Hydrogen Borrowing-Based Methods for the Synthesis of Quaternary Stereocentres: Supplementary Information

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1. General Experimental

Microwave vials and vial caps (containing a resealing Silicone/PTFE septum) were purchased from Kinesis (Cole-Palmer) and were used without flame-drying. All other reactions were carried out in flame-dried glassware under an atmosphere of nitrogen unless stated otherwise. Room temperature (RT) refers to 20 – 25 °C. Temperatures of 0 °C were obtained using an ice/water bath and temperatures of –78 °C were obtained using a dry ice/acetone bath. Heating was achieved using an oil bath equipped with a contact thermometer.

PhMe, CH_2Cl_2, Et_2O, tetrahydrofuran, MeCN and 1,4-dioxane were purified by filtration through activated alumina columns employing the method of Grubbs et al. [1] Water was purified by an Elix® UV-10 system. All other solvents and reagents were used as supplied by major chemical suppliers without prior purification.

Thin layer chromatography (TLC) was performed on Merck Kieselgel 60 F_{254} 0.25 mm pre-coated aluminium plates. TLC plates were visualized under UV light (λ = 254 nm) and/or by staining with potassium permanganate solution, phosphomolybdic acid stain, bromocresol green stain or vanillin in acidic ethanol (Vanillin stain). Flash chromatography was performed using VWR silica gel 60 (40 – 63 µm particle size) or (15 – 40 µm particle size) using head pressure by means of a nitrogen line.

NMR spectroscopy was carried out using Bruker 400 MHz, 500 MHz or 600 MHz (with helium-cooled broadband cryoprobe) spectrometers in the deuterated solvent stated, using the residual non-deuterated solvent signal as an internal reference. Chemical shifts are quoted in ppm with signal splittings recorded as singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), hextet (h), multiplet (m). Higher multiplicities are indicated by combinations of these abbreviations, for example: doublet of doublets (dd). The abbreviation br. denotes broad. Coupling constants, J, are rounded to the nearest 0.1 Hz and are presented as observed. Unless otherwise stated, all NMR experiments were performed at 298 K. Systematic names were generated by the computer program ChemDraw 23.0.1 according to the guidelines specified by the International Union of Pure and Applied Chemistry (IUPAC). Where a pentamethylphenyl (Ph*) group is employed, peak broadening and splitting due to restricted rotation may be observed in both the ^{1}H and ^{13}C NMR spectra, resulting in more resonances than initially expected based upon symmetry. For inseparable mixtures of diastereomers (>[75:25] d.r.) both isomers are reported separately and the structure of the major diastereomer is shown. When ^{1}H and ^{13}C NMR data for the major diastereoisomer is reported, any signals that overlap with the minor isomer have been integrated without the contribution from the minor isomer being included. In such a case, signals of the minor isomer are not reported. For equimolar mixtures of diastereomers (d.r. ≤ [75:25]), ^{1}H NMR data for isomers is reported together.

Melting points were determined using a Griffin melting point apparatus and are uncorrected. Infrared spectra were recorded neat or as a thin film on a Bruker Tensor 27 spectrometer equipped with an attenuated total reflectance attachment with internal calibration. Absorption maxima (λ_{max}) are quoted in wavenumbers (cm^{-1}). The abbreviation br. denotes broad.

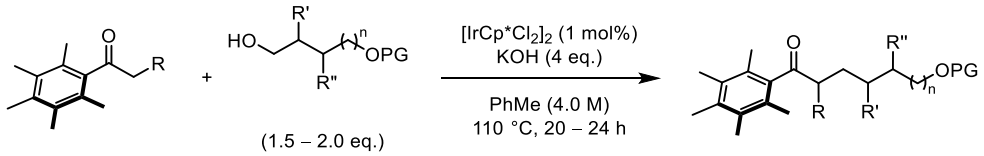
Low-resolution mass spectra were recorded on a Waters LCT Premier XE bench-top orthogonal acceleration time-of-flight LC-MS system (loop injection mode). High Resolution Mass spectrometry was carried out using

flow injection analysis and was performed on an ACQUITY I-Class PLUS UPLC System (Waters, Milford, MA, USA) coupled to an ACQUITY RDa mass spectrometer (Waters, Milford, MA, USA) equipped with an ESI probe and a TOF mass analyser. In positive ion mode, the flow rate was set to 0.300 mL/min using a 50% methanol(aq) + 0.1% formic acid eluent. Scan parameters were set as follows: analyser mode, full scan; scan range, 50 2000 m/z; scan rate, 2 Hz; cone voltage, 30 V; capillary voltage, 1.5 kV; desolvation temperature, 550 °C; and intelligent data capture, on. In negative ion mode, the flow rate was set to 0.300 mL/min using a 50% $methanol_{(aq)}$ + 0.1% formic acid eluent. Scan parameters were set as follows: analyser mode, full scan; scan range, 50 2000 m/z; scan rate, 2 Hz; cone voltage, 40 V; capillary voltage, 0.8 kV; desolvation temperature, 550 °C; and intelligent data capture, on. Electrospray ionisation (ESI) HRMS were also recorded on a Thermo Exactive orbitrap spectrometer equipped with a Waters Equity LC system, with a flow rate of 0.2 mL/min using water:methanol:formic acid (10:89.9:0.1) as eluent. The system uses an orbitrap mass analyser and a heated electrospray ionisation (HESI-II) probe for ESI^+ and has a resolution of 50,000 FWHM under conditions for maximum sensitivity, with an accuracy of better than 5 ppm for 24 h following external calibration on the day of analysis. The mass reported is that containing the most abundant isotopes, with each value rounded to 4 decimal places and within 5 ppm of the calculated mass.

Single crystal X-ray data collection and structure determination were performed by Timothy C. Jenkins in the Chemistry Research Laboratory, University of Oxford. Crystals were mounted on MiTeGen loops using perfluoropolyether oil and rapidly transferred to a goniometer head on a diffractometer fitted with an Oxford CryoSystems CryoStream open-flow nitrogen cooling device. [2] Data collections were either carried out at 150 K using an (Rigaku) Oxford Diffraction Supernova A diffractometer, or at 100 K using a high flux Rigaku Synergy DW rotating anode diffractometer using mirror-monochromated Cu Kα radiation (λ = 1.54184 Å). Data were processed using CryAlisPro, the structure was then solved using charge-flipping algorithm SUPERFLIP[3] and refined by full-matrix least squares using CRYSTALS. [4, 5] Structures are visualised and represented using Mercury.

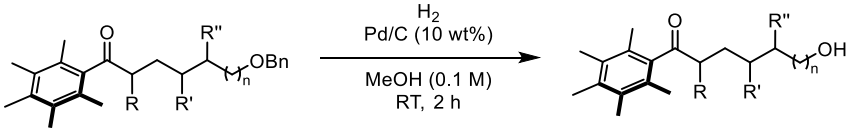
2. General Procedures

General Procedure A: Hydrogen Borrowing Alkylation with mono-protected diols



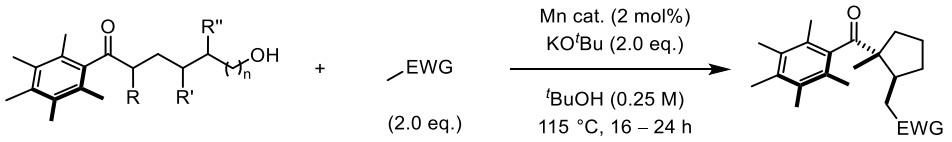
Ph* ketone (1.00 eq.), mono-protected diol (1.50 –2.00 eq.), $[IrCp^*Cl_2]_2$ (1.0 mol%) and KOH (4.00 eq.) were added to a 10 – 20 mL microwave vial. The vial was sealed evacuated and back-filled with Ar (3 times) and PhMe (4.0 M, degassed with Ar (balloon)) was added. The reaction was heated at 110 °C for 20 – 24 h, cooled to room temperature, filtered through a silica plug (Et_2O elution) and concentrated *in vacuo*. Purification was accomplished *via* flash column chromatography as indicated.

General Procedure B: Benzyl Deprotection



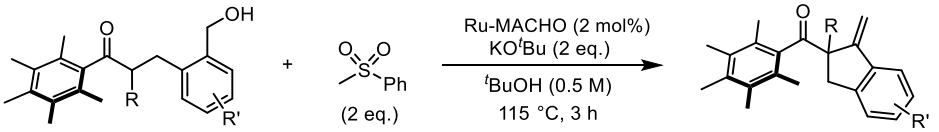
Benzyl ether substrate (1.00 eq.) was dissolved in MeOH (0.1 M) and the solution was degassed with nitrogen (balloon) for 10 min. Pd/C (10% Pd on carbon, 10 wt%) was added and a balloon of hydrogen gas was attached. H_2 was bubbled through the reaction mixture for 10 min and then the mixture was stirred vigorously at RT for 2 h. The crude reaction mixture was filtered through a Celite® pad (washed with CH_2Cl_2) and concentrated *in vacuo.* Purification was accomplished *via* flash column chromatography as indicated.

General Procedure C: Acceptorless dehydrogenation-intramolecular conjugate addition



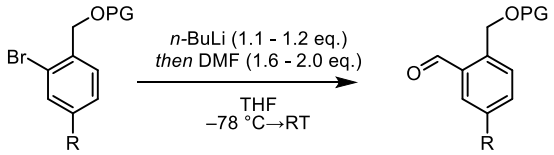
Hydroxy-ketone substrate (0.300 mmol, 1.00 eq.), nucleophile (0.600 mmol, 2.00 eq.), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (2.0 mol%) and KO^{t}Bu (0.600 mmol, 2.00 eq.) were added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and back-filled with Ar (3 times) and ^{t}BuOH (0.25 M, degassed with Ar (balloon)) was added. The reaction was heated at 115 °C for 16 – 24 h, cooled to RT, filtered through a silica pad (Et_2O/CH_2Cl_2 elution) and concentrated *in vacuo*. Purification was accomplished *via* flash column chromatography as indicated.

General Procedure D: Acceptorless dehydrogenation to access exocyclic alkenes



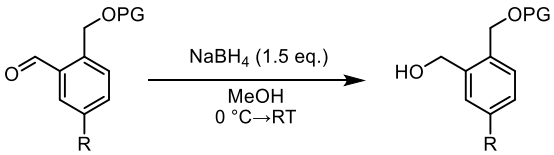
Ph* hydroxy-ketone substrate (1.00 eq.), methyl phenyl sulfone (2.00 eq.), Ru-MACHO® (1.0 mol%) and KO^{t}Bu (2.00 eq.) added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and back-filled with Ar (3 times) and ^{t}BuOH (0.50 M, degassed with Ar (balloon)) was added. The reaction was heated at 115 °C for 3 h, cooled to RT, filtered through a silica pad and concentrated *in vacuo*. Purification was accomplished *via* flash column chromatography as indicated.

General Procedure E: Lithium-Halogen Exchange of Benzyl Ethers



n-BuLi (2.5 M in hexanes, 1.10 – 1.20 eq.) was added slowly to a solution of aryl bromide (1.00 eq.) in THF (0.30 M) at –78 °C. The mixture was stirred at –78 °C for 40 min and *N,N*-dimethylformamide (1.60 – 2.00 eq.) was added. The reaction was warmed to RT, stirred for 2 h and quenched with the addition of sat. aq. NH_4Cl. The mixture was diluted with EtOAc and water, the layers separated and the aqueous phase extracted three times with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Purification was accomplished *via* flash column chromatography as indicated.

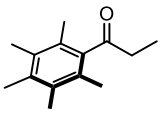
General Procedure F: Reduction of aryl aldehydes



Aryl aldehyde (1.00 eq.) was dissolved in MeOH (0.30 M) and the solution was cooled to 0 °C. $NaBH_4$ (1.50 eq.) was added, the reaction allowed to warm to RT and stirred for 2 h. The reaction was quenched by addition of sat. aq. NH_4Cl and the mixture concentrated *in vacuo*. The residue was diluted with EtOAc and water, the layers separated and the aqueous phase extracted three times with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification, when required, was conducted *via* flash column chromatography as indicated.

3. Preparation and Characterisation of Compounds

S1 1-(2,3,4,5,6-Pentamethylphenyl)propan-1-one



Pentamethylbenzene (5.00 g, 33.8 mmol) and proprionyl chloride (3.2 mL, 37 mmol) were dissolved in CH_2Cl_2 (150 mL) and the mixture was cooled to 0 °C. $AlCl_3$ (5.43 g, 40.8 mmol) was added portionwise and the reaction was allowed to warm to RT and stirred for 1 h. The crude reaction mixture was poured onto ice (approx. 150 g) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL) and the combined organic layers were washed with satd. aq. $NaHCO_3$, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 98:2 ⟶ 96:4) gave the *title compound* as a white solid (5.63 g, 81%).

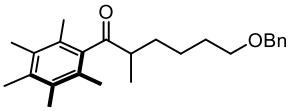
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.69 (q, *J* = 7.2 Hz, 2H), 2.23 (s, 3H), 2.19 (s, 6H), 2.09 (s, 6H), 1.20 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 212.9, 141.0, 135.4, 133.2, 127.5, 38.9, 17.3, 16.8, 16.1, 7.7;

m/z (ESI$^+$) Found ([M+H]$^+$) = 205, $C_{14}H_{21}O$ requires 205.

The spectral data matched that previously reported in the literature. [6]

S2 6-(Benzyloxy)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



Ketone **S1** (2.04 g, 10.0 mmol), $[IrCp^*Cl_2]_2$ (80 mg, 1.0 mol%), KOH (2.24 g, 40.0 mmol), 4-benzyloxy-1-butanol (3.5 mL, 20 mmol) and PhMe (2.5 mL) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 96:4 ⟶ 90:10) gave the *title compound* as a colourless oil (3.10 g, 85%).

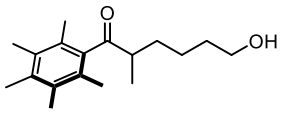
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 5H), 4.49 (s, 2H), 3.46 (t, *J* = 6.4 Hz, 2H), 2.91 – 2.69 (m, 1H), 2.23 (s, 3H), 2.18 (s, 6H), 2.08 (s, 6H), 1.86 – 1.76 (m, 1H), 1.71 – 1.47 (m, 3H), 1.45 – 1.30 (m, 2H), 1.14 (d, *J* = 7.0 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 215.1, 140.2, 138.7, 135.5, 133.2, 128.5, 128.4, 127.8, 127.6, 73.1, 70.3, 48.5, 31.7, 30.0, 24.2, 18.1, 16.8, 16.2, 15.3;

IR (film) ν_{max}/cm^{-1} 2935, 2862, 1693, 1100, 734, 698;

HRMS (ESI$^+$) $C_{25}H_{35}O_2^+$ ([M+H]$^+$) requires 367.2632; found 367.2639, Δ 1.98 ppm.

1a 6-Hydroxy-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



Benzyl ether **S2** (2.09 g, 5.70 mmol) was subjected to **General Procedure B** in MeOH (10 mL) with Pd (10% on carbon) (209 mg, 10 wt%) for 2 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 70:30 → 60:40) gave the *title compound* as a white solid (1.44 g, 92%).

m.p. = 39–41 °C;

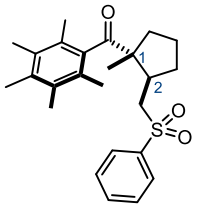
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (t, *J* = 6.4 Hz, 2H), 2.87 – 2.71 (m, 1H), 2.23 (s, 3H), 2.18 (s, 6H), 2.09 (s, 6H), 1.88 – 1.75 (m, 1H), 1.63 – 1.32 (m, 5H), 1.15 (d, *J* = 7.0 Hz, 3H);

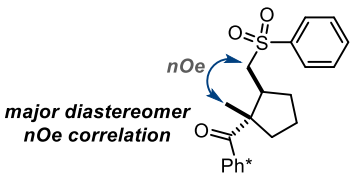
^{13}C NMR (101 MHz, $CDCl_3$) δ 215.1, 140.1, 135.6, 133.2, 128.3, 62.8, 48.5, 32.9, 31.6, 23.6, 18.0, 16.8, 16.1, 15.4;

IR (film) ν_{max}/cm^{-1} 3371, 2935, 2342, 1692, 1575, 1457, 1070, 1043, 923;

HRMS (ESI$^+$) $C_{18}H_{29}O_2^+$ ([M+H]$^+$) requires 277.2162; found 277.2163, Δ 0.26 ppm.

3a (1-Methyl-2-((phenylsulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone





Hydroxy-ketone **1a** (83 mg, 0.30 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* reverse phase flash column chromatography (eluent water: MeCN 70:30 → MeCN) gave the *title compound* as a white solid (99 mg, 80%, [93:7] d.r.*)

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The relative stereochemistry was assigned by nOe and X-Ray crystallography analysis.

Major (1*RS*, 2*RS*) diastereomer:

m.p. = 164 – 166 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.86 (m, 2H), 7.70 – 7.62 (m, 1H), 7.60 – 7.53 (m, 2H), 3.56 (dd, *J* = 13.8, 2.1 Hz, 1H), 2.99 (dd, *J* = 13.8, 11.9 Hz, 1H), 2.62 – 2.52 (m, 1H), 2.35 – 2.25 (m, 1H), 2.22 (s, 3H), 2.14 (s, 6H), 2.01 (s, 3H), 1.92 (s, 3H), 1.90 – 1.76 (m, 1H), 1.75 – 1.53 (m, 4H), 1.12 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 217.4, 140.3, 138.7, 135.3, 133.7, 133.5, 133.1, 129.4, 128.1, 128.0, 127.9, 58.6, 58.1, 39.5, 36.7, 29.6, 22.1, 19.2, 18.5, 18.4, 16.8, 16.3, 16.1;

IR (film) ν_{max}/cm^{-1} 2926, 1678, 1447, 1306, 1147, 756;

HRMS (ESI$^+$) $C_{25}H_{32}NaO_3S^+$ ([M+Na]$^+$) requires 435.1964; found 435.1975, Δ 2.47 ppm.

Minor (1*SR*, 2*RS*) diastereomer:

m.p. = 138 – 140 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.69 – 7.63 (m, 1H), 7.60 – 7.54 (m, 2H), 3.65 – 3.32 (m, 2H), 2.34 (dtd, *J* = 10.3, 7.5, 2.4 Hz, 1H), 2.21 (s, 3H), 2.19 – 2.15 (m, 4H), 2.14 (s, 3H), 2.12 – 2.04 (m, 1H), 2.04 – 1.98 (m, 4H), 1.94 (s, 3H), 1.80 – 1.70 (m, 2H), 1.56 – 1.50 (m, 1H), 1.12 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.6, 140.3, 139.4, 135.3, 133.7, 133.5, 133.0, 129.4, 128.1, 127.9, 127.8, 60.2, 58.5, 45.0, 39.0, 31.0, 24.2, 22.0, 18.7, 18.4, 16.8, 16.3, 16.0;

IR (film) ν_{max}/cm^{-1} 2967, 1679, 1448, 1306, 1150, 1087, 917, 738;

HRMS (ESI^+) $C_{25}H_{33}O_3S^+$ ($[M+H]^+$) requires 413.2145; found 413.2148, Δ 0.73 ppm.

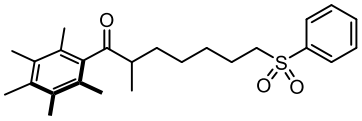
Scale-Up Procedure:

Hydroxy-ketone **1a** (1.10 g, 4.00 mmol), methyl phenyl sulfone (1.25 g, 8.00 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (40 mg, 2.0 mol%) and KO^{t}Bu (898 mg, 8.00 mmol) were added to a 125 mL pressure tube. The pressure tube was evacuated and back-filled with Ar (3 times), ^{t}BuOH (degassed with Ar (balloon) (16 mL)) was added and the tube was sealed under an Ar atmosphere. The reaction was heated at 115 °C for 16 h, cooled to RT, filtered through a silica pad (Et_2O/CH_2Cl_2 elution) and concentrated *in vacuo*. Purification *via* reverse phase flash column chromatography (eluent water: MeCN 70:30 → MeCN) gave the *title compound* as a white solid (1.20 g, 73%, [94:6] d.r.*)

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The spectroscopic data were identical to that given above.

4 2-Methyl-1-(2,3,4,5,6-pentamethylphenyl)-7-(phenylsulfonyl)heptan-1-one



Hydroxy-ketone **1a** (83 mg, 0.30 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), Ru-MACHO® (3.6 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and back-filled with Ar (3 times) and ^{t}BuOH (1.2 mL) was added. The reaction was heated at 115 °C for 24 h, cooled to RT, filtered through a silica pad (Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 87:5:8 → 85:5:10) gave the *title compound* as a white solid (68 mg, 55%, isolated in conjunction with 35 mg, 28% cyclised product **3a** [89:11] d.r.*)

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

m.p. = 82 – 84 °C;

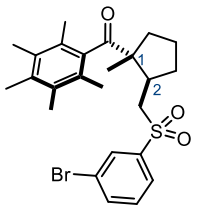
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 – 7.86 (m, 2H), 7.69 – 7.61 (m, 1H), 7.60 – 7.53 (m, 2H), 3.14 – 3.02 (m, 2H), 2.80 – 2.67 (m, 1H), 2.23 (s, 3H), 2.18 (s, 6H), 2.06 (s, 6H), 1.78 – 1.66 (m, 3H), 1.45 – 1.20 (m, 5H), 1.10 (d, *J* = 7.0 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 214.8, 140.0, 139.4, 135.6, 133.8, 133.2, 129.4, 128.3, 128.2, 56.3, 48.3, 31.5, 28.6, 26.9, 22.7, 18.0, 16.9, 16.2, 15.4;

IR (film) ν_{max}/cm^{-1} 2940, 1691, 1447, 1306, 1148, 1088, 922, 733, 690;

HRMS (ESI$^+$) $C_{25}H_{34}NaO_3S^+$ ([M+Na]$^+$) requires 437.2121; found 437.2120, Δ 0.21 ppm.

3b (2-(((3-Bromophenyl)sulfonyl)methyl)-1-methylcyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **1a** (83 mg, 0.30 mmol), 3-bromophenyl methyl sulfone (141 mg, 0.600 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/EtOAc, 91:5:4) gave separable diastereomers of the *title compound* as a white solid (106 mg, 72%, [95:5] d.r.*)

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The relative stereochemistry was assigned by X-ray crystallography analysis.

Major (1*RS*, 2*RS*) diastereomer:

m.p. = 118 – 120 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (t, *J* = 1.9 Hz, 1H), 7.84 – 7.80 (m, 1H), 7.80 – 7.75 (m, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 3.57 (dd, *J* = 13.8, 2.1 Hz, 1H), 3.00 (dd, *J* = 13.8, 11.9 Hz, 1H), 2.63 – 2.54 (m, 1H), 2.34 – 2.27 (m, 1H), 2.23 (s, 3H), 2.18 – 2.12 (m, 6H), 2.02 (s, 3H), 1.96 (s, 3H), 1.87 – 1.79 (m, 1H), 1.76 – 1.54 (m, 4H), 1.13 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.4, 142.2, 138.7, 136.9, 135.4, 133.5, 133.2, 131.0, 131.0, 128.1, 127.9, 126.6, 123.4, 58.6, 58.3, 39.4, 36.6, 29.7, 22.1, 19.2, 18.5, 18.4, 16.8, 16.4, 16.1;

IR (film) ν_{max}/cm^{-1} 2968, 1677, 1572, 1412, 1318, 1217, 1149, 1099, 926 ;

HRMS (ESI$^+$) [$C_{25}H_{32}{}^{79}BrO_3S$]$^+$ ([M+H]$^+$) requires 491.1250; found 491.1244, Δ 1.32 ppm.

Minor (1*SR*, 2*RS*) diastereomer:

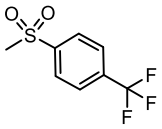
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (t, *J* = 1.8 Hz, 1H), 7.87 (ddd, *J* = 7.8, 1.8, 1.0 Hz, 1H), 7.79 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H), 3.58 – 3.42 (m, 2H), 2.36 (dtd, *J* = 10.3, 7.4, 2.3 Hz, 1H), 2.22 (s, 3H), 2.20 – 2.17 (m, 1H), 2.16 (s, 3H), 2.15 (s, 3H), 2.13 – 2.05 (m, 1H), 2.04 – 1.97 (m, 4H), 1.96 (s, 3H), 1.83 – 1.71 (m, 2H), 1.61 – 1.49 (m, 1H), 1.14 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.7, 142.3, 139.3, 136.9, 135.3, 133.5, 133.0, 131.1, 131.0, 127.9, 127.7, 126.7, 123.5, 60.2, 58.6, 44.8, 39.0, 31.1, 24.3, 22.0, 18.7, 18.4, 16.8, 16.3, 16.0;

IR (film) ν_{max}/cm^{-1} 2930, 1679, 1572, 1461, 1414, 1318, 1217, 1150, 1097;

HRMS (ESI$^+$) [$C_{25}H_{32}{}^{79}BrO_3S$]$^+$ ([M+H]$^+$) requires 491.1250; found 491.1245, Δ 1.01 ppm.

S3 1-(Methylsulfonyl)-4-(trifluoromethyl)benzene



Mg turnings (608 mg, 24.9 mmol) were heated with stirring under vacuum in a two-necked flask for 10 min and allowed to cool to RT. THF (5 mL) and a single iodine crystal were added and 4-bromobenzotrifluoride (1.40 mL, 10.0 mmol) was added slowly. The mixture was refluxed for a further 5 min, cooled to RT and diluted with THF (5 mL). The cooled Grignard reagent was added slowly to a suspension of (1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide) adduct (2.40 g, 10.0 mmol) in THF (30 mL) at –40 °C. The reaction mixture was stirred at –40 °C for 1 h, allowed to warm to RT and the THF was removed under a stream of N_2. The residue was dissolved in *N*,*N*-dimethylformamide (DMF, 40 mL) and MeI (1.9 mL, 30 mmol) was added. The resulting suspension was heated to 75 °C overnight, cooled to RT, filtered under reduced pressure and the filtrate concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 75:5:20) gave the *title compound* as a yellow solid (732 mg, 33%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 – 8.00 (m, 2H), 7.96 – 7.75 (m, 2H), 3.09 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 144.0, 135.6 (q, J^2_{C-F} = 33.2 Hz), 128.1, 126.6 (q, J^3_{C-F} = 3.8 Hz), 123.1 (q, J^1_{C-F} = 273.2 Hz), 44.4;

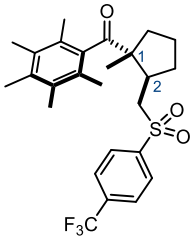
^{19}F NMR (471 MHz, $CDCl_3$) δ -63.2;

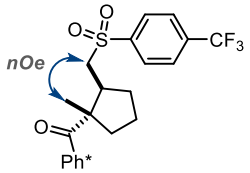
HRMS (ESI$^+$) $C_8H_7F_3NaO_2S^+$ ([M+Na]$^+$) requires 247.0011; found 247.0011, Δ 0.01 ppm.

The spectroscopic data were consistent with that present in the literature. [7]

3c

(1-Methyl-2-(((4-(trifluoromethyl)phenyl)sulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone





major trans diastereomer nOe correlation

Hydroxy-ketone **1a** (83 mg, 0.30 mmol), sulfone **S3** (134 mg, 0.600 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 90:5:5) gave separable

diastereomers of the *title compound* as a white solid (70 mg, 48%, [94:6] d.r., isolated in conjunction with **S4** 45 mg, 36%).*

*d.r. calculated post-purification due to overlapping peaks in the crude NMR

The relative stereochemistry was assigned by nOe and X-ray crystallography analysis.

Major (1*RS*, 2*RS*) diastereomer:

m.p. = 140 – 142 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 – 7.98 (m, 2H), 7.93 – 7.73 (m, 2H), 3.63 (dd, *J* = 13.9, 2.1 Hz, 1H), 3.03 (dd, *J* = 13.9, 11.9 Hz, 1H), 2.54 (dddd, *J* = 12.0, 10.2, 8.3, 2.1 Hz, 1H), 2.30 (m, 1H), 2.22 (s, 3H), 2.15 (s, 3H), 2.14 (s, 3H), 2.02 (s, 3H), 1.88 (s, 3H), 1.81 (dt, *J* = 12.0, 9.5 Hz, 1H), 1.76 – 1.56 (m, 4H), 1.13 (s, 3H);

^{13}C NMR ({^{19}F} 126 MHz, $CDCl_3$) δ 217.3, 143.6, 138.6, 135.5, 135.4, 133.5, 133.2, 128.7, 128.0, 127.7, 126.6, 123.3, 58.6, 58.1, 39.4, 36.4, 29.6, 22.0, 19.2, 18.5, 18.3, 16.8, 16.3, 16.0;

^{19}F NMR (565 MHz, $CDCl_3$) δ -63.2;

IR (film) ν_{max}/cm^{-1} 2953, 1679, 1404, 1325, 1174, 1017, 916, 846;

HRMS (ESI$^+$) $C_{26}H_{31}F_3NaO_3S^+$ ([M+Na]$^+$) requires 503.1838; found 503.1835, Δ 0.58 ppm.

Minor (1*SR*, 2*RS*) diastereomer:

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 – 8.01 (m, 2H), 7.86 (d, *J* = 8.2 Hz, 2H), 3.59 – 3.47 (m, 2H), 2.42 – 2.31 (m, 1H), 2.21 (s, 3H), 2.20 – 2.15 (m, 4H), 2.14 (s, 3H), 2.12 – 2.07 (m, 1H), 2.06 – 1.97 (m, 4H), 1.92 (s, 3H), 1.82 – 1.68 (m, 2H), 1.56 (dt, *J* = 13.3, 8.1 Hz, 1H), 1.14 (s, 3H);

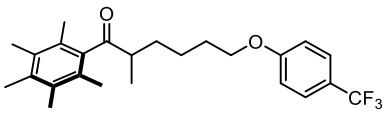
^{13}C NMR (151 MHz, $CDCl_3$) δ 217.6, 143.9, 139.2, 135.5 (q, J^2_{C-F} = 33.3 Hz), 135.4, 133.5, 133.0, 128.8, 127.9, 127.6, 126.6 (q, J^3_{C-F} = 3.6 Hz), 123.3 (q, J^1_{C-F} = 273.0 Hz), 60.2, 58.4, 44.8, 38.9, 31.1, 24.2, 22.0, 18.7, 18.4, 16.8, 16.3, 16.0;

^{19}F NMR (565 MHz, $CDCl_3$) δ -63.2.

IR (film) ν_{max}/cm^{-1} 2945, 1694, 1617, 1520, 1331, 1260, 1179, 1162, 1121, 1069, 639;

HRMS (ESI$^+$) $C_{26}H_{32}F_3O_3S^+$ ([M+H]$^+$) requires 481.2019; found 481.2014, Δ 0.90 ppm.

S4 2-Methyl-1-(2,3,4,5,6-pentamethylphenyl)-6-(4-(trifluoromethyl)phenoxy)hexan-1-one



Hydroxy-ketone **1a** (83 mg, 0.30 mmol), sulfone **S3** (134 mg, 0.600 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 90:5:5) gave the *title compound* as a colourless oil (45 mg, 36%, isolated in conjunction with **3c** 70 mg, 48%, [94:6] d.r.)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 – 7.45 (m, 2H), 6.92 (d, *J* = 8.6 Hz, 2H), 3.99 (t, *J* = 6.4 Hz, 2H), 2.89 – 2.75 (m, 1H), 2.24 (s, 3H), 2.18 (s, 6H), 2.09 (s, 6H), 1.91 – 1.74 (m, 3H), 1.67 – 1.58 (m, 1H), 1.53 – 1.39 (m, 2H), 1.17 (d, *J* = 7.0 Hz, 3H);

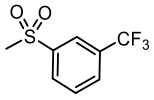
^{13}C NMR (151 MHz, $CDCl_3$) δ 214.9, 161.6, 140.1, 135.6, 133.3, 128.4, 127.0 (q, J^3_{C-F} = 3.7 Hz), 123.7 (q, J^1_{C-F} = 271.4 Hz), 122.9 (q, J^2_{C-F} = 32.7 Hz), 114.6, 68.1, 48.4, 31.6, 29.4, 24.0, 18.1, 16.9, 16.2, 15.4;

^{19}F NMR (565 MHz, $CDCl_3$) δ -61.5;

IR (film) ν_{max}/cm^{-1} 2946, 1694, 1617, 1520, 1384, 1331, 1260, 1179, 1162, 1121, 1069, 924;

HRMS (ESI^+) $C_{25}H_{32}F_3O_2^+$ ($[M+H]^+$) requires 421.2349; found 421.2341, Δ 1.89 ppm.

S5 1-(Methylsulfonyl)-3-(trifluoromethyl)benzene



Mg turnings (613 mg, 25.0 mmol) were heated with stirring under vacuum in a two-necked flask for 10 min and allowed to cool to RT. THF (5 mL) and a single iodine crystal were added and 3-bromobenzotrifluoride (1.40 mL, 10.0 mmol) was added slowly. The mixture was refluxed for a further 5 min, cooled to RT and diluted with THF (5 mL). The cooled Grignard reagent was added slowly to a suspension of (1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide) adduct, 2.40 g, 10.0 mmol) in THF (30 mL) at –40 °C. The reaction mixture was stirred at –40 °C for 2 h, allowed to warm to RT and the THF was removed under a stream of N_2. The residue was dissolved in *N*,*N*-dimethylformamide (DMF, 40 mL) and MeI (1.9 mL, 30 mmol) was added. The resulting suspension was heated to 75 °C overnight, cooled to RT, and Et_2O (50 mL) was added. The resulting suspension was filtered through a Celite® pad and the filtrate concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 80:5:15 → 70:5:25) gave the *title compound* as a yellow solid (921 mg, 41%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.16 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.93 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.75 (t, *J* = 7.8 Hz, 1H), 3.10 (s, 3H);

^{13}C NMR ({^{19}F} 126 MHz, $CDCl_3$) δ 141.9, 132.3, 130.9, 130.6, 130.4, 124.8, 123.2, 44.6;

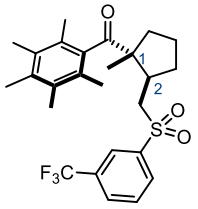
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.9;

m/z (ESI^+) Found ($[M+H]^+$) = 247, $C_8H_7F_3NaO_2S$ requires 247;

The spectroscopic data matched that previously reported in the literature. [8]

3d

1-Methyl-2-(((3-(trifluoromethyl)phenyl)sulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **1a** (83 mg, 0.30 mmol), sulfone **S5** (134 mg, 0.600 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h.

Purification *via* sequential flash column chromatography (reverse phase (eluent water/MeCN 30:70 → MeCN), then normal phase (eluent Pentane/CH_2Cl_2/Et_2O, 90:5:5)) gave separable diastereomers of the *title compound* as a white solid (86 mg, 60%, [91:9] d.r.*).

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The relative stereochemistry was assigned by X-ray crystallography analysis.

Major (1*RS*, 2*RS*) diastereomer:

m.p. = 129 – 131 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 – 8.17 (m, 1H), 8.09 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.95 – 7.90 (m, 1H), 7.74 (t, *J* = 7.8 Hz, 1H), 3.62 (dd, *J* = 13.8, 2.1 Hz, 1H), 3.04 (dd, *J* = 13.8, 11.9 Hz, 1H), 2.60 (dddd, *J* = 12.1, 10.2, 8.3, 2.1 Hz, 1H), 2.32 (m, 1H), 2.22 (s, 3H), 2.15 (s, 6H), 2.02 (s, 3H), 1.93 (s, 3H), 1.89 – 1.78 (m, 1H), 1.77 – 1.54 (m, 4H), 1.13 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.4, 141.6, 138.7, 135.4, 133.5, 133.2, 132.2 (q, $J^2_{C–F}$ = 33.5 Hz), 131.4, 130.5 (q, $J^3_{C–F}$ = 3.6 Hz), 130.3, 128.0, 127.8, 125.2 (q, $J^3_{C–F}$ = 3.9 Hz), 123.3 (q, $J^1_{C–F}$ = 273.1 Hz), 58.6, 58.2, 39.5, 36.6, 29.7, 22.1, 19.2, 18.5, 18.4, 16.8, 16.3, 16.0;

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.8;

IR (film) ν_{max}/cm^{-1} 2970, 1677, 1328, 1306, 1175, 1146, 1102, 1073, 771, 755;

HRMS (ESI$^+$) $[C_{26}H_{32}F_3O_3S]^+$ ($[M+H]^+$) requires 481.2019; found 481.2014, Δ 0.90 ppm.

Minor (1*SR*, 2*RS*) diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.17 (m, 1H), 8.14 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.93 (ddt, *J* = 7.8, 1.8, 0.9 Hz, 1H), 7.75 (tt, *J* = 7.9, 0.7 Hz, 1H), 3.63 – 3.41 (m, 2H), 2.44 – 2.33 (m, 1H), 2.21 (s, 3H), 2.20 – 2.15 (m, 4H), 2.14 (s, 3H), 2.13 – 2.05 (m, 1H), 2.05 – 1.97 (m, 4H), 1.95 (s, 3H), 1.76 (m, 2H), 1.56 (dt, *J* = 13.2, 8.1 Hz, 1H), 1.15 (s, 3H);

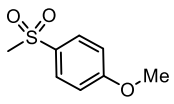
^{13}C NMR (151 MHz, $CDCl_3$) δ 217.7, 141.7, 139.2, 135.4, 133.5, 133.0, 132.2 (q, $J^2_{C–F}$ = 33.6 Hz), 131.4, 130.5 (q, $J^3_{C–F}$ = 3.5 Hz), 130.3, 127.9, 127.7, 125.3 (q, $J^3_{C–F}$ = 3.9 Hz), 123.3 (q, $J^1_{C–F}$ = 272.8 Hz), 60.2, 58.6, 44.8, 39.0, 31.1, 24.3, 22.0, 18.6, 18.4, 16.8, 16.3, 16.0;

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.8;

IR (film) ν_{max}/cm^{-1} 2934, 1680, 1461, 1384, 1329, 1306, 1218, 1175, 1148, 1102, 1073, 762;

HRMS (ESI$^+$) $[C_{26}H_{32}F_3O_3S]^+$ ($[M+H]^+$) requires 481.2019; found 481.2015, Δ 0.72 ppm.

