = 0.48 (20% ether in petrol); **IR** (neat): 3125w, 2113s, 1699s, 1384s, 1248s; **δ_H** (400 MHz, $CDCl_3$) = 4.76 (br s, 1H, CHN_2), 3.87 (s, 2H, CH_2), 0.95 (s, 9H, CMe_3); **δ_C** (100 MHz, $CDCl_3$) = 73.9 (CH_2), 46.1 (CHN_2), 31.5 (CMe_3), 26.4 (C*Me*$_3$); ***m/z (FI): 156 (M^+, 100%), 157 (M + H^+, 12); HRMS: M^+ found 156.0900, $C_7H_{12}N_2O_2$ requires 156.0899.

Isopropyl diazoacetate, 2.03g[6]



2.03g was prepared following the typical procedure using isopropanol (450 μL, 5.95 mmol). The residue was purified by flash chromatography (5% Et_2O in petrol) to afford the diazoacetate **2.03g** (325 mg, 43%) as a yellow oil.

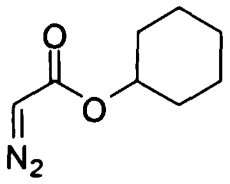
R*$_f$** = 0.47 (30% Et_2O in petrol); **IR** (neat): 2110s, 1652s, 1379m, 1329m; **δ_H** (400 MHz, $CDCl_3$) = 5.09 (heptet, 1H, *J* = 6.3, OCH), 4.71 (br s, 1H, CHN_2), 1.26 (d, 6H, *J* = 6.3, 2 × CH_3); **δ_C** (100 MHz, $CDCl_3$) = 166.5 (CO_2), 68.4 (OCH), 46.3 (CHN_2), 22.0 (2 × CH_3); ***m/z (FI): 128 (M^+, 100%), 129 (M + H^+, 5); HRMS: M^+ found 128.0584, $C_5H_8N_2O_2$ requires 128.0586.

---

[5] A. Nakamura, A. Konishi, Y. Tatsuno, S. Otsuka, *J. Am. Chem. Soc.* **1978**, *100*, 3443–3448.

[6] M. Thap, O. P. Strausz, H. E. Gunning, *J. Am. Chem. Soc.* **1969**, *91*, 1261–1263.

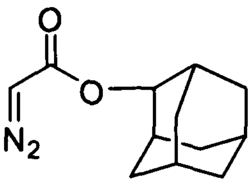
Cyclohexyl diazoacetate, 2.03h[7]



2.03h was prepared following the typical procedure using cyclohexanol (0.50 mL, 4.73 mmol). The residue was purified by flash chromatography (5% Et_2O in petrol) to afford the diazoacetate **2.03h** (673 mg, 84%) as a yellow oil.

R*f** = 0.57 (30% Et_2O in petrol); **IR** (neat): 2939s, 2110s, 1690s, 1451m, 1378s; **δ_H** (400 MHz, $CDCl_3$) = 4.90–4.78 (m, 1H, OCH), 4.74 (br s, 1H, CHN_2), 1.98–1.20 (m, 10H, 5 × CH_2); **δ_C** (100 MHz, $CDCl_3$) = 166.4 (CO_2), 73.2 (OCH), 46.3 (CHN_2), 31.8, 25.3 and 23.7 (3 × CH_2); ***m/z (FI): 168 (M^+, 100%), 169 (M + H^+, 15); HRMS: M^+ found 168.0901, $C_8H_{12}N_2O_2$ requires 168.0899.

2-Adamantyl diazoacetate, 2.03i[8]



2.03i was prepared following the typical procedure using 2-adamantanol (1.20 g, 7.88 mmol). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the diazoacetate **2.03i** (1.33 g, 77%) as a yellow oil.

R*f** = 0.57 (30% Et_2O in petrol); **IR** (neat): 2977w, 2910s, 2858s, 2112s, 1692s, 1452s, 1375s, 1333s, 1248s, 1190s; **δ_H** (400 MHz, $CDCl_3$) = 5.10 (t, 1H, *J* = 3.3, OCH), 4.74 (br s, 1H, CHN_2), 2.03–1.96 (m, 4H, 2 × CH_2), 1.87–1.74 (m, 8H, 2 × CH, 3 × CH_2), 1.61–1.54 (m, 2H, 2 × CH); **δ_C** (100 MHz, $CDCl_3$) = 166.2 (CO_2), 77.5 (OCH), 46.3 (CHN_2), 37.3, 2 × 36.3 and 2 × 31.7 (5 × CH_2), 2 × 32.0, 27.2 and 26.9 (4 × CH); ***m/z (FI): 220 (M, 100%), 221 (M + H^+, 18); HRMS: M^+ found 220.1204, $C_{12}H_{16}N_2O_2$ requires 220.1212.

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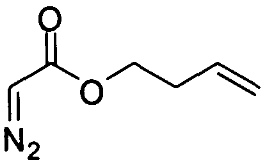
[7] T. Aratani, Y. Yoneyoshi, T.Nagase, *Tetrahedron Lett.* **1977**, *30*, 2599–2602.

[8] M. P. Doyle, *et. al. Recueil des Travaux Chimiques des Pays-Bas* **1995**, *114*, 163–170.

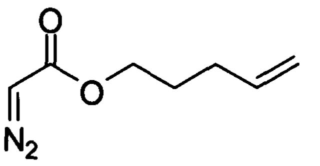
But-3-enyl diazoacetate, 2.06a[9]



2.06a was prepared following the typical procedure using 3-buten-1-ol (0.25 mL, 2.91 mmol). The residue was purified by flash chromatography (5% EtOAc in hexane) to afford the diazoester **2.06a** (223 mg, 55%) as a yellow oil.

R*f** = 0.18 (10% EtOAc in hexane); **IR** (neat): 2985s, 2112s, 1696s; **δH** (400 MHz, $CDCl_3$) = 5.86–5.62 (m, 1H, =CH), 5.68–5.00 (m, 2H, $=CH_2$), 4.72 (br s, 1H, CHN_2), 4.18 (t, 2H, *J* = 6.8, OCH_2), 2.46–2.28 (m, 2H, CH_2); **δC** (100 MHz, $CDCl_3$) = 134.2 (=CH), 117.8 ($=CH_2$), 64.3 9 (OCH_2), 33.7 (CH_2); ***m/z (FI): 121 (70%), 140 (M^+, 100%), 141 ($M + H^+$, 17); HRMS: M^+ found 140.0582, $C_6H_8N_2O_2$ requires 140.0586.

Pent-4-enyl diazoacetate, 2.06b[10]



2.06b was prepared following the typical procedure using 4-penten-1-ol (1.10 mL, 10.7 mmol). The residue was purified by flash chromatography (5% EtOAc in hexane) to afford the diazoester **2.06b** (1.04 g, 63%) as a yellow oil.

R*f** = 0.14 (10% EtOAc in hexane); **IR** (neat): 2956s, 2113s, 1697s, 1450s, 1398s, 1242s, 1187s; **δH** (400 MHz, $CDCl_3$) = 5.88–5.74 (m, 1H, =CH), 5.08–4.96 (m, 2H, $=CH_2$), 5.74 (br s, 1H, CHN_2), 4.16 (t, 2H, *J* = 6.6, OCH_2), 2.18–2.06 (m, 2H, CH_2), 1.80–1.68 (m, 2H, CH_2); **δC** (100 MHz, $CDCl_3$) = 137.4 (=CH), 115.3 ($=CH_2$), 64.3 (OCH_2), 46.1 (CHN_2), 29.9 and 27.9 (2 × CH_2); ***m/z (FI): 154 (M^+, 52%), 155 ($M + H^+$, 50), 170 (100); HRMS: M^+ found 154.0742, $C_7H_{10}N_2O_2$ requires 154.0742.

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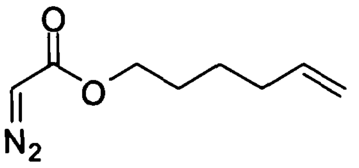
[9] C. J. Moody, A. M. Z. Slawin, D. Willows, *Org. Biomol. Chem.* **2003**, *1*, 2716–2722.

[10] M. P. Doyle, I. M. Phillips, *Tetrahedron Lett.* **2001**, *42*, 3155–3158.

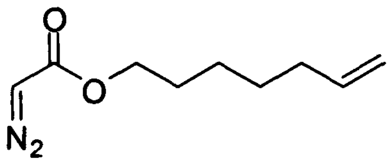
Hex-5-enyl diazoacetate, 2.06c[10]



2.06c was prepared following the typical procedure using 5-hexen-1-ol (0.95 mL, 7.92 mmol). The residue was purified by flash chromatography (5% EtOAc in hexane) to afford the diazoacetate **2.06c** (1.20 g, 90%) as a yellow oil.

R*f** = 0.34 (10% EtOAc in hexane); **IR** (neat): 2938s, 2111s, 1696s, 1243s, 1186s; **δ_H** (400 MHz, $CDCl_3$) = 5.82–5.68 (m, 1H, =CH), 5.06–4.90 (m, 2H, $=CH_2$), 4.74 (br s, 1H, CHN_2), 4.16 (t, 2H, *J* = 6.7, OCH_2), 2.16–1.96 (m, 2H, $=CHCH_2$), 1.76–1.56 (m, 2H, OCH_2CH_2), 1.56–1.36 (m, 2H, $OCH_2CH_2CH_2$); **δ_C** (100 MHz, $CDCl_3$) = 138.3 (=CH), 114.8 ($=CH_2$), 64.7 (OCH_2), 46.1 (CHN_2), 33.2, 28.2 and 25.1 (3 × CH_2); ***m/z (FI): 168 (M^+, 25%), 169 (M + H^+, 100); HRMS: M + H^+ found 169.0973, $C_8H_{13}N_2O_2$ requires 169.0977.

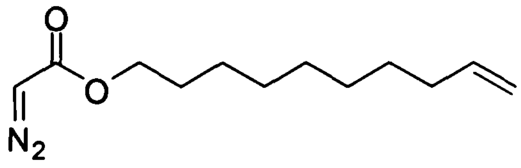
Hept-6-enyl diazoacetate, 2.06d



2.06d was prepared following the typical procedure using 6-hepten-1-ol (1.27 g, 11.1 mmol). The residue was purified by flash chromatography (5% EtOAc in hexane) to afford the diazoester **2.06d** (1.90 g, 94%) as a yellow oil.

R*f** = 0.34 (20% EtOAc in hexane); **IR** (neat): 2933s, 2111s, 1696s, 1398s, 1359s, 1241s, 1185s; **δ_H** (400 MHz, $CDCl_3$) = 5.88–5.72 (m, 1H, =CH), 4.90–5.06 (m, 2H, $=CH_2$), 4.73 (br s, 1H, CHN_2), 4.16 (t, 2H, *J* = 6.7, OCH_2), 2.06 (q, 2H, *J* = 7.0, $=CHCH_2$), 1.69–1.62 (m, 2H, OCH_2CH_2), 1.48–1.30 (m, 4H, 2 × CH_2); **δ_C** (100 MHz, $CDCl_3$) = 138.6 (=CH), 114.5 ($=CH_2$), 64.9 (OCH_2), 46.1 (CHN_2), 33.5 ($=CHCH_2$), 28.6, 28.4 and 25.3 (3 × CH_2); ***m/z (FI): 121 (100%), 170 (40), 169 (M + H^+, 50); HRMS: M + H^+ found 183.1132, $C_9H_{15}N_2O_2$ requires 183.1134.

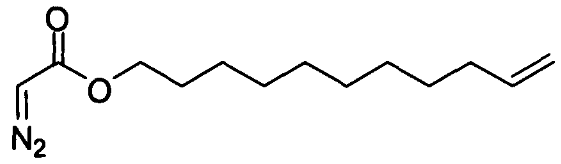
Dec-9-enyl diazoacetate, 2.06e[10]



2.06e was prepared following the typical procedure using 9-decen-1-ol (0.75 mL, 4.21 mmol). The residue was purified by flash chromatography (5% EtOAc in hexane) to afford the diazoester **2.06e** (911 mg, 96%) as a yellow oil.

R*$_f$** = 0.67 (30% EtOAc in hexane); **IR** (neat): 2928s, 2110s, 1697s, 1242s, 1186s; δ_H (400 MHz, $CDCl_3$) = 5.36–5.22 (m, 1H, =CH), 5.04–4.90 (m, 2H, $=CH_2$), 4.74 (br s, 1H, CHN_2), 4.14 (t, 2H, *J* = 6.7, OCH_2), 2.04 (q, 2H, *J* = 6.8, $=CHCH_2$), 1.68–1.61 (m, 2H, OCH_2CH_2), 1.24–1.44 (m, 10H, 5 × CH_2); δ_C (100 MHz, $CDCl_3$) = 139.2 (=CH), 114.2 ($=CH_2$), 65.1 (OCH_2), 46.2 (CHN_2), 33.8, 29.3, 29.2, 29.0, 28.8, 28.7 and 25.8 (7 × CH_2); ***m/z (FI): 224 (M^+, 8%), 225 ($M + H^+$, 100), 226 (40); HRMS: $M + H^+$ found 225.1604, $C_{12}H_{21}N_2O_2$ requires 225.1603.

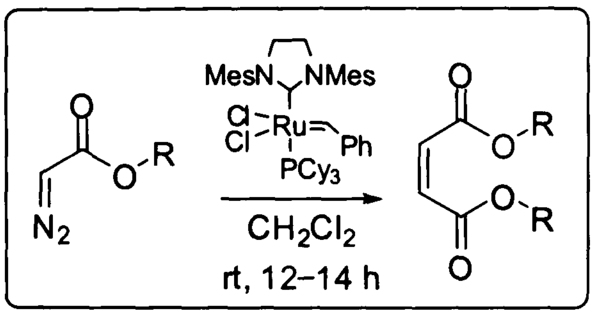
Undec-10-enyl diazoacetate, 2.06f



2.06f was prepared following the typical procedure using 10-undecen-1-ol (1.90 mL, 9.50 mmol). The residue was purified by flash chromatography (5% EtOAc in petrol) to afford the diazoester **2.06f** (2.05 g, 91%) as a yellow oil.

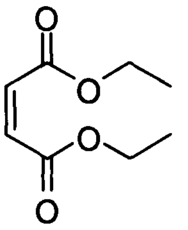
R*$_f$** = 0.30 (10% EtOAc in hexane); **IR** (neat): 2927s, 2110s, 1698s, 1241s, 1186s; δ_H (400 MHz, $CDCl_3$) = 5.82–5.72 (m, 2H, =CH), 4.98–4.88 (m, 2H, $=CH_2$), 4.71 (br s, 1H, CHN_2), 4.12 (t, 2H, *J* = 6.8, OCH_2), 2.04–1.98 (m, 2H, $=CHCH_2$), 1.64–1.57 (m, 2H, OCH_2CH_2), 1.40–1.16 (m, 12H, 6 × CH_2); δ_C (100 MHz, $CDCl_3$) = 139.0 (=CH), 114.1 ($=CH_2$), 64.9 (OCH_2), 46.0 (CHN_2), 33.7, 29.4, 29.3, 29.2, 29.0, 28.8, 28.7 and 25.7 (8 × CH_2); ***m/z (FI): 238 (M^+, 8%), 239 ($M + H^+$, 100), 308 (100); HRMS: $M + H^+$ found 239.1764, $C_{13}H_{23}N_2O_2$ requires 239.1760.

5.3. Homo-coupling of a-Diazoacetates



General Procedure: Grubbs 2nd generation catalyst **1.50** (0.005 equiv., 0.5 mol%) was added to a solution of diazoacetate (1.0 equiv.) in CH_2Cl_2. The mixture was stirred at room temperature for 12–16h. The mixture was concentrated under reduced pressure and purified by flash chromatography.

Diethyl maleate, 2.04a[11]


Z:*E* 98:2

2.04a was prepared following the general procedure using ethyl diazoacetate **2.03a** (0.10 mL, 0.952 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* 98:2 by GC-MS) was purified by flash chromatography (5% Et_2O in petrol) to afford the maleate **2.04a** (78.0 mg, 95%) as a pale yellow liquid.

R*f** = 0.56 (30% Et_2O in petrol); **IR** (neat): 2985s, 2936s, 1730s, 1639s, 1447s, 1405s, 1384s, 1214s, 1163s, 1096m; δ_H (400 MHz, $CDCl_3$) = 6.20 (s, 2H, 2 × =CH), 4.21 (q, 4H, J = 7.1, 2 × CH_2), 1.27 (t, 6H, J = 7.1, 2 × CH_3); δ_C (100 MHz, $CDCl_3$) 165.2 (2 × CO_2), 129.7 (2 × =CH), 61.5 (2 × CH_2), 31.9 (2 × CH_3); ***m/z (CI): 127 (20%), 144 (5), 173 (M + H^+, 100), 190 (M + NH_4^+, 5); HRMS: M + NH_4^+ found 190.1079, $C_8H_{16}NO_4$ requires 190.1072.

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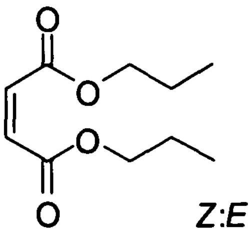
[11] N. Suzuki, Y. Kaneko, T. Tsukanaka, T. Nomoto, Y. Ayaguchi, Y. Izawa, *Tetrahedron* **1985**, *41*, 2387–2392.

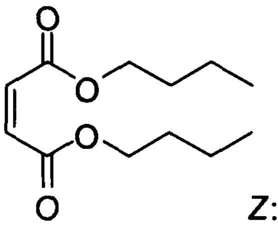
Di-*n*-propyl maleate, 2.04b[12]



2.04b was prepared following the general procedure using *n*-propyl diazoacetate **2.03b** (52.0 mg, 0.406 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* 95:5 by GC-MS) was purified by flash chromatography (10% Et_2O in petrol) to afford the maleate **2.04b** (34.0 mg, 84%) as a yellow liquid.

R**f** = 0.40 (30% Et_2O in petrol); **IR** (neat): 1726s, 1408s, 1266s; **δH** (400 MHz, $CDCl_3$) = 6.24 (s, 2H, 2 × =CH), 4.15 (t, 4H, *J* = 7.0, 2 × OCH_2), 1.70 (sextet, 4H, *J* = 7.0, 2 × OCH_2CH_2), 0.92 (t, 3H, *J* = 7.0, 2 × CH_3); **δC** (100 MHz, $CDCl_3$) = 165.4 (2 × CO_2), 129.8 (2 × =CH), 66.8 (2 × OCH_2), 21.8 (2 × OCH_2CH_2), 10.3 (2 × CH_3); ***m/z*** (CI): 201 (M + H^+, 85%), 203 (30), 218 (M + NH_4^+, 85), 220 (100); HRMS: M + H^+ found 201.1122, $C_{10}H_{17}O_4$ requires 201.1121.

Di-*n*-butyl maleate, 2.04c[12]



2.04c was prepared following the general procedure using *n*-butyl diazoacetate **2.03c** (96.0 mg, 0.676 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* 86:14 by GC-MS) was purified by flash chromatography (10% Et_2O in petrol) to afford the maleate **2.04c** (57.0 mg, 74%) as a yellow liquid.

R**f** = 0.48 (30% Et_2O in petrol); **IR** (neat): 2961s, 2875m, 1731s, 1644m, 1466m, 1406s, 1377m, 1210s, 1165s; **δH** (400 MHz, $CDCl_3$) = 6.23 (s, 2H, 2 × =CH), 4.19 (t, 4H, *J* = 6.7, 2 × OCH_2), 1.58–1.70 (m, 4H, 2 × OCH_2CH_2), 1.40 (hextet, 4H, *J* = 7.3, CH_2CH_3), 0.94 (t, 6H, *J* = 7.3, 2 × CH_3); **δC** (100 MHz, $CDCl_3$) 165.4 (2 × CO_2), 129.7 (2 × =CH), 65.2 (2 × OCH_2), 30.4 (2 × OCH_2CH_2), 19.1 (2 × CH_2CH_3), 13.6 (2 × CH_3); ***m/z*** (CI): 190 (100%), 192 (72), 229 (15); HRMS: M + H^+ found 229.1437, $C_{12}H_{21}O_4$ requires 229.1434.

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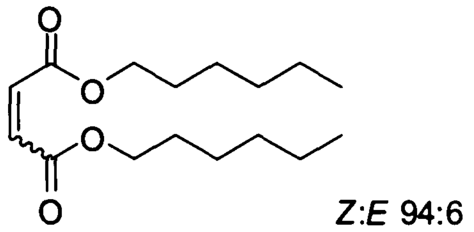
[12] C. R. Reddy, P. Iyengar, G. Nagendrappa, B. S. J. Prakash, *Catal. Lett.* **2005**, *101*, 87–91.

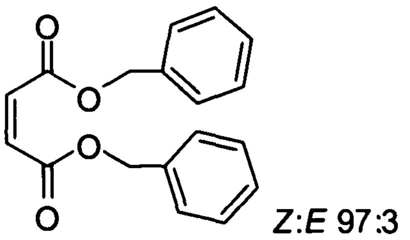
Di-*n*-hexyl maleate, 2.04d[13]



2.04d was prepared following the general using from *n*-hexyl diazoacetate **2.03d** (90.0 mg, 0.529 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* 94:6 by GC-MS) was purified by flash chromatography (10% Et_2O in petrol) to afford an inseparable mixture of *Z* and *E*-isomers **2.04d** (74.0 mg, 98%) as a yellow liquid.

R*f** = 0.38 (30% Et_2O in petrol); **IR** (neat): 2957s, 2860s, 1731s, 1645m, 1467m, 1406m, 1213s, 1164s; **δ_H** (400 MHz, $CDCl_3$) ***Z*-isomer** = 6.23 (s, 2H, 2 × =CH), 4.17 (t, 4H, *J* = 6.8, 2 × OCH_2), 1.70–1.50 (m, 4H, 2 × OCH_2CH_2), 1.42–1.20 (m, 12H, 6 × CH_2), 0.89 (t, 6H, *J* = 6.6, 2 × CH_3); discernible data for ***E*-isomer** = 6.85 (s, 2H, 2 × =CH); **δ_C** (100 MHz, $CDCl_3$) ***Z*-isomer** = 165.3 (2 × CO_2), 129.7 (2 × =CH), 65.5 (2 × OCH_2), 31.4, 28.4, 25.5 and 22.5 (8 × CH_2), 13.9 (2 × CH_3); discernible data for ***E*-isomer** = 165.1 (2 × CO_2), 133.6 (2 × =CH), 64.6 (2 × OCH_2), 31.3, 29.6, 25.4 and 22.4 (8 × CH_2), 13.9 (2 × CH_3); ***m/z (CI): 52 (20%) 302 (M + NH_4^+, 100), 304 (20); HRMS: M + H^+ found 285.2061, $C_{16}H_{29}O_4$ requires 285.2060.

Dibenzyl maleate, 2.04e[14]



2.04e prepared following the general procedure using benzyl diazoacetate **2.03e** (80.0 mg, 0.454 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* 97:3 by GC-MS) was purified by flash chromatography (10% Et_2O in petrol) to afford the maleate **2.04e** (53.0 mg, 79%) as a yellow liquid.

R*f** = 0.31 (30% Et_2O in petrol); **IR** (neat): 1725s, 1644s, 1498w, 1401w, 1364w; **δ_H** (400 MHz, $CDCl_3$) = 7.30–7.42 (m, 10H, Ar), 6.30 (s, 2H, 2 × =CH), 5.64 (s, 4H, 2 × CH_2); **δ_C** (100 MHz, $CDCl_3$) = 164.9 (2 × CO_2), 135.1 (2 × Ar, quat.), 129.8 (2 × =CH), 2 × 128.6 and 128.5 (6 × Ar), 67.1 (2 × CH_2); ***m/z (CI): 297 (M + H^+, 15%), 314 (M + NH_4^+, 100), 316 (40); HRMS: M + NH_4^+ found 314.1386, $C_{18}H_{20}O_4N$ requires 314.1387.

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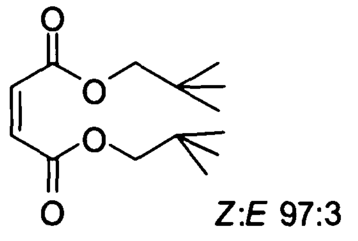
[13] P. Hua, Z. Sha, *Yingyong Huagong* **2002**, *31*, 3–8.
[14] M. E. Jung, K. Shishido, L. H. Davis, *J. Org. Chem.* **1982**, *47*, 891–892.

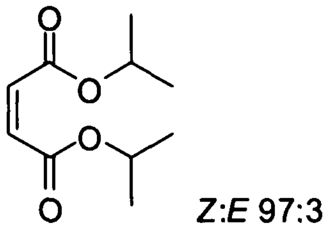
Dineopentyl maleate, 2.04f[15]



2.04f was prepared following the general procedure using neopentyl diazoacetate **2.03f** (100 mg, 0.641 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* 97:3 by GC-MS) was purified by flash chromatography (10% Et_2O in petrol) to afford the maleate **2.04f** (65.0 mg, 79%) as a yellow oil.

R*_f** = 0.48 (20% Et_2O in petrol); **IR** (neat): 2962s, 1729s, 1646m, 1479s, 1410s, 1393s, 1368s, 1217s, 1165s; **δ_H** (400 MHz, $CDCl_3$) = 6.27 (s, 2H, 2 × =CH), 3.88 (s, 4H, 2 × CH_2), 0.95 (s, 18H, 2 × CMe_3); **δ_C** (100 MHz, $CDCl_3$) = 165.4 (2 × CO_2), 129.7 (2 × =CH), 74.6 (2 × CH_2), 31.3 (2 × *C*Me_3), 26.4 (2 × C*Me*$_3$); ***m/z (CI): 187 (10%), 257 (M + H^+,10), 274 (M + NH_4^+, 100); HRMS: M + H^+ found 257.1751, $C_{14}H_{25}O_4$ requires 257.1753.

Diisopropyl maleate, 2.04g[16]



2.04g prepared following the general procedure using isopropyl diazoacetate **2.03g** (54.0 mg, 0.422 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* 97:3 by GC-MS) was purified by flash chromatography (5% Et_2O in petrol) to afford the maleate **2.04g** (40.0 mg, 95%) as a yellow liquid.

R*_f** = 0.43 (30% Et_2O in petrol); **IR** (neat): 2983s, 1726s, 1624m, 1469w, 1402m, 1219s, 1105s; **δ_H** (400 MHz, $CDCl_3$) = 6.19 (s, 2H, 2 × =CH), 5.12 (heptet, 2H, *J* = 6.2, 2 × CH), 1.30 (d, 12H, *J* = 6.3, 4 × CH_3); **δ_C** (100 MHz, $CDCl_3$) = 164.8 (2 × CO_2), 129.8 (2 × =CH), 68.9 (2 × OCH_2), 21.7 (2 × CH_3); ***m/z (CI): 201 (M + H^+, 100%), 203 (65), 218 (M + NH_4^+, 30), 220 (85); HRMS: M + H found 201.1119, $C_{10}H_{17}O_4$ requires 201.1121.

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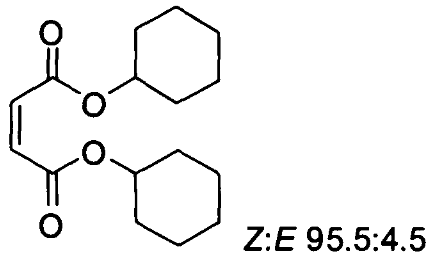
[15] J. W. Larsen, D. Lee, *Energy Fuels* **2006**, *20*, 257–261.

[16] A. Goti, S. Cicchi, M. Cacciarini, F. Cardona, V. Fedi, A. Brandi, *Eur. J. Org. Chem.* **2000**, 3633–3645.

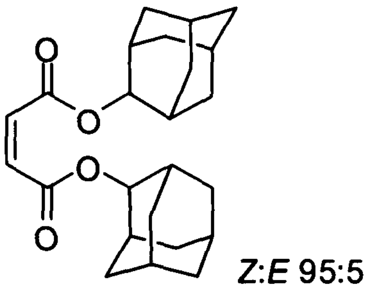
Dicyclohexyl maleate, 2.04h[17]



2.04h was prepared following the general procedure using cyclohexyl diazoacetate **2.03h** (70.0 mg, 0.417 mmol) in CH_2Cl_2 (3 mL). The residue (*Z*:*E* 95.5:4.5 by GC-MS) was purified by flash chromatography (10% Et_2O in petrol) to afford the maleate **2.04h** (48.0 mg, 82%) as a colourless oil.

R*f** = 0.51 (30% Et_2O in petrol); **IR** (neat): 2938s, 2860s, 1726s, 1644s, 1452s, 1401s, 1366s, 1213s, 1167s; δ_H (400 MHz, $CDCl_3$) = 6.20 (s, 2H, 2 × =CH), 4.82–4.92 (m, 2H, 2 × CH), 1.88–1.92 (m, 4H, 2 × CH_2), 1.80–1.70 (m, 4H, 2 × CH_2), 1.60–1.52 (m, 2H, 2 × CH of CH_2), 1.52–1.30 (m, 8H, 4 × CH_2), 1.30–1.20 (m, 2H, 2 × CH of CH_2); δ_C (100 MHz, $CDCl_3$) = 164.8 (2 × CO_2), 129.9 (2 × =CH), 73.8 (2 × CH), 31.4, 25.3 and 23.8 (10 × CH_2 cyclohexyl); ***m/z (CI): 281 (M + H^+, 100%), 298 (M + NH_4^+, 35), 300 (15); HRMS: M + H^+ found 281.1749, $C_{16}H_{25}O_4$ requires 281.1747.

Di-2-adamantyl maleate, 2.04i[18]



2.04i was prepared following the general procedure starting from 2-adamantyl diazoacetate **2.03i** (95.0 mg, 0.432 mmol) in CH_2Cl_2 (3 mL). The residue (*Z*:*E* 95:5 by GC-MS) was purified by flash chromatography (5% Et_2O in petrol) to afford the maleate **2.04i** (62.0 mg, 75%) as a yellow liquid.

***R*f** = 0.54 (30% Et_2O in petrol); **IR** (neat): 2912s, 2858s, 1719s, 1642w, 1453s, 1402s, 1382m, 1365w, 1215s, 1169s, 1101s; δ_H (400 MHz, $CDCl_3$) = 6.26 (s, 2H, 2 × =CH), 5.05 (t, 2H, $J = 3.5$, 2 × OCH), 2.06–1.99 (m, 8H, 4 × CH_2), 1.87–1.74 (m, 16H, 6 × CH and 5 × CH_2), 1.61–1.54 (m, 4H, 2 × CH and CH_2); δ_C (100 MHz, $CDCl_3$) = 164.8 (2 × CO_2), 129.9 (2 × =CH), 78.2 (2 ×

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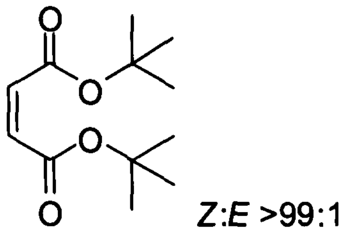
[17] H. Yamashita, T. Mukaiyama, *Chem. Lett.* **1985**, *3*, 363–366.

[18] A. M. Polyakova, Yu. G. Gololobov, M. D. Suchkova, K. A. Mager, N. G. Senchenya, T. I. Guseva, *Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya* **1986**, *12*, 2808–2809.

OCH), 37.3, 2 × 36.3 and 2 × 31.6 (10 × CH_2), 2 × 31.7, 27.2 and 26.9 (8 × CH); ***m/z*** (CI): 135 (40%), 152 (38), 385 (M + H^+, 100), 402 (M + NH_4^+, 10); HRMS: M + H^+ found 385.2384, $C_{24}H_{33}O_4$ requires 385.2379.

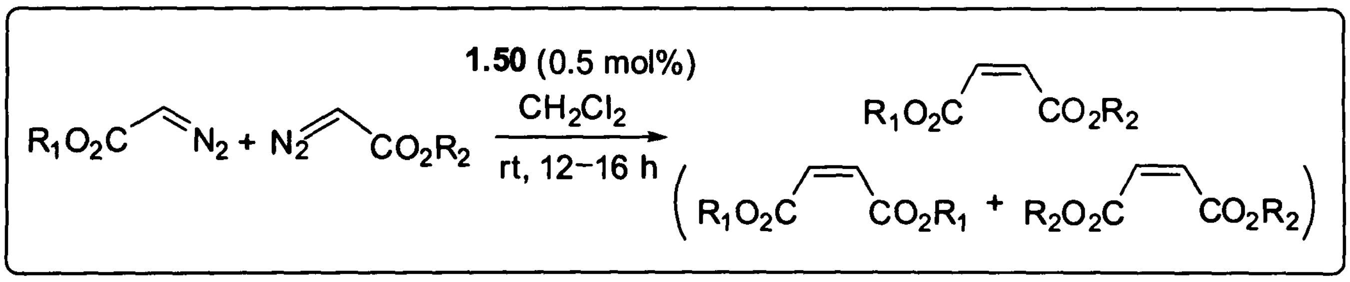
Di-*tert*-butyl maleate, 2.04j[19]



2.04j was prepared following the general procedure using *tert*-butyl diazoacetate **2.03j** (0.10 mL, 0.722 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* >99:1 by GC-MS) was purified by flash chromatography (10% Et_2O in petrol) to afford the maleate **2.04j** (82.0 mg, quant.) as a yellow oil.

R*f** = 0.44 (20% Et_2O in petrol); **IR** (neat): 2935s, 1721s, 1642m, 1478m, 1395s, 1370s, 1217s, 1144s; **δ_H** (400 MHz, $CDCl_3$) = 6.06 (s, 2H, 2 × =CH), 1.54 (s, 18H, 2 × CMe_3); **δ_C** (100 MHz, $CDCl_3$) = 164.5 (2 × CO_2), 130.1 (2 × =CH), 81.8 (2 × *C*Me_3), 28.0 (2 × C*Me*$_3$); ***m/z (CI): 190 (100%), 192 (70), 229 (M + H^+, 15); HRMS: M + H^+ found 229.1437, $C_{12}H_{21}O_4$ requires 229.1434.

5.4. Hetero-coupling of α-Diazoacetates



General procedure: Grubbs' 2nd generation catalyst **1.50** (0.005 equiv., 0.5 mol%) was added to a solution of mixture of diazoacetates (1.0 equiv. each) in CH_2Cl_2. The reaction mixture was stirred at room temperature for 12–16 h, concentrated under reduced pressure and purified by flash chromatography.

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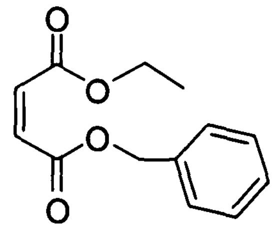
[19] Y. Iwasawa, K. Nonoshita, K. Tomimoto, *Tetrahedron Lett.* **1995**, *36*, 7459–62.

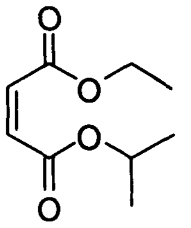
Benzyl ethyl maleate, 2.05a[20]



Z:*E* 98:2

2.05a was prepared following the general procedure using ethyl diazoacetate **2.03a** (43.5 μL, 0.414 mmol) and benzyl diazoacetate **2.03e** (73.0 mg, 0.414 mmol) in CH_2Cl_2 (5 mL). The crude mixture was analysed by GC-MS. The reaction mixture comprised of inseparable mixture of benzyl ethyl maleate **2.05a** (*Z*:*E* 98:2), diethyl maleate **2.04a** and dibenzyl maleate **2.04e** in 63:18:18 ratio.

Ethyl isopropyl maleate, 2.05b



Z:*E* 98:2

2.05b was prepared following the general procedure using ethyl diazoacetate **2.03a** (36.5 mg, 0.320 mmol) and isopropyl diazoacetate **2.03g** (41.0 mg, 0.320 mmol) in CH_2Cl_2 (4.5 mL). The residue (*Z*:*E* 98:2 by GC-MS) was purified by flash chromatography (5% Et_2O in petrol) to afford the maleate **2.05b** (25.0 mg, 42%) as a colourless liquid.

$\boldsymbol{R}_f$ = 0.44 (30% Et_2O in petrol); **IR** (neat): 2980s, 1708s, 1646s, 1450m, 1390s, 1210s, 1141s; $\boldsymbol{\delta}_H$ (400 MHz, $CDCl_3$) = 6.22 (s, 2H, 2 × =CH), 5.13 (heptet, 1H, *J* = 6.3, C*H*Me$_2$), 4.25 (q, 2H, *J* = 7.2, OCH_2), 1.36–1.26 (m, 9H, 3 × CH_3); $\boldsymbol{\delta}_C$ (100 MHz, $CDCl_3$) = 165.3 and 164.8 (2 × CO_2), 130.2 and 129.4 (2 × =CH), 68.9 (CH), 61.2 (OCH_2), 21.7 (C*Me*$_2$) 14.0 (CH_2CH_3); ***m/z*** (CI): 70 (40%), 87 (38), 131 (65), 187 (M + H^+, 100), 204 (M + NH_4^+, 15); HRMS: M + H^+ found 187.0977, $C_9H_{15}O_4$ requires 187.0970.

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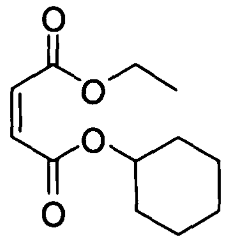
[20] E. Dziwinski, J. Hetper, *J. Chromatogr.* **1986**, *367*, 201–206.

Ethyl cyclohexyl maleate, 2.05c

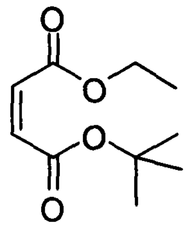


Z:*E* >99:1

2.05c was prepared following the general procedure using ethyl diazoacetate **2.03a** (15.0 mg, 0.131 mmol) and cyclohexyl diazoacetate **2.03h** (22.0 mg, 0.131 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* >99:1 by GC-MS) was purified by flash chromatography (5→10% Et_2O in petrol) to afford the maleate **2.05c** (17.0 mg, 57%) as a yellow liquid.

R_f = 0.46 (30% Et_2O in petrol); **IR** (neat): 2900s, 2846m, 1725s, 1640s, 1457m, 1403m, 1210s, 1164s; δ_H (400 MHz, $CDCl_3$) = 6.22 (s, 2H, 2 × =CH), 4.91–4.84 (m, 1H, OCH), 4.25 (q, 2H, J = 7.1, OCH_2), 1.94–1.90 (m, 2H, CH_2 cyclohexyl), 1.77–1.72 (m, 2H, CH_2 cyclohexyl), 1.62–1.54 (m, 2H, CH_2 cyclohexyl), 1.32 (t, 3H, J = 7.1, CH_3), 1.50–1.21 (m, 4H, 2 × CH_2 cyclohexyl); δ_C (100 MHz, $CDCl_3$) = 165.3 and 164.8 (2 × CO_2), 130.2 and 129.4 (2 × =CH), 73.9 (OCH), 61.2 (OCH_2), 31.4, 25.3 and 23.7 (3 × CH_2 cyclohexyl), 14.0 (CH_3); ***m/z*** (CI): 145 (53%), 162 (25), 227 (M + H^+, 100), 244 (M + NH_4^+, 10); HRMS: M + NH_4^+ found 244.1545, $C_{12}H_{22}NO_4$ requires 244.1549.

tert-Butyl ethyl maleate, 2.05d

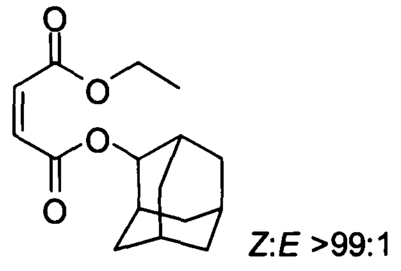


Z:*E* >99:1

2.05d was prepared following the general procedure using ethyl diazoacetate **2.03a** (76.0 µL, 0.722 mmol) and *tert*-butyl diazoacetate **2.03j** (100 µL, 0.722 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* >99:1 by GC-MS) was purified by flash chromatography (5% Et_2O in petrol) to afford the maleate **2.05d** (61.0 mg, 42%) as a yellow liquid.

R_f = 0.35 (20% Et_2O in petrol); **IR** (neat): 2982s, 1728s, 1640s, 1458m, 1397s, 1369s, 1218s, 1151s; δ_H (400 MHz, $CDCl_3$) = 6.13 (d, 2H, J = 3.6, 2 × =CH), 4.25 (q, 2H, J = 7.1, OCH_2), 1.51 (s, 9H, CMe_3), 1.31 (t, 3H, J = 7.1, CH_2CH_3); δ_C (100 MHz, $CDCl_3$) = 165.3 and 164. 4 (2 × CO_2), 131.4 and 128.3 (2 × =CH), 82.2 (CMe_3), 61.0 (OCH_2), 27.9 (CMe_3), 14.1 (CH_2CH_3); ***m/z*** (CI): 104 (30%), 162 (100), 164 (85), 201 (M + H^+, 35), 203 (15), 220 (M + NH_4^+, 55); HRMS: M + H^+ found 201.1122, $C_{10}H_{17}O_4$ requires 201.1121.

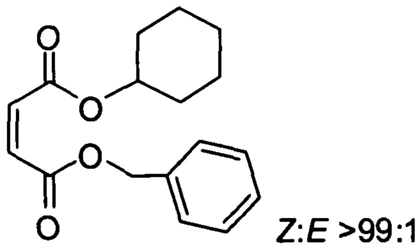
2-Adamantyl ethyl maleate, 2.05e



2.05e was prepared following the general procedure using ethyl diazoacetate **2.03a** (13.0 μL, 0.123 mmol) and 2-adamantyl diazoacetate **2.03i** (27.0 mg, 0.123 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* >99:1 by GC-MS) was purified by flash chromatography (5% Et_2O in petrol) to afford the maleate **2.05e** (15.0 mg, 44%) as a yellow liquid.

R*f** = 0.48 (30% Et_2O in petrol); **IR** (neat): 2908s, 2856m, 1728s, 1642s, 1453m, 1403m, 1209s, 1164s, 1101w; **δ_H** (400 MHz, $CDCl_3$) = 6.25 (d, 2H, *J* = 8.1, 2 × =CH), 5.06 (t, 1H, *J* = 3.2, OCH), 4.25 (q, 2H, *J* = 7.1, OCH_2), 2.07–1.99 (m, 4H, 2 × CH_2), 1.90–1.74 (m, 6H, 2 × CH and 2 × CH_2), 1.60–1.56 (m, 4H, 2 × CH and CH_2), 1.31 (t, 3H, *J* = 7.1, CH_3); δ_C (100 MHz, $CDCl_3$) = 165.4 and 164.7 (2 × CO_2), 130.2 and 129.5 (2 × =CH), 78.3 (OCH), 61.2 (OCH_2), 37.3, 2 × 36.3 and 2 × 31.7 (5 × CH_2 adamantyl), 2 × 31.6, 27.1 and 26.9 (4 × CH adamantyl), 14.0 (CH_3); ***m/z (CI): 148 (80%), 152 (20), 279 (M + H^+, 100), 296 (M + NH_4^+, 10); HRMS: M + H^+ found 279.1592, $C_{16}H_{23}O_4$ requires 279.1596.

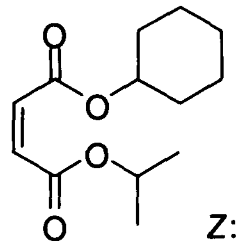
Benyl cyclohexyl maleate, 2.05f



2.05f was prepared following the general procedure using benzyl diazoacetate **2.03e** (29.4 mg, 0.167 mmol) and cyclohexyl diazoacetate **2.03h** (28.0 mg, 0.167 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* >99:1 by GC-MS) was purified by flash chromatography (10% Et_2O in petrol) to afford the maleate **2.05f** (24.0 mg, 50%) as a yellow liquid.