S6 1-Methoxy-4-(methylsulfonyl)benzene



Mg turnings (304 mg, 12.5 mmol) were heated with stirring under vacuum in a two-necked flask for 10 min and allowed to cool to RT. THF (5 mL) and a single iodine crystal were added and 4-bromoanisole (0.63 mL, 5.00 mmol) was added slowly. The mixture was refluxed for a further 5 min, cooled to RT and diluted with THF (5 mL). The cooled Grignard reagent was added slowly to a suspension of

(1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide) adduct, 1.20 g, 5.00 mmol) in THF (10 mL) at –40 °C. The reaction mixture was stirred at –40 °C for 1 h, allowed to warm to RT and the THF was removed under a stream of N_2. The residue was dissolved in *N*,*N*-dimethylformamide (DMF, 40 mL) and MeI (0.93 mL, 15.0 mmol) was added. The resulting suspension was heated to 75 °C overnight, cooled to RT, filtered under reduced pressure and the filtrate concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 70:5:25) gave the *title compound* as a white solid (538 mg, 58%).

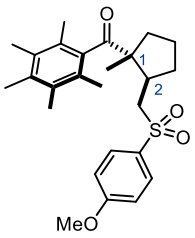
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.74 (m, 2H), 7.10 – 6.90 (m, 2H), 3.89 (s, 3H), 3.03 (s, 3H);

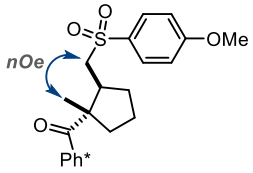
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 132.5, 129.7, 114.6, 55.8, 45.0;

HRMS (ESI$^+$) $C_8H_{11}O_3S^+$ ([M+H]$^+$) requires 187.0423; found 187.0423, Δ 0.51 ppm.

The spectroscopic data were consistent with that present in the literature. [9]

3e (2-(((4-Methoxyphenyl)sulfonyl)methyl)-1-methylcyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone





major trans diastereomer nOe correlation

Hydroxy-ketone **1a** (83 mg, 0.30 mmol), sulfone **S6** (112 mg, 0.600 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* sequential reverse phase flash column chromatography (eluent H_2O/MeCN 80:20 ⟶ 5:95) and normal phase flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 80:5:15) gave the *title compound* as a white solid (97 mg, 73%, [95:5] d.r.)*

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The spectroscopic data were collected on the diastereomeric mixture. The relative stereochemistry was assigned by nOe analysis.

m.p. = 143 – 145 °C;

Major (1*RS*, 2*RS*) diastereomer (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 – 7.77 (m, 2H), 7.05 – 6.99 (m, 2H), 3.89 (s, 3H), 3.53 (dd, *J* = 13.8, 2.1 Hz, 1H), 2.96 (dd, *J* = 13.8, 11.9 Hz, 1H), 2.56 (dddd, *J* = 12.0, 10.2, 8.3, 2.1 Hz, 1H), 2.33 – 2.24 (m, 1H), 2.22 (s, 3H), 2.18 – 2.12 (m, 6H), 2.01 (s, 3H), 1.94 (s, 3H), 1.87 – 1.77 (m, 1H), 1.73 – 1.52 (m, 4H), 1.11 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.4, 163.8, 138.8, 135.3, 133.5, 133.1, 132.0, 130.2, 128.1, 128.0, 114.6, 58.7, 58.4, 55.8, 39.7, 36.8, 29.7, 22.1, 19.2, 18.4, 18.4, 16.8, 16.3, 16.0;

Selected characteristic peaks for the minor (1*SR*, 2*RS*) diastereomer (from the mixture):

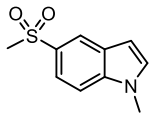
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 – 7.83 (m, 2H), 3.48 (m, 1H), 3.44 (dd, *J* = 14.4, 2.4 Hz, 1H), 2.21 (s, 3H), 1.96 (s, 3H), 1.13 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.4, 163.6, 139.3, 135.1, 132.8, 131.9, 130.1, 127.7, 60.1, 58.6, 45.1, 38.9, 30.8, 24.1, 21.9, 18.6, 16.1, 15.9;

IR (film) ν_{max}/cm^{-1} 3018, 1720, 1676, 1579, 1317, 1297, 1262, 1144, 1091, 1027, 838, 808;

HRMS (ESI$^+$) $C_{26}H_{35}O_4S^+$ ([M+H]$^+$) requires 443.2251; found 443.2246, Δ 1.09 ppm.

S7 1-Methyl-5-(methylsulfonyl)-1*H*-indole



5-Bromo-1-methyl-1*H*-indole (1.99 g, 9.50 mmol) was dissolved in THF (20 mL) and cooled to –78 °C. *n*-BuLi (4.0 mL, 2.5 M in hexanes, 10 mL) was added dropwise and the resulting mixture allowed to stir at –78 °C for 1 h. The mixture was transferred *via* syringe to a suspension of DABSO ((1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide) adduct), 2.40 g, 10.0 mmol) in THF (20 mL) at –40 °C. The reaction mixture was stirred at –40 °C for 2 h, allowed to warm to RT and the THF was removed under a stream of N_2. The residue was dissolved in *N*,*N*-dimethylformamide (DMF, 40 mL) and MeI (1.8 mL, 29 mmol) was added. The resulting suspension was heated to 75 °C overnight, cooled to RT, and Et_2O (50 mL) was added. The resulting suspension was filtered through a Celite® pad and the filtrate concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 80:10:10 → 40:10:50) gave the *title compound* as a yellow solid (751 mg, 38%.)

m.p. = 112 – 114 °C;

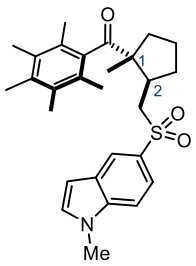
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.76 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.45 (dt, *J* = 8.7, 0.8 Hz, 1H), 7.21 (d, *J* = 3.2 Hz, 1H), 6.64 (dd, *J* = 3.2, 0.9 Hz, 1H), 3.86 (s, 3H), 3.07 (s, 3H;

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 131.6, 131.5, 128.2, 121.9, 120.1, 110.0, 103.0, 45.4, 33.3;

IR (film) ν_{max}/cm^{-1} 2927, 1697, 1601, 1574, 1513, 1484, 1449, 1345, 1305, 1209, 1140, 1063, 960;

HRMS (ESI$^+$) $[C_{10}H_{11}NNaO_2S]^+$ ([M+Na]$^+$) requires 232.0403; found 232.0402, Δ 0.30 ppm.

3f (1-Methyl-2-(((1-methyl-1*H*-indol-5-yl)sulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **1a** (83 mg, 0.30 mmol), sulfone **S7** (126 mg, 0.600 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/EtOAc, 85:5:10 → 83:5:12) gave inseparable diastereomers of the *title compound* as a tan solid (97 mg, 69%, [94:6] d.r.)

The spectroscopic data were collected on the diastereomeric mixture. The relative stereochemistry was assigned by analogy with other products.

m.p. = 158 – 160 ° C;

Major (1*RS*, 2*RS*) diastereomer (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (d, *J* = 1.7 Hz, 1H), 7.69 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.21 (d, *J* = 3.1 Hz, 1H), 6.64 (d, *J* = 3.1 Hz, 1H), 3.87 (s, 3H), 3.56 (dd, *J* = 13.9, 2.1 Hz, 1H), 3.01 (dd, *J* = 13.8, 11.9 Hz, 1H), 2.60 (dddd, *J* = 12.0, 10.1, 8.2, 2.1 Hz, 1H), 2.37 – 2.26 (m, 1H), 2.21 (s, 3H), 2.13 (s, 3H), 2.11 (s, 3H), 2.00 (s, 3H), 1.87 (s, 3H), 1.85 – 1.77 (m, 1H), 1.74 – 1.58 (m, 4H), 1.10 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.4, 139.0, 138.8, 135.2, 133.4, 133.0, 131.4, 130.9, 128.2, 128.1, 128.1, 122.5, 120.7, 109.9, 103.1, 58.8, 58.7, 39.9, 36.9, 33.3, 29.8, 22.2, 19.2, 18.35, 18.38, 16.8, 16.3, 16.0;

Selected characteristic peaks for the minor (1*SR*, 2*RS*) diastereomer (from the mixture):

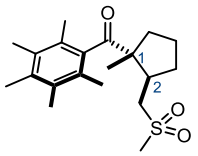
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (d, *J* = 1.8 Hz, 1H), 7.74 (dd, *J* = 8.7, 1.8 Hz, 1H), 3.53 – 3.47 (m, 2H), 2.15 (s, 3H), 2.01 (s, 3H), 1.94 (s, 3H), 1.11 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.5, 139.5, 135.1, 132.9, 130.9, 128.0, 127.9, 122.6, 120.8, 103.1, 60.2, 59.1, 45.4, 39.0, 31.0, 29.8, 24.2, 22.1, 18.7, 16.2, 16.0;

IR (film) ν_{max}/cm^{-1} 2979, 1679, 1608, 1514, 1345, 1328, 1303, 1282, 1138, 1063, 919;

HRMS (ESI$^+$) $[C_{28}H_{36}NO_3S]^+$ ([M+H]$^+$) requires 466.2410; found 466.2409, Δ 0.24 ppm.

3g (1-Methyl-2-((methylsulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **1a** (83 mg, 0.30 mmol), dimethyl sulfone (141 mg, 1.50 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 65:10:25 → 60:10:30) gave separable diastereomers of the *title compound* as a white solid (93 mg, 88%, >[95:5] d.r.)*

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The relative stereochemistry was assigned by X-Ray crystallography analysis.

Major (1*RS*, 2*RS*) diastereomer

m.p. = 164 – 166 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.51 (dd, *J* = 13.7, 2.1 Hz, 1H), 2.94 – 2.83 (m, 4H), 2.69 (tdd, *J* = 12.2, 9.3, 2.1 Hz, 1H), 2.40 – 2.29 (m, 1H), 2.23 (s, 3H), 2.18 (s, 3H), 2.17 (s, 3H), 2.12 (s, 3H), 2.07 (s, 3H), 1.93 – 1.88 (m, 1H), 1.79 – 1.62 (m, 3H), 1.62 – 1.53 (m, 1H), 1.16 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.6, 138.7, 135.5, 133.7, 133.1, 128.1, 128.0, 58.8, 56.5, 42.0, 39.4, 36.8, 29.8, 22.1, 19.3, 18.8, 18.5, 16.8, 16.4, 16.1;

IR (film) ν_{max}/cm^{-1} 2960, 1678, 1588, 1470, 1416, 1385, 1302, 1260, 1227, 1137, 1098;

HRMS (ESI$^+$) $C_{20}H_{31}O_3S^+$ ([M+H]$^+$) requires 351.1988; found 351.1979, Δ 2.68 ppm.

Minor (1*SR*, 2*RS*) diastereomer:

m.p. = 127 – 129 °C;

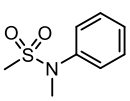
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.48 (dd, *J* = 14.0, 11.2 Hz, 1H), 3.39 (dd, *J* = 14.1, 2.1 Hz, 1H), 2.97 (s, 3H), 2.42 (dtd, *J* = 10.6, 7.9, 2.1 Hz, 1H), 2.29 – 2.25 (m, 1H), 2.25 – 2.20 (m, 4H), 2.18 (s, 3H), 2.17 (s, 3H), 2.15 – 2.07 (m, 1H), 2.06 (s, 3H), 2.05 (s, 3H), 1.85 – 1.75 (m, 2H), 1.63 – 1.57 (m, 1H), 1.21 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.7, 139.2, 135.4, 133.5, 133.1, 128.0, 127.9, 60.3, 56.7, 44.5, 42.4, 38.9, 31.2, 24.3, 22.1, 18.9, 18.5, 16.8, 16.3, 16.0;

IR (film) ν_{max}/cm^{-1} 2933, 1679, 1461, 1414, 1385, 1303, 1265, 1141, 1097, 965, 916, 842, 760, 735;

HRMS (ESI$^+$) $[C_{20}H_{31}O_3S]^+$ ([M+H]$^+$) requires 351.1988; found 351.1986, Δ 0.68 ppm.

S8 *N*-Methyl-*N*-phenylmethanesulfonamide



A solution of *N*-methylaniline (1.0 mL, 9.2 mmol) and NEt_3 (1.3 mL, 9.2 mmol) in CH_2Cl_2 (20 mL) was cooled to –20 °C. Methanesulfonyl chloride (1.1 mL, 14 mmol) was added dropwise and the reaction was allowed to warm to RT for 6 h. The reaction was quenched with the addition of 3 mL sat. aq. NH_4Cl and diluted

further with CH_2Cl_2 (50 mL) and water (50 mL). The layers were separated and the aqueous layer extracted with CH_2Cl_2 (2 × 60 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/EtOAc, 85:15 → 80:20) gave the title compound as a white solid (1.56 g, 92%).

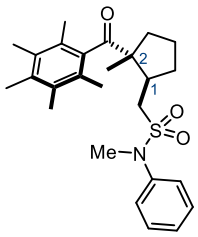
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.35 (m, 4H), 7.33 – 7.27 (m, 1H), 3.33 (s, 3H), 2.84 (s, 3H);

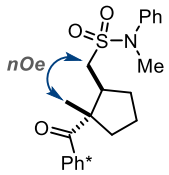
^{13}C NMR (101 MHz, $CDCl_3$) δ 141.6, 129.5, 127.6, 126.3, 38.2, 35.3;

m/z (ESI^+) Found ($[M+H]^+$) = 186, $C_8H_{12}NO_2S$ requires 186.

The spectroscopic data were consistent with that present in the literature. [10]

3h *N*-Methyl-1-(2-methyl-2-(2,3,4,5,6-pentamethylbenzoyl)cyclopentyl)-*N*-phenylmethanesulfonamide





major trans diastereomer nOe correlation

Hydroxy-ketone **1a** (83 mg, 0.30 mmol), sulfonamide **S8** (111 mg, 0.600 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 90:5:5) gave separable diastereomers of the *title compound* as a white solid (102 mg, 77%, [93:7] d.r.)*

*d.r. calculated post-purification due to overlapping peaks in the crude NMR

The relative stereochemistry was assigned by nOe and X-ray crystallography analysis.

Major (1*RS*, 2*RS*) diastereomer:

m.p. = 118 – 120 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.37 (m, 4H), 7.30 – 7.26 (m, 1H), 3.49 (dd, *J* = 13.3, 2.3 Hz, 1H), 3.33 (s, 3H), 2.80 (dd, *J* = 13.4, 11.9 Hz, 1H), 2.65 (dddd, *J* = 12.2, 10.4, 8.2, 2.3 Hz, 1H), 2.30 – 2.23 (m, 1H), 2.22 (s, 3H), 2.16 (s, 3H), 2.15 (s, 3H) ,2.00 (s, 6H), 1.93 – 1.81 (m, 1H), 1.73 – 1.59 (m, 3H), 1.59 – 1.52 (m, 1H), 1.10 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.6, 141.6, 138.6, 135.3, 133.6, 133.0, 129.4, 128.2, 128.1, 127.3, 126.5, 58.8, 50.3, 40.1, 38.3, 37.1, 29.6, 21.9, 19.2, 18.5, 18.0, 16.8, 16.3, 16.0;

IR (film) ν_{max}/cm^{-1} 3020, 1676, 1597, 1494, 1360, 1146, 1028, 926, 873, 698;

HRMS (ESI^+) $C_{26}H_{39}NO_3S^+$ ($[M+H]^+$) requires 442.2410; found 442.2402, Δ 1.97 ppm

Minor (1*SR*, 2*RS*) diastereomer:

m.p. = 118 – 120 °C;

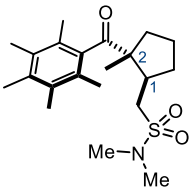
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 – 7.35 (m, 4H), 7.30 – 7.24 (m, 1H), 3.39 – 3.32 (m, 4H), 3.26 (dd, *J* = 13.9, 11.3 Hz, 1H), 2.46 – 2.34 (m, 1H), 2.24 – 2.17 (m, 5H), 2.16 (s, 3H), 2.14 – 2.09 (m, 4H), 2.02 (s, 3H), 1.86 (s, 3H), 1.83 – 1.66 (m, 2H), 1.60 (ddd, *J* = 13.1, 8.6, 6.4 Hz, 1H), 1.10 (s, 3H);

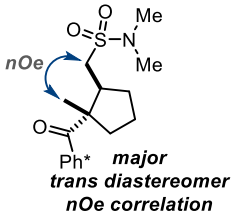
^{13}C NMR (151 MHz, $CDCl_3$) δ 218.4, 141.7, 139.7, 135.3, 133.4, 133.0, 129.4, 127.8, 127.5, 127.3, 126.4, 59.8, 50.6, 45.4, 39.4, 38.3, 30.9, 24.5, 22.0, 18.2, 18.1, 16.8, 16.3, 16.0;

IR (film) ν_{max}/cm^{-1} 3026, 2944, 1678, 1493, 1457, 1344, 1268, 1218, 1174, 1077, 920, 898, 869;

HRMS (ESI$^+$) $C_{26}H_{39}NO_3S^+$ ([M+H]$^+$) requires 442.2410; found 442.2401, Δ 2.04 ppm**.**

3i *N*,*N*-Dimethyl-1-(2-methyl-2-(2,3,4,5,6-pentamethylbenzoyl)cyclopentyl)methanesulfonamide





Hydroxy-ketone **1a** (83 mg, 0.30 mmol), *N*,*N*-dimethylmethanesulfonamide (74 mg, 0.60 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 80:20 → 72:28) gave separable diastereomers of the *title compound* as a white solid (93 mg, 82%, [91:9] d.r.)

The relative stereochemistry was assigned by nOe and X-ray crystallography analysis.

Major (1*RS*, 2*RS*) diastereomer:

m.p. = 138 – 140 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.33 (dd, *J* = 13.3, 2.2 Hz, 1H), 2.85 (s, 6H), 2.72 (dd, *J* = 13.3, 11.9 Hz, 1H), 2.61 (dddd, *J* = 12.1, 10.2, 8.2, 2.2 Hz, 1H), 2.30 (dtd, *J* = 12.8, 8.4, 3.8 Hz, 1H), 2.22 (s, 3H), 2.18 (s, 3H), 2.12 (s, 3H), 2.06 (s, 3H), 1.93 – 1.82 (m, 1H), 1.75 – 1.51 (m, 4H), 1.16 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.6, 138.7, 135.4, 133.6, 133.1, 128.2, 128.1, 58.8, 48.7, 39.9, 37.5, 36.9, 29.7, 21.9, 19.3, 18.6, 18.2, 16.8, 16.4, 16.0;

IR (film) ν_{max}/cm^{-1} 2967, 1679, 1461, 1357, 1333, 1260, 1218, 1150, 1094, 960, 926;

HRMS (ESI$^+$) $C_{21}H_{33}NaNO_3S^+$ ([M+Na]$^+$) requires 402.2073; found 402.2061, Δ 2.97 ppm**.**

Minor (1*SR*, 2*RS*) diastereomer:

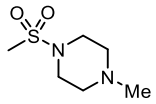
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.26 (dd, *J* = 14.0, 2.1 Hz, 1H), 3.17 (dd, *J* = 13.9, 11.2 Hz, 1H), 2.88 (s, 6H), 2.47 – 2.34 (m, 1H), 2.27 – 2.19 (m, 5H), 2.18 (s, 3H), 2.17 (s, 3H), 2.13 (ddt, *J* = 13.6, 9.4, 5.9 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.88 – 1.71 (m, 2H), 1.62 (ddd, *J* = 13.2, 8.6, 6.7 Hz, 1H), 1.18 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 218.4, 139.7, 135.3, 133.5, 133.0, 127.9, 127.6, 59.9, 49.3, 45.4, 39.2, 37.6, 31.0, 24.6, 21.9, 18.5, 18.3, 16.8, 16.3, 16.0;

IR (film) ν_{max}/cm^{-1} 2959, 1679, 1650, 1461, 1333, 1266, 1219, 1151, 1097, 960, 923, 898;

HRMS (ESI$^+$) $C_{21}H_{34}NO_3S^+$ ([M+H]$^+$) requires 380.2254; found 380.2244, Δ 2.71 ppm**.**

S9 1-Methyl-4-(methylsulfonyl)piperazine



1-Methylpiperazine (1.11 mL, 10.0 mmol) and NEt_3 (2.1 mL, 15 mmol) were dissolved in CH_2Cl_2 (70 mL) and the mixture was cooled to 0 °C. Methanesulfonyl chloride (0.81 mL, 10.5 mmol) was added slowly, the mixture allowed to warm to RT and stirred for 1 h. The reaction mixture was diluted with 1 M NaOH (100 mL), the layers separated and the aqueous layer extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with NH_4Cl (2 × 100 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give the *title compound* as an off-white solid, which required no further purification (477 mg, 27%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.27 (t, *J* = 5.0 Hz, 4H), 2.78 (s, 2H), 2.54 (t, *J* = 5.0 Hz, 4H), 2.35 (s, 3H);

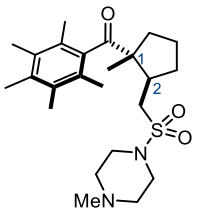
^{13}C NMR (101 MHz, $CDCl_3$) δ 54.4, 45.9, 45.8, 34.4;

m/z (ESI^+) Found ($[M+H]^+$) =179, [$C_6H_{15}N_2O_2S$] requires 179.

The spectroscopic data matched that previously reported in the literature. [11]

3j

(1-Methyl-2-(((4-methylpiperazin-1-yl)sulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **1a** (83 mg, 0.30 mmol), sulfonamide **S9** (107 mg, 0.600 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent CH_2Cl_2/7 N NH_3 in MeOH, 99.2:0.8 → 99:1) gave inseparable diastereomers of the *title compound* as a white solid (103 mg, 79%, [93:7] d.r.*)

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The spectroscopic data were collected on the diastereomeric mixture. The relative stereochemistry was assigned by analogy with other products.

m.p. = 153 – 155 °C;

Major (1*RS*, 2*RS*) diastereomer (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.30 (dd, *J* = 13.0, 2.0 Hz, 1H), 3.25 (t, *J* = 5.0 Hz, 4H), 2.69 (dd, *J* = 13.0, 11.8 Hz, 1H), 2.62 (dddd, *J* = 11.9, 10.0, 8.0, 1.9 Hz, 1H), 2.48 (t, *J* = 4.9 Hz, 4H), 2.33 (s, 3H), 2.31 – 2.25 (m, 1H), 2.22 (s, 3H,), 2.17 (s, 3H), 2.16 (s, 3H), 2.11 (s, 3H), 2.06 (s, 3H), 1.95 – 1.86 (m, 1H), 1.75 – 1.62 (m, 3H), 1.62 – 1.53 (m, 1H,), 1.14 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.5, 138.8, 135.3, 133.6, 133.1, 128.2, 128.0, 58.8, 54.7, 49.7, 46.1, 45.7, 39.8, 37.0, 29.8, 21.9, 19.3, 18.7, 18.4, 16.8, 16.4, 16.1;

Selected characteristic peaks for the minor (1*SR*, 2*RS*) diastereomer (from the mixture):

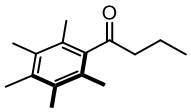
^{1}H NMR (600 MHz, $CDCl_3$) δ 2.05 (s, 3H), 1.18 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.9, 139.6, 135.3, 133.5, 133.0, 127.9, 127.6, 60.0, 50.5, 45.7, 45.4, 39.2, 31.1, 24.5, 22.0, 18.6, 18.4, 16.8, 16.3, 16.0;

IR (film) ν_{max}/cm^{-1} 2943, 2799, 1677, 1456, 1341, 1327, 1289, 1164, 1146, 951, 916;

HRMS (ESI$^+$) $[C_{24}H_{39}N_2O_3S]^+$ ([M+H]$^+$) requires 435.2676; found 435.2676, Δ 1.44 ppm.

S10 1-(2,3,4,5,6-Pentamethylphenyl)butan-1-one



$AlCl_3$ (5.43 g, 40.8 mmol) was added portionwise (over 5 min) to a stirred solution of butyryl chloride (3.94 g, 38.0 mmol) and pentamethylbenzene (5.00 g, 33.8 mmol) in CH_2Cl_2 (160 mL) at 0 °C. The reaction was allowed to warm to RT, stirred for 2 h and was then poured onto ice (approx. 200 g) and diluted with $NaHCO_3$ (100 mL). The layers were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 200 mL). The combined organic layers were washed with $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated *in vacuo.* Purification *via* flash column chromatography (eluent Pentane → Pentane/Et_2O 96:4) gave the *title compound* as a white solid (5.95 g, 80%);

m.p. = 76 – 78 °C;

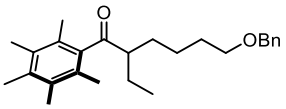
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (t, *J* = 7.3 Hz, 2H), 2.23 (s, 3H), 2.18 (s, 6H), 2.10 (s, 6H), 1.75 (h, *J* = 7.4 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 212.2, 140.9, 135.4, 133.2, 127.5, 47.7, 17.3, 16.8, 16.1, 13.9;

IR (film) ν_{max}/cm^{-1} 2934, 1700, 1456, 1133, 913, 742;

HRMS (ESI$^+$) $C_{15}H_{23}O^+$ ([M+H]$^+$) requires 219.1743; found 219.1744, Δ 0.09 ppm.

S11 6-(Benzyloxy)-2-ethyl-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



Ketone **S10** (1.65 g, 7.50 mmol), $[Ir(cod)Cl]_2$ (50 mg, 1.0 mol%), dppBz (67 mg, 2.0 mol%) and KOH (1.68 g, 30.0 mmol) were added to a 10 – 20 mL microwave vial. The vial was sealed and purged with Ar (balloon) for 5 min. PhMe (1.9 mL) and 4-benzyloxy-1-butanol (2.91 g, 15.0 mmol) were added. The reaction was heated at 110 °C for 18 h, cooled to room temperature, filtered through a silica plug (elution with Et_2O) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 96:4) gave the *title compound* as a colourless oil (2.22 g, 78%).

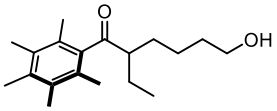
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.26 (m, 5H), 4.48 (s, 2H), 3.45 (t, *J* = 6.6 Hz, 2H), 2.68 (p, *J* = 6.2 Hz, 1H), 2.23 (s, 3H), 2.17 (s, 6H), 2.09 (s, 6H), 1.83 – 1.66 (m, 2H), 1.66 – 1.57 (m, 2H), 1.54 – 1.40 (m, 4H), 0.94 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 214.0, 140.1, 138.8, 135.5, 133.2, 128.6, 128.5, 127.8, 127.6, 73.1, 70.3, 54.9, 30.2, 28.6, 24.0, 22.2, 18.0, 16.9, 16.2, 11.9;

IR (film) ν_{max}/cm^{-1} 2937, 2862, 1691, 1454, 1100, 1028, 996, 910;

HRMS (ESI$^+$) $C_{26}H_{37}O_2^+$ ([M+H]$^+$) requires 381.2788; found 318.2786, Δ 0.64 ppm.

1k 2-Ethyl-6-hydroxy-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



Benzyl ether **S11** (1.94 g, 5.11 mmol) was subjected to **General Procedure B** in MeOH (55 mL) with Pd (10% on carbon) (194 mg, 10 wt%) for 1 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 60:40 → 50:50) gave the *title compound* as a white solid (1.36 g, 92%).

m.p. = 55 – 57 °C

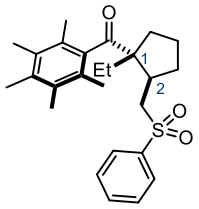
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (t, *J* = 6.5 Hz, 2H), 2.73 – 2.56 (m, 1H), 2.23 (s, 3H), 2.18 (s, 6H), 2.09 (s, 6H), 1.82 – 1.66 (m, 2H), 1.63 – 1.37 (m, 6H), 0.95 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 214.1, 140.0, 135.6, 133.2, 128.6, 62.8, 54.9, 33.1, 28.3, 23.5, 22.3, 18.0, 16.9, 16.2, 12.0;

IR (film) ν_{max}/cm^{-1} 3400, 2936, 2873, 1693, 1458, 1383, 1300, 1263, 1071, 997;

HRMS (ESI$^+$) $C_{19}H_{30}O^+$ ([M+H]$^+$) requires 291.2319; found 291.2318, Δ 0.26 ppm.

3k (1-Ethyl-2-((phenylsulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **1k** (87 mg, 0.30 mmol), phenyl methyl sulfone (94 mg, 0.60 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 88:5:7 → 87:5:8) gave the *title compound* as a white solid (72 mg, 56%, [87:13] d.r.)

The spectroscopic data were collected on the diastereomeric mixture. The relative stereochemistry was assigned by analogy with the other products.

m.p. = 143 – 145 °C;

Major (1*RS*, 2*RS*) diastereomer (from the mixture)**:**

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 – 7.77 (m, 2H), 7.67 – 7.62 (m, 1H), 7.57 – 7.52 (m, 2H), 3.19 (dd, *J* = 13.6, 2.3 Hz, 1H), 2.97 (dd, *J* = 13.6, 12.2 Hz, 1H), 2.71 – 2.62 (m, 1H), 2.31 – 2.22 (m, 4H), 2.17 (s, 3H), 2.16 (s,

3H), 2.09 – 2.03 (m, 7H), 1.93 – 1.84 (m, 1H), 1.77 (m, 1H), 1.69 – 1.58 (m, 3H), 1.25 – 1.17 (m, 1H), 0.94 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 215.3, 140.8, 137.4, 135.4, 133.7, 133.6, 133.0, 129.4, 129.3, 129.0, 127.8, 63.5, 57.8, 39.6, 31.3, 29.6, 22.4, 21.9, 19.0, 18.3, 16.8, 16.4, 16.0, 9.3;

Selected characteristic peaks for the minor (1*SR*, 2*RS*) diastereomer (from the mixture):

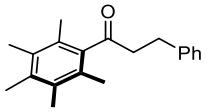
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 – 7.90 (m, 2H), 7.62 – 7.60 (m, 2H), 3.58 – 3.45 (m, 2H), 2.49 – 2.41 (m, 1H), 2.23 (s, 3H), 2.17 (s, 3H), 2.16 (s, 3H), 2.00 (s, 3H), 0.68 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.4, 140.2, 139.4, 135.3, 133.4, 133.1, 128.2, 128.1, 63.6, 58.6, 40.5, 33.6, 26.8, 22.6, 19.1, 18.9, 16.8, 16.3, 16.1, 8.2;

IR (film) ν_{max}/cm^{-1} 2965, 2880, 1673, 1448, 1307, 1148, 914, 736;

HRMS (ESI$^+$) $C_{26}H_{35}O_3S^+$ ([M+H]$^+$) requires 427.2301; found 427.2295, Δ 1.46 ppm.

S12 1-(2,3,4,5,6-Pentamethylphenyl)-3-phenylpropan-1-one



3-Phenylpropanoic acid (4.50 g, 30.0 mmol) was dissolved in thionyl chloride (5.3 mL, 73 mmol) and the mixture was refluxed for 16 h. Once cooled to RT, the reaction mixture was concentrated *in vacuo*. The crude acyl chloride was dissolved in CH_2Cl_2 (10 mL) and added to a solution of pentamethylbenzene (4.40 g, 30.0 mmol) in CH_2Cl_2 (90 mL) at 0 °C. $AlCl_3$ (5.00 g, 37.5 mmol) was added portion-wise and the mixture was stirred at RT for 1 h. The crude reaction mixture was poured onto ice (approx. 150 g) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL) and the combined organic layers were washed sequentially with satd. aq. $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane: Et_2O, 98:2) gave the title compound as a pale yellow solid (3.88 g, 46%).

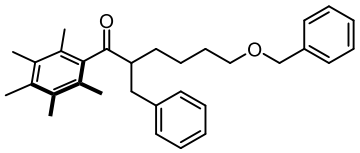
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.12 (m, 5H), 3.11 – 3.04 (m, 2H), 3.04 – 2.95 (m, 2H), 2.24 (s, 3H), 2.18 (s, 6H), 2.06 (s, 6H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 210.9, 141.0, 140.5, 135.5, 133.1, 128.5, 128.5, 127.4, 126.1, 47.1, 29.4, 17.1, 16.7, 15.9;

m/z (ESI$^+$) Found ([M+H$^+$) = 281, $C_{20}H_{25}O$ requires 281.

The spectroscopic data matched that previously reported in the literature. [12]

S13 2-Benzyl-6-(benzyloxy)-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



Ketone **S12** (840 mg, 3.0 mmol), $[Ir(cod)Cl]_2$ (20 mg, 1.0 mol%), dppBz (27 mg, 2.0 mol%) and KOH (673 mg, 12.0 mmol) were added to a 5 – 10 mL microwave vial. The vial was sealed and purged with Ar (balloon) for 5 min. PhMe (0.75 mL) and 4-benzyloxy-butanol (1.62 g, 9.00 mmol) were added. The reaction was heated at 110 °C for 28 h, cooled to room temperature, filtered through a silica plug (Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5) gave the *title compound* as a colourless oil (1.33 g, 95%).

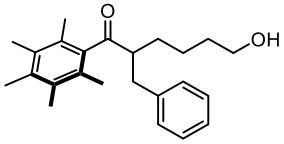
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 6.83 (m, 10H), 4.44 (s, 2H), 3.37 (t, *J* = 6.4 Hz, 2H), 3.17 (dd, *J* = 13.5, 6.2 Hz, 1H), 3.06 (ddd, *J* = 11.5, 7.4, 5.7 Hz, 1H), 2.67 (dd, *J* = 13.5, 7.5 Hz, 1H), 2.22 (s, 3H), 2.15 (s, 6H), 2.02 (br s, 6H), 1.78 – 1.67 (m, 1H), 1.57 – 1.48 (m, 2H), 1.48 – 1.31 (m, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 212.9, 140.4, 139.6, 138.7, 135.7, 133.2, 129.5, 128.7, 128.5, 128.4, 127.7, 127.6, 126.2, 73.0, 70.2, 56.0, 35.6, 30.0, 29.5, 24.0, 17.8, 16.9, 16.1;

IR (film) ν_{max}/cm^{-1} 2937, 2858, 1691, 1495, 1454, 1362, 1303, 1260, 1204, 1099, 1028, 913, 735, 699;

HRMS (ESI$^+$) $C_{31}H_{39}O_2^+$ ([M+H]$^+$) requires 443.2945; found 443.2945, Δ 0.15 ppm.

1l 2-Benzyl-6-hydroxy-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



Benzyl ether **S13** (1.24 g, 2.80 mmol) was subjected to **General Procedure B** in MeOH (25 mL) with Pd (10% on carbon) (124 mg, 10 wt%) for 2 h. The *title compound* was obtained as a white solid which was used without further purification (980 mg, 99%);

m.p. = 86 – 88 °C;

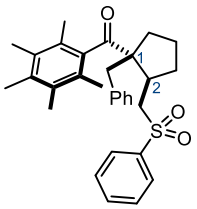
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.22 (m, 2H), 7.21 – 7.14 (m, 3H), 3.63 – 3.49 (m, 2H), 3.16 (dd, *J* = 13.5, 5.9 Hz, 1H), 3.11 – 2.99 (m, 1H), 2.65 (dd, *J* = 13.5, 8.0 Hz, 1H), 2.23 (s, 3H), 2.16 (s, 6H), 2.00 (br s, 6H), 1.72 (m, 1H), 1.54 – 1.30 (m, 5H), 1.24 (t, *J* = 5.5 Hz, 1H);

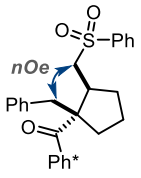
^{13}C NMR (101 MHz, $CDCl_3$) δ 213.0, 140.3, 139.6, 135.8, 133.3, 129.4, 128.7, 128.4, 126.3, 62.7, 56.0, 35.8, 32.9, 29.2, 23.5, 17.9, 16.9, 16.2;

IR (film) ν_{max}/cm^{-1} 3392, 2937, 1689, 1454, 1383, 1302, 1260, 1126, 1070, 1030, 913;

HRMS (ESI$^+$) $C_{24}H_{33}O_2^+$ ([M+H]$^+$) requires 353.2475; found 353.2476, Δ 0.28 ppm.

3l ((1*S*,2*R*))-1-Benzyl-2-((phenylsulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone





nOe correlation

Hydroxy-ketone **1l** (106 mg, 0.300 mmol), phenyl methyl sulfone (94 mg, 0.60 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 89:5:6) gave a single diastereomer of the *title compound* as an off-white solid (45 mg, 31%, >[95:5] d.r.)

The relative stereochemistry was assigned by nOe and X-ray crystallography analysis.

m.p. = 174 – 176 °C;

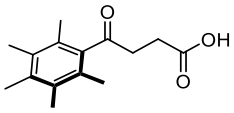
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 – 7.89 (m, 2H), 7.72 – 7.66 (m, 1H), 7.63 – 7.57 (m, 2H), 7.25 – 7.17 (m, 5H), 3.51 (dd, *J* = 13.6, 2.3 Hz, 1H), 3.42 (dd, *J* = 12.9, 1.6 Hz, 1H), 3.18 (dd, *J* = 13.7, 12.2 Hz, 1H), 2.73 (dtd, *J* = 12.0, 9.4, 2.3 Hz, 1H), 2.42 – 2.35 (m, 1H), 2.33 (d, *J* = 12.9 Hz, 1H), 2.18 (s, 3H), 2.17 (s, 3H), 2.08 (s, 3H), 2.07 – 2.03 (m, 1H), 1.96 (s, 3H), 1.94 – 1.86 (m, 1H), 1.82 – 1.74 (m, 2H), 1.65 – 1.57 (m, 1H), 1.12 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 214.0, 141.0, 137.8, 136.1, 135.6, 133.9, 133.6, 132.7, 131.6, 130.3, 129.6, 128.2, 127.9, 126.8, 65.1, 57.6, 40.1, 33.1, 30.6, 29.1, 22.1, 18.0, 17.3, 16.8, 16.5, 15.6;

IR (film) ν_{max}/cm^{-1} 2954, 1673, 1494, 1448, 1308, 1217, 1149, 1112, 1086, 899;

HRMS (ESI$^+$) $[C_{31}H_{36}NaO_3S]^+$ ([M+Na]$^+$) requires 511.2277; found 511.2272, Δ 1.11 ppm.

S14 4-Oxo-4-(2,3,4,5,6-pentamethylphenyl)butanoic acid



$AlCl_3$ (9.00 g, 67.0 mmol) was added portion-wise (over 5 min) to a stirred solution of succinic anhydride (3.10 g, 30.7 mmol) and pentamethylbenzene (5.00 g, 33.7 mmol) in CH_2Cl_2 (100 mL) at RT. The reaction was stirred for 5 min at RT and was then poured into cold 1 M HCl (100 mL). The layers were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with 1 M HCl (2 × 100 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent CH_2Cl_2/MeOH, 97:3 → 95:5) gave the *title compound* as a white solid (5.25 g, 68%).

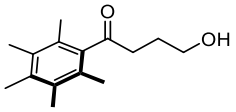
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.02 (t, *J* = 6.4 Hz, 2H), 2.78 (t, *J* = 6.4 Hz, 2H), 2.24 (s, 3H), 2.19 (s, 6H), 2.12 (s, 6H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.6, 178.4 , 139.8, 135.8, 133.3, 127.7, 40.1, 27.6, 17.2, 16.8, 16.1;

m/z (ESI$^+$) Found ([M+Na]$^+$) = 271, $C_{15}H_{20}NaO_3$ requires 271.

The spectroscopic data matched that previously reported in the literature. [12]

S15 4-Hydroxy-1-(2,3,4,5,6-Pentamethylphenyl)butan-1-one



$BH_3{\cdot}SMe_2$ (3.1 mL, 33 mmol) was added dropwise (over 5 min) to a solution of acid **S14** (5.38 g, 21.7 mmol) in THF (100 mL) at 0 °C. The resulting solution was allowed to warm slowly to RT overnight (16 h), subsequently cooled to 0 °C and then quenched with MeOH (16 mL) and water (40 mL). The mixture was concentrated *in* vacuo, diluted further with water (100 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with satd. aq. $NaHCO_3$, dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 60:40 → 30:70) gave the *title compound* as a white solid (5.05 g, 99%).

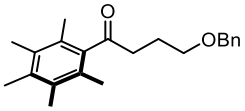
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (t, *J* = 6.1 Hz, 2H), 2.82 (t, *J* = 6.9 Hz, 2H), 2.23 (s, 3H), 2.19 (s, 6H), 2.10 (s, 6H), 2.06 – 1.94 (m, 2H), 1.78 (s, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 212.6, 140.6, 135.6, 133.2, 127.4, 62.5, 42.6, 26.3, 17.3, 16.8, 16.1;

m/z (ESI$^+$) Found ([M+Na]$^+$) = 257, $C_{15}H_{22}NaO_2$ requires 257.

The spectroscopic data matched that previously reported in the literature. [12]

S16 4-(Benzyloxy)-1-(2,3,4,5,6-pentamethylphenyl)butan-1-one



Benzyl bromide (0.54 mL, 4.5 mmol) and DIPEA (0.83 mL, 4.8 mmol) were added to alcohol **S15** (702 mg, 3.00 mmol) and KI (50 mg, 0.30 mmol) in a 10 mL round-bottomed flask. The mixture was heated to 150 °C for 3 h, cooled to RT and diluted with EtOAc (20 mL) and water (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5 → 92:8) gave the *title compound* as a white solid (901 mg, 93%).

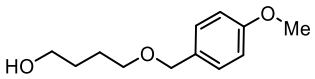
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 5H), 4.51 (s, 2H), 3.59 (t, *J* = 6.1 Hz, 2H), 2.81 (t, *J* = 7.2 Hz, 2H), 2.23 (s, 3H), 2.18 (s, 6H), 2.09 (s, 6H), 2.07 – 1.99 (m, 2H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 211.8, 140.8, 138.6, 135.5, 133.2, 128.5, 127.8, 127.7, 127.5, 73.0, 69.4, 42.2, 23.6, 17.3, 16.8, 16.1;

m/z (ESI$^+$) Found ([M+H]$^+$) =325, [$C_{22}H_{29}O_2$] requires 325.

The spectroscopic data matched that present in the literature.[13]

S17 4-((4-Methoxybenzyl)oxy)butan-1-ol



1,4-butanediol (1.46 mL, 16.5 mmol) was added to a stirred suspension of NaH (660 mg, 16.5 mmol, 60% dispersed in mineral oil) and tetrabutylammonium iodide (1.11 g, 3.00 mmol) in THF (60 mL) at 0 °C. 4-Methoxybenzyl chloride (2.03 mL, 15.0 mmol) was added and the reaction was warmed to RT, stirred for 1 h, then heated to 60 °C for 16 h. The crude reaction mixture was poured into satd. $NaHCO_3$ and vigorously stirred for 10 min. The layers were separated and the aqueous layer was extracted with EtOAc (2 × 80 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 70:30 → 50:50) gave the *title compound* as a pale yellow oil (2.79 g, 89%).

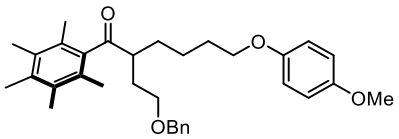
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 2H), 6.91 – 6.83 (m, 2H), 4.45 (s, 2H), 3.80 (s, 3H), 3.63 (t, *J* = 5.8 Hz, 2H), 3.49 (t, *J* = 5.7 Hz, 2H), 2.13 (s, 1H), 1.87 – 1.48 (m, 4H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 130.3, 129.5, 114.0, 72.9, 70.2, 62.9, 55.4, 30.4, 26.9;

m/z (ESI$^+$) Found ([M+Na]$^+$) = 233, $C_{12}H_{18}NaO_3$ requires 233;

The spectroscopic data matched that previously reported in the literature. [14]

S18 2-(2-(Benzyloxy)ethyl)-6-((4-methoxybenzyl)oxy)-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



Ketone **S16** (648 mg, 2.00 mmol), 4-((4-methoxybenzyl)oxy)butan-1-ol **S17** (840 mg, 4.00 mmol), $[Ir(Cp^*)Cl_2]_2$ (16 mg, 1.0 mol%), KOH (449 mg, 8.00 mmol) and PhMe (0.5 mL, 4.0 M) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 85:15 → 80:20) gave the *title compound* as a colourless oil (867 mg, 84%).

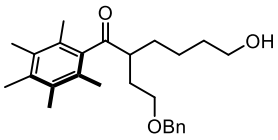
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 2H), 7.30 – 7.26 (m, 3H), 7.25 – 7.20 (m, 2H), 6.88 – 6.84 (m, 2H), 4.47 – 4.41 (m, 2H), 4.39 (s, 2H), 3.80 (s, 3H), 3.59 – 3.50 (m, 2H), 3.38 (t, *J* = 6.5 Hz, 2H), 2.96 (p, *J* = 6.1 Hz, 1H), 2.23 (s, 3H), 2.17 (s, 6H), 2.11 (dt, *J* = 13.9, 6.6 Hz, 1H), 2.07 (s, 6H), 1.79 – 1.67 (m, 2H), 1.65 – 1.50 (m, 2H), 1.50 – 1.30 (m, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 213.7, 159.3, 139.8, 138.6, 135.6, 133.2, 130.8, 129.4, 128.6, 128.5, 127.7, 127.6, 113.9, 72.9, 72.7, 70.0, 68.4, 55.4, 50.3, 30.0, 29.7, 29.2, 24.1, 17.9, 16.9, 16.2;

IR (film) ν_{max}/cm^{-1} 2942, 2862, 1689, 1614, 1512, 1455, 1363, 1301, 1247, 1099, 1036, 820;

HRMS (ESI$^+$) $[C_{34}H_{45}O_4]^+$ ([M+H]$^+$) requires 517.3312; found 517.3322, Δ 1.88 ppm.

1m 2-(2-(Benzyloxy)ethyl)-6-hydroxy-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



PMB ether **S18** (850 mg, 1.65 mmol) was dissolved in a mixture of CH_2Cl_2 (14.5 mL)/water (1.5 mL) and DDQ (561 g, 2.47 mmol) was added at RT. The mixture was stirred at RT for 3 h, quenched with sat. $NaHCO_3$ (20 mL) and diluted with water (20 mL) and CH_2Cl_2 (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/EtOAc, 80:20) gave the *title compound* as a colourless oil (544 mg, 83%).

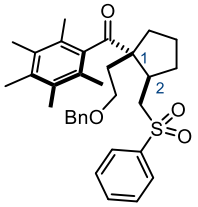
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 2H), 7.30 – 7.27 (m, 3H), 4.49 – 4.38 (m, 2H), 3.59 (t, *J* = 6.4 Hz, 2H), 3.57 – 3.51 (m, 2H), 2.97 (p, *J* = 6.1 Hz, 1H), 2.23 (s, 3H), 2.17 (s, 6H), 2.14 – 2.06 (m, 7H), 1.80 – 1.66 (m, 2H), 1.58 – 1.49 (m, 2H), 1.49 – 1.37 (m, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 213.8, 139.7, 138.5, 135.7, 133.2, 128.6, 128.5, 127.8, 127.7, 72.9, 68.3, 62.7, 50.3, 32.9, 29.3, 29.2, 23.5, 18.0, 16.9, 16.2;

IR (film) ν_{max}/cm^{-1} 3441, 3007, 2938, 1689, 1544, 1454, 1218, 1092, 699;

HRMS (ESI$^+$) $[C_{26}H_{37}O_3]^+$ ($[M+H]^+$) requires 397.2737; found 397.2735, Δ 0.49 ppm.

3m (1-(2-(Benzyloxy)ethyl)-2-((phenylsulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **1m** (119 mg, 0.300 mmol), phenyl methyl sulfone (94 mg, 0.60 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* sequential flash column chromatography *via* normal phase (eluent Pentane/CH_2Cl_2/Et_2O, 88:5:7 → Pentane/CH_2Cl_2/EtOAc 85:5:10), then reverse phase (eluent water/MeCN, 70:30 → MeCN) gave a mixture of diastereomers of the *title compound* as a colourless oil (40 mg, 25%, [91:9] d.r.*)

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The spectroscopic data were collected on the diastereomeric mixture. The relative stereochemistry was assigned by analogy with the other products.

Major (1*RS*, 2*RS*) diastereomer (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 – 7.76 (m, 2H), 7.72 – 7.62 (m, 1H), 7.57 (t, *J* = 7.7 Hz, 2H), 7.41 – 7.29 (m, 5H), 4.56 – 4.45 (m, 2H), 3.70 – 3.57 (m, 2H), 3.22 (dd, *J* = 13.7, 2.3 Hz, 1H), 3.04 (t, *J* = 12.8 Hz, 1H), 2.77 – 2.62 (m, 1H), 2.36 – 2.28 (m, 1H), 2.27 (s, 3H), 2.20 (s, 3H), 2.19 – 2.14 (m, 4H), 2.13 – 2.05 (m, 4H), 2.03 (s, 3H), 1.88 – 1.79 (m, 1H), 1.79 – 1.54 (m, 4H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 215.0, 140.8, 138.3, 137.2, 135.5, 133.7, 133.7, 133.0, 129.4, 129.1, 129.0, 128.5, 127.8, 127.7, 73.3, 67.1, 62.1, 57.8, 39.9, 32.5, 29.4, 29.1, 22.4, 19.1, 18.3, 16.8, 16.4, 16.0;

Fewer ^{13}C resonances observed than expected due to overlapping peaks in the Ar region.

Selected characteristic peaks of the minor (1*SR*, 2*RS*) diastereomer (from the mixture):

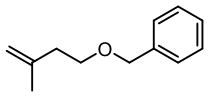
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 7.5 Hz, 2H), 4.28 (s, 2H), 3.49 (d, *J* = 6.6 Hz, 2H), 3.31 – 3.24 (m, 1H), 2.55 – 2.43 (m, 1H), 2.20 (s, 3H), 2.14 (s, 3H), 2.12 (s, 3H), 1.97 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 216.6, 140.2, 139.2, 135.4, 133.5, 133.1, 128.5, 128.1, 127.7, 73.1, 66.6, 62.5, 58.4, 42.3, 35.0, 34.1, 30.9, 29.8, 22.4, 19.0, 18.8, 16.8, 16.3, 16.1;

IR (film) ν_{max}/cm^{-1} 2934, 2877, 1674, 1448, 1306, 1218, 1148, 1086, 690;

HRMS (ESI$^+$) $[C_{33}H_{41}O_4S]^+$ ([M+H]$^+$) requires 533.2720; found 533.2711, Δ 1.79 ppm.

S19 (((3-Methylbut-3-en-1-yl)oxy)methyl)benzene



NaH (60% in mineral oil, 1.58 g, 39.6 mmol) was added to a stirred solution of 3-methyl-3-buten-1-ol (2.0 mL, 20 mmol) in THF (80 mL) at RT and the mixture was stirred at RT for 45 min. The mixture was cooled to 0 °C and benzyl bromide (2.3 mL, 19 mmol) was added dropwise. The reaction was allowed to warm to RT overnight, cooled to 0 °C and quenched with the addition of satd. aq NH_4Cl (20 mL). The mixture was diluted with EtOAc (50 mL) and water (75 mL), the layers separated and the aqueous layer extracted with EtOAc (2 × 80 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane: Et_2O, 99.5:0.5 ⟶ 99:1) gave the title compound as a colourless oil (2.54 g, 75%).

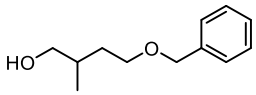
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.20 (m, 5H), 4.75 – 4.70 (m, 1H), 4.67 (dq, *J* = 2.1, 1.1 Hz, 1H), 4.46 (s, 2H), 3.52 (t, *J* = 6.9 Hz, 2H), 2.35 – 2.19 (m, 2H), 1.68 (t, *J* = 1.2 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.9, 138.5, 128.4, 127.7, 127.6, 111.5, 72.9, 68.7, 37.8, 22.7;

m/z (ESI$^+$) Found ([M+Na]$^+$) = 199, $C_{12}H_{16}NaO$ requires 199;

The spectroscopic data matched that previously reported in the literature. [15]

S20 4-(Benzyloxy)-2-methylbutan-1-ol



$BH_3{\cdot}SMe_2$ (2.7 mL, 28 mmol) was added dropwise to a solution of alkene **S19** (1.67 g, 9.53 mmol) in THF (75 mL) at 0 °C. The reaction was allowed to warm to RT and stirred overnight. A suspension of sodium perborate tetrahydrate (7.33 g, 47.6 mmol) in water (20 mL) was added slowly at 0 °C and the reaction was stirred at RT for 4 h. The mixture was diluted with satd. aq. NH_4Cl (70 mL) and Et_2O (50 mL), the layers were separated and the aqueous layer was extracted with Et_2O (2 × 100 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane: Et_2O, 65:35 → 50:50) gave the title compound as a colourless oil (1.63 g, 88%)

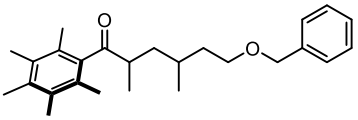
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 4.52 (s, 2H), 3.60 (ddd, *J* = 9.4, 6.2, 4.9 Hz, 1H), 3.55 – 3.47 (m, 2H), 3.43 (dd, *J* = 10.9, 6.6 Hz, 1H), 2.15 (br s, 1H), 1.89 – 1.73 (m, 1H), 1.75 – 1.63 (m, 1H), 1.58 (dtd, *J* = 14.5, 6.1, 4.6 Hz, 1H), 0.92 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.1, 128.6, 127.9, 127.9, 73.3, 68.8, 68.3, 34.3, 34.2, 17.4;

m/z (ESI$^+$) Found ([M+H]$^+$) = 195, $C_{12}H_{19}O_2$ requires 195.

The spectroscopic data matched that previously reported in the literature. [16]

S21 6-(Benzyloxy)-2,4-dimethyl-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



Ph* ethyl ketone **S1** (2.10 g, 10.3 mmol), $[IrCp^*Cl_2]_2$ (41 mg, 1.0 mol%) and KOH (1.16 g, 20.6 mmol) were added to 10 – 20 mL microwave vial. The vial was sealed and evacuated and back-filled with Ar (3 times). Alcohol **S20** (1.00 g, 5.15 mmol) and PhMe (1.3 mL, degassed with Ar (balloon)) were added and the reaction was heated to 110 °C for 30 h. The crude reaction mixture was filtered through a silica plug and concentrated *in vacuo*. The mixture was passed through a silica plug to remove excess Ph* ethyl ketone (elution with Pentane/Et_2O, 98:2 → 90:10) and concentrated *in vacuo*. The crude mixture was dissolved in MeOH (40 mL) and degassed with N_2 (balloon). PtO_2 (215 mg, 15 wt%) was added, H_2 was bubbled through the mixture for 15 min and the reaction was left under an atmosphere of H_2 for 3 h. The reaction mixture was filtered through a Celite® pad (washed with CH_2Cl_2) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 97:3 → 95:5) gave the *title compound* as a colourless oil (449 mg, 23%, 1:3.6 d.r.)*

*N.B. d.r. was calculated after purification and is the result of challenging purification of the diastereomeric mixture from other side products. The d.r. of the crude reaction mixture was 1:1.1,

representing an unselective reaction. The relative stereochemistry is unassigned. The spectroscopic data were collected on the diastereomeric mixture.

Major diastereomer (from the mixture)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 4.49 (s, 2H), 3.56 – 3.44 (m, 2H), 2.94 – 2.80 (m, 1H), 2.23 (s, 3H), 2.18 (s, 6H), 2.08 (s, 6H), 1.78 – 1.67 (m, 1H), 1.66 – 1.58 (m, 1H), 1.55 – 1.43 (m, 3H), 1.11 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 6.5 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 215.7, 140.2, 138.7, 135.5, 133.2, 128.5, 128.3, 127.8, 127.7, 73.1, 68.4, 46.0, 38.6, 37.9, 27.2, 18.9, 18.1, 16.9, 16.2, 15.1;

Selected characteristic peaks of the minor diastereomer (from the mixture)

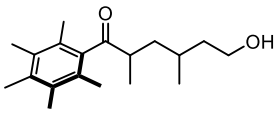
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.48 – 4.41 (m, 2H), 2.23 (s, 3H), 1.13 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.2 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 133.1, 128.5, 127.7, 127.6, 68.6, 46.1, 39.5, 35.6, 27.7, 20.9, 15.9;

IR (film) ν_{max}/cm^{-1} 2932, 2859, 1694, 1455, 1101, 1029, 915, 738, 699, 639;

HRMS (ESI$^+$) $C_{26}H_{37}O_2^+$ ([M+H]$^+$) requires 381.2788; found 381.2789, Δ 0.23 ppm.

1n 6-Hydroxy-2,4-dimethyl-1-(2,3,4,5,6-pentamethylphenyl)hexan-1-one



Ketone **S21** (445 mg, 1.18 mmol, [1:3.6] d.r.) dissolved in MeOH (12 mL) and the mixture was degassed with N_2 (balloon). Pd (10% on carbon) (45 mg, 10 wt%) was added and a balloon of hydrogen gas was attached. H_2 was bubbled through the reaction mixture for 15 min and then the mixture was stirred vigorously at RT for 3 h. The crude reaction mixture was filtered through a Celite® pad (washed with CH_2Cl_2) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 75:25 → 60:40) gave the title compound as a colourless oil (316 mg, 92%, 1:3.6 d.r.).

The relative stereochemistry is unassigned. The spectroscopic data were collected on the diastereomeric mixture.

Major diastereomer (from the mixture)**:**

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 – 3.52 (m, 2H), 2.97 – 2.83 (m, 1H), 2.23 (s, 3H), 2.18 (s, 6H), 2.09 (s, 6H) 1.76 – 1.66 (m, 1H), 1.64 – 1.41 (m, 4H), 1.26 (br. s, 1H), (d, *J* = 7.0 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 215.6, 140.2, 135.6, 133.2, 128.3, 61.0, 45.9, 41.0, 38.8, 26.8, 18.8, 18.1, 16.9, 16.2, 15.1;

Selected characteristic peaks for the minor diastereomer (from the mixture):

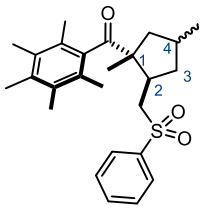
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 – 3.73 (m, 1H), 1.88 (dt, *J* = 13.4, 6.5 Hz, 1H), 1.41 – 1.32 (m, 1H), 1.17 (dt, *J* = 13.9, 7.1 Hz, 1H), 0.95 (d, *J* = 6.6 Hz, 3H);

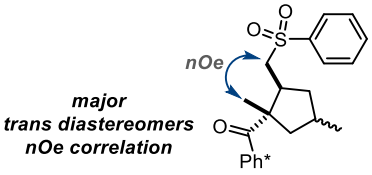
^{13}C NMR (126 MHz, $CDCl_3$) δ 215.6, 139.8, 135.6, 60.9, 46.2, 39.0, 27.3, 21.0, 18.1, 16.6;

IR (film) ν_{max}/cm^{-1} 3397, 2932, 1693, 1459, 1382, 1062, 921, 736, 647,

HRMS (ESI$^+$) $C_{19}H_{31}OS^+$ ([M+H]$^+$) requires 291.2319; found 291.2320, Δ 0.48 ppm.

3n (1,4-Dimethyl-2-((phenylsulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone





Hydroxy-ketone **1n** (87 mg, 0.30 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 80:5:15) gave the *title compound* as a white solid (112 mg, 88%, [50:45:3:2] d.r. ([*trans*':*trans*'':*cis*':*cis*'']))

Due to overlapping peaks, the d.r. could not be determined from the crude NMR and therefore was determined post-purification. The two "*trans"* diastereomers were inseparable and therefore the data for both isomers is reported together as observed. Equally, the two "*cis"* diastereomers were inseparable and therefore the data for both isomers is reported together as observed.

The relative stereochemistry between the ketone and sulfone substituents was assigned by nOe analysis.

Data for the major "*trans"* ((1*R*,2*R*,4*SR*) & (1*S*,2*S*,4*RS*)) diastereomers

m.p. = 164 – 165 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 – 7.77 (m, 4H), 7.70 – 7.60 (m, 2H), 7.60 – 7.49 (m, 4H), 3.52 (m, 2H), 3.02 (dd, *J* = 13.8, 11.9 Hz, 1H), 2.97 (dd, *J* = 13.8, 12.00 Hz, 1H), 2.72 (dtd, *J* = 11.5, 9.3, 2.1 Hz, 1H), 2.65 (tdd, *J* = 12.0, 6.2, 2.2 Hz, 1H), 2.49 (dt, *J* = 12.7, 6.4 Hz, 1H), 2.33 (dd, *J* = 13.8, 9.8 Hz, 1H), 2.22 (s, 3H), 2.22 (s, 3H), 2.21 – 2.12 (m, 13H), 2.02 – 1.96 (m, 7H), 1.93 (s, 3H), 1.92 – 1.89 (m, 4H), 1.89 – 1.82 (m, 1H), 1.79 (dd, *J* = 12.6, 7.2 Hz, 1H), 1.37 (dd, *J* = 12.6, 10.3 Hz, 1H), 1.22 (td, *J* = 12.4, 11.1 Hz, 1H), 1.17 (s, 3H), 1.16 – 1.10 (m, 4H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 218.1, 217.3, 140.2, 138.9, 135.3, 135.3, 133.7, 133.7, 133.5, 133.4, 133.10, 133.09, 129.42, 129.40, 128.1, 128.0, 127.9, 127.8, 127.8, 59.5, 58.3, 58.2, 57.8, 46.0, 45.6, 40.7, 39.9, 38.5, 37.8, 32.6, 30.6, 22.5, 21.8, 21.4, 19.2, 19.0, 18.6, 18.44, 18.38, 16.80, 16.78, 16.34, 16.33, 16.11, 16.07;*

Fewer peaks than expected due to overlapping signals in aromatic region of the 13C spectrum.

IR (film) ν_{max}/cm^{-1} 2953, 1676, 1448, 1307, 1150, 1088, 923, 791, 760, 690;

HRMS (ESI$^+$) $C_{26}H_{35}O_3S^+$ ([M+H]$^+$) requires 427.2301; found 427.2306, Δ 1.06 ppm.

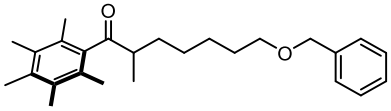
Data for the minor "*cis*" diastereomers, (1*R*,2*S*,4*SR*) & (1*S*,2*R*,4*RS*):

m.p. = 110 – 112 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 – 7.93 (m, 2H), 7.93 – 7.89 (m, 2H), 7.69 – 7.63 (m, 2H), 7.58 (m, 4H), 3.61 (dd, *J* = 14.3, 11.1 Hz, 1H), 3.54 (dd, *J* = 14.4, 2.0 Hz, 1H), 3.45 – 3.35 (m, 2H), 2.50 – 2.43 (m, 1H), 2.44 – 2.36 (m, 2H), 2.36 – 2.30 (m, 1H), 2.25 – 2.17 (m, 8H), 2.16 (s, 3H), 2.15 (s, 3H) 2.14 – 2.11 (m, 7H), 2.02 (s, 3H), 2.02 (s, 3H), 1.95 (s, 3H), 1.91 (s, 3H), 1.81 (dd, *J* = 9.0, 3.1 Hz, 2H), 1.65 (m, 1H), 1.57 – 1.53 (m, 1H), 1.17 (s, 3H), 1.13 – 1.07 (m, 4H), 1.04 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.2 Hz, 3H);

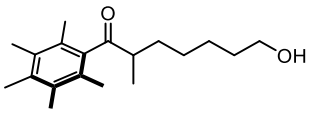
^{13}C NMR (151 MHz, $CDCl_3$) δ 218.9, 217.1, 140.5, 140.3, 140.1, 139.0, 135.3, 135.3, 133.7, 133.7, 133.5, 133.5, 133.0, 132.9, 129.43, 129.42, 128.1, 128.04, 127.98, 127.5, 127.3, 61.5, 60.4, 59.4, 58.2, 49.0, 47.9, 45.2, 44.8, 41.5, 39.6, 32.3, 30.8, 26.1, 24.8, 22.0, 20.8, 19.0, 18.5, 18.3, 18.1, 16.83, 16.76, 16.3, 16.0;
Fewer peaks than expected due to overlapping signals in aromatic region of the 13C spectrum.
IR (film) ν_{max}/cm^{-1} 2955, 1680, 1507, 1385, 1307, 1149, 1087, 999, 921;
HRMS (ESI$^+$) $C_{26}H_{35}O_3S^+$ ([M+H]$^+$) requires 427.2301; found 427.2313, Δ 2.70 ppm.

S22 7-(Benzyloxy)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)heptan-1-one



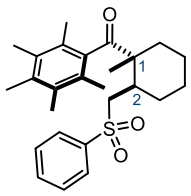
Ph* ethyl ketone **1a** (1.63 g, 8.00 mmol), $[IrCp^*Cl_2]_2$ (64 mg, 1.0 mol%), KOH (1.80 g, 32.0 mmol), 5-benzyloxylpentan-1-ol (3.1 mL, 16 mmol) and PhMe (2.0 mL) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5 → 92:8) gave the *title compound* as a colourless oil which solidified on standing (2.71 g, 89%);
m.p. = 66 – 68 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 5H), 4.49 (s, 2H), 3.45 (t, *J* = 6.5 Hz, 2H), 2.90 – 2.67 (m, 1H), 2.23 (s, 3H), 2.18 (s, 6H), 2.08 (s, 6H), 1.85 – 1.71 (m, 1H), 1.66 – 1.59 (m, 2H), 1.50 – 1.22 (m, 5H), 1.14 (d, *J* = 7.0 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 215.2, 140.2, 138.8, 135.5, 133.2, 128.5, 128.4, 127.8, 127.6, 73.0, 70.5, 48.5, 31.8, 29.8, 27.3, 26.4, 18.1, 16.9, 16.2, 15.3;
IR (film) ν_{max}/cm^{-1} 2935, 2858, 1693, 1454, 1100, 1028, 990, 923, 735, 698;
HRMS (ESI$^+$) $C_{26}H_{37}O_2^+$ ([M+H]$^+$) requires 381.2788; found 381.2788, Δ 0.08 ppm.

1o 7-Hydroxy-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)heptan-1-one



Benzyl ether **S22** (2.53 g, 6.66 mmol) was subjected to **General Procedure B** in MeOH (70 mL) with Pd (10% on carbon) (253 mg, 10 wt%) for 2 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 70:30 → 60:40) gave the *title compound* as a white solid (1.35 g, 70%).
m.p. = 31 – 33 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.6 Hz, 2H), 2.78 (dqd, *J* = 8.3, 6.9, 4.4 Hz, 1H), 2.23 (s, 3H), 2.18 (s, 6H), 2.09 (s, 6H), 1.85 – 1.74 (m, 1H), 1.56 (tdd, *J* = 8.2, 6.7, 3.8 Hz), 1.51 – 1.22 (m, 6H), 1.14 (d, *J* = 7.0 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 215.2, 140.1, 135.6, 133.2, 128.4, 63.1, 48.5, 32.8, 31.8, 27.3, 26.0, 18.1, 16.9, 16.2, 15.3;
IR (film) ν_{max}/cm^{-1} 3367, 2934, 2860, 1692, 1456, 1382, 1304, 1260, 1055, 990, 925, 732, 688;
HRMS (ESI$^+$) $C_{19}H_{31}O_2^+$ ([M+H]$^+$) requires 291.2318; found 291.2319, Δ 0.05 ppm.

3o (1-Methyl-2-((phenylsulfonyl)methyl)cyclohexyl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **1o** (87 mg, 0.30 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O/CH_2Cl_2, 85:10:5) gave the *title compound* as a white solid (100 mg, 78%, [88:12] d.r.*)

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The spectroscopic data were collected on the diastereomeric mixture. The relative stereochemistry was assigned by analogy with other products.

m.p. = 195 – 197 °C;

Major (1*RS*,2*RS*) diastereomer (from the mixture)**:**

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.85 (m, 2H), 7.70 – 7.60 (m, 1H), 7.59 – 7.49 (m, 2H), 4.10 (dd, *J* = 14.0, 1.5 Hz, 1H), 2.89 (dd, *J* = 14.0, 10.8 Hz, 1H), 2.62 – 2.49 (m, 1H), 2.49 – 2.38 (m, 1H), 2.21 (s, 3H), 2.19 – 2.10 (m, 6H), 1.99 (s, 3H), 1.97 (s, 3H), 1.75 – 1.61 (m, 1H), 1.61 – 1.20 (m, 6H), 1.19 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 219.1, 140.7, 139.6, 135.1, 133.6, 133.3, 133.1, 129.4, 128.0, 127.7, 127.6, 58.3, 50.5, 36.3, 36.2, 28.6, 25.4, 21.0, 19.2, 19.1, 16.8, 16.7, 16.3, 16.2;

Selected characteristic peaks for the minor (1*RS*,2*SR*) diastereomer (from the mixture):

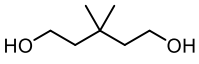
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.56 (dd, *J* = 14.4, 1.3 Hz, 1H), 3.46 (dd, *J* = 14.4, 9.2 Hz, 1H), 2.21 (s, 3H), 2.14 (s, 6H), 2.04 (s, 6H), 2.00 (s, 6H), 1.05 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.4, 140.5, 139.1, 135.1, 133.7, 133.4, 133.1, 129.4, 128.2, 57.8, 52.6, 40.0, 35.2, 28.0, 24.7, 23.8, 22.3, 19.2, 19.0, 16.3, 16.1;

IR (film) ν_{max}/cm^{-1} 2935, 2866, 1680, 1448, 1305, 1150, 1087, 910, 737;

HRMS (ESI$^+$) $C_{26}H_{35}O_3S^+$ ([M+H]$^+$) requires 427.2301; found 427.2309, Δ 1.76 ppm.

S23 3,3-Dimethylpentane-1,5-diol



3,3-Dimethylpentanedioc acid (3.50 g, 21.9 mmol) was added portion-wise to a suspension of $LiAlH_4$ (2.49 g, 65.7 mmol) in THF (110 mL) at 0 °C. A reflux condenser was added and the mixture was heated to reflux for 16 h, cooled to 0 °C and diluted with Et_2O (50 mL). The reaction was quenched with sequential dropwise addition of water (2.5 mL), aqueous NaOH (15% w/v, 2.5 mL) and water (7.5 mL). $MgSO_4$ was added, the mixture was stirred vigorously for 15 min and filtered under reduced pressure. The filtrate was

concentrated *in vacuo*. Purification *via* flash column chromatography (eluent CH_2Cl_2/EtOAc, 40:60) gave the *title compound* as a colourless oil (2.79 g, 96%).

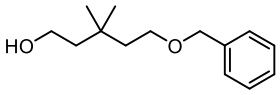
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 – 3.60 (m, 4H), 2.06 (br s, 2H), 1.57 (t, *J* = 7.0 Hz), 0.94 (s, 6H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 59.8, 44.2, 31.8, 28.2;

m/z (ESI$^+$) Found ([M+Na]$^+$) = 155, $C_7H_{16}NaO_2$ requires 155;

The spectral data matched that previously reported in the literature. [17]

S24 5-(Benzyloxy)-3,3-dimethylpentan-1-ol



Diol **S23** (2.48 g, 19.0 mmol) was dissolved in dry THF (20 mL) and NaH (60% dispersed in mineral oil, 752 mg, 19.0 mmol) was added at RT. The mixture was stirred at RT for 1 h, cooled to 0 °C and benzyl bromide (2.3 mL, 19 mmol) was added dropwise. The resulting mixture was allowed to warm to RT overnight, cooled to 0 °C and quenched with the addition of satd. NH_4Cl (5 mL) and diluted with EtOAc (50 mL) and water (50 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 60:40) gave the *title compound* as a colourless oil (1.48 g, 35%).

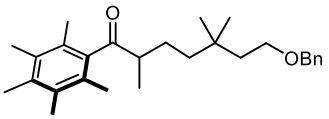
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H), 4.50 (s, 2H), 3.70 (t, *J* = 7.2 Hz, 2H), 3.55 (t, *J* = 6.9 Hz, 2H), 1.71 – 1.59 (m, 3H), 1.56 (t, *J* = 7.2 Hz, 2H), 0.93 (s, 6H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 128.5, 127.8, 127.8, 73.3, 67.5, 59.9, 44.5, 41.3, 31.8, 28.2;

m/z (ESI$^+$) Found ([M+H]$^+$) = 223, $C_{14}H_{23}O_2$ requires 223;

The spectral data matched that previously reported in the literature. [18]

S25 7-(Benzyloxy)-2,5,5-trimethyl-1-(2,3,4,5,6-pentamethylphenyl)heptan-1-one



Ph* ethyl ketone **S1** (612 mg, 3.00 mmol), $[Ir(cod)Cl]_2$ (20 mg, 1.0 mol%), dppBz (27 mg, 2.0 mol%), and KOH (673 mg, 12.0 mmol) were added to a 10 – 20 mL microwave vial. The vial was sealed and purged with Ar (balloon) for 5 min. PhMe (0.75 mL) and alcohol **S24** (1.00 g, 4.50 mmol) were added. The reaction was heated at 110 °C for 18 h, cooled to room temperature, filtered through a silica plug (elution with Et_2O) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 96:4 → 95:5) gave the *title compound* as a colourless oil (1.12 g, 91%).

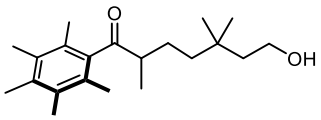
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 4.48 (s, 2H), 3.51 (t, *J* = 7.5 Hz, 2H), 2.78 – 2.63 (m, 1H), 2.23 (s, 3H), 2.18 (s, 6H), 2.08 (s, 6H), 1.88 – 1.76 (m, 1H), 1.65 – 1.54 (m, 2H), 1.37 – 1.24 (m, 2H), 1.22 – 1.14 (m, 1H), 1.11 (d, *J* = 7.1 Hz, 3H), 0.89 (s, 6H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 215.2, 140.2, 138.8, 135.5, 133.2, 128.5, 127.7, 127.6, 73.1, 67.6, 49.0, 41.0, 40.1, 32.3, 27.6, 27.5, 26.4, 18.1, 16.8, 16.2, 15.7;

IR (film) ν_{max}/cm^{-1} 2936, 2869, 1694, 1454, 1101, 1028, 924, 736, 698, 630;

HRMS (ESI$^+$) $C_{28}H_{41}O_2^+$ ([M+H]$^+$) requires 409.3101; found 409.3107, Δ 1.44 ppm.

1p 7-Hydroxy-2,5,5-trimethyl-1-(2,3,4,5,6-pentamethylphenyl)heptan-1-one



Benzyl ether **S25** (1.11 g, 2.70 mmol) was subjected to **General Procedure B** in MeOH (25 mL) with Pd (10% on carbon) (111 mg, 10 wt%) for 2 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 65:35) gave the *title compound* as a colourless oil (859 mg, 99%).

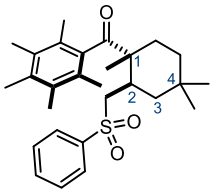
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.69 (t, *J* = 8.0 Hz, 2H), 2.70 (td, *J* = 7.5, 5.1 Hz, 1H), 2.24 (s, 3H), 2.18 (s, 6H), 2.09 (s, 6H), 1.87 – 1.78 (m, 1H), 1.53 (td, *J* = 7.2, 1.9 Hz, 2H), 1.37 – 1.29 (m, 2H), 1.25 – 1.17 (m, 1H), 1.13 (d, *J* = 7.1 Hz, 3H), 0.90 (s, 6H);

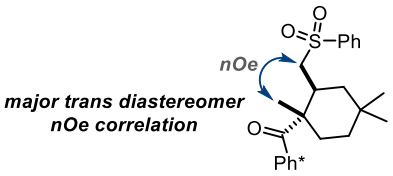
^{13}C NMR (151 MHz, $CDCl_3$) δ 215.2, 140.2, 135.6, 133.2, 128.4, 60.0, 49.0, 44.5, 40.0, 32.4, 27.6, 27.5, 26.4, 18.1, 16.9, 16.2, 15.9;

IR (film) ν_{max}/cm^{-1} 3358, 2938, 2872, 1693, 1459, 1385, 1302, 1261, 1146, 1123, 1051, 1021, 988, 925, 737, 635;

HRMS (ESI$^+$) $C_{21}H_{35}O_2^+$ ([M+H]$^+$) requires 319.2632; found 319.2638, Δ 2.00 ppm.