R*f** = 0.47 (30% Et_2O in petrol); **IR** (neat): 2939s, 2869s, 1728s, 1643m, 1598s, 1454s, 1401m, 1365m, 1214s, 1164s, 1037m; **δ_H** (400 MHz, $CDCl_3$) = 7.40–7.30 (m, 5H, Ar), 6.25 (d, 2H, *J* = 6.0, 2 × =CH), 5.22 (s, 2H, CH_2Ar), 4.89–4.77 (m, 1H, C(1)H cyclohexyl), 1.91–1.83 (m, 2H, CH_2 cyclohexyl), 1.78–1.68 (m, 2H, CH_2 cyclohexyl), 1.59–1.49 (m, 2H, CH_2 cyclohexyl), 1.44–1.18 (m, 4H, 2 × CH_2 cyclohexyl); δ_C (100 MHz, $CDCl_3$) = 165.1 and 164.7 (2 × CO_2), 135.2 (Ar, quat.), 131.0 (=CH), 128.7, 128.6, 128.5 and 128.4 (3 × Ar and =CH), 74.1 (OCH), 67.1 (OCH_2), 31.4, 25.3 and 23.8 (3 × CH_2 cyclohexyl); ***m/z (CI): 148 (75%), 289 (M + H^+, 35), 306 (M + NH_4^+, 100); HRMS: M + NH_4^+ found 306.1703, $C_{17}H_{24}NO_4$ requires 306.1705.

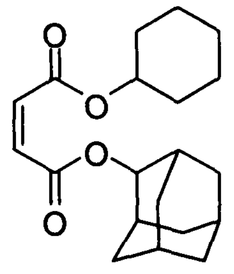
Cyclohexyl isopropyl maleate, 2.05g



Z:*E* >99:1

Following the general procedure using cyclohexyl diazoacetate **2.03h** (26.0 mg, 0.156 mmol) and isopropyl diazoacetate **2.03g** (20.0 mg, 0.156 mmol) in CH_2Cl_2 (5 mL). The crude mixture was analysed by ^{1}H-NMR. The reaction mixture comprised of inseparable mixture of cyclohexyl isopropyl maleate **2.05g** (*Z*:*E* >99:1), dicyclohexyl maleate **2.04h** and diisopropyl maleate **2.04g** in 52:24:24 ratio.

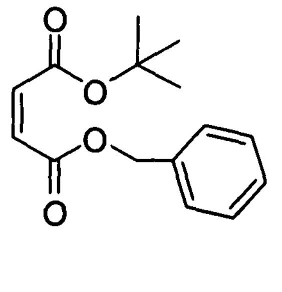
2-Adamantyl cyclohexyl maleate, 2.05h



Z:*E* >99:1

Following the general procedure using 2-adamantyl diazoacetate **2.03i** (28.0 mg, 0.127 mmol) and cyclohexyl diazoacetate **2.03h** (21.0 mg, 0.127 mmol) in CH_2Cl_2 (5 mL). The crude mixture was analysed by ^{1}H-NMR. The reaction mixture comprised of inseparable mixture of 2-adamantyl cyclohexyl maleate **2.05h** (*Z*:*E* >99:1), di-2-adamantyl maleate **2.04i** and dicyclohexyl maleate **2.04h** in 48:19:33 ratio.

Benzyl *tert*-butyl maleate, 2.05i

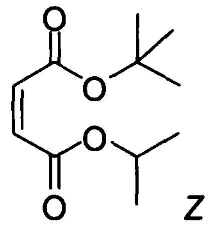


Z:*E* 97:3

2.05i was prepared following the general procedure using benzyl diazoacetate **2.03e** (60.0 mg, 0.341 mmol) and *tert*-butyl diazoacetate **2.03j** (47.0 µL, 0.341 mmol) in CH_2Cl_2 (5 mL). The residue (*Z*:*E* 97:3 by GC-MS) was purified by flash chromatography (5% Et_2O in petrol) to afford the maleate **2.05i** (40.0 mg, 45%) as a yellow liquid.

R**f** = 0.69 (30% Et_2O in petrol); **IR** (neat): 2980s, 1727s, 1641m, 1498m, 1456s, 1397s, 1213s, 1149s; **δH** (400 MHz, $CDCl_3$) = 7.40–7.30 (m, 5H, Ar), 6.19 (d, 2H, *J* = 2.7, 2 × =CH), 5.23 (s, 2H, OCH_2), 1.49 (s, 9H, CMe_3); **δC** (100 MHz, $CDCl_3$) = 165.1 and 164.3 (2 × CO_2), 135.3 (Ar, quat.), 135.0 and 127.8 (2 × =CH), 128.6, 128.5 and 127.4 (3 × Ar), 82.3 (CMe_3), 66.8 (OCH_2), 27.9 (CMe_3); ***m/z*** (CI): 224 (100%), 226 (20), 263 ($M + H^+$, 15), 280 ($M + NH_4^+$, 15); HRMS: $M + H^+$ found 263.1280, $C_{15}H_{19}O_4$ requires 263.1278.

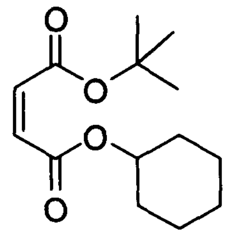
tert-Butyl isopropyl maleate, 2.05j[21]



Z:*E* >99:1

Following the general procedure using isopropyl diazoacetate **2.03g** (53.0 mg, 0.414 mmol) and *tert*-butyl diazoacetate **2.03j** (57.0 μL, 0.414 mmol) in CH_2Cl_2 (5 mL). The crude mixture was analysed by GC. The reaction mixture comprised of inseparable mixture of *tert*-butyl isopropyl maleate **2.05j** (*Z*:*E* >99:1), diisopropyl maleate **2.04g** and di-*tert*-butyl maleate **2.04j** in 50:25:25 ratio.

tert-Butyl cyclohexyl maleate, 2.05k



Z:*E* >99:1

Following the general procedure using cyclohexyl diazoacetate **2.03h** (26.0 mg, 0.155 mmol) and *tert*-butyl diazoacetates **2.03j** (21.4 μL, 0.155 mmol) in CH_2Cl_2 (5 mL). The crude mixture was analysed by ^{1}H-NMR. The reaction mixture comprised of inseparable mixture of *tert*-butyl cyclohexyl maleate **2.05k** (*Z*:*E* >99:1), dicyclohexyl maleate **2.04h** and di-*tert*-butyl maleate **2.04j** in 50: 35:15 ratio.

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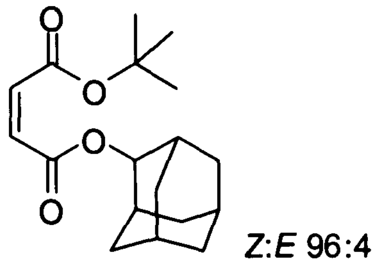
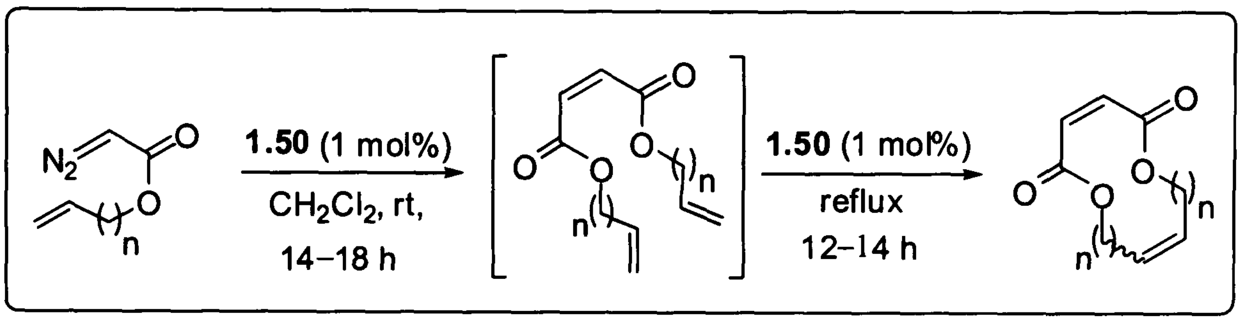
[21] T. Otsu, M. Yoshioka, T. Sunagawa, *J. Polym. Sci., Part A: Polym. Chem.* **1992**, *30*, 1347–1354.

2-Adamantyl *tert*-butyl maleate, 2.05l



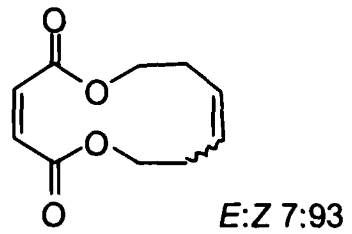
Following the general procedure using 2-adamantyl diazoacetate **2.03i** (67.0 mg, 0.304 mmol) and *tert*-butyl diazoacetate **2.03j** (42.0 μL, 0.304 mmol) in CH_2Cl_2 (10 mL). The crude mixture was analysed by ^{1}H-NMR. The reaction mixture comprised of inseparable mixture of 2-adamantyl *tert*-butyl maleate **2.05l** (*Z*:*E* 96:4), di-2-adamantyl maleate **2.04i** and di-*tert*-butyl maleate **2.04j** in 50:25:25 ratio.

5.5. Macrocyclic Dilactones from Alkenyl Diazoacetates



General procedure: Grubbs' 2nd generation catalyst **1.50** (0.01 equiv., 1 mol%) was added to a solution of diazoacetate (1.0 equiv.) in CH_2Cl_2 and the mixture was stirred at room temperature for 14–18 h. Further catalyst **1.50** (0.01 equiv., 1 mol%) and, in some cases, CH_2Cl_2 was added, and the reaction mixture was then refluxed for 12–14 h. The mixture was concentrated under reduced pressure and purified by flash chromatography.

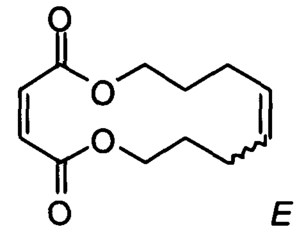
1,6-Dioxa-cyclododeca-3,9-diene-2,5-dione, 2.08a



2.08a was prepared following the general procedure using but-3-enyl diazoacetate **2.06a** (50.0 mg, 0.357 mmol) in CH_2Cl_2 (5 + 66 mL). The residue was purified by flash chromatography (5→10% Et_2O in petrol) to afford the dilactone **2.08a** (17.0 mg, 49%, *E*:*Z* 7:93 by GC-MS) as a yellow liquid.

R*$_f$** = 0.22 (30% Et$_2$O in petrol); **IR** (neat): 2962w, 2254s, 1794s, 1382w, 1261m, 1100s; δ_H (400 MHz, CDCl$_3$) ***Z*-isomer** = 6.18 (s, 2H, 2 × =CHCO), 5.62–5.54 (m, 2H, 2 × =C*H*CH$_2$), 4.28–4.25 (m, 4H, 2 × OCH$_2$), 2.54–2.49 (m, 4H, 2 × =CHC*H*$_2$); discernible data for ***E*-isomer** = 6.16 (s, 2H, 2 × =CHCO), 5.42–5.39 (m, 2H, 2 × =C*H*CH$_2$), 2.44–2.40 (m, 4H, 2 × =CHC*H*$_2$); δ_C (100 MHz, CDCl$_3$) ***Z*-isomer** = 165.1 (2 × CO$_2$), 128.7 and 128.6 (4 × =CH), 64.8 (2 × OCH$_2$), 26.4 (2 × =CH*C*H$_2$); discernible data for ***E*-isomer** = 129.2 (2 × =CH), 63.3 (2 × OCH$_2$), 32.5 (2 × =CH*C*H$_2$); ***m/z (CI): 197 (M + H$^+$, 30%), 214 (M + NH$_4^+$, 100), 215 (10); HRMS: M + H$^+$ found 197.0816, $C_{10}H_{13}O_4$ requires 197.0814.

1,6-Dioxa-cyclotetradeca-3,10-diene-2,5-dione, 2.08b

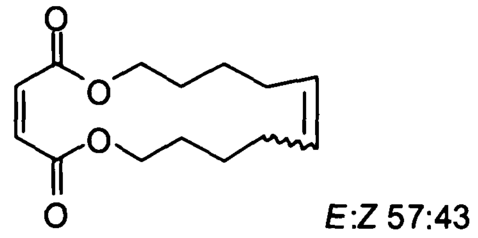


E:*Z* 30:70

2.08b was prepared following the general procedure using pent-4-enyl diazoacetate **2.06b** (53.0 mg, 0.344 mmol) in CH$_2$Cl$_2$ (5 mL). The residue was purified by flash chromatography (5→10% EtOAc in hexane) to afford dilactone **2.08b** (20.0 mg, 53%, *E*:*Z* 30:70 by GC-MS) as a yellow liquid.

R*$_f$** = 0.45 (50% EtOAc in hexane); **IR** (neat): 2401s, 1725s, 1297m, 1216s; δ_H (400 MHz, CDCl$_3$) ***Z*-isomer** = 6.24 (s, 2H, 2 × =CHCO), 5.48–5.38 (m, 2H, 2 × =C*H*CH$_2$), 4.18–4.15 (m, 4H, 2 × OCH$_2$), 2.16–2.26 (m, 4H, 2 ×=CHC*H*$_2$), 1.70–1.76 (m, 4H, 2 × =CHCH$_2$C*H*$_2$); discernible data for ***E*-isomer** = 6.24 (s, 2H, 2 × =CH), 4.23–4.21 (m, 4H, 2 × OCH$_2$), 1.76–1.84 (m, 4H, 2 × =CHCH$_2$C*H*$_2$); δ_C (100 MHz, CDCl$_3$) ***Z*-isomer** = 165.3 (2 × CO$_2$), 129.6 (2 × =CH), 129.4 (2 × =CH), 63.9 (2 × OCH$_2$), 27.7 (2 × =CH*C*H$_2$), 22.8 (2 × OCH$_2$*C*H$_2$); discernible data for ***E*-isomer** = 165.2 (2 × CO$_2$), 130.3 and 129.6 (4 × =CH), 64.9 (2 × OCH$_2$), 30.2 (2 × =CH*C*H$_2$), 27.2 (2 × OCH$_2$*C*H$_2$); ***m/z (CI): 93 (15%), 109 (15), 225 (M + H$^+$, 100), 242 (M + NH$_4^+$, 25); HRMS: M + H$^+$ found 225.1129, $C_{12}H_{17}O_4$ requires 225.1127.

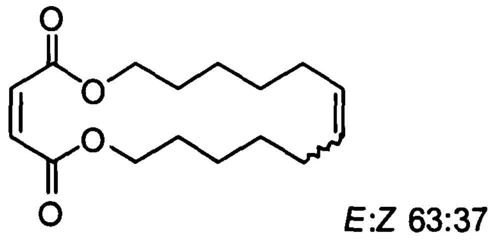
1,6-Dioxa-cyclohexadeca-3,11-diene-2,5-dione, 2.08c



2.08c was prepared following the general procedure using hex-5-enyl diazoacetate **2.06c** (50.0 mg, 0.297 mmol) in CH_2Cl_2 (4 + 55 mL). The residue was purified by flash chromatography (15% Et_2O in petrol) to afford dilactone **2.08c** (16.0 mg, 43%, *E*:*Z* 57:43 by GC-MS) as a pale yellow liquid.

R*f** = 0.35 (30% Et_2O in petrol); **IR** (neat): 2400w, 1724s, 1216s; **δH** (400 MHz, $CDCl_3$) ***E*-isomer** = 6.22 (s, 2H, 2 × =CHCO), 5.38–5.35 (m, 2H, 2 × =C*H*CH_2), 4.17 (t, 4H, *J* = 7.4, 2 × OCH_2), 2.02–2.14 (m, 4H, 2 × =CHCH_2), 1.70–1.64 (m, 4H, 2 × OCH_2CH_2), 1.48–1.38 (m, 4H, 2 × =$CHCH_2CH_2$); discernible data for ***Z*-isomer** = 6.23 (s, 2H, 2 × =CHCO), 5.43–5.34 (m, 2H, 2 × =C*H*CH_2), 4.19 (t, 4H, *J* = 6.7, 2 × OCH_2), 1.76–1.71 (m, 4H, 2 × OCH_2CH_2); **δC** (100 MHz, $CDCl_3$) ***E*-isomer** = 165.2 (2 × CO_2), 131.1 and 129.5 (4 × =CH), 65.2 (2 × OCH_2), 31.4 (2 × =CHCH_2), 26.8 (2 × OCH_2CH_2), 24.2 (2 × =$CHCH_2CH_2$); discernible data for ***Z*-isomer** = 165.3 (2 × CO_2), 129.8 and 129.5 (4 × =CH), 64.7 (2 × OCH_2), 27.4 (2 × =$CHCH_2$), 26.2 and 25.2 (4 × CH_2); ***m/z (CI): 137 (15%), 253 (M + H^+, 100), 270 (M + NH_4^+, 15); HRMS: M + H^+ found 253.1448, $C_{14}H_{21}O_4$ requires 253.1440.

1,6-Dioxa-cyclooctadeca-3,12-diene-2,5-dione, 2.08d

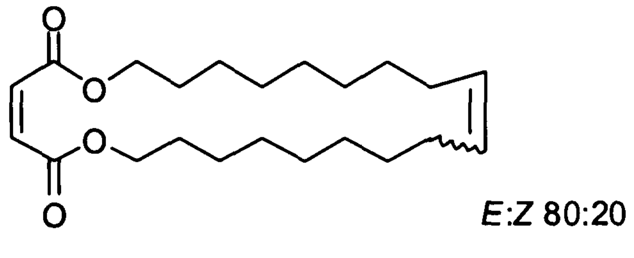


2.08d was prepared following the general procedure using hept-6-enyl diazoacetate **2.06d** (50.0 mg, 0.275 mmol) in CH_2Cl_2 (4 + 51 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the dilactone **2.08d** (16.0 mg, 42%, *E*:*Z* 63:37 by GC-MS) as a pale yellow liquid.

***R*f** = 0.40 (20% Et_2O in petrol); **IR** (neat): 2920s, 2254m, 1720s, 1450w, 1216s; **δH** (400 MHz, $CDCl_3$) ***E*-isomer** = 6.23 (s, 2H, 2 × =CHCO), 5.34 (t, 2H, *J* = 4.1, 2 × =C*H*CH_2), 4.10–4.26 (m, 4H, 2 × OCH_2), 2.10–1.96 (m, 4H, 2 × =CHCH_2), 1.72–1.58 (m, 4H, 2 × OCH_2CH_2), 1.50–1.22 (m, 8H, 2 × =$CHCH_2CH_2CH_2$); **δC** (100 MHz, $CDCl_3$) ***E*-isomer** = 165.4 (2 × CO_2), 130.8 and 129.6 (4 × =CH), 65.5 (2 × OCH_2), 32.1 (2 × =$CHCH_2$), 28.6, 28.4 and 25.0 (6 × CH_2);

discernible data for **Z-isomer** = 165.3 (2 × CO_2), 129.9 (2 × =CH), 65.3 (2 × OCH_2), 28.7, 28.2, 25.6 and 24.8 (8 × CH_2); ***m/z*** (CI): 95 (10%), 281 ($M + H^+$, 100), 298 ($M + NH_4^+$, 25); HRMS: $M + H^+$ found 281.1758, $C_{16}H_{25}O_4$ requires 281.1753.

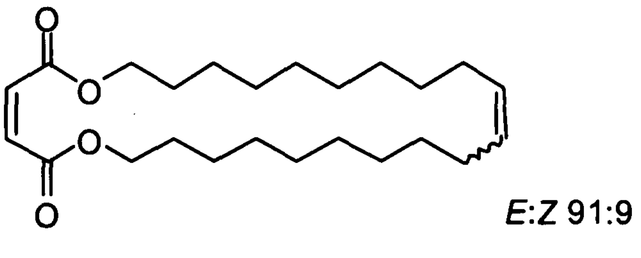
1,6-Dioxa-cyclotetracosa-3,15-diene-2,5-dione, 2.08e



2.08e was prepared following the general procedure using dec-9-enyl diazoacetate **2.06e** (174 mg, 0.777 mmol) in CH_2Cl_2 (25 mL). The residue was purified by flash chromatography (5→10% EtOAc in hexane) to afford the dilactone **2.08e** (68.0 mg, 48%, *E*:*Z* 80:20 from GC-MS) as a pale yellow liquid.

R*f** = 0.52 (30% EtOAc in hexane); **IR** (neat): 2929s, 2857s, 2254m, 1724s, 1466w, 1216s; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 6.23 (s, 2H, 2 × =CHCO), 5.32–5.30 (m, 2H, 2 × =C*H*CH_2), 4.15 (t, 4H, *J* = 7.2, 2 × OCH_2), 2.02–1.92 (m, 4H, 2 × =CHC*H*$_2$), 1.60–1.72 (m, 4H, 2 × OCH_2C*H*$_2$), 1.20–1.44 (m, 20H, 10 × CH_2); discernible data for **Z-isomer** = 6.28 (s, 2H, 2 × =CHCO), 5.38–5.34 (m, 2H, 2 × =C*H*CH_2); δ_C (100 MHz, $CDCl_3$) ***E*-isomer** = 165.3 (2 × CO_2), 130.9 and 129.5 (4 × =CH), 65.4 (2 × OCH_2), 32.1 (2 × =CH*C*H_2), 29.4, 29.2, 28.8, 28.5, 28.1 and 25.5 (12 × CH_2); discernible data for **Z-isomer** = 129.9 and 125.2 (4 × =CH), 65.5 (2 × OCH_2), 29.4, 29.3, 29.1, 26.8 and 25.7 (10 × CH_2); ***m/z (CI): 70 (48%), 148 (48), 365 ($M + H^+$, 100), 382 ($M + NH_4^+$, 50); HRMS: $M + H^+$ found 365.2697 $C_{22}H_{37}O_4$ requires 365.2692.

1,6-Dioxa-cyclohexacosa-3,16-diene-2,5-dione, 2.08f

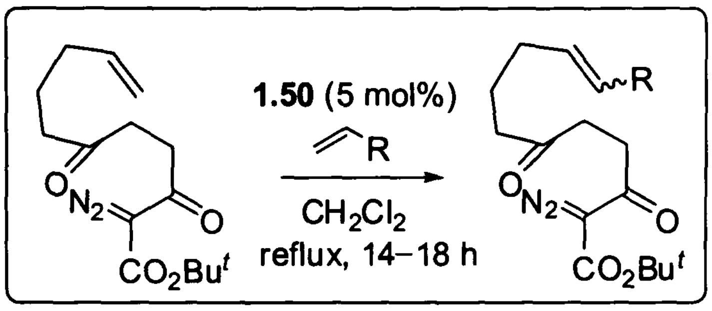


2.08f was prepared following the general procedure using undec-10-enyl diazoacetate **2.06f** (46.0 mg, 0.193 mmol) in CH_2Cl_2 (3 + 35 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the dilactone **2.08f** (21.0 mg, 55%, *E*:*Z* 91:9 from GC-MS) as a yellow liquid.

***R*f** = 0.38 (20% Et_2O in petrol); **IR** (neat): 2929s, 2254s, 1723s, 1468w, 1216s; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 6.23 (s, 2H, 2 × =CHCO), 5.36–5.40 (m, 2H, 2 × =C*H*CH_2), 4.18 (t, 4H, *J* =

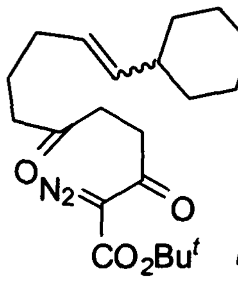
6.8, 2 × OCH_2), 2.00–1.86 (m, 4H, 2 × $=CHCH_2$), 1.60–1.72 (m, 4H, 2 × OCH_2CH_2), 1.20–1.32 (m, 24H, 12 × CH_2); discernible data for **Z-isomer** = 5.35 (t, 2H; *J* = 5.3, 2 × $=CHCH_2$), 4.14–4.08 (t, 4H, *J* = 4.8, 2 × OCH_2), 2.06–2.01 (m, 4H, 2 × $=CHCH_2$); δ_C (100 MHz, $CDCl_3$) ***E*-isomer** = 165.4 (2 × CO_2), 130.2 and 129.8 (4 × =CH), 65.5 (2 × OCH_2), 32.6 (2 × $=CHCH_2$), 29.7, 29.5, 29.4, 29.2, 29.1, 28.4 and 25.8 (14 × CH_2); discernible data for ***Z*-isomer** = 129.8 (2 × =CH), 27.2 (2 × CH_2); ***m/z*** (CI): 70 (15%), 393 (M + H^+, 100); HRMS: M + H^+ found 393.3007, $C_{24}H_{41}O_4$ requires 393.3005.

5.6. Cross Metathesis of a-Diazo-β-ketoester 3.14



General procedure: Grubbs 2nd generation catalyst **1.50** (5 mol%) was added to a solution of *tert*-butyl 2-diazo-3,6-dioxo-10-undecenoate **3.14**[22] (1.0 equiv.) and olefin (5–10 equiv.) in CH_2Cl_2 (*c* = 15–20 mM). The mixture was heated under reflux for 14–18 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure and purified by flash chromatography.

tert-Butyl 11-cyclohexyl-2-diazo-3,6-dioxoundec-10-enoate, 3.22a



E:*Z* 85:15

3.22a was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and vinylcyclohexane (186 μL, 1.36 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the diazoester **3.22a** (40.0 mg, 78%, *E*:*Z* 85:15 from ^1H NMR) as a pale yellow oil.

***R*f** = 0.51 (30% Et_2O in petrol); **IR** (neat): 2928s, 2853m, 2401s, 2254s, 2137s, 1709s, 1647s, 1371s, 1316s, 1216s, 1136m; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 5.38–5.18 (m, 2H, 2 × =CH),

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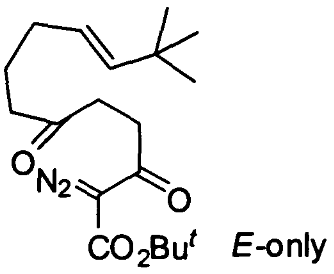
[22] D. M. Hodgson, P. A. Stupple, F. Y. T. M. Pierard, A. H. Labande, C. Johnstone, *Chem. Eur. J.* **2001**, *7*, 4465–4476.

3.08 and 2.70 (2 × t, 4H, J = 6.2, (CO)$_2$CH$_2$CH$_2$), 2.44 (t, 2H, J = 7.4, COCH$_2$), 2.02–1.94 (m, 2H, =CHC*H*$_2$), 1.92–1.80 (m, 1H, C(1)H cyclohexyl), 1.74–1.54 (m, 7H, COCH$_2$C*H*$_2$, 2 × CH$_2$ and CH of CH$_2$ cyclohexyl), 1.50 (s, 9H, CMe$_3$), 1.30–0.96 (m, 5H, 2 × CH$_2$ and CH of CH$_2$ cyclohexyl); discernible data for ***Z*-isomer** = 2.08–2.00 (m, 2H, =CHC*H*$_2$); **δ_C** (100 MHz, CDCl$_3$) ***E*-isomer** = 209.3 and 191.7 (2 × CO), 160.5 (CO$_2$), 137.5 and 126.5 (2 × =CH), 83.1 (*C*Me$_3$), 41.9, 40.6, 36.2, 34.2, 33.2, 31.9, 26.2, 26.1, 23.5 (8 × CH$_2$ and C(1)H cyclohexyl) and 28.3 (C*Me*$_3$); discernible data for ***Z*-isomer** = 136.9 and 126.8 (2 × =CH), 42.2, 36.0, 33.2, 25.9, 23.6 (5 × CH$_2$); ***m/z*** (CI): 330 (85%), 334 (95), 337 (60), 349 (60), 364 (50), 377 (M + H$^+$, 100); HRMS (ES+): M + H$^+$ found 377.2434, C$_{21}$H$_{33}$N$_2$O$_4$ requires 377.2435.

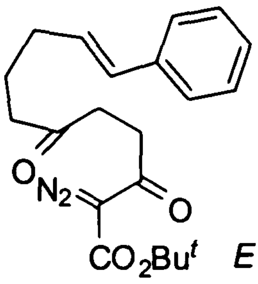
(*E*)-*tert*-Butyl 2-diazo-12,12-dimethyl-3,6-dioxotridec-10-enoate, 3.22b



3.22b was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and 3,3-dimethyl-1-butene (175 μL, 1.36 mmol) in CH$_2$Cl$_2$ (10 mL). The residue was purified by flash chromatography (10% Et$_2$O in petrol) to afford the diazoester **3.22b** (35.2 mg, 74%) as a yellow oil.

R*$_f$** = 0.43 (30% Et$_2$O in petrol); **IR** (neat): 2963s, 2873m, 2136s, 1720s, 1640w, 1383s, 1352w, 1112s; **δ_H** (400 MHz, CDCl$_3$) = 5.44 (dt, 1H, J = 15.4 and 1.3, =C*H*CMe$_3$), 5.25 (dt, 1H, J = 15.5 and 6.6, =C*H*CH$_2$), 3.09 and 2.73 (2 × t, 4H, J = 6.1, (CO)$_2$CH$_2$CH$_2$), 2.46 (t, 2H, J = 7.6, COCH$_2$), 2.02–1.95 (m, 2H, =CHC*H*$_2$), 1.65 (quintet, 2H, J = 7.4, COCH$_2$C*H*$_2$), 1.53 (s, 9H, OCMe$_3$), 0.98 (s, 9H, CMe$_3$); **δ_C** (100 MHz, CDCl$_3$) = 209.4 and 191.7 (2 × CO), 160.5 (CO$_2$), 142.5 (=*C*HCMe$_3$), 123.6 (=*C*HCH$_2$), 83.2 (O*C*Me$_3$), 42.0 (CO*C*H$_2$), 36.1 and 34.2 ((CO)$_2$*C*H$_2$*C*H$_2$), 32.8 (*C*Me$_3$), 31.9 (=CH*C*H$_2$), 29.7 (C*Me*$_3$), 28.3 (OC*Me*$_3$), 23.7 (COCH$_2$*C*H$_2$); ***m/z (CI): 312 (70%), 340 (40), 351 (M + H$^+$, 100), 368 (M + NH$_4^+$, 40); HRMS (ES+): M + H$^+$ found 351.2279, C$_{19}$H$_{31}$N$_2$O$_4$ requires 351.2278.

(*E*)-*tert*-Butyl 2-diazo-11-phenyl-3,6-dioxoundec-10-enoate, 3.22c

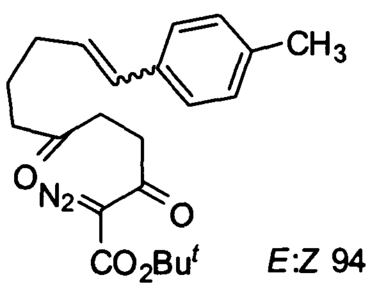


E-only

3.22c was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and styrene (156 μL, 1.36 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the diazoester **3.22c** (41.0 mg, 81%) as a yellow oil.

R*~f~** = 0.65 (50% Et_2O in petrol); **IR** (neat): 3019s, 2400m, 2253m, 2137s, 1708s, 1647s, 1523w, 1476w, 1371s, 1316s, 1215s, 1134s; δ_H (400 MHz, $CDCl_3$) = 7.36–7.24 (m, 4H, Ar), 7.20 (tt, 1H, *J* = 7.1 and 1.3, Ar), 6.39 (d, 1H, *J* = 15.8, =C*H*Ar), 6.17 (dt, 1H, *J* = 15.8 and 6.9, =C*H*CH_2), 3.10 and 2.72 (2 × t, 4H, *J* = 6.2, $(CO)_2CH_2CH_2$), 2.53 (t, 2H, *J* = 7.4, $COCH_2$), 2.25–1.99 (m, 2H, =$CHCH_2$), 1.79 (quintet, 2H, *J* = 7.4, $COCH_2CH_2$), 1.53 (s, 9H, CMe_3); δ_C (100 MHz, $CDCl_3$) = 209.1 and 191.6 (2 × CO), 160.5 (CO_2), 137.6 (Ar, quat.), 130.6 and 129.9 (2 × =CH), 128.4, 126.9 and 125.9 (3 × Ar), 83.1 (CMe_3), 41.9 ($COCH_2$), 36.2 and 34.3 ($(CO)_2CH_2CH_2$), 32.3 (=$CHCH_2$), 28.3 (CMe_3), 23.2 ($COCH_2CH_2$); ***m/z (CI): 306 (10%), 315 (30), 332 (100), 371 (M + H^+, 30), 388 (M + NH_4^+, 40); HRMS (ES+): M + NH_4^+ found 388.2229, $C_{21}H_{30}N_3O_4$ requires 388.2231.

***tert*-Butyl 2-diazo-11-(4-methyl)phenyl-3,6-dioxoundec-10-enoate, 3.22d**



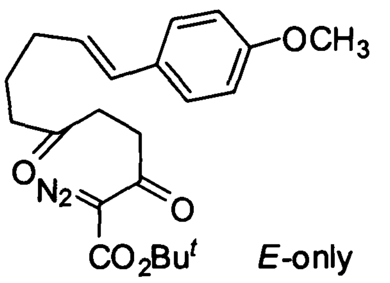
E:*Z* 94:6

3.22d was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and 4-methylstyrene (179 μL, 1.36 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the diazoester **3.22d** (36.0 mg, 69%, *E*:*Z* 94:6 from ^1H NMR) as a yellow oil.

***R*~f~** = 0.39 (30% Et_2O in petrol); **IR** (neat): 2921m, 2133s, 1716s, 1630s, 1512s, 1404w, 1383s, 1319w, 1181s; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 7.86–7.82 (m, 2H, Ar), 7.70 (d, 2H, *J* = 7.8, Ar), 6.95 (d, 1H, *J* =15.9, =C*H*Ar), 6.70 (dt, 1H, *J* = 15.9 and 7.0, =C*H*CH_2), 3.71 and 3.32 (2 × t, 4H, *J* = 6.2, $(CO)_2CH_2CH_2$), 3.14 (t, 2H, *J* = 7.4, $COCH_2$), 2.92 (s, 3H, CH_3), 2.85–2.78 (m, 2H,

=CHC*H*$_2$), 2.38 (quintet, 2H, *J* = 7.3, COCH$_2$C*H*$_2$), 2.14 (s, 9H, CMe$_3$); discernible data for ***Z*-isomer** = 7.64–7.61 (m, 1H, Ar), 2.23 (s, 9H, CMe$_3$); δ_C (100 MHz, CDCl$_3$) ***E*-isomer** = 209.2 and 191.7 (2 × CO), 160.5 (CO$_2$), 136.6 and 134.8 (2 × Ar, quat.), 130.4 and 128.8 (2 × =CH), 129.2 and 125.8 (2 × Ar), 83.2 (*C*Me$_3$), 41.9 (CO*C*H$_2$), 36.2 and 34.3 ((CO)$_2$*C*H$_2$*C*H$_2$), 32.3 (=CH*C*H$_2$), 28.3 (C*Me*$_3$), 23.3 (COCH$_2$*C*H$_2$), 21.1 (CH$_3$); discernible data for ***Z*-isomer** = 209.8 and 192.2 (2 × CO), 161.2 (CO$_2$), 137.2 and 135.4 (2 × Ar, quat.), 130.0 and 129.5 (2 × =CH), 128.8 and 126.4 (2 × Ar), 83.8 (*C*Me$_3$), 42.6 (CO*C*H$_2$), 36.8 and 34.8 ((CO)$_2$*C*H$_2$*C*H$_2$), 32.9 (=CH*C*H$_2$), 28.9 (C*Me*$_3$), 23.9 (COCH$_2$*C*H$_2$), 21.7(CH$_3$); ***m/z*** (CI): 220 (55%), 262 (45), 276 (80), 320 (55), 346 (100), 376 (60), 385 (M + H$^+$, 25), 402 (M + NH$_4^+$,15); HRMS (ES+): M + H$^+$ found 385.2120, $C_{22}H_{29}N_2O_4$ requires 385.2122.

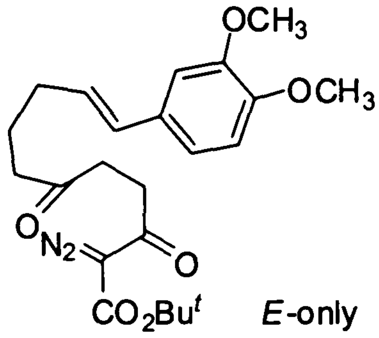
(*E*)-*tert*-Butyl 2-diazo-11-(4-methoxy)phenyl-3,6-dioxoundec-10-enoate, 3.22e



3.22e was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and 4-methoxystyrene (181 μL, 1.36 mmol) in CH$_2$Cl$_2$ (10 mL). The residue was purified by flash chromatography (10% Et$_2$O in petrol) to afford the diazoester **3.22e** (25.0 mg, 46%, 74% based on recovered starting material) as a yellow oil.

R*$_f$** = 0.32 (30% Et$_2$O in petrol); **IR** (neat): 3020s, 2401m, 2254m, 2137m, 1710s, 1648m, 1511s, 1371m, 1316m, 1216s, 1134w; δ_H (400 MHz, CDCl$_3$) = 7.36 (d, 2H, *J* = 8.7, Ar), 6.81 (d, 2H, *J* = 8.7, Ar), 6.38 (d, 1H, *J* = 15.8, =C*H*Ar), 6.02 (dt, 1H, *J* = 15.8 and 7.0, =C*H*CH$_2$), 3.78 (s, 3H, OCH$_3$), 3.10 and 2.72 (2 × t, 4H, *J* = 6.4, (CO)$_2$CH$_2$CH$_2$), 2.52 (t, 2H, *J* = 7.3, COC*H*$_2$), 2.24–2.16 (m, 2H, =CHC*H*$_2$), 1.76 (quintet, 2H, *J* = 7.3, COCH$_2$C*H*$_2$), 1.52 (s, 9H, CMe$_3$); δ_C (100 MHz, CDCl$_3$) = 209.2 and 191.6 (2 × CO), 160.5 (CO$_2$), 158.7 and 130.4 (2 × Ar, quat.), 129.9 and 127.7 (2 × =CH), 127.0 and 113.8 (2 × Ar), 83.2 (*C*Me$_3$), 55.2 (OCH$_3$), 41.9 (CO*C*H$_2$), 36.2 and 34.2 ((CO)$_2$*C*H$_2$*C*H$_2$), 32.3 (=CH*C*H$_2$), 28.3 (C*Me*$_3$), 23.4 (COCH$_2$*C*H$_2$); ***m/z (CI): 292 (90%), 336 (90), 362 (100), 392 (30), 401 (M + H$^+$, 5), 418 (M + NH$_4^+$, 20); HRMS (ES+): M + H$^+$ found 401.2072, $C_{22}H_{29}N_2O_5$ requires 401.2071.

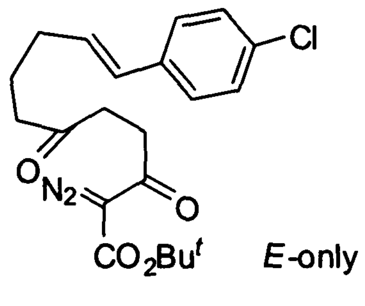
(*E*)-*tert*-Butyl 2-diazo-11-(3,4-dimethoxy)phenyl-3,6-dioxoundec-10-enoate, 3.22f



3.22f was prepared following the general procedure using diazoester **3.14** (51.0 mg, 0.173 mmol) and 3,4-dimethoxystyrene[23] (77.0 μL, 0.519 mmol) in CH_2Cl_2 (12 mL). The residue was purified by flash chromatography (5% Et_2O in petrol) to afford the diazoester **3.22f** (27.0 mg, 36%) as a yellow oil.

R*f** = 0.16 (40% Et_2O in petrol); **IR** (neat): 3020s, 2400m, 2256m, 2136m, 1710s, 1645m, 1510s, 1374m, 1315m, 1216s, 1133w; **δH** (400 MHz, $CDCl_3$) = 6.91–6.79 (m, 3H, Ar), 6.33 (d, 1H, *J* = 15.9, =C*H*Ar), 6.04 (dt, 1H, *J* = 15.9 and 6.9, =C*H*CH_2), 3.90 and 3.87 (2 × s, 6H, 2 × OCH_3), 3.10 and 2.73 (2 × t, 4H, *J* = 6.2, $(CO)_2CH_2CH_2$), 2.54 (t, 2H, *J* = 7.4, COC*H*$_2$), 2.24–2.19 (m, 2H, =CHC*H*$_2$), 1.78 (quintet, 2H, *J* = 7.4, $COCH_2C$*H*$_2$), 1.53 (s, 9H, CMe_3); **δC** (100 MHz, $CDCl_3$) = 209.2 and 191.7 (2 × CO), 160.5 (CO_2), 148.9, 148.7 and 148.3 (3 × Ar, quat.), 130.2 and 128.0 (2 × =CH), 118.8, 111.1, and 108.4 (3 × Ar), 83.2 (*C*Me_3), 55.9 and 55.8 (2 × OCH_3), 41.9 (CO*C*H_2), 36.2 and 34.3 ($(CO)_2CH_2CH_2$), 32.3 (=CH*C*H_2), 28.3 (C*Me*$_3$), 23.4 ($COCH_2CH_2$); ***m/z (CI): 184 (30%), 301 (100), 320 (35), 431 ($M + H^+$, 2); HRMS (ES+): $M + Na^+$ found 453.1996, $C_{23}H_{30}NaN_2O_6$ requires 453.1996.

(*E*)-*tert*-Butyl 2-diazo-11-(4-chloro)phenyl-3,6-dioxoundec-10-enoate, 3.22g



3.22g was prepared following the general procedure using diazoester **3.14** (126 mg, 0.428 mmol) and 4-chlorostyrene (257 μL, 2.14 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the diazoester **3.22g** (131 mg, 76%) as a pale yellow oil.

***R*f** = 0.32 (30% Et_2O in petrol); **IR** (neat): 2958s, 2400m, 2254s, 2137s, 1708s, 1647s, 1490s, 1370s, 1316s, 1216s, 1133s, 1092m, 1012m; **δH** (400 MHz, $CDCl_3$) = 7.26–7.22 (s br, 4H, Ar),

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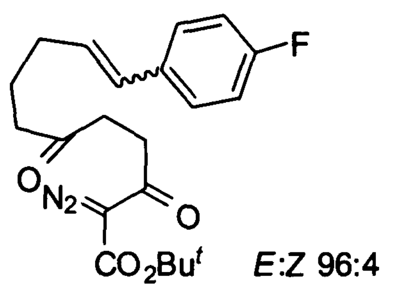
[23] M. C. Pampín, J. C. Estévez, R. J. Estévez, L. Castedo, *Arkivoc* **2003**, *15*, 29–38.

6.33 (d, 1H, J = 15.8, =CHAr), 6.15 (dt, 1H, J = 15.8 and 6.9, =CHCH$_2$), 3.10 and 2.72 (2 × t, 4H, J = 6.1, (CO)$_2$CH$_2$CH$_2$), 2.53 (t, 2H, J = 7.3, COCH_2), 2.24–2.18 (m, 2H, =CHCH_2), 1.78 (quintet, 2H, J = 7.3, COCH$_2$CH_2), 1.53 (s, 9H, CMe$_3$); **δ_C** (100 MHz, CDCl$_3$) = 209.0 and 191.6 (2 × CO), 160.5 (CO$_2$), 136.1 and 132.4 (2 × Ar, quat.), 130.7 and 129.4 (2 × =CH), 128.6 and 127.2 (2 × Ar), 83.2 (CMe$_3$), 41.9 (COCH$_2$), 36.2 and 34.3 ((CO)$_2C$H$_2C$H$_2$), 32.3 (=CHCH$_2$), 28.3 (CMe_3), 23.1 (COCH$_2C$H$_2$); ***m/z*** (CI): 326 (20%), 349 (25), 366 (100), 405 (M + H$^+$, 32), 468 (36); **HRMS** (ES+): M + H$^+$ found 405.1570, $C_{21}H_{26}{}^{35}ClN_2O_4$ requires 405.1576.

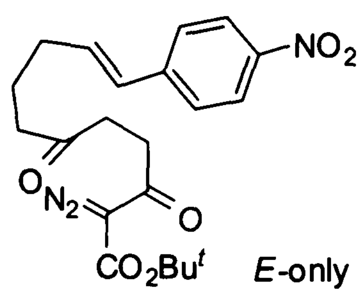
***tert*-Butyl 2-diazo-11-(4-fluoro)phenyl-3,6-dioxoundec-10-enoate, 3.22h**



3.22h was prepared following the general procedure using diazoester **3.14** (40 mg, 0.136 mmol) and 4-fluorostyrene (162 µL, 1.36 mmol) in CH$_2$Cl$_2$ (10 mL). The residue was purified by flash chromatography (10→30% Et$_2$O in petrol) to afford the diazoester **3.22h** (40 mg, 76%, *E*:*Z* 96:4 from ^{1}H NMR) as a yellow oil.