3p (2,3,4,5,6-Pentamethylphenyl)(1,4,4-trimethyl-2-((phenylsulfonyl)methyl)cyclohexyl)methanone





Hydroxy-ketone **1p** (95 mg, 0.30 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 88:5:7 → 87:5:8) gave inseparable diastereomers of the *title compound* as a white solid (131 mg, 96%, [93:7] d.r.)*

*d.r. calculated post-purification due to overlapping peaks in the crude NMR

The spectroscopic data were collected on the diastereomeric mixture. The relative stereochemistry was assigned by nOe and X-ray crystallography analysis.

m.p. = 175 – 177 °C;

Major (1*RS*,2*RS*) diastereomer (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 – 7.89 (m, 2H), 7.68 – 7.60 (m, 1H), 7.61 – 7.52 (m, 2H), 4.16 (dd, *J* = 14.0, 1.4 Hz, 1H), 2.85 (dd, *J* = 14.0, 10.8 Hz, 1H), 2.68 (dddd, *J* = 12.3, 10.8, 4.0, 1.4 Hz, 1H), 2.21 (s, 3H), 2.17 – 2.13 (m, 6H), 2.13 – 2.08 (m, 1H), 2.00 (s, 3H), 1.92 (s, 3H), 1.62 (td, *J* = 14.0, 4.1 Hz, 1H), 1.33 – 1.23 (m, 3H), 1.19 – 1.08 (m, 4H), 0.92 (s, 3H), 0.89 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 219.2, 140.4, 139.7, 135.1, 133.6, 133.3, 133.2, 129.3, 128.2, 127.7, 127.5, 58.2, 50.2, 41.2, 33.8, 32.8, 32.5, 32.1, 30.3, 24.4, 19.1, 19.0, 16.8, 16.4, 16.3, 16.2;

Selected characteristic peaks for the minor (1*RS*,2*SR*) diastereomer (from the mixture):

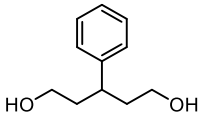
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.43 (dd, *J* = 14.6, 1.8 Hz, 1H), 3.39 (dd, *J* = 14.6, 7.9 Hz, 1H), 2.06 (s, 3H), 2.02 (s, 3H), 1.86 (dt, *J* = 14.2, 3.1 Hz, 1H), 1.50 (dt, *J* = 12.2, 2.9 Hz, 1H), 1.43 – 1.34 (m, 2H), 0.98 (s, 3H), 0.88 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 216.3, 139.9, 138.5, 135.2, 133.7, 133.4, 133.0, 129.4, 128.3, 59.4, 52.6, 42.8, 38.5, 35.8, 33.3, 32.8, 30.5, 26.1, 24.1, 19.6, 19.0, 16.8, 16.4, 16.1;

IR (film) ν_{max}/cm^{-1} 2953, 1678, 1473, 1448, 1317, 1305, 1151, 1087, 910, 760;

HRMS (ESI^+) $[C_{28}H_{39}O_3S]^+$ ($[M+H]^+$) requires 455.2614; found 415.2608, Δ 1.48 ppm.

S26 3-Phenylpentane-1,5-diol



$LiAlH_4$ (1.37 g, 36.1 mmol) was added to a stirred solution of 3-phenylglutaric acid (2.50 g, 12.0 mmol) in THF at 0 °C. The resulting suspension was warmed to RT and then heated at reflux for 16 h. The reaction was cooled to 0 °C, diluted with Et_2O and quenched with sequential dropwise addition of H_2O (1.4 mL), aq. NaOH (15% w/v, 1.4 mL) and H_2O (4.1 mL). $MgSO_4$ was added and the resulting suspension was stirred vigorously for 15 min and then filtered under reduced pressure. The filtrate was concentrated *in vacuo*. Purification *via* flash column chromatography (eluent CH_2Cl_2/MeOH, 95:5 → 80:20) gave the *title compound* as a colourless oil (1.84 g, 85%).

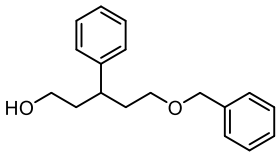
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H), 7.24 – 7.16 (m, 3H), 3.62 – 3.53 (m, 2H), 3.53 – 3.42 (m, 2H), 2.92 (tt, *J* = 10.0, 5.2 Hz, 1H), 2.02 – 1.91 (m, 2H), 1.91 – 1.77 (m, 2H), 1.36 (s, 2H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 128.8, 127.7, 126.6, 61.1, 39.6, 39.0;

m/z (ESI^+) Found ($[M+Na]^+$) = 203, $C_{11}H_{16}NaO_2$ requires 203;

The spectroscopic data were consistent with that present in the literature. [19]

S27 5-(Benzyloxy)-3-phenylpentan-1-ol



Diol **S26** (1.79 g, 9.94 mmol) was dissolved in *N,N*-dimethylformamide (20 mL) and cooled to 0 °C. NaH (400 mg, 10.0 mmol, 60% dispersed in mineral oil) was added, the reaction was allowed to warm to RT and stirred for 1 h. BnBr (1.08 mL, 9.04 mmol) was added and the reaction allowed to stir at RT overnight. The reaction was cooled to 0 °C, quenched by addition of sat. aq. NH_4Cl (20 mL) and diluted with EtOAc (100 mL) and water (100 mL). The layers were separated and the aqueous layer extracted with EtOAc (100 mL). The combined organic phases were washed with brine (three times), dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/EtOAc, 80:20 → 70:30) gave the *title compound* as a colourless oil (888 mg, 36%).

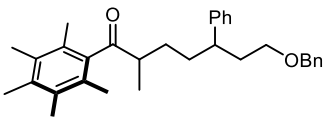
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 7H), 7.23 – 7.18 (m, 1H), 7.18 – 7.14 (m, 2H), 4.42 (d, *J* = 11.9 Hz, 1H), 4.38 (d, *J* = 11.9 Hz, 1H), 3.54 (ddd, *J* = 10.7, 6.9, 5.5 Hz, 1H), 3.47 (ddd, *J* = 10.7, 7.3, 6.5 Hz, 1H), 3.37 (ddd, *J* = 9.4, 6.7, 5.1 Hz, 1H), 3.27 (ddd, *J* = 9.4, 7.9, 6.2 Hz, 1H), 2.92 (tt, *J* = 10.0, 5.1 Hz, 1H), 2.08 – 1.98 (m, 1H), 1.94 (dtd, *J* = 14.1, 7.2, 5.2 Hz, 1H), 1.90 – 1.77 (m, 2H), 1.40 (br s, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.5, 138.6, 128.7, 128.5, 127.8, 127.83, 127.79, 126.5, 73.1, 68.4, 61.2, 39.7, 39.2, 36.9;

IR (film) ν_{max}/cm^{-1} 3433, 2935, 2865, 1694, 1495, 1454, 1206, 1052, 912, 736, 702;

HRMS (ESI$^+$) $C_{18}H_{23}O_2^+$ ([M+H]$^+$) requires 271.1693; found 271.1690, Δ 1.05 ppm.

S28 7-(Benzyloxy)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)-5-phenylheptan-1-one



Ph* ethyl ketone **S1** (384 mg, 1.88 mmol), alcohol **S27** (888 mg, 3.25 mmol), $[IrCp^*Cl_2]_2$ (15 mg, 1.0 mol%), KOH (422 mg, 7.52 mmol) and PhMe (0.47 mL) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5 → 92:8) gave the *title compound* as a pale yellow oil (769 mg, 90% [51:49] d.r.)

The spectroscopic data were collected on the diastereomeric mixture. The relative stereochemistry is unassigned.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 10H), 7.25 – 7.20 (m, 4H), 7.20 – 7.13 (m, 2H), 7.12 – 7.08 (m, 2H), 7.08 – 7.03 (m, 2H), 4.43 – 4.34 (m, 4H), 3.34 (m, 2H), 3.23 (m, 2H), 2.77 – 2.63 (m, 4H), 2.23 (s, 3H),

2.22 (s, 3H), 2.16 (s, 6H), 2.15 (s, 6H), 2.09 – 1.88 (m, 14H), 1.85 – 1.73 (m, 3H), 1.73 – 1.58 (m, 5H), 1.34 – 1.25 (m, 1H), 1.18 – 1.11 (m, 1H), 1.09 (d, *J* = 7.0 Hz, 3H), 1.07 (d, *J* = 6.9 Hz, 3H);*

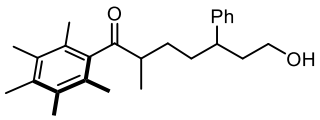
^{13}C NMR (151 MHz, $CDCl_3$) δ 214.9, 145.0, 144.6, 140.13, 140.11, 138.72, 138.70, 135.5, 135.4, 133.09, 133.12, 128.5, 128.35, 128.3, 127.8, 127.6, 126.2, 73.1, 73.0, 68.49, 68.47, 48.5, 48.2, 42.9, 42.5, 37.1, 36.6, 34.6, 34.4, 30.0, 29.7, 18.01, 18.0, 16.84, 16.8, 16.1, 16.1, 15.6, 15.1;*

IR (film) ν_{max}/cm^{-1} 2938, 2863, 1694, 1454, 1115, 1076, 914, 736, 701;

HRMS (ESI^+) $C_{32}H_{41}O_2^+$ ($[M+H]^+$) requires 457.3101; found 457.3096, Δ 1.05 ppm.

* N.B. Total proton count doubled due to the presence of 2 diastereomers. Fewer peaks than expected in the ^{13}C spectrum due to overlapping signals of different diastereomers.

1q 7-Hydroxy-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)-5-phenylheptan-1-one



Ketone **S28** (753 mg, 1.65 mmol, [51:49] d.r.) was subjected to **General Procedure B** in MeOH (17 mL) with Pd (10% on carbon) (75 mg, 10 wt%) for 3 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 65:35 → 60:40) gave the title compound as a colourless oil (560 mg, 93%, [52:48] d.r.)

The spectroscopic data were collected on the diastereomeric mixture. The relative stereochemistry is unassigned.

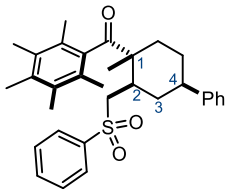
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 4H), 7.20 – 7.15 (m, 2H), 7.14 – 7.11 (m, 2H), 7.11 – 7.04 (m, 2H), 3.59 – 3.48 (m, 2H), 3.48 – 3.39 (m, 2H), 2.79 – 2.70 (m, 1H), 2.70 – 2.60 (m, 3H), 2.23 (s, 3H), 2.22 (s, 3H), 2.16 (s, 6H), 2.15 (s, 6H), 2.00 (br s, 12H), 1.96 – 1.86 (m, 2H), 1.85 – 1.72 (m, 3H), 1.72 – 1.54 (m, 5H), 1.40 (br s, 1H), 1.36 – 1.28 (m, 2H), 1.22 – 1.13 (m, 1H), 1.10 (d, *J* = 7.0 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H);

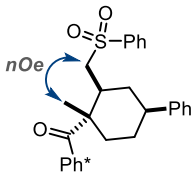
^{13}C NMR (151 MHz, $CDCl_3$) δ 214.9, 214.9, 144.9, 144.5, 140.1, 140.07 135.5, 135.5, 133.14, 133.1, 128.6, 128.34, 128.3, 127.7, 126.4, 61.23, 61.2, 48.4, 48.2, 42.9, 42.6, 39.9, 39.4, 34.6, 34.5, 30.0, 29.7, 18.02, 18.0, 16.83, 16.8, 16.1, 15.6, 15.2;*

IR (film) ν_{max}/cm^{-1} 3458, 2934, 1694, 1541, 1383, 1053, 925, 762, 703, 652

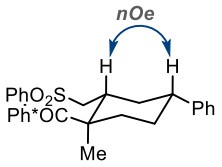
HRMS (ESI^+) $C_{25}H_{34}NaO_2^+$ ($[M+Na]^+$) requires 389.2451; found 389.2441, Δ 2.64 ppm.

3q (1-Methyl-4-phenyl-2-((phenylsulfonyl)methyl)cyclohexyl)(2,3,4,5,6-pentamethylphenyl)methanone





trans diastereomer nOe correlation



major all- trans diastereomer nOe correlation

Hydroxy-ketone **1q** (100 mg, 0.300 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure C** in ^{t}BuOH (1.2 mL) at 115 °C for 16 h. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/Et_2O, 97.5:0.5:2 → 80:5:15) gave inseparable diastereomers of the *title compound* as a white solid (108 mg, 72%, [81:5:10:4] d.r. [*trans*':*trans*'':*cis*':*cis*'']).*

*d.r. calculated post-purification due to overlapping peaks in the crude NMR. The labels ' and '' refer to different diastereomers. The labels *cis* and *trans* relate to the relative stereochemistry about the bond between the Ph* ketone and sulfone substituent. The single prime label indicates the major component with each relative stereochemistry, and the double prime label indicates the minor component. The *cis* diastereomers were assigned based on the position of the protons α- to the sulfone, by analogy with the other *cis* diastereomers. The mixture was further purified by recrystallisation (vapor diffusion over three days using $CHCl_3$ as the solvent and MeOH as the precipitant) to give the major diastereomer as a single diastereomer which was assigned as (1*RS*,2*RS*,4*RS*) by nOe and X-ray crystallography analysis.

m.p. = 185 – 188 °C;

Major all-*trans* diastereomer (1*RS*,2*RS*,4*RS*) (*trans'*):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.89 (m, 2H), 7.69 – 7.62 (m, 1H), 7.62 – 7.54 (m, 2H), 7.33 – 7.27 (m, 2H), 7.23 – 7.13 (m, 3H), 4.17 (dd, *J* = 13.8, 1.3 Hz, 1H), 2.94 (dd, *J* = 13.8, 10.8 Hz, 1H), 2.87 – 2.77 (m, 1H), 2.68 (dtd, *J* = 13.7, 3.8, 1.8 Hz, 1H), 2.62 – 2.48 (m, 1H) , 2.24 (s, 3H), 2.18 (s, 3H), 2.17 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H), 1.76 – 1.53 (m, 5H), 1.28 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 218.8, 145.8, 140.7, 139.5, 135.2, 133.6, 133.4, 133.2, 129.4, 128.6, 128.0, 127.6, 127.6, 126.9, 126.4, 58.0, 49.9, 43.1, 36.5, 36.2, 35.9, 28.4, 19.22, 19.18, 16.9, 16.8, 16.3, 16.2;

Selected characteristic peaks of the minor diastereomers (1*RS*,2*RS*,4*SR* -*trans*'') (1*RS*,2*SR*,4*RS*-*cis'*) and 1*RS*,2*SR*,4*SR*-*cis''*) (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.53 – 7.49 (m, 2H), 7.42 (dt, *J* = 8.3, 1.1 Hz, 2H), 7.38 – 7.34 (m, 2H), 4.27 (d, *J* = 14.4 Hz, 1H, *trans''*), 3.88 (dt, *J* = 14.6, 1.9 Hz, 1H, *cis''*), 3.72 (dd, *J* = 14.6, 11.5 Hz, 1H, *cis''*), 3.51 (dd, *J* = 14.5, 1.6 Hz, 1H, *cis'*), 3.45 (dd, *J* = 14.5, 8.5 Hz, 1H, *cis'*), 3.12 – 3.06 (m, 2H), 3.02 (dd, *J* = 14.3, 10.5 Hz, 1H, *trans''*), 2.17 (s, 3H), 2.14 (s, 3H), 2.12 (s, 3H), 2.02 (s, 3H), 1.97 (s, 3H), 1.49 – 1.43 (m, 1H), 1.27 (s, 3H), 1.26 (s, 3H), 1.24 – 1.19 (m, 1H), 1.10 (s, 3H, *cis'*);**

^{13}C NMR (151 MHz, $CDCl_3$) δ 219.0, 218.6, 216.3, 146.0, 145.5, 142.8, 140.7, 140.1, 139.7, 139.6, 139.6, 138.5, 135.2, 135.1, 134.8, 133.7, 133.5, 133.4, 133.2, 133.1, 133.0, 133.0, 132.9, 129.4, 129.3, 129.2,

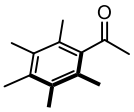
128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.8, 127.5, 127.4, 127.3, 127.2, 126.9, 126.9, 126.3, 126.2, 125.8, 59.2, 57.6, 55.2, 52.4, 51.1, 49.3, 44.0, 42.6, 37.7, 37.6, 36.5, 36.1, 35.5, 31.9, 31.7, 31.4, 30.7, 30.6, 27.4, 26.0, 21.9, 19.5, 19.0, 18.8, 18.7, 18.6, 18.2, 16.6, 16.6, 16.2, 16.0, 16.0.*

** N.B. the labels cis' and cis'' are assigned arbitrarily and indicate peaks belonging to different diastereomers

IR (film) ν_{max}/cm^{-1} 3027, 2935, 1680, 1495, 1448, 1306, 1218, 1151, 1086, 910, 839;

HRMS (ESI$^+$) $[C_{28}H_{39}O_3S]^+$ ($[M+H]^+$) requires 503.2614; found 503.2612, Δ 0.49 ppm.

S30 1-(2,3,4,5,6-Pentamethylphenyl)ethan-1-one



A solution of pentamethylbenzene (5.00 g, 33.7 mmol) and acetyl chloride (2.1 mL, 29 mmol) in CH_2Cl_2 (200 mL) was cooled in an ice bath. $AlCl_3$ (4.38 g, 32.9 mmol) was added portion-wise over 5 minutes, the resulting mixture was allowed to warm to RT and stirred for 90 min. After completion, the reaction mixture was poured onto crushed ice (approx. 200 g). Once the ice had melted, the layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 × 100 mL), the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 97:3 → 90:10) gave the *title compound* as a white solid (4.66 g, 85%).

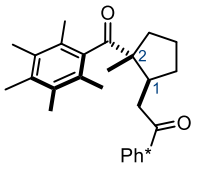
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (3 H, s), 2.24 (3 H, s), 2.19 (6 H, s), 2.13 (6 H, s);

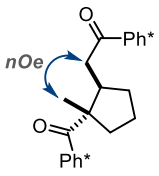
^{13}C NMR (101 MHz, $CDCl_3$) δ 210.2, 141.1, 135.5, 133.2, 127.1, 33.3, 17.2, 16.8, 16.1;

m/z (ESI$^+$) Found ($[M+Na]^+$) = 213, $C_{13}H_{18}NaO$ requires 213.

The spectroscopic data matched that previously reported in the literature. [20]

3r 2-((1*SR*,2*RS*)-2-Methyl-2-(2,3,4,5,6-pentamethylbenzoyl)cyclopentyl)-1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one





Hydroxy-ketone **1a** (83 mg, 0.30 mmol), Ph* methyl ketone (114 mg, 0.600 mmol), Ir(cod)acac (4.8 mg, 4.0 mol%), cataCXium® A (17.2 mg, 16.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) added to a 2 – 5 mL microwave vial. The vial was sealed and evacuated and back-filled with Ar (3 times) and ^{t}BuOH (1.2 mL, degassed with Ar (balloon)) was added. The reaction was heated at 110 °C for 24 h, cooled to RT, filtered through a silica pad (Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column

chromatography (eluent Pentane/Et_2O, 98:2 → 92:8) gave the *title compound* as a white solid (93 mg, 69%, >[95:5] d.r.)

The relative stereochemistry was assigned by nOe analysis.

m.p. = 159 – 161 °C;

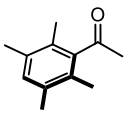
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.95 (dd, *J* = 19.1, 1.7 Hz, 1H), 2.80 – 2.62 (m, 1H), 2.52 (dd, *J* = 19.1, 11.3 Hz, 1H), 2.32 – 2.21 (m, 1H), 2.16 (s, 3H), 2.15 (s, 3H), 2.20 – 2.17 (m, 9H), 2.16 (s, 3H), 1.99 (m, 12H), 1.92 – 1.84 (m, 1H), 1.68 – 1.56 (m, 3H), 1.31 – 1.17 (m, 1H), 1.05 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 218.0, 210.8, 140.8, 139.0, 135.5, 135.0, 133.5, 133.2, 132.8, 128.5, 128.1, 127.3, 58.3, 47.0, 39.7, 37.3, 30.4, 22.0, 19.3, 18.2, 18.1, 17.1, 16.8, 16.8, 16.4, 16.1, 16.0;

IR (film) ν_{max}/cm^{-1} 2988, 2942, 1700, 1677, 1513, 1462, 1447, 1407, 1382, 1303, 1262, 1226, 1111, 912;

HRMS (ESI$^+$) $C_{31}H_{43}O_2^+$ ([M+H]$^+$) requires 447.3258; found 447.3255, Δ 0.51 ppm.

S31 1-(2,3,5,6-tetramethylphenyl)ethan-1-one



Aluminium trichloride (2.97 g, 22.3 mmol) was added portion-wise to a solution of durene (2.50 g, 18.6 mmol) and acetyl chloride (1.34 mL, 20.5 mmol) in CH_2Cl_2 (75 mL) at 0 °C. The reaction mixture was warmed to RT, stirred for 30 min and then poured onto crushed ice (approx. 100 g). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed sequentially with satd. aq. $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 98:2 → 90:10) gave the *title compound* as a white solid (3.07 g, 94%).

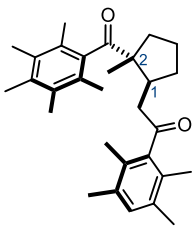
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (s, 1H), 2.46 (s, 3H), 2.21 (s, 6H), 2.09 (s, 6H);

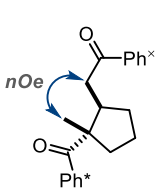
^{13}C NMR (101 MHz, $CDCl_3$) δ 210.0, 143.2, 134.5, 131.6, 127.7, 32.9, 19.6, 16.0;

m/z (ESI$^+$) Found ([M+H]$^+$) = 177, $C_{12}H_{17}O$ requires 177.

The spectroscopic data matched that previously reported in the literature. [21]

3s 2-(2-Methyl-2-(2,3,4,5,6-pentamethylbenzoyl)cyclopentyl)-1-(2,3,5,6-tetramethylphenyl)ethan-1-one





Hydroxy-ketone **1a** (83 mg, 0.30 mmol), Ph$^×$ methyl ketone **S31** (106 mg, 0.600 mmol), Ir(cod)acac (4.8 mg, 4.0 mol%), cataCXium® A (17.2 mg, 16.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were added to a 2 – 5 mL

microwave vial. The vial was sealed, evacuated and back-filled with Ar (3 times) and ^{t}BuOH (1.2 mL, degassed with Ar (balloon)) was added. The reaction was heated at 115 °C for 16 h, cooled to RT, filtered through a silica pad (Et_2O/CH_2Cl_2 elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 98:2 → 95:5) gave an inseparable mixture of diastereomers of the *title compound* as a white solid (107 mg, 83%, [95:5] d.r.*)

*d.r. calculated post-purification due to overlapping peaks in the crude NMR. The relative stereochemistry was assigned by nOe analysis.

m.p. = 147 – 150 °C;

Major (1*SR,* 2*RS*) diastereomer (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.95 (s, 1H), 3.05 (dd, *J* = 19.2, 1.7 Hz, 1H), 2.81 – 2.73 (m, 1H), 2.61 (dd, *J* = 19.1, 11.3 Hz, 1H), 2.38 – 2.28 (m, 1H), 2.23 (s, 3H), 2.21 (s, 6H), 2.19 (s, 3H), 2.16 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 2.02 (s, 6H), 1.99 – 1.91 (m, 1H), 1.74 – 1.61 (m, 3H), 1.39 – 1.30 (m, 1H), 1.14 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.9, 210.5, 143.0, 138.9, 135.1, 134.5, 133.5, 132.8, 131.6, 128.5, 128.1, 127.9, 58.3, 46.7, 39.6, 37.2, 30.4, 22.0, 19.6, 19.3, 18.5, 18.1, 16.7, 16.4, 16.0, 15.9;

Selected characteristic peaks of the minor (1*RS,* 2*RS*) diastereomer (from the mixture):

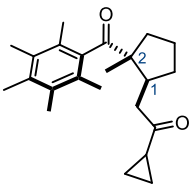
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.08 – 3.07 (m, 1H), 1.17 (s, 3H);

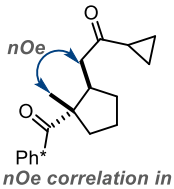
^{13}C NMR (151 MHz, $CDCl_3$) δ 218.6, 211.5, 143.0, 140.5, 134.9, 133.4, 132.8, 128.0, 127.4, 58.7, 47.4, 45.4, 39.2, 31.8, 29.8, 24.7, 21.7, 18.3, 18.2, 16.2, 16.0;

IR (film) ν_{max}/cm^{-1} 2941, 1703, 1674, 1469, 1378, 1303, 1260, 1219, 1109, 980;

HRMS (ESI^{+}) $[C_{30}H_{40}NaO_2]^{+}$ ([M+Na]$^{+}$) requires 455.2913; found 455.2921, Δ 1.61 ppm.

3t 1-Cyclopropyl-2-(2-methyl-2-(2,3,4,5,6-pentamethylbenzoyl)cyclopentyl)ethan-1-one





nOe correlation in major trans diastereomer

Hydroxy-ketone **1a** (83 mg, 0.30 mmol), Ir(cod)acac (4.8 mg, 4.0 mol%), cataCXium® A (17.2 mg, 16.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) added to a 2 – 5 mL microwave vial. The vial was sealed and evacuated and back-filled wit Ar (3 times) and ^{t}BuOH (1.2 mL, degassed with Ar (balloon)) and cyclopropyl methyl ketone (59 µL, 0.60 mmol) were added. The reaction was heated at 115 °C for 24 h, cooled to RT, filtered through a silica pad (Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5 → 92:8) gave inseparable diastereomers of the *title compound* as a colourless solid (61 mg, 60%, [92:8] d.r.)

The spectroscopic data were collected on the mixture. The relative stereochemistry was assigned by nOe analysis.

m.p. = 61 – 63 °C;

Major (1*SR,* 2*RS*) diastereomer (from the mixture):

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.95 (dd, *J* = 16.6, 2.2 Hz, 1H), 2.63 – 2.54 (m, 1H), 2.42 (dd, *J* = 16.6, 11.4 Hz, 1H), 2.22 (s, 3H), 2.16 (m, 6H), 2.08 – 2.03 (m, 4H), 2.02 (s, 3H), 1.95 – 1.79 (m, 2H), 1.72 – 1.59 (m, 3H), 1.34 – 1.19 (m, 1H), 1.15 (s, 2H), 1.05 – 0.91 (m, 2H), 0.92 – 0.73 (m, 2H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 218.1, 210.1, 138.9, 135.1, 133.5, 132.8, 128.5, 128.2, 58.5, 44.7, 40.8, 37.6, 30.3, 22.0, 20.8, 19.2, 18.4, 17.8, 16.7, 16.3, 16.0, 10.9, 10.5;

Selected characteristic peaks for the minor (1*RS,* 2*RS*) diastereomer (from the mixture):

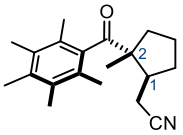
^{1}H NMR (600 MHz, $CDCl_3$) δ 2.91 – 2.87 (m, 2H), 1.10 (s, 3H);

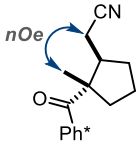
^{13}C NMR (151 MHz, $CDCl_3$) δ 218.7, 210.9, 140.6, 134.9, 133.3, 127.8, 127.5, 58.5, 46.4, 45.5, 39.3, 31.5, 24.7, 21.5, 21.3, 18.2, 16.8, 16.3, 10.8, 10.7;

IR (film) ν_{max}/cm^{-1} 2960, 1699, 1678, 1447, 1386, 1302, 1261, 1196, 1114, 1071, 1016, 924, 737, 630;

HRMS (ESI$^+$) $C_{23}H_{32}NaO_2^+$ ([M+Na]$^+$) requires 363.2295; found 363.2299, Δ 1.20 ppm.

3u 2-(2-Methyl-2-(2,3,4,5,6-pentamethylbenzoyl)cyclopentyl)acetonitrile





major trans diastereomer nOe correlation

Hydroxy-ketone **1a** (83 mg, 0.30 mmol), bromodicarbonyl[bis[2-(diisopropylphosphino)ethyl]amine]manganese(I), **Mn cat** (3.0 mg, 2.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) were added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and back-filled with Ar (3 times) and ^{t}BuOH (1.2 mL) and MeCN (78 µL, 1.5 mmol) were added. The reaction was heated at 115 °C for 16 h, cooled to RT, filtered through a silica pad (Et_2O/CH_2Cl_2 elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 96:4 ⟶ 92:8) gave separable diastereomers of the *title compound* as a white solid (14 mg, 15%, [96:4] d.r.*)

*d.r. calculated post-purification due to overlapping peaks in the crude NMR.

The relative stereochemistry was assigned by nOe analysis.

Major (1*SR*, 2RS) diastereomer:

m.p. = 97 – 99 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.69 (dd, *J* = 16.7, 3.6 Hz, 1H), 2.47 (tdd, *J* = 10.5, 8.2, 3.5 Hz, 1H), 2.30 – 2.24 (m, 1H), 2.23 (s, 3H), 2.21 – 2.17 (m, 4H), 2.17 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 2.03 – 1.93 (m, 1H), 1.78 – 1.62 (m, 3H), 1.61 – 1.51 (m, 1H), 1.14 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.4, 138.6, 135.5, 133.6, 133.2, 128.1, 127.7, 119.5, 58.0, 42.1, 38.1, 30.1, 21.6, 19.2, 18.6, 18.5, 17.9, 16.8, 16.4, 16.1;

IR (film) ν_{max}/cm^{-1} 2952, 2248, 1680, 1473, 1385, 1303, 1264, 1218, 1114, 924;

HRMS (ESI$^+$) $[C_{20}H_{27}NO]^+$ ([M+H]$^+$) requires 298.2165; found 298.2163, Δ 0.79 ppm.

Minor (1*RS*, 2*RS*) Diastereomer:

m.p. = 90 – 92 °C;

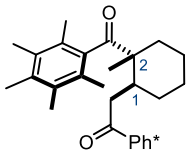
^{1}H NMR (600 MHz, $CDCl_3$) δ 2.70 – 2.58 (m, 2H), 2.28 (ddd, *J* = 13.2, 9.5, 6.8 Hz, 1H), 2.23 (s, 3H), 2.22 – 2.15 (m, 8H), 2.05 (s, 3H), 2.05 (s, 3H), 1.97 (td, *J* = 9.1, 4.6 Hz, 1H), 1.92 – 1.83 (m, 1H), 1.83 – 1.75 (m, 1H), 1.69 (ddd, *J* = 13.7, 8.8, 5.3 Hz, 1H), 1.11 (s, 3H);

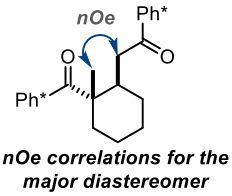
^{13}C NMR (151 MHz, $CDCl_3$) δ 218.2, 139.9, 135.3, 133.5, 133.0, 127.7, 127.1, 120.2, 58.1, 47.5, 39.2, 31.1, 24.6, 21.1, 20.2, 18.3, 18.1, 16.8, 16.3, 16.0;

IR (film) ν_{max}/cm^{-1} 2937, 2244, 1680, 1460, 1263, 1221, 1079, 1023, 920;

HRMS (ESI$^+$) $[C_{20}H_{28}NNaO]^+$ ([M+Na]$^+$) requires 320.1985; found 320.1283, Δ 0.49 ppm.

3v 2-(2-Methyl-2-(2,3,4,5,6-pentamethylbenzoyl)cyclohexyl)-1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one





nOe correlations for the major diastereomer

Hydroxy-ketone **1o** (87 mg, 0.30 mmol), Ph* methyl ketone (114 mg, 0.600 mmol), [Ir(cod)acac] (2.4 mg, 1.0 mol%), cataCXium® A (4.3 mg, 4.0 mol%) and KOH (67 mg, 1.2 mmol) were added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and backfilled with Ar (3 times) and PhMe (1.2 mL, degassed with Ar (balloon)) was added. The reaction was heated at 115 °C for 24 h, cooled to RT, filtered through a silica pad (Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 98:2 → 94:6) gave the *title compound* as a white solid (100 mg, 72% [86:14] d.r.);

The spectroscopic data were collected on the mixture. The relative stereochemistry was assigned by nOe analysis.

m.p. = 203 – 205 °C;

Major (1*SR*, 2*RS*) diastereomer (from the mixture)**:**

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.44 – 3.38 (m, 1H, *J* = 19.7, 1.3 Hz), 2.75 (dddd, *J* = 11.6, 10.4, 4.0, 1.2 Hz, 1H), 2.49 (dd, *J* = 19.8, 10.4 Hz, 1H), 2.24 (s, 3H), 2.22 (s, 3H), 2.19 (s, 9H), 2.16 (s, 3H), 2.12 (s, 3H), 2.10 (s, 6H), 2.02 (s, 4H), 1.69 – 1.65 (m, 1H), 1.62 – 1.58 (m, 1H), 1.54 – 1.45 (m, 2H), 1.42 – 1.28 (m, 2H), 1.19 (m, 4H),

^{13}C NMR (151 MHz, $CDCl_3$) δ 219.1, 210.6, 140.9, 139.7, 135.4, 134.8, 133.4, 133.2, 132.9, 128.0, 127.8, 127.6, 51.2, 48.1, 35.8, 34.7, 29.1, 25.8, 21.4, 19.4, 19.3, 16.9, 16.8, 16.8, 16.3, 16.1, 16.1, 16.1;

Selected characteristic peaks for the minor (1*RS*, 2*RS*) diastereomer (from the mixture)**:**

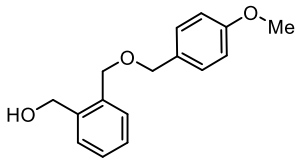
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.13 (d, *J* = 6.0 Hz, 1H), 2.22 (s, 3H), 2.16 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.00 (br. s, 6H), 1.93 – 1.87 (m, 1H), 1.16 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 218.2, 211.1, 141.0, 139.9, 135.4, 133.2, 133.2, 133.0, 128.2, 128.1, 127.5, 51.9, 46.3, 27.3, 24.1, 19.3, 18.9, 17.0, 16.3;

IR (film) ν_{max}/cm^{-1} 2931, 2860, 1699, 1677, 1447, 1381, 1304, 1270, 1256, 1171, 1116, 1084, 987, 909, 732;

HRMS (ESI$^+$) $C_{32}H_{45}O_2^+$ ([M+H]$^+$) requires 461.3414; found 461.3414, Δ 0.05 ppm.

S32 (2-(((4-Methoxybenzyl)oxy)methyl)phenyl)methanol



NaH (1.45 g, 36.2 mmol, 60% dispersed in mineral oil) was added portion-wise to a stirred solution of 1,2-benzenedimethanol (5.00 g, 36.2 mmol) and KI (2.72 g, 16.4 mmol) in *N,N*-dimethylformamide (55 mL) at –20 °C and the mixture was stirred for 1 h. 4-Methoxybenzyl chloride (4.44 mL, 32.8 mmol) was added, the reaction allowed to warm to RT and stirred for 2 h. The mixture was cooled to 0 °C, quenched with the addition of satd. NH_4Cl (20 mL) and diluted with Et_2O (100 mL) and water (100 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2 × 150 mL). The combined organic phases were washed with brine (3 times), dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/EtOAc, 85:15 → 82:18) gave the *title compound* as a colourless oil (6.18 g, 73%).

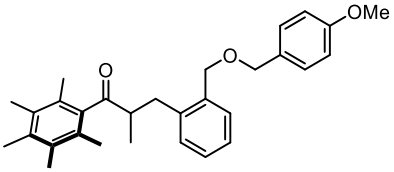
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 1H), 7.37 – 7.32 (m, 1H), 7.32 – 7.25 (m, 4H), 6.93 – 6.83 (m, 2H), 4.65 (s, 2H), 4.62 (s, 2H), 4.52 (s, 2H), 3.81 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 140.8, 136.1, 130.3, 129.9, 129.9, 129.5, 129.1, 128.1, 114.1, 72.3, 71.2, 64.0, 55.4;

m/z (ESI^+) Found ($[M+Na]^+$) = 281, $C_{16}H_{18}NaO$ requires 281.

The spectroscopic data matched that previously reported in the literature. [22]

S33 3-(2-(((4-Methoxybenzyl)oxy)methyl)phenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



Ph* ethyl ketone **S1** (722 mg, 3.54 mmol), alcohol **S32** (1.83 g, 7.08 mmol), $[IrCp^*Cl_2]_2$ (28 mg, 1.0 mol%), KOH (794 mg, 14.6 mmol) and PhMe (0.90 mL, 4.0 M) were subjected to **General Procedure A** at 110 °C for 20 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 93:7 → 90:10) gave the *title compound* as a colourless oil (1.41 g, 90%).

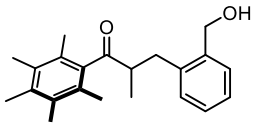
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.24 – 7.14 (m, 5H), 6.89 – 6.80 (m, 2H), 4.49 – 4.40 (m, 2H), 4.38 (s, 2H), 3.80 (s, 3H), 3.31 (dd, *J* = 13.8, 4.5 Hz, 1H), 3.09 (dqd, *J* = 9.7, 7.0, 4.5 Hz, 1H), 2.63 (dd, *J* = 13.8, 9.8 Hz, 1H), 2.23 (s, 3H), 2.17 (s, 6H), 2.13 – 1.88 (m, 6H), 1.06 (d, *J* = 7.0 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 214.1, 159.4, 139.7, 138.7, 136.5, 135.7, 133.2, 130.8, 130.4, 129.7, 129.5, 128.5, 127.9, 126.5, 113.9, 72.2, 69.9, 55.4, 50.0, 34.3, 18.0, 16.9, 16.2, 15.4;

IR (film) ν_{max}/cm^{-1} 2905, 2872, 1695, 1657, 1514, 1454, 1302, 1249, 1082, 1038, 925;

HRMS (ESI$^+$) $C_{30}H_{36}NaO_3^+$ ([M+Na]$^+$) requires 467.2557; found 467.2564, Δ 1.56 ppm.