R*$_f$** = 0.31 (30% Et$_2$O in petrol); **IR** (neat): 2980s, 2974s, 2136s, 1720s, 1640s, 1510s, 1390m, 1322m, 1232s, 1110s; **δ_H** (400 MHz, CDCl$_3$) ***E*-isomer** = 7.31–7.27 (m, 2H, Ar), 6.98 (2 × d, 2H, J = 8.7, Ar), 6.34 (d, 1H, J = 15.9, =CHAr), 6.08 (dt, 1H, J = 15.9 and 7.0, =CHCH$_2$), 3.10 and 2.72 (2 × t, 4H, J = 6.0, (CO)$_2$CH$_2$CH$_2$), 2.54 (t, 2H, J = 7.3, COCH_2), 2.25–2.18 (m, 2H, =CHCH_2), 1.78 (quintet, 2H, J = 7.3, COCH$_2$CH_2), 1.53 (s, 9H, CMe_3); discernible data for ***Z*-isomer** = 2.64–2.58 (m, 2H, COCH$_2$), 1.39 (s, 9H, CMe$_3$); **δ_C** (100 MHz, CDCl$_3$) ***E*-isomer** = 209.1 and 191.7 (2 × CO), 161.9 (d, $J_{C\text{-}F}$ = 244, C-F, quat.), 160.5 (CO$_2$), 133.8 (d, $J_{C\text{-}F}$ = 3, Ar, quat.), 129.7 and 129.4 (2 × =CH), 127.4 (d, $J_{C\text{-}F}$ = 7, Ar), 115.3 (d, $J_{C\text{-}F}$ = 21, Ar), 83.2 (CMe$_3$), 41.9 (COCH$_2$), 36.2 and 34.3 ((CO)$_2C$H$_2C$H$_2$), 32.3 (=CHCH$_2$), 28.3 (CMe_3), 23.2 (COCH$_2C$H$_2$); **δ_F** (376 MHz, CDCl$_3$) = –115.6; ***m/z (CI): 366 (100%), 378 (80), 396 (50), 389 (M + H$^+$, 10), 406 (M + NH$_4^+$, 40), 422 (55); **HRMS** (ES+): M + H$^+$ found 389.1870, $C_{21}H_{26}{}^{19}FN_2O_4$ requires 389.1877.

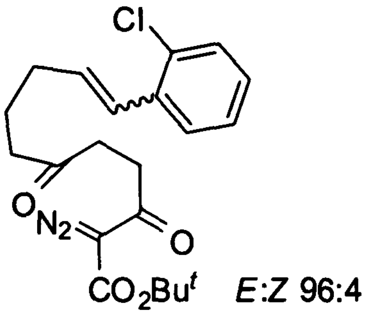
(*E*)-*tert*-Butyl 2-diazo-11-(4-nitro)phenyl-3,6-dioxoundec-10-enoate, 3.22i



3.22i was prepared following the general procedure using diazoester **3.14** (42.0 mg, 0.143 mmol) and 4-nitrostyrene[24] (213 mg, 1.43 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (20→30% Et_2O in petrol) to afford the diazoester **3.22i** (47.0 mg, 79%) as a yellow oil.

R*f** = 0.22 (30% Et_2O in petrol); **IR** (neat): 3685w, 3019s, 2400m, 2254m, 2137m, 1709s, 1649m, 1597m, 1517s, 1371m, 1344s, 1316m, 1215s, 1133w; δ_H (400 MHz, $CDCl_3$) = 8.12 (d, 2H, *J* = 8.8, Ar), 7.43 (d, 2H, *J* = 8.8, Ar), 6.45 (d, 1H, *J* = 16.0, =C*H*Ar), 6.38 (dt, 1H, *J* = 15.9 and 6.4, =C*H*CH_2), 3.09 and 2.71 (2 × t, 4H, *J* = 6.1, $(CO)_2CH_2CH_2$), 2.54 (t, 2H, *J* = 7.2, COC*H*$_2$), 2.30–2.25 (m, 2H, =CHC*H*$_2$), 1.80 (quintet, 2H, *J* = 7.3, $COCH_2C$*H*$_2$), 1.51 (s, 9H, CMe_3); δ_C (100 MHz, $CDCl_3$) = 208.8 and 191.6 (2 × CO), 160.5 (CO_2), 146.5 and 144.1 (2 × Ar, quat.) 135.4 and 128.8 (2 × =CH), 126.4 and 123.9 (2 × Ar), 83.2 (*C*Me_3), 41.8 (CO*C*H_2), 36.2 and 34.3 ($(CO)_2$*C*H_2*C*H_2), 32.4 (=CH*C*H_2), 28.3 (C*Me*$_3$), 22.8 ($COCH_2$*C*H_2); ***m/z (CI): 360 (5%), 377 (100), 378 (20), 416 (M + H^+, 5); HRMS (ES+): M + H^+ found 416.1816, $C_{21}H_{26}N_3O_6$ requires 416.1816.

tert-Butyl 2-diazo-11-(2-chloro)phenyl-3,6-dioxoundec-10-enoate, 3.22j



3.22j was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and 2-chlorostyrene (174 μL, 1.36 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→20% Et_2O in petrol) to afford the diazoester **3.22j** (49.0 mg, 89%, *E*:*Z* 96:4 from ^1H NMR) as a yellow oil.

***R*f** = 0.37 (30% Et_2O in petrol); **IR** (neat): 3067s, 2133s, 1720s, 1628s, 1594s, 1473s, 1439s, 1417s, 1278m, 1129s, 1044s; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 8.08 (d, 1H, *J* = 7.8, Ar), 7.91 (d,

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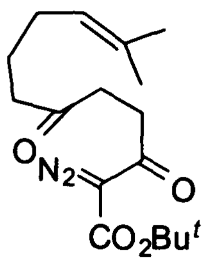
[24] S. P. Jacober, R. P. Hanzlik, *J. Am. Chem. Soc.* **1986**, *108*, 1594–1597.

1H, *J* = 8.1, Ar), 7.82–7.70 (m, 2H, Ar), 7.35 (d, 1H, *J* = 15.6, =C*H*Ar), 6.72 (dt, 1H, *J* = 15.7 and 7.2, =C*H*CH$_2$), 3.70 and 3.33 (2 × t, 4H, *J* = 6.0, (CO)$_2$CH$_2$CH$_2$), 3.15 (t, 2H, *J* = 7.3, COCH$_2$), 2.40–2.85 (m, 2H, =CHC*H*$_2$), 2.40 (quintet, 2H, *J* = 7.3, COCH$_2$C*H*$_2$), 2.12 (s, 9H, CMe$_3$); discernible data for ***Z*-isomer** = 8.19 (d, 2H, *J* = 7.6, Ar), 3.06 (t, 2H, *J* = 7.4, COCH$_2$); **δ$_C$** (100 MHz, CDCl$_3$) ***E*-isomer** = 209.7 and 192.3 (2 × CO), 161.1 (CO$_2$), 136.3 and 133.1 (2 × Ar, quat.), 133.5, 130.1, 128.6 127.4, 127.3, 127.2 (4 × Ar and 2 × =CH), 83.8 (*C*Me$_3$), 42.5 (CO*C*H$_2$), 36.8 and 34.9 ((CO)$_2$*C*H$_2$*C*H$_2$), 33.1 (=CH*C*H$_2$), 28.9 (C*Me*$_3$), 23.7 (COCH$_2$*C*H$_2$); discernible data for ***Z*-isomer** = 128.9, 127.8 and 126.9 (3 × Ar), 24.1 (CMe$_3$); ***m/z*** (CI): 132 (45%), 323 (20), 340 (75), 349 (90), 366 (80), 377 (25), 396 (100), 422 (10), 405 (M + H$^+$, 60); HRMS (ES+): M + H$^+$ found 405.1576, $C_{21}H_{26}{}^{35}ClN_2O_4$ requires 405.1576.

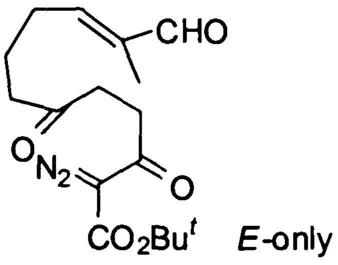
***tert*-Butyl 2-diazo-11-methyl-3,6-dioxododec-10-enoate, 3.22k**



3.22k was prepared following the general procedure using diazoester **3.14** (45.0 mg, 0.153 mmol) and amylene (162 μL, 1.53 mmol) in CH$_2$Cl$_2$ (12 mL). The residue was purified by flash chromatography (10% Et$_2$O in petrol) to afford the diazoester **3.22k** (38.0 mg, 77%) as a pale yellow oil.

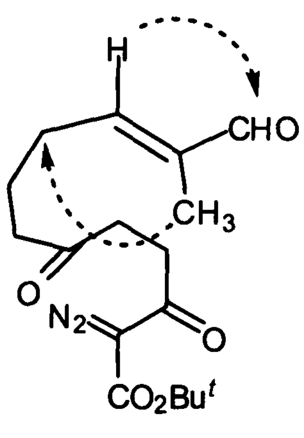
R*$_f$** = 0.51 (30% Et$_2$O in petrol); **IR** (neat): 2960s, 2875m, 2130s, 1720s, 1640w, 1380s, 1358w, 1116s; **δ$_H$** (400 MHz, CDCl$_3$) = 5.10–5.06 (m, 1H, =CH), 3.09 and 2.73 (2 × t, 4H, *J* = 6.0, (CO)$_2$CH$_2$CH$_2$), 2.46 (t, 2H, *J* = 7.6, COCH$_2$), 2.02–1.96 (m, 2H, =CHC*H*$_2$), 1.68 and 1.59 (2 × s, 6H, =CMe$_2$), 1.67–1.61 (m, 2H, COCH$_2$C*H*$_2$), 1.53 (s, 9H, CMe$_3$); **δ$_C$** (100 MHz, CDCl$_3$) = 209.4 and 191.7 (2 × CO), 160.5 (CO$_2$), 132.3 (=*C*Me$_2$), 123.7 (=CH), 83.2 (*C*Me$_3$), 42.2 (CO*C*H$_2$), 36.1 and 34.2 ((CO)$_2$*C*H$_2$*C*H$_2$), 28.3 (C*Me*$_3$), 27.4 (=CH*C*H$_2$), 25.7 and 17.7 (=C*Me*$_2$), 23.9 (COCH$_2$*C*H$_2$); ***m/z (CI): 323 (M + H$^+$, 70%), 340 (100), 354 (20); HRMS (ES+): M + H$^+$ found 323.1961, $C_{17}H_{27}N_2O_4$ requires 323.1965.

(*E*)-*tert*-Butyl 2-diazo-11-methyl-3,6,12-trioxododec-10-enoate, 3.22l

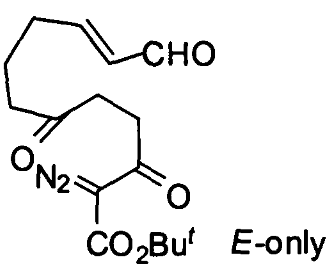


3.22l was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and methacrolein (112 µL, 1.36 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (40% Et_2O in petrol) to afford the diazoester **3.22l** (38.0 mg, 83%) as a yellow oil.

R*f** = 0.13 (30% Et_2O in petrol); **IR** (neat): 2970s, 2873s, 2133s, 1725s, 1640w, 1371w, 1216s, 1112s; δ_H (400 MHz, $CDCl_3$) = 9.39 (s, 1H, CHO), 6.46–6.50 (m, 1H, =CH), 3.11 and 2.72 (2 × t, 4H, *J* = 6.0, $(CO)_2CH_2CH_2$), 2.56 (t, 2H, *J* = 7.3, $COCH_2$), 2.40–2.35 (m, 2H, =CHC*H*$_2$), 1.81 (quintet, 2H, *J* = 7.4, $COCH_2CH_2$), 1.74 (d, 3H, *J* = 1.0, CH_3), 1.53 (s, 9H, CMe_3); δ_C (100 MHz, $CDCl_3$) = 208.5 and 191.6 (2 × CO), 195.3 (CHO), 160.5 (CO_2), 153.6 (=CH), 139.9 (=C), 83.2 (*C*Me_3), 41.8 (CO*C*H_2), 36.1 and 34.3 ($(CO)_2CH_2CH_2$), 28.3 (=CH*C*H_2), 28.2 (C*Me*$_3$), 22.3 ($COCH_2CH_2$), 9.2 (CH_3); ***m/z (ES+): 225 (10%), 298 (65), 314 (25), 325 (65), 354 (M + NH_4^+, 15), 351 (100), 372 (8); HRMS: M + NH_4^+ found 354.2025, $C_{17}H_{28}N_3O_5$ requires 354.2023. Key NOE enhancements supporting the stereochemical assignments are shown below:



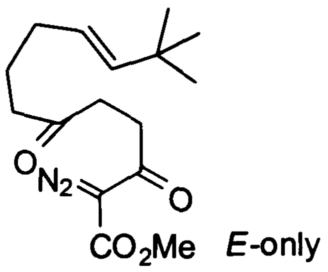
(*E*)-*tert*-Butyl 2-diazo-3,6,12-trioxododec-10-enoate, 3.22m



3.22m was prepared following the general procedure using diazoester **3.14** (42.0 mg, 0.143 mmol) and crotonaldehyde (59.0 µL, 0.715 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (35→40% Et_2O in petrol) to afford the diazoester **3.22m** (35.0 mg, 76%) as a pale yellow oil.

R*f** = 0.26 (50% Et_2O in petrol); **IR** (neat): 2974s, 2870s, 2133s, 1720s, 1640m, 1371w, 1216s, 1132s; δ_H (400 MHz, $CDCl_3$) = 9.51 (d, 1H, *J* = 7.9, CHO), 6.82 (dt, 1H, *J* = 15.7 and 6.8, =C*H*CH_2), 6.16–6.10 (m, 1H, =C*H*CHO), 3.14–3.11 and 2.73–2.70 (2 × m, 4H, $(CO)_2CH_2CH_2$), 2.56 (t, 2H, *J* = 7.2, $COCH_2$), 2.39–2.34 (m, 2H, =CHC*H*$_2$), 1.83 (quintet, 2H, *J* = 7.3, $COCH_2$C*H*$_2$), 1.53 (s, 9H, CMe_3); δ_C (100 MHz, $CDCl_3$) = 208.4 and 191.6 (2 × CO), 194.0 (CHO), 160.5 (CO_2), 157.7 (=*C*HCHO), 133.3 (=*C*HCH_2), 83.3 (*C*Me_3), 41.6 (CO*C*H$_2$), 36.2 and 34.4 ($(CO)_2$*C*H$_2$*C*H$_2$), 31.9 (=CH*C*H$_2$), 28.3 (C*Me*$_3$), 21.7 ($COCH_2$*C*H$_2$); ***m/z (CI): 170 (10%), 284 (80), 314 (35), 323 (M + H^+, 10), 340 (M + NH_4^+, 100); HRMS (ES+): M + H^+ found 323.1602 $C_{16}H_{23}N_2O_5$ requires 323.1601.

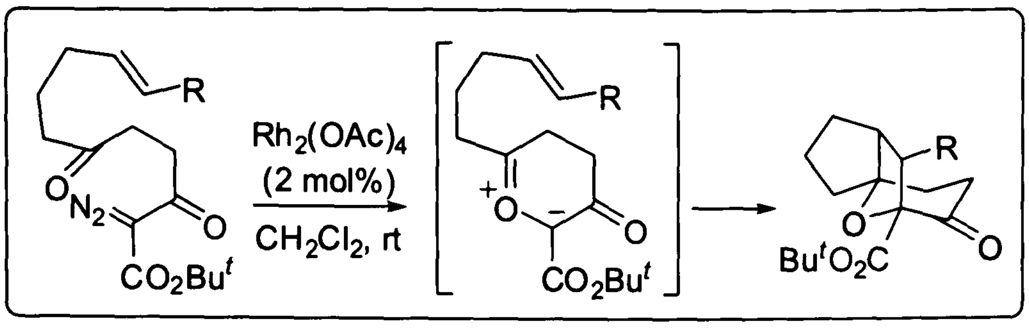
(*E*)-Methyl 2-diazo-12,12-dimethyl-3,6-dioxotridec-10-enoate, 3.22n



3.22n was prepared following the general procedure using diazoester **3.14** (CO_2Bu^t = CO_2Me)[5] (40.0 mg, 0.158 mmol) and 3,3-dimethyl-1-butene (204 µL, 1.58 mmol) in CH_2Cl_2 (12 mL). The residue was was purified with flash chromatography (15% Et_2O in petrol) to afford the diazoester **3.22n** (10.0 mg, 20%) as a yellow oil.

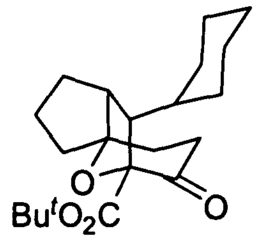
R*f** = 0.29 (30% Et_2O in petrol); **IR** (neat): 2970s, 2873s, 2137s, 1726s, 1640w, 1371w, 1214s, 1115s; δ_H (400 MHz, $CDCl_3$) = 5.45 (d, 1H, *J* = 15.5, =C*H*CMe_3), 5.30–5.24 (m, 1H, =C*H*CH_2), 3.85 (s, 3H, OCH_3), 3.15–3.08 and 2.88–2.74 (2 × m, 4H, $(CO)_2CH_2CH_2$), 2.48–2.40 (m, 2H, $COCH_2$), 2.02–1.95 (m, 2H, =CHC*H*$_2$), 1.70–1.58 (m, 2H, $COCH_2$C*H*$_2$), 0.98 (s, 9H, CMe_3); δ_C (100 MHz, $CDCl_3$) = 209.0 and 191.2 (2 × CO), 161.8 (CO_2), 142.5 (=*C*HCMe_3), 123.6 (=*C*HCH_2), 52.2 (OCH_3), 41.9 (CO*C*H$_2$), 36.2 and 34.1 ($(CO)_2$*C*H$_2$*C*H$_2$), 32.8 (*C*Me_3), 31.9 (=CH*C*H$_2$), 29.7 (C*Me*$_3$), 23.7 ($COCH_2$*C*H$_2$); ***m/z (CI): 270 (30%), 300 (100), 309 (M + H^+, 30), 326 (M + NH_4^+, 25); HRMS (ES+): M + H^+ found 309.1808, $C_{16}H_{25}N_2O_4$ requires 309.1809.

5.7. Tandem Carbonyl Ylide Formation-Intramolecular Cycloadditions



General procedure: Anhydrous rhodium acetate dimer (2 mol%) was added to a stirred solution of olefin **3.22** (obtained by cross-metathesis) in CH_2Cl_2 (c = 15–20 mM). After 3 h the reaction mixture was concentrated under reduced pressure and purified by flash chromatography.

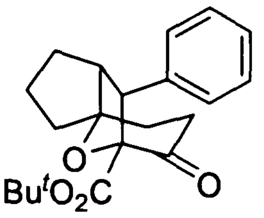
6-Cyclohexyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23a



3.23a was prepared following the general procedure using diazoester **3.22a** (57.0 mg, 0.152 mmol) in CH_2Cl_2 (8 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the cycloadduct **3.23a** (41.1 mg, 78%) as a pale yellow oil.

R*f** = 0.45 (30% Et_2O in petrol); **IR** (neat): 3020s, 2200w, 1725m, 1216s; **δ_H** (400 MHz, $CDCl_3$) = 2.74–2.58 (m, 1H, CH of CH_2), 2.46–2.34 (m, 2H, CH_2), 2.22–2.17 (m, 1H, CH), 2.10 (t, 1H, J = 7.9, CH), 2.00 (dd, 1H, J = 13.4 and 3.4, CH), 1.94–1.54 (m, 10H, 5 × CH_2), 1.46 (s, 9H, CMe_3), 1.46–1.36 (m, 1H, CH of CH_2), 1.30–0.96 (m, 6H, 3 × CH_2); **δ_C** (100 MHz, $CDCl_3$) = 205.3 (CO), 166.5 (CO_2), 92.8 and 91.9 (2 × COC, quat.), 82.2 (CMe_3), 59.9, 51.8 and 39.3 (3 × CH), 37.5, 35.6, 34.5, 32.5, 32.4, 32.3, 26.5, 26.3, 26.2 and 24.5 (10 × CH_2), 27.8 ($C\mathit{Me}_3$); ***m/z (CI): 293 (10%), 310 (100), 349 (M + H^+, 15), 366 (M + NH_4^+, 15); HRMS (ES+): M + H^+ found 349.2369, $C_{21}H_{33}O_4$ requires 349.2373.

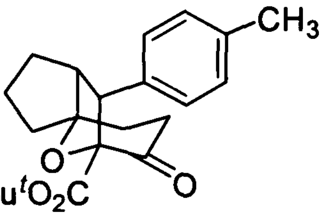
8-Oxo-6-phenyl-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23c



3.23c was prepared following the general procedure using diazoester **3.22c** (53.0 mg, 0.143 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (20% Et_2O in petrol) to afford the cycloadduct **3.23c** (41.3 mg, 84%) as a pale yellow oil.

R*$_f$** = 0.44 (50% Et_2O in petrol); **IR** (neat): 2959s, 2872s, 2400s, 2253s, 1734s, 1458s, 1370w, 1217s, 1158w; **δ_H** (400 MHz, $CDCl_3$) = 7.32–7.20 (m, 5H, Ar), 3.40 (d, 1H, *J* = 8.1, C*H*Ar), 2.88–2.68 (m, 2H, C*H*CH$_2$ and CH of CH$_2$), 2.62–2.48 (m, 2H, CH$_2$), 2.17 (dd, 1H, *J* = 7.6 and 5.8, CH of CH$_2$), 2.12–1.82 (m, 3H, CH of CH$_2$ and CH$_2$), 1.82–1.78 (m, 2H, CH$_2$), 1.58–1.50 (m, 1H, CH of CH$_2$), 1.54 (s, 9H, CMe$_3$); **δ_C** (100 MHz, $CDCl_3$) = 203.7 (CO), 166.3 (CO$_2$), 137.4 (Ar, quat.), 128.6, 128.1 and 126.9 (3 × Ar), 93.5 and 91.8 (2 × COC, quat.), 82.6 (*C*Me$_3$), 60.5 (*C*HAr) and 53.9 (*C*HCH$_2$), 37.2, 36.3, 33.5, 33.1 and 24.5 (5 × CH$_2$), 27.8 (C*Me*$_3$); ***m/z (ES+): 304 (100%), 360 (M + NH_4^+, 62); HRMS: M + NH_4^+ found 360.2167, $C_{21}H_{30}NO_4$ requires 360.2169.

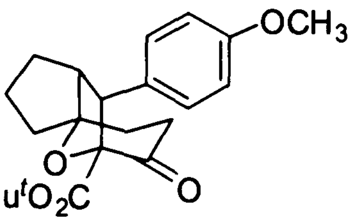
6-(4-Methyl)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23d



3.23d was prepared following the general procedure using diazoester **3.22d** (30.0 mg, 0.0781 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (20% Et_2O in petrol) to afford the cycloadduct **3.23d** (24.0 mg, 86%) as a yellow oil.

R*$_f$** = 0.34 (30% Et_2O in petrol); **IR** (neat): 3019m, 2957m, 1721s, 1517w, 1451w, 1370m, 1321m, 1257w, 1216s, 1158m, 1084m; δ_H (400 MHz, $CDCl_3$) = 7.14–7.06 (m, 4H, Ar), 3.38 (d, 1H, *J* = 8.1, C*H*Ar), 2.76–2.67 (m, 2H, C*H*CH$_2$ and CH of CH$_2$), 2.60–2.48 (m, 2H, CH$_2$), 2.31 (s, 3H, CH$_3$), 2.15 (dd, 1H, *J* = 13.4 and 5.9, CH of CH$_2$), 2.06–1.82 (m, 2H, CH$_2$), 1.78–1.69 (m, 2H, CH$_2$), 1.56–1.47 (m, 2H, CH$_2$), 1.40 (s, 9H, CMe$_3$); δ_C (100 MHz, $CDCl_3$) = 203.8 (CO), 166.3 (CO$_2$), 136.6 and 134.1 (2 × Ar, quat.), 128.8 and 128.5 (2 × Ar), 93.6 and 91.7 (2 × COC, quat.), 82.6 (*C*Me$_3$), 60.1 (*C*HAr), 53.8 (*C*HCH$_2$), 37.3, 36.2, 33.4, 33.1 and 25.2 (5 × CH$_2$), 27.9 (C*Me*$_3$), 21.0 (CH$_3$); ***m/z (CI): 274 (10%), 318 (100), 374 (M + NH_4^+, 2); HRMS (ES+): M + NH_4^+ found 374.2329, $C_{22}H_{32}NO_4$ requires 374.2326.

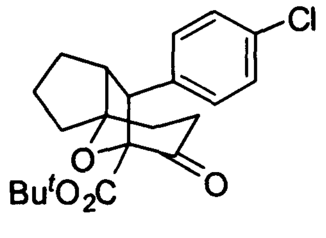
6-(4-Methoxy)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23e



3.23e was prepared following the general procedure using diazoester **3.22e** (41.0 mg, 0.102 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (30% Et_2O in petrol) to afford the cycloadduct **3.23e** (38.0 mg, quant.) as a colourless oil.

R*$_f$** = 0.15 (30% Et_2O in petrol); **IR** (neat): 3020s, 2200w, 1722s, 1515m, 1370m, 1216s; **δ_H** (400 MHz, $CDCl_3$) = 7.16 (d, 2H, *J* = 8.7, Ar), 6.80 (d, 2H, *J* = 8.7, Ar), 3.76 (s, 3H, OCH_3), 3.38 (d, 1H, *J* = 8.1, C*H*Ar), 2.76–2.64 (m, 2H, C*H*CH_2 and CH of CH_2), 2.60–2.48 (m, 2H, CH_2), 2.14 (dd, 1H, *J* = 13.3 and 5.8, CH of CH_2), 2.08–1.80 (m, 3H, CH of CH_2 and CH_2), 1.80–1.64 (m, 2H, CH_2), 1.58–1.46 (m, 1H, CH of CH_2), 1.38 (s, 9H, CMe_3); **δ_C** (100 MHz, $CDCl_3$) = 203.9 (CO), 166.3 (CO_2), 158.9 and 129.1 (2 × Ar, quat.), 129.7 and 127.4 (2 × Ar), 93.6 and 91.7 (2 × COC, quat.), 82.6 (*C*Me_3), 59.6 (*C*HAr), 55.1 (OCH_3), 53.8 (*C*HCH_2), 37.3, 36.2, 33.3, 33.0, 24.5 (5 × CH_2), 27.8 (C*Me*$_3$); ***m/z (CI): 334 (100%), 335 (20), 390 (M + NH_4^+, 40); HRMS (ES+): M + NH_4^+ found 390.2277, $C_{22}H_{32}NO_5$ requires 390.2275.

6-(4-Chloro)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23g

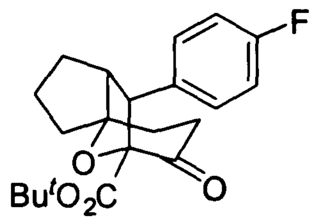


3.23g was prepared following the general procedure using diazoester **3.22g** (50.0 mg, 0.123 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (20% Et_2O in petrol) to afford the cycloadduct **3.23g** (38.0 mg, 82%) as a pale yellow oil.

***R*$_f$** = 0.27 (30% ether in petrol); **IR** (neat): 2950m, 2401w, 1703s, 1647s, 1490s, 1370s, 1316s, 1216s, 1133s; **δ_H** (400 MHz, $CDCl_3$) = 7.26 (d, 2H, *J* = 8.5, Ar), 7.18 (d, 2H, *J* = 8.5, Ar), 3.50 (d, 1H, *J* = 8.1, C*H*Ar), 2.80–2.70 (m, 1H, CH of CH_2), 2.66–2.62 (m, 1H, C*H*CH_2), 2.60–2.44 (m, 2H, CH_2), 2.16 (dd, 1H, *J* = 7.9 and 5.6, CH of CH_2), 2.08–1.82 (m, 2H, CH_2), 1.82–1.66 (m, 2H, CH_2), 1.58–1.46 (m, 2H, CH_2), 1.38 (s, 9H, CMe_3); **δ_C** (100 MHz, $CDCl_3$) = 203.9 (CO), 166.0 (CO_2), 135.7 and 132.8 (2 × Ar, quat.), 130.0 and 128.2 (2 × Ar), 93.5 and 91.8 (2 × COC, quat.), 82.9 (*C*Me_3), 59.5 (*C*HAr), 53.8 (*C*HCH_2), 37.3, 36.0, 33.1, 33.0 and 24.5 (5 × CH_2), 27.8

(C*Me*$_3$); ***m/z*** (CI): 338 (100%), 340 (35), 394 (M + NH_4^+, 100), 396 (35); HRMS (ES+): M + NH_4^+ found 394.1783, $C_{21}H_{29}{}^{35}ClNO_4$ requires 394.1780.

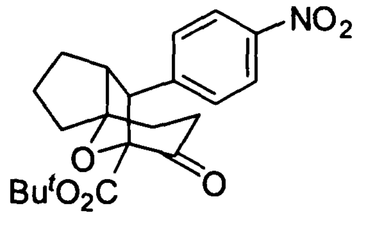
6-(4-Fluoro)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23h



3.23h was prepared following the general procedure using diazoester **3.22h** (33.0 mg, 0.0850 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (20% Et_2O in petrol) to afford the cycloadduct **3.23h** (27.0 mg, 88%) as a yellow oil.

R*$_f$** = 0.28 (30% Et_2O in petrol); **IR** (neat): 2957s, 1738s, 1607m, 1513s, 1451w, 1394s, 1370s, 1322s, 1232s, 1161s, 1140m, 1085s; **δ_H** (400 MHz, $CDCl_3$) = 7.24–7.18 (m, 2H, Ar), 7.00–6.92 (m, 2H, Ar), 3.40 (d, 1H, *J* = 8.3, C*H*Ar), 2.78–2.70 (m, 1H, CH of CH_2), 2.65 (td, 1H, *J* = 8.3 and 1.6, C*H*CH$_2$), 2.57–2.46 (m, 2H, CH_2), 2.16 (dd, 1H, *J* = 13.4 and 5.9, CH of CH_2), 2.08–1.83 (m, 2H, CH_2), 1.80–1.68 (m, 2H, CH_2), 1.57–1.46 (m, 2H, CH_2), 1.40 (s, 9H, CMe_3); **δ_C** (100 MHz, $CDCl_3$) = 204.0 (CO), 166.2 (CO_2), 161.8 (d, $J_{C\text{-}F}$ = 244, C-F, quat.), 132.9 (d, $J_{C\text{-}F}$ = 3, Ar, quat.), 130.2 (d, $J_{C\text{-}F}$ = 7, Ar), 114.9 (d, $J_{C\text{-}F}$ = 21.0, Ar), 93.4 and 91.8 (2 × COC, quat.), 82.8 (*C*Me$_3$), 59.5 (*C*HAr), 53.9 (*C*HCH$_2$), 37.3, 36.1, 33.2, 32.9 and 24.5 (5 × CH_2), 27.8 (C*Me*$_3$); **δ_F** (376 MHz, $CDCl_3$) = −115.7; ***m/z (CI): 305 (45%), 322 (100), 378 (M + NH_4^+, 10); HRMS (ES+): M + NH_4^+ found 378.2078, $C_{21}H_{29}{}^{19}FNO_4$ requires 378.2075.

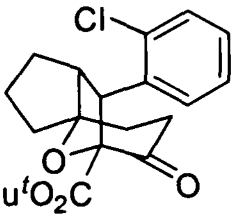
6-(4-Nitro)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23i



3.23i was prepared following the general procedure using diazoester **3.22i** (40.0 mg, 0.0964 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (30% Et_2O in petrol) to afford the cycloadduct **3.23i** (37.2 mg, quant.) as a pale yellow oil.

R*$_f$** = 0.13 (30% Et_2O in petrol); **IR** (neat): 2960m, 2401w, 1722s, 1601w, 1522s, 1371w, 1350s, 1216s, 1086w; **δ_H** (400 MHz, $CDCl_3$) = 8.12 (d, 2H, *J* = 7.2, Ar), 7.42 (d, 2H, *J* = 8.8, Ar), 3.54 (d, 1H, *J* = 8.2, C*H*Ar), 2.85–2.75 (m, 1H, CH of CH_2), 2.68–2.65 (m, 1H, C*H*CH$_2$), 2.54–2.44 (m, 2H, CH_2), 2.18 (dd, 1H, *J* = 7.9 and 5.0, CH of CH_2), 2.12–1.84 (m, 3H, CH of CH_2 and CH_2), 1.84–1.76 (m, 1H, CH of CH_2), 1.76–1.66 (m, 1H, CH of CH_2), 1.62–1.48 (m, 1H, CH of CH_2), 1.38 (s, 9H, CMe_3); δ_C (100 MHz, $CDCl_3$) = 204.2 (CO), 165.7 (CO_2), 146.9 and 144.8 (2 × Ar, quat.), 129.7 and 123.2 (2 × Ar), 93.6 and 92.1 (2 × COC, quat.), 83.3 (*C*Me₃), 59.6 (C*H*Ar), 53.7 (*C*HCH₂), 37.3, 35.8, 32.9, 32.7 and 24.4 (5 × CH_2), 27.8 (C*Me*₃); ***m/z (CI): 319 (30%), 349 (60), 375 (35), 405 (M + NH_4^+, 100); HRMS (ES+): M + NH_4^+ found 405.2021, $C_{21}H_{29}N_2O_6$ requires 405.2020.

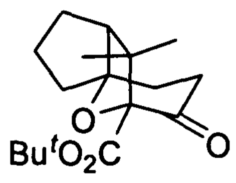
6-(2-Chloro)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23j



3.23j was prepared following the general procedure using diazoester **3.22j** (22.0 mg, 0.0544 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (30% Et_2O in petrol) to afford the cycloadduct **3.23j** (16.0 mg, 78%) as a pale yellow oil.

R*f** = 0.15 (30% Et_2O in petrol); **IR** (neat): 3020s, 1720s, 1370w, 1216s, 1159w, 1085w; δ_H (400 MHz, $CDCl_3$) = 7.38 (dd, 1H, *J* = 7.0 and 2.1, Ar), 7.19–7.12 (m, 2H, Ar), 7.04 (dd, 1H, *J* = 7.3 and 2.0, Ar), 4.04 (d, 1H, *J* = 9.1, C*H*Ar), 2.90–2.74 (m, 2H, CH_2), 2.66–2.54 (m, 2H, C*H*CH₂ and CH of CH_2), 2.20 (dd, 1H, *J* = 13.0 and 5.8, CH of CH_2), 2.11–2.00 (m, 2H, CH_2), 1.83–1.62 (m, 3H, CH of CH_2 and CH_2), 1.55–1.46 (m, 1H, CH of CH_2), 1.26 (s, 9H, CMe_3); δ_C (100 MHz, $CDCl_3$) = 203.5 (CO), 165.5 (CO_2), 135.8 and 135.2 (2 × Ar, quat.), 129.7, 127.9, 127.8 and 126.8 (4 × Ar), 92.9 and 91.7 (2 × COC, quat.), 82.6 (*C*Me₃), 55.2 and 54.9 (2 × CH), 37.3, 36.7, 33.2, 31.5 and 24.1 (5 × CH_2), 27.4 (C*Me*₃); ***m/z (CI): 294 (20%), 338 (100), 340 (20), 394 (M + NH_4^+, 2); HRMS (ES+): M + NH_4^+ found 394.1773, $C_{21}H_{29}{}^{35}ClNO_4$ requires 394.1780.

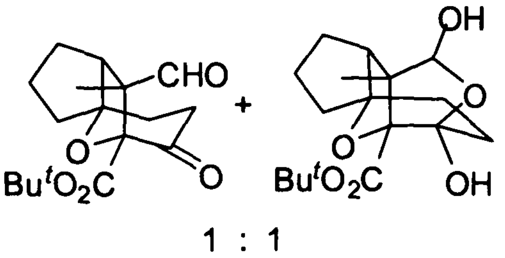
6,6-Dimethyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23k



3.23k was prepared following the general procedure using diazoester **3.22k** (31.0 mg, 0.0963 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (15% Et_2O in petrol) to afford the cycloadduct **3.23k** (21.0 mg, 74%) as a colourless oil.

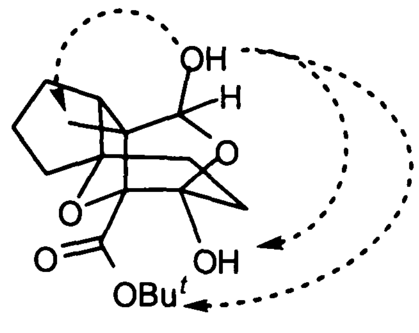
R*f** = 0.48 (30% Et_2O in petrol); **IR** (neat): 2962s, 1743s, 1740s, 1457m, 1416w, 1392s, 1368s, 1301s, 1259m, 1169s, 1095s, 1032m; δ_H (400 MHz, $CDCl_3$) = 2.70–2.63 (m, 1H, CH of CH_2), 2.54–2.37 (m, 2H, CH_2), 2.28 (dd, 1H, *J* = 9.0 and 2.0, C*H*CH_2), 2.14–2.09 (m, 1H, CH of CH_2), 1.87–1.42 (m, 6H, 3 × CH_2), 1.52 (s, 9H, CMe_3), 1.17 and 1.08 (2 × s, 6H, C*Me*$_2$); δ_C (100 MHz, $CDCl_3$) = 203.2 (CO), 165.8 (CO_2), 96.8 and 91.3 (2 × COC, quat.), 82.3 (*C*Me_3), 56.9 (*C*HCH_2), 48.1 (*C*Me_2), 36.9, 36.4, 34.4, 27.7 and 26.6 (5 × CH_2), 27.9 (C*Me*$_3$), 24.4 and 19.9 (C*Me*$_2$); ***m/z (CI): 256 (100%), 295 (M + H^+, 5), 312 (M + NH_4^+, 15); HRMS (ES+): M + H^+ found 295.1908, $C_{17}H_{27}O_4$ requires 295.1904.

6-Formyl-6-methyl-8-oxo-11-oxa-tricyclo[5.3.1.$0^{1,5}$]undecane-7-*tert*-butyl carboxylate, 3.231

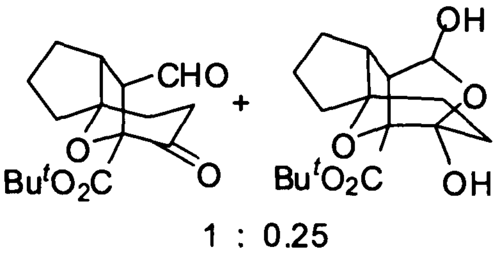


3.231 was prepared following the general procedure using diazoester **3.221** (34.0 mg, 0.101 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (50% Et_2O in petrol) to afford the cycloadduct **3.231** (24.0 mg, 77%, as 1:1 mixture of the desired cycloadduct **3.231** and its cyclic hydrate **3.241**) as a yellow oil.

R*$_f$** = 0.12 (40% Et_2O in petrol); **IR** (neat): 3020s, 1725m, 1371w, 1216s, 1101w; δ_H (400 MHz, $CDCl_3$) **mixture** of cycloadduct and cyclic hydrate = 9.63 (s, 1H, CHO), 5.21 (d, 1H, *J* = 12.2, OH), 4.94 (d, 1H, *J* = 12.2, C*H*OH), 3.57 (br s, 1H, OH), 3.00 (dd, 1H, *J* = 8.2 and 2.9, CH), 2.75–2.68 (m, 1H, CH of CH_2), 2.59–2.44 (m, 2H, CH_2), 2.22–2.14 (m, 1H, CH of CH_2), 2.10–1.98 (m, 3H, CH and CH_2), 1.97–1.86 (m, 2H, CH_2), 1.80–1.58 (m, 12H, 6 × CH_2), 1.56 and 1.53 (2 × s, 18H, 2 × CMe_3), 1.32 and 1.07 (2 × s, 6H, 2 × CH_3); discernible data for cycloadduct **3.231** = 9.63 (s, 1H, CHO); discernible data for cyclic hydrate **3.241** = 5.21 (d, 1H, *J* = 12.2, OH), 4.94 (d, 1H, *J* = 12.2, C*H*OH), 3.57 (br s, 1H, OH); δ_C (100 MHz, $CDCl_3$) **mixture** of cycloadduct and cyclic hydrate = 203.2 (CO), 200.9 (CHO), 170.6 and 164.2 (2 × CO_2), 106.1 (quat.), 103.9 (CH), 96.2, 96.0, 92.6, 90.7, 85.2 and 83.8 (6 × O–C, quat.), 62.1 and 60.3 (2 × quat.), 59.0 and 49.9 (2 × CH), 38.6, 37.1, 35.7, 34.0, 30.5, 30.2, 28.2, 27.7, 26.7 and 25.9 (10 × CH_2), 28.1 and 27.9 (2 × C*Me*$_3$), 13.3 and 13.2 (2 × CH_3); discernible data for cycloadduct **3.231** = 203.2 (CO), 200.9 (CHO); discernible data for cyclic hydrate **3.241** = 106.1 (quat.), 103.9 (CH); ***m/z (CI): 253 (25%), 270 (100), 326 (M + NH_4^+, 15); HRMS (ES+): M + NH_4^+ found 326.1966, $C_{17}H_{28}NO_5$ requires 326.1962. Key NOE enhancements supporting the stereochemical assignments are shown below:



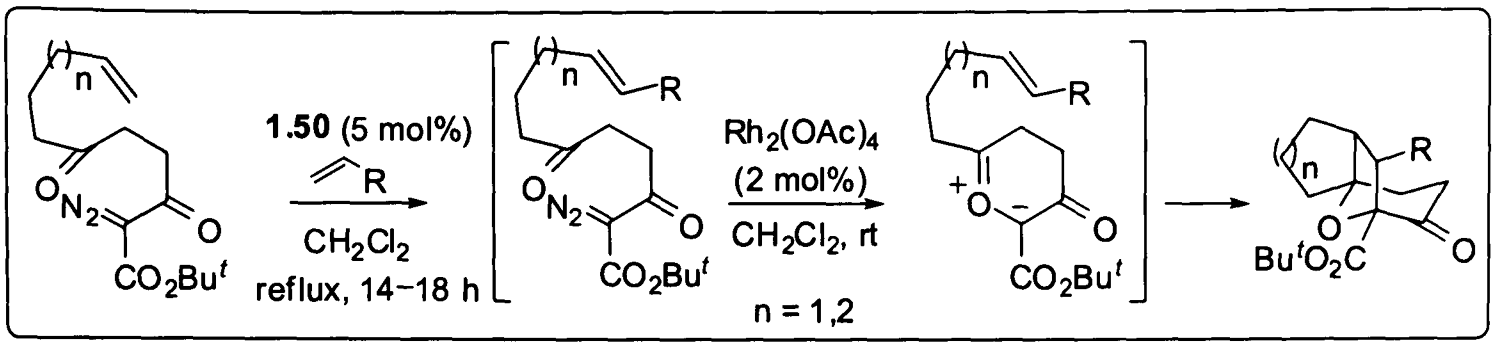
6-Formyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23m



3.23m was prepared following the general procedure using diazoester **3.22m** (26.0 mg, 0.0807 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (45% Et_2O in petrol) to afford the cycloadduct **3.23m** (20.1 mg, 85%, as 1:0.25 mixture of the cycloadduct **3.23m** and its cyclic hydrate **3.24m**) as a yellow oil.

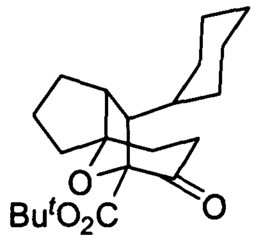
$\boldsymbol{R_f}$ = 0.16 (50% Et_2O in petrol); **IR** (neat): 2962s, 1726s, 1453m, 1370s, 1324m, 1258m, 1158s, 1102s; δ_H (400 MHz, $CDCl_3$) cycloadduct **3.23m** = 9.84 (d, 1H, J = 1.3, CHO), 3.21 (dd, 1H, J = 7.0 and 1.2, C*H*CHO), 2.94–2.89 (m, 1H, C*H*CH$_2$), 2.70–2.60 (m, 2H, CH$_2$), 2.52–2.42 (m, 2H, CH$_2$), 2.16–2.08 (m, 1H, CH of CH$_2$), 1.98–1.80 (m, 4H, 2 × CH$_2$), 1.80–1.68 (m, 1H, CH of CH$_2$), 1.53 (s, 9H, CMe$_3$); discernible data for cyclic hydrate **3.24m** = 5.75 (d, 1H, J = 11.9, OH), 5.25 (d, 1H, J = 11.8, C*H*OH); δ_C (100 MHz, $CDCl_3$) cycloadduct **3.23m** = 203.3 (CO), 198.6 (CHO), 165.6 (CO$_2$), 93.6 and 92.2 (2 × COC, quat.), 83.9 (*C*Me$_3$), 66.0 (*C*HCHO), 45.6 (*C*HCH$_2$), 37.1, 35.2, 33.1, 33.0 and 24.9 (5 × CH$_2$), 27.9 (C*Me*$_3$); discernible data for cyclic hydrate **3.24m** = 106.9 (quat.), 101.6 (CH), 95.4 and 91.6 (2 × COC, quat.), 84.8 (*C*Me$_3$), 62.8 and 54.9 (2 × CH), 38.6, 33.8, 30.6, 29.4, and 25.1 (5 × CH$_2$), 27.7 (C*Me*$_3$); ***m/z*** (CI): 256 (100%), 272 (32), 295 (M + H$^+$, 10), 312 (M + NH$_4^+$, 100), 328 (25); HRMS (ES+): M + NH$_4^+$ found 312.1803, $C_{16}H_{26}NO_5$ requires 312.1805.

5.8. One-Pot Cross Metathesis/ Intramolecular Cycloadditions



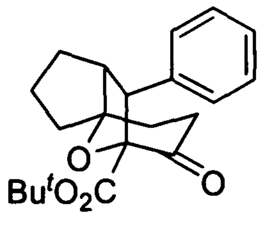
General procedure: Grubbs 2nd generation catalyst **1.50** (5 mol%) was added to a solution of α-diazo-β-ketoester (1.0 equiv.) and olefin (5–10 equiv.) in CH_2Cl_2 (*c* = 14–20 mM) and the reaction mixture was heated to reflux for 14–18 h. After cooling to room temperature anhydrous rhodium acetate dimer (2 mol%) added and the reaction mixture was stirred at room temperature for 3 h. The mixture was then concentrated under reduced pressure and purified by flash chromatography.

6-Cyclohexyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23a



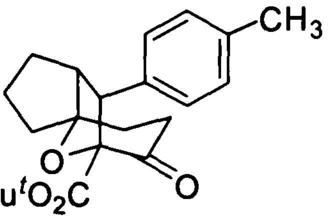
3.23a was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and vinylcyclohexane (186 µL, 1.36 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the cycloadduct **3.23a** (30.0 mg, 63%) as a yellow oil. Spectroscopic data as described above (pp. 129).

8-Oxo-6-phenyl-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23c



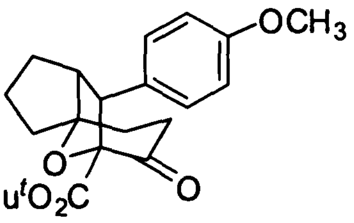
3.23c was prepared following the general procedure using diazoester **3.14** (147 mg, 0.50 mmol) and styrene (229 µL, 2.00 mmol) in CH_2Cl_2 (30 mL). The residue was purified by flash chromatography (30% Et_2O in petrol) to afford the cycloadduct **3.23c** (125 mg, 73%) as a yellow oil. Spectroscopic data as described above (pp. 129).

6-(4-Methyl)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23d



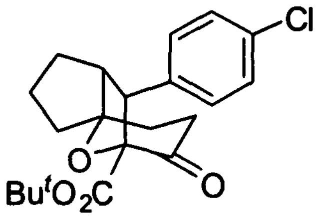
3.23d was prepared following the general procedure using diazoester **3.14** (42.0 mg, 0.143 mmol) and 4-methylstyrene (188 μL, 1.43 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→20% Et_2O in petrol) to afford the cycloadduct **3.23d** (39.0 mg, 77%) as a yellow oil. Spectroscopic data as described above (pp. 130).

6-(4-Methoxy)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23e



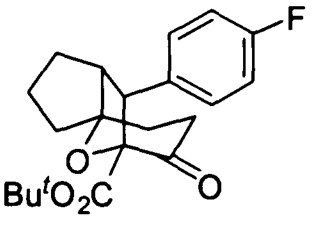
3.23e was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and 4-methoxystyrene (181 μL, 1.36 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the cycloadduct **3.23e** (22.0 mg, 43%) as a yellow oil. Spectroscopic data as described above (pp. 130).

6-(4-Chloro)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23g



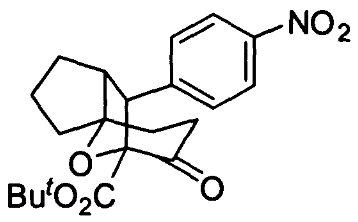
3.23g was prepared following the general procedure using diazoester **3.14** (130 mg, 0.442 mmol) and 4-chlorostyrene (212 μL, 1.77 mmol) in CH_2Cl_2 (25 mL). The residue was purified by flash chromatography (20% Et_2O in petrol) to afford the cycloadduct **3.23g** (113 mg, 68%) as a yellow oil. Spectroscopic data as described above (pp. 131).

6-(4-Fluoro)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23h



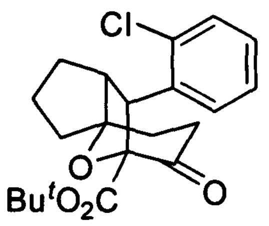
3.23h was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and 4-fluorostyrene (162 μL, 1.36 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the cycloadduct **3.23h** (37.0 mg, 75%) as a yellow oil. Spectroscopic data as described above (pp. 132).

6-(4-Nitro)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23i



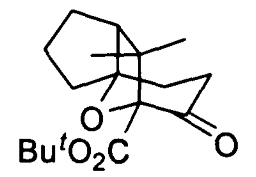
3.23i was prepared following the general procedure using diazoester **3.14** (193 mg, 0.656 mmol) and 4-nitrostyrene (489 mg, 3.28 mmol) in CH_2Cl_2 (32 mL). The residue was purified by flash chromatography (30% Et_2O in petrol) to afford the cycloadduct **3.23i** (192 mg, 76%) as a pale yellow oil. Spectroscopic data as described above (pp. 132).

6-(2-Chloro)phenyl-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23j



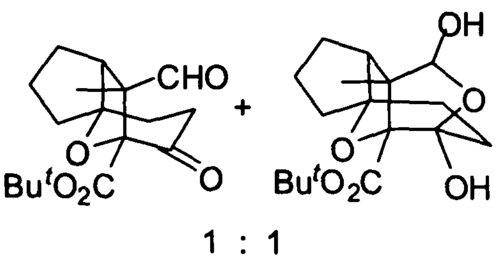
3.23j was prepared following the general procedure using diazoester **3.14** (43.0 mg, 0.146 mmol) and 2-chlorostyrene (187 μL, 1.46 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→20% Et_2O in petrol) to afford the cycloadduct **3.23j** (44.0 mg, 80%) as a yellow oil. Spectroscopic data as described above (pp. 133).

6,6-Dimethyl-8-oxo-11-oxatricyclo[5.3.1.$0^{1,5}$]undecane-7-*tert*-butyl carboxylate, 3.23k



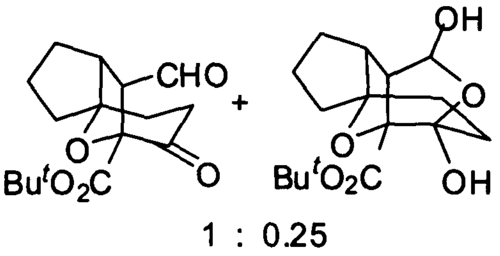
3.23k was prepared following the general procedure using diazoester **3.14** (42.0 mg, 0.143 mmol) and amylene (151 μL, 1.43 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (15% Et_2O in petrol) to afford the cycloadduct **3.23k** (33.0 mg, 79%) as a colourless oil. Spectroscopic data as described above (pp. 133).

6-Formyl-6-methyl-8-oxo-11-oxa-tricyclo[5.3.1.$0^{1,5}$]undecane-7-*tert*-butyl carboxylate, 3.23l



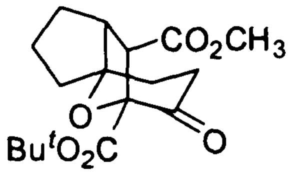
3.23l was prepared following the general procedure using diazoester **3.14** (42.0 mg, 0.143 mmol) and methacrolein (118 μL, 1.43 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (50% Et_2O in petrol) to afford the cycloadduct **3.23l** (38.0 mg, 86%, as 1:1 mixture of the desired cycloadduct **3.23l** and its cyclic hydrate **3.24l**) as a yellow oil. Spectroscopic data as described above (pp. 134).

6-Formyl-8-oxo-11-oxatricyclo[5.3.1.$0^{1,5}$]undecane-7-*tert*-butyl carboxylate, 3.23m



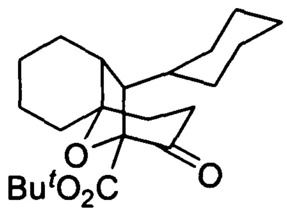
3.23m was prepared following the general procedure using diazoester **3.14** (40.0 mg, 0.136 mmol) and crotonaldehyde (56.0 μL, 0.680 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (40% Et_2O in petrol) to afford the cycloadduct **3.23m** (28.0 mg, 70%, as 1:0.25 mixture of the cycloadduct **3.23m** and its cyclic hydrate **3.24m**) as a yellow oil. Spectroscopic data as described above (pp. 135).

6-Carbomethoxy-8-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undecane-7-*tert*-butyl carboxylate, 3.23n[25]



3.23n was prepared following the general procedure using diazoester **3.14** (245 mg, 0.840 mmol) and methyl acrylate (180 μL, 2.08 mmol) in CH_2Cl_2 (40 mL). The residue was purified by flash chromatography (30% Et_2O in petrol) to afford the cycloadduct **3.23n** (186 mg, 69%) as a yellow oil. Spectroscopic data consistent with lit.

7-Cyclohexyl-9-oxo-12-oxatricyclo[6.3.1.0^{1,6}]dodecane-8-*tert*-butyl carboxylate, 3.26a



3.26a was prepared following the general procedure using diazoester **3.25**[25] (41.0 mg, 0.133 mmol) and vinylcyclohexane (182 μL, 1.33 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the cycloadduct was obtained **3.26a** (24.0 mg, 50%) as a yellow oil.

R*f** = 0.58 (30% Et_2O in petrol); **IR** (neat): 2929s, 2358s, 1727s, 1368s, 1318m, 1155s, 1078s; δ_H (400 MHz, $CDCl_3$) = 2.70–2.58 (m, 1H, CH of CH_2), 2.48–2.30 (m, 1H, CH of CH_2), 2.24 (dd, 1H, J = 10.4 and 4.3, CH), 210–1.95 (m, 2H, CH_2), 1.90–1.52 (m, 10H, CH, CH of CH_2 and 4 × CH_2), 1.49 (s, 9H, CMe_3), 1.40–0.88 (m, 10H, CH, CH of CH_2 and 4 × CH_2); δ_C (100 MHz, $CDCl_3$) = 204.7 (CO), 167.2 (CO_2), 91.3, 82.2 and 80.4 (3 × O–C, quat.), 58.6, 46.3 and 39.0 (3 × CH), 35.2, 33.9, 33.5, 32.8, 32.7, 31.1, 26.5, 26.3, 26.2, 21.6, 19.4 (11 × CH_2), 27.8 (CMe_3); ***m/z (CI): 363 ($M + H^+$, 100%), 380 ($M + NH_4^+$, 100), 382 (50); HRMS (ES+): $M + H^+$ found 363.2532, $C_{22}H_{35}O_4$ requires 363.2530.

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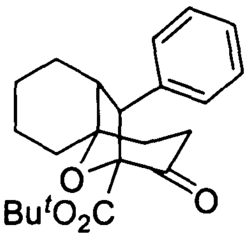
[25] D. M. Hodgson, A. H. Labande, F. Y. T. M. Pierard, M. Á. E. Castro, *J. Org. Chem* **2003**, *68*, 6153–6159.

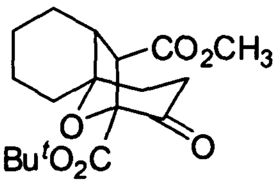
9-Oxo-7-phenyl-12-oxatricyclo[6.3.1.0^{1,6}]dodecane-8- *tert*-butyl carboxylate, 3.26b



3.26b was prepared following the general procedure using diazoester **3.25** (226 mg, 0.734 mmol) and styrene (336 μL, 2.94 mmol) in CH_2Cl_2 (40 mL). The residue was purified by flash chromatography (20% Et_2O in petrol) to afford the cycloadduct **3.26b** (172mg, 66%) as a yellow oil.

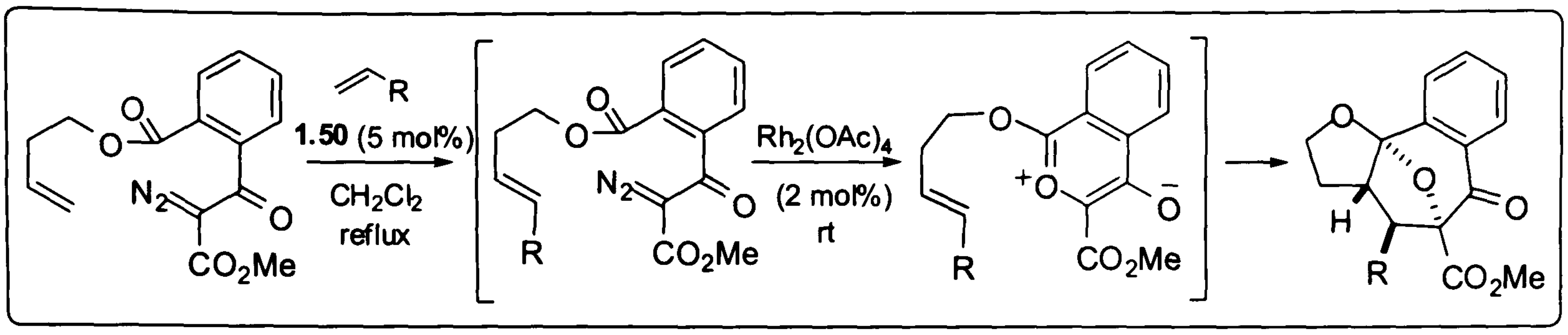
R*$_f$** = 0.54 (50% Et_2O in petrol); **IR** (neat): 2961s, 2872s, 2405s, 2253s, 1730s, 1450s, 1374s, 1220s, 1160w, 1080m; **δ_H** (400 MHz, $CDCl_3$) = 7.34 (d, 2H, *J* = 7.5, Ar), 7.26 (t, 2H, *J* = 7.6, Ar), 7.20 (d, 1H, *J* = 7.4, Ar), 3.66 (d, 1H, *J* = 5.4, C*H*Ar), 2.52–2.42 (m, 2H, C*H*CH_2 and CH of CH_2), 2.26–1.88 (m, 7H, CH of CH_2 and 3 × CH_2), 1.80–1.50 (m, 3H, CH of CH_2 and CH_2), 1.56 (s, 9H, CMe_3), 1.52–1.28 (m, 1H, CH of CH_2); **δ_C** (100 MHz, $CDCl_3$) = 203.2 (CO), 167.1 (CO_2), 137.4 (Ar, quat.), 128.3, 128.2 and 126.9 (3 × Ar), 91.6, 82.7 and 80.9 (3 × O–C, quat.), 58.0 (*C*HAr), 47.6 (*C*HCH_2), 36.9, 34.4, 32.7, 29.8, 21.0 and 19.0 (6 × CH_2), 27.9 (C*Me*$_3$); ***m/z (CI): 318 (100%), 357 (M + H^+, 5), 374 (M + NH_4^+, 60); HRMS (ES+): M + NH_4^+ found 374.2325, $C_{22}H_{32}NO_4$ requires 374.2326.

7-Carbomethoxy-9-oxo-12-oxatricyclo[6.3.1.0^{1,6}]dodecane-8-*tert*-butyl carboxylate, 3.26c[25]



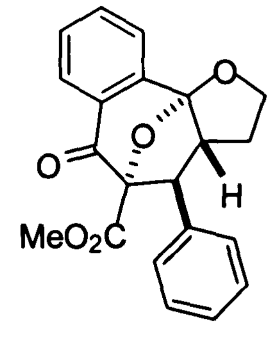
3.26c was prepared following the general procedure using diazoester **3.25** (116 mg, 0.376 mmol) and methyl acrylate (68.0 μL, 0.752 mmol) in CH_2Cl_2 (20 mL). The residue was purified by flash chromatography (20% Et_2O in petrol) to afford the cycloadduct **3.26c** (80.0 mg, 63%) as a yellow oil. Spectroscopic data consistent with lit.

5.9. One-Pot Cross Metatyhesis/ Oxidopyrylium Formation-Cycloaddition



General procedure: Grubbs' 2nd generation catalyst **1.50** (5 mol%) was added to a solution of α-diazo-β-ketoester **3.27**[26] (1.0 equiv.) and olefin (5–10 equiv.) in CH_2Cl_2 (c = 15–20 mM) and the reaction mixture was heated to reflux for 14–18 h. After cooling to room temperature anhydrous rhodium acetate dimer (2 mol%) added and the reaction mixture was stirred at room temperature for 3 h. The mixture was then concentrated under reduced pressure and purified by flash chromatography.

9,10-Benzo-7-carbomethoxy-6-phenyl-2,11-dioxatricyclo[5.3.1.0^{1,5}]undecane-8-one, 3.29a



3.29a was prepared following the general procedure using diazoester **3.27** (40.0 mg, 0.132 mmol) and styrene (152 μL, 1.32 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (5→20% Et_2O in petrol) to afford the cycloadduct **3.29a** (40.0 mg, 86%) as a yellow oil.

R_f = 0.40 (50% Et_2O in petrol); **IR** (neat): 2954m, 1751s, 1702s, 1603m, 1455m, 1283m, 1251m, 1154w, 1086m; δ_H (400 MHz, $CDCl_3$) = 7.97 (d, 1H, J = 7.3, Ar), 7.75–7.66 (m, 2H, Ar), 7.58–7.48 (m, 1H, Ar), 7.24–7.16 (m, 3H, Ar), 7.02–6.94 (m, 2H, Ar), 4.64 (q, 1H, J = 7.8, OCH_aH_b), 4.54–4.44 (m, 1H, OCH_aH_b), 4.15 (d, 1H, J = 5.1, CHPh), 3.84 (s, 3H, OCH_3), 3.08–3.00 (m, 1H, $CHCH_2$), 2.60–2.46 (m, 1H, $CHCH_aH_b$), 2.26–2.14 (m, 1H, $CHCH_aH_b$); δ_C (100 MHz, $CDCl_3$) = 190.1 (CO), 167.4 (CO_2), 143.7, 135.7 and 130.6 (3 × Ar, quat.), 134.7, 129.3, 128.9, 128.3, 127.6, 127.2 and 122.2 (7 × Ar), 114.0 and 94.4 (2 × quat.), 71.8 (OCH_2), 55.6 and 55.2 (2 × CH), 53.0 (OCH_3), 33.5 ($CHCH_2$); ***m/z*** (CI): 131 (100%), 351 ($M + H^+$, 90),

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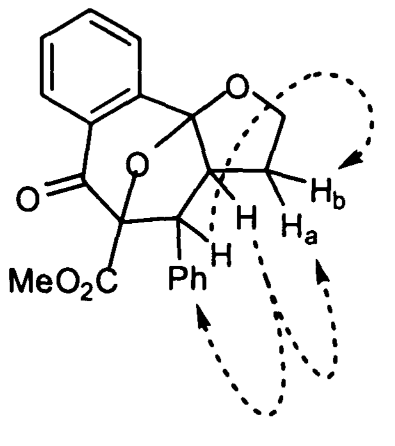
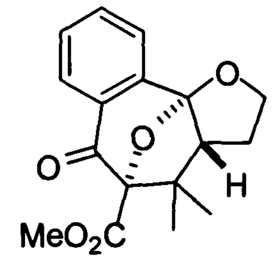
[26] D. M. Hodgson, P. A. Stupple, C. Johnstone, *Arkivoc* **2003**, *7*, 49–58.

368 (M + NH_4^+, 10); HRMS: M + H^+ found 351.1233, $C_{21}H_{19}O_5$ requires 351.1232. Key NOE enhancements supporting the stereochemical assignments are shown below:



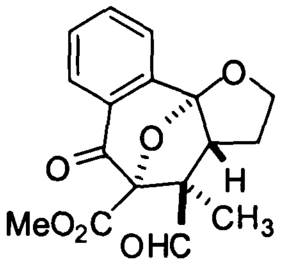
9,10-Benzo-7-carbomethoxy-6,6-dimethyl-2,11-dioxatricyclo[5.3.1.$0^{1,5}$]undecane-8-one, 3.29b



3.29b was prepared following the general procedure using diazoester **3.27** (37.0 mg, 0.123 mmol) and amylene (130 μL, 1.23 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the cycloadduct **3.29b** (30.6 mg, 83%) as a yellow oil.

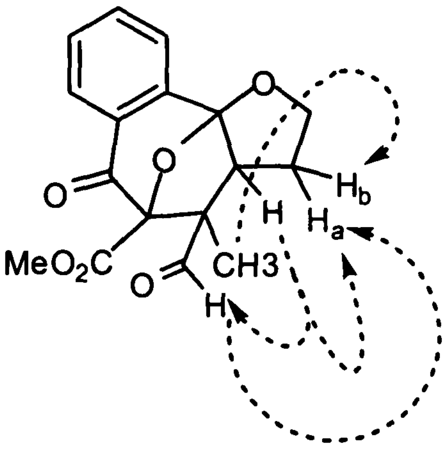
R*f** = 0.27 (50% Et_2O in petrol); **IR** (neat): 2957m, 1751s, 1699s, 1602, 1457m, 1366m, 1291s, 1255s, 1110s, 1089s, 1038m; **δ_H** (400 MHz, $CDCl_3$) = 8.01 (d, 1H, *J* = 7.7, Ar), 7.64–7.50 (m, 2H, Ar), 7.46 (t, 1H, *J* = 7.4, Ar), 4.44–4.38 (m, 2H, OCH_2), 3.87 (s, 3H, OCH_3), 2.51 (dd, 1H, *J* = 9.6 and 4.1, C*H*CH$_2$), 2.20–2.04 (m, 2H, CHC*H*$_2$), 1.27 and 1.21 (2 × s, 6H, C*Me*$_2$); **δ_C** (100 MHz, $CDCl_3$) = 190.2 (CO), 165.8 (CO_2), 145.4 and 129.6 (2 × Ar, quat.), 134.3, 128.7, 127.6 and 121.3 (4 × Ar), 112.3 and 96.4 (2 × quat.), 71.6 (OCH_2), 59.6 (*C*HCH$_2$), 52.5 (OCH_3), 44.7 (*C*Me$_2$), 27.2 (CH*C*H$_2$), 26.4 and 22.4 (C*Me*$_2$); ***m/z (CI): 173 (35%), 221 (15), 238 (85), 303 (M + H^+, 100), 320 (M + NH_4^+, 35); HRMS: M + H^+ found 303.1226, $C_{17}H_{19}O_5$ requires 303.1232.

9,10-Benzo-7-carbomethoxy-6-formyl-6-methyl-2,11-dioxatricyclo[5.3.1.0^{1,5}] undecane-8-one, 3.29c

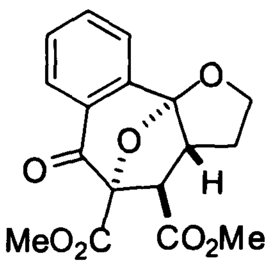


3.29c was prepared following the general procedure using diazoester **3.27** (37.0 mg, 0.123 mmol) and methacrolein (101 μL, 1.23 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→60% EtOAc in hexane) to afford the cycloadduct **3.29c** (21.0 mg, 54%) as a yellow oil.

R*f** = 0.23 (60% EtOAc in hexane); **IR** (neat): 1751s, 1703s, 1438m, 1284m, 1085w; **δ**$_H$ (400 MHz, $CDCl_3$) = 9.68 (s, 1H, CHO), 7.95 (d, 1H, *J* = 7.8, Ar), 7.68–7.56 (m, 2H, Ar), 7.47 (td, 1H, *J* = 7.4 and 1.5, Ar), 4.47–4.43 (m, 1H, OCH_aH_b), 4.37–4.31 (m, 1H, OCH_aH_b), 3.91 (s, 3H, OCH_3), 3.31 (dd, 1H, *J* = 10.6 and 3.0, C*H*CH_2), 2.20–2.11 (m, 1H, CHCH_aH_b), 2.05–1.99 (m, 1H, CHCH_aH_b), 1.51 (s, 3H, CH_3); **δ**$_C$ (100 MHz, $CDCl_3$) = 199.8 (CHO), 189.1 (CO), 165.0 (CO_2), 144.4 and 129.2 (2 × Ar, quat.), 134.8, 129.1, 127.9 and 121.3 (4 × Ar), 112.9 and 95.2 (2 × quat.), 71.8 (OCH_2), 58.7 (*C*CH, quat.), 53.1 (OCH_3), 52.2 (*C*HCH_2), 26.8 (CH*C*H_2), 15.1 (CH_3); ***m/z (CI): 317 (M + H^+, 82%), 334 (M + NH_4^+, 100); HRMS: M + H^+ found 317.1022, $C_{17}H_{17}O_6$ requires 317.1025. Key NOE enhancements supporting the stereochemical assignments are shown below:

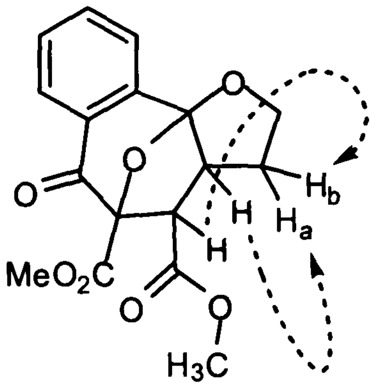


9,10-Benzo-6,7-dicarbomethoxy-2,11-dioxatricyclo[5.3.1.$0^{1,5}$]undecane-8-one, 3.29d

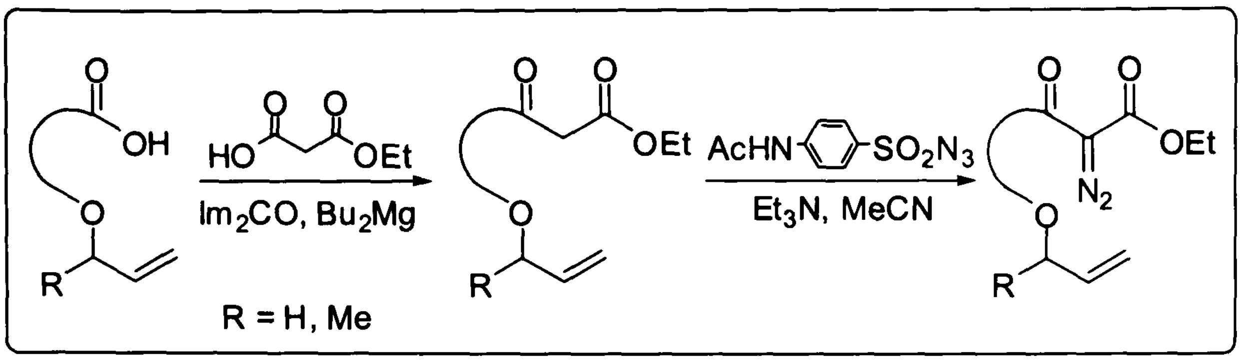


3.29d was prepared following the general procedure using diazoester **3.27** (36.0 mg, 0.119 mmol) and methyl acrylate (107 μL, 1.19 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→40% Et_2O in petrol) to afford the cycloadduct **3.29d** (27.0 mg, 68%) as a white solid.

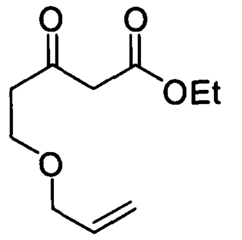
R*f** = 0.18 (60% Et_2O in petrol); **IR** (KBr): 2956m, 1752s, 1704s, 1603m, 1438m, 1367m, 1285s, 1205s, 1085s; **m.p.** = 147–148 °C; **δ_H** (400 MHz, $CDCl_3$) = 8.04 (d, 1H, *J* = 7.6, Ar), 7.66–7.54 (m, 2H, Ar), 7.51 (td, 1H, *J* = 7.5 and 1.5, Ar), 4.58–4.50 (m, 1H, OCH_aH_b), 4.48–4.38 (m, 1H, OCH_aH_b), 3.89 and 3.68 (2 × s, 6H, 2 × OCH_3), 3.74 (d, 1H, *J* = 4.8, $CHCO_2CH_3$), 3.12–3.04 (m, 1H, $CHCH_2$), 2.58–2.45 (m, 1H, $CHCH_aH_b$), 2.10–1.98 (m, 1H, $CHCH_aH_b$); **δ_C** (100 MHz, $CDCl_3$) = 189.5 (CO), 170.4 and 166.6 (2 × CO_2), 143.1 and 130.1 (2 × Ar, quat.), 134.4, 129.3, 127.3 and 121.9 (4 × Ar), 114.5 and 91.8 (2 × quat.), 71.6 (OCH_2), 54.8 ($CHCO_2CH_3$), 53.3 ($CHCH_2$), 52.7 and 52.5 (2 × OCH_3), 32.4 ($CHCH_2$); ***m/z (CI): 333 ($M + H^+$, 100%), 350 ($M + NH_4^+$, 80); HRMS: $M + H^+$ found 333.0972, $C_{17}H_{17}O_7$ requires 333.0974. Key NOE enhancements supporting the stereochemical assignments are shown below:



5.10. Synthesis of α-Diazo-β-ketoesters



Ethyl 5-(allyloxy)-3-oxopentanoate, 4.19



β-Ketoester **4.19** was prepared by homologation carboxylic acid **4.18**[27] following Masamune's procedure.[28] Carbonyl diimidazole (2.76 g, 17.0 mmol) was added to a stirred solution of 3-(allyloxy)propanoic acid **4.18** (2.01 g, 15.5 mmol) in THF (20 mL) at 0 °C. After 15 min the reaction mixture was allowed to warm to room temperature for 1 h. *mono*-Ethyl malonate (2.00 mL, 17.0 mmol) in THF (20 mL), was cooled to –78 °C and to this solution Bu$_2$Mg (17.0 mL of a 1.0 M solution in heptane, 17.0 mmol) was added *via* a syringe. The reaction was allowed to stir at –78 °C for 15 min and then at room temperature for 1 h. The solvent was removed under reduced pressure to give the Mg salt of *mono*-ethyl malonate. Acyl imidazolide was added *via* a cannula to the Mg salt. After 18 h the reaction was quenched by the addition of 10% aq. citric acid solution (20 mL). The aq. phase was extracted with Et$_2$O (3 × 40 mL) and the combined organic extracts were washed with sat. aq. NaHCO$_3$ solution (3 × 30 mL), aq. NaCl (3 × 30 mL), dried (MgSO$_4$) and concentrated under reduced pressure. The crude was purified by flash chromatography (5→30% Et$_2$O in petrol) to afford the β-ketoester **4.19** (2.3 g, 73%) as a colourless oil.

***R*$_f$** = 0.16 (30% ether in petrol); **IR** (neat): 2985s, 1720s, 1648s, 1360m, 1230w, 1091m; δ_H (400 MHz, CDCl$_3$) = 5.93–5.84 (m, 1H, =CH), 5.26 (dq, 1H, *J* = 17.2 and 1.4, =CH_aH$_b$), 5.18 (dq, 1H, *J* = 10.4 and 1.4, =CH$_a$$H_b$), 4.20 (q, 2H, *J* = 7.1, OCH_2CH$_3$), 3.97 (dt, 2H, *J* = 5.6 and 1.4, =CHCH_2), 3.71 (t, 2H, *J* = 6.2, COCH$_2$CH_2), 3.49 (s, 2H, (CO)$_2$CH$_2$)), 2.82 (t, 2H, *J* = 6.2, COCH_2CH$_2$), 1.28 (t, 3H, *J* = 7.1, CH$_3$); δ_C (100 MHz, CDCl$_3$) = 201.4 (CO), 167.1 (CO$_2$), 134.4 (=CH), 117.2 (=CH$_2$), 72.1 (=CHCH$_2$), 64.8 (COCH$_2$CH$_2$), 61.4 (OCH$_2$CH$_3$), 49.8 (CO)$_2$CH$_2$)),

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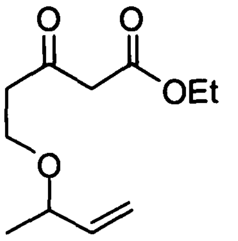
[27] B. Simonot, G. Rousseau, *Synth. Commun.* **1993**, *23*, 549–560.

[28] a) D. W. Brooks, L. D. L. Lu, S. Masamune, *Angew. Chem. Int. Ed.* **1979**, *18*, 72–74; b) M. Ghosh, M. J. Miller, *Tetrahedron* **1996**, *52*, 4225–4238.

43.1 ($COCH_2CH_2$), 14.1 (CH_3); **HRMS** (ES+): M + Na^+ found 223.0934, $C_{10}H_{16}NaO_4$ requires 223.0941.

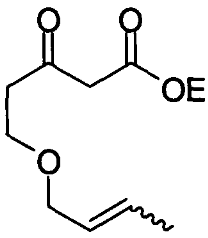
Ethyl 5-(but-3-en-2-yloxy)-3-oxopentanoate, 4.26



β-Ketoester **4.26** was prepared by homologation of carboxylic acid following the procedure mentioned above starting from 3-(but-3-en-2-yloxy) propanoic acid **4.25** (5.00 g, 34.7 mmol). The crude was purified by flash chromatography (5→10% Et_2O in petrol) to afford the β-ketoester **4.26** (4.0 g, 54%) as a colourless oil.

R*f** = 0.42 (40% Et_2O in petrol); **IR** (neat): 2981s, 1717s, 1645s, 1369m, 1311w, 1238w, 1097m; δ_H (400 MHz, $CDCl_3$) = 5.71–5.67 (m, 1H, =CH), 5.20–5.12 (m, 2H, =CH_2), 4.20 (q, 2H, *J* = 7.2, OCH_2CH_3), 3.85–3.78 (m, 1H, $CHCH_3$), 3.73 (dt, 1H, *J* = 9.8 and 6.2, $COCH_2CH_aH_b$), 3.58 (dt, 1H, *J* = 9.8 and 6.3, $COCH_2CH_aH_b$), 3.49 (s, 2H, $(CO)_2CH_2$), 2.78 (td, 2H, *J* = 6.2 and 0.9, $COCH_2$), 1.28 (t, 3H, *J* = 7.2, OCH_2CH_3), 1.22 (d, 3H, *J* = 6.3, $CHCH_3$); δ_C (100 MHz, $CDCl_3$) = 201.7 (CO), 167.1 (CO_2), 139.9 (=CH), 116.1 (=CH_2), 77.4 ($CHCH_3$), 62.9 ($COCH_2CH_2$), 61.3 (OCH_2CH_3), 49.8 ($(CO)_2CH_2$), 43.3 ($COCH_2$), 21.2 ($CHCH_3$), 14.1 (OCH_2CH_3); ***m/z (ES+): 215 (M + H^+, 7%), 237 (M + Na^+, 100); HRMS: M + Na^+ found 237.1095, $C_{11}H_{18}NaO_4$ requires 237.1097.

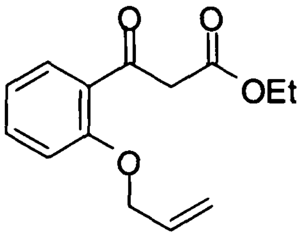
Ethyl 5-(but-2-enyloxy)-3-oxopentanoate, 4.39



β-Ketoester **4.39** was prepared by homologation of carboxylic acid following the procedure mentioned above starting from 3-(but-2-enyloxy)propanoic acid **4.38**[27] (1.28 g, 8.89 mmol). The crude was purified by flash chromatography (5→10% Et_2O in petrol) to afford the β-ketoester **4.39** (1.39 g, 73%) as a colourless oil.

***R*f** = 0.39 (40% Et_2O in petrol); **IR** (neat): 2981s, 1710s, 1642s, 1311w, 1230w, 1095m; δ_H (400 MHz, $CDCl_3$) = 5.76–5.67 and 5.59-5.51 (2 × m, 2 × =CH), 4.20 (q, 2H, *J* = 7.2, OCH_2CH_3), 3.91–3.89 (m, 2H, =$CHCH_2$), 3.68 (t, 2H, *J* = 6.2, $COCH_2CH_2$), 3.49 (s, 2H, $(CO)_2CH_2$), 2.80 (t, 2H, J = 6.2, $COCH_2$), 1.72–1.69 (m, 3H, $=CHCH_3$), 1.28 (t, 3H, J = 7.2, OCH_2CH_3); δ_C (100 MHz, $CDCl_3$) = 201.5 (CO), 167.1 (CO_2), 129.8 and 127.2 (2 × $=CH_2$), 71.8 ($=CHCH_2$), 64.5 ($COCH_2CH_2$), 61.3 (OCH_2CH_3), 49.8 ($(CO)_2CH_2$), 43.1 ($COCH_2$), 17.8 ($=CHCH_3$), 14.1 (OCH_2CH_3); **HRMS**: M + Na^+ found 237.1097, $C_{11}H_{18}NaO_4$ requires 237.1097.

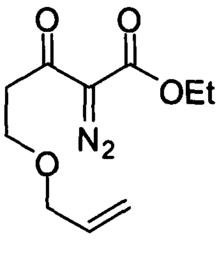
Ethyl 3-(2-(allyloxy)phenyl)-3-oxopropanoate, 4.33b



β-Ketoester **4.33b** was prepared by homologation of carboxylic acid following the procedure mentioned above starting from 2-(allyloxy)benzoic acid **4.32** (3.00 g, 16.8 mmol). The crude was purified by flash chromatography (10→30% Et_2O in petrol) to afford the β-ketoester **4.33b** (2.7 g, 65%) as a colourless oil.

R_f = 0.39 (30% Et_2O in petrol); **IR** (neat): 2981s, 1717s, 1640s, 1369m, 1097m; δ_H (400 MHz, $CDCl_3$) = 7.90–7.85 (m, 1H, Ar), 7.50–7.46 (m, 1H, Ar), 7.04 (td, 1H, J = 15.1 and 1.4, Ar), 6.95 (d, 1H, J = 8.4, Ar), 6.16–6.06 (m, 1H, =CH), 5.45–5.32 (m, 2H, $=CH_2$), 4.65 (dt, 2H, J = 5.5 and 1.4, $=CHCH_2$), 4.15 (q, 2H, J = 7.2, OCH_2CH_3), 4.02 (s, 2H, $COCH_2$), 1.25 (t, 3H, J = 7.2, CH_3); δ_C (100 MHz, $CDCl_3$) = 193.4 (CO), 168.2 (CO_2), 158.1 and 126.7 (2 × Ar, quat.), 134.5, 132.3, and 131.2 (2 × Ar, =CH), 120.9 and 112.7 (2 × Ar), 118.7 ($=CH_2$), 69.5 ($=CHCH_2$), 60.9 (OCH_2CH_3), 50.6 ($COCH_2$), 14.1 (CH_3); ***m/z*** (ES+): 249 (M + H^+, 86%), 271 (M + Na^+, 100); HRMS: M + Na^+ found 271.0938, $C_{14}H_{16}NaO_4$ requires 271.0941.

Ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate, 4.20[29]



4.20 was prepared by diazo transfer using *p*-acetamidobenzenesulfonylazide following lit. procedure.[30] To a solution of ethyl 5-(allyloxy)-3-oxopentanoate **4.19** (2.26 g, 11.3 mmol) in acetonitrile (40 mL) was added Et_3N (1.90 mL, 13.5 mmol) and *p*-acetamidobenzenesulfonyl

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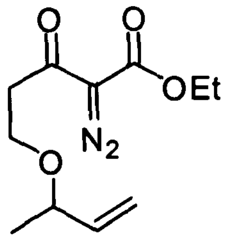
[29] N. McCarthy, M. A. McKervey, T. Ye, M. McCann, E. Murphy, M. P. Doyle, *Tetrahedron Lett.* **1992**, *33*, 5983–5986.

[30] Y.-H. Lim, K. F. McGee, S. McN. Sieburth, *J. Org. Chem.* **2002**, *67*, 6535–6538.

azide (3.25 g, 13.5 mmol). The reaction mixture was allowed to stir at room temperature for 2 h during which time a white precipitate was formed. The mixture was washed with sat. aq. NH_4Cl (20 mL) and the aq. layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with 10% aq. KOH (3 × 30 mL), sat. aq. $NaHCO_3$ (3 × 30 mL) and sat. aq. NaCl (3 × 30 mL), dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography (5→30% ether in petrol) to afford the diazoester **4.20** (2.24 g, 92%) as a yellow oil.

$\boldsymbol{R_f}$ = 0.45 (40% ether in petrol); **IR** (neat): 2975m, 2139s, 1720s, 1645s, 1373m, 1220w, 1087s; δ_H (400 MHz, $CDCl_3$) = 5.95–5.85 (m, 1H, =CH), 5.27 (dq, 1H, *J* = 17.3 and 1.4, $=CH_aH_b$), 5.17 (dq, 1H, *J* = 10.4 and 1.4, $=CH_aH_b$), 4.23 (q, 2H, *J* = 7.1, OCH_2CH_3), 4.00 (dt, 2H, *J* = 5.7 and 1.4, $=CHCH_2$), 3.78 (t, 2H, *J* = 6.2, $COCH_2CH_2$), 3.15 (t, 2H, *J* = 6.2, $COCH_2CH_2$), 1.33 (t, 3H, *J* = 7.1, CH_3); δ_C (100 MHz, $CDCl_3$) = 190.6 (CO), 161.3 (CO_2), 134.7 (=CH), 117.1 ($=CH_2$), 72.0 ($=CHCH_2$), 64.9 ($COCH_2CH_2$), 61.4 (OCH_2CH_3), 40.3 ($COCH_2CH_2$), 14.3 (CH_3); **HRMS** (ES+): M + Na^+ found 249.0838, $C_{10}H_{14}N_2NaO_4$ requires 249.0846.

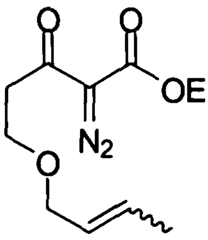
Ethyl 5-(but-3-en-2-yloxy)-2-diazo-3-oxopentanoate, 4.27



4.27 was prepared by diazo transfer using *p*-acetamidobenzenesulfonyl azide following the procedure mentioned above starting from ethyl 5-(but-3-en-2-yloxy)-3-oxopentanoate **4.26** (2.50 g, 11.7 mmol). The crude was purified by flash chromatography (5→10% Et_2O in petrol) to afford the diazoester **4.27** (2.4 g, 86%) as a yellow oil.

$\boldsymbol{R_f}$ = 0.50 (40% Et_2O in petrol); **IR** (neat): 2981s, 2136s, 1719s, 1656s, 1447m, 1373s, 1304s, 1214s, 1098s, 1020m; δ_H (400 MHz, $CDCl_3$) = 5.78–5.69 (m, 1H, =CH), 5.22–5.11 (m, 2H, $=CH_2$), 4.30 (q, 2H, *J* = 7.2, OCH_2CH_3), 3.89–3.84 (m, 1H, $CHCH_3$), 3.80 (dt, 1H, *J* = 9.8 and 6.2, $COCH_2CH_aH_b$), 3.66 (dt, 1H, *J* = 9.8 and 6.2, $COCH_2CH_aH_b$), 3.12 (td, 2H, *J* = 6.2 and 1.0, $COCH_2$), 1.33 (t, 3H, *J* = 7.2, OCH_2CH_3), 1.22 (d, 3H, *J* = 6.3, $CHCH_3$); δ_C (100 MHz, $CDCl_3$) = 190.7 (CO), 161.3 (CO_2), 140.2 (=CH), 115.8 ($=CH_2$), 77.1 ($CHCH_3$), 62.9 ($COCH_2CH_2$), 61.4 (OCH_2CH_3), 40.6 ($COCH_2$), 21.2 ($CHCH_3$), 14.3 (OCH_2CH_3); ***m/z*** (ES+): 241 (M + H^+, 46%), 263 (M + Na^+, 100); HRMS: M + Na^+ found 263.1002, $C_{11}H_{16}N_2NaO_4$ requires 263.1002.