11a 3-(2-(Hydroxymethyl)phenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



2,3-Dichloro-5,6-dicyano-*p*-benzoquinone, DDQ (1.08 g, 4.76 mmol) was added to a stirred solution of ether **S33** (1.41 g, 3.17 mmol) in a mixture of CH_2Cl_2:water (28.8 mL: 3.2 mL). The reaction was stirred at RT for 3 h and quenched by the addition of sat. $NaHCO_3$ (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 75:25 → 70:30) gave the *title compound* as a colourless oil (996 mg, 97%).

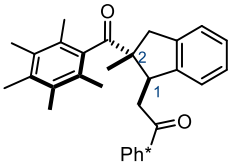
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 1H), 7.25 – 7.19 (m, 3H), 4.76 (d, *J* = 12.3 Hz, 1H), 4.65 (d, *J* = 12.3 Hz, 1H), 3.36 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.18 (dqd, *J* = 8.7, 7.2, 5.6 Hz, 1H), 2.68 (dd, *J* = 14.0, 8.7 Hz, 1H), 2.23 (s, 3H), 2.19 – 2.11 (m, 6H), 2.03 (br s, 6H), 1.11 (d, *J* = 7.2 Hz, 3H);

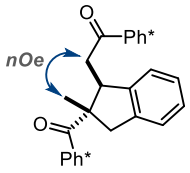
^{13}C NMR (151 MHz, $CDCl_3$) δ 214.5, 139.5, 139.0, 138.3, 135.8, 133.3, 130.7, 129.1, 128.4, 128.0, 126.8, 63.3, 50.2, 34.1, 18.0, 16.9, 16.1, 16.1;

IR (film) ν_{max}/cm^{-1} 3420, 2937, 2875, 1692, 1455, 1384, 1307, 1084, 1043, 1014, 925, 747;

HRMS (ESI$^+$) $C_{22}H_{28}NaO_2^+$ ([M+Na]$^+$) requires 347.1982; found 347.1984, Δ 0.70 ppm.

3w 2-(2-Methyl-2-(2,3,4,5,6-pentamethylbenzoyl)-2,3-dihydro-1*H*-inden-1-yl)-1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one





major diastereomer
nOe correlation

Hydroxy-ketone **11** (97 mg, 0.30 mmol), Ph* methyl ketone **S30** (114 mg, 0.600 mmol), [Ir(cod)acac] (4.8 mg, 4.0 mol%), cataCXium® A (17.2 mg, 16.0 mol%) and KO^{t}Bu (68 mg, 0.60 mmol) added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and back-filled with Ar (3 times) and ^{t}BuOH (1.2 mL, degassed with Ar (balloon)) was added. The reaction was heated at 115 °C for 24 h, cooled to RT, filtered through a silica pad (Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 98:2 → 95:5) gave separable diastereomers of the *title compound* as a white solid (44 mg, 34%, [94:6] d.r.)

*d.r. was determined post-purification due to overlapping peaks

The relative stereochemistry was assigned by nOe analysis.

Major (1*RS*, 2*RS*) diastereomer:

m.p. = 201 – 203 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.5 Hz, 1H), 7.21 – 7.16 (m, 1H), 7.16 – 7.12 (m, 1H), 7.10 (d, *J* = 7.3 Hz, 1H), 4.28 (d, *J* = 10.1 Hz, 1H), 3.61 (dd, *J* = 19.8, 1.5 Hz, 1H), 3.28 (d, *J* = 15.3 Hz, 1H), 2.97 (dd, *J* = 19.7, 10.3 Hz, 1H), 2.78 (d, *J* = 15.3 Hz, 1H), 2.27 (s, 3H), 2.25 – 2.20 (m, 15H), 2.19 (s, 3H), 2.17 (s, 3H), 2.14 (s, 3H), 2.12 (s, 3H), 1.25 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 216.9, 210.6, 143.8, 141.2, 140.5, 139.3, 135.7, 135.4, 133.7, 133.3, 133.0, 128.1, 128.0, 127.7, 126.9, 126.8, 124.9, 124.4, 60.5, 46.4, 44.4, 43.4, 20.0, 19.2, 19.0, 17.4, 16.9, 16.8, 16.4, 16.2, 16.1;

IR (film) ν_{max}/cm^{-1} 3016, 2928, 1699, 1451, 1218, 1116, 932, 760;

HRMS (ESI$^+$) $C_{35}H_{43}O_2^+$ ([M+H]$^+$) requires 495.3258; found 495.3254, Δ 0.65 ppm.

Minor (1*SR*, 2*RS*) diastereomer:

m.p. = 212 – 214 °C;

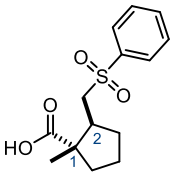
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 – 7.46 (m, 1H), 7.18 – 7.10 (m, 3H), 3.97 (dd, *J* = 10.8, 2.0 Hz, 1H), 3.61 (d, *J* = 15.2 Hz, 1H), 3.35 (dd, *J* = 20.2, 2.1 Hz, 1H), 3.09 (dd, *J* = 20.2, 10.8 Hz, 1H), 2.80 (d, *J* = 15.2 Hz, 1H), 2.22 (s, 3H), 2.21 (s, 3H), 2.19 (s, 3H), 2.15 – 2.10 (m, 12H), 2.05 – 1.76 (m, 9H), 1.22 (s, 3H);

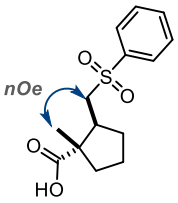
^{13}C NMR (151 MHz, $CDCl_3$) δ 218.4, 210.7, 146.4, 141.0, 140.7, 140.6, 135.7, 135.4, 133.6, 133.3, 133.0, 128.0, 127.8, 127.2, 127.2, 126.9, 126.3, 125.1, 59.4, 50.4, 49.1, 45.8, 25.7, 18.1, 18.1, 17.1, 17.0, 17.0, 16.4, 16.2, 16.2;

IR (film) ν_{max}/cm^{-1} 2950, 1703, 1677, 1309, 924, 762;

HRMS (ESI$^+$) $C_{35}H_{43}O_2^+$ ([M+H]$^+$) requires 495.3258; found 495.3266, Δ 1.70 ppm.

5 (1*SR*,2*SR*)-1-Methyl-2-((phenylsulfonyl)methyl)cyclopentane-1-carboxylic acid





A 2 – 5 mL microwave vial was charged with ketone **3a** (62 mg, 0.15 mmol, >[95:5] d.r.) and 1,1,1,3,3,3-hexafluoroisopropanol (1.5 mL) and 37% aq. HCl (12 M, 0.3 mL). The resulting mixture was stirred at 65 °C for 16 h, cooled to RT and diluted with CH_2Cl_2 (10 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo.* Purification *via* flash column chromatography (eluent CH_2Cl_2/EtOAc/HCO_2H 89.95:10:0.05) gave the *title compound* as a white solid (39 mg, 93%).

The relative stereochemistry was assigned by nOe and X-ray crystallography analysis.

m.p. = 112 – 114 °C;

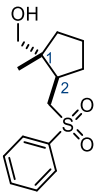
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.80 (m, 2H), 7.73 – 7.61 (m, 1H), 7.57 (t, *J* = 7.6 Hz, 2H), 3.43 (dd, *J* = 13.8, 2.8 Hz, 1H), 2.99 (dd, *J* = 13.8, 10.9 Hz, 1H), 2.64 (tdd, *J* = 10.9, 7.9, 2.8 Hz, 1H), 2.31 – 2.17 (m, 1H), 2.17 – 1.97 (m, 1H), 1.83 – 1.70 (m, 2H), 1.70 – 1.58 (m, 1H), 1.58 – 1.41 (m, 1H), 1.08 (s, 3H);

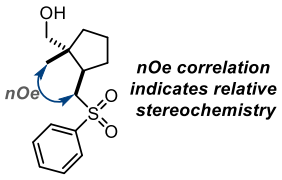
^{13}C NMR (101 MHz, $CDCl_3$) δ 182.3, 139.8, 133.8, 129.4, 128.1, 58.1, 51.4, 40.7, 37.4, 30.1, 22.2, 18.0;

IR (film) ν_{max}/cm^{-1} 3067, 2917, 1698, 1472, 1448, 1408, 1304, 1260, 1146, 1086, 1000, 913, 831, 744, 689;

HRMS (ESI$^-$) $C_{14}H_{17}O_4S^-$ ([M-H]$^-$) requires 281.0853; found 281.0853, Δ 0.16 ppm.

6 ((1*RS*,2*RS*)-1-Methyl-2-((phenylsulfonyl)methyl)cyclopentyl)methanol





Ketone **3a** (62 mg, 0.15 mmol, >[95:5 d.r.]) was dissolved in CH_2Cl_2 (0.75 mL) and the solution was cooled to –17 °C (ice/salt bath). Br_2 (21 µL, 0.40 mmol) was added dropwise and the resulting solution was stirred at –17 °C for 40 min. The reaction mixture was then warmed to RT, the majority of the volatiles were removed under a stream of nitrogen and the resulting solid was dried *in vacuo* (0.2 mmHg) for 30 sec. The residue was dissolved in THF (1.5 mL) and the resulting stirred solution was cooled to 0 °C. $LiAlH_4$ (29 mg, 0.75 mmol) was added in a single portion and the reaction mixture was stirred for 3 h at 0 °C. The resulting mixture was diluted with Et_2O (1.5 mL) and quenched by sequential dropwise addition of H_2O (30 µL), aq. NaOH (15% w/v, 30 µL) and H_2O (150 µL). $MgSO_4$ was added and the resulting suspension was stirred vigorously for 15 min and then filtered and concentrated *in vacuo*. Purification *via* flash column chromatography (Pentane/CH_2Cl_2/Et_2O, 60:5:35) gave the *title compound* as a colourless oil (34.4 mg, 86%).

The relative stereochemistry was assigned by nOe analysis.

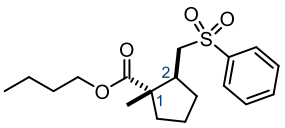
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.87 (m, 2H), 7.68 – 7.61 (m, 1H), 7.60 – 7.50 (m, 2H), 3.57 – 3.31 (m, 3H), 2.94 (dd, *J* = 14.0, 9.7 Hz, 1H), 2.20 (tdd, *J* = 10.5, 8.0, 2.9 Hz, 1H), 2.11 – 1.94 (m, 1H), 1.77 – 1.61 (m, 1H), 1.62 – 1.48 (m, 2H), 1.47 – 1.35 (m, 1H), 1.35 – 1.23 (m, 1H), 0.79 (s, 3H);

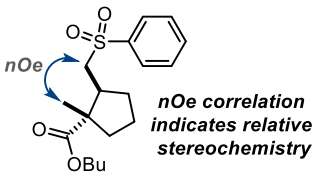
^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 133.7, 129.4, 128.0, 70.1, 58.4, 46.2, 39.1, 35.8, 31.5, 21.8, 18.1;

IR (film) ν_{max}/cm^{-1} 3539, 2954, 2873, 1448, 1304, 1146, 1086, 745, 689;

HRMS (ESI$^+$) $[C_{14}H_{20}NaO_3S]^+$ ([M+Na]$^+$) requires 291.1025; found 291.1019, Δ 2.21 ppm.

7 Butyl (1*RS*,2*RS*)-1-methyl-2-((phenylsulfonyl)methyl)cyclopentane-1-carboxylate





Ph* ketone **3a** (32 mg, 0.10 mmol, >[95:5] d.r.) was dissolved in CH_2Cl_2 (0.5 mL) and the solution was cooled to –17 °C (ice/salt bath). Br_2 (10 µL, 0.20 mmol) was added dropwise and the resulting solution was stirred at –17 °C for 20 min. *n*-BuOH (28 µL, 0.30 mmol) was added and the reaction was allowed to warm to RT overnight. The reaction was diluted with CH_2Cl_2 (10 mL) and sat. aq. $Na_2S_2O_3$ (10 mL), the layers were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash

column chromatography (Pentane/CH_2Cl_2/Et_2O 80:5:15) gave the *title compound* as a colourless oil (30 mg, 90%, >[95:5] d.r.)

The relative stereochemistry was assigned by nOe analysis.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 – 7.77 (m, 2H), 7.70 – 7.61 (m, 1H), 7.61 – 7.50 (m, 2H), 3.98 (td, *J* = 6.6, 2.9 Hz, 2H), 3.42 (dd, *J* = 13.8, 2.6 Hz, 1H), 2.97 (dd, *J* = 13.8, 11.1 Hz, 1H), 2.57 (tdd, *J* = 10.9, 8.0, 2.6 Hz, 1H), 2.28 – 2.13 (m, 1H), 2.04 (ddd, *J* = 12.9, 10.0, 8.1 Hz, 1H), 1.71 (m, 2H), 1.63 – 1.43 (m, 4H), 1.38 – 1.27 (m, 2H), 1.03 (s, 3H), 0.91 (t, *J* = 7.4 Hz, 3H);

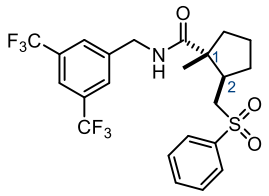
^{13}C NMR (126 MHz, $CDCl_3$) δ 176.6, 139.9, 133.7, 129.4, 128.1, 64.7, 58.3, 51.7, 40.7, 37.2, 30.7, 29.9, 22.1, 19.3, 18.1, 13.9;

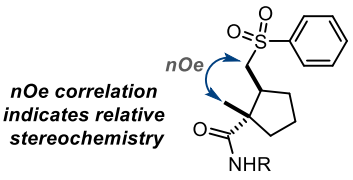
IR (film) ν_{max}/cm^{-1} 2964, 2876, 1723, 1653, 1554, 1448, 1308, 1196, 1148, 1117, 1087;

HRMS (ESI$^+$) $[C_{18}H_{27}O_4S]^+$ ([M+H]$^+$) requires 339.1625; found 339.1620, Δ 1.40 ppm.

8

(1*RS*,2*RS*)-*N*-(3,5-Bis(trifluoromethyl)benzyl)-1-methyl-2-((phenylsulfonyl)methyl)cyclopentane-1-carboxamide





Ph* ketone **3a** (32 mg, 0.10 mmol, >[95:5] d.r.) was dissolved in CH_2Cl_2 (0.5 mL) and the solution was cooled to –17 °C (ice/salt bath). Br_2 (10 µL, 0.20 mmol) was added dropwise and the resulting solution was stirred at –17 °C for 20 min. ^{i}Pr$_2$NEt(70 µL, 0.40 mmol) and (3,5-bis(trifluoromethyl)phenyl)methanamine (73 mg, 0.30 mmol) were added sequentially and the reaction was allowed to warm to RT overnight. The reaction was diluted with CH_2Cl_2 (10 mL) and sat. aq. $Na_2S_2O_3$ (10 mL), the layers were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were washed with 1 M HCl and brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (Pentane/CH_2Cl_2/EtOAc 70:5:25) gave the *title compound* as a tan solid (50 mg, 99%, >[95:5] d.r.)

The relative stereochemistry was assigned by nOe and X-ray crystallography analysis.

m.p. = 122 – 124 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 2H), 7.76 (s, 1H), 7.69 (s, 2H), 7.67 – 7.59 (m, 1H), 7.54 (t, *J* = 7.7 Hz, 2H), 6.50 – 6.39 (m, 1H), 4.56 – 4.45 (m, 2H), 3.53 (dd, *J* = 13.9, 3.4 Hz, 1H), 2.98 (dd, *J* = 13.9, 9.8 Hz, 1H), 2.68 (tdd, *J* = 10.5, 8.1, 3.4 Hz, 1H), 2.16 (dtd, *J* = 13.0, 8.3, 4.4 Hz, 1H), 1.99 – 1.88 (m, 1H), 1.82 – 1.67 (m, 2H), 1.67 – 1.59 (m, 1H), 1.56 – 1.45 (m, 1H), 1.11 (s, 3H);

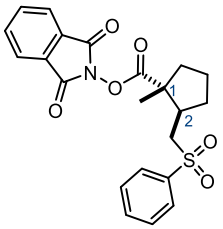
^{13}C NMR (151 MHz, $CDCl_3$) δ 177.0, 141.5, 139.6, 133.9, 132.0 (q, $J^2_{C–F}$ = 33.4 Hz), 129.4, 128.0, 127.8 (q, $J^3_{C–F}$ = 3.8 Hz), 123.4 (q, $J^1_{C–F}$ = 273.0 Hz), 121.4 (hept, $J^3_{C–F}$ = 3.8 Hz), 58.2, 51.7, 42.8, 40.1, 38.1, 30.2, 22.0, 18.7;

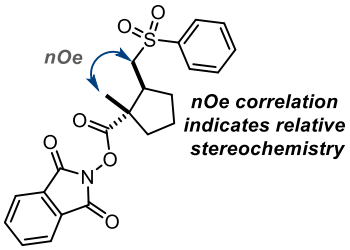
^{19}F NMR (565 MHz, $CDCl_3$) δ -62.9;

IR (film) ν_{max}/cm^{-1} 3380, 2967, 1637, 1510, 1386, 1362, 1280, 1170, 1143, 1127, 1100;

HRMS (ESI$^+$) $[C_{23}H_{24}F_6NO_3S]^+$ ([M+H]$^+$) requires 508.1376; found 508.1373, Δ 0.46 ppm.

9 1,3-Dioxoisoindolin-2-yl (1*RS*,2*RS*)-1-methyl-2-((phenylsulfonyl)methyl)cyclopentane-1-carboxylate





Ketone **3a** (41 mg, 0.10 mmol, >[95:5] d.r.) was dissolved in CH_2Cl_2 (0.5 mL) and the solution was cooled to –17 °C (ice/salt bath). Br_2 (21 µL, 0.40 mmol) was added dropwise and the mixture was stirred at –17 °C for 20 min. *N*-hydroxyphthalimide (65 mg, 0.40 mmol) and ^{i}Pr$_2$NEt (70 µL, 0.40 mmol) were added sequentially and the reaction was allowed to warm to RT and stirred for 16 h. The mixture was diluted with CH_2Cl_2 (10 mL) and sat. aq. $Na_2S_2O_3$ (10 mL), the layers separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/CH_2Cl_2/EtOAc, 75:5:20) gave the *title compound* as a colourless oil (42 mg, 99%).

The relative stereochemistry was assigned by nOe analysis.

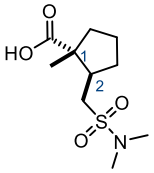
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 – 7.95 (m, 2H), 7.92 – 7.84 (m, 2H), 7.83 – 7.78 (m, 2H), 7.65 – 7.59 (m, 1H), 7.58 – 7.53 (m, 2H), 3.62 (dd, *J* = 13.7, 2.5 Hz, 1H), 3.04 (dd, *J* = 13.7, 11.6 Hz, 1H), 2.79 (tdd, *J* = 11.1, 7.9, 2.5 Hz, 1H), 2.44 – 2.35 (m, 1H) 2.35 – 2.26 (m, 1H), 1.92 – 1.79 (m, 3H), 1.65 (dddd, *J* = 18.2, 11.2, 9.2, 5.0 Hz, 1H), 1.27 (s, 3H);

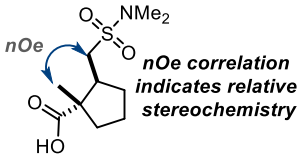
^{13}C NMR (151 MHz, $CDCl_3$) δ 172.9, 161.9, 139.7, 134.9, 133.8, 129.4, 129.1, 128.2, 124.1, 57.6, 51.1, 41.5, 37.4, 29.3, 22.2, 17.7;

IR (film) ν_{max}/cm^{-1} 2934, 1783, 1745, 1370, 1307, 1149, 1085, 1025, 911, 878, 738, 698;

HRMS (ESI$^+$) $[C_{22}H_{22}NO_6S]^+$ ([M+H]$^+$) requires 428.1162; found 428.1158, Δ 0.93 ppm.

10 (1*RS*,2*RS*)-2-((*N*,*N*-Dimethylsulfamoyl)methyl)-1-methylcyclopentane-1-carboxylic acid





Ketone **3i** (38 mg, 0.10 mmol, >[95:5] d.r.) was dissolved in CH_2Cl_2 (0.5 mL) and the solution was cooled to –17 °C (ice/salt bath). Br_2 (21 µL, 0.40 mmol) was added dropwise and the resulting solution was stirred at –17 °C for 40 min. The reaction mixture was then warmed to RT, the majority of the volatiles were

removed under a stream of nitrogen and the resulting solid was dried *in vacuo* (0.2 mmHg) for 30 sec. The residue was dissolved in THF (1.0 mL), sat. aq. $NaHCO_3$ (1.0 mL) was added and the mixture was stirred at RT for 3 h. The reaction was diluted with CH_2Cl_2 (5 mL) and 3 M HCl (5 mL), the layers were separated and the aqueous phase extracted with CH_2Cl_2 (3 × 15 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (CH_2Cl_2/MeOH/HCO_2H, 99.15:0.8:0.05) gave the *title compound* as a white solid (24.2 mg, 97%, >[95:5] d.r.)

The relative stereochemistry was assigned by nOe analysis.

m.p. = 93 – 95 °C;

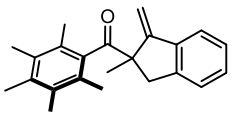
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.35 – 3.19 (m, 1H), 2.88 (s, 6H), 2.83 – 2.63 (m, 2H), 2.32 (dtd, *J* = 12.7, 7.5, 5.0 Hz, 1H), 2.21 – 2.06 (m, 1H), 1.87 – 1.72 (m, 2H), 1.72 – 1.63 (m, 1H), 1.61 – 1.49 (m, 1H), 1.12 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3, 51.4, 49.6, 41.1, 37.7, 37.6, 30.2, 22.1, 17.8;

IR (film) ν_{max}/cm^{-1} 2973, 2925, 1693, 1329, 1281, 1144, 957, 776, 713;

HRMS (ESI$^-$) $[C_{10}H_{18}NO_4S]^-$ ([M-H]$^-$) requires 248.0962; found 248.0959, Δ 1.02 ppm.

12a (2-Methyl-1-methylene-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11a** (97 mg, 0.30 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), Ru-MACHO® (3.6 mg, 1.0 mol%), KO^{t}Bu (68 mg, 0.60 mmol) were subjected to **General Procedure D** with ^{t}BuOH (0.6 mL) at 115 °C for 3 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.2:0.8 ⟶ 99:1) gave the *title compound* as a white solid (81 mg, 85%).

m.p. = 71 – 73 °C;

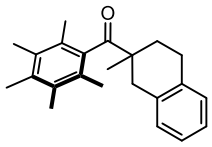
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.40 (m, 1H), 7.22 – 7.13 (m, 2H), 7.10 (m, 1H), 5.67 (s, 1H), 5.33 (s, 1H), 3.50 (d, *J* = 16.9 Hz, 1H), 2.89 (d, *J* = 16.9 Hz, 1H), 2.19 (s, 3H), 2.17 (s, 3H), 2.05 (s, 6H), 1.85 (s, 3H), 1.65 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 215.7, 153.8, 143.3, 139.7, 139.5, 135.1, 133.1, 132.7, 128.9, 128.1, 127.7, 126.9, 125.2, 121.1, 106.2, 59.6, 42.9, 29.0, 18.7, 18.3, 16.8, 16.2, 16.1;

IR (film) ν_{max}/cm^{-1} 2932, 1691, 1476, 1438, 1262, 1217, 1101, 932, 896, 780, 762;

HRMS (ESI$^+$) $C_{23}H_{26}NaO^+$ ([M+Na]$^+$) requires 341.1876; found 341.1874, Δ 0.56 ppm.

13a (2-Methyl-1,2,3,4-tetrahydronaphthalen-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11a** (97 mg, 0.30 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), $[IrCp^*Cl_2]_2$ (2.4 mg, 1.0 mol%) and KOH (67 mg, 1.2 mmol) were added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and backfilled with Ar (3 times) and PhMe (0.6 mL) was added. The reaction was heated at 115 °C for 24 h, cooled to RT, filtered through a silica pad (Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.2:0.8 → 99:1) gave the *title compound* as a white solid (67 mg, 70%).

m.p. = 110 – 111 °C;

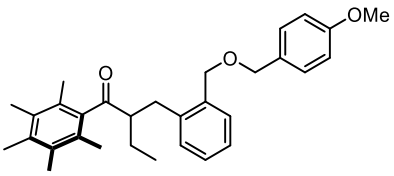
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.14 – 7.07 (m, 3H), 7.07 – 7.03 (m, 1H), 3.20 (d, *J* = 16.2 Hz, 1H), 2.84 (dd, *J* = 9.1, 4.3 Hz, 2H), 2.74 (dd, *J* = 16.2, 2.4 Hz, 1H), 2.24 (s, 3H), 2.19 (s, 3H), 2.19 (s, 3H), 2.13 (s, 6H), 2.05 (dt, *J* = 13.0, 9.2 Hz, 1H), 1.93 – 1.84 (m, 1H), 1.19 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 219.8, 139.8, 135.0, 135.0, 135.0, 133.3, 133.2, 129.9, 128.8, 127.6, 126.0, 126.0, 47.9, 39.0, 31.5, 25.8, 20.9, 19.2, 19.1, 16.8, 16.25, 16.3;

IR (film) ν_{max}/cm^{-1} 2927, 1686, 1583, 1496, 1453, 1382, 1303, 1260, 1080, 990, 908, 752;

HRMS (ESI$^+$) $C_{23}H_{28}NaO^+$ ([M+Na]$^+$) requires 343.2032; found 343.2035, Δ 0.76 ppm.

S34 2-(2-(((4-Methoxybenzyl)oxy)methyl)benzyl)-1-(2,3,4,5,6-pentamethylphenyl)butan-1-one



Ph* propyl ketone **S10** (654 mg, 3.00 mmol), alcohol **S32** (1.55 g, 6.00 mmol), $[IrCp^*Cl_2]_2$ (36 mg, 1.5 mol%), KOH (673 mg, 12.0 mmol) and PhMe (0.75 mL) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5 → 94:6) gave the *title compound* as a colourless oil (1.06 g, 77%).

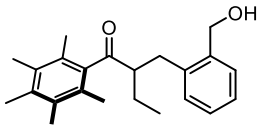
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.32 (m, 1H), 7.25 – 7.20 (m, 3H), 7.20 – 7.16 (m, 2H), 6.88 – 6.84 (m, 2H), 4.45 (d, *J* = 11.4 Hz, 1H), 4.42 (d, *J* = 11.4 Hz), 4.37 (s, 2H), 3.80 (s, 3H), 3.21 (dd, *J* = 13.9, 6.5 Hz, 1H), 3.08 – 2.97 (m, 1H), 2.71 (dd, *J* = 13.9, 7.3 Hz, 1H), 2.22 (s, 3H), 2.21 – 1.68 (m, 13H), 1.48 – 1.39 (m, 1H), 0.93 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 212.5, 159.3, 139.6, 139.0, 136.5, 135.7, 133.2, 131.0, 130.5, 129.6, 129.4, 129.0, 127.9, 126.5, 113.9, 72.2, 69.9, 56.8, 55.4, 31.9, 22.9, 17.7, 16.9, 16.2, 12.2;

IR (film) ν_{max}/cm^{-1} 2934, 1692, 1613, 1514, 1464, 1302, 1249, 1075, 1037, 822, 755;

HRMS (ESI$^+$) $C_{31}H_{39}O_3^+$ ([M+H]$^+$) requires 458.2894; found 458.2886, Δ 1.61 ppm.

11b 2-(2-(Hydroxymethyl)benzyl)-1-(2,3,4,5,6-pentamethylphenyl)butan-1-one



2,3-Dichloro-5,6-dicyano-*p*-benzoquinone, DDQ (182 mg, 0.800 mmol) was added to a stirred solution of PMB ether **S34** (243 g, 0.531 mmol) in a mixture of CH_2Cl_2:water (5.4 mL: 0.6 mL). The reaction was stirred at RT for 3 h and quenched by the addition of sat. $NaHCO_3$ (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 82:18 → 70:30) gave the *title compound* as a colourless oil (167 mg, 93%).

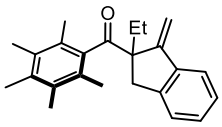
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 1H), 7.26 – 7.16 (m, 3H), 4.80 (d, *J* = 12.3 Hz, 1H), 4.62 (d, *J* = 12.3 Hz, 1H), 3.28 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.11 (tt, *J* = 8.0, 5.7 Hz, 1H), 2.79 (dd, *J* = 14.0, 5.7 Hz, 1H), 2.22 (s, 3H), 2.14 (br s, 6H), 2.03 – 1.58 (m, 7H), 1.51 – 1.40 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 213.2, 139.3, 139.1, 138.6, 135.8, 133.2, 130.8, 129.3, 128.9, 127.9, 126.7, 63.3, 57.3, 30.9, 23.5, 17.7, 16.9, 16.1, 12.4;

IR (film) ν_{max}/cm^{-1} 3446, 2932, 1691, 1456, 1384, 1301, 1260, 1139, 1090, 1042, 945;

HRMS (ESI$^+$) $C_{23}H_{30}NaO_2^+$ ([M+Na]$^+$) requires 361.2138; found 361.2131, Δ 2.03 ppm.

12b (2-Ethyl-1-methylene-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11b** (101 mg, 0.300 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), Ru-MACHO® (3.6 mg, 1.0 mol%), KO^{t}Bu (68 mg, 0.60 mmol) and ^{t}BuOH (0.6 mL) were subjected to **General Procedure D** at 115 °C for 3 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.2:0.8 → 99:1) gave the *title compound* as a white solid (76 mg, 76%.)

m.p. = 110 – 111 °C

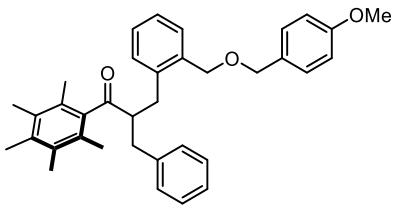
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.37 (m, 1H), 7.23 – 7.14 (m, 2H), 7.14 – 7.01 (m, 1H), 5.75 (s, 1H), 5.27 (s, 1H), 3.42 (d, *J* = 17.4 Hz, 1H), 2.98 (d, *J* = 17.4 Hz, 1H), 2.31 (dq, *J* = 13.4, 7.4 Hz), 2.19 (s, 3H), 2.16 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H), 1.96 (dq, *J* = 13.4, 7.4 Hz, 1H), 1.85 (s, 3H), 0.76 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 215.8, 151.1, 144.0, 140.6, 139.9, 135.0, 133.1, 132.6, 128.8, 128.3, 127.8, 126.8, 124.9, 120.6, 106.5, 63.8, 39.1, 33.8, 18.6, 18.3, 16.8, 16.2, 16.1, 8.6;

IR (film) ν_{max}/cm^{-1} 2938, 1687, 1635, 1476, 1462, 1302, 1260, 900, 779, 761, 730;

HRMS (ESI$^+$) $C_{24}H_{29}O^+$ ([M+H]$^+$) requires 333.2213; found 333.2212, Δ 0.31 ppm.

S35 2-Benzyl-3-(2-(((4-methoxybenzyl)oxy)methyl)phenyl)-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one

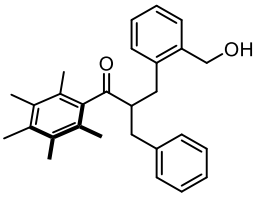


Ph* ketone **S12** (840 mg, 3.00 mmol), alcohol **S32** (1.55 g, 6.00 mmol), $[IrCp^*Cl_2]_2$ (36 mg, 1.5 mol%), KOH (673 mg, 12.0 mmol) and PhMe (0.75 mL) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 96:4 → 95:5) gave the *title compound* as a colourless oil (831 mg, 53%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 1H), 7.24 – 7.14 (m, 8H), 7.09 – 7.03 (m, 2H), 6.89 – 6.83 (m, 2H), 4.24 – 4.13 (m, 4H), 3.81 (s, 3H), 3.36 (p, *J* = 6.9 Hz, 1H), 3.26 (dd, *J* = 13.8, 6.8 Hz, 1H), 3.17 (dd, *J* = 13.3, 6.7 Hz, 1H), 2.64 (dd, *J* = 13.8, 7.0 Hz, 1H), 2.55 (dd, *J* = 13.3, 6.9 Hz, 1H), 2.21 (s, 3H), 2.11 (s, 6H), 1.78 (br s, 6H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 211.4, 159.3, 140.1, 139.0, 138.4, 136.6, 135.9, 133.2, 131.1, 130.6, 129.7, 129.5, 129.3, 129.1, 128.4, 127.8, 126.6, 126.3, 113.9, 72.1, 69.7, 58.3, 55.4, 35.8, 32.2, 17.5, 16.9, 16.1;
IR (film) ν_{max}/cm^{-1} 2929, 1694, 1613, 1514, 1455, 1302, 1249, 1174, 1077, 1037, 902, 822;
HRMS (ESI^+) $C_{36}H_{40}NaO_3^+$ ($[M+Na]^+$) requires 543.2870; found 543.2861, Δ 1.65 ppm.

11c 2-Benzyl-3-(2-(hydroxymethyl)phenyl)-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



2,3-Dichloro-5,6-dicyano-*p*-benzoquinone, DDQ (571 mg, 2.52 mmol) was added to a stirred solution of PMB ether **S35** (818 mg, 1.57 mmol) in a mixture of CH_2Cl_2:water (13.5 mL: 1.5 mL). The reaction was stirred at RT for 3 h, quenched by the addition of sat. $NaHCO_3$ (30 mL) and diluted with CH_2Cl_2 (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 82:18 → 70:30) gave the *title compound* as a solid glass (464 mg, 74%).

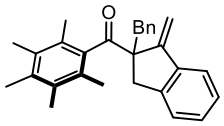
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 1H), 7.28 – 7.23 (m, 2H), 7.22 – 7.14 (m, 4H), 7.14 – 7.09 (m, 2H), 4.55 (d, *J* = 12.3 Hz, 1H), 4.39 (d, *J* = 12.3 Hz, 1H), 3.46 (tt, *J* = 8.4, 5.3 Hz, 1H), 3.30 (dd, *J* = 14.0, 8.4 Hz, 1H), 3.20 (dd, *J* = 13.4, 5.3 Hz, 1H), 2.65 (dd, *J* = 14.0, 5.3 Hz, 1H), 2.53 (dd, *J* = 13.4, 8.4 Hz, 1H), 2.22 (s, 3H), 2.14 (s, 6H), 1.85 (br s, 6H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 212.2, 139.8, 139.0, 138.8, 138.2, 136.0, 133.3, 130.7, 129.4, 129.2, 128.9, 128.5, 127.8, 126.7, 126.5, 63.1, 58.4, 36.6, 31.0, 17.7, 16.9, 16.1;

IR (film) ν_{max}/cm^{-1} 3443, 3025, 2926, 1692, 1454, 1301, 1260, 1217, 1125, 1008, 904;

HRMS (ESI$^+$) $C_{28}H_{33}O_2^+$ ([M+H]$^+$) requires 401.2475; found 401.2465, Δ 2.47 ppm.

12c (2-Benzyl-1-methylene-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11c** (120 mg, 0.300 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), Ru-MACHO® (3.6 mg, 1.0 mol%), KO^{t}Bu (68 mg, 0.60 mmol) and ^{t}BuOH (0.6 mL) were subjected to **General Procedure D** at 115 °C for 3 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.2:0.8 ⟶ 99:1) gave the *title compound* as a white solid (61 mg, 51%.)

m.p. = 104 – 106 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.33 (m, 1H), 7.24 – 7.19 (m, 2H), 7.14 – 6.99 (m, 5H), 6.92 – 6.82 (m, 1H), 5.86 (s, 1H), 5.55 (s, 1H), 3.43 (dd, *J* = 13.4, 1.7 Hz, 2H), 3.28 (d, *J* = 17.1 Hz, 1H), 3.20 (d, *J* = 17.1 Hz, 1H), 2.16 (s, 3H), 2.13 (s, 3H), 2.01 (s, 3H), 1.89 (s, 3H), 1.86 (s, 3H);

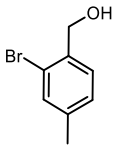
^{13}C NMR (101 MHz, $CDCl_3$) δ 214.1, 152.0, 143.8, 139.8, 139.4, 137.5, 135.2, 133.2, 132.5, 131.2, 128.7, 128.3, 127.9, 127.8, 126.6, 126.5, 124.7, 120.7, 107.3, 64.5, 46.1, 38.3, 18.4, 18.1, 16.8, 16.3, 16.0;

IR (film) ν_{max}/cm^{-1} 3026, 2924, 1686, 1633, 1475, 1454, 1302, 1259, 1219, 1135, 903;

m/z (ESI$^+$) Found ([M+Na]$^+$) = 417, $C_{29}H_{30}NaO$ requires 417;

HRMS (ESI$^+$) $C_{29}H_{30}NaO^+$ ([M+Na]$^+$) requires 417.2189; found 417.2181, Δ 1.87 ppm.

S36 (2-Bromo-4-methylphenyl)methanol



2-Bromo-4-methybenzaldehyde (5.00 g, 25.1 mmol) was dissolved in MeOH (80 mL) and cooled to 0 °C. $NaBH_4$ (1.42 g, 37.7 mmol) was added, the reaction allowed to warm to RT and stirred for 2 h. The reaction was quenched with water (20 mL) and the mixture was concentrated *in vacuo*. The residue was dissolved in EtOAc (150 mL) and diluted with water (120 mL). The layers were separated and the aqueous phase extracted with EtOAc (2 × 150 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give the *title compound* as a colourless oil which required no further purification (5.05 g, 100%).

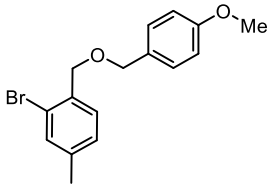
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.33 (d, *J* = 7.7 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 4.71 (s, 2H), 2.33 (s, 3H), 1.93 (s, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 136.8, 133.2, 129.1, 128.5, 122.7, 65.1, 20.9;

m/z (ESI$^+$) [$C_8H_{10}{}^{79}BrO$] requires 201; mass not found.