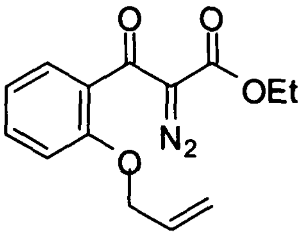
Ethyl 5-(but-2-enyloxy)-2-diazo-3-oxopentanoate, 4.40



4.40 was prepared by diazo transfer using *p*-acetamidobenzenesulfonyl azide following the procedure mentioned above starting from ethyl 5-(but-2-enyloxy)-3-oxopentanoate **4.39** (1.25 g, 5.84 mmol). The crude was purified by flash chromatography (5→20% Et_2O in petrol) to afford the diazoester **4.40** (1.33 g, 95%) as a yellow oil.

***R*f** = 0.49 (40% Et_2O in petrol); **IR** (neat): 2980s, 2138s, 1720s, 1650s, 1214s, 1098s; δ_H (400 MHz, $CDCl_3$) = 5.75–5.66 and 5.59–5.52 (2 × m, 2H, 2 × =CH), 4.29 (q, 2H, *J* = 7.1, OC*H*$_2$CH$_3$), 3.91 (dd, 2H, *J* = 6.1 and 1.1, =CHC*H*$_2$), 3.74 (t, 2H, *J* = 6.2, COCH$_2$C*H*$_2$), 3.13 (t, 2H, *J* = 6.2, COCH$_2$), 1.70 (dd, 3H, *J* = 6.3 and 1.0, =CHC*H*$_3$), 1.32 (t, 3H, *J* = 7.1, OCH$_2$C*H*$_3$); δ_C (100 MHz, $CDCl_3$) = 190.6 (CO), 161.2 (CO_2), 129.6 and 127.4 (2 × =CH$_2$), 71.7 (=CH*C*H$_2$), 64.6 (COCH$_2$*C*H$_2$), 61.4 (O*C*H$_2$CH$_3$), 40.3 (CO*C*H$_2$), 17.7 (=CH*C*H$_3$), 14.3 (OCH$_2$*C*H$_3$); HRMS: M + Na$^+$ found 263.0999, $C_{11}H_{16}N_2NaO_4$ requires 263.1002.

Ethyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate, 4.34b

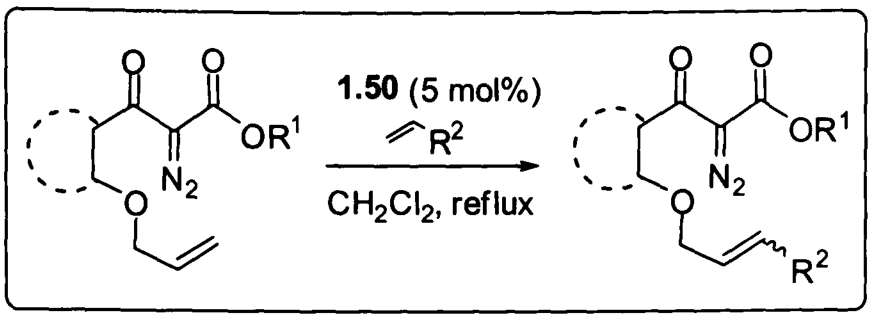


4.34b was prepared by diazo transfer using *p*-acetamidobenzenesulfonyl azide following the procedure mentioned above starting from ethyl 3-(2-(allyloxy)phenyl)-3-oxopropanoate **4.33b** (2.71 g, 10.9 mmol). The crude was purified by flash chromatography (20% Et_2O in petrol) to afford the diazoester **4.34b** (2.9 g, 97%) as a yellow oil.

***R*f** = 0.35 (30% Et_2O in petrol); **IR** (neat): 3078m, 2984s, 2138s, 1728s, 1629s, 1488s, 1451m, 1371s, 1320s, 1165s, 1017s; δ_H (400 MHz, $CDCl_3$) = 7.44–7.39 (m, 1H, Ar), 7.34 (dd, 1H, *J* = 7.6 and 1.7, Ar), 7.01 (td, 1H, *J* = 7.6 and 1.0, Ar), 6.89 (d, 1H, *J* = 8.3, Ar), 6.04–5.94 (m, 1H, =CH), 5.38 (dq, 1H, *J* = 17.2 and 1.5, =C*H*$_a$H$_b$), 5.27 (dq, 1H, *J* = 10.6 and 1.5, =CH$_a$*H*$_b$), 4.55 (dt, 2H, *J* = 5.1 and 1.5, =CHC*H*$_2$), 4.18 (q, 2H, *J* = 7.2, OC*H*$_2$CH$_3$), 1.21 (t, 3H, *J* = 7.2, CH$_3$); δ_C (100 MHz, $CDCl_3$) = 186.2 (CO), 160.9 (CO_2), 156.0 and 128.3 (2 × Ar. quat.), 132.7 (=CH), 132.3, 128.7, 120.8 and 111.9 (4 × Ar), 117.4 (=CH$_2$), 69.2 (=CH*C*H$_2$), 61.3 (O*C*H$_2$CH$_3$), 14.2 (CH$_3$);

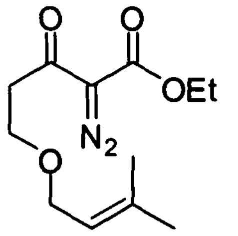
m/z (FI): 274 (M^+, 100%), 275 ($M + H^+$, 100); HRMS: M^+ found 274.0945, $C_{14}H_{14}N_2O_4$ requires 274.0954.

5.11. Cross-Metathesis of α-Diazo-β-ketoesters 4.20 & 4.34a



General procedure: Grubbs 2nd generation catalyst **1.50** (5 mol%) was added to a solution of diazoester (1.0 equiv.) and olefin (5–10 equiv.) in CH_2Cl_2 (*c* = 15–20 mM). The mixture was heated under reflux for 14–18 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure and purified by flash chromatography.

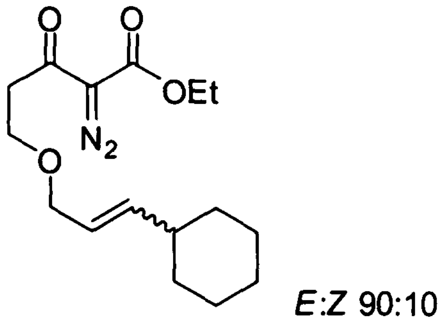
Ethyl 2-diazo-5-(3-methylbut-2-enyloxy)-3-oxopentanoate, 4.30a



4.30a was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (52.0 mg, 0.230 mmol) and amylene (243 μL, 2.30 mmol) in CH_2Cl_2 (15 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the diazoester **4.30a** (48.0 mg, 82%) as a yellow oil.

***R*f** = 0.31 (30% Et_2O in petrol); **IR** (neat): 2143s, 1718s, 1655s, 1373m, 1301m, 1216w, 1091s; δ_H (400 MHz, $CDCl_3$) = 5.35–5.31 (m, 1H, =CH), 4.29 (q, 2H, *J* = 7.2, OCH_2CH_3), 3.98 (d, 2H, *J* = 6.8, $=CHCH_2$), 3.76 (t, 2H, *J* = 6.3, $COCH_2CH_2$), 3,14 (t, 2H, *J* = 6.2, $COCH_2$), 1.74 and 1.67 (2 × s, 6H, CMe_2), 1.32 (t, 3H, *J* = 7.1, CH_3); δ_C (100 MHz, $CDCl_3$) = 190.7 (CO), 161.3 (CO_2), 137.1 (=C), 120.9 (=CH), 67.4 ($=CHCH_2$), 64.7 ($COCH_2CH_2$), 61.4 (OCH_2CH_3), 40.4 ($COCH_2$), 25.8 and 18.0 (CMe_2), 14.3 (CH_3); *m/z* (CI): 187 (80%), 204 (40), 255 ($M + H^+$, 30), 272 ($M + NH_4^+$, 10); HRMS (ES+): $M + H^+$ found 255.1339, $C_{12}H_{19}N_2O_4$ requires 255.1339.

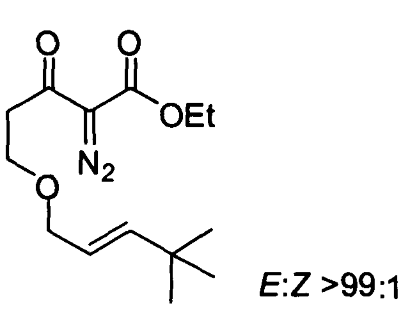
Ethyl 5-(3-cyclohexylallyloxy)-2-diazo-3-oxopentanoate, 4.30b



4.30b was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (47.0 mg, 0.208 mmol) and vinylcyclohexane (284 μL, 2.08 mmol) in CH_2Cl_2 (15 mL). The residue was purified by flash chromatography (5→15% Et_2O in petrol) to afford the diazoester **4.30b** (57.0 mg, 89%, *E*:*Z* 90:10 by ^1H NMR) as a yellow oil.

R*f** = 0.46 (30% Et_2O in petrol); **IR** (neat): 2925s, 2852s, 2134s, 1719s, 1658s, 1449m, 1373s, 1302s, 1219m, 1101m, 1020m; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 5.65 (dd, 1H, *J* = 15.5 and 6.4, $=CHC_6H_{11}$), 5.46 (dtd, 1H, *J* = 15.4, 6.2 and 1.1, $=CHCH_2$), 4.30 (q, 2H, *J* = 7.2, OCH_2CH_3), 3.94 (d, 2H, *J* = 6.1, $=CHCH_2$), 3.75 (t, 2H, *J* = 6.3, $COCH_2CH_2$), 3.14 (t, 2H, *J* = 6.3, $COCH_2$), 2.02–1.90 (m, 1H, C(1)H cyclohexyl), 1.76–1.56 (m, 6H, 3 × CH_2 cyclohexyl), 1.33 (t, 3H, *J* = 7.2, CH_3), 1.32–1.00 (m, 4H, 2 × CH_2 cyclohexyl); discernible data for ***Z*-isomer** = 5.42–5.39 (m, 1H, =CH), 5.30 (dd, 1H, *J* = 3.5 and 1.7, =CH); δ_C (100 MHz, $CDCl_3$) ***E*-isomer** = 190.7 (CO), 161.3 (CO_2), 140.6 and 123.5 (2 × =CH), 72.0 ($=CHCH_2$), 64.5 ($COCH_2CH_2$), 61.5 (OCH_2CH_3), 40.4 and 40.3 ($COCH_2$ and C(1)H cyclohexyl), 32.7, 26.1 and 26.0 (3 × CH_2 cyclohexyl), 14.3 (CH_3); ***m/z (CI): 204 (45%), 300 (55), 309 (M + H^+, 85), 326 (M + NH_4^+, 50); HRMS (ES+): M + H^+ found 309.1810, $C_{16}H_{25}N_2O_4$ requires 309.1809.

(*E*)-Ethyl 2-diazo-5-(4,4-dimethylpent-2-enyloxy)-3-oxopentanoate, 4.30c

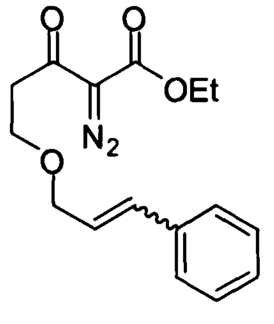


4.30c was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (53.0 mg, 0.234 mmol) and 3,3-dimethyl-1-butene (301 μL, 2.34 mmol) in CH_2Cl_2 (15 mL). The residue was purified by flash chromatography (7→30% Et_2O in petrol) to afford the diazoester **4.30c** (33.0 mg, 50%, *E*:*Z* >99:1 by ^1H NMR) as a yellow oil.

***R*f** = 0.34 (30% Et_2O in petrol); **IR** (neat): 2960m, 2135s, 1719s, 1658s, 1372s, 1302s, 1108m; δ_H (400 MHz, $CDCl_3$) = 5.70 (dt, 1H, *J* = 15.7 and 1.2, $=CHCMe_3$), 5.44 (dt, 1H, *J* = 15.7 and 6.0,

=C*H*CH$_2$), 4.30 (q, 2H, *J* = 7.2, OC*H*$_2$CH$_3$), 3.95 (dd, 2H, *J* = 6.0 and 1.2, =CHC*H*$_2$), 3.75 (t, 2H, *J* = 6.5, COCH$_2$C*H*$_2$), 3.15 (t, 2H, *J* = 6.5, COCH$_2$), 1.33 (t, 3H, *J* = 7.2, OCH$_2$C*H*$_3$), 1.01 (s, 9H, CMe$_3$); **δ$_C$** (100 MHz, CDCl$_3$) = 190.7 (CO), 161.2 (CO$_2$), 145.4 (=*C*HCMe$_3$), 120.9 (=*C*HCH$_2$), 72.1 (=CH*C*H$_2$), 64.6 (COCH$_2$*C*H$_2$), 61.4 (O*C*H$_2$CH$_3$), 40.3 (CO*C*H$_2$), 32.9 (*C*Me$_3$), 29.4 (C*Me*$_3$), 14.3 (OCH$_2$*C*H$_3$); ***m/z*** (CI): 274 (25%), 283 (M + H$^+$, 100), 300 (M + NH$_4^+$, 15); HRMS (ES+): M + H$^+$ found 283.1652, $C_{14}H_{23}N_2O_4$ requires 283.1652.

Ethyl 2-diazo-3-oxo-5-(3-phenylallyloxy)pentanoate, 4.30d

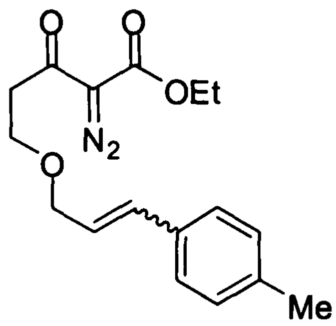


E:*Z* 94:6

4.30d was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (53.0 mg, 0.234 mmol) and styrene (268 μL, 2.34 mmol) in CH$_2$Cl$_2$ (15 mL). The residue was purified by flash chromatography (10→30% Et$_2$O in petrol) to afford the diazoester **4.30d** (33.0 mg, 47%, *E*:*Z* 94:6 by ^{1}H NMR) as a yellow oil.

R*$_f$** = 0.22 (30% Et$_2$O in petrol); **IR** (neat): 2870m, 2135s, 1716s, 1654s, 1373s, 1302s, 1219m, 1107s, 1020m; **δ$_H$** (400 MHz, CDCl$_3$) ***E*-isomer** = 7.40–7.22 (m, 5H, Ar), 6.60 (d, 1H, *J* = 15.9, =CHPh), 6.28 (dt, 1H, *J* = 15.9 and 6.1, =C*H*CH$_2$), 4.30 (q, 2H, *J* = 7.1, OC*H*$_2$CH$_3$), 4.18 (dd, 2H, *J* = 6.1 and 1.5, =C*H*CH$_2$), 3.84 (t, 2H, *J* = 6.2, COCH$_2$C*H*$_2$), 3.18 (t, 2H, *J* = 6.2, COCH$_2$), 1.33 (t, 3H, *J* = 7.1, CH$_3$); discernible data for ***Z*-isomer** = 3.73 (t, 2H, *J* = 6.1, COCH$_2$C*H*$_2$), 3.14 (t, 2H, *J* = 6.2, COCH$_2$); **δ$_C$** (100 MHz, CDCl$_3$) ***E*-isomer** = 190.6 (CO), 161.2 (CO$_2$), 136.7 (Ar, quat.), 132.5 (=*C*HPh), 128.5, 127.6 and 126.4 (3 × Ar), 125.9 (=*C*HCH$_2$), 71.6 (=CH*C*H$_2$), 64.9 (COCH$_2$*C*H$_2$), 61.4 (O*C*H$_2$CH$_3$), 40.3 (CO*C*H$_2$), 14.3 (CH$_3$); ***m/z (CI): 203 (40%), 294 (40), 303 (M + H$^+$, 20), 320 (M + NH$_4^+$, 100); HRMS (ES+): M + NH$_4^+$ found 320.1606, $C_{16}H_{22}N_3O_4$ requires 320.1605.

Ethyl 2-diazo-3-oxo-5-(3-p-tolylallyloxy)pentanoate, 4.30e

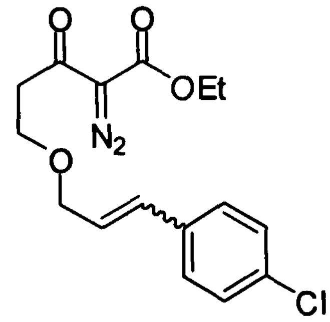


E:*Z* 98:2

4.30e was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (45.0 mg, 0.199 mmol) and 4-methylstyrene (262 μL, 1.99 mmol) in CH_2Cl_2 (15 mL). The residue was purified by flash chromatography (5→20% Et_2O in petrol) to afford the diazoester **4.30e** (41.0 mg, 65%, *E*:*Z* 98:2 by ^{1}H NMR) as a yellow oil.

R_f = 0.22 (30% Et_2O in petrol); **IR** (neat): 2924w, 2135s, 1716s, 1655s, 1372s, 1302s, 1099s; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 7.28 (d, 2H, *J* = 8.0, Ar), 7.12 (d, 2H, *J* = 8.0, Ar), 6.57 (d, 1H, *J* = 15.9, =C*H*Ar), 6.22 (dt, 1H, *J* = 15.9 and 6.2, =C*H*CH_2), 4.30 (q, 2H, *J* = 7.2, OC*H*$_2$$CH_3$), 4.16 (dd, 2H, *J* = 6.2 and 1.4, =CHC*H*$_2$), 3.83 (t, 2H, *J* = 6.2, $COCH_2$C*H*$_2$), 3.18 (t, 2H, *J* = 6.2, $COCH_2$), 2.34 (s, 3H, C*H*$_3$Ar), 1.33 (t, 3H, *J* = 7.1, OCH_2C*H*$_3$); discernible data for ***Z*-isomer** = 3.73 (t, 2H, *J* = 6.2, $COCH_2$C*H*$_2$); δ_C (100 MHz, $CDCl_3$) ***E*-isomer** = 190.6 (CO), 161.3 (CO_2), 137.5 and 133.9 (2 × Ar, quat.), 132.5 (=*C*HAr), 129.2 and 126.4 (2 × Ar), 124.9 (=*C*HCH_2), 71.8 (=CH*C*H$_2$), 64.8 ($COCH_2$*C*H$_2$), 61.5 (O*C*H$_2$$CH_3$), 40.3 (CO*C*H$_2$), 21.2 (*C*H$_3$Ar), 14.3 ($OCH_2$*C*H$_3$); ***m/z*** (ES+): 311 (10%), 339.1315 (M + Na^+, 100); HRMS: M + Na^+ found 339.1315, $C_{17}H_{20}N_2NaO_4$ requires 339.1315.

Ethyl 5-(3-(4-chlorophenyl)allyloxy)-2-diazo-3-oxopentanoate, 4.30f



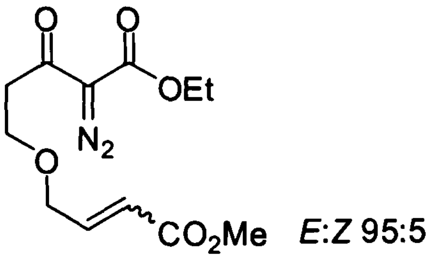
E:*Z* 97:3

4.30f was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (46.0 mg, 0.203 mmol) and 4-chlorostyrene (244 μL, 2.03 mmol) in CH_2Cl_2 (15 mL). The crude was purified by flash chromatography (5→25% Et_2O in petrol) to afford the diazoester **4.30f** (37.0 mg, 54%, *E*:*Z* 97:3 by ^{1}H NMR) as a yellow oil.

R_f = 0.25 (30% Et_2O in petrol); **IR** (neat): 2136s, 1716s, 1656s, 1491m, 1373s, 1303s, 1219m, 1091s, 1014m; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 7.32–7.26 (m, 4H, Ar), 6.55 (dt, 1H, *J* = 15.9

and 1.5, =C*H*Ar), 6.25 (dt, 1H, *J* = 15.9 and 6.0, =C*H*CH$_2$), 4.29 (q, 2H, *J* = 7.2, OC*H*$_2$CH$_3$), 4.15 (dd, 2H, *J* = 6.1 and 1.5, =CHC*H*$_2$), 3.83 (t, 2H, *J* = 6.1, COCH$_2$C*H*$_2$), 3.18 (t, 2H, *J* = 6.2, COCH$_2$), 1.32 (t, 3H, *J* = 7.2, CH$_3$); discernible data for ***Z*-isomer** = 3.72 (t, 2H, *J* = 6.2, COCH$_2$); δ_C (100 MHz, CDCl$_3$) ***E*-isomer** = 190.6 (CO), 161.2 (CO$_2$), 135.2 and 133.2 (2 × Ar, quat.), 131.0 (=*C*HAr), 128.7 and 127.7 (2 × Ar), 126.7 (=*C*HCH$_2$), 71.4 (=CH*C*H$_2$), 65.0 (COCH$_2$*C*H$_2$), 61.5 (O*C*H$_2$CH$_3$), 40.3 (CO*C*H$_2$), 14.3 (CH$_3$); ***m/z*** (ES+): 354 (M + NH$_4^+$, 4%), 359 (M + Na$^+$, 100); HRMS: M + Na$^+$ found 359.0770, $C_{16}H_{17}{}^{35}ClN_2NaO_4$ requires 359.0769.

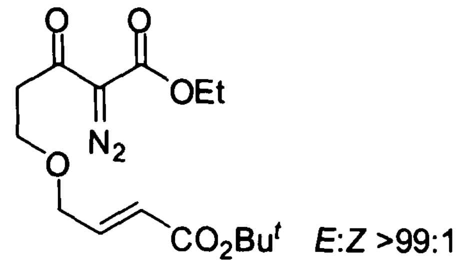
Ethyl 2-diazo-5-(4-methoxy-4-oxobut-2-enyloxy)-3-oxopentanoate, 4.30g



4.30g was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (52.0 mg, 0.230 mmol) and methyl acrylate (207 µL, 2.30 mmol) in CH$_2$Cl$_2$ (15 mL). The residue was purified by flash chromatography (10→30% Et$_2$O in petrol) to afford the diazoester **4.30g** (56.0 mg, 86%, *E*:*Z* 95:5 by ^{1}H NMR) as a yellow oil.

R*$_f$** = 0.18 (40% Et$_2$O in petrol); **IR** (neat): 2956w, 2137s, 1720s, 1656s, 1437w, 1374m, 1305s, 1133m; δ_H (400 MHz, CDCl$_3$) ***E*-isomer** = 6.94 (dt, 1H, *J* = 15.9 and 4.1, =C*H*CH$_2$), 6.06 (dt, 1H, *J* = 15.8 and 2.0, =C*H*CO$_2$), 4.30 (q, 2H, *J* = 7.1, OC*H*$_2$CH$_3$), 4.16 (dd, 2H, *J* = 4.2 and 2.0, =CHC*H*$_2$), 3.81 (t, 2H, *J* = 6.2, COCH$_2$C*H*$_2$), 3.73 (s, 3H, OCH$_3$) 3.16 (t, 2H, *J* = 6.2, COCH$_2$), 1.33 (t, 3H, *J* = 7.2, CH$_3$); discernible data for ***Z*-isomer** = 6.38 (dt, 1H, *J* = 11.8 and 4.9, =C*H*CH$_2$), 5.81 (dt, 1H, *J* = 11.8 and 2.4, =CH), 4.58 (dd, 2H, 4.8 and 2.5, =CHC*H*$_2$); δ_C (100 MHz, CDCl$_3$) ***E*-isomer** = 190.4 (CO), 162.7 and 161.2 (2 × CO$_2$), 144.5 (=*C*HCH$_2$), 120.8 (=*C*HCO$_2$), 69.5 (=CH*C*H$_2$), 65.7 (COCH$_2$*C*H$_2$), 61.5 (O*C*H$_2$CH$_3$), 51.5 (OCH$_3$), 40.1 (CO*C*H$_2$), 14.3 (OCH$_2$*C*H$_3$); ***m/z (CI): 276 (15%), 285 (M + H$^+$, 25), 302 (M + NH$_4^+$, 75); HRMS (ES+): M + Na$^+$ found 307.0897, $C_{12}H_{16}N_2O_6Na$ requires 307.0901.

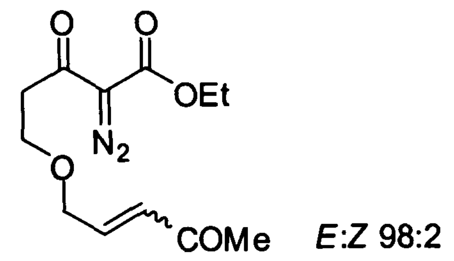
(*E*)-Ethyl 5-(4-butoxy-4-oxobut-2-enyloxy)-2-diazo-3-oxopentanoate, 4.30h



4.30h was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (47.0 mg, 0.208 mmol) and *tert*-butyl acrylate (304 μL, 2.08 mmol) in CH_2Cl_2 (15 mL). The residue was purified by flash chromatography (5→25% Et_2O in petrol) to afford the diazoester **4.30h** (53.0 mg, 78%, *E*:*Z* >99:1 by ^{1}H NMR) as a yellow oil.

R*f** = 0.23 (40% Et_2O in petrol); **IR** (neat): 2980s, 2136s, 1716s, 1659s, 1457w, 1369s, 1307s, 1154s, 1021w; **δH** (400 MHz, $CDCl_3$) = 6.82 (dt, 1H, *J* = 15.7 and 4.5, =C*H*CH$_2$), 5.96 (dt, 1H, *J* = 15.7 and 2.0, =C*H*CO$_2$), 4.30 (q, 2H, *J* = 7.2, OC*H*$_2$CH$_3$), 4.13 (dd, 2H, *J* = 4.5 and 2.0, =CHC*H*$_2$), 3.81 (t, 2H, *J* = 6.2, COCH$_2$C*H*$_2$), 3.16 (t, 2H, *J* = 6.2, COCH$_2$), 1.48 (s, 9H, CM*e*$_3$), 1.34 (t, 3H, *J* = 7.2, OCH$_2$C*H*$_3$); **δC** (100 MHz, $CDCl_3$) = 190.5 (CO), 165.6 and 161.2 (2 × CO$_2$), 142.8 (=*C*HCH$_2$), 123.2 (=*C*HCO$_2$), 80.3 (*C*Me$_3$), 69.7 (=CH*C*H$_2$), 65.7 (COCH$_2$*C*H$_2$), 61.5 (O*C*H$_2$CH$_3$), 40.2 (CO*C*H$_2$), 28.1 (C*Me*$_3$), 14.3 (OCH$_2$*C*H$_3$); ***m/z (CI): 262 (20%), 288 (85), 344 (M + NH_4^+, 100); HRMS (ES+): M + NH_4^+ found 344.1815, $C_{15}H_{26}N_3O_6$ requires 344.1816.

Ethyl 2-diazo-3-oxo-5-(4-oxopent-2-enyloxy)pentanoate, 4.30i

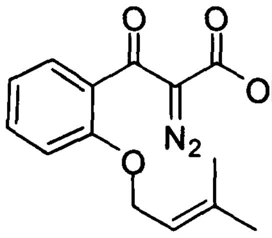


4.30i was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (54.0 mg, 0.239 mmol) and methyl vinyl ketone (194 μL, 2.39 mmol) in CH_2Cl_2 (15 mL). The crude was purified by flash chromatography (10→30% Et_2O in petrol) to afford the diazoester **4.30i** (55.0 mg, 86%, *E*:*Z* 98:2 by ^{1}H NMR) as a yellow oil.

***R*f** = 0.14 (50% Et_2O in petrol); **IR** (neat): 2985w, 2138s, 1717s, 1680m, 1373s, 1304s, 1256m, 1219w, 1134s, 1020m; **δH** (400 MHz, $CDCl_3$) ***E*-isomer** = 6.76 (dt, 1H, *J* = 16.0 and 4.3, =C*H*CH$_2$), 6.28 (dt, 1H, *J* = 16.0 and 1.9, =C*H*CO), 4.30 (q, 2H, *J* = 7.2, OC*H*$_2$CH$_3$), 4.19 (dd, 2H, *J* = 4.4 and 1.9, =CHC*H*$_2$), 3.83 (t, 2H, *J* = 6.2, COCH$_2$C*H*$_2$), 3.17 (t, 2H, *J* = 6.2, COC*H*$_2$), 2.27 (s, 3H, OCH$_3$), 1.34 (t, 3H, *J* = 7.1, CH$_3$); discernible data for ***Z*-isomer** = 5.79–5.77 (m, 1H, =CH), 4.53 (dd, 2H, *J* = 4.3 and 2.0, =CHC*H*$_2$); **δC** (100 MHz, $CDCl_3$) ***E*-isomer** = 198.2 and

190.4 (2 × CO), 161.2 (CO_2), 142.9 (=CHCH_2), 130.3 (=CHCO), 69.7 (=CHCH$_2$), 65.7 ($COCH_2CH_2$), 61.5 (OCH_2CH_3), 40.1 ($COCH_2$), 27.3 ($COCH_3$), 14.3 (OCH_2CH_3); ***m/z*** (CI): 260 (25%), 269 (M + H^+, 10), 286 (M + NH_4^+, 100); HRMS (ES+): M + H^+ found 269.1134, $C_{12}H_{17}N_2O_5$ requires 269.1132.

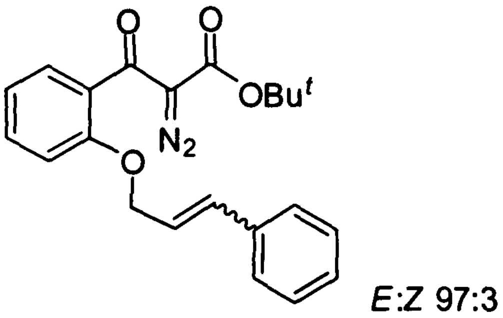
tert-Butyl 2-diazo-3-(2-(3-methylbut-2-enyloxy)phenyl)-3-oxopropanoate, 4.36a



4.36a was prepared by general procedure using *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a**[31] (44.0 mg, 0.146 mmol) and amylene (154 μL, 1.46 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (7→10% Et_2O in petrol) to afford the diazoester **4.36a** (39.0 mg, 81%) as a yellow oil.

R*f** = 0.46 (30% Et_2O in petrol); **IR** (neat): 2979m, 2139s, 1724s, 1631s, 1488m, 1452s, 1369m, 1321s, 1256s, 1149s; **δ_H** (400 MHz, $CDCl_3$) = 7.41–7.36 (m, 1H, Ar), 7.30 (dd, 1H, *J* = 7.5 and 1.7, Ar), 6.98 (td, 1H, *J* = 7.5 and 0.7, Ar), 6.88 (d, 1H, *J* = 8.3, Ar), 5.42–5.38 (m, 1H, =CH), 4.55 (d, 2H, *J* = 6.6, OCH_2), 1.78 and 1.71 (2 × s, 6H, CMe_2), 1.37 (s, 9H, CMe_3); **δ_C** (100 MHz, $CDCl_3$) = 186.8 (CO), 160.2 (CO_2), 156.1 and 128.8 (2 × Ar, quat.), 137.2 (=C, quat.), 132.0, 128.5, 120.5 and 111.9 (4 × Ar), 119.6 (=CH), 82.6 (CMe_3), 65.6 (OCH_2), 28.0 (CMe_3), 25.7 and 18.2 (CMe_2); ***m/z (FI): 330 (M^+, 100%), 331 (M + H^+, 28); HRMS: M^+ found 330.1584, $C_{18}H_{22}N_2O_4$ requires 330.1580.

tert-Butyl 3-(2-(cinnamyloxy)phenyl)-2-diazo-3-oxopropanoate, 4.36b



4.36b was prepared following the general procedure using *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (50.0 mg, 0.166 mmol) and styrene (190 μL, 1.66 mmol) in CH_2Cl_2

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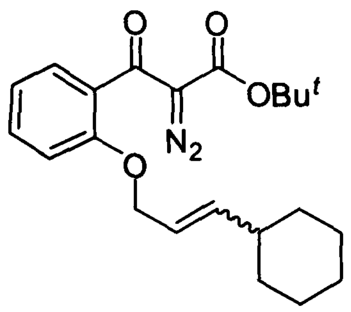
[31] D. M. Hodgson, M. Petroliagi, *Tetrahedron: Asymmetry* **2001**, *12*, 877–881.

(10 mL). The residue was purified by flash chromatography (10→20% Et_2O in petrol) to afford the diazoester **4.36b** (50.0 mg, 80%, *E*:*Z* 97:3) as a yellow oil.

R*f** = 0.36 (30% Et_2O in petrol); **IR** (neat): 2979m, 2140s, 1722s, 1691m, 1488s, 1451s, 1370s, 1322m, 1250s, 1163s, 1127s; **δ_H** (400 MHz, $CDCl_3$) ***E*-isomer** = 7.44–7.29 (m, 7H, Ar), 7.03 (dt, 1H, *J* = 7.6 and 1.0, Ar), 6.95 (d, 1H, *J* = 8.3, Ar), 6.72 (dt, 1H, *J* = 16.2 and 1.5, =C*H*Ar), 3.48 (dt, 1H, *J* = 16.2 and 5.2, =C*H*CH_2), 4.74 (dd, 2H, *J* = 5.3 and 1.5, OCH_2), 1.36 (s, 9H, CMe_3); discernible data for ***Z*-isomer** = 4.85–4.83 (m, 2H, OCH_2); **δ_C** (100 MHz, $CDCl_3$) = 186.8 (CO), 160.1 (CO_2), 155.9, 136.3 and 128.8 (3 × Ar, quat.), 132.4 (=*C*HAr), 132.2, 128.6, 128.6, 127.9, 126.5, 120.8 and 111.9 (7 × Ar), 123.9 (=*C*HCH_2), 82.7 (*C*Me_3), 68.9 (OCH_2), 28.0 (C*Me*$_3$); ***m/z (CI): 117 (100%), 340 (35), 379 (M + H^+, 18); HRMS (ES+): M + H^+ found 379.1652, $C_{22}H_{23}N_2O_4$ requires 379.1652.

tert-Butyl 3-(2-(3-cyclohexylallyloxy)phenyl)-2-diazo-3-oxopropanoate, 4.36c

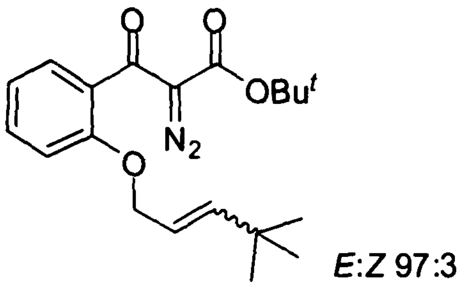


E:*Z* 92:8

4.36c was prepared following the general procedure using *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (43.0 mg, 0.142 mmol) and vinylcyclohexane (194 μL, 1.42 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (5→10% Et_2O in petrol) to afford the diazoester **4.36c** (48.0 mg, 88%, *E*:*Z* 92:8 by ^1H NMR) as a yellow oil.

R*f** = 0.41 (30% Et_2O in petrol); **IR** (neat): 2927w, 2138m, 1721s, 1637s, 1488w, 1451w, 1369w, 1320s, 1250w, 1109w; **δ_H** (400 MHz, $CDCl_3$) ***E*-isomer** = 7.41–7.36 (m, 1H, Ar), 7.31 (dd, 1H, *J* = 7.6 and 1.7, Ar), 6.98 (td, 1H, *J* = 7.6 and 0.7, Ar), 6.88 (d, 1H, *J* = 8.3, Ar), 5.75 (dd, 1H, *J* = 15.7 and 6.8, =C*H*C_6H_{11}), 5.58 (dtd, 1H, *J* = 15.7, 5.6 and 1.3, =CHCH_2), 4.49 (d, 2H, *J* = 5.6, OCH_2), 2.04–2.97 (m, 1H, C(1)H cyclohexyl), 1.75–1.05 (m, 10H, 5 × CH_2 cyclohexyl), 1.37 (s, 9H, CMe_3); discernible data for ***Z*-isomer** = 5.50–5.49 (m, 1H, =CH), 4.62 (d, 2H, *J* = 5.6, OCH_2); **δ_C** (100 MHz, $CDCl_3$) ***E*-isomer** = 186.8 (CO), 160.2 (CO_2), 156.1 and 128.7 (2 × Ar, quat.), 140.6 (=*C*HC_6H_{11}), 132.1, 128.6, 121.8 and 111.9 (4 × Ar), 120.6 (=*C*HCH_2), 82.6 (*C*Me_3), 69.3 (OCH_2), 40.4 (C(1)H, cyclohexyl), 32.6, 26.1 and 25.9 (3 × CH_2 cyclohexyl), 28.1 (C*Me*$_3$); ***m/z (FI): 356 (30%), 384 (M^+, 100), 385 (M + H^+, 30); HRMS (ES+): M + Na^+ found 407.1941, $C_{22}H_{28}N_2NaO_4$ requires 407.1941.

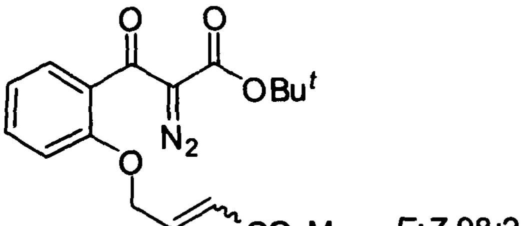
tert-Butyl 2-diazo-3-(2-(4,4-dimethylpent-2-enyloxy)phenyl)-3-oxopropanoate, 4.36d



4.36d was prepared following the general procedure using *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (48.0 mg, 0.159 mmol) and 3,3-dimethyl-1-butene (204 μL, 1.59 mmol) in CH_2Cl_2 (12 mL). The residue was purified by flash chromatography (5→10% Et_2O in petrol) to afford the diazoester **4.36d** (42.0 mg, 74%, *E*:*Z* 97:3 by ^1H NMR) as a yellow oil.

R*$_f$** = 0.57 (30% Et_2O in petrol); **IR** (neat): 2138m, 1640s, 1487w, 1452w, 1369w, 1319m, 1248m, 1149w; **δ$_H$** (400 MHz, $CDCl_3$) ***E*-isomer** = 7.41–7.37 (m, 1H, Ar), 7.32 (dd, 1H, *J* = 7.6 and 1.7, Ar), 6.99 (t, 1H, *J* = 7.5, Ar), 6.88 (d, 1H, *J* = 8.3, Ar), 5.83 (dt, 1H, *J* = 15.8 and 1.4, (=C*H*CMe$_3$), 5.54 (dt, 1H, *J* = 15.9 and 5.5, =C*H*CH$_2$), 4.50 (dd, 2H, *J* = 5.5 and 1.3, OCH$_2$), 1.38 and 1.04 (2 × s, 18H, 2 × CMe$_3$); discernible data for ***Z*-isomer** = 4.62 (dd, 2H, *J* = 6.1 and 1.3, OCH$_2$); **δ$_C$** (100 MHz, $CDCl_3$) ***E*-isomer** = 186.7 (CO), 160.2 (CO$_2$), 156.1 and 128.7 (2 × Ar, quat.), 145.4 (=*C*HCMe$_3$), 132.1, 128.6, 119.3 and 111.9 (4 × Ar), 120.6 (=C*H*CH$_2$), 82.6 (O*C*Me$_3$), 69.3 (OCH$_2$), 33.0 (*C*Me$_3$), 29.3 and 28.0 (2 × C*Me*$_3$); ***m/z (FI): 358 (M$^+$, 100%), 359 (M + H$^+$, 28); HRMS (ES+): M + Na$^+$ found 381.1785, $C_{20}H_{26}N_2NaO_4$ requires 381.1785.

Methyl 4-(2-(3-*tert*-butoxy-2-diazo-3-oxopropanoyl)phenoxy)but-2-enoate, 4.36e

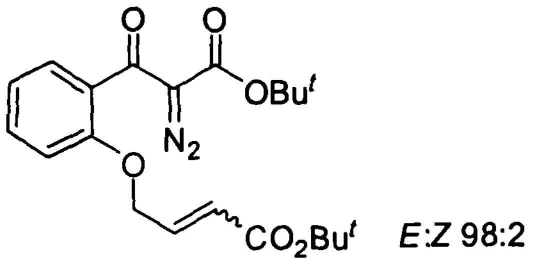


4.36e was prepared following the general procedure using *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (44 mg, 0.146 mmol) and methyl acrylate (131 μL, 1.46 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the diazoester **4.36e** (47.5 mg, 90%, *E*:*Z* 98:2 by ^1H NMR) as a yellow oil.

***R*$_f$** = 0.17 (40% Et_2O in petrol); **IR** (neat): 2141m, 1720s, 1637s, 1489w, 1453w, 1370w, 1321m, 1250w, 1171w; **δ$_H$** (400 MHz, $CDCl_3$) ***E*-isomer** = 7.43–7.38 (m, 1H, Ar), 7.33 (dd, 1H, *J* = 7.6 and 1.7, Ar), 7.08–7.02 (m, 2H, Ar and =C*H*CH$_2$), 6.85 (d, 1H, *J* = 8.4, Ar), 6.18 (dt, 1H, *J* = 15.7 and 2.2, =C*H*CO$_2$), 4.72 (dd, 2H, *J* = 3.8 and 2.3, OCH$_2$), 3.76 (s, 3H, OCH$_3$), 1.37 (s, 9H, CMe$_3$); discernible data for ***Z*-isomer** = 4.83 (dd, 2H, *J* = 4.4 and 1.9, OCH$_2$); **δ$_C$** (100 MHz, $CDCl_3$) ***E*-**

isomer = 186.5 (CO), 166.4 and 159.8 (2 × CO_2), 155.2 and 128.7 (2 × Ar, quat.), 142.1 (=C*H*CH_2), 132.2, 128.7, 121.5 and 111.8 (4 × Ar), 121.4 (=*C*HCO_2), 82.9 (*C*Me_3), 67.0 (OCH_2), 51.7 (OCH_3), 28.0 (C*Me*$_3$); ***m/z*** (FI): 360 (M^+, 100%), 361 (M + H^+, 25); HRMS (ES+): M + Na^+ found 383.1214, $C_{18}H_{20}N_2NaO_6$ requires 383.1214.

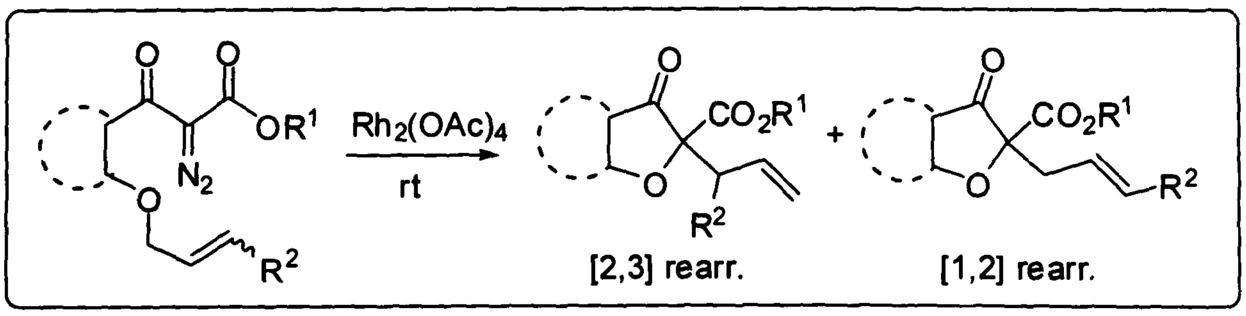
***tert*-Butyl 4-(2-(3-*tert*-butoxy-2-diazo-3-oxopropanoyl)phenoxy)but-2-enoate, 4.36f**



4.36f was prepared following the general procedure using *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (43.0 mg, 0.142 mmol) and *tert*-butyl acrylate (208 μL, 1.42 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the diazoester **4.36f** (51.0 mg, 89%, *E*:*Z* 98:2 by ^1H NMR) as a yellow oil.

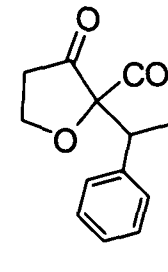
R*$_f$** = 0.33 (40% Et_2O in petrol); **IR** (neat): 2140m, 1718s, 1633m, 1489w, 1454w, 1369w, 1320s, 1153s; **δ_H** (400 MHz, $CDCl_3$) ***E*-isomer** = 7.43–7.39 (m, 1H, Ar), 7.33 (dd, 1H, *J* = 7.6 and 1.7, Ar), 7.04 (td, 1H, *J* = 7.6 and 0.9, Ar), 6.94 (dt, 1H, *J* = 15.7 and 3.8, =C*H*CH_2), 6.85 (d, 1H, *J* = 8.4, Ar), 6.10 (dt, 1H, *J* = 15.7 and 2.1, =C*H*CO_2), 4.69 (dd, 2H, *J* = 3.8 and 2.0, OCH_2), 1.49 and 1.38 (2 × s, 18H, 2 × CMe_3); discernible data for ***Z*-isomer** = 4.81 (dd, 2H, *J* = 4.5 and 2.0, OCH_2); **δ_C** (100 MHz, $CDCl_3$) ***E*-isomer** = 186.6 (CO), 165.2 and 159.8 (2 × CO_2), 155.4 and 128.8 (2 × Ar, quat.), 140.5 (=C*H*CH_2), 132.2, 128.6, 121.3 and 111.8 (4 × Ar), 123.7 (=*C*HCO_2), 82.8 and 80.7 (2 × *C*Me_3), 67.1 (OCH_2), 28.1 and 28.0 (2 × C*Me*$_3$); ***m/z (FI): 402 (M^+, 100%), 403 (M + H^+, 28); HRMS (ES+): M + Na^+ found 425.1681, $C_{21}H_{26}N_2NaO_6$ requires 425.1683.

5.12. Tandem Oxonium Ylide Formation-Rearrangement



General procedure: Anhydrous rhodium acetate dimer (4 mol%) was added to a solution of diazoester (obtained by cross-metathesis) in CH_2Cl_2 (*c* = 12–20 mM) and the reaction mixture was stirred at room temperature till consumption of the starting material (generally 8–12 h). The reaction mixture was concentrated under reduced pressure and purified by flash chromatography.

Ethyl 3-oxo-2-(1-phenylallyl)tetrahydrofuran-2-carboxylate, 4.21d

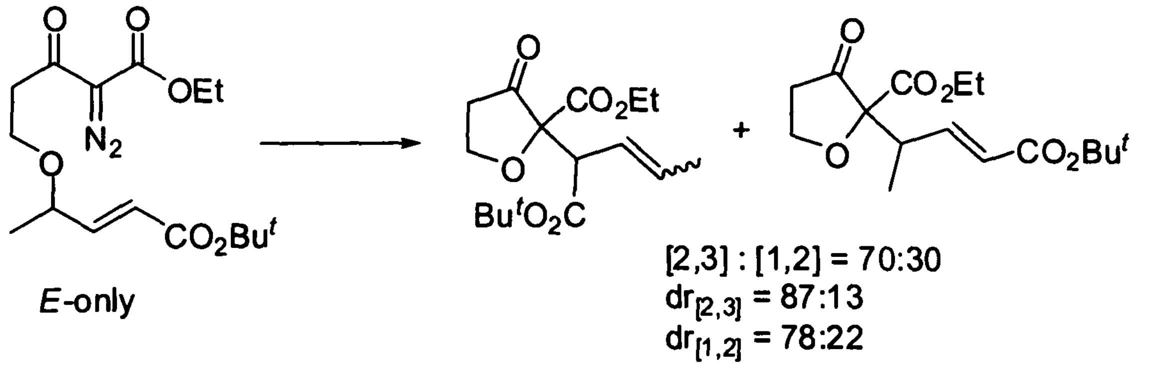


dr = 94:6

4.21d was prepared following the general procedure using ethyl 2-diazo-3-oxo-5-(3-phenylallyloxy)pentanoate **4.30d** (7.00 mg, 0.0232 mmol) in CH_2Cl_2 (2 mL). The residue was purified by flash chromatography (30% Et_2O in petrol) to afford the dihydrofuranone **4.21d** (6.00 mg, 94%, dr = 94:6 by ^1H NMR) as a yellow oil.

R*f** = 0.26 (30% Et_2O in petrol); **IR** (neat): 2983s, 1766s, 1741s, 1466w, 1409w, 1233s, 1093s, 1024s; δ_H (400 MHz, $CDCl_3$) **major** diastereomer = 7.33–7.20 (m, 5H, Ar), 6.22–6.13 (m, 1H, =CH), 5.26–5.17 (m, 2H, $=CH_2$), 4.34–4.18 (m, 5H, C*H*Ar, $COCH_2CH_2$, OCH_2CH_3), 2.28–2.21 (m, 1H, $COCH_aH_b$), 1.65 (dt, 1H, *J* = 18.2 and 10.2, $COCH_aH_b$), 1.33 (t, 3H, *J* = 7.2, CH_3); discernible data for **minor** diastereomer = 6.04–5.95 (m, 1H, =CH), 5.19–5.08 (m, 2H, $=CH_2$), 4.04–3.95 (m, 2H, OCH_2CH_3), 2.56–2.54 (m, 2H, C*H*Ar), 1.01 (t, 3H, *J* = 7.1, OCH_2CH_3); δ_C (100 MHz, $CDCl_3$) **major** diastereomer = 208.8 (CO), 167.3 (CO_2), 137.4 (Ar, quat.), 135.1 (=CH), 130.0, 128.3 and 127.3 (3 × Ar), 118.2 ($=CH_2$), 89.4 (O–C, quat.), 64.7 ($COCH_2CH_2$), 62.3 (OCH_2CH_3), 54.2 (*C*HAr), 36.2 ($COCH_2$), 14.2 (CH_3); ***m/z (CI): 275 ($M + H^+$, 100%), 292 ($M + NH_4^+$, 40); HRMS: $M + H^+$ found 275.1282, $C_{16}H_{19}O_4$ requires 275.1283.

Ethyl 2-(1-*tert*-butoxy-1-oxopent-3-en-2-yl)-3-oxotetrahydrofuran-2-carboxylate, 4.28

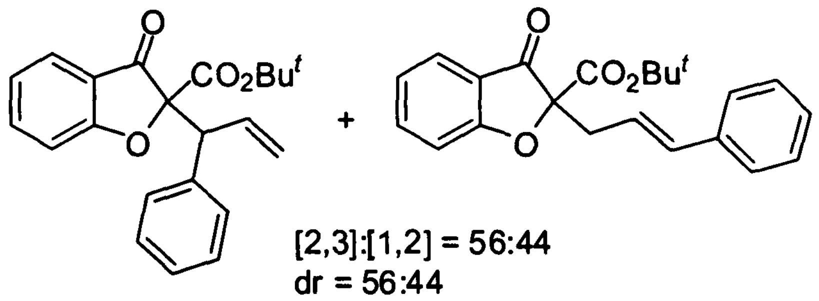


[2,3] : [1,2] = 70:30
$dr_{[2,3]}$ = 87:13
$dr_{[1,2]}$ = 78:22

4.28 was prepared following the general procedure mentioned above starting (*E*)-*tert*-butyl 4-(4-diazo-5-ethoxy-3,5-dioxopentyloxy)pent-2-enoate **4.29** (27.0 mg, 0.0794 mmol) in CH_2Cl_2 (5 mL). The residue was purified by flash chromatography (20% Et_2O in petrol) to afford the dihydrofuranone **4.28** (24.0 mg, 97%, [2,3]:[1,2] = 70:30, dr$_{[2,3]}$ = 87:13, dr$_{[1,2]}$ = 78:22 by ^{1}H NMR) as a yellow oil.

R*$_f$** = 0.40 (40% Et$_2$O in petrol); **IR** (neat): 2981m, 1769m, 1727s, 1645s, 1455m, 1369m, 1252s, 1154s, 1022w; **δ_H** (400 MHz, CDCl$_3$) **major** diastereomer of **[2,3]**-rearr. = 5.77 (dq, 2H, *J* = 15.3 and 6.4, =C*H*CH$_3$), 5.50 (ddq, 2H, *J* = 15.3, 9.2 and 1.5, =C*H*CH), 4.47–4.33 (m, 2H, COCH$_2$C*H*$_2$), 4.27–4.10 (m, 2H, OC*H*$_2$CH$_3$), 3.96 (d, 1H, *J* = 9.2, =CHC*H*), 2.92–2.83 (m, 1H, COC*H*$_a$H$_b$), 2.59–2.48 (m, 1H, COCH$_a$*H*$_b$), 1.68 (dd, 3H, *J* = 6.4 and 1.5, =CHC*H*$_3$), 1.41 (s, 9H, CMe$_3$), 1.25 (t, 3H, *J* = 7.1, OCH$_2$C*H*$_3$); discernible data of **minor** diastereomer of **[2,3]**-rearr. = 3.84 (d, 1H, *J* = 9.3, =CHC*H*); discernible data of **major** diastereomer of **[1,2]**-rearr. = 6.74 (dd, 1H, *J* = 15.8 and 8.2, =C*H*CH), 5.81 (dd, 1H, *J* = 15.8 and 1.0, =C*H*CO$_2$), 3.27–3.21 (m, 1H, =CHC*H*), 1.00 (d, 3H, *J* = 6.8, CHC*H*$_3$); discernible data of **minor** diastereomer of **[1,2]**-rearr. = 6.65 (dd, 1H, *J* = 15.7 and 9.1, =C*H*CH), 1.12 (d, 3H, *J* = 6.8, CHC*H*$_3$); **δ_C** (100 MHz, CDCl$_3$) **major** diastereomer of **[2,3]**-rearr. = 208.1 (CO), 169.6 and 167.0 (2 × CO$_2$), 131.8 (=*C*HCH$_3$), 122.9 (=*C*HCH), 87.2 (O–C, quat.), 82.0 (*C*Me$_3$), 64.8 (COCH$_2$*C*H$_2$), 62.2 (O*C*H$_2$CH$_3$), 54.9 (=CH*C*H), 35.4 (CO*C*H$_2$), 27.9 (C*Me*$_3$), 18.0 (=CH*C*H$_3$), 14.1 (OCH$_2$*C*H$_3$); ***m/z (CI): 257 (45%), 274 (100), 313 (M + H$^+$, 2), 330 (M + NH$_4^+$, 1); HRMS: M + H$^+$ found 313.1656, $C_{16}H_{25}O_6$ requires 313.1651.

Butyl 3-oxo-2-(1-phenylallyl)-2,3-dihydrobenzofuran-2-carboxylate, 4.35b

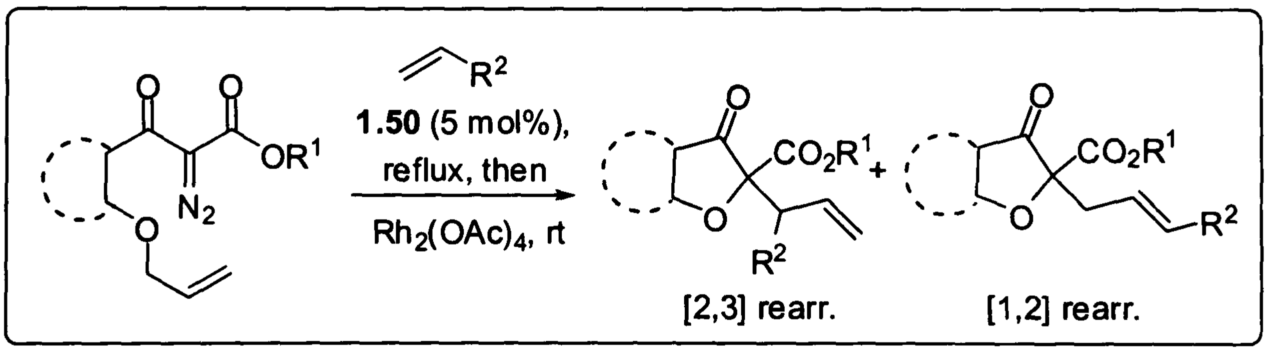


4.35b was prepared following the general procedure using (*E*)-butyl 3-(2-(cinnamyloxy)phenyl)-2-diazo-3-oxopropanoate **4.36b** (42.0 mg, 0.112 mmol) in CH$_2$Cl$_2$ (7 mL). The residue was purified by flash chromatography (20% Et$_2$O in petrol) to afford the benzofuranone **4.35b** (39.0 mg, quant. as 56:44 mixture of [2,3] and [1,2]-rearrangement products, dr of [2,3] = 56:44, determined by ^{1}H NMR) as a yellow oil.

***R*$_f$** = 0.38 (30% Et$_2$O in petrol); **IR** (neat): 1725s, 1613s, 1477s, 1463s, 1370m, 1253s, 1156s; δ_H (400 MHz, CDCl$_3$) **mixture** of **[2,3]** and **[1,2]**-rearr. = 7.70–6.88 (m, 27H, Ar), 6.57 (dt, 1H, *J* = 15.9 and 1.1, =C*H*Ph), 6.39–6.30 (m, 1H, =C*H*CHPh), 6.10 (dt, 1H, *J* = 15.9 and 7.3, =C*H*CH$_2$), 5.77–5.68 (m, 1H, =C*H*CHPh), 5.38 (dt, 1H, *J* = 16.9 and 1.2, =C*H*$_a$H$_b$), 5.32–5.30 (m, 1H, =CH$_a$*H*$_b$), 5.09 (dt, 1H, *J* = 16.9 and 1.3, =C*H*$_a$H$_b$), 4.93–4.91 (m, 1H, =CH$_a$*H*$_b$), 4.50 (d, 1H, *J* =

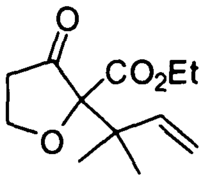
8.6, C*H*Ph), 4.44 (d, 1H, *J* = 8.6, C*H*Ph), 3.20 (ddd, 1H, *J* = 14.5, 7.7 and 1.3, =CHC*H*$_a$H$_b$), 2.90 (ddd, 1H, *J* = 14.5, 6.9 and 1.4, =CHCH$_a$*H*$_b$), 1.50, 1.46 and 1.18 (3 × s, 27H, 3 × CMe$_3$); discernible data of **major** diastereomer of **[2,3]**-rearr. = 6.39–6.30 (m, 1H, =C*H*CHPh), 5.38 (dt, 1H, *J* = 16.9 and 1.2, =C*H*$_a$H$_b$), 5.32–5.30 (m, 1H, =CH$_a$*H*$_b$), 4.50 (d, 1H, *J* = 8.6, C*H*Ph); discernible data of **minor** diastereomer of **[2,3]**-rearr. = 5.77–5.68 (m, 1H, =C*H*CHPh), 5.09 (dt, 1H, *J* = 16.9 and 1.3, =C*H*$_a$H$_b$), 4.93–4.91 (m, 1H, =CH$_a$*H*$_b$), 4.44 (d, 1H, *J* = 8.6, C*H*Ph); discernible data of **[1,2]**-rearr. product = 6.57 (dt, 1H, *J* = 15.9 and 1.1, =C*H*Ph), 6.10 (dt, 1H, *J* = 15.9 and 7.3, =C*H*CH$_2$), 3.20 (ddd, 1H, *J* = 14.5, 7.7 and 1.3, =CHC*H*$_a$H$_b$), 2.90 (ddd, 1H, *J* = 14.5, 6.9 and 1.4, =CHCH$_a$*H*$_b$); δ$_C$ (100 MHz, CDCl$_3$) **mixture** of **[1,2]** and **[2,3]**-rear. = 195.9, 195.2 and 194.6 (3 × CO), 172.7, 172.4 and 172.3 (3 × CO$_2$), 164.2, 163.6, 162.8, 138.8, 136.8 and 136.0 (6 × Ar, quat.), 138.5, 138.5, 138.1, 135.2, 134.8, 134.1, 129.4, 128.9, 128.5, 128.4, 128.1, 127.5, 127.3, 127.2, 126.3, 124.9, 124.8, 124.5, 122.6, 122.5, 122.1, 121.4, 113.5, 113.4 and 112.9 (25 CH, 4 × =CH, 21 × Ar), 120.0, 119.9 and 119.6 (3 × Ar, quat.), 118.9 and 118.7 (2 × =CH$_2$), 94.5, 94.0 and 91.5 (3 × O–C, quat.), 83.9, 83.8 and 83.7 (3 × *C*Me$_3$), 54.8 and 53.6 (2 × *C*HPh), 37.5 (=CH*C*H$_2$), 27.8 and 27.4 (3 × C*Me*$_3$); discernible data of **[1,2]**-rearr. product = 37.5 (=CH*C*H$_2$); discernible data of **[2,3]**-rearr. products = 118.9 and 118.7 (2 × =CH$_2$), 54.8 and 53.6 (2 × *C*HPh); ***m/z*** (ES+): 368 (M + NH$_4^+$, 25%), 373 (M + Na$^+$, 100); HRMS: M + Na$^+$ found 373.1408 C$_{22}$H$_{22}$NaO$_4$ requires 373.1410.

5.13. One-Pot Cross-Metathesis/ Oxonium Ylide Formation-Rearrangement



General procedure: Grubbs 2$^{\text{nd}}$ generation catalyst **1.50** (5 mol%) was added to a solution of diazoester (1.0 equiv.) and olefin (5–10 equiv.) in CH$_2$Cl$_2$ (*c* = 15–20 mM) and the reaction mixture was heated to reflux for 14 h. After cooling to room temperature anhydrous rhodium acetate dimer (2–4 mol%) added and the reaction mixture was stirred at room temperature until consumption of the diazoester (generally 8–12 h). The mixture was then concentrated under reduced pressure and purified by flash chromatography

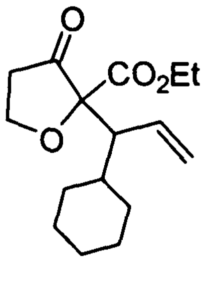
Ethyl 2-(2-methylbut-3-en-2-yl)-3-oxotetrahydrofuran-2-carboxylate, 4.21a



4.21a was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (47.0 mg, 0.208 mmol) and amylene (220 μL, 2.08 mmol) in CH_2Cl_2 (13 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the dihydrofuranone **4.21a** (41.0 mg, 87%) as a yellow oil.

R*$_f$** = 0.52 (40% Et_2O in petrol); **IR** (neat): 2984w, 1740s, 1640s, 1466w, 1409w, 1365w, 1232s, 1151s, 1093s, 1024s; **δ_H** (400 MHz, $CDCl_3$) = 6.00 (dd, 1H, *J* = 17.4 and 10.8, =CH), 5.08–5.02 (m, 2H, =CH_2), 4.39–4.33 (m, 1H, $COCH_2CH_aH_b$), 4.27–4.19 (m, 2H, OCH_2CH_3), 4.09–4.02 (m, 1H, $COCH_2CH_aH_b$), 2.55–2.50 (m, 2H, $COCH_2$), 1.28 (t, 3H, *J* = 7.2, OCH_2CH_3), 1.21 and 1.95 (2 × s, 6H, CMe_2); **δ_C** (100 MHz, $CDCl_3$) = 208.9 (CO), 166.9 (CO_2), 142.4 (=CH), 113.7 (=CH_2), 88.6 (O–C, quat.), 63.8 ($COCH_2CH_2$), 61.7 (OCH_2CH_3), 43.2 (CMe_2), 37.8 ($COCH_2$), 22.6 and 21.7 (CMe_2), 14.2 (OCH_2CH_3); ***m/z (CI): 158 (100%), 227 ($M + H^+$, 30); HRMS: $M + H^+$ found 227.1276, $C_{12}H_{19}O_4$ requires 227.1283.

Ethyl 2-(1-cyclohexylallyl)-3-oxotetrahydrofuran-2-carboxylate, 4.21b

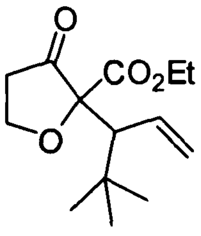


dr = 90:10

4.21b was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (46.0 mg, 0.203 mmol) and vinylcyclohexane (277 μL, 2.03 mmol) in CH_2Cl_2 (15 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the dihydrofuranone **4.21b** (45.0 mg, 79%, dr = 90:10 by ^{1}H NMR) as a yellow oil.

R*$_f$** = 0.31 (30% Et_2O in petrol); **IR** (neat): 2925s, 1766m, 1739s, 1639s, 1449w, 1407w, 1367w, 1233s, 1147m, 1119m, 1097m, 1052w; **δ_H** (400 MHz, $CDCl_3$) **major** diastereomer = 5.75 (dt, 1H, *J* = 17.0 and 10.2, =CH), 5.12 (dd, 1H, *J* = 10.2 and 2.1, =CH_aH_b), 5.04 (dd, 1H, *J* = 17.0 and 2.1, =CH_aH_b), 4.44–4.39 (m, 1H, $COCH_2CH_aH_b$), 4.27–4.08 (m, 3H, $COCH_2CH_aH_b$ and OCH_2CH_3), 2.70 (dd, 1H, *J* = 10.2 and 3.8, CHC_6H_{11}), 2.76–2.54 (m, 2H, $COCH_2$), 1.94–0.88 (m, 11H, cyclohexyl), 1.25 (t, 3H, *J* = 7.1, CH_3); discernible data for **minor** diastereomer = 5.66 (dt, 1H, *J* = 17.4 and 10.2, =CH), 5.02 (dd, 1H, *J* = 17.2 and 2.1, =CH_aH_b), 2.78 (dd, 1H, *J* = 10.1 and 4.1, C*H*C_6H_{11}), 2.43–2.38 (m, 2H, $COCH_2$); δ_C (100 MHz, $CDCl_3$) **major** diastereomer = 209.5 (CO), 167.3 (CO_2), 134.1 (=CH), 119.1 (=CH_2), 90.3 (O–C, quat.), 63.6 ($COCH_2$*C*H_2), 62.0 (O*C*H_2CH_3), 54.3 (*C*HC_6H_{11}), 38.7 (C(1)H cyclohexyl), 36.4 (CO*C*H_2), 33.0, 29.8, 26.6, 26.5 and 26.2 (5 × CH_2 cyclohexyl), 14.1 (CH_3); discernible data for **minor** diastereomer = 133.6 (=CH), 120.2 (=CH_2), 90.1 (O–C, quat.), 64.5 ($COCH_2$*C*H_2), 62.0 (O*C*H_2CH_3), 54.4 (*C*HC_6H_{11}), 39.2 (C(1)H cyclohexyl), 36.3 (CO*C*H_2CH_2), 31.9, 26.7 (2 × CH_2 cyclohexyl); ***m/z (CI): 158 (100%), 207 (20), 281 (M + H^+, 10); HRMS (ES+): M + H^+ found 281.1747, $C_{16}H_{25}O_4$ requires 281.1747.

Ethyl 2-(4,4-dimethylpent-1-en-3-yl)-3-oxotetrahydrofuran-2-carboxylate, 4.21c

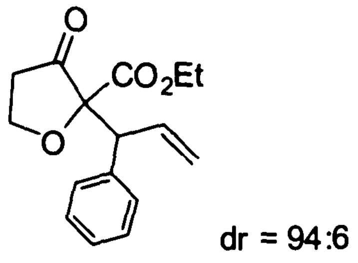


dr = 94:6

4.21c was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (42.0 mg, 0.186 mmol) and 3,3-dimethyl-1-butene (239 μL, 1.86 mmol) in CH_2Cl_2 (13 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the dihydrofuranone **4.21c** (23.0 mg, 49%, dr = 94:6 by ^{1}H NMR) as a yellow oil.

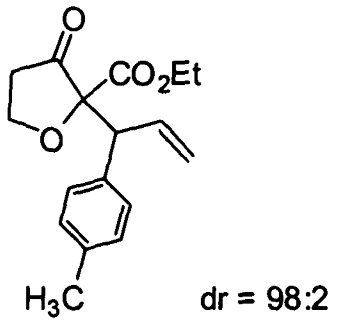
R*$_f$** = 0.23 (30% Et_2O in petrol); **IR** (neat): 2961s, 1765s, 1739s, 1365w, 1223s, 1189s, 1142s, 1063s, 1007s; δ_H (400 MHz, $CDCl_3$) **major** diastereomer = 5.85 (dt, 1H, *J* = 17.2 and 10.2, =CH), 5.15 (dd, 1H, *J* = 10.2 and 2.1, =CH_aH_b), 5.05 (dd, 1H, *J* = 17.2 and 2.1, =CH_aH_b), 4.47 (td, 1H, *J* = 9.8 and 2.8, $COCH_2$CH_aH_b), 4.26–4.19 (m, 1H, $COCH_2CH_aH_b$), 4.11 (q, 2H, *J* = 7.2, O$CH_2$$CH_3$), 2.81–2.71 (m, 2H, C*H*CMe_3 and COCH_aH_b), 2.51–2.44 (m, 1H, COCH_aH_b), 1.25 (t, 3H, *J* = 7.2, OCH_2CH_3), 0.92 (s, 9H, CMe_3); discernible data for **minor** diastereomer = 2.85 (d, 1H, *J* = 10.1, C*H*CMe_3), 0.96 (s, 9H, CMe_3); δ_C (100 MHz, $CDCl_3$) **major** diastereomer = 209.6 (CO), 167.4 (CO_2), 134.8 (=CH), 113.7 (=CH_2), 90.5 (O–C, quat.), 63.1 ($COCH_2$*C*H_2), 62.2 (O*C*H_2CH_3), 56.8 (*C*HCMe_3), 34.9 (CO*C*H_2), 34.3 (*C*Me_3), 29.3 (C*Me*$_3$), 14.0 (OCH_2*C*H_3); ***m/z (CI): 199 (10%), 255 (M + H^+, 100), 272 (M + NH_4^+, 80); HRMS: M + H^+ found 255.1591, $C_{14}H_{23}O_4$ requires 255.1596.

Ethyl 3-oxo-2-(1-phenylallyl)tetrahydrofuran-2-carboxylate, 4.21d



4.21d was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (40.0 mg, 0.177 mmol) and styrene (202 μL, 1.77 mmol) in CH_2Cl_2 (12 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the dihydrofuranone **4.21d** (32.0 mg, 66%, dr = 94:6 by ^1H NMR) as a yellow oil. Spectroscopic data as above (pp. 161).

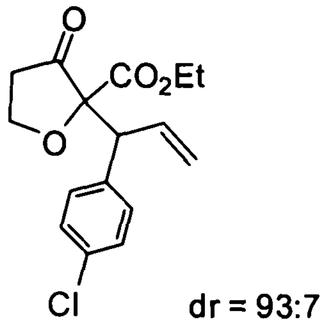
Ethyl 3-oxo-2-(1-p-tolylallyl)tetrahydrofuran-2-carboxylate, 4.21e



4.21e was following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (46.0 mg, 0.203 mmol) and 4-methylstyrene (267 μL, 2.03 mmol) in CH_2Cl_2 (15 mL). The crude was purified by flash chromatography (5→25% Et_2O in petrol) to afford the dihydrofuranone **4.21e** (37.0 mg, 63%, dr = 98:2 by GC-MS) as a yellow oil.

$\boldsymbol{R}_\mathbf{f}$ = 0.31 (30% Et_2O in petrol); **IR** (neat): 1763s, 1737s, 1467w, 1238w, 1217s, 1132m, 1066w, 1023w; $\boldsymbol{\delta}_\mathbf{H}$ (400 MHz, $CDCl_3$) **major** diastereomer = 7.19 (d, 2H, *J* = 8.0, Ar), 7.08 (d, 2H, *J* = 8.0, Ar), 6.19–6.10 (m, 1H, =CH), 5.23–5.15 (m, 2H, =CH_2), 4.34–4.18 (m, 5H, C*H*Ar, $COCH_2CH_2$, OCH_2CH_3), 2.31–2.20 (m, 1H, $COCH_aH_b$), 2.30 (s, 3H, CH_3Ar), 1.69 (dt, 1H, *J* = 18.2 and 10.2, $COCH_aH_b$), 1.32 (t, 3H, *J* = 7.1, OCH_2CH_3); discernible data for **minor** diastereomer = 6.03–5.94 (m, 1H, =CH), 5.10–5.06 (m, 2H, =CH_2), 4.03–3.97 (m, 2H, OCH_2CH_3), 1.04 (t, 3H, *J* = 7.2, OCH_2CH_3); $\boldsymbol{\delta}_\mathbf{C}$ (100 MHz, $CDCl_3$) **major** diastereomer = 208.8 (CO), 167.4 (CO_2), 136.9 and 134.4 (2 × Ar, quat.), 135.31 (=CH), 129.8 and 128.9 (2 × Ar), 117.9 (=CH_2), 89.4 (O–C, quat.), 64.7 ($COCH_2CH_2$), 62.2 (OCH_2CH_3), 53.9 (CHAr), 36.2 ($COCH_2$), 21.3 (CH_3Ar), 14.2 (OCH_2CH_3); ***m/z*** (CI): 131 (100%), 289 (M + H^+, 30), 306 (M + NH_4^+, 20); HRMS: M + NH_4^+ found 306.1706, $C_{17}H_{24}NO_4$ requires 306.1705.

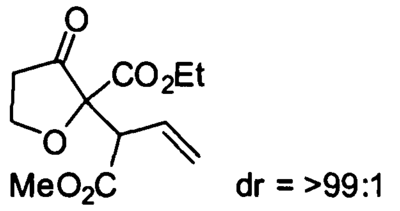
Ethyl 2-(1-(4-chlorophenyl)allyl)-3-oxotetrahydrofuran-2-carboxylate, 4.21f



4.21f was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (44.0 mg, 0.195 mmol) and 4-chlorostyrene (234 µL, 1.95 mmol) in CH_2Cl_2 (15 mL). The residue was purified by flash chromatography (5→25% Et_2O in petrol) to afford the dihydrofuranone **4.21f** (30.5 mg, 51%, dr = 93:7 by ^1H NMR) as a colourless oil, which crystallises upon standing.

R**f** = 0.37 (40% Et_2O in petrol); **m.p.** 103–104 °C; **IR** (neat): 1767s, 1739s, 1491s, 1405w, 1235s, 1132s, 1092m, 1015m; **δ_H** (400 MHz, $CDCl_3$) **major** diastereomer = 7.45–7.23 (m, 4H, Ar), 6.15–6.06 (m, 1H, =CH), 5.24–5.18 (m, 2H, =CH_2), 4.32–4.19 (m, 5H, C*H*Ar, $COCH_2CH_2$, OCH_2CH_3), 2.32–2.25 (m, 1H, $COCH_aH_bCH_2$), 1.73 (dt, 1H, *J* = 18.4 and 10.3, $COCH_aH_bCH_2$), 1.32 (t, 3H, *J* = 7.2, OCH_2CH_3); discernible data for **minor** diastereomer = 5.97–5.88 (m, 1H, =CH), 5.11–5.06 (m, 2H, =CH_2), 4.06–3.97 (m, 2H, OCH_2CH_3), 1.05 (t, 3H, *J* = 7.1, OCH_2CH_3); **δ_C** (100 MHz, $CDCl_3$) **major** diastereomer = 208.5 (CO), 167.1 (CO_2), 135.9 and 133.3 (2 × Ar, quat.), 134.7 (=CH), 131.4 and 128.4 (2 × Ar), 118.6 (=CH_2), 89.2 (O–C, quat.), 64.7 ($COCH_2CH_2$), 62.4 (OCH_2CH_3), 53.4 (CHAr), 36.2 ($COCH_2$), 14.2 (CH_3); ***m/z*** (CI): 148 (65%), 151 (100), 309 (M + H^+, 12), 326 (M + NH_4^+, 15); HRMS: M + NH_4^+ found 326.1160, $C_{16}H_{21}N^{35}ClO_4$ requires 326.1159.

Ethyl 2-(1-methoxy-1-oxobut-3-en-2-yl)-3-oxotetrahydrofuran-2-carboxylate, 4.21g

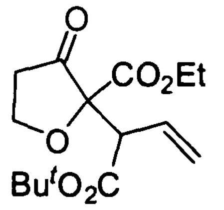


4.21g was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (47.0 mg, 0.208 mmol) and methyl acrylate (187 µL, 2.08 mmol) in CH_2Cl_2 (15 mL). The residue was purified by flash chromatography (10→30% Et_2O in petrol) to afford the dihydrofuranone **4.21g** (43.0 mg, 81%, dr = >99:1) as a yellow oil.

R**f** = 0.12 (30% Et_2O in petrol); **IR** (neat): 1735m, 1642s, 1439w, 1238s, 1150w, 1062m, 1020m; **δ_H** (400 MHz, $CDCl_3$) = 5.94–5.85 (m, 1H, =CH), 5.23–5.28 (m, 2H, =CH_2), 4.49–4.37 (m, 2H,

$COCH_2CH_2$), 4.27–4.14 (m, 3H, $CHCO_2$ and OCH_2CH_3), 3.68 (s, 3H, OCH_3), 2.97–2.87 (m, 1H, $COCH_aH_b$), 2.59–2.51 (m, 1H, $COCH_aH_b$), 1.27 (t, 3H, J = 7.2, OCH_2CH_3); δ_C (100 MHz, $CDCl_3$) = 208.0 (CO), 170.5 and 166.8 (2 × CO_2), 129.8 (=CH), 121.4 (=CH_2), 86.7 (O–C, quat.), 65.1 ($COCH_2CH_2$), 62.4 (OCH_2CH_3), 54.9 ($CHCO_2$), 52.5 (OCH_3), 35.2 ($COCH_2$), 14.1 (OCH_2CH_3); ***m/z*** (CI): 184 (95%), 225 (45), 257 (M + H^+, 100), 274 (M + NH_4^+, 2); HRMS: M + NH_4^+ found 274.1295, $C_{12}H_{20}NO_6$ requires 274.1291.

Ethyl 2-(1-*tert*-butoxy-1-oxobut-3-en-2-yl)-3-oxotetrahydrofuran-2-carboxylate, 4.21h

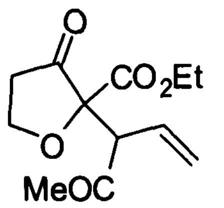


dr = 98:2

4.21h was prepared following the general procedure using ethyl 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (40.0 mg, 0.177 mmol) and *tert*-butyl acrylate (259 μL, 1.77 mmol) in CH_2Cl_2 (14 mL). The residue was purified by flash chromatography (5→30% Et_2O in petrol) to afford the dihydrofuranone **4.21h** (43.5 mg, 82%, dr = 98:2 by ^1H NMR) as a yellow oil.

R*f** = 0.25 (30% Et_2O in petrol); **IR** (neat): 3020s, 1768s, 1728s, 1370m, 1216s, 1154s, 1021m; δ_H (400 MHz, $CDCl_3$) **major** diastereomer = 5.92–5.82 (m, 1H, =CH), 5.26–5.21 (m, 2H, =CH_2), 4.48–4.35 (m, 2H, $COCH_2CH_2$), 4.26–4.12 (m, 2H, OCH_2CH_3), 4.04 (d, 1H, J = 9.3, $CHCO_2$), 2.94–2.85 (m, 1H, $COCH_aH_b$), 2.58–2.49 (m, 1H, $COCH_aH_b$), 1.42 (s, 9H, CMe_3), 1.27 (t, 3H, J = 7.1, OCH_2CH_3); discernible data for **minor** diastereomer = 3.90 (d, 1H, J = 9.3, $CHCO_2$), 3.04–2.96 (m, 1H, $COCH_aH_b$); δ_C (100 MHz, $CDCl_3$) **major** diastereomer = 208.1 (CO), 169.1 and 167.0 (2 × CO_2), 130.5 (=CH), 120.6 (=CH_2), 86.8 (O–C, quat.), 82.2 (CMe_3), 64.9 ($COCH_2CH_2$), 62.3 (OCH_2CH_3), 55.8 ($CHCO_2$), 35.3 ($COCH_2$), 27.9 (CMe_3), 14.1 (OCH_2CH_3); discernible data for **minor** diastereomer = 28.1 (CMe_3); ***m/z (CI): 225 (15%), 243 (85), 260 (100), 299 (M + H, 2); HRMS: M + H^+ found 299.1493, $C_{15}H_{23}O_6$ requires 299.1495.

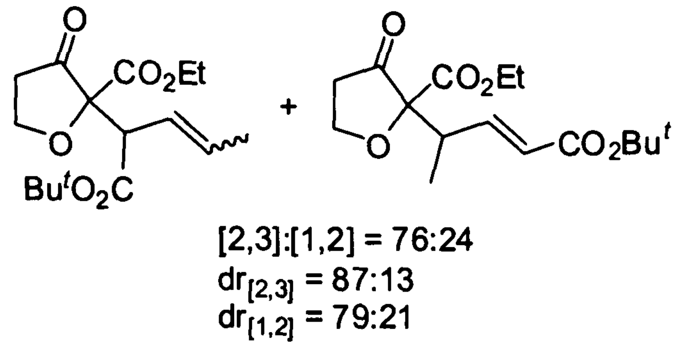
Ethyl 3-oxo-2-(4-oxopent-1-en-3-yl)tetrahydrofuran-2-carboxylate, 4.21i



dr = 84:16

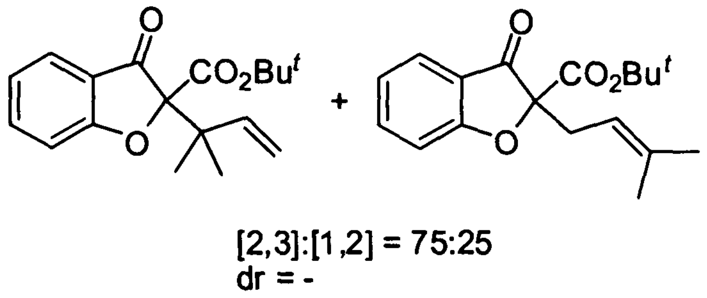
4.21i was prepared following the general procedure using 5-(allyloxy)-2-diazo-3-oxopentanoate **4.20** (49.0 mg, 0.217 mmol) and methyl vinyl ketone (176 μL, 2.17 mmol) in CH_2Cl_2 (15 mL). The crude was purified by flash chromatography (10→30% Et_2O in petrol) to afford the dihydrofuranone **4.21i** (45.0 mg, 86%, dr = 84:16, which changes to 54:46 with time, each diastereomer exist in keto-enol form $d_{1(\text{major})}$ = 2:1, $d_{2(\text{minor})}$ = 3:1, by ^{1}H NMR) as a yellow oil.

Ethyl 2-(1-*tert*-butoxy-1-oxopent-3-en-2-yl)-3-oxotetrahydrofuran-2-carboxylate, 4.28



4.28 was prepared in one-pot following the general procedure using ethyl 5-(but-3-en-2-yloxy)-2-diazo-3-oxopentanoate **4.27** (50.0 mg, 0.208 mmol) and *tert*-butyl acrylate (304 μL, 2.08 mmol) in CH_2Cl_2 (15 mL). The crude was purified by flash chromatography (20% Et_2O in petrol) to afford the dihydrofuranone **4.28** (44.0 mg, 68%, [2,3]:[1,2] = 76:24, $dr_{[2,3]}$ = 87:13, $dr_{[1,2]}$ = 79:21 by ^{1}H NMR) as a yellow oil. Spectroscopic data as above (pp. 161).

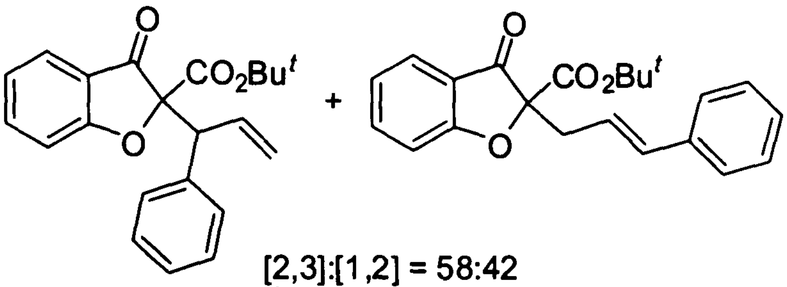
tert-Butyl 2-(2-methylbut-3-en-2-yl)-3-oxo-2,3-dihydrobenzofuran-2-carboxylate, 4.35a



4.35a was prepapred following the general procedure using *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a**[13] (45.0 mg, 0.149 mmol) and amylene (158 μL, 1.49 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the benzofuranone **4.35a** (25.0 mg, 56% as 75:25 mixture of [2,3] and [1,2]-rearrangement products, determined by ^{1}H NMR) as a yellow oil.

R*f** = 0.52 (30% Et_2O in petrol); **IR** (neat): 1722s, 1671s, 1478m, 1216s, 1155m; δ_H (400 MHz, $CDCl_3$) **[2,3]**-rearr. = 7.66–7.59 (m, 2H, Ar), 7.22–7.19 (m, 1H, Ar), 7.10–7.06 (m, 1H, Ar), 6.15 (dd, 1H, J = 17.4 and 10.8, =CH), 5.09 (dd, 1H, J = 17.4 and 1.0, =CH_aH$_b$), 5.04 (dd, 1H, J = 10.7 and 1.0, =CH$_a$$H_b$), 1.45 (s, 9H, CMe_3), 1.27 (s, 6H, CMe_2); discernible data for **[1,2]**-rearr. product = 3.01 (dd, 1H, J = 14.9 and 7.9, =CHCH_aH$_b$), 2.68 (dd, 1H, J = 14.9 and 6.9, =CHCH$_a$$H_b$), 1.66 and 1.63 (2 × s, 6H, CMe_2), 1.39 (s, 9H, CMe_3); δ_C (100 MHz, $CDCl_3$) **[2,3]**-rearr. = 195.1 (CO), 171.6 (CO_2), 163.6 and 121.1 (2 × Ar, quat.), 141.5 (=CH), 138.0, 124.5, 122.1 and 113.0 (4 × Ar), 113.8 (=CH_2), 93.9 (O–C, quat.), 83.6 (CMe_3), 44.1 (CMe_2), 27.8 (CMe_3), 22.2 and 21.8 (CMe_2); discernible data for **[1,2]**-rearr. product = 140.6, 138.2, 124.7, 122.2, 115.5 and 113.3 (2 × =CH, 4 × Ar), 92.0 (O–C, quat.), 83.5 (CMe_3), 32.9 (=$CHCH_2$), 27.7 (CMe_3), 27.6 and 25.8 (CMe_2); ***m/z (ES+): 179 (100%), 269 (M + Na^+, 60), 320 (M + NH_4^+, 6); HRMS: M + Na^+ found 325.1411, $C_{18}H_{22}NaO_4$ requires 325.1410.

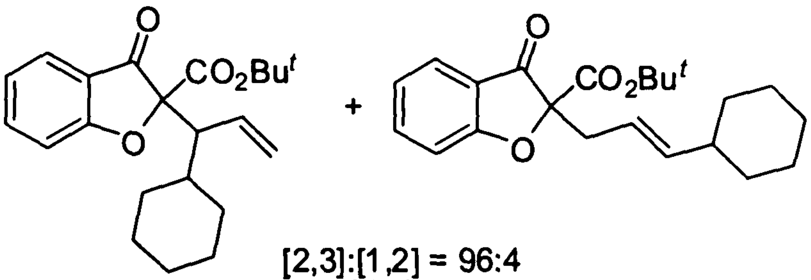
tert-Butyl 3-oxo-2-(1-phenylallyl)-2,3-dihydrobenzofuran-2-carboxylate, 4.35b



[2,3]:[1,2] = 58:42
dr = 56:44

4.35b was prepared in one-pot following the general procedure using *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (48.0 mg, 0.159 mmol) and styrene (182 μL, 1.59 mmol) in CH_2Cl_2 (12 mL). The residue was purified by flash chromatography (10% Et_2O in petrol) to afford the benzofuranone **4.35b** (40.0 mg, 72%, [2,3]:[1,2] = 58:42, dr = 56:44 by ^1H NMR) as a yellow oil. Spectroscopic data as mentioned above (pp. 162).

tert-Butyl 2-(1-cyclohexylallyl)-3-oxo-2,3-dihydrobenzofuran-2-carboxylate, 4.35c



[2,3]:[1,2] = 96:4
dr = 55:45

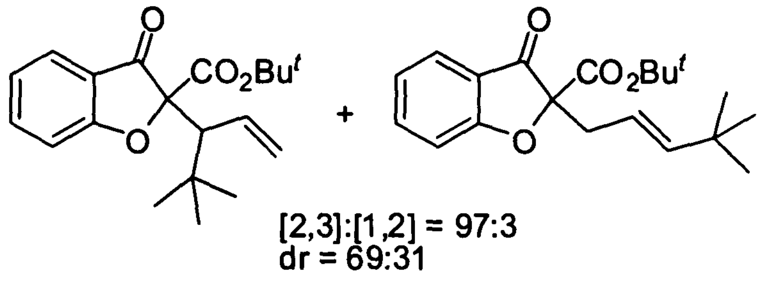
4.35c was prepared in one-pot following the general procedure using *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (33.0 mg, 0.109 mmol) and vinylcyclohexane (149 μL, 1.09 mmol) in CH_2Cl_2 (10 mL). The residue was purified by flash chromatography (petrol→10% Et_2O in petrol) to afford the benzofuranone **4.35c** (36.0 mg, 92%, [2,3]:[1,2] = 96:4, dr = 55:45 by ^1H NMR) as a yellow oil.