The spectroscopic data matched that previously reported in the literature. [23]

S37 2-Bromo-1-(((4-methoxybenzyl)oxy)methyl)-4-methylbenzene



Alcohol **S36** (5.05 g, 25.1 mmol) was dissolved in *N*,*N*-dimethylformamide (50 mL) and cooled to 0 °C. NaH (60%, dispersed in mineral oil, 1.11 g, 27.6 mmol) was added and the reaction stirred for 30 min at 0 °C. 4-Methoxybenzyl chloride (3.75 mL, 27.6 mmol) was added, the mixture warmed to RT and stirred for 16 h. The reaction was quenched with the addition of NH_4Cl (20 mL) and diluted with Et_2O (200 mL) and water (200 mL). They layers were separated and the aqueous phase was extracted with Et_2O (2 × 150 mL). The combined organic phases were washed with brine (3 × 200 mL) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99:1 → 98:2) gave the *title compound* as a colourless oil (6.93 g, 86%).

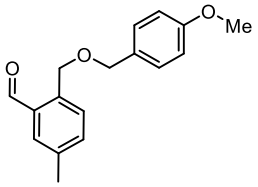
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 2H), 7.35 – 7.29 (m, 2H), 7.11 (dd, *J* = 8.1, 1.7 Hz, 1H), 6.94 – 6.85 (m, 2H), 4.57 (s, 2H), 4.55 (s, 2H), 3.81 (s, 3H), 2.32 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 139.2, 134.7, 133.1, 130.4, 129.6, 129.4, 128.3, 123.0, 114.0, 72.4, 71.3, 55.4, 20.9;

IR (film) ν_{max}/cm^{-1} 2836, 1612, 1514, 1456, 1356, 1249, 1174, 1093, 1039, 822;

HRMS (ESI$^+$) [$C_{16}H_{17}{}^{79}BrNaO_2$]$^+$ ([M+Na]$^+$) requires 343.0304; found 343.0302, Δ 0.51 ppm.

S38 2-(((4-Methoxybenzyl)oxy)methyl)-5-methylbenzaldehyde



Aryl Bromide **S37** (5.14 g, 16.0 mmol) was subjected to **General Procedure E** with *n*-BuLi (2.5 M in hexanes, 7.7 mL, 19.2 mmol) and *N,N*-dimethylformamide (2.5 mL, 32 mmol) in THF (53 mL). Purification *via* flash column chromatography (eluent Pentane/Et_2O, 5:95 → 85:15) gave the *title compound* as a colourless oil (4.07 g, 94%).

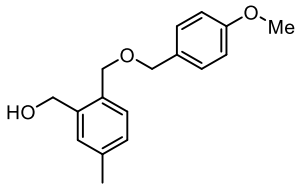
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.67 (d, *J* = 2.0 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.39 (ddd, *J* = 7.7, 2.0, 0.8 Hz, 1H), 7.35 – 7.27 (m, 2H), 6.97 – 6.75 (m, 2H), 4.89 (s, 2H), 4.56 (s, 2H), 3.81 (s, $3H_3$), 2.42 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 159.5, 138.1, 137.9, 134.7, 133.7, 132.5, 130.3, 129.6, 128.9, 114.0, 72.6, 69.2, 55.4, 21.0;

IR (film) ν_{max}/cm^{-1} 2838, 1688, 1613, 1571, 1514, 1359, 1302, 1248, 1084, 1036, 826, 774, 758;

HRMS (ESI$^+$) $[C_{17}H_{19}O_3]^+$ ([M+H]$^+$) requires 271.1329; found 271.1323, Δ 2.26 ppm.

S39 (2-(((4-Methoxybenzyl)oxy)methyl)-5-methylphenyl)methanol



Aldehyde **S38** (4.06 g, 15.0 mmol) was subjected to **General Procedure F** with $NaBH_4$ (1.42 g, 37.7 mmol) in MeOH (80 mL). The *title compound* was formed as a colourless oil which required no further purification (3.59 g, 88%).

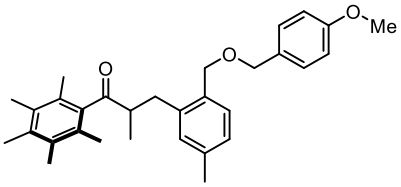
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 8.7, 2.0 Hz, 2H), 7.22 (d, *J* = 1.8 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.10 (dd, *J* = 7.6, 1.9 Hz, 1H), 6.92 – 6.84 (m, 2H), 4.61 (s, 2H), 4.59 (s, 2H), 4.50 (s, 2H), 3.81 (s, 3H), 2.70 (s, 1H), 2.36 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 140.7, 138.9, 133.1, 130.8, 130.4, 129.9, 129.6, 128.6, 114.1, 72.2, 71.1, 64.1, 55.4, 21.2;

IR (film) ν_{max}/cm^{-1} 3395, 2862, 1613, 1586, 1514, 1360, 1302, 1249, 1175, 1035, 822, 760;

HRMS (ESI$^+$) $[C_{17}H_{21}O_3]^+$ ([M+H]$^+$) requires 273.1485; found 273.1484, Δ 0.55 ppm.

S40 3-(2-(((4-Methoxybenzyl)oxy)methyl)-5-methylphenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



Ph* ethyl ketone **S1** (816 mg, 4.00 mmol), alcohol **S39** (2.18 g, 8.00 mmol), $[IrCp^*Cl_2]_2$ (32 mg, 1.0 mol%), KOH (898 mg, 16.0 mmol) and PhMe (1.0 mL, 4.0 M, degassed with Ar) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5 → 90:10) gave the *title compound* as a colourless oil (1.41 g, 69%).

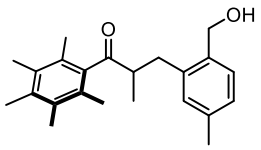
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 3H), 7.02 – 6.97 (m, 2H), 6.88 – 6.82 (m, 2H), 4.43 – 4.36 (m, 2H), 4.35 (s, 2H), 3.80 (s, 3H), 3.27 (dd, *J* = 13.8, 4.5 Hz, 1H), 3.15 – 3.05 (m, 1H), 2.59 (dd, *J* = 13.8, 9.7 Hz, 1H), 2.30 (s, 3H), 2.23 (s, 3H), 2.16 (br s, 6H), 2.09 (br s, 6H), 1.05 (d, *J* = 7.0 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 214.3, 159.3, 139.8, 138.7, 137.6, 135.6, 133.5, 133.2, 131.6, 130.5, 129.9, 129.4, 128.5, 127.2, 113.9, 72.0, 69.8, 55.4, 50.0, 34.3, 21.3, 18.0, 16.9, 16.2, 15.4;

IR (film) ν_{max}/cm^{-1} 2931, 1694, 1614, 1514, 1456, 1248, 1173, 1076, 1037, 825, 763;

HRMS (ESI$^+$) $[C_{31}H_{39}O_3]^+$ ([M+H]$^+$) requires 459.2894; found 459.2892, Δ 0.28 ppm.

11d 3-(2-(Hydroxymethyl)-5-methylphenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



PMB ether **S40** (1.75 g, 3.82 mmol) was dissolved in a mixture of CH_2Cl_2 (36 mL)/water (4 mL) and DDQ (1.30 g, 5.73 mmol) was added at RT. The mixture was stirred at RT for 3 h, quenched with sat. $NaHCO_3$ (20 mL) and diluted with water (20 mL) and CH_2Cl_2 (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 70 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O 95:5 → 70:30) gave the *title compound* as a white solid (643 mg, 50%).

m.p. = 91 – 93 °C;

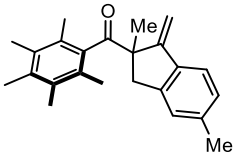
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 7.5 Hz, 1H), 7.05 – 7.00 (m, 2H), 4.71 (d, *J* = 12.1 Hz, 1H), 4.59 (d, *J* = 12.1 Hz, 1H), 3.32 (dd, *J* = 13.9, 5.6 Hz, 1H), 3.24 – 3.12 (m, 1H), 2.65 (dd, *J* = 13.9, 8.6 Hz, 1H), 2.31 (s, 3H), 2.23 (s, 3H), 2.17 (br s, 6H), 2.05 (br s, 6H), 1.11 (d, *J* = 7.1 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 214.6, 139.6, 138.2, 137.6, 136.1, 135.7, 133.3, 131.4, 129.2, 128.4, 127.4, 63.1, 50.2, 34.1, 21.2, 18.0, 16.9, 16.2, 16.1;

IR (film) ν_{max}/cm^{-1} 3348, 2934, 1783, 1746, 1456, 1385, 1306, 1219, 1085, 999, 923;

HRMS (ESI$^+$) $[C_{23}H_{30}NaO_2]^+$ ([M+Na]$^+$) requires 361.2138; found 361.2133, Δ 1.52 ppm.

12d (2,5-Dimethyl-1-methylene-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11d** (102 mg, 0.300 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), Ru-MACHO® (3.6 mg, 1.0 mol%), KO^{t}Bu (68 mg, 0.60 mmol) and ^{t}BuOH (0.6 mL) were subjected to **General Procedure D** at 115 °C for 3 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.2:0.8) gave the *title compound* as a white solid (69 mg, 69%.)

m.p. = 145 – 147 °C;

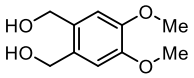
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.8 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.92 (s, 1H), 5.59 (s, 1H), 5.25 (s, 1H), 3.47 (d, *J* = 16.9 Hz, 1H), 2.83 (d, *J* = 16.9 Hz, 1H), 2.31 (s, 3H), 2.19 (s, 3H), 2.17 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H), 1.87 (s, 3H), 1.63 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 215.8, 153.7, 143.5, 139.8, 138.9, 136.9, 135.0, 133.1, 132.6, 128.1, 128.0, 127.7, 125.7, 120.9, 105.2, 59.8, 42.8, 29.1, 21.6, 18.7, 18.3, 16.8, 16.2, 16.1;

IR (film) ν_{max}/cm^{-1} 3021, 1684, 1633, 1609, 1439, 1365, 1301, 1263, 1145, 913, 885, 815;

HRMS (ESI$^+$) $[C_{24}H_{28}ONa]^+$ ([M+Na]$^+$) requires 355.2032; found 355.2023, Δ 0.15 ppm.

S41 (4,5-Dimethoxy-1,2-phenylene)dimethanol



$LiAlH_4$ (854 mg, 22.5 mmol) was added portion-wise to a solution of 5,6-dimethoxyisobenzofuran-1(3*H*)-one (1.46 g, 7.50 mmol) in THF (25 mL). The mixture was heated to reflux for 4 h, cooled to 0 °C, and quenched with sequential dropwise addition of water (0.85 mL), NaOH (15% w/v, 0.85 mL) and water (2.6 mL). The mixture was diluted with $CHCl_3$ (25 mL), Na_2SO_4 was added and the mixture was stirred vigorously for 15 min. The mixture was filtered and concentrated *in vacuo* to give the *title compound* as a pale pink solid, which was used without further purification (990 mg, 66%.)

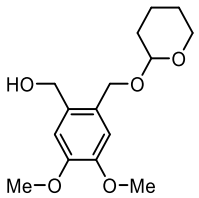
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (s, 2H), 4.69 (s, 4H), 3.90 (s, 6H), 2.47 – 2.22 (m, 2H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.7, 132.1, 113.4 2 × *C*(3), 64.1 2 × *C*(1), 56.2 2 × *C*(5);

m/z (ESI$^+$) Found ([M+Na]$^+$) = 221, $[C_{10}H_{14}NaO_4]$ requires 221;

The spectroscopic data matched that previously reported in the literature. [24]

S42 (4,5-Dimethoxy-2-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)phenyl)methanol



Diol **S41** (990 mg, 5.00 mmol) was suspended in CH_2Cl_2 (10 mL) and 3,4-dihydro-2*H*-pyran (0.22 mL, 2.41 mmol) and pyridinium *p*-toluenesulfonate (61 mg, 0.24 mmol) were added. The mixture was heated at 45 °C for 4 h, cooled to RT and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/EtOAc, 60:40) gave the *title compound* as a colourless oil (345 mg, 51%).

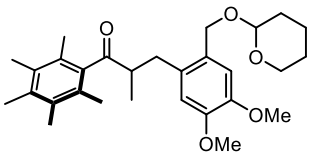
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (s, 1H), 6.88 (s, 1H), 4.84 (d, *J* = 11.5 Hz, 1H), 4.73 (t, *J* = 3.4 Hz, 1H), 4.68 – 4.58 (m, 2H), 4.55 (d, *J* = 11.5 Hz, 1H), 3.93 – 3.84 (m, 7H), 3.62 – 3.52 (m, 1H), 1.87 – 1.67 (m, 2H), 1.67 – 1.48 (m, 4H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.9, 148.4, 133.4, 128.3, 113.8, 113.3, 97.8, 67.7, 63.6, 62.5, 56.2, 56.1, 30.6, 25.4, 19.4;

IR (film) ν_{max}/cm^{-1} 3449, 2943, 1610, 1519, 1466, 1346, 1283, 1210, 1109, 1026, 907;

HRMS (ESI$^+$) $[C_{15}H_{22}NaO_5]^+$ ([M+Na]$^+$) requires 305.1360; found 305.1352, Δ 2.18 ppm.

S43 3-(4,5-Dimethoxy-2-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)phenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



Ph* ethyl ketone **S1** (161 mg, 0.79 mmol), alcohol **S41** (335 mg, 1.19 mmol), $[IrCp^*Cl_2]_2$ (6.3 mg, 1.0 mol%), KOH (177 mg, 3.16 mmol) and PhMe (0.2 mL) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 80:20 → 70:30) gave the *title compound* as a colourless oil (352 mg, 95%, [49:51] d.r.)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (s, 1H), 6.88 (s, 1H), 6.77 – 6.69 (m, 2H), 4.67 (dd, *J* = 18.3, 11.6 Hz, 2H), 4.61 – 4.56 (m, 1H), 4.49 (t, *J* = 3.6 Hz, 1H), 4.40 (dd, *J* = 13.1, 11.6 Hz, 2H), 3.93 – 3.80 (m, 14H), 3.55 – 3.45 (m, 2H), 3.27 (dd, *J* = 13.8, 5.5 Hz, 2H), 3.16 – 3.04 (m, 2H), 2.63 (dt, *J* = 13.7, 8.3 Hz, 2H), 2.23 (2 × s, 6H), 2.17 (s, 12H), 2.03 (s, 12H), 1.86 – 1.73 (m, 2H), 1.72 – 1.43 (m, 10H), 1.09 (2 × d, *J* = 7.1 Hz, 6H);

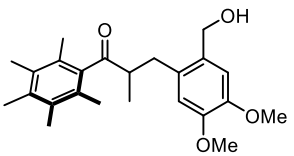
^{13}C NMR (101 MHz, $CDCl_3$) δ 214.3, 214.2, 148.4, 148.3, 147.4, 147.4, 139.8, 139.7, 135.7, 133.3, 131.4, 131.2, 128.6, 128.5, 128.4, 114.3, 114.1, 113.3, 113.0, 98.1, 98.0, 66.7, 66.6, 62.54, 62.53, 56.11, 56.07 50.3, 50.3, 34.2, 34.1, 30.8, 25.6, 19.7, 17.9, 16.9, 16.2, 16.1, 15.7;

IR (film) ν_{max}/cm^{-1} 2945, 1694, 1519, 1465, 1350, 1277, 1203, 1111, 1037, 1022, 870, 815;

HRMS (ESI$^+$) $[C_{29}H_{40}NaO_5]^+$ ([M+Na]$^+$) requires 491.2768; found 491.2755, Δ 2.62 ppm.

N.B. the product was found to decompose slowly in $CDCl_3$

11e 3-(2-(Hydroxymethyl)-4,5-dimethoxyphenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



THP-protected alcohol **S43** (330 mg, 0.700 mmol) was dissolved in MeOH (7 mL). $TsOH{\cdot}H_2O$ (13 mg, 0.07 mmol) was added and the reaction was stirred at RT for 4 h. The mixture was diluted with EtOAc

(20 mL) and water (20 mL), the layers separated and the aqueous layer extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/EtOAc, 90:10 → 70:30) gave the *title compound* as a white solid (126 g, 47%)

m.p. = 138 – 140 °C;

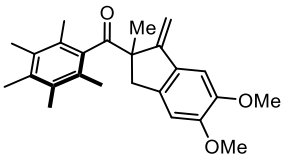
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.94 (s, 1H), 6.76 (s, 1H), 4.75 (d, *J* = 12.1 Hz, 1H), 4.59 (d, *J* = 12.1 Hz, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 3.34 (dd, *J* = 14.0, 6.6 Hz, 1H), 3.19 (h, *J* = 7.2 Hz, 1H), 2.66 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.25 (s, 3H), 2.19 (s, 6H), 2.11 (br s, 3H), 1.96 (br s, 3H), 1.16 (d, *J* = 7.2 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 214.5, 148.4, 147.6, 139.4, 135.9, 133.3, 131.3, 130.6, 128.4 (br.), 113.9, 112.4, 63.0, 56.1, 56.1, 50.6, 33.9, 17.9, 16.9, 16.6, 16.1;

IR (film) ν_{max}/cm^{-1} 3519, 2939, 1693, 1611, 1518, 1466, 1333, 1273, 1127, 1105, 911;

HRMS (ESI$^+$) $[C_{24}H_{32}O_4Na]^+$ ($[M+Na]^+$) requires 407.2193; found 407.2180, Δ 3.11 ppm.

12e (5,6-Dimethoxy-2-methyl-1-methylene-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11e** (58 mg, 0.15 mmol), methyl phenyl sulfone (47 mg, 0.30 mmol), Ru-MACHO® (1.8 mg, 1.0 mol%), KO^{t}Bu (34 mg, 0.30 mmol) and ^{t}BuOH (0.3 mL) were subjected to **General Procedure D** at 115 °C for 3 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 92:8 → 90:10) gave the *title compound* as a white solid (52 mg, 92%.)

m.p. = 160 – 162 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (s, 1H), 6.60 (s, 1H), 5.45 (s, 1H), 5.20 (s, 1H), 3.90 (s, 3H), 3.83 (s, 3H), 3.44 (d, *J* = 16.6 Hz, 1H), 2.82 (d, *J* = 16.6 Hz, 1H), 2.20 (s, 3H), 2.17 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 1.87 (s, 3H), 1.64 (s, 3H);

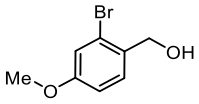
^{13}C NMR (101 MHz, $CDCl_3$) δ 215.8, 154.1, 150.7, 149.0, 139.9, 135.9, 135.0, 133.1, 132.6, 131.8, 128.1, 127.7, 107.3, 103.5, 103.2, 60.1, 56.1, 56.1, 42.8, 29.1, 18.7, 18.3, 16.8, 16.2, 16.1;

IR (film) ν_{max}/cm^{-1} 2998, 1685, 1604, 1503, 1466, 1315, 1271, 1219, 1070, 987, 905;

HRMS (ESI$^+$) $[C_{25}H_{30}NaO_3]^+$ ($[M+Na]^+$) requires 401.2087; found 401.2082, Δ 1.24 ppm.

N.B. the product was found to decompose slowly in $CDCl_3$

S44 (2-Bromo-4-methoxyphenyl)methanol



2-Bromo-4-methoxybenzaldehyde (5.38 g, 25.0 mmol) was dissolved in MeOH (80 mL) and the solution cooled to 0 °C. $NaBH_4$ (1.42 g, 37.5 mmol) was added, the reaction allowed to warm to RT and stirred for 2 h. The reaction was quenched by addition of water (10 mL) and the mixture concentrated *in vacuo*. The residue was diluted with EtOAc (200 mL) and water (200 mL), the layers were separated and the aqueous phase extracted with EtOAc (3 × 200 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give the *title compound* as a colourless oil that required no further purification (5.29 g, 97%.)

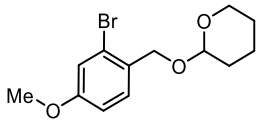
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 1H), 7.11 (d, *J* = 2.6 Hz, 1H), 6.86 (dd, *J* = 8.5, 2.6 Hz, 1H), 4.68 (s, 2H), 3.80 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 131.9, 130.1, 123.4, 118.1, 113.5, 64.8, 55.6;

m/z (ESI$^+$) [$C_8H_{10}{}^{79}BrO_2$] requires 217; mass not found.

The spectroscopic data matched that previously reported in the literature. [25]

S45 2-((2-Bromo-4-methoxybenzyl)oxy)tetrahydro-2*H*-pyran



Alcohol **S44** (5.27 g, 24.3 mmol) was dissolved in CH_2Cl_2 (80 mL) and 3,4-dihydro-2*H*-pyran (3.3 mL, 37 mmol) and pyridinium *p*-toluenesulfonate (611 mg, 2.43 mmol) were added. The mixture was stirred overnight at RT and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99:1 → 94:6) gave the *title compound* as a colourless oil (6.25 g, 85%).

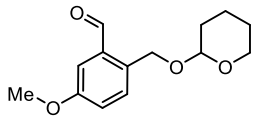
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.34 (m, 1H), 7.11 (d, *J* = 2.6 Hz, 1H), 6.85 (dd, *J* = 8.5, 2.6 Hz, 1H), 4.80 – 4.71 (m, 2H), 4.52 (d, *J* = 12.4 Hz, 1H), 3.98 – 3.89 (m, 1H), 3.79 (s, 3H), 3.60 – 3.52 (m, 1H), 1.95 – 1.81 (m, 1H), 1.81 – 1.46 (m, 5H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 130.5, 129.9, 123.8, 118.1, 113.5, 98.4, 68.5, 62.3, 55.7, 30.7, 25.6, 19.5;

IR (film) ν_{max}/cm^{-1} 2944, 1606, 1570, 1496, 1440, 1241, 1135, 1038, 975, 907, 869;

HRMS (ESI$^+$) [$C_{13}H_{17}{}^{79}BrNaO_3$]$^+$ ([M+Na]$^+$) requires 323.0253; found 323.0251, Δ 0.67 ppm.

S46 5-Methoxy-2-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)benzaldehyde



Aryl bromide **S45** (4.22 g, 14.0 mmol) was subjected to **General Procedure E** using *n*-BuLi (2.5 M in hexanes, 6.8 mL, 16.8 mmol) and *N,N*-dimethylformamide (1.75 mL, 22.6 mmol) in THF (50 mL). Purification *via* flash column chromatography (eluent Pentane/Et_2O, 92:8 → 80:20) gave the *title compound* as a colourless oil (3.21 g, 92%).

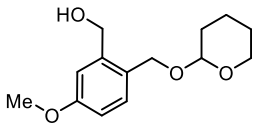
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 (s, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.41 (d, *J* = 2.8 Hz, 1H), 7.11 (dd, *J* = 8.4, 2.8 Hz, 1H), 5.13 – 5.05 (m, 1H), 4.82 (d, *J* = 12.8 Hz, 1H), 4.73 (dd, *J* = 4.2, 2.9 Hz, 1H), 3.86 (s, 4H), 3.60 – 3.50 (m, 1H), 1.92 – 1.77 (m, 1H), 1.73 (tdd, *J* = 9.2, 4.0, 2.9 Hz, 1H), 1.67 – 1.49 (m, 4H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.1, 159.6, 135.2, 133.1, 131.2, 120.4, 114.2, 98.3, 65.8, 62.6, 55.7, 30.7, 25.5, 19.6;

IR (film) ν_{max}/cm^{-1} 2945, 1693, 1610, 1575, 1503, 1318, 1282, 1258, 1027;

HRMS (ESI$^+$) $[C_{14}H_{18}O_4Na]^+$ ([M+Na]$^+$) requires 273.1079; found 273.1089, Δ 2.88 ppm.

S47 (5-Methoxy-2-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)phenyl)methanol



Aldehyde **S46** (3.10 g, 12.4 mmol) was subjected to **General Procedure F** with $NaBH_4$ (703 mg, 18.6 mmol) in MeOH (40 mL). The *title compound* was formed as a colourless oil that required no further purification (3.13 g, 100%.)

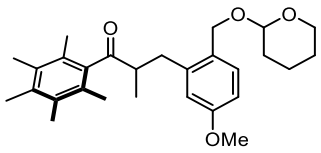
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.3 Hz, 1H), 6.97 (d, *J* = 2.8 Hz, 1H), 6.81 (dd, *J* = 8.3, 2.7 Hz, 1H), 4.85 (d, *J* = 11.4 Hz, 1H), 4.72 (t, *J* = 3.4 Hz, 1H), 4.71 – 4.61 (m, 2H), 4.54 (d, *J* = 11.4 Hz, 1H), 3.89 (ddd, *J* = 11.5, 8.2, 3.1 Hz, 1H), 3.82 (s, 3H), 3.62 – 3.53 (m, 1H), 1.86 – 1.67 (m, 2H), 1.67 – 1.45 (m, 4H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 142.2, 132.0, 128.0, 115.4, 113.1, 97.8, 67.6, 64.0, 62.5, 55.5, 30.6, 25.4, 19.4;

IR (film) ν_{max}/cm^{-1} 3453, 2945, 2870, 1613, 1582, 1265, 1120, 1035;

HRMS (ESI$^+$) $[C_{14}H_{20}O_4Na]^+$ ([M+Na]$^+$) requires 275.1254; found 275.1250, Δ 1.29 ppm.

S48 3-(5-Methoxy-2-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)phenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



Ph* ethyl ketone **S1** (714 mg, 3.50 mmol), alcohol **S47** (1.76 g, 7.00 mmol), $[IrCp^*Cl_2]_2$ (32 mg, 1.0 mol%), KOH (898 mg, 16.0 mmol) and PhMe (1.0 mL) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5 → 75:25) gave the *title compound* as a pale-yellow oil (1.12 g, 73%, [45:55]).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.16 (m, 2H), 6.76 – 6.60 (m, 4H), 4.71 – 4.59 (m, 2H), 4.57 (t, *J* = 3.6 Hz, 1H), 4.42 (t, *J* = 3.5 Hz, 1H), 4.40 – 4.29 (m, 2H), 3.84 (dddd, *J* = 11.5, 8.6, 5.4, 3.3 Hz, 2H), 3.75 (s, 6H), 3.47 (dd, *J* = 10.9, 5.1 Hz, 2H), 3.27 (ddd, *J* = 13.8, 4.7, 2.1 Hz, 2H), 3.18 – 3.04 (m, 2H), 2.63 (dt, *J* = 13.7, 9.3 Hz, 2H), 2.20 (2 × s, 6H), 2.15 (d, *J* = 2.3 Hz, 12H), 2.11 – 1.92 (m, 12H), 1.83 – 1.72 (m, 2H), 1.72 – 1.34 (m, 10H), 1.06 (d, *J* = 7.0 Hz, 6H);

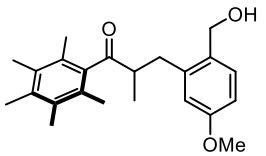
^{13}C NMR (101 MHz, $CDCl_3$) δ 214.3, 214.2, 159.3, 159.2, 140.6, 140.4, 139.8, 139.7, 135.7, 133.2, 131.5, 131.3, 128.8, 128.6, 128.5, 116.7, 116.4, 111.54, 111.46, 97.9, 97.7, 66.6, 66.5, 62.3, 62.3, 55.4, 49.9, 49.8, 34.7, 34.5, 30.7, 25.6, 19.6, 18.0, 16.9, 16.2, 15.7, 15.3;

IR (film) ν_{max}/cm^{-1} 2936, 1695, 1613, 1579, 1504, 1464, 1262, 1114, 1011, 902;

HRMS (ESI^+) $[C_{28}H_{39}O_4]^+$ ($[M+H]^+$) requires 439.2843; found 439.2843, Δ 0.10 ppm.

N.B. the product was found to decompose slowly in $CDCl_3$.

11f 3-(2-(Hydroxymethyl)-5-methoxyphenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



THP-protected alcohol **S48** (1.11 g, 2.53 mmol) was dissolved in THF (20 mL) and aqueous HCl (3 M, 5 mL) was added. The mixture was stirred at RT for 16 h and was diluted with water (20 mL) and EtOAc (30 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2 × 30 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 70:30 → 60:40) gave the *title compound* as a colourless oil (231 mg, 26%.)

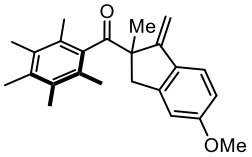
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.2 Hz, 1H), 6.78 – 6.71 (m, 2H), 4.68 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 3.79 (s, 3H), 3.34 (dd, *J* = 13.9, 5.7 Hz, 1H), 3.24 – 3.15 (m, 1H), 2.67 (dd, *J* = 13.9, 8.5 Hz, 1H), 2.23 (s, 3H), 2.17 (s, 6H), 2.13 – 1.93 (m, 6H), 1.12 (d, *J* = 7.2 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 214.4, 159.3, 140.1, 139.5, 135.8, 133.3, 131.5, 130.8, 128.4, 116.5, 111.7, 62.9, 55.4, 50.2, 34.3, 18.0, 16.9, 16.1;

IR (film) ν_{max}/cm^{-1} 3438, 2944, 1689, 1611, 1579, 1502, 1309, 1260, 1162, 1051, 921;

HRMS (ESI$^+$) $[C_{23}H_{30}NaO_3]^+$ ([M+Na]$^+$) requires 377.2087; found 377.2078, Δ 2.37 ppm.

12f (5-Methoxy-2-methyl-1-methylene-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11f** (53 mg, 0.15 mmol), methyl phenyl sulfone (47 mg, 0.30 mmol), Ru-MACHO® (1.8 mg, 1.0 mol%), KO^{t}Bu (34 mg, 0.30 mmol) and ^{t}BuOH (0.3 mL) were subjected to **General Procedure D** at 115 °C for 3 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 98.8:1.2 → 98.4:1.6) gave the *title compound* as a white solid (43 mg, 82%.)

m.p. = 158 – 160 °C;

^{1}H NMR (400 MHz, C_6D_6) δ 7.24 (d, *J* = 8.5 Hz, 1H), 6.72 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.43 – 6.35 (m, 1H), 5.55 (s, 1H), 5.53 (s, 1H), 3.61 (d, *J* = 17.0 Hz, 1H), 3.20 (s, 3H), 2.69 (d, *J* = 17.0 Hz, 1H), 2.03 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 1.94 (s, 3H), 1.78 (s, 3H), 1.73 (s, 3H);

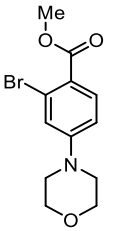
^{13}C NMR (101 MHz, C_6D_6) δ 214.3, 161.3, 154.1, 145.4, 140.6, 134.7, 133.2, 132.8, 132.5, 128.2, 127.9, 122.4, 114.7, 109.4, 103.7, 60.1, 54.8, 43.1, 29.3, 18.7, 18.5, 16.6, 16.0;

IR (film) ν_{max}/cm^{-1} 3052, 1730, 1682, 1604, 1493, 1304, 1258, 1150, 908, 883, 838;

HRMS (ESI$^+$) $[C_{24}H_{28}NaO_2]^+$ ([M+Na]$^+$) requires 371.1982; found 371.1974, Δ 1.90 ppm.

N.B. the product was found to decompose slowly in $CDCl_3$

S49 Methyl 2-Bromo-4-morpholinobenzoate



Methyl 2-bromo-4-fluorobenzoate (5.00 g, 21.4 mmol) and morpholine (9.4 mL, 110 mmol) were dissolved in DMSO (20 mL) and the mixture was heated to 120 °C for 2 h. The mixture was cooled to RT, diluted with water (100 mL) and EtOAc (100 mL) and the layers separated. The aqueous layer was extracted with EtOAc (2 × 100 mL) and the combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/EtOAc, 85:15 → 80:20) gave the *title compound* as a colourless oil (5.23 g, 78%.)

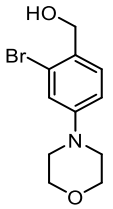
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.8 Hz, 1H), 7.10 (d, *J* = 2.6 Hz, 1H), 6.78 (dd, *J* = 8.9, 2.6 Hz, 1H), 3.87 (s, 3H), 3.86 – 3.80 (m, 4H), 3.32 – 3.22 (m, 4H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 153.8, 133.3, 124.4, 120.5, 119.8, 112.4, 66.6, 52.1, 47.6;

m/z (ESI$^+$) Found ([M+H]$^+$) = 300, [$C_{12}H_{15}{}^{79}BrNO_3$] requires 300.

The spectroscopic data were consistent with that reported in the literature. [26]

S50 (2-Bromo-4-morpholinophenyl)methanol



Methyl Ester **S49** (5.20 g, 17.3 mmol) was dissolved in THF (80 mL) and cooled to 0 °C. $LiAlH_4$ (657 mg, 17.3 mmol) was added and the mixture was warmed to RT and stirred for 1 h. The reaction was cooled to 0 °C and quenched by sequential dropwise addition of H_2O (0.66 mL), aq. NaOH (15% w/v, 0.66 mL) and H_2O (2.0 mL). $MgSO_4$ was added, the resulting suspension stirred vigorously for 15 min and then filtered and concentrated *in vacuo*. Purification *via* column chromatography (Pentane/EtOAc, 80:20 → 75:25) gave the *title compound* as a colourless oil (3.80 g, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 2.4 Hz, 1H), 6.85 (dd, *J* = 8.5, 2.5 Hz, 1H),

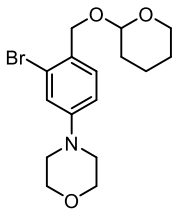
4.66 (s, 2H), 3.97 – 3.74 (m, 4H), 3.23 – 3.02 (m, 4H), 1.97 (s, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.9, 130.9, 130.2, 124.1, 119.5, 114.7, 66.8, 64.9, 49.0;

IR (film) ν_{max}/cm^{-1} 3431, 2829, 1605, 1552, 1498, 1450, 1380, 1232, 1121, 942, 761;

HRMS (ESI$^+$) $[C_{11}H_{15}{}^{79}BrNO_2]^+$ ([M+H]$^+$) requires 272.0281; found 272.0277, Δ 1.33 ppm.

S51 4-(3-Bromo-4-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)phenyl)morpholine



Alcohol **S50** (3.78 g, 13.9 mmol) was dissolved in CH_2Cl_2 (50 mL) and 3,4-dihydro-2*H*-pyran (1.9 mL, 21 mmol) and pyridinium *p*-toluenesulfonate (349 mg, 1.39 mmol) was added. The reaction was stirred at RT for 16 h, filtered through a SiO_2 plug (CH_2Cl_2/Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (Pentane/EtOAc, 95:5 → 90:10) gave the *title compound* as a colourless oil (2.30 g, 46%).

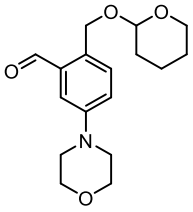
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.5 Hz, 1H), 7.08 (d, *J* = 2.5 Hz, 1H), 6.84 (dd, *J* = 8.5, 2.5 Hz, 1H), 4.80 – 4.72 (m, 2H), 4.51 (d, *J* = 12.3 Hz, 1H), 3.98 – 3.89 (m, 1H), 3.89 – 3.80 (m, 4H), 3.63 – 3.51 (m, 1H), 3.18 – 3.07 (m, 4H), 1.95 – 1.81 (m, 1H), 1.80 – 1.46 (m, 5H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 130.5, 128.7, 124.4, 119.5, 114.6, 98.3, 68.5, 66.8, 62.3, 49.1, 30.7, 25.6, 19.5;

IR (film) ν_{max}/cm^{-1} 2947, 2856, 1605, 1553, 1500, 1450, 1230, 1122, 1035, 943, 907, 869, 812;

HRMS (ESI$^+$) $[C_{16}H_{22}{}^{79}BrNaNO_3]^+$ ([M+Na]$^+$) requires 378.0675; found 378.0674, Δ 0.31 ppm.

S52 5-Morpholino-2-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)benzaldehyde



Aryl bromide **S51** (2.28 g, 6.39 mmol) was subjected to **General Procedure E** using *n*-BuLi (2.5 M in hexanes, 3.1 mL, 7.66 mmol) and *N,N*-dimethylformamide (1.0 mL, 13.0 mmol) in THF (21 mL). Purification *via* flash column chromatography (eluent Pentane/EtOAc, 88:12 → 80:20) gave the *title compound* as a yellow oil (1.37 g, 70%).

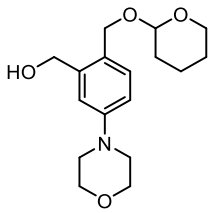
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.32 (s, 1H), 7.54 – 7.33 (m, 2H), 7.19 – 7.02 (m, 1H), 5.08 (d, *J* = 12.8 Hz, 1H), 4.81 (d, *J* = 12.8 Hz, 1H), 4.73 (t, *J* = 3.6 Hz, 1H), 4.00 – 3.77 (m, 5H), 3.63 – 3.51 (m, 1H), 3.29 – 3.14 (m, 4H), 1.83 (ddt, *J* = 12.6, 7.6, 4.5 Hz, 1H), 1.73 (ddt, *J* = 13.1, 9.6, 3.4 Hz, 1H), 1.66 – 1.44 (m, 4H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 192.5, 150.8, 134.9, 132.2, 131.0, 120.9, 116.8, 98.3, 66.7, 65.9, 62.6, 49.3, 30.7, 25.6, 19.6;

IR (film) ν_{max}/cm^{-1} 2948, 2855, 1693, 1606, 1508, 1348, 1245, 1123, 1034, 969, 886, 765;

HRMS (ESI$^+$) $[C_{17}H_{24}NO_4]^+$ ([M+H]$^+$) requires 306.1700; found 306.1700, Δ 0.12 ppm.

S53 (5-Morpholino-2-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)phenyl)methanol



Aldehyde **S52** (1.36 g, 4.45 mmol) was subjected to **General Procedure F** with $NaBH_4$ (252 mg, 6.67 mmol) in MeOH (15 mL). The *title compound* was formed as a colourless oil that required no further purification (1.36 g, 99%.)