R

R_f = 0.52 (30% ether in petrol); **IR** (neat): 2927s, 1726s, 1613s, 1477s, 1463s, 1370s, 1299s, 1155s, 1012m; δ_H (400 MHz, $CDCl_3$) **mixture** of diastereomers of **[2,3]**-rearr. = 7.68–7.58 (m, 4H, Ar), 7.27–7.22 (m, 2H, Ar), 7.13–7.05 (m, 2H, Ar), 5.95 (dt, 1H, *J* = 17.0 and 10.2, =CHC_6H_{11}), 5.36 (dt, 1H, *J* = 17.0 and 10.1, =CHC_6H_{11}), 5.26 (dd, 1H, *J* = 10.1 and 2.0,

=C*H*$_a$H$_b$), 5.21 (dd, 1H, *J* = 16.9 and 2.0, =CH$_a$*H*$_b$), 5.08 (dd, 1H, *J* = 16.9 and 2.0, =C*H*$_a$H$_b$), 4.95 (dd, 1H, *J* = 10.2 and 2.0, =CH$_a$*H*$_b$), 3.09–3.04 (m, 2H, 2 × C*H*C_6H_{11}), 2.11–2.07 (m, 1H, CH of CH_2 cyclohexyl), 1.77–0.83 (m, 21H, 2 × C(1)H, CH of CH_2 and 9 × CH_2, cyclohexyl), 1.48 and 1.41 (2 × s, 18H, 2 × CMe_3); discernible data for **major** diastereomer of **[2,3]**-rearr. = 5.95 (dt, 1H, *J* = 17.2 and 10.2, =C*H*C_6H_{11}), 5.26 (dd, 1H, *J* = 10.1 and 2.0, =C*H*$_a$H$_b$), 5.21 (dd, 1H, *J* = 16.9 and 2.0, =CH$_a$*H*$_b$); discernible data for **minor** diastereomer of **[2,3]**-rearr. = 5.36 (dt, 1H, J = 16.9 and 10.1, =C*H*C_6H_{11}), 5.08 (dd, 1H, *J* = 16.9 and 2.0, =C*H*$_a$H$_b$), 4.95 (dd, 1H, *J* = 10.2 and 2.0, =CH$_a$*H*$_b$); discernible data of **[1,2]**-rearr. product = 2.92 (dd, *J* = 14.4 and 7.6, 1H, =CHC*H*$_a$H$_b$), 2.69 (dd, 1H, *J* = 14.4 and 6.8, =CHCH$_a$*H*$_b$); δ_C (100 MHz, $CDCl_3$) **mixture** of diastereomers of **[2,3]**-rearr. = 195.7 and 195.6 (2 × CO), 172.5 and 172.3 (2 × CO_2), 164.4, 164.0, 120.5 and 119.9 (4 × Ar, quat.), 138.3, 138.1, 124.7, 122.3, 122.2, 113.4 and 113.2 (7 × Ar), 133.3 and 131.6 (2 × =CH), 120.4 and 119.7 (2 × =CH_2), 95.6 and 95.4 (2 × O–C, quat.), 83.6 and 83.5 (2 × *C*Me$_3$), 54.2 and 53.8 (2 × *C*HC_6H_{11}), 39.4 and 38.1 (2 × C(1)H, cyclohexyl), 32.9, 32.2, 29.5, 29.3, 26.8, 26.6, 26.4, 26.4, 26.2 and 26.1 (10 × CH_2, cyclohexyl), 27.8 and 27.7 (2 × C*Me*$_3$); ***m/z*** (ES+): 301 (100%), 357 (4), 374 (M + NH_4^+, 39), 379 (M + Na^+, 65); HRMS: M + Na^+ found 379.1880, $C_{22}H_{28}NaO_4$ requires 379.1880.

tert-Butyl 2-(4,4-dimethylpent-1-en-3-yl)-3-oxo-2,3-dihydrobenzofuran-2-carboxylate, 4.35d



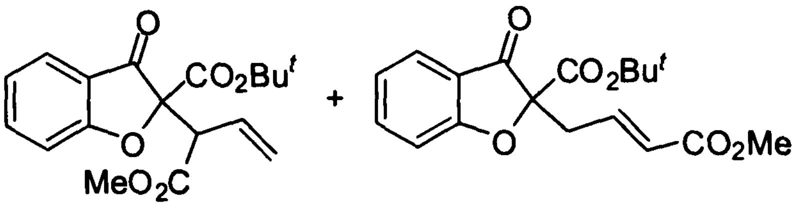
[2,3]:[1,2] = 97:3
dr = 69:31

4.35d was prepared in one-pot following the general procedure mentioned above starting from *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (52.0 mg, 0.172 mmol) and 3,3-dimethyl-1-butene (221 μL, 1.72 mmol) in CH_2Cl_2 (10 mL). The crude was purified by flash chromatography (10% Et_2O in petrol) to afford the benzofuranone **4.35d** (49.0 mg, 86%, [2,3]:[1,2] = 97:3, dr = 69:31 by ^{1}H NMR) as a yellow oil.

***R*$_f$** = 0.48 (30% Et_2O in petrol); **IR** (neat): 2979m, 1728s, 1613s, 1476s, 1369s, 1253s, 1156s, 1010s; δ_H (400 MHz, $CDCl_3$) **mixture** of diastereomers of **[2,3]**-rearr. = 7.68–7.58 (m, 4H, Ar), 7.27–7.23 (m, 2H, Ar), 7.13–7.06 (m, 2H, Ar), 6.04 (dt, 1H, *J* = 17.2 and 10.2, =CH), 5.37–5.27 (m, 1H, =CH), 5.30 (dd, 1H, *J* = 10.3 and 2.0, =C*H*$_a$H$_b$), 5.23 (dd, 1H, *J* = 17.2 and 2.0, =CH$_a$*H*$_b$), 5.11 (dd, 1H, *J* = 17.2 and 2.0, =C*H*$_a$H$_b$), 5.01 (dd, 1H, *J* = 10.1 and 2.0, =CH$_a$*H*$_b$), 3.15 (d, 1H, *J* = 10.2, C*H*CMe$_3$), 3.11 (d, 1H, *J* = 10.1, C*H*CMe$_3$), 1.43 and 1.39 (2 × s, 18H, 2 × $OCMe_3$), 1.07 and 0.84 (2 × s, 18H, 2 × CMe_3); discernible data for **major** diastereomer of **[2,3]**-rearr. = 6.04

(dt, 1H, *J* = 17.2 and 10.2, =CH), 5.30 (dd, 1H, *J* = 10.3 and 2.0, =C*H*$_a$H$_b$), 5.23 (dd, 1H, *J* = 17.2 and 2.0, =CH$_a$*H*$_b$), 3.15 (d, 1H, *J* = 10.2, C*H*CMe$_3$); discernible data for **minor** diastereomer of **[2,3]**-rearr. = 5.37–5.27 (m, 1H, =CH), 5.11 (dd, 1H, *J* = 17.2 and 2.0, =C*H*$_a$H$_b$), 5.01 (dd, 1H, *J* = 10.1 and 2.0, =CH$_a$*H*$_b$), 3.11 (d, 1H, *J* = 10.1, C*H*CMe$_3$); discernible data for **[1,2]**-rearr. product = 2.94–2.88 (m, 1H, =CHC*H*$_a$H$_b$), 2.75–2.69 (m, 1H, =CHCH$_a$*H*$_b$); δ_C (100 MHz, $CDCl_3$) **major** diastereomer of **[2,3]**-rearr. = 195.6 (CO), 171.3 (CO_2), 164.4 and 119.7 (2 × Ar, quat.), 138.1, 124.8, 122.4 and 113.4 (4 × Ar), 134.0 (=CH), 120.0 (=CH_2), 95.8 (O–C, quat.), 83.5 (O*C*Me$_3$), 57.0 (*C*HCMe$_3$), 34.5 (CH*C*Me$_3$), 29.5 and 27.6 (2 × C*Me*$_3$); discernible data for **minor** diastereomer of **[2,3]**-rearr. = 196.1(CO), 172.5 (CO_2), 165.1 (Ar, quat.), 138.0, 124.7, 122.2 and 113.1 (4 × Ar), 132.5 (=CH), 120.5 (=CH_2), 94.9 (O–C, quat.), 56.3 (*C*HCMe$_3$), 34.5 (CH*C*Me$_3$), 29.3 and 27.8 (2 × C*Me*$_3$); ***m/z*** (CI): 231 (100%), 248 (80), 292 (50), 331 (M +H$^+$, 4), 348 (M + NH$_4^+$, 30); HRMS (ES+): M + NH$_4^+$ found 348.2170, $C_{20}H_{30}NO_4$ requires 348.2169.

tert-Butyl 2-(1-methoxy-1-oxobut-3-en-2-yl)-3-oxo-2,3-dihydrobenzofuran-2-carboxylate, 4.35e



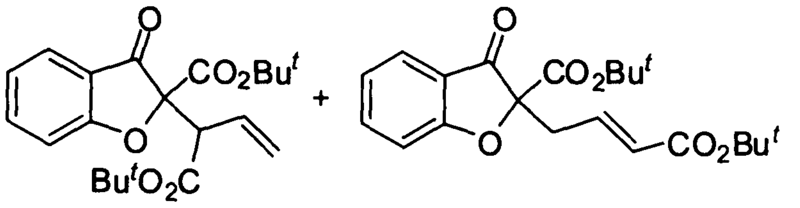
[2,3]:[1,2] = 95:5
dr = 91:9

4.35e was prepared in one-pot following the general procedure mentioned above starting from *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (46.0 mg, 0.152 mmol) and methyl acrylate (137 μL, 1.52 mmol) in CH_2Cl_2 (12 mL). The crude was purified by flash chromatography (5→20% Et_2O in petrol) to afford the benzofuranone **4.35e** (40.0 mg, 79%, [2,3]:[1,2] = 95:5, dr = 91:9 by ^{1}H NMR) as a yellow oil.

***R*~f~**

R_f = 0.43 (40% Et_2O in petrol); **IR** (neat): 2970w, 1742s, 1615s, 1463s, 1371m, 1253s, 1155s, 1102w, 1027m; δ_H (400 MHz, $CDCl_3$) **major** diastereomer of **[2,3]**-rearr. = 7.21–7.62 (m, 2H, Ar), 7.27–7.23 (m, 1H, Ar), 7.13–7.06 (m, 1H, Ar), 6.13–6.04 (m, 1H, =CH), 5.48–5.43 (m, 2H, =CH_2), 4.37 (d, 1H, *J* = 9.3, $CHCO_2$), 3.52 (s, 3H, OCH_3), 1.43 (s, 9H, CMe_3); discernible data for **minor** diastereomer of **[2,3]**-rearr. = 4.28 (d, 1H, *J* = 9.3, $CHCO_2$), 3.78 (s, 3H, OCH_3); discernible data for **[1,2]**-rearr. product = 3.70 (s, 3H, OCH_3), 3.19 (ddd, 1H, *J* = 15.0, 7.5 and 1.4, =CHC*H*$_a$H$_b$), 2.83 (ddd, 1H, *J* = 15.0, 7.5 and 1.4, =CHCH$_a$*H*$_b$); δ_C (100 MHz, $CDCl_3$) **major** diastereomer of **[2,3]**-rearr. = 194.2 (CO), 172.0 and 169.5 (2 × CO_2), 162.9 and 120.3 (2 × Ar, quat.), 137.9, 124.6, 122.5 and 113.2 (4 × Ar), 129.4 (=CH), 122.0 (=CH_2), 91.3 (O–C, quat.), 84.3 (*C*Me$_3$), 53.6 (*C*HCO$_2$), 52.4 (OCH$_3$), 27.7 (C*Me*$_3$); ***m/z*** (CI): 250 (100%), 294 (48), 294 (50), 333 (M +H$^+$, 18), 350 (M + NH$_4^+$, 40); HRMS (ES+): M + H$^+$ found 333.1334, $C_{18}H_{21}O_6$ requires 333.1333.

***tert*-butyl 2-(1-*tert*-butoxy-1-oxobut-3-en-2-yl)-3-oxo-2,3-dihydrobenzofuran-2-carboxylate, 4.35f**

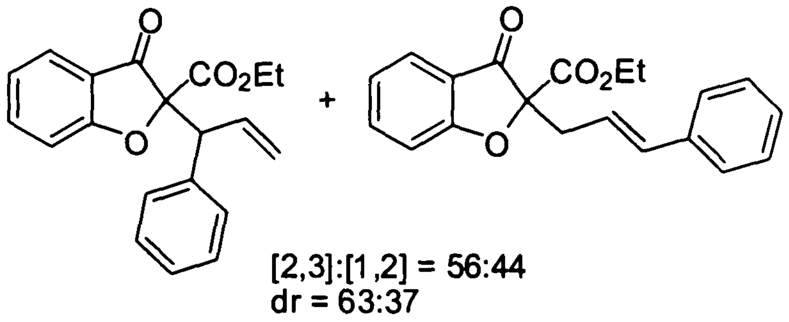


[2,3]:[1,2] = 98:2
dr = 93:7

4.35f was prepared in one-pot following the general procedure mentioned above starting from *tert*-butyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34a** (42.0 mg, 0.139 mmol) and *tert*-butyl acrylate (203 μL, 1.39 mmol) in CH_2Cl_2 (12 mL). The crude was purified by flash chromatography (5→15% Et_2O in petrol) to afford the benzofuranone **4.35f** (43.0 mg, 83%, [2,3]:[1,2] = 98:2, dr = 93:7 by ^{1}H NMR) as a yellow oil, which crystallises upon standing.

R*$_f$** = 0.52 (40% Et_2O in petrol); **m.p.** 64–65 °C; **IR** (neat): 2981w, 1735s, 1614s, 1463m, 1370s, 1252s, 1150s, 1026w; **δ$_H$** (400 MHz, CDCl$_3$) **major** diastereomer of **[2,3]**-rearr. = 7.69–7.62 (m, 2H, Ar), 7.27–7.23 (m, 1H, Ar), 7.13 (t, 1H, *J* = 7.8, Ar), 6.12–6.03 (m, 1H, =CH), 5.42–5.38 (m, 2H, =CH$_2$), 4.20 (d, 1H, *J* = 9.3, CHCO$_2$), 1.43 and 1.09 (2 × s, 18H, 2 × CMe$_3$); discernible data for **minor** diastereomer of **[2,3]**-rearr. = 5.60–5.51 (m, 1H, =CH), 5.30–5.26 (m, 1H, =C*H*$_a$H$_b$), 5.12–5.09 (m, 1H, =CH$_a$*H*$_b$); discernible data for **[1,2]**-rearr. product = 3.17 (ddd, 1H, *J* =14.9, 7.5 and 1.4, =CHC*H*$_a$H$_b$), 2.75 (ddd, 1H, *J* = 14.9, 7.3 and 1.3, =CHCH$_a$*H*$_b$); **δ$_C$** (100 MHz, CDCl$_3$) **major** diastereomer of **[2,3]**-rearr. = 193.9 (CO), 172.1 and 167.6 (2 × CO$_2$), 162.9 and 120.5 (2 × Ar, quat.), 137.9, 124.7, 122.5 and 113.3 (4 × Ar), 130.1 (=CH), 121.5 (=CH$_2$), 91.6 (O–C, quat.), 84.2 and 82.5 (2 × *C*Me$_3$), 54.2 (*C*HCO$_2$), 27.7 and 27.4 (2 × C*Me*$_3$); ***m/z (CI): 236 (100%), 336 (70), 375 (M +H$^+$, 18), 392 (M + NH$_4^+$, 20); HRMS (ES+): M + H$^+$ found 375.1801, $C_{21}H_{27}O_6$ requires 375.1802.

Ethyl 2-(1-phenylallyl)-3-oxo-2,3-dihydrobenzofuran-2-carboxylate, 4.35b′



4.35b′ was prepared following the general procedure using ethyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34b**[32] (54.0 mg, 0.197 mmol) and styrene (225 µL, 1.97 mmol) in CH_2Cl_2 (15 mL). The residue was purified by flash chromatography (5→15% Et_2O in petrol) to afford the benzofuranone **4.35b′** (39.0 mg, 61%, [2,3]:[1,2] = 56:44, dr = 63:37 by ^{1}H NMR) as a yellow oil.

$\boldsymbol{R_f}$ = 0.50 (40% Et_2O in petrol); **IR** (neat): 1751s, 1725s, 1612s, 1476s, 1463, 1300m, 1234s, 1147w, 1025m; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) **mixture** of **[1,2]** and **[2,3]**-rearr. products = 7.71–6.89 (m, 27H, Ar), 6.57 (d, 1H, J = 15.7, =CHPh), 6.39–6.29 (m, 1H, =CHCHPh), 6.08 (dt, 1H, J = 15.7 and 7.4, =CHCH$_2$), 5.80–5.72 (m, 1H, =CHCHPh), 5.40–5.36 (m, 1H, =CH_aH$_b$), 5.31–5.28 (m, 1H, =CH$_a$$H_b$), 5.16–5.12 (m, 1H, =C$H_aH_b$), 4.97–4.94 (m, 1H, =CH$_a$$H_b$), 4.55 (d, 1H, J = 8.6, CHPh), 4.49 (d, 1H, J = 8.6, CHPh), 4.32–4.21 (m, 8H, 2 × OCH_2), 4.02 (q, 2H, J = 7.1, OCH_2), 3.26–3.21 (m, 1H, =CHCH_aH$_b$), 2.99–2.94 (m, 1H, =CHCH$_a$$H_b$), 1.32, 1.26 and 1.00 (3 × t, 9H, J = 7.1, 3 × CH_3); discernible data of **major** diastereomer of **[2,3]**-rearr. = 6.39–6.29 (m, 1H, =CHCHPh), 5.40–5.36 (m, 1H, =CH_aH$_b$), 5.31–5.28 (m, 1H, =CH$_a$$H_b$), 4.55 (d, 1H, J = 8.6, CHPh); discernible data of **minor** diastereomer of **[2,3]**-rearr. = 5.80–5.72 (m, 1H, =CHCHPh), 5.16–5.12 (m, 1H, =CH_aH$_b$), 4.97–4.94 (m, 1H, =CH$_a$$H_b$), 4.49 (d, 1H, J = 8.6, CHPh); discernible data of **[1,2]**-rearr. product = 6.57 (d, 1H, J = 15.7, =CHPh), 6.08 (dt, 1H, J = 15.7 and 7.4, =CHCH$_2$), 3.26–3.21 (m, 1H, =CHCH_aH$_b$), 2.99–2.94 (m, 1H, =CHCH$_a$$H_b$); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) **mixture** of **[1,2]** and **[2,3]**-rearr. products = 195.6, 194.7 and 194.2 (3 × CO), 172.6, 172.3 and 172.2 (3 × CO_2), 165.4, 164.9, 164.7, 138.2, 136.8 and 135.6 (6 × Ar, quat.), 138.6, 138.3, 135.5, 134.6, 133.5, 129.4, 128.8, 128.6, 128.4, 128.1, 127.6, 127.4, 126.3, 124.9, 124.8, 124.6, 122.8, 122.7, 122.3, 120.9, 113.6, 113.5 and 113.1 (23 CH: 4 × =CH, 19 × Ar), 119.9, 119.8 and 119.5 (3 × Ar, quat.), 119.5 and 118.9 (2 × =CH_2), 94.2, 93.9 and 91.0 (3 × O–C, quat.), 62.8, 62.7 and 62.5 (3 × OCH_2), 54.8 and 53.9 (2 × CHPh), 37.7 (=CHCH$_2$), 14.1, 14.0 and 13.7 (3 × CH_3); discernible data of **[2,3]**-rearr. products = 119.5 and 118.9 (2 × =CH_2), 54.8 and 53.9 (2 × CHPh); discernible data of **[1,2]**-rearr. product = 37.7 (=CHCH$_2$); ***m/z*** (ES+): 323 (M + H$^+$,

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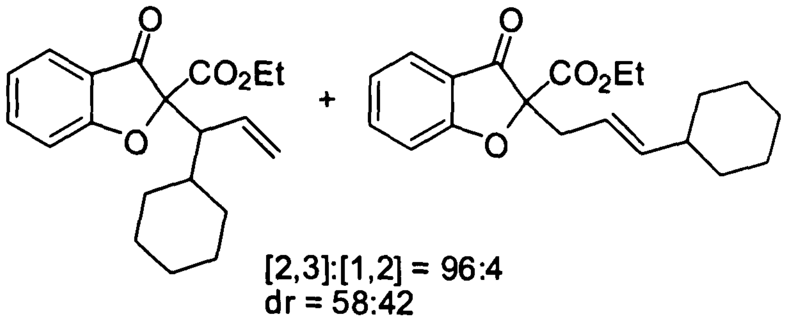
[32] a) M. C. Pirrung, J. A. Werner, *J. Am. Chem. Soc.* **1986**, *108*, 6060–6062; b) G. K. Murphy, F. G. West, *Org. Lett.* **2006**, *8*, 4359–4361.

12%), 340 (M + NH_4^+, 5), 345 (M + Na^+, 100); HRMS: M + Na^+ found 345.1096, $C_{20}H_{18}NaO_4$ requires 345.1097.

Ethyl 2-(1-cyclohexylallyl)-3-oxo-2,3-dihydrobenzofuran-2-carboxylate, 4.35c′

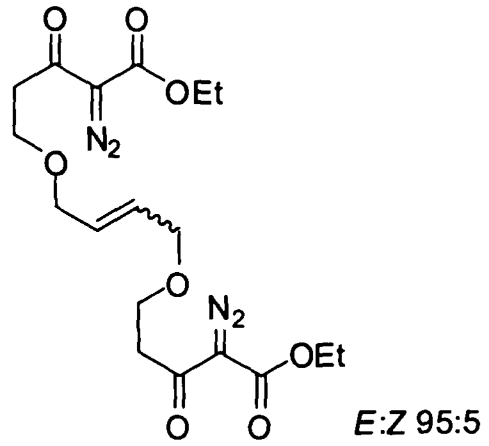


4.35c′ was prepared following the general procedure using ethyl 3-(2-(allyloxy)phenyl)-2-diazo-3-oxopropanoate **4.34b** (48.0 mg, 0.175 mmol) and vinylcyclohexane (239 μL, 1.75 mmol) in CH_2Cl_2 (12 mL). The residue was purified by flash chromatography (5→10% Et_2O in petrol) to afford the benzofuranone **4.35c′** (41.2 mg, 72%, [2,3]:[1,2] = 96:4, dr = 58:42 by ^1H NMR) as a yellow oil.

R*f** = 0.66 (40% Et_2O in petrol); **IR** (neat): 2926s, 1751s, 1611s, 1476w, 1463s, 1368w, 1324m, 1299m, 1231s, 1025s; δ_H (400 MHz, $CDCl_3$) **mixture** of diastereomers of **[2,3]**-rearr. = 7.69–7.59 (m, 4H, Ar), 7.27–7.24 (m, 2H, Ar), 7.15–7.07 (m, 2H, Ar), 5.94 (dt, 1H, *J* = 16.9 and 10.2, =C*H*CH), 5.37 (dt, 1H, *J* = 17.0 and 10.1, =C*H*CH), 5.26–5.18 (m, 2H, =CH_2), 5.10 (dd, 1H, *J* = 17.0 and 1.9, =C$H_a$$H_b$), 4.97 (dd, 1H, *J* = 10.1 and 2.0, =C$H_a$$H_b$), 4.32–4.14 (m, 4H, 2 × OCH_2), 3.13–3.09 (m, 2H, 2 × C*H*C_6H_{11}), 2.06–2.09 (m, 1H, CH of CH_2 cyclohexyl), 1.77–0.83 (m, 21H, CH of CH_2, 2 × C(1)H, 9 × CH_2 cyclohexyl), 1.30 and 1.25 (2 × t, 6H, *J* = 7.1, 2 × CH_3); discernible data for **major** diastereomer of **[2,3]**-rearr. = 5.94 (dt, 1H, *J* = 16.9 and 10.2, =CH), 5.26–5.18 (m, 2H, =CH_2); discernible data for **minor** diastereomer of **[2,3]**-rearr. = 5.37 (dt, 1H, *J* = 17.0 and 10.1, =CH), 5.10 (dd, 1H, *J* = 17.0 and 1.9, =C$H_a$$H_b$), 4.97 (dd, 1H, *J* = 10.1 and 2.0, =C$H_a$$H_b$); discernible data for **[1,2]**-rearr. product = 2.98–2.93 (m, 1H, =CHC$H_a$$H_b$), 2.79–2.74 (m, 1H, =CHC$H_a$$H_b$); δ_C (100 MHz, $CDCl_3$) **mixture** of diastereomers of **[2,3]**-rearr. = 195.4 and 195.2 (2 × CO), 172.4 and 172.2 (2 × CO_2), 165.6, 165.3, 120.3 and 119.8 (4 × Ar, quat.), 138.5, 138.3, 124.8, 122.6, 122.5, 113.5 and 113.3 (7 × Ar), 133.2 and 131.3 (2 × =CH), 120.8 and 119.9 (2 × =CH_2), 95.4 and 94.9 (2 × O–C, quat.), 62.6 and 62.5 (2 × OCH_2), 54.5 and 54.2 (2 × *C*HC_6H_{11}), 39.4 and 38.0 (2 × C(1)H, cyclohexyl), 32.9, 31.9, 29.5, 29.3, 26.7, 26.5, 26.4, 26.3, 26.1 and 26.0 (10 × CH_2, cycloehxyl), 14.1 and 14.0 (2 × CH_3); ***m/z (ES+): 329 (M + H^+, 25%), 346 (M + NH_4^+, 5), 351 (M + Na^+, 100); HRMS: M + Na^+ found 351.1570, $C_{20}H_{24}NaO_4$ requires 351.1567.

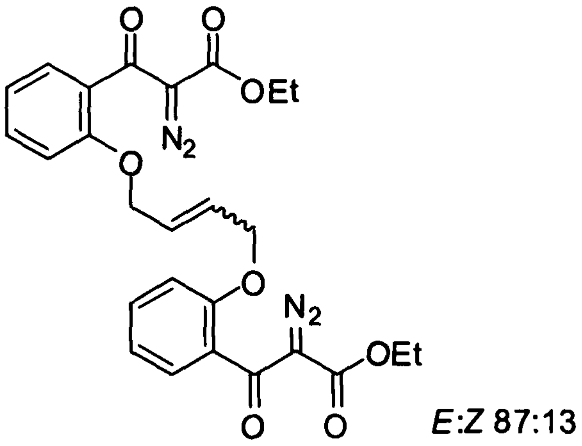
Spectroscopic data for compounds isolated for characterisation:

Diethyl 5,5'-(but-2-ene-1,4-diylbis(oxy))bis(2-diazo-3-oxopentanoate), 4.41



E:*Z* 95:5, determined by ^{1}H-NMR; ***R*$_f$** = 0.21 (60% Et_2O in petrol); **IR** (neat): 2136s, 1716s, 1652s, 1373m, 1303s, 1137m, 1020m; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 5.79–5.78 (m, 2H, 2 × =CH), 4.30 (q, 4H, *J* = 7.2, 2 × OCH_2CH$_3$), 4.00–3.98 (m, 4H, 2 × =CHCH_2), 3.76 (t, 4H, *J* = 6.2, 2 × COCH$_2$CH_2), 3.14 (t, 4H, *J* = 6.2, 2 × COCH$_2$), 1.33 (t, 6H, *J* = 7.1, 2 × OCH$_2$CH_3); discernible data for ***Z*-isomer** = 5.70–5.68 (m, 2H, 2 × =CH), 4.07–3.98 (m, 4H, 2 × =CHCH_2); δ_C (100 MHz, $CDCl_3$) ***E*-isomer** = 190.6 (2 × CO), 161.2 (2 × CO_2), 129.4 (2 × =CH), 70.9 (2 × =CHCH_2), 64.9 (2 × COCH$_2$CH$_2$), 61.5 (2 × OCH_2CH$_3$), 40.3 (2 × COCH_2), 14.3 (2 × OCH$_2$CH$_3$); ***m/z*** (ES+): 391 (100%), 425 (M + H$^+$, 24), 447 (M + Na$^+$, 75); HRMS: M + Na$^+$ found 447.1490, $C_{18}H_{24}N_4NaO_8$ requires 447.1486.

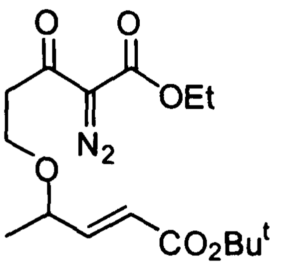
Diethyl 3,3'-(2,2'-(but-2-ene-1,4-diylbis(oxy))bis(2,1-phenylene))bis(2-diazo-3-oxopropanoate), 4.44



E:*Z* 87:13, determined by ^{1}H-NMR; ***R*$_f$** = 0.38 (60% Et_2O in petrol); **IR** (neat): 2140s, 1721s, 1628s, 1487w, 1451m, 1394m, 1370m, 1321s, 1257m, 1162w, 1110w; δ_H (400 MHz, $CDCl_3$) ***E*-isomer** = 7.42–7.38 (m, 2H, Ar), 7.32 (dd, 2H, *J* = 7.6 and 1.7, Ar), 7.02 (td, 2H, *J* = 7.6 and 1.0, Ar), 6.88 (d, 2H, *J* = 8.3, Ar), 5.99 (t, 2H, *J* = 2.3, 2 × =CH), 4.60–4.59 (m, 4H, 2 × OCH_2), 1.36 (s, 18H, 2 × CMe_3); discernible data for ***Z*-isomer** = 5.86 (t, 2H, *J* = 3.5, 2 × =CH), 4.66 (d, 4H, *J*

= 3.5, 2 × OCH$_2$); δ$_C$ (100 MHz, CDCl$_3$) ***E*-isomer** = 186.6 (2 × CO), 160.1, 157.3 and 128.7 (2 × CO$_2$, 4 × Ar, quat.), 132.1, 128.6, 127.4, 120.9 and 111.9 (8 × Ar and 2 × =CH), 82.7 (2 × *C*Me$_3$), 68.1 (2 × OCH$_2$), 28.0 (2 × C*Me*$_3$); ***m/z*** (ES+): 594 (M + NH$_4^+$, 19), 599 (M + Na$^+$, 100); HRMS: M + Na$^+$ found 599.2115, $C_{30}H_{32}N_4NaO_8$ requires 599.2112.

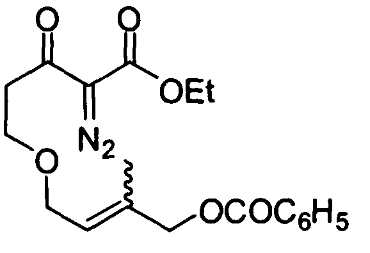
(*E*)-*tert*-Butyl 4-(4-diazo-5-ethoxy-3,5-dioxopentyloxy)pent-2-enoate, 4.29



E-only

R*$_f$** = 0.43 (40% Et$_2$O in petrol); **IR** (neat): 2979m, 2135s, 1715s, 1656s, 1370s, 1303s, 1154s; **δ$_H$** (400 MHz, CDCl$_3$) = 6.72 (dd, 1H, *J* = 15.7 and 6.3, =C*H*CH), 5.88 (dd, 1H, *J* = 15.7 and 1.4, =CHCO), 4.30 (q, 2H, *J* = 7.2, OC*H*$_2$CH$_3$), 4.07–4.00 (m, 1H, C*H*CH$_3$), 3.79–3.68 (m, 2H, COCH$_2$C*H*$_2$), 3.20–3.05 (m, 2H, COCH$_2$), 1.48 (s, 9H, CMe$_3$), 1.33 (t, 3H, *J* = 7.2, OCH$_2$C*H*$_3$), 1.25 (d, 3H, *J* = 6.3, CHC*H*$_3$); **δ$_C$** (100 MHz, CDCl$_3$) = 190.5 (CO), 165.7 and 161.2 (2 × CO$_2$), 147.9 (=*C*HCH), 122.9 (=*C*HCO), 80.4 (*C*Me$_3$), 74.9 (*C*HCH$_3$), 63.7 (COCH$_2$*C*H$_2$), 61.5 (O*C*H$_2$CH3), 40.5 (CO*C*H$_2$), 28.1 (C*Me*$_3$), 20.6 (CH*C*H$_3$), 14.3 (OCH$_2$*C*H$_3$); ***m/z (ES+): 297 (20%), 335 (4), 363 (M + Na$^+$, 100); HRMS: M + Na$^+$ found 363.1521, $C_{16}H_{24}N_2NaO_6$ requires 363.1527.

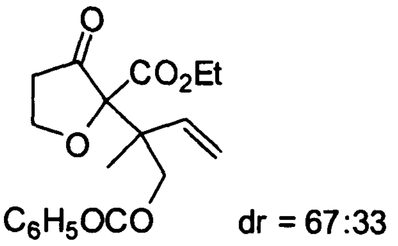
4-(4-Diazo-5-ethoxy-3,5-dioxopentyloxy)-2-methylbut-2-enyl benzoate, 4.42



E:*Z* 75:25

E:*Z* 75:25, determined by ^{1}H-NMR; ***R*$_f$** = 0.63 (60% Et$_2$O in petrol); **IR** (neat): 2136s, 1713m, 1648s, 1373w, 1302m, 1219w, 1107w, 1020w; **δ$_H$** (400 MHz, CDCl$_3$) ***E*-isomer** = 8.08–8.02 (m, 2H, Ar), 7.58 (t, 1H, *J* = 7.4, Ar), 7.46–7.42 (m, 2H, Ar), 5.74 (tq, 1H, *J* = 6.5 and 1.3, =CH), 4.86 (s, 2H, =CC*H*$_2$), 4.32 (q, 2H, *J* = 7.2, OC*H*$_2$CH$_3$), 4.08 (d, 2H, *J* = 6.5, =CHC*H*$_2$), 3.80 (t, 2H, *J* = 6.0, COCH$_2$C*H*$_2$), 3.14 (t, 2H, *J* = 6.0, COC*H*$_2$), 1.80 (s, br, 3H, =CCH$_3$), 1.32 (t, 3H, *J* = 7.2, OCH$_2$C*H*$_3$); discernible data for ***Z*-isomer** = 5.64 (t, 1H, *J* = 6.6, =CH), 4.88 (s, 2H, =CC*H*$_2$), 4.12 (d, 2H, *J* = 6.6, =CHC*H*$_2$), 1.88 (s, br, 3H, =CCH$_3$), 1.20 (t, 3H, *J* = 6.9, OCH$_2$C*H*$_3$); **δ$_C$** (100 MHz, CDCl$_3$) *E*-isomer = 190.5 (CO), 166.4 and 161.2 (2 × CO$_2$), 134.1 and 129.6 (2 × C, quat.), 132.9, 129.6 and 128.3 (3 × Ar), 124.6 (=CH), 69.3 (=CCH$_2$), 67.1 (=CHC*H*$_2$), 65.8 (COCH$_2$C*H*$_2$), 61.4 (OC*H*$_2$CH$_3$), 40.3 (COCH$_2$), 14.3 and 14.2 (2 × CH$_3$); ***m/z*** (ES+): 369 (97%), 375 (M + H$^+$, 4), 397 (M + Na$^+$, 100); HRMS: M + Na$^+$ found 397.1374, $C_{19}H_{22}N_2NaO_6$ requires 397.1370.

Ethyl 2-(1-(benzoyloxy)-2-methylbut-3-en-2-yl)-3-oxotetrahydrofuran-2-carboxylate, 4.43



dr determined by ^{1}H-NMR; ***R*$_f$** = 0.29 (60% Et$_2$O in petrol); **IR** (neat): 2361s, 2342s, 1718m, 1647m, 1456w, 1271w, 1097w; **δ$_H$** (400 MHz, CDCl$_3$) **mixture** of diastereomers = 7.98–7.96 (m, 4H, Ar), 7.60–7.55 (m, 2H, Ar), 7.48–7.43 (m, 4H, Ar), 6.39 (dd, 1H, *J* = 17.7 and 10.8, =CH), 6.03 (dd, 1H, *J* = 19.9 and 10.6, =CH), 5.28–5.25 (m, 2H, =CH$_2$), 5.24–5.18 (m, 2H, =CH$_2$), 4.60 (d, 1H, *J* = 10.8, C$_q$C*H*$_a$H$_b$), 4.50 (d, 1H, *J* = 10.8, C$_q$C*H*$_a$H$_b$), 4.39–4.12 (m, 10H, 2 × OC*H*$_2$CH$_3$, 2 × COCH$_2$C*H*$_2$, 2 × C$_q$CH$_a$*H*$_b$), 2.60–2.42 (m, 4H, COCH$_2$), 1.56 (s, 3H, C$_q$CH$_3$), 1.38 (s, 3H, C$_q$CH$_3$), 1.29–1.24 (m, 6H, 2 × OCH$_2$C*H*$_3$); discernible data for **major** diastereomer = 6.03 (dd, 1H, *J* = 19.9 and 10.6, =CH), 5.28–5.25 (m, 2H, =CH$_2$), 4.60 (d, 1H, *J* = 10.8, C$_q$C*H*$_a$H$_b$), 1.56 (s, 3H, C$_q$CH$_3$), discernible data for **minor** diastereomer = 6.39 (dd, 1H, *J* = 17.7 and 10.8, =CH), 5.24–5.18 (m, 2H, =CH$_2$), 4.50 (d, 1H, *J* = 10.8, C$_q$C*H*$_a$H$_b$), 1.38 (s, 3H, C$_q$CH$_3$); **δ$_C$** (100 MHz, CDCl$_3$) **major** diastereomer = 208.1 (CO), 166.5 and 166.2 (2 × CO$_2$), 137.8 (=CH), 133.2, 129.6 and 128.6 (3 × Ar), 129.8 (Ar, quat.), 116.8 (=CH$_2$), 86.6 (O–C, quat.), 68.3 (CCH$_2$), 64.0 and 62.1 (OCH$_2$CH$_3$ and COCH$_2$CH$_2$), 47.8 (C, quat.), 37.1 (COCH$_2$), 16.2 (CCH$_3$), 14.1 (OCH$_2$CH$_3$); discernible data for **minor** diastereomer = 208.1 (CO), 166.5 and 166.1 (2 × CO$_2$), 133.1, 129.7 and 128.4 (3 × Ar), 116.2 (=CH$_2$), 86.8 (O–C, quat.), 68.5 (C$_q$CH$_2$), 64.1 (OCH$_2$), 47.4 (C, quat.), 37.2 (COCH$_2$), 16.6 (C$_q$CH$_3$); ***m/z*** (CI): 105 (72%), 225 (100), 347 (M + H$^+$, 30); HRMS: M + H$^+$ found 347.1495, $C_{19}H_{23}O_6$ requires 347.1495.