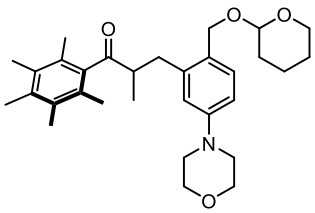
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 1H), 6.97 (d, *J* = 2.7 Hz, 1H), 6.81 (dd, *J* = 8.4, 2.6 Hz, 1H), 4.84 (d, *J* = 11.4 Hz, 1H), 4.73 (t, *J* = 3.5 Hz, 1H), 4.68 (dd, *J* = 12.2, 6.1 Hz, 1H), 4.62 (dd, *J* = 12.2, 6.6 Hz, 1H), 4.52 (d, *J* = 11.4 Hz, 1H), 3.94 – 3.81 (m, 5H), 3.63 – 3.50 (m, 1H), 3.24 (t, *J* = 6.5 Hz, 1H), 3.21 – 3.13 (m, 4H), 1.85 – 1.66 (m, 2H), 1.66 – 1.47 (m, 4H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.7, 141.7, 131.8, 127.0, 117.0, 114.5, 97.7, 67.7, 67.0, 64.4, 62.4, 49.2, 30.6, 25.4, 19.4;

IR (film) ν_{max}/cm^{-1} 3408, 2943, 2858, 1725, 1613, 1506, 1451, 1240, 1118, 1023, 759;

HRMS (ESI$^+$) $[C_{17}H_{26}NO_4]^+$ ([M+H]$^+$) requires 308.1856; found 308.1852, Δ 1.39 ppm.

S54 2-Methyl-3-(5-morpholino-2-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)phenyl)-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



Ph* ethyl ketone **S1** (592 mg, 2.90 mmol), alcohol **S53** (1.34 g, 4.36 mmol), $[IrCp^*Cl_2]_2$ (23 mg, 1.0 mol%), KOH (651 mg, 11.6 mmol) and PhMe (0.73 mL) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 85:15 → 70:30) gave the *title compound* as a pale yellow oil (952 mg, 66%, [46:54] d.r.)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.20 (m, 2H), 6.85 – 6.71 (m, 4H), 4.69 (d, *J* = 11.6 Hz, 1H), 4.64 (d, *J* = 11.4 Hz, 1H), 4.59 (t, *J* = 3.6 Hz, 1H), 4.45 (t, *J* = 3.5 Hz, 1H), 4.38 (d, *J* = 11.6 Hz, 1H), 4.34 (d, *J* = 11.4 Hz, 1H), 3.93 – 3.76 (m, 10H), 3.56 – 3.46 (m, 2H), 3.41 – 3.28 (m, 2H), 3.20 – 3.04 (m, 10H), 2.74 – 2.57 (m, 2H), 2.23 (s, 3H), 2.23 (s, 3H), 2.17 (s, 12H), 1.98 (br s, 12H), 1.84 – 1.76 (m, 2H), 1.70 – 1.42 (m, 10H), 1.10 (2 × d, *J* = 7.0 Hz, 6H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 214.3, 214.2, 151.04, 150.95, 140.1, 139.9, 139.8, 139.7, 135.7, 133.2, 131.3, 131.1, 128.5, 128.0, 127.8, 118.6, 118.3, 113.6, 113.6, 97.8, 97.7, 67.0, 66.7, 66.6, 62.3, 62.2, 50.0, 49.9, 49.5, 35.0, 34.8, 30.7, 25.6, 19.6, 19.6, 17.9, 16.9, 16.2, 16.1, 15.7;

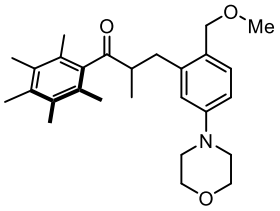
Fewer peaks than expected in 13C spectrum due to overlapping peaks

IR (film) ν_{max}/cm^{-1} 2948, 1693, 1612, 1452, 1237, 1122, 1022, 975;

HRMS (ESI^+) $[C_{31}H_{44}NO_4]^+$ ($[M+H]^+$) requires 494.3265; found 494.3250, Δ 3.05 ppm.

N.B. the product was found to decompose slowly in $CDCl_3$

S55 3-(2-(Methoxymethyl)-5-morpholinophenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



THP-protected alcohol **S54** (927 mg, 1.88 mmol) was dissolved in MeOH:water (18 mL: 2 mL) and *p*-toluenesulfonic acid monohydrate (393 mg, 2.07 mmol) was added. The mixture was stirred at RT for 16 h, then heated to 65 °C for 2 h. The mixture was cooled to RT, quenched with the addition of $NaHCO_3$ (10 mL) and diluted with EtOAc (50 mL) and water (40 mL). The layers were separated and the aqueous

phase extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 80:20 → 70:30) gave the *title compound* as a white solid (583 mg, 73%).

m.p. = 114 – 116 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.4 Hz, 1H), 6.78 (s, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 4.34 – 4.20 (m, 2H), 3.85 (t, *J* = 4.7 Hz, 4H), 3.32 (dd, *J* = 13.4, 5.0 Hz, 1H), 3.25 (s, 3H), 3.20 – 3.07 (m, 5H), 2.59 (dd, *J* = 13.6, 8.9 Hz, 1H), 2.23 (s, 3H), 2.17 (br s, 6H), 2.05 (br s, 6H), 1.11 (d, *J* = 7.1 Hz, 3H);

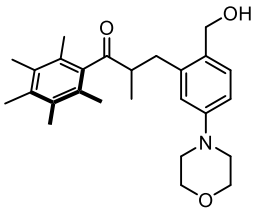
^{13}C NMR (151 MHz, $CDCl_3$) δ 214.3, 151.1, 140.1, 139.8, 135.7, 133.2, 131.1, 128.5, 127.9, 118.5, 113.6, 72.6, 67.0, 58.0, 50.2, 49.5, 35.0, 17.9, 16.9, 16.2, 15.9;

IR (film) ν_{max}/cm^{-1} 2859, 1693, 1610, 1509, 1452, 1380, 1242, 1123, 1088, 971, 925, 890;

HRMS (ESI$^+$) $[C_{27}H_{37}NNaO_3]^+$ ([M+Na]$^+$) requires 446.2666; found 446.2662, Δ 0.82 ppm.

N.B. the product was found to decompose slowly in $CDCl_3$

11g 3-(2-(Hydroxymethyl)-5-morpholinophenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



Methyl ether **S55** (500 mg, 1.18 mmol) was dissolved in THF: water (15 mL: 10 mL) and *p*-toluenesulfonic acid monohydrate (449 mg, 2.36 mmol) was added. The mixture was stirred at RT for 24 h. The reaction was quenched with the addition of sat. aq. $NaHCO_3$ (20 mL), and diluted with EtOAc (20 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2 × 20 mL). The combined aqueous phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 80:20 → 60:40) gave the *title compound* as a white solid (256 mg, 53%).

m.p. = 55 – 57 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.3 Hz, 1H), 6.79 (s, 2H), 4.67 (dd, *J* = 12.0, 4.0 Hz, 1H), 4.56 (dd, *J* = 12.0, 5.1 Hz, 1H), 3.86 (t, *J* = 4.8 Hz, 4H), 3.36 (dd, *J* = 13.7, 6.1 Hz, 1H), 3.24 – 3.16 (m, 1H), 3.16 – 3.10 (m, 4H), 2.67 (dd, *J* = 13.7, 7.9 Hz, 1H), 2.23 (s, 3H), 2.16 (s, 6H), 2.01 (s, 6H), 1.13 (d, *J* = 7.2 Hz, 3H);

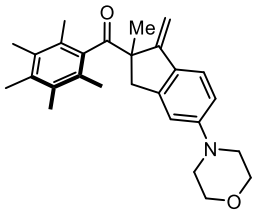
^{13}C NMR (126 MHz, $CDCl_3$) δ 214.4, 151.0, 139.5, 139.5, 135.8, 133.3, 130.8, 130.5, 128.4, 118.2, 113.9, 67.0, 62.9, 50.2, 49.5, 34.6, 17.9, 16.8, 16.4, 16.1;

IR (film) ν_{max}/cm^{-1} 3458, 2979, 1692, 1610, 1507, 1452, 1267, 1240, 1122, 912;

HRMS (ESI$^+$) $[C_{26}H_{35}NNaO_3]^+$ ([M+Na]$^+$) requires 432.2509; found 432.2503, Δ 1.35 ppm.

N.B. the product was found to decompose slowly in $CDCl_3$

12g (2-Methyl-1-methylene-5-morpholino-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11g** (123 mg, 0.300 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), Ru-MACHO® (3.6 mg, 1.0 mol%), KO^{t}Bu (68 mg, 0.60 mmol) and ^{t}BuOH (0.6 mL) were subjected to **General Procedure D** at 115 °C for 3 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 90:10 ⟶ 88:12) gave the *title compound* as an off-white solid (51 mg, 42%.)

m.p. = 155 – 157 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.5 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 6.62 (s, 1H), 5.48 (s, 1H), 5.16 (s, 1H), 3.92 – 3.75 (m, 4H), 3.46 (d, *J* = 16.8 Hz, 1H), 3.18 – 3.07 (m, 4H), 2.83 (d, *J* = 16.8 Hz, 1H), 2.19 (s, 3H), 2.17 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H), 1.88 (s, 3H), 1.63 (s, 3H);

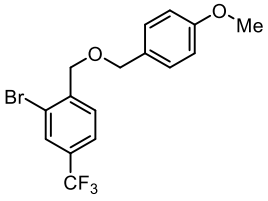
^{13}C NMR (151 MHz, $CDCl_3$) δ 215.7, 153.4, 152.3, 144.8, 139.8, 135.0, 133.1, 132.6, 131.8, 128.1, 127.7, 121.9, 115.1, 111.2, 103.5, 67.0, 60.0, 49.5, 43.1, 29.1, 18.7, 18.3, 16.8, 16.2, 16.1;

IR (film) ν_{max}/cm^{-1} 2852, 1689, 1608, 1499, 1450, 1243, 1123, 1041, 964, 883;

HRMS (ESI$^+$) $[C_{27}H_{33}NNaO_2]^+$ ([M+Na]$^+$) requires 426.2404; found 426.2399, Δ 1.14 ppm.

N.B. the product was found to decompose slowly in $CDCl_3$

S56 2-Bromo-1-(((4-methoxybenzyl)oxy)methyl)-4-(trifluoromethyl)benzene



NaH (60% in mineral oil, 864 mg, 21.6 mmol) was added portion-wise to a solution of (2-bromo-4-(trifluoromethyl)phenyl)methanol (5.00 g, 19.6 mmol) in DMF (20 mL) at 0 °C and the mixture was stirred for 30 min. 4-Methoxybenzyl chloride (2.9 mL, 21 mmol) was added, the mixture warmed to

RT and stirred for 2 h. The reaction was quenched with the addition of sat. aq. NH_4Cl (15 mL) and the mixture was diluted with Et_2O (150 mL) and water (150 mL). The layers were separated and the aqueous phase extracted with Et_2O (2 × 150 mL). The combined organic phases were washed with brine (3 × 100 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane → Pentane/ Et_2O 95:5) gave the *title compound* as a colourless oil (6.54 g, 89%.)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 – 7.78 (m, 1H), 7.67 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.58 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.36 – 7.29 (m, 2H), 6.97 – 6.83 (m, 2H), 4.62 (s, 2H), 4.60 (s, 2H), 3.82 (s, 3H);

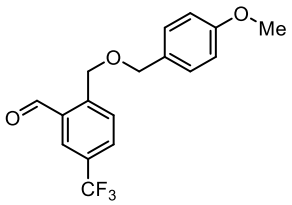
^{13}C NMR (151 MHz, $CDCl_3$) δ 159.6, 142.2, 131.1 (q, J^2_{C-F} = 32.9 Hz), 129.9, 129.6, 129.4 (q, J^3_{C-F} = 3.8 Hz), 129.1, 124.4 (q, J^3_{C-F} = 3.7 Hz), 123.4 (q, J^1_{C-F} = 272.5 Hz), 122.4, 114.1, 72.9, 70.9, 55.4;

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.6;

IR (film) ν_{max}/cm^{-1} 2838, 1614, 1515, 1323, 1251, 1173, 1132, 1078, 1040, 833;

HRMS (ESI$^+$) $[C_{16}H_{14}{}^{79}BrF_3NaO_2]^+$ ([M+Na]$^+$) requires 397.0022; found 397.0014, Δ 1.88 ppm.

S57 2-(((4-Methoxybenzyl)oxy)methyl)-5-(trifluoromethyl)benzaldehyde



Aryl Bromide **S56** (5.00 g, 13.3 mmol) was subjected to **General Procedure E** using *n*-BuLi (2.5 M in hexanes, 6.4 mL, 16.0 mmol) and *N,N*-dimethylformamide (1.65 mL, 21.3 mmol) in THF (45 mL). Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5 → 90:10) gave the *title compound* as a colourless oil (3.13 g, 73%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.11 (d, *J* = 1.8 Hz, 1H), 7.91 – 7.70 (m, 2H), 7.35 – 7.28 (m, 2H), 6.95 – 6.84 (m, 2H), 4.98 (s, 2H), 4.61 (s, 2H), 3.82 (s, 3H);

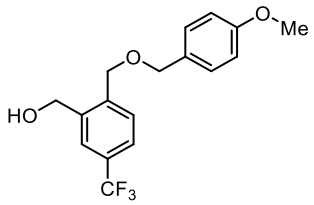
^{13}C NMR (151 MHz, $CDCl_3$) δ 191.5, 159.6, 145.1, 133.7, 130.5 (q, J^2_{C-F} = 33.5 Hz), 130.3 (q, J^3_{C-F} = 3.6 Hz), 129.8, 129.6, 129.2 (q, J^3_{C-F} = 3.8 Hz), 129.0, 123.7 (q, J^1_{C-F} = 272.3 Hz), 114.1, 73.0, 68.9, 55.4;

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.8;

IR (film) ν_{max}/cm^{-1} 2839, 1707, 1615, 1515, 1333, 1250, 1179, 1132, 1082, 1036, 846;

HRMS (ESI$^+$) $[C_{17}H_{15}F_3NaO_3]^+$ ([M+Na]$^+$) requires 347.0866; found 347.0860, Δ 1.69 ppm.

S58 (2-(((4-Methoxybenzyl)oxy)methyl)-5-(trifluoromethyl)phenyl)methanol



Aldehyde **S57** (3.13 g, 9.65 mmol) was subjected to **General Procedure F** with $NaBH_4$ (548 mg, 14.5 mmol) in MeOH (28 mL). The *title compound* was formed as a colourless oil that required no further purification (3.12 g, 99%.)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 – 7.67 (m, 1H), 7.55 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.31 – 7.25 (m, 2H), 6.93 – 6.87 (m, 2H), 4.69 (s, 2H), 4.63 (s, 2H), 4.53 (s, 2H), 3.81 (s, 3H);

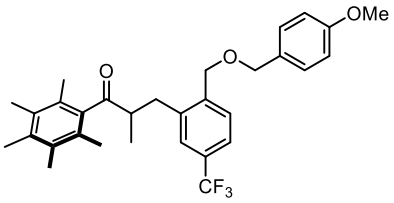
^{13}C NMR (151 MHz, $CDCl_3$) δ 159.7, 141.1, 139.9, 130.9 (q, $J^2_{C–F}$ = 32.4 Hz), 130.1, 129.9, 129.2, 126.1 (q, $J^3_{C–F}$ = 3.8 Hz), 124.8 (q, $J^3_{C–F}$ = 3.8 Hz), 124.5 (q, $J^1_{C–F}$ = 272.5 Hz), 114.2, 72.7, 70.2, 63.2, 55.4;

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.6;

IR (film) ν_{max}/cm^{-1} 3446, 2839, 1614, 1515, 1332, 1251, 1167, 1127, 1081, 1037, 837;

HRMS (ESI$^+$) $[C_{17}H_{17}NaF_3O_3]^+$ ([M+Na]$^+$) requires 349.1022; found 349.1017, Δ 1.31 ppm.

S59 3-(2-(((4-Methoxybenzyl)oxy)methyl)-5-(trifluoromethyl)phenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



Ph* ethyl ketone **S1** (816 mg, 4.00 mmol), alcohol **S58** (2.61 g, 8.00 mmol), $[IrCp^*Cl_2]_2$ (32 mg, 1.0 mol%), KOH (898 mg, 16.0 mmol) and PhMe (1.0 mL) were subjected to **General Procedure A** at 110 °C for 24 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 94:6 → 85:15) gave the *title compound* as a pale-yellow oil (1.41 g, 69%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.0 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.26 – 7.23 (m, 2H), 6.91 – 6.85 (m, 2H), 4.52 (s, 2H), 4.45 (s, 2H), 3.81 (s, 3H), 3.32 (dd, *J* = 14.0, 5.1 Hz, 1H), 3.16 – 2.96 (m, 1H), 2.68 (dd, *J* = 14.0, 9.1 Hz, 1H), 2.23 (s, 3H), 2.17 (br s, 6H), 1.95 (br s, 6H), 1.07 (d, *J* = 7.1 Hz, 3H);

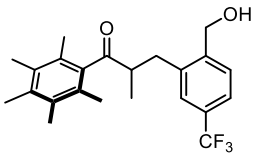
^{13}C NMR (151 MHz, $CDCl_3$) δ 213.5, 159.5, 140.6, 139.4, 139.3, 135.9, 133.3, 130.0, 129.9 (q, $J^2_{C–F}$ = 32.2 Hz), 129.5, 129.5, 128.4, 127.2 (q, $J^3_{C–F}$ = 3.7 Hz), 126.1 (q, $J^1_{C–F}$ = 273.1 Hz), 123.3 (q, $J^3_{C–F}$ = 3.5 Hz), 114.0, 72.6, 69.1, 55.4, 49.7 34.1, 18.0, 16.9, 16.1, 15.7;

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.53;

IR (film) ν_{max}/cm^{-1} 2910, 1696, 1614, 1514, 1333, 1250, 1165, 1126, 1084, 1038, 911, 834;

HRMS (ESI$^+$) $[C_{31}H_{35}F_3NaO_3]^+$ ([M+Na]$^+$) requires 535.2431; found 535.2419, Δ 2.19 ppm.

11h 3-(2-(Hydroxymethyl)-5-(trifluoromethyl)phenyl)-2-methyl-1-(2,3,4,5,6-pentamethylphenyl)propan-1-one



Ketone **S59** (1.40 g, 2.73 mmol) was dissolved in a mixture of CH_2Cl_2:water (24 mL: 3 mL) and DDQ (931 mg, 4.10 mmol) was added at RT. The mixture was stirred at RT for 3 h, quenched with sat. aq. $NaHCO_3$ (20 mL) and diluted with water (20 mL) and CH_2Cl_2 (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O 80:20 → 65:35) gave the *title compound* as a white solid (674 mg, 63%).

m.p. = 101 – 103 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.9 Hz, 1H), 7.51 – 7.43 (m, 2H), 4.88 (d, *J* = 12.9 Hz, 1H), 4.72 (d, *J* = 12.9 Hz, 1H), 3.39 (dd, *J* = 14.1, 6.6 Hz, 1H), 3.29 – 3.14 (m, 1H), 2.71 (dd, *J* = 14.1, 7.7 Hz, 1H), 2.23 (s, 3H), 2.16 (s, 6H), 2.12 – 1.74 (br s, 6H), 1.14 (d, *J* = 7.2 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 214.1, 142.9, 139.1, 138.8, 136.0, 133.4, 129.9 (q, J^2_{C-F} = 32.2 Hz), 129.1, 128.4, 127.1 (q, J^3_{C-F} = 3.6 Hz), 124.3 (q, J^1_{C-F} = 271.8 Hz), 123.5 (q, J^3_{C-F} = 3.4 Hz), 62.6, 50.0, 33.8, 17.9, 16.9, 16.5, 16.1;

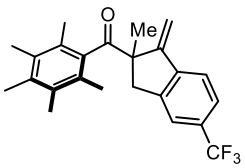
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.6;

IR (film) ν_{max}/cm^{-1} 3446, 2936, 1694, 1457, 1421, 1333, 1164, 1126, 1082, 913;

m/z (ESI$^+$) Found ([M+H]$^+$) = 393, $[C_{23}H_{28}F_3O_2]$ requires 393;

HRMS (ESI$^+$) $[C_{23}H_{28}F_3O_2]^+$ ([M+H]$^+$) requires 393.2036; found 393.2027, Δ 2.20 ppm.

12h (2-Methyl-1-methylene-5-(trifluoromethyl)-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11h** (118 mg, 0.300 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), Ru-MACHO® (3.6 mg, 1.0 mol%), KO^{t}Bu (68 mg, 0.60 mmol) and ^{t}BuOH (0.6 mL) were subjected to **General Procedure**

D at 115 °C for 3 h. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.3:0.7) gave the *title compound* as a white solid (50 mg, 43%.)

m.p. = 126 – 128 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.36 (s, 1H), 5.78 (s, 1H), 5.45 (s, 1H), 3.54 (d, *J* = 17.1 Hz, 1H), 2.92 (d, *J* = 17.1 Hz, 1H), 2.20 (s, 3H), 2.17 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.83 (s, 3H), 1.66 (s, 3H);

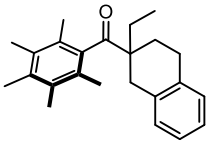
^{13}C NMR (151 MHz, $CDCl_3$) δ 214.9, 152.6, 143.7, 142.9, 139.2, 135.4, 133.3, 132.9, 130.8 (q, $J^2_{C–F}$ = 32.0 Hz), 128.0, 127.5, 124.4 (q, $J^1_{C–F}$ = 271.9 Hz), 124.1 (q, $J^3_{C–F}$ = 3.8 Hz), 122.2 (q, $J^3_{C–F}$ = 4.0 Hz), 121.3, 109.0, 59.9, 42.6, 28.8, 18.8, 18.4, 16.8, 16.2, 16.1;

^{19}F NMR (471 MHz, $CDCl_3$) δ -62.2;

IR (film) ν_{max}/cm^{-1} 2935, 1691, 1433, 1335, 1322, 1167, 1127, 1079, 990, 914, 842;

HRMS (ESI$^+$) $[C_{24}H_{25}F_3NaO]^+$ ([M+Na]$^+$) requires 409.1750; found 409.1747, Δ 0.56 ppm.

13b (2-Ethyl-1,2,3,4-tetrahydronaphthalen-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11b** (101 mg, 0.30 mmol), ethyl phenyl sulfone (94 mg, 0.60 mmol), $[IrCp^*Cl_2]_2$ (4.8 mg, 2.0 mol%) and KOH (67 mg, 1.2 mmol) were added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and back-filled with Ar (3 times) and PhMe (0.6 mL, degassed with Ar (balloon)) was added. The reaction was heated at 115 °C for 24 h, cooled to RT, filtered through a silica pad (Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.2:0.8) and subsequent recrystallisation (vapor diffusion over three days using $CHCl_3$ as the solvent and MeOH as the precipitant) gave the *title compound* as a white solid (21 mg, 21%).

m.p. = 93 – 95 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.04 (m, 3H), 7.04 – 6.99 (m, 1H), 3.07 (d, *J* = 16.2 Hz, 1H), 2.84 – 2.77 (m, 2H), 2.74 (dd, *J* = 16.3, 2.3 Hz, 1H), 2.24 (s, 3H), 2.19 (s, 3H), 2.18 (s, 3H), 2.12 (s, 3H), 2.09 (s, 4H), 2.00 – 1.89 (m, 1H), 1.79 – 1.60 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H);

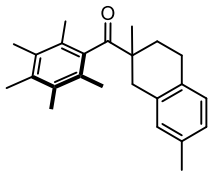
^{13}C NMR (126 MHz, $CDCl_3$) δ 217.7, 139.5, 135.4, 135.1, 135.0, 133.2, 133.18, 129.7, 128.6, 128.1, 125.9, 125.87, 51.2, 36.9, 28.6, 25.9, 25.5, 19.12, 19.09, 16.8, 16.3, 16.2, 8.9;*

IR (film) ν_{max}/cm^{-1} 2934, 1682, 1495, 1452, 1383, 1302, 1258, 1158, 1083, 999, 888;

HRMS (ESI$^+$) $[C_{24}H_{30}NaO]^+$ ([M+Na]$^+$) requires 357.2189; found 357.2180, Δ 2.36 ppm.

*Fewer ^{13}C peaks than expected due to overlapping peaks in the aromatic region

13c (2,7-Dimethyl-1,2,3,4-tetrahydronaphthalen-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Hydroxy-ketone **11d** (102 mg, 0.300 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol), $[IrCp^*Cl_2]_2$ (2.4 mg, 1.0 mol%) and KOH (67 mg, 1.2 mmol) were added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and back-filled with Ar (3 times) and PhMe (0.6 mL, degassed with Ar (balloon)) was added. The reaction was heated at 115 °C for 24 h, cooled to RT, filtered through a silica pad (Et_2O elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.2:0.8 → 99:1) gave the *title compound* as a white solid (67 mg, 67%).

m.p. = 127 – 129 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.98 (d, *J* = 7.7 Hz, 1H), 6.93 (dd, *J* = 7.8, 1.9 Hz, 1H), 6.87 (s, 1H), 3.16 (d, *J* = 16.2 Hz, 1H), 2.80 (dd, *J* = 9.3, 4.2 Hz, 2H), 2.69 (dd, *J* = 16.3, 2.3 Hz, 1H), 2.27 (s, 3H), 2.24 (s, 3H), 2.19 (s, 3H), 2.18 (s, 3H), 2.13 (s, 3H), 2.12 (s, 3H), 2.06 – 1.97 (m, 1H), 1.92 – 1.80 (m, 1H), 1.19 (s, 3H);

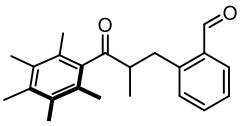
^{13}C NMR (151 MHz, $CDCl_3$) δ 219.9, 139.9, 135.4, 135.0, 134.8, 133.2, 133.2, 131.9, 130.4, 128.7, 127.6, 126.8, 47.9, 39.0, 31.6, 25.4, 21.1, 20.8, 19.2, 19.1, 16.8, 16.2;*

IR (film) ν_{max}/cm^{-1} 2980, 2931, 1684, 1506, 1455, 1384, 1301, 1113, 1076, 987, 911, 806;

HRMS (ESI$^+$) $[C_{24}H_{30}NaO]^+$ ([M+Na]$^+$) requires 357.2189; found 357.2188, Δ 0.31 ppm.

*Fewer ^{13}C peaks than expected due to overlapping peaks in the aromatic region

14 2-(2-Methyl-3-oxo-3-(2,3,4,5,6-pentamethylphenyl)propyl)benzaldehyde



Dess-Martin periodinane (1.27 g, 3.00 mmol) was added to a solution of hydroxy-ketone **11a** (810 mg, 2.50 mmol) in CH_2Cl_2 (12.5 mL) at 0 °C. The mixture was warmed to RT, stirred for 4 h and quenched with aq. Na_2SO_3 (10 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 95:5 → 90:10) gave the *title compound* as a colourless oil (800 mg, 99%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 10.21 (s, 1H), 7.82 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.50 (td, *J* = 7.5, 1.5 Hz, 1H), 7.42 – 7.35 (m, 2H), 3.66 (dd, *J* = 12.9, 5.7 Hz, 1H), 3.17 – 3.10 (m, 1H), 3.08 (dd, *J* = 12.9, 8.1 Hz, 1H), 2.22 (s, 3H), 2.16 (s, 6H), 2.12 – 1.84 (br s, 6H), 1.09 (d, *J* = 7.1 Hz, 3H);

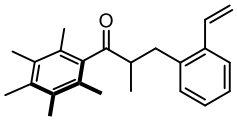
^{13}C NMR (151 MHz, $CDCl_3$) δ 213.6, 192.6, 142.8, 139.4, 135.7, 134.4, 133.7, 133.2, 132.9, 128.5, 127.1, 50.4, 34.4, 17.9, 16.8, 16.2, 16.1;*

IR (film) ν_{max}/cm^{-1} 2932, 1697, 1600, 1574, 1453, 1383, 1292, 1211, 1163, 1085, 925, 758, 667 ;

HRMS (ESI$^+$) $[C_{22}H_{27}O_2]^+$ ([M+H]$^+$) requires 323.2006; found 323.2004, Δ 0.56 ppm.

*Fewer ^{13}C peaks than expected due to overlapping peaks in the aromatic region.

15 2-Methyl-1-(2,3,4,5,6-pentamethylphenyl)-3-(2-vinylphenyl)propan-1-one



Methyltriphenylphosphonium bromide (446 mg, 1.25 mmol) was suspended in THF (2.5 mL) and the suspension was cooled to –78 °C. *n*-BuLi (2.5 M in hexanes, 0.5 mL, 1.25 mmol) was added dropwise, the mixture allowed to warm to 0 °C and stirred for 1 h. The mixture was cooled to –78 °C and a solution of aldehyde **14** (322 mg, 1.00 mmol) in THF (2.5 mL) was added slowly. The mixture was allowed to warm to RT, stirred for 3 h, quenched with satd. NH_4Cl (5 mL) and diluted with Et_2O (5 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.2:0.8 → 98:2) gave the *title compound* as a colourless oil (123 mg, 38%.)

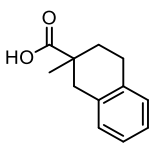
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 1H), 7.23 – 7.18 (m, 2H), 7.16 (dt, *J* = 5.5, 3.5 Hz, 1H), 6.83 (dd, *J* = 17.3, 10.9 Hz, 1H), 5.61 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.21 (dd, *J* = 10.9, 1.4 Hz, 1H), 3.35 (dd, *J* = 13.8, 4.5 Hz, 1H), 3.04 (dqd, *J* = 9.5, 7.1, 4.5 Hz, 1H), 2.63 (dd, *J* = 13.8, 9.6 Hz, 1H), 2.24 (s, 3H), 2.18 (s, 6H), 2.05 (s, 6H), 1.04 (d, *J* = 7.1 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 214.1, 139.6, 137.6, 137.0, 135.7, 134.7, 133.2, 131.1, 128.5, 127.8, 126.8, 126.1, 115.7, 49.8, 35.2, 17.9, 16.9, 16.1, 15.3;

IR (film) ν_{max}/cm^{-1} 2982, 2934, 1694, 1449, 1384, 1318, 1259, 1151, 1086, 1050, 910;

HRMS (ESI$^+$) $[C_{23}H_{29}O]^+$ ([M+H]$^+$) requires 321.2213; found 321.2213, Δ 0.15 ppm.

16 2-Methyl-1,2,3,4-tetrahydronaphthalene-2-carboxylic acid



Ketone **13a** (64 mg, 0.20 mmol) was dissolved in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) (1.7 mL) in a 2 – 5 mL microwave vial. The vial was sealed, HCl (12 M, 0.34 mL) was added and the reaction was heated

at 65 °C for 16 h. The reaction was cooled to RT and diluted with CH_2Cl_2 (15 mL) and water (15 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent CH_2Cl_2/EtOAc/HCO_2H 97.95:2:0.05) gave the *title compound* as an off-white solid (37.5 mg, 99%.)

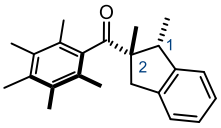
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 – 6.95 (m, 4H), 3.24 (d, *J* = 16.4 Hz, 1H), 2.97 – 2.86 (m, 1H), 2.87 – 2.76 (m, 1H), 2.67 (d, *J* = 16.4 Hz, 1H), 2.20 – 2.10 (m, 1H), 1.82 – 1.68 (m, 1H), 1.32 (s, 3H);

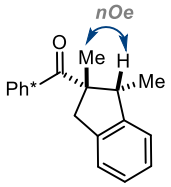
^{13}C NMR (151 MHz, $CDCl_3$) δ 183.6, 135.1, 134.8, 129.4, 128.9, 126.03, 125.96, 41.7, 38.4, 31.7, 26.2, 24.3;

HRMS (ESI^-) $C_{12}H_{14}O_2^-$ ($[M-H]^-$) requires 189.0921; found 189.0913, Δ 4.18 ppm.

The spectroscopic data were consistent with that present in the literature. [27]

17 ((1*RS*,2*SR*)-1,2-Dimethyl-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone





Alkene **12a** (64 mg, 0.20 mmol) was dissolved in MeOH (5 mL, degassed with N_2 (balloon)). Pd/C (13 mg, 10% on carbon, 20 wt% loading w.r.t. **12a**) was added, a balloon of H_2 was attached and the gas was bubbled through the mixture for 15 min. The mixture was left under an atmosphere of H_2 for 2 h. The reaction mixture was filtered through a Celite® pad (washed with CH_2Cl_2) and concentrated *in vacuo* to give the *title compound* as a white solid that required no further purification (64 mg, 99%, >[95:5] d.r.)

The relative stereochemistry was assigned by nOe and X-ray crystallography analysis.

m.p. = 147 – 148 °C;

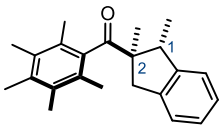
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 – 7.17 (m, 2H), 7.17 – 7.11 (m, 2H), 3.66 (d, *J* = 15.2 Hz, 1H), 3.17 (q, *J* = 7.1 Hz, 1H), 2.77 (d, *J* = 15.2 Hz, 1H), 2.23 (s, 3H), 2.20 (s, 3H), 2.18 – 2.13 (m, 6H), 2.00 (s, 3H), 1.38 (d, *J* = 7.2 Hz, 3H), 1.15 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 217.7, 147.9, 141.1, 140.3, 134.9, 133.3, 132.7, 127.9, 127.1, 126.8, 126.6, 125.0, 124.1, 58.5, 52.5, 45.3, 25.8, 19.4, 17.8, 17.7, 16.8, 16.2, 16.1;

IR (film) ν_{max}/cm^{-1} 2968, 2931, 1683, 1479, 1453, 1381, 1260, 1178, 1153, 1085, 1071, 924, 911;

HRMS (ESI^+) $[C_{23}H_{29}O]^+$ ($[M+H]^+$) requires 321.2213; found 321.2211, Δ 0.61 ppm.

18 ((1*RS*,2*RS*)-1,2-Dimethyl-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone



Alkene **12a** (64 mg, 0.20 mmol) was dissolved in CH_2Cl_2 (6 mL, degassed with N_2 (balloon)) and a 1 mL aliquot of a solution of Crabtree's catalyst ($[Ir(cod)pyPCy_3]^+PF_6^-$, 64 mg, in 4 mL CH_2Cl_2) was added. A balloon of H_2 was attached and bubbled through the solution for 2 min. The reaction was left under an atmosphere of H_2 and aliquots (3 × 1 mL) of the catalyst solution were added every 10 min. The solution was left under an atmosphere of H_2 for 2 h, filtered through a Celite® pad (washed with CH_2Cl_2) and concentrated *in vacuo.* Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.2:0.8 ⟶ 99.1:0.9) gave the *title compound* as a white solid (44 mg, 68%, >[95:5] d.r.)

The relative stereochemistry was assigned by X-ray crystallography analysis.

m.p. = 105 – 106 °C;

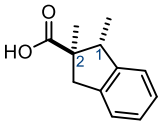
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 – 7.15 (m, 1H), 7.14 – 7.09 (m, 3H), 3.60 (q, *J* = 7.1 Hz, 1H), 3.36 (d, *J* = 15.3 Hz, 1H), 2.81 (d, *J* = 15.3 Hz, 1H), 2.22 (s, 3H), 2.19 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.11 (s, 3H), 1.32 (d, *J* = 7.1 Hz, 3H), 1.18 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 217.3, 145.4, 141.1, 139.3, 135.2, 133.5, 133.0, 128.3, 128.0, 126.7, 126.6, 124.3, 123.4, 61.8, 44.7, 44.6, 19.2, 18.7, 18.2, 16.7, 16.3, 16.1, 12.7;

IR (film) ν_{max}/cm^{-1} 2939, 1683, 1460, 1381, 1306, 1260, 1149, 1080, 989, 913;

HRMS (ESI$^+$) $[C_{23}H_{29}O]^+$ ($[M+H]^+$) requires 321.2213; found 321.2211, Δ 0.70 ppm.

19 (1*RS*,2*RS*)-1,2-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylic acid



Ketone **18** (32 mg, 0.10 mmol) was dissolved in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (1.0 mL) and HCl (37% aq, 0.2 mL) was added. The reaction was heated at 65 °C for 18 h, cooled to RT and diluted with water (10 mL) and CH_2Cl_2 (10 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification *via* flash column chromatography (CH_2Cl_2/EtOAc/HCO_2H, 97.95:2:0.05) afforded the title compound as a colourless oil (19.0 mg, 99%, >[95:5] d.r.)

The relative stereochemistry was assigned by analogy with parent compound **18.**

m.p. = 70 – 72 °C;

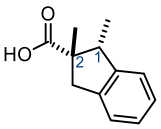
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.03 (m, 4H), 3.64 (q, *J* = 7.1 Hz, 1H), 3.50 (d, *J* = 15.6 Hz, 1H), 2.80 (d, *J* = 15.6 Hz, 1H), 1.33 (d, *J* = 7.1 Hz, 3H), 1.18 (s, 3H);

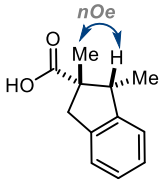
^{13}C NMR (101 MHz, $CDCl_3$) δ 183.8, 145.6, 140.6, 126.8, 126.8, 124.5, 123.5, 53.5, 45.6, 43.6, 18.3, 13.3;

IR (film) ν_{max}/cm^{-1} 2976, 1703, 1547, 1477, 1405, 1328, 1269, 1018, 942, 759, 734;

HRMS (ESI$^-$) $[C_{12}H_{13}O_2]^-$ ([M-H]$^-$) requires 189.0921; found 189.0915, Δ 2.97 ppm.

20 (1*RS*,2*SR*)-1,2-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylic acid





Ketone **17** (32 mg, 0.10 mmol) was dissolved in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (1.0 mL) and HCl (37% aq, 0.2 mL) was added. The reaction was heated at 65 °C for 18 h, cooled to RT and diluted with water (10 mL) and CH_2Cl_2 (10 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (CH_2Cl_2/EtOAc/HCO_2H, 97.95:2:0.05) afforded the title compound as a colourless oil (18.6 mg, 97%, [>95:5] d.r.).

The relative stereochemistry was assigned by nOe analysis.