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REFERENCES

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Chapter 3: Intramolecular Carbonyl Ylide Cycloadditions

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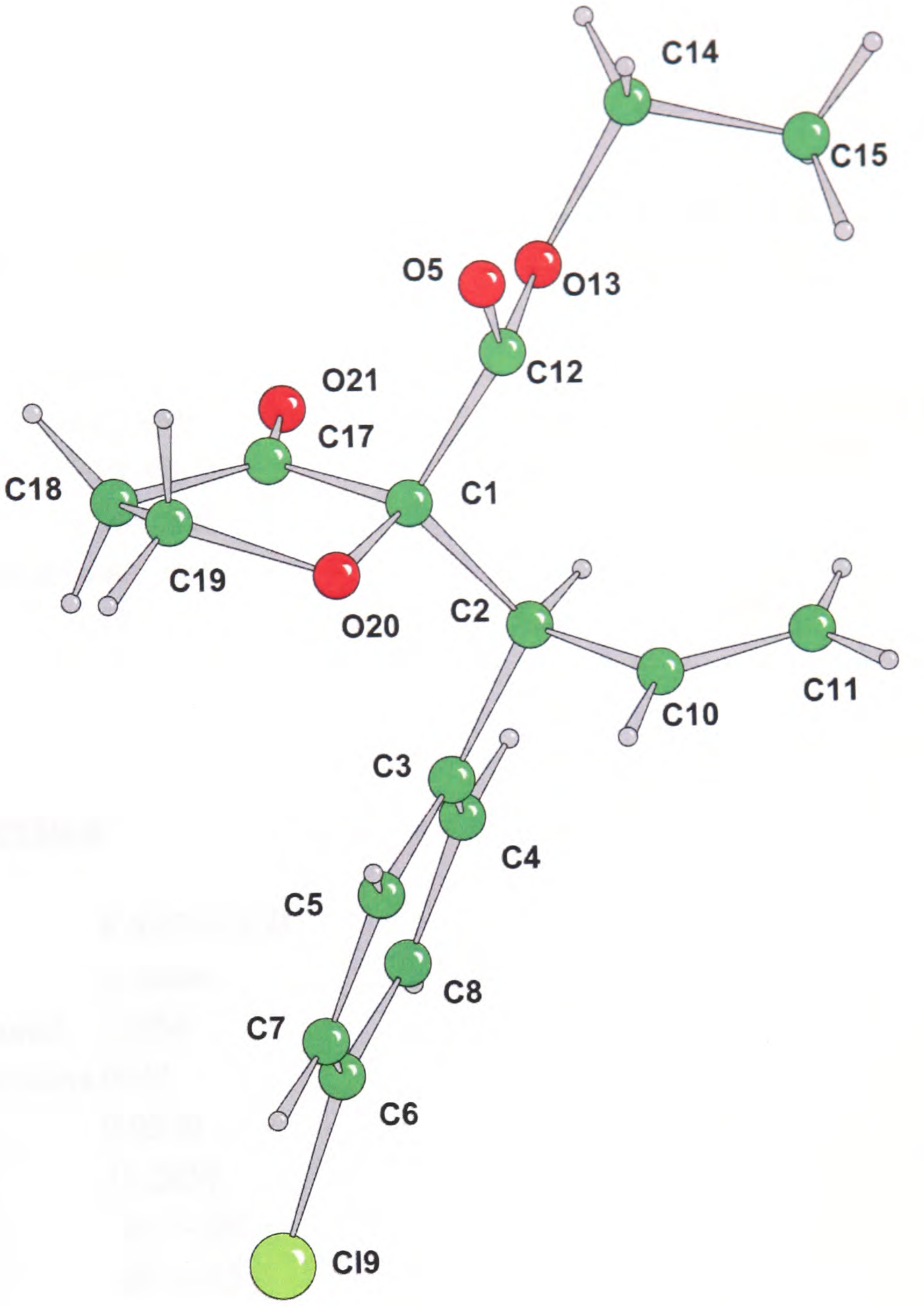
APPENDICES

Single X-Ray diffraction report for $C_{16}H_{16}Cl_1O_4$ (4.21f)



06-10-16

8241543 Compound TJD020

Crystal Data

$a = 20.3909(6)$ Å $\alpha = 90°$
$b = 20.0916(6)$ Å $\beta = 92.1017(18)°$
$c = 7.4099(2)$ Å $\gamma = 90°$

Volume	3033.69(15) Å^3	Crystal Class	Monoclinic
Space group	C 1 2/c 1	Z =	8
Formula	$C_{16}H_{16}Cl_1O_4$	M_r	307.75
Cell determined from	3615 reflections	Cell θ range =	1 - 28°
Temperature	150K		
Shape	plate		
Colour	colourless	Size	0.20 × 0.20 × 0.80 mm
D_x	1.35 Mg m^{-3}	F000	1288.000
μ	0.264 mm^{-1}		
Absorption correction	multi-scan		
T_{min}	0.73	T_{max}	0.95

Data Collection

Diffractometer	KAPPACCD
Scan type	ω scans
Reflections measured	28266
Independent reflections	6943
Rint	0.0530
θ_{max}	28.2650
h =	-26 → 26
k =	-26 → 25
l =	-9 → 9

Refinement

$\Delta\rho_{min}$ =	-1.45 e Å^{-3}
$\Delta\rho_{max}$ =	1.64 e Å^{-3}
Reflections used	6917
Cutoff: I >	-10.00σ(I)
Parameters refined	246
S =	0.98
R-factor	0.096
weighted R-factor	0.151
Δ/σ_{max}	0.0051
Refinement on	F²
w =	$1/[\sigma^2(F_{obs}^2) + (0.043 \times P)^2 + 11.140 \times P + 0.000 + 0.000 \times \sin\theta]$, $P = 0.333 \times \max(F_{obs}^2,0) + 0.667 \times F_{calc}^2$

Parameters

Label	*x*	*y*	*z*	$U_{iso/equiv}$	Occupancy
C2	0.70052(9)	0.35237(9)	0.8008(2)	0.0302	1.0000
C3	0.75430(9)	0.38007(9)	0.6848(2)	0.0268	1.0000
C4	0.79582(9)	0.33564(9)	0.5996(2)	0.0280	1.0000
C5	0.84952(9)	0.35789(10)	0.5078(3)	0.0320	1.0000
C6	0.86226(9)	0.42552(10)	0.5008(3)	0.0348	1.0000
C7	0.82116(10)	0.47094(10)	0.5795(3)	0.0393	1.0000
Cl9	0.93175(3)	0.45461(3)	0.39730(9)	0.0555	1.0000
C12	0.58086(9)	0.33952(9)	0.8588(2)	0.0349	1.0000
C17	0.61639(8)	0.35335(9)	0.5354(2)	0.0255	1.0000
C18	0.59662(9)	0.41632(9)	0.4370(2)	0.0277	1.0000
C19	0.58135(9)	0.46385(9)	0.5879(2)	0.0267	1.0000
O20	0.62255(6)	0.44246(6)	0.74051(16)	0.0284	1.0000
C1	0.62978(9)	0.37244(9)	0.7342(2)	0.0256	1.0000
C8	0.76781(10)	0.44808(10)	0.6712(3)	0.0355	1.0000
O21	0.62285(7)	0.29854(6)	0.47403(19)	0.0370	1.0000
C15	0.5707(6)	0.1960(6)	1.0727(15)	0.0480	0.211(4)
O5	0.5333(5)	0.3678(4)	0.915(2)	0.0445	0.211(4)
C14	0.5337(4)	0.2232(4)	0.9102(13)	0.0417	0.211(4)
O13	0.5805(4)	0.2681(3)	0.8099(10)	0.0340	0.211(4)
O131	0.59050(10)	0.27527(10)	0.8741(3)	0.0338	0.789(4)

C141	0.55290(14)	0.24058(12)	1.0087(4)	0.0419	0.789(4)
O105	0.54358(14)	0.36991(12)	0.9518(5)	0.0443	0.789(4)
C151	0.57432(16)	0.16896(15)	1.0090(4)	0.0475	0.789(4)
C110	0.6978(7)	0.3498(12)	1.0056(12)	0.0325	0.109(5)
C111	0.7488(10)	0.3607(14)	1.1119(17)	0.0513	0.109(5)
C10	0.71322(12)	0.37614(10)	0.9935(3)	0.0325	0.891(5)
C11	0.72099(14)	0.33512(15)	1.1307(3)	0.0513	0.891(5)
H41	0.78692(9)	0.28896(9)	0.6064(2)	0.0358	1.0000
H51	0.87643(9)	0.32636(10)	0.4476(3)	0.0381	1.0000
H71	0.83011(10)	0.51807(10)	0.5719(3)	0.0470	1.0000
H181	0.55860(9)	0.40663(9)	0.3534(2)	0.0336	1.0000
H182	0.63245(9)	0.43290(9)	0.3698(2)	0.0331	1.0000
H191	0.53520(9)	0.46061(9)	0.6194(2)	0.0314	1.0000
H192	0.59223(9)	0.51059(9)	0.5605(2)	0.0322	1.0000
H81	0.74035(10)	0.48000(10)	0.7293(3)	0.0425	1.0000
H151	0.5425(6)	0.1737(6)	1.1550(15)	0.0728	0.211(4)
H152	0.5965(6)	0.1640(6)	1.0085(15)	0.0736	0.211(4)
H153	0.5982(6)	0.2269(6)	1.1395(15)	0.0731	0.211(4)
H141	0.5101(4)	0.1927(4)	0.8331(13)	0.0590	0.211(4)
H142	0.5024(4)	0.2510(4)	0.9739(13)	0.0595	0.211(4)
H1411	0.50540(14)	0.24376(12)	0.9813(4)	0.0542	0.789(4)
H1412	0.56256(14)	0.25774(12)	1.1315(4)	0.0521	0.789(4)
H1511	0.54879(16)	0.14752(15)	1.1022(4)	0.0737	0.789(4)
H1512	0.56277(16)	0.15014(15)	0.8905(4)	0.0737	0.789(4)
H1513	0.62195(16)	0.16461(15)	1.0362(4)	0.0749	0.789(4)
H1101	0.6565(7)	0.3467(12)	1.0533(12)	0.0380	0.109(5)
H1111	0.7438(10)	0.3599(14)	1.2360(17)	0.0570	0.109(5)
H1112	0.7903(10)	0.3643(14)	1.0660(17)	0.0570	0.109(5)
H101	0.71549(12)	0.42485(10)	1.0142(3)	0.0405	0.891(5)
H111	0.71952(14)	0.28857(15)	1.1078(3)	0.0675	0.891(5)
H112	0.72866(14)	0.35248(15)	1.2470(3)	0.0660	0.891(5)

Thermal Parameters

Label	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C2	0.0264(10)	0.0396(11)	0.0248(9)	0.0047(8)	0.0050(7)	0.0113(8)
C3	0.0231(9)	0.0322(10)	0.0250(9)	0.0009(7)	-0.0005(7)	0.0040(7)
C4	0.0258(9)	0.0301(10)	0.0279(9)	-0.0012(7)	0.0004(7)	0.0034(7)
C5	0.0269(10)	0.0354(10)	0.0338(10)	-0.0017(8)	0.0045(8)	0.0042(8)
C6	0.0220(10)	0.0415(12)	0.0409(11)	0.0046(9)	0.0023(8)	-0.0011(8)
C7	0.0325(11)	0.0318(11)	0.0535(13)	0.0037(9)	0.0018(9)	-0.0010(9)
Cl9	0.0314(3)	0.0591(4)	0.0768(4)	0.0090(3)	0.0140(3)	-0.0061(3)
C12	0.0310(10)	0.0364(11)	0.0381(11)	0.0103(9)	0.0102(8)	0.0112(8)
C17	0.0191(9)	0.0246(9)	0.0332(10)	-0.0008(7)	0.0067(7)	-0.0018(7)
C18	0.0289(10)	0.0281(10)	0.0263(9)	0.0035(7)	0.0030(7)	-0.0001(8)
C19	0.0275(9)	0.0244(9)	0.0283(9)	0.0038(7)	0.0012(7)	0.0036(7)
O20	0.0320(7)	0.0253(6)	0.0279(7)	-0.0025(5)	-0.0008(5)	0.0083(5)
C1	0.0275(9)	0.0220(9)	0.0277(9)	0.0028(7)	0.0059(7)	0.0078(7)
C8	0.0329(11)	0.0302(10)	0.0434(11)	-0.0034(9)	0.0021(9)	0.0063(8)
O21	0.0423(8)	0.0261(7)	0.0432(8)	-0.0067(6)	0.0078(6)	0.0027(6)
C15	0.060(2)	0.031(2)	0.054(2)	0.0086(15)	0.0062(18)	-0.0056(18)
O5	0.0380(15)	0.0522(13)	0.045(2)	0.0138(12)	0.0196(15)	0.0199(12)
C14	0.0430(19)	0.0368(18)	0.046(2)	0.0110(16)	0.0173(16)	-0.0064(15)
O13	0.0379(14)	0.0324(12)	0.0326(16)	0.0090(13)	0.0138(13)	0.0034(11)
O131	0.0378(11)	0.0315(9)	0.0330(13)	0.0080(9)	0.0142(10)	0.0024(7)
C141	0.0432(17)	0.0367(15)	0.0469(18)	0.0107(13)	0.0174(14)	-0.0065(12)
O105	0.0379(13)	0.0516(10)	0.045(2)	0.0134(9)	0.0196(13)	0.0193(8)
C151	0.0591(18)	0.0300(17)	0.054(2)	0.0087(13)	0.0067(15)	-0.0056(15)
C110	0.0244(16)	0.0450(18)	0.0285(14)	0.0040(14)	0.0069(13)	0.0014(14)
C111	0.045(2)	0.079(2)	0.0302(16)	0.0113(16)	0.0076(15)	0.0230(17)
C10	0.0245(13)	0.0451(16)	0.0285(11)	0.0040(10)	0.0068(8)	0.0013(11)
C11	0.0454(18)	0.079(2)	0.0302(12)	0.0114(12)	0.0080(11)	0.0232(15)

Distances

C2	C3	1.523(3)Å		C2	C1	1.560(2)Å
C2	C110	1.522(9)Å		C2	C10	1.519(3)Å
C3	C4	1.397(2)Å		C3	C8	1.398(3)Å
C4	C5	1.384(3)Å		C4	H41	0.957Å
C5	C6	1.385(3)Å		C5	H51	0.959Å
C6	C7	1.383(3)Å		C6	Cl9	1.737(2)Å
C7	C8	1.382(3)Å		C7	H71	0.966Å
C12	C1	1.534(2)Å		C12	O5	1.210(9)Å
C12	O13	1.480(7)Å		C12	O131	1.310(3)Å
C12	O105	1.210(3)Å		C17	C18	1.508(2)Å
C17	C1	1.537(2)Å		C17	O21	1.200(2)Å
C18	C19	1.511(2)Å		C18	H181	0.994Å
C18	H182	0.959Å		C19	O20	1.449(2)Å
C19	H191	0.980Å		C19	H192	0.988Å
O20	C1	1.416(2)Å		C8	H81	0.963Å
C15	C14	1.500(9)Å		C15	C141	1.070(11)Å
C15	C151	0.725(13)Å		C15	H151	0.964Å
C15	H152	0.967Å		C15	H153	0.961Å
C15	H1511	1.098Å		C15	H1513	1.259Å
O5	O105	0.34(2)Å		C14	O13	1.526(8)Å
C14	O131	1.590(7)Å		C14	C141	0.887(9)Å
C14	C151	1.539(9)Å		C14	H141	0.955Å
C14	H142	0.981Å		C14	H1411	0.896Å
O13	O131	0.530(8)Å		O13	C141	1.689(7)Å
O131	C141	1.457(3)Å		C141	C151	1.504(4)Å
C141	H142	1.072Å		C141	H1411	0.984Å
C141	H1412	0.986Å		C151	H151	1.285Å
C151	H152	0.464Å		C151	H1511	0.980Å
C151	H1512	0.977Å		C151	H1513	0.988Å
C110	C111	1.299(10)Å		C110	C10	0.623(18)Å
C110	C11	1.066(14)Å		C110	H1101	0.927Å
C111	C10	1.159(14)Å		C111	C11	0.78(2)Å
C111	H1111	0.929Å		C111	H1112	0.928Å
C111	H112	1.108Å		C10	C11	1.314(3)Å
C10	H101	0.991Å		C11	H1111	1.023Å
C11	H111	0.951Å		C11	H112	0.937Å
H151	H1511	0.671Å		H152	H1513	0.551Å

H142	H1411	0.166Å		H1111	H112	0.355Å

Angles

C3	C2	C1	113.80(14)°		C3	C2	C110	128.9(5)°
C1	C2	C110	104.9(7)°		C3	C2	C10	108.30(16)°
C1	C2	C10	109.87(15)°		C110	C2	C10	23.6(7)°
C2	C3	C4	118.83(16)°		C2	C3	C8	123.06(16)°
C4	C3	C8	117.89(17)°		C3	C4	C5	121.28(18)°
C3	C4	H41	118.909°		C5	C4	H41	119.811°
C4	C5	C6	119.22(18)°		C4	C5	H51	119.446°
C6	C5	H51	121.316°		C5	C6	C7	120.96(18)°
C5	C6	Cl9	120.26(16)°		C7	C6	Cl9	118.76(16)°
C6	C7	C8	119.23(19)°		C6	C7	H71	120.228°
C8	C7	H71	120.533°		C1	C12	O5	123.4(6)°
C1	C12	O13	105.5(3)°		O5	C12	O13	122.85(10)°
C1	C12	O131	112.23(13)°		O5	C12	O131	123.5(5)°
O13	C12	O131	20.8(3)°		C1	C12	O105	124.15(16)°
O5	C12	O105	16.3(10)°		O13	C12	O105	129.2(3)°
O131	C12	O105	122.90(9)°		C18	C17	C1	106.80(14)°
C18	C17	O21	128.16(17)°		C1	C17	O21	125.01(16)°
C17	C18	C19	103.37(14)°		C17	C18	H181	108.993°
C19	C18	H181	114.059°		C17	C18	H182	110.309°
C19	C18	H182	110.246°		H181	C18	H182	109.682°
C18	C19	O20	105.11(14)°		C18	C19	H191	111.101°
O20	C19	H191	109.172°		C18	C19	H192	113.242°
O20	C19	H192	108.324°		H191	C19	H192	109.698°
C19	O20	C1	109.08(13)°		C2	C1	C12	108.19(14)°
C2	C1	C17	111.61(14)°		C12	C1	C17	111.90(15)°
C2	C1	O20	110.03(15)°		C12	C1	O20	109.75(14)°
C17	C1	O20	105.35(13)°		C3	C8	C7	121.39(18)°
C3	C8	H81	119.948°		C7	C8	H81	118.641°
C14	C15	C141	35.6(5)°		C14	C15	C151	79.1(10)°
C141	C15	C151	112.3(12)°		C14	C15	H151	112.501°
C141	C15	H151	117.934°		C151	C15	H151	98.039°
C14	C15	H152	96.592°		C141	C15	H152	121.372°
C151	C15	H152	27.331°		H151	C15	H152	110.488°
C14	C15	H153	116.417°		C141	C15	H153	82.532°
C151	C15	H153	138.452°		H151	C15	H153	108.873°

H152	C15	H153	111.459°	
C141	C15	H1511	134.188°	
H151	C15	H1511	37.283°	
C14	C15	H1513	114.070°	
C151	C15	H1513	51.642°	
H152	C15	H1513	24.447°	
H153	C15	H1513	87.844°	
C12	O5	O105	82.0(20)°	
C15	C14	O131	91.5(4)°	
C15	C14	C141	44.7(6)°	
O131	C14	C141	65.0(4)°	
O13	C14	C151	108.3(5)°	
C141	C14	C151	70.9(6)°	
O13	C14	H141	113.455°	
C141	C14	H141	160.287°	
C15	C14	H142	97.908°	
O131	C14	H142	101.366°	
C151	C14	H142	121.464°	
O13	C14	H1411	116.256°	
C141	C14	H1411	67.021°	
H141	C14	H142	109.366°	
H142	C14	H1411	8.735°	
C12	O13	O131	61.3(8)°	
C12	O13	C141	95.9(3)°	
O131	O13	C141	55.7(8)°	
C12	O131	O13	98.0(9)°	
C12	O131	C141	116.71(9)°	
O13	O131	C141	106.9(9)°	
C15	C141	O13	122.8(7)°	
C15	C141	O131	121.6(7)°	
O13	C141	O131	17.5(3)°	
C14	C141	C151	75.2(6)°	
O131	C141	C151	107.38(9)°	
C14	C141	H142	59.200°	
O131	C141	H142	105.466°	
C15	C141	H1411	117.449°	
O13	C141	H1411	99.005°	
C151	C141	H1411	110.246°	
C14	C141	H1412	164.556°	

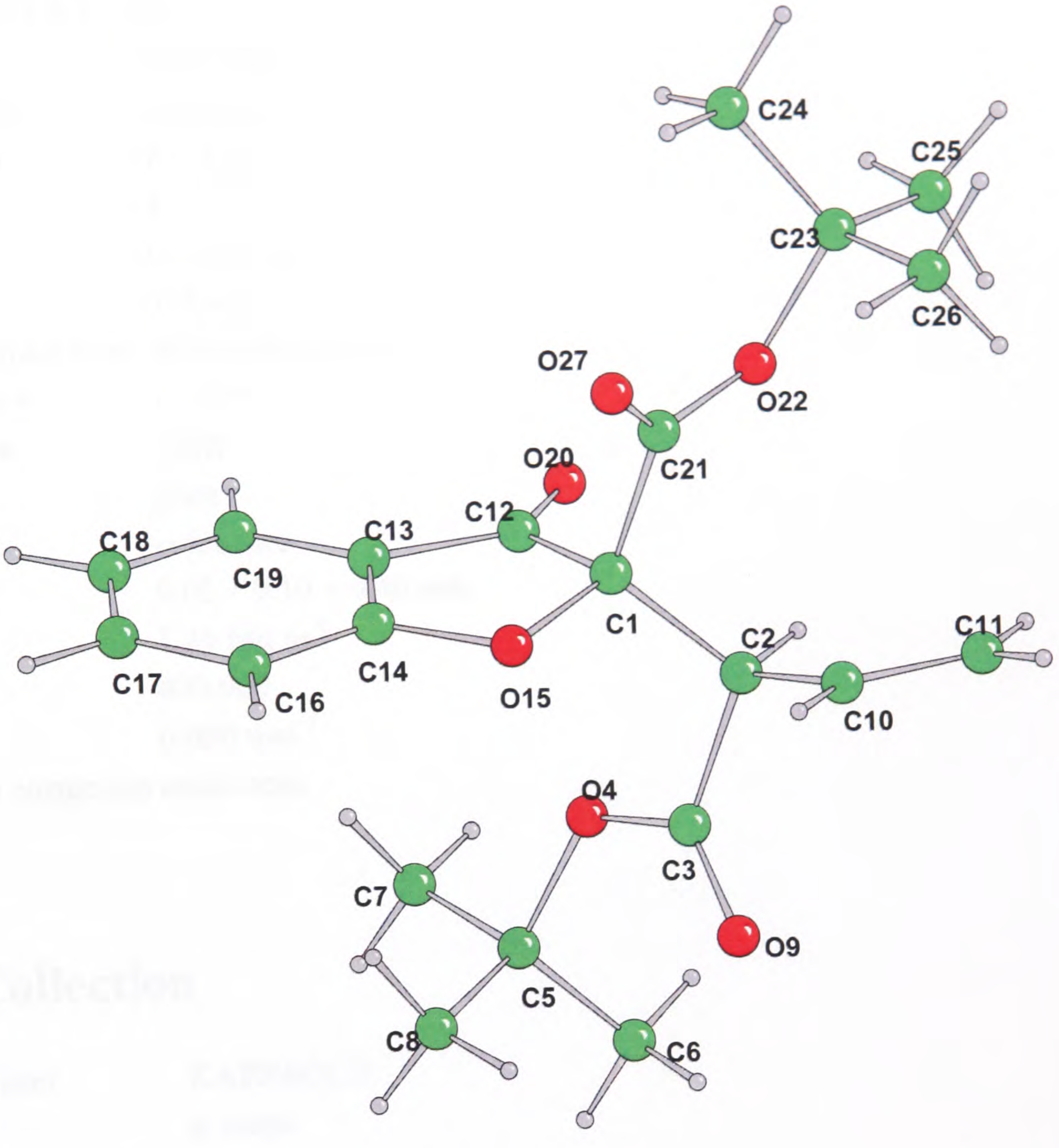
C14	C15	H1511	106.670°
C151	C15	H1511	61.023°
H152	C15	H1511	74.954°
C141	C15	H1513	126.551°
H151	C15	H1513	114.944°
H153	C15	H1511	134.768°
H1511	C15	H1513	86.822°
C15	C14	O13	107.46(10)°
O13	C14	O131	19.4(3)°
O13	C14	C141	84.4(5)°
C15	C14	C151	27.6(5)°
O131	C14	C151	99.4(5)°
C15	C14	H141	118.241°
O131	C14	H141	132.435°
C151	C14	H141	94.586°
O13	C14	H142	109.123°
C141	C14	H142	69.859°
C15	C14	H1411	90.656°
O131	C14	H1411	106.552°
C151	C14	H1411	113.155°
H141	C14	H1411	109.074°
C12	O13	C14	116.80(10)°
C14	O13	O131	87.1(8)°
C14	O13	C141	31.5(3)°
C12	O131	C14	123.7(4)°
C14	O131	O13	73.4(8)°
C14	O131	C141	33.5(4)°
C15	C141	C14	99.7(8)°
C14	C141	O13	64.1(5)°
C14	C141	O131	81.5(5)°
C15	C141	C151	26.5(7)°
O13	C141	C151	102.0(3)°
C15	C141	H142	125.238°
O13	C141	H142	94.279°
C151	C141	H142	117.613°
C14	C141	H1411	56.932°
O131	C141	H1411	111.504°
C15	C141	H1412	80.244°
O13	C141	H1412	128.920°

O131	C141	H1412	111.822°	
H142	C141	H1411	7.871°	
H1411	C141	H1412	109.211°	
C15	C151	C14	73.3(8)°	
C14	C151	C141	33.9(3)°	
C14	C151	H151	93.900°	
C15	C151	H152	106.770°	
C141	C151	H152	119.246°	
C15	C151	H1511	78.612°	
C141	C151	H1511	105.085°	
H152	C151	H1511	117.134°	
C14	C151	H1512	74.842°	
H151	C151	H1512	132.295°	
C15	C151	H1513	93.225°	
C141	C151	H1513	111.602°	
H152	C151	H1513	14.165°	
H1511	C151	H1513	111.159°	
C2	C110	C111	122.78(10)°	
C111	C110	C10	63.1(12)°	
C111	C110	C11	37.0(13)°	
C2	C110	H1101	116.657°	
C10	C110	H1101	125.603°	
C110	C111	C10	28.6(9)°	
C10	C111	C11	82.7(14)°	
C10	C111	H1111	131.775°	
C110	C111	H1112	120.799°	
C11	C111	H1112	142.535°	
C110	C111	H112	101.986°	
C11	C111	H112	56.354°	
H1112	C111	H112	135.764°	
C2	C10	C111	135.0(12)°	
C2	C10	C11	122.79(9)°	
C111	C10	C11	36.2(12)°	
C110	C10	H101	146.711°	
C11	C10	H101	119.762°	
C110	C11	C10	28.0(9)°	
C110	C11	H1111	134.662°	
C10	C11	H1111	108.917°	
C111	C11	H111	129.379°	

C151	C141	H1412	106.547°
H142	C141	H1412	108.108°
C12	O105	O5	82(2)°
C15	C151	C141	41.2(8)°
C15	C151	H151	47.975°
C141	C151	H151	76.962°
C14	C151	H152	131.050°
H151	C151	H152	123.118°
C14	C151	H1511	110.875°
H151	C151	H1511	30.902°
C15	C151	H1512	147.951°
C141	C151	H1512	107.961°
H152	C151	H1512	96.477°
C14	C151	H1513	131.887°
H151	C151	H1513	110.953°
H1511	C151	H1512	110.270°
H1512	C151	H1513	110.589°
C2	C110	C10	77.9(9)°
C2	C110	C11	147.6(17)°
C10	C110	C11	98.7(15)°
C111	C110	H1101	119.889°
C11	C110	H1101	91.753°
C110	C111	C11	55.1(12)°
C110	C111	H1111	118.876°
C11	C111	H1111	72.870°
C10	C111	H1112	104.862°
H1111	C111	H1112	119.919°
C10	C111	H112	118.773°
H1111	C111	H112	17.374°
C2	C10	C110	78.4(9)°
C110	C10	C111	88.2(14)°
C110	C10	C11	53.4(12)°
C2	C10	H101	117.446°
C111	C10	H101	97.024°
C110	C11	C111	87.9(13)°
C111	C11	C10	61.1(11)°
C111	C11	H1111	60.221°
C110	C11	H111	96.232°
C10	C11	H111	118.531°

H1111	C11	H111	128.616°		C110	C11	H112	138.501°
C111	C11	H112	79.679°		C10	C11	H112	119.276°
H1111	C11	H112	20.248°		H111	C11	H112	122.180°
C15	H151	C151	33.986°		C15	H151	H1511	82.263°
C151	H151	H1511	48.564°		C15	H152	C151	45.899°
C15	H152	H1513	108.919°		C151	H152	H1513	153.939°
C14	H142	C141	50.941°		C14	H142	H1411	54.944°
C141	H142	H1411	54.186°		C14	H1411	C141	56.048°
C14	H1411	H142	116.321°		C141	H1411	H142	117.944°
C15	H1511	C151	40.365°		C15	H1511	H151	60.454°
C151	H1511	H151	100.534°		C15	H1513	C151	35.132°
C15	H1513	H152	46.634°		C151	H1513	H152	11.896°
C111	H1111	C11	46.909°		C111	H1111	H112	111.174°
C11	H1111	H112	66.133°		C111	H112	C11	43.967°
C111	H112	H1111	51.452°		C11	H112	H1111	93.620°

Single X-Ray diffraction report for $C_{21}H_{26}O_6$ (4.35f)



06-11-07

11071035 Compound

Crystal Data

a = 11.2466(2) Å $\alpha = 90°$
b = 10.6685(2) Å $\beta = 90.4637(8)°$
c = 16.7518(3) Å $\gamma = 90°$

Volume	2009.89(6) Å^3
Crystal Class	Monoclinic
Space group	P 1 2_1/a 1
Z =	4
Formula	$C_{21} H_{26} O_6$
M_r	374.43
Cell determined from	4830 reflections
Cell θ range =	1 - 27°
Temperature	150K
Shape	plate
Colour	colourless
Size	0.02 × 0.10 × 0.40 mm
D_x	1.24 Mg m^{-3}
F000	800.000
μ	0.090 mm^{-1}
Absorption correction	multi-scan

Data Collection

Diffractometer	KAPPACCD
Scan type	ω scans
Reflections measured	8999
Independent reflections	4603
Rint	0.0004
θ_{max}	27.4987
h =	$-14 \rightarrow 14$
k =	$-13 \rightarrow 13$
l =	$-21 \rightarrow 21$

Refinement

$\Delta\rho_{min}$ =	-0.19 e Å^{-3}
$\Delta\rho_{max}$ =	0.14 e Å^{-3}
Reflections used	2256
Cutoff: I >	3.00σ(I)
Parameters refined	244
S =	1.11
R-factor	0.033
weighted R-factor	0.037
Δ/σ_{max}	0.0002
Refinement on	F
w =	$w' \times [1 - (\Delta F_{obs} / 6 \times \Delta F_{est})^2]^2$
w′ =	$[P_0T_0'(x) + P_1T_1'(x) + ...P_{n-1}T_{n-1}'(x)]^{-1}$, where P_i are the coefficients of a Chebychev series in $t_i(x)$, and x = $F_{calc}/F_{calcmax}$.
P_0 - P_{n-1} =	0.401 0.231 0.177

Parameters

Label	*x*	*y*	*z*	$U_{iso/equiv}$	Occupancy
C1	0.36884(15)	0.15735(16)	0.28960(10)	0.0239	1.0000
C2	0.30508(16)	0.27578(16)	0.26011(10)	0.0256	1.0000
C3	0.27839(16)	0.26635(17)	0.17061(10)	0.0260	1.0000
O4	0.22888(11)	0.15666(11)	0.15318(7)	0.0294	1.0000
C5	0.19303(17)	0.12361(19)	0.07031(10)	0.0309	1.0000
C6	0.0999(2)	0.2160(2)	0.04031(14)	0.0487	1.0000
C7	0.1394(2)	-0.0057(2)	0.08060(13)	0.0498	1.0000
C8	0.3016(2)	0.1175(2)	0.01786(13)	0.0508	1.0000
O9	0.29880(13)	0.34958(12)	0.12359(7)	0.0371	1.0000
C10	0.37579(19)	0.39226(17)	0.27770(10)	0.0323	1.0000
C11	0.3324(2)	0.48775(19)	0.31749(12)	0.0473	1.0000
C12	0.29228(16)	0.03605(16)	0.28970(10)	0.0259	1.0000
C13	0.36722(16)	0.05732(16)	0.25040(10)	0.0264	1.0000
C14	0.46679(17)	0.00415(17)	0.22224(10)	0.0269	1.0000
O15	0.46792(11)	0.13056(11)	0.23757(7)	0.0265	1.0000
C16	0.55605(18)	0.05676(18)	0.18092(11)	0.0338	1.0000
C17	0.5400(2)	0.18432(19)	0.16894(12)	0.0419	1.0000

C18	0.4401(2)	0.24846(19)	0.19651(12)	0.0412	1.0000
C19	0.35225(19)	0.18538(17)	0.23710(11)	0.0338	1.0000
O20	0.19480(11)	0.02508(12)	0.31889(8)	0.0328	1.0000
C21	0.42145(16)	0.17597(16)	0.37447(10)	0.0249	1.0000
O22	0.33418(10)	0.20596(11)	0.42353(7)	0.0260	1.0000
C23	0.35872(16)	0.24321(17)	0.50812(10)	0.0270	1.0000
C24	0.41826(17)	0.13642(19)	0.55283(11)	0.0323	1.0000
C25	0.23488(17)	0.2670(2)	0.53933(11)	0.0379	1.0000
C26	0.43064(18)	0.36327(18)	0.50794(11)	0.0349	1.0000
O27	0.52505(11)	0.16299(13)	0.38974(7)	0.0333	1.0000
H21	0.22475(16)	0.28144(16)	0.28887(10)	0.0337	1.0000
H61	0.0682(2)	0.1851(2)	0.01146(14)	0.0748	1.0000
H62	0.1384(2)	0.2976(2)	0.03265(14)	0.0754	1.0000
H63	0.0343(2)	0.2222(2)	0.08037(14)	0.0756	1.0000
H71	0.1149(2)	-0.0390(2)	0.02775(13)	0.0798	1.0000
H72	0.2009(2)	-0.0606(2)	0.10537(13)	0.0801	1.0000
H73	0.0703(2)	0.0012(2)	0.11601(13)	0.0804	1.0000
H81	0.2757(2)	0.0817(2)	0.03383(13)	0.0777	1.0000
H82	0.3315(2)	0.2041(2)	0.01173(13)	0.0787	1.0000
H83	0.3608(2)	0.0637(2)	0.04538(13)	0.0784	1.0000
H101	0.45924(19)	0.39497(17)	0.25845(10)	0.0424	1.0000
H111	0.3810(2)	0.56008(19)	0.32838(12)	0.0614	1.0000
H112	0.2520(2)	0.48495(19)	0.33779(12)	0.0627	1.0000
H161	0.62547(18)	0.01075(18)	0.16238(11)	0.0440	1.0000
H171	0.6015(2)	0.23039(19)	0.14033(12)	0.0529	1.0000
H181	0.4322(2)	0.33819(19)	0.18583(12)	0.0511	1.0000
H191	0.28168(19)	0.22923(17)	0.25622(11)	0.0431	1.0000
H241	0.42141(17)	0.15792(19)	0.61040(11)	0.0524	1.0000
H242	0.50163(17)	0.12419(19)	0.53291(11)	0.0522	1.0000
H243	0.36996(17)	0.05970(19)	0.54484(11)	0.0522	1.0000
H251	0.23894(17)	0.3031(2)	0.59358(11)	0.0608	1.0000
H252	0.19360(17)	0.3260(2)	0.50226(11)	0.0610	1.0000
H253	0.19034(17)	0.1876(2)	0.54143(11)	0.0612	1.0000
H261	0.44638(18)	0.38682(18)	0.56383(11)	0.0564	1.0000
H262	0.50690(18)	0.34849(18)	0.47941(11)	0.0562	1.0000
H263	0.38295(18)	0.42855(18)	0.48062(11)	0.0562	1.0000

Thermal Parameters

Label	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0260(9)	0.0233(9)	0.0225(8)	-0.0010(7)	0.0039(7)	0.0011(7)
C2	0.0311(10)	0.0218(9)	0.0238(9)	-0.0001(7)	0.0016(7)	0.0025(8)
C3	0.0275(9)	0.0237(9)	0.0267(9)	-0.0011(8)	0.0027(7)	0.0025(8)
O4	0.0393(7)	0.0257(7)	0.0232(6)	-0.0004(5)	-0.0038(5)	-0.0054(6)
C5	0.0360(11)	0.0349(11)	0.0218(9)	-0.0016(8)	-0.0029(8)	-0.0067(8)
C6	0.0468(13)	0.0537(14)	0.0452(12)	0.0038(11)	-0.0184(10)	0.0001(11)
C7	0.0677(16)	0.0421(13)	0.0393(12)	-0.0010(10)	-0.0114(11)	-0.0205(12)
C8	0.0472(13)	0.0648(16)	0.0404(12)	-0.0194(11)	0.0076(10)	-0.0115(12)
O9	0.0528(9)	0.0306(7)	0.0277(7)	0.0029(6)	-0.0027(6)	-0.0086(7)
C10	0.0455(12)	0.0255(10)	0.0259(9)	0.0027(8)	-0.0044(8)	-0.0024(9)
C11	0.0792(17)	0.0265(11)	0.0360(11)	-0.0021(9)	-0.0057(11)	0.0005(11)
C12	0.0317(10)	0.0255(9)	0.0205(8)	0.0021(7)	-0.0018(8)	-0.0005(8)
C13	0.0352(10)	0.0230(9)	0.0211(9)	0.0007(7)	-0.0001(8)	0.0012(8)
C14	0.0359(11)	0.0219(9)	0.0229(8)	-0.0004(7)	-0.0007(8)	0.0014(8)
O15	0.0314(7)	0.0226(6)	0.0257(6)	-0.0027(5)	0.0060(5)	0.0004(5)
C16	0.0396(11)	0.0299(11)	0.0320(10)	-0.0013(8)	0.0068(9)	0.0040(9)
C17	0.0567(14)	0.0336(12)	0.0357(11)	-0.0034(9)	0.0106(10)	0.0123(10)
C18	0.0663(15)	0.0231(10)	0.0344(11)	-0.0028(8)	0.0088(10)	0.0045(10)
C19	0.0495(12)	0.0237(10)	0.0282(9)	0.0006(8)	0.0006(9)	-0.0044(9)
O20	0.0310(7)	0.0338(8)	0.0336(7)	0.0010(6)	0.0048(6)	-0.0045(6)
C21	0.0288(10)	0.0194(9)	0.0266(9)	0.0005(7)	0.0029(8)	-0.0008(8)
O22	0.0263(7)	0.0309(7)	0.0209(6)	-0.0031(5)	0.0000(5)	0.0005(5)
C23	0.0292(10)	0.0308(10)	0.0209(8)	-0.0023(7)	-0.0023(7)	-0.0001(8)
C24	0.0342(10)	0.0336(11)	0.0290(9)	0.0033(8)	-0.0011(8)	-0.0020(9)
C25	0.0342(11)	0.0532(13)	0.0264(10)	-0.0054(9)	0.0026(8)	0.0073(10)
C26	0.0397(11)	0.0305(10)	0.0343(10)	-0.0032(9)	-0.0076(8)	-0.0028(9)
O27	0.0268(7)	0.0415(8)	0.0316(7)	-0.0007(6)	-0.0007(5)	0.0048(6)

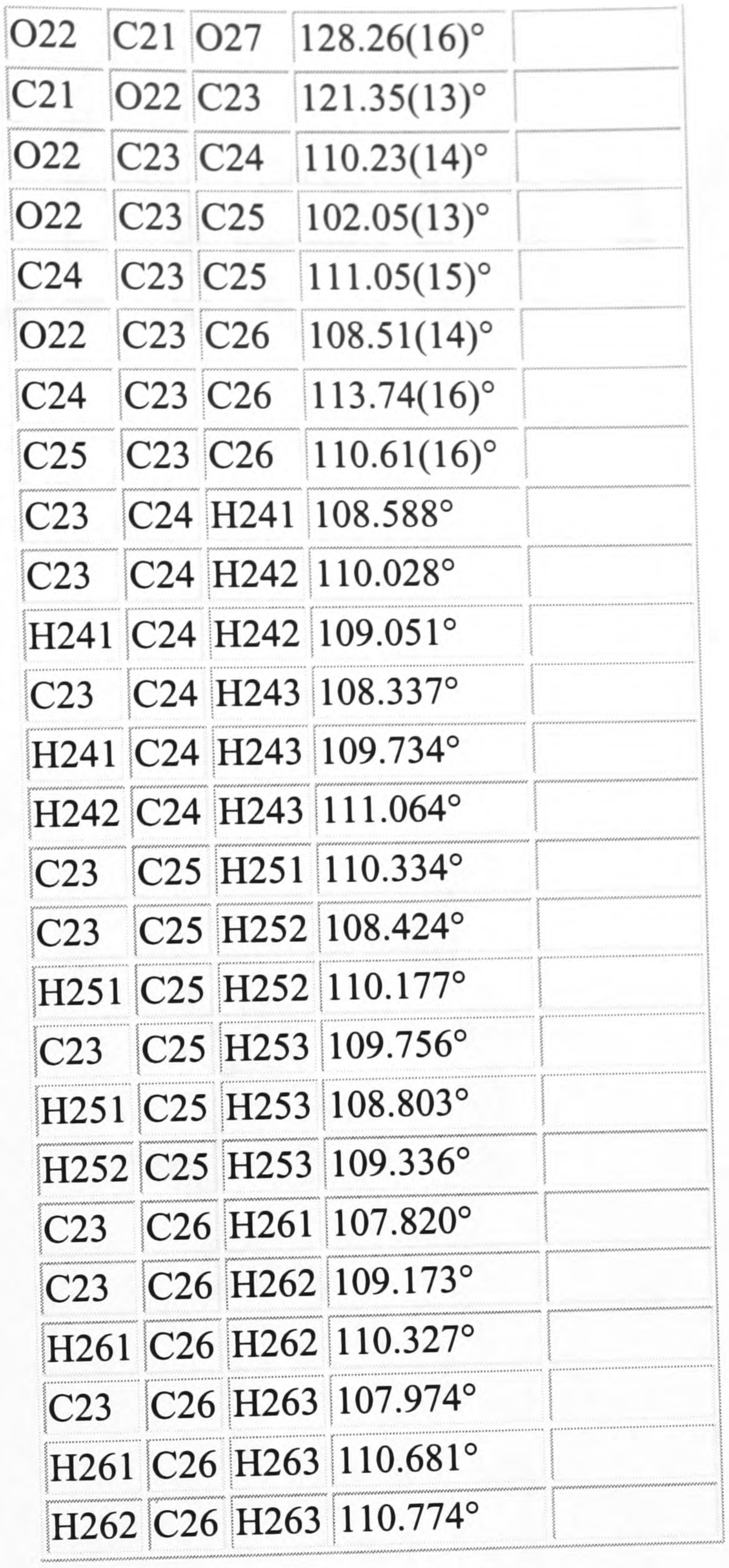
Distances

C1	C2	1.533(2)Å		C14	C16	1.386(3)Å
C1	C12	1.554(2)Å		C16	C17	1.387(3)Å
C1	O15	1.4487(19)Å		C16	H161	0.975Å
C1	C21	1.548(2)Å		C17	C18	1.397(3)Å
C2	C3	1.530(2)Å		C17	H171	0.977Å
C2	C10	1.503(3)Å		C18	C19	1.380(3)Å
C2	H21	1.029Å		C18	H181	0.978Å
C3	O4	1.327(2)Å		C19	H191	0.978Å
C3	O9	1.210(2)Å		C21	O22	1.325(2)Å
O4	C5	1.485(2)Å		C21	O27	1.199(2)Å
C5	C6	1.520(3)Å		O22	C23	1.495(2)Å
C5	C7	1.516(3)Å		C23	C24	1.516(3)Å
C5	C8	1.511(3)Å		C23	C25	1.513(2)Å
C6	H61	0.991Å		C23	C26	1.515(3)Å
C6	H62	0.981Å		C24	H241	0.992Å
C6	H63	1.004Å		C24	H242	1.006Å
C7	H71	0.991Å		C24	H243	0.991Å
C7	H72	0.995Å		C25	H251	0.988Å
C7	H73	0.984Å		C25	H252	0.996Å
C8	H81	0.988Å		C25	H253	0.985Å
C8	H82	0.989Å		C26	H261	0.984Å
C8	H83	0.990Å		C26	H262	0.998Å
C10	C11	1.314(3)Å		C26	H263	0.989Å
C10	H101	0.995Å				
C11	H111	0.963Å				
C11	H112	0.968Å				
C12	C13	1.465(2)Å				
C12	O20	1.210(2)Å				
C13	C14	1.384(3)Å				
C13	C19	1.394(3)Å				
C14	O15	1.373(2)Å				

Angles

C2	C1	C12	115.40(14)°	
C2	C1	O15	109.20(13)°	
C12	C1	O15	105.38(13)°	
C2	C1	C21	111.38(14)°	
C12	C1	C21	108.26(13)°	
O15	C1	C21	106.72(13)°	
C1	C2	C3	110.44(14)°	
C1	C2	C10	111.89(15)°	
C3	C2	C10	110.23(14)°	
C1	C2	H21	107.913°	
C3	C2	H21	107.259°	
C10	C2	H21	108.953°	
C2	C3	O4	110.62(14)°	
C2	C3	O9	123.56(16)°	
O4	C3	O9	125.81(16)°	
C3	O4	C5	121.68(13)°	
O4	C5	C6	109.64(16)°	
O4	C5	C7	102.42(14)°	
C6	C5	C7	110.71(18)°	
O4	C5	C8	109.83(15)°	
C6	C5	C8	113.15(18)°	
C7	C5	C8	110.55(18)°	
C5	C6	H61	108.446°	
C5	C6	H62	108.418°	
H61	C6	H62	109.636°	
C5	C6	H63	109.264°	
H61	C6	H63	110.177°	
H62	C6	H63	110.845°	
C5	C7	H71	109.438°	
C5	C7	H72	107.858°	
H71	C7	H72	110.406°	
C5	C7	H73	108.498°	
H71	C7	H73	110.542°	
C13	C19	H191	120.931°	
C18	C19	H191	120.990°	
C1	C21	O22	108.74(14)°	
C1	C21	O27	123.00(15)°	

H72	C7	H73	110.034°
C5	C8	H81	107.021°
C5	C8	H82	107.279°
H81	C8	H82	111.619°
C5	C8	H83	107.327°
H81	C8	H83	112.071°
H82	C8	H83	111.217°
C2	C10	C11	122.8(2)°
C2	C10	H101	117.338°
C11	C10	H101	119.817°
C10	C11	H111	120.318°
C10	C11	H112	120.393°
H111	C11	H112	119.254°
C1	C12	C13	104.18(14)°
C1	C12	O20	125.79(16)°
C13	C12	O20	129.99(17)°
C12	C13	C14	107.53(16)°
C12	C13	C19	132.00(18)°
C14	C13	C19	120.46(17)°
C13	C14	O15	114.08(15)°
C13	C14	C16	122.65(17)°
O15	C14	C16	123.26(16)°
C1	O15	C14	107.48(13)°
C14	C16	C17	116.00(19)°
C14	C16	H161	120.535°
C17	C16	H161	123.459°
C16	C17	C18	122.46(19)°
C16	C17	H171	118.206°
C18	C17	H171	119.330°
C17	C18	C19	120.34(19)°
C17	C18	H181	119.443°
C19	C18	H181	120.202°
C13	C19	C18	118.08(19)°



O22	C21	O27	128.26(16)°	
C21	O22	C23	121.35(13)°	
O22	C23	C24	110.23(14)°	
O22	C23	C25	102.05(13)°	
C24	C23	C25	111.05(15)°	
O22	C23	C26	108.51(14)°	
C24	C23	C26	113.74(16)°	
C25	C23	C26	110.61(16)°	
C23	C24	H241	108.588°	
C23	C24	H242	110.028°	
H241	C24	H242	109.051°	
C23	C24	H243	108.337°	
H241	C24	H243	109.734°	
H242	C24	H243	111.064°	
C23	C25	H251	110.334°	
C23	C25	H252	108.424°	
H251	C25	H252	110.177°	
C23	C25	H253	109.756°	
H251	C25	H253	108.803°	
H252	C25	H253	109.336°	
C23	C26	H261	107.820°	
C23	C26	H262	109.173°	
H261	C26	H262	110.327°	
C23	C26	H263	107.974°	
H261	C26	H263	110.681°	
H262	C26	H263	110.774°	