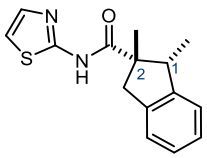
^{1}H NMR (600 MHz, $CDCl_3$) δ 11.43 (br s, 1H), 7.23 – 7.12 (m, 4H), 3.60 (d, *J* = 16.0 Hz, 1H), 3.13 (q, *J* = 7.2 Hz, 1H), 2.72 (d, *J* = 16.0 Hz, 1H), 1.40 (s, 3H), 1.23 (d, *J* = 7.1 Hz, 3H);

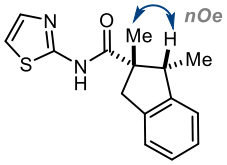
^{13}C NMR (151 MHz, $CDCl_3$) δ 182.2, 146.3, 140.8, 126.9, 126.8, 124.8, 124.0, 53.8, 50.1 41.1, 24.9, 17.3;

m/z (ESI$^-$) Found ([M-H]$^-$) = 189, $[C_{12}H_{13}O_2]$ requires 189.

The spectroscopic data matched that already reported in the literature. [28]

21 (1*RS*,2*SR*)-1,2-Dimethyl-*N*-(thiazol-2-yl)-2,3-dihydro-1*H*-indene-2-carboxamide





Carboxylic acid **20** (19 mg, 0.10 mmol) was dissolved in MeCN (1.0 mL) and added to a 2 – 5 mL microwave vial. 2-Aminothiazole (12 mg, 0.12 mmol), *N*-ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide hydrochloride (32 mg, 0.17 mmol), 1-hydroxybenzotriazole (16 mg, 0.12 mmol) and DIPEA (38 µL, 0.22 mmol) were added. The microwave vial was sealed and the reaction was heated at 85 °C for 16 h.

The reaction was cooled to RT and diluted with EtOAc (15 mL) and water (15 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 15 mL). The combined organic phases were washed with brine, dried over $NaSO_4$ and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent PhMe/EtOAc, 96:4) gave the *title compound* as a white solid (17 mg, 63%, >[95:5] d.r.)

The relative stereochemistry was assigned by nOe analysis.

m.p. = 134 – 136 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (br s, 1H), 7.39 (d, *J* = 3.5 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.27 – 7.22 (m, 2H), 7.22 – 7.15 (m, 1H), 6.95 (d, *J* = 3.5 Hz, 1H), 3.57 (d, *J* = 16.2 Hz, 1H), 3.22 (q, *J* = 7.1 Hz, 1H), 2.95 (d, *J* = 16.1 Hz, 1H), 1.51 (s, 3H), 1.21 (d, *J* = 7.2 Hz, 3H);

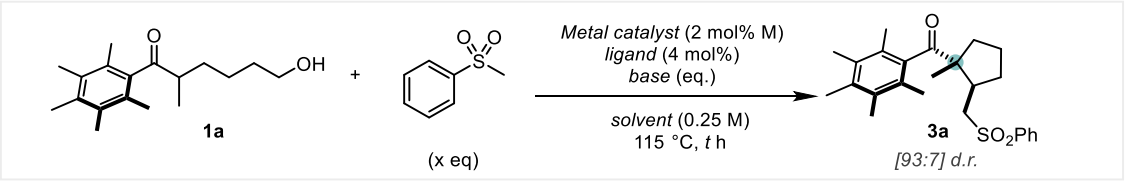
^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 158.2, 146.2, 140.1, 137.4, 127.8, 127.7, 125.1, 124.2, 113.8, 54.7, 50.0, 41.8, 24.1, 15.7;

IR (film) ν_{max}/cm^{-1} 3188, 2965, 1679, 1536, 1480, 1320, 1273, 1161, 1011, 912;

HRMS (ESI^+) $[C_{15}H_{17}N_2OS]^+$ ($[M+H]^+$) requires 273.1056; found 273.1045, Δ 4.00 ppm.

4. Optimisation Tables

Table S1: Acceptorless Dehydrogenation-Intramolecular Conjugate Addition Cascade

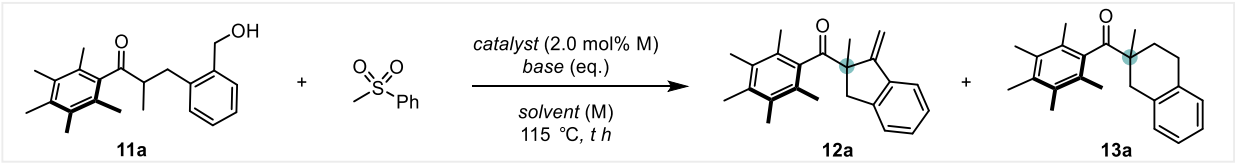


Entry	M Catalyst	Ligand	$PhSO_2Me$ equiv	Base (eq.)	Solvent	Reaction time (h)	Yield (%)[a]	
							1a	3a
1	Ir(cod)acac	cataCXium® A	2	KO^{t}Bu (2)	^{t}BuOH	24	-	73 *(77)*
2	Ir(cod)acac	dppBz	2	KO^{t}Bu (2)	^{t}BuOH	24	4	71
3	Ir(cod)acac	PPh_3	2	KO^{t}Bu (2)	^{t}BuOH	24	5	73
4	$[IrCp^*Cl_2]_2$	-	2	KO^{t}Bu (2)	^{t}BuOH	24	20	50
5	Ru-MACHO®	-	2	KO^{t}Bu (2)	^{t}BuOH	24	4	26[b]
7	**Mn cat**	-	2	KO^{t}Bu (2)	^{t}BuOH	24	-	74 *(75)*
8	-	-	2	KO^{t}Bu (2)	^{t}BuOH	24	79	-
9	**Mn cat**	-	2	KO^{t}Bu (1)	^{t}BuOH	24	-	64
10	**Mn cat**	-	2	KO^{t}Bu (0.5)	^{t}BuOH	24	84	-
11	**Mn cat**	-	2	NaO^{t}Bu (2)	^{t}BuOH	24	51	17
12	**Mn cat**	-	2	KOH (2)	PhMe	24	11	57
13	**Mn cat**	-	2	KOH (4)	PhMe	24	4	38
14	**Mn cat**	-	1.5	KO^{t}Bu (2)	^{t}BuOH	24	-	64
15	**Mn cat**	-	2	KO^{t}Bu (2)	^{t}BuOH	16	-	77 *(80)*
16	**Mn cat**	-	2	KO^{t}Bu (2)	^{t}BuOH	4	13	55
17	Ir(cod)acac	cataCXium® A	2	KO^{t}Bu (2)	^{t}BuOH	16	2	69

[a] Yield determined via ^{1}H quantitative NMR using 1,1,2,2-tetrachloroethane as an internal standard, isolated yields are given in parentheses

[b] acyclic side product **4** isolated in 55% yield.

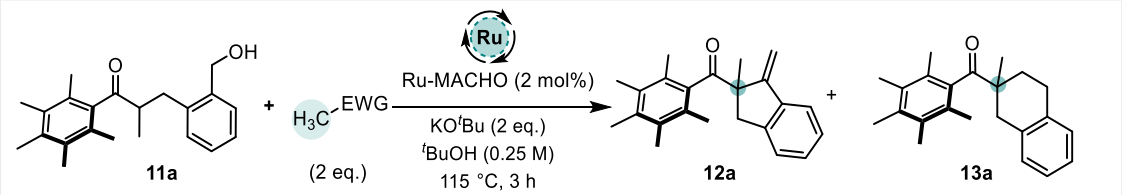
Table S2: Reaction with benzylic alcohol substrates



Entry	Catalyst (mol%)/ligand (mol%)	Base (Eq)	Solvent (M)	Time (h)	NMR Yield (%)[a]		
					11a	12a	13a
1	[Ir(cod)acac] (2)/cataCXiumA (4)	KO^{t}Bu (2)	^{t}BuOH (0.25)	24	31	21 *(24)*	18 *(18)*
2	[Ir(cod)acac] (2)/cataCXiumA (4)	KOH (4)	PhMe (0.25)	24	-	19 *(22)*	45 *(40)*
3	[IrCp*$_2$Cl$_2$]$_2$ (1)	KOH (4)	PhMe (0.25)	24	11	21	44 *(41)*
4	Ru-MACHO (2)	KOH (4)	PhMe (0.25)	24	-	62	-
5	**Mn cat** (2)	KOH (4)	PhMe (0.25)	24	-	50	-
6	[Ir(cod)acac] (2)/cataCXiumA (4)	KOH (4)	PhMe (0.5)	24	-	20	42
7	[IrCp*$_2$Cl$_2$]$_2$ (1)	KOH (4)	PhMe (0.5)	24	1	12	71 *(70)*
8	[IrCp*$_2$Cl$_2$]$_2$ (1)	KOH (4)	PhMe (1)	24	-	13	50
9	[IrCp*$_2$Cl$_2$]$_2$ (1)	KOH (4)	PhMe (2)	24	-	11	55
10	[IrCp*$_2$Cl$_2$]$_2$ (1)	KO^{t}Bu (2)	^{t}BuOH (0.5)	24	27	7	44
11	[IrCp*$_2$Cl$_2$]$_2$ (1)	KO^{t}Bu (2)	^{t}BuOH (0.25)	3	42	3	5
12	Ru-MACHO (2)	KO^{t}Bu (2)	^{t}BuOH (0.25)	24	0	70	
13	Ru-MACHO (2)	KO^{t}Bu (2)	^{t}BuOH (0.25)	2	7	77 *(76)*	-
14	Ru-MACHO (2)	KO^{t}Bu (2)	^{t}BuOH (0.25)	3	5	80 *(81)*	-
15	Ru-MACHO (2)	KO^{t}Bu (2)	^{t}BuOH (0.25)	6	2	79	-
16	Ru-MACHO (2)	KOH (4)	PhMe (0.25)	2	8	74	-
17	Ru-MACHO (2)	KOH (4)	PhMe (0.5)	24	0	82 *(82)*	-
18	Ru-MACHO (2)	KO^{t}Bu (2)	^{t}BuOH (0.5)	3	1	85 (*85*)	-
19	Ru-MACHO (2)	KOH (4)	PhMe (0.5)	3	-	84 *(84)*	-

[a] Yield determined via ^{1}H quantitative NMR using 1,1,2,2-tetrachloroethane as an internal standard, isolated yields are given in parentheses

Table S3: Alternative sulfone nucleophiles with benzylic alcohol substrates (Ruthenium-catalysed method)



Entry	Nucleophile	Yield (%)[a]		
		11a	12a	13a
1	A	-	85 (85)	-
2	B	-	71	-
3	C	-	69	-
4	D	-	79 (74)	-

[a]Yield determined via ^{1}H quantitative NMR using 1,1,2,2-tetrachloroethane as an internal standard. Isolated yields are given in parentheses.

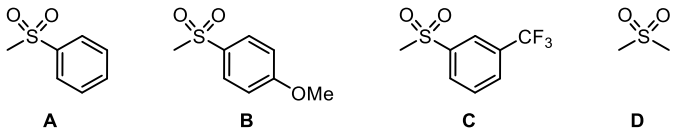
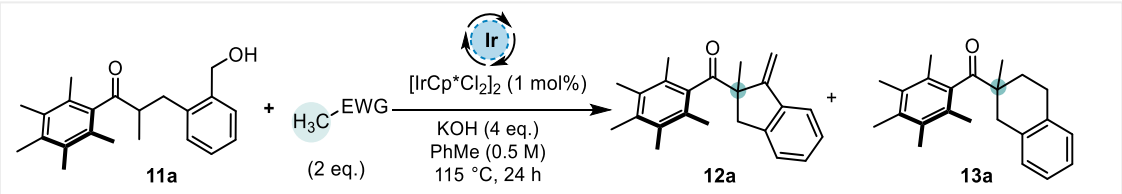
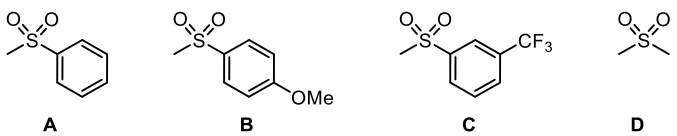


Table S4: Alternative sulfone nucleophiles with benzylic alcohol substrates (Iridium-catalysed method)



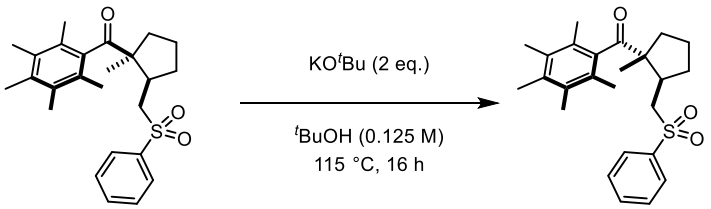
Entry	Nucleophile	Yield (%)[a]		
		11a	12a	13a
1	A	1	12	71 (70)
2	B	5	19	55
3	C		19	10
4	D	-	26	43

[a] Yield determined via ^{1}H quantitative NMR using 1,1,2,2-tetrachloroethane as an internal standard. Isolated yields are given in parentheses.



5. Mechanistic Experiments

5.1 Resubjection of *cis*-3a with base



Ketone ***cis*-3a** (12.1 mg, 0.029 mmol) and KO^{t}Bu (6.5 mg, 0.058 mmol) were added to a 1.75 mL vial. The vial was evacuated and back-filled with Ar (5 times). ^{t}BuOH (230 µL, 0.125 M) was added, the vial sealed under Ar and the reaction was heated at 115 °C for 16 h. The mixture was cooled to RT, filtered through a silica plug (Et_2O/CH_2Cl_2) and concentrated *in vacuo*. Purification *via* preparative thin layer chromatography eluent Pentane/CH_2Cl_2/Et_2O, 70:5:25) gave the *title compound* as a white solid (9.6 mg, 79%, [93:7] d.r.)

The spectroscopic data were consistent with that reported above for **3a**.

5.2 Measurement of gas evolution

To demonstrate that gas was evolved over the course of the acceptorless dehydrogenation-conjugate addition reaction, the amount of gas evolved during the reaction was measured. The experiment was set up by piercing the reaction microwave vial septum with a cannula and collecting the gas evolved in an inverted measuring cylinder (see **Figure S1** for experimental setup). The results of this experiment are depicted in **Figure S2**. Since heating the reaction solvent to 115 °C in a microwave vial would cause an increase in vapour pressure, ^{t}AmOH was first heated under our gas collection apparatus.* The expansion of the reaction headspace was complete within 1 h and constituted approximately 6.5 mL of gas. This volume was subtracted from all readings in the hydrogen evolution experiment to give an accurate representation of the amount of gas evolved in the reaction. Over the course of the reaction, a total of approximately 7 cm^3 of gas was evolved (averaged over two repeats). The expected amount of gas evolved assuming full conversion was calculated to be 7.26 cm^3 using the ideal gas law. Therefore, the results of the gas collection experiment are consistent with the alcohol undergoing almost full conversion to the corresponding aldehyde and an equivalent of hydrogen gas being evolved to enable catalyst turnover.

* ^{t}AmOH was used for this study in place of ^{t}BuOH as the lower boiling point of ^{t}BuOH was incompatible with the experiment setup. A control experiment indicated that the product **3a** was formed in comparable yield when using ^{t}AmOH as the solvent.

Figure S1: Experimental Setup for measurement of gas evolution

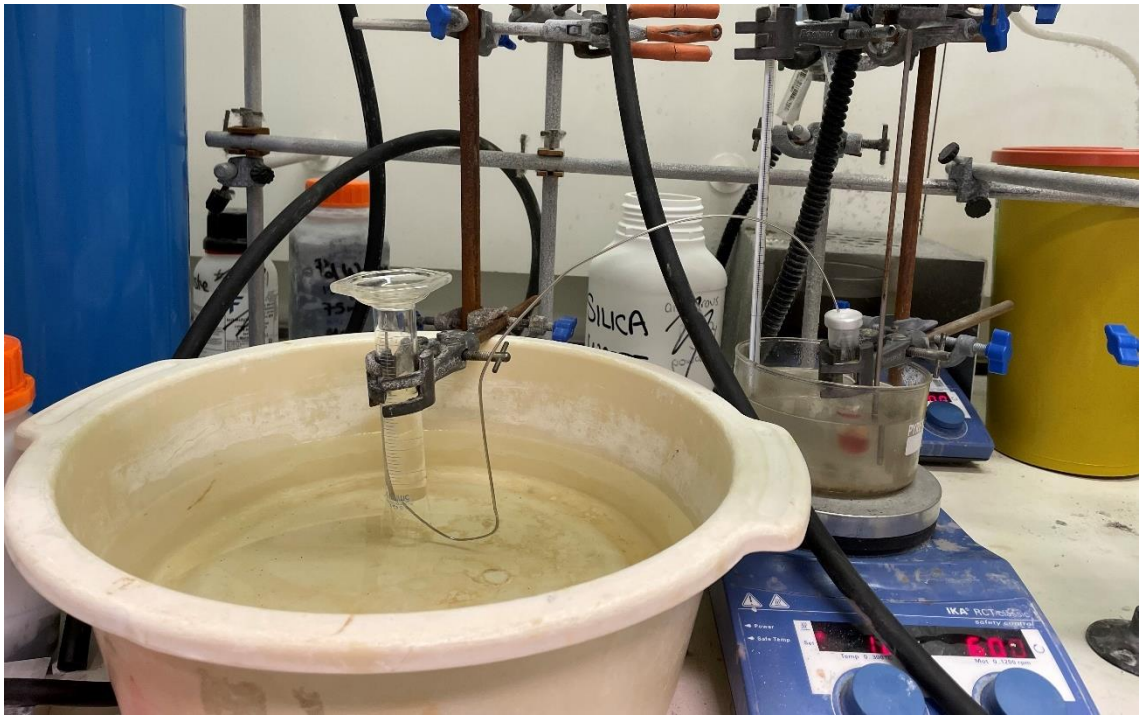
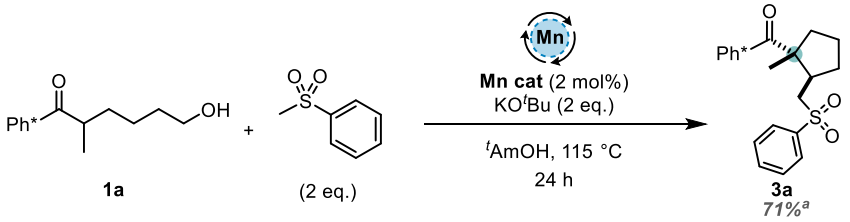
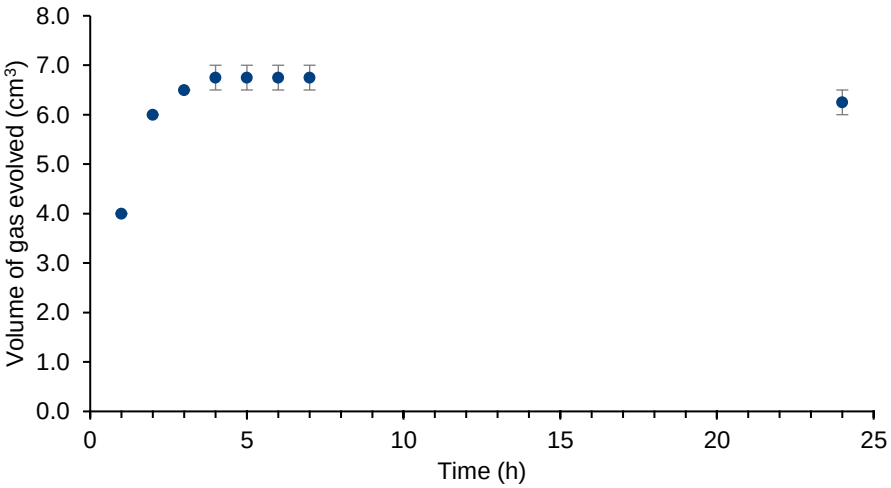


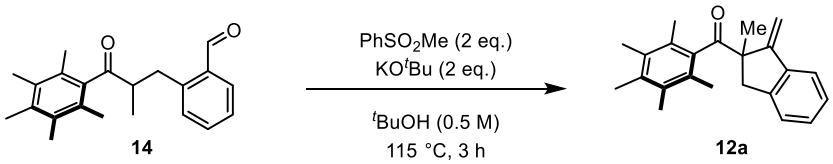
Figure S2: Graph showing gas evolution over the course of the acceptorless dehydrogenative coupling reaction to give **3a**





[a]*Yield determined via ^{1}H quantitative NMR using 1,1,2,2-tetrachloroethane as an internal standard*

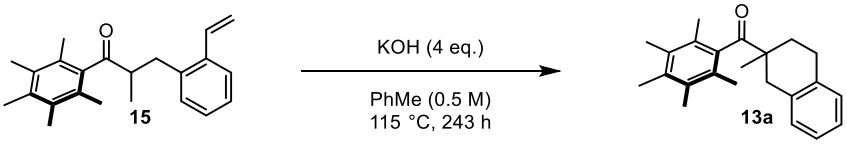
5.3 Metal-free experiment with aldehyde 14



Aldehyde **14** (97 mg, 0.30 mmol), methyl phenyl sulfone (94 mg, 0.60 mmol) and KO^{t}Bu (68 mg, 0.60 mmol) were added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and back-filled with Ar (3 times) and ^{t}BuOH (0.6 mL, degassed with Ar (balloon)) was added. The reaction was heated at 115 °C for 3 h, cooled to RT, filtered through a silica pad (Et_2O/CH_2Cl_2 elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99.1:0.9 → 99:1) gave the *title compound* as a white solid (92 mg, 96%).

The spectroscopic data were consistent with that reported above for **12a**.

5.4 Metal-free experiment with styrene 15



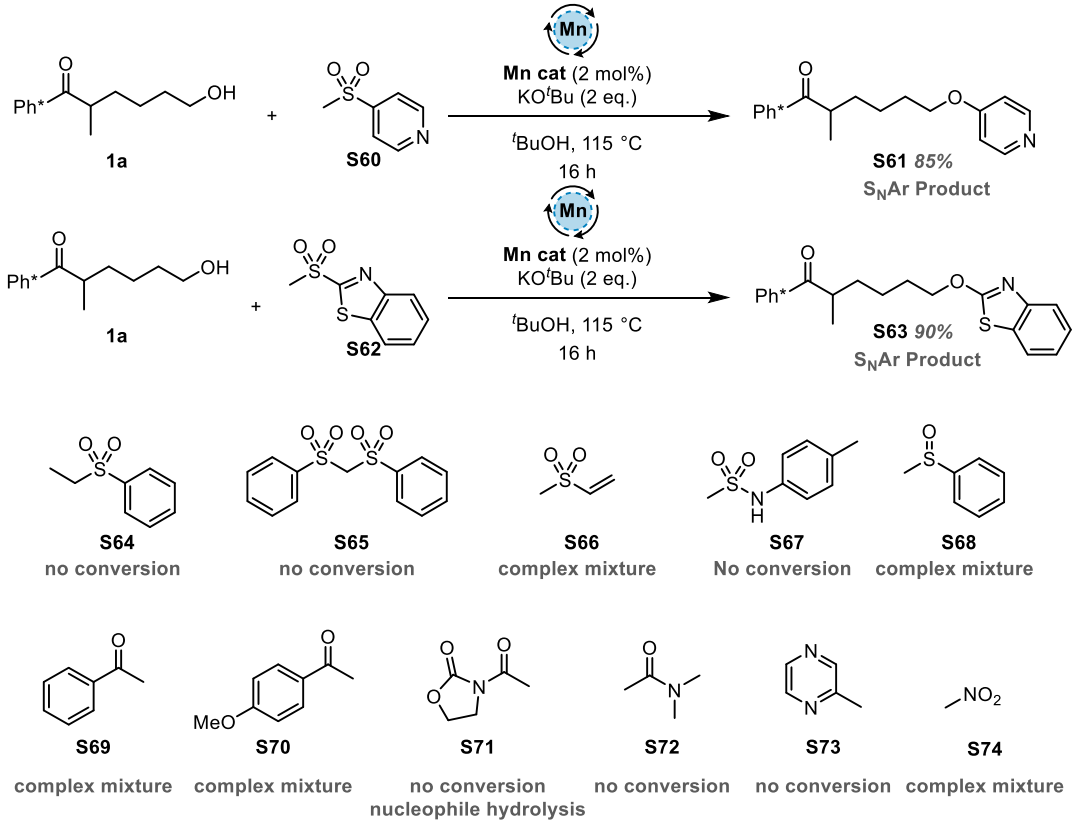
Styrene **15** (40 mg, 0.125 mmol) and KOH (28 mg, 0.50 mmol) were added to a 2 – 5 mL microwave vial. The vial was sealed, evacuated and backfilled with Ar (3 times) and PhMe (0.25 mL, degassed with Ar (balloon)) was added. The reaction was heated at 115 °C for 24 h, cooled to RT, filtered through a silica pad (Et_2O/CH_2Cl_2 elution) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Pentane/Et_2O, 99:1) gave the *title compound* as a white solid (28 mg, 70%).

The spectroscopic data were consistent with that reported above for **13a**.

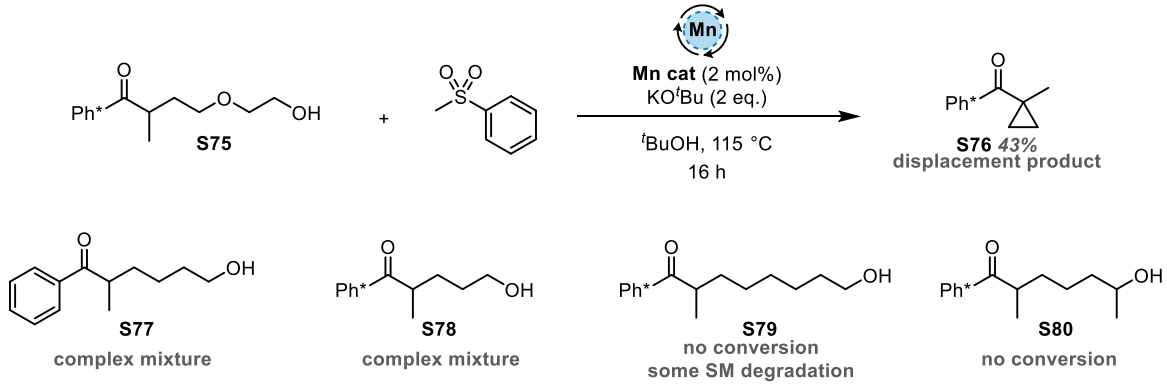
6. List of Unsuccessful Substrates

The following substrates were unsuccessful in the acceptorless dehydrogenation-intramolecular conjugate addition reaction. The outcome of reactions using these substrates is indicated below.

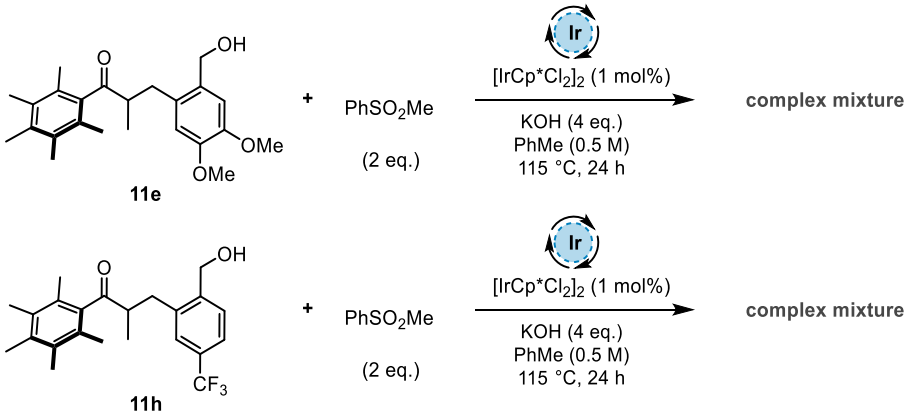
6.1 Unsuccessful Nucleophiles



6.2 Unsuccessful hydroxy-ketones



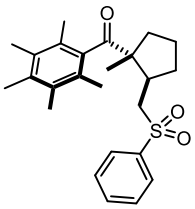
6.3 Unsuccessful benzylic hydroxy-ketones for the Ir-catalysed hydrogen borrowing reaction

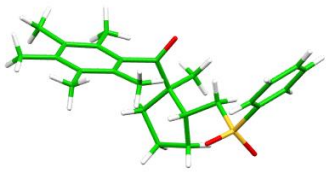


7. X-Ray Crystallography Data

(1-Methyl-2-((phenylsulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone (3a):

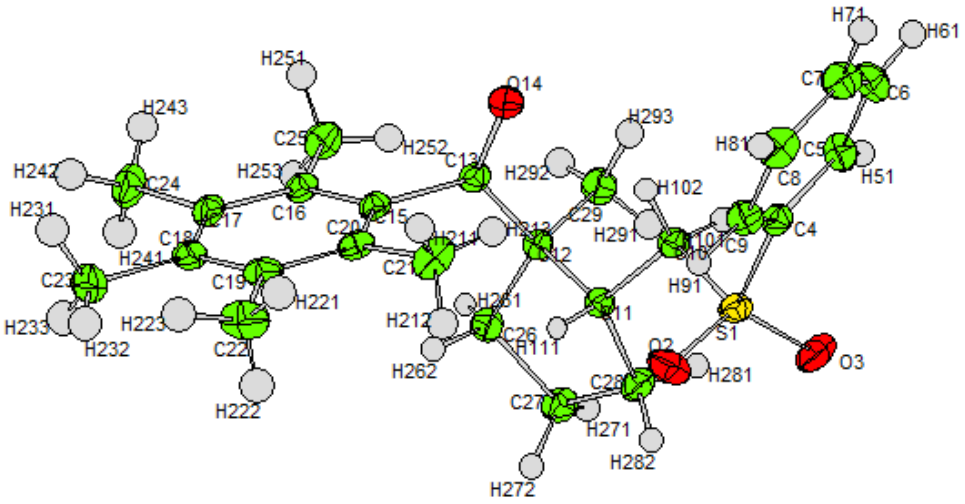
Recrystallised from hexane/CH_2Cl_2/MeOH





Formula C25 H32 O3 S

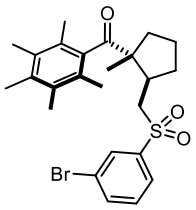
Crystal Class	orthorhombic	Space Group	P b c a
a	8.9910(1)	alpha	90
b	14.5710(1)	beta	90
c	32.8041(2)	gamma	90
Volume	4297.59(6)	Z	8
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.28	Mr	412.59
Mu	1.517	Temperature (K)	150
Size	0.01 × 0.10 × 0.30		
Colour	clear pale colourless	Shape	lath
Cell from	36412 Reflections	Theta range	6 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.85-0.98
Reflections measured	106899	Independent reflections	4496
Rint	0.053	Theta max	76.13
Hmin, Hmax	-11 11		
Kmin, Kmax	-18 17		
Lmin, Lmax	-41 41		
Refinement on Fsqd			
R-factor	0.038	Weighted R-factor	0.098
Max shift/su	0.0008		
Delta Rho min	-0.38	Delta Rho max	0.30
Reflections used	4496	sigma(I) limit	-3.00
Number of parameters	262	Goodness of fit	0.977

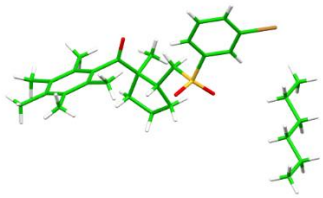


Thermal ellipsoids are drawn at the 50% probability level.

(2-(((3-Bromophenyl)sulfonyl)methyl)-1-methylcyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone (3b):

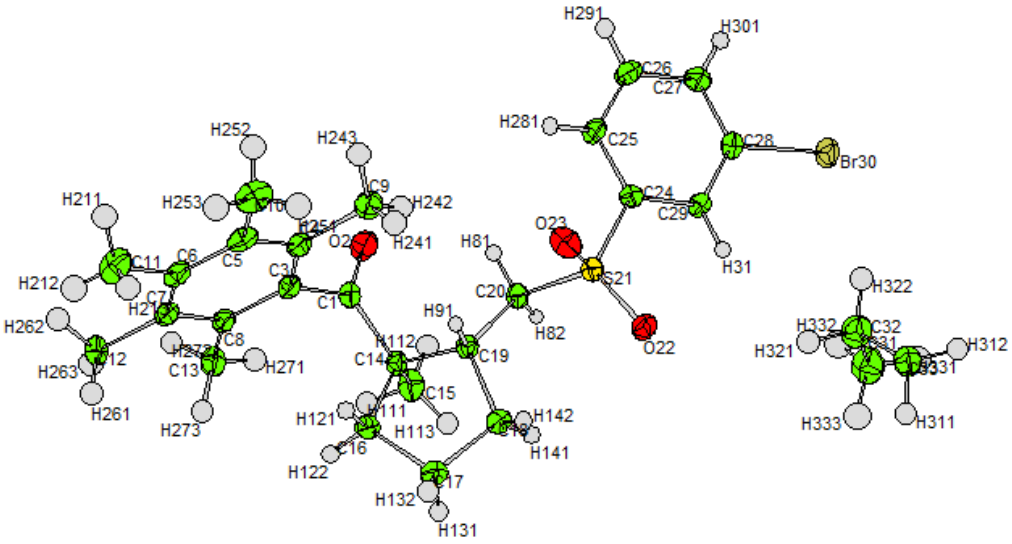
Recrystallised from $CHCl_3$/MTBE/Hexane





Formula C25 H31 Br O3 S, 0.5(C6 H14)

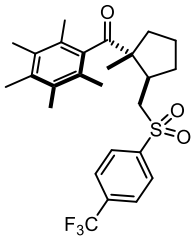
Crystal Class	monoclinic	Space Group	P 21/c
a	19.7734(2)	alpha	90
b	8.9224(1)	beta	105.1963(11)
c	15.2607(2)	gamma	90
Volume	2598.24(5)	Z	4
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.37	Mr	534.58
Mu	3.114	Temperature (K)	150
Size	0.20 × 0.20 × 0.50		
Colour	translucent pale colourless	Shape	needle
Cell from	14898 Reflections	Theta range	5 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.20-0.54
Reflections measured	19027	Independent reflections	5386
Rint	0.033	Theta max	74.76
Hmin, Hmax	-24 24		
Kmin, Kmax	-11 11		
Lmin, Lmax	-19 16		
Refinement on Fsqd			
R-factor	0.036	Weighted R-factor	0.1004
Max shift/su	0.0008		
Delta Rho min	-0.56	Delta Rho max	0.63
Reflections used	5386	sigma(I) limit	-3.00
Number of parameters	298	Goodness of fit	0.996

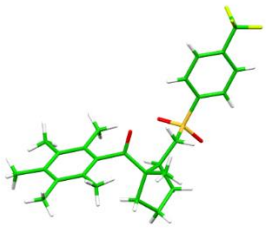


Thermal ellipsoids are drawn at the 50% probability level.

1-Methyl-2-(((4-(trifluoromethyl)phenyl)sulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone (3c):

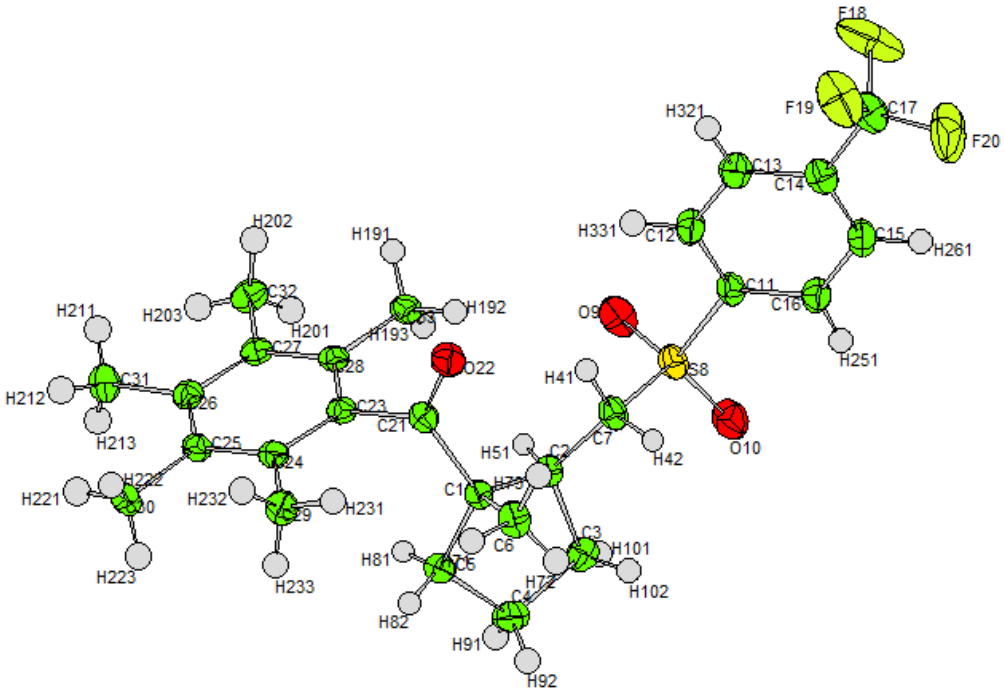
Recrystallised from $CHCl_3$/Hexane





Formula C26 H31 F3 O3 S

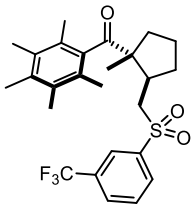
Crystal Class	triclinic	Space Group	P -1
a	7.4347(2)	alpha	103.4840(18)
b	8.8266(2)	beta	92.5338(18)
c	18.8432(4)	gamma	98.6062(18)
Volume	1184.89(5)	Z	2
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.35	Mr	480.59
Mu	1.643	Temperature (K)	150
Size	0.20 × 0.20 × 0.20		
Colour	translucent pale colourless	Shape	cube
Cell from	17028 Reflections	Theta range	5 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.65-0.72
Reflections measured	22626	Independent reflections	4902
Rint	0.022	Theta max	73.98
Hmin, Hmax	-8 9		
Kmin, Kmax	-11 11		
Lmin, Lmax	-23 23		
Refinement on Fsqd			
R-factor	0.037	Weighted R-factor	0.1024
Max shift/su	0.0006		
Delta Rho min	-0.36	Delta Rho max	0.34
Reflections used	4902	sigma(I) limit	-3.00
Number of parameters	298	Goodness of fit	0.9841

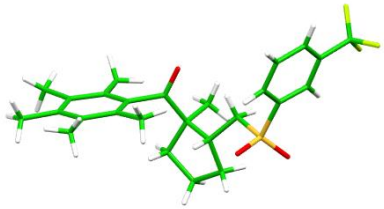


Thermal ellipsoids are drawn at the 50% probability level.

1-Methyl-2-(((3-(trifluoromethyl)phenyl)sulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone (3d):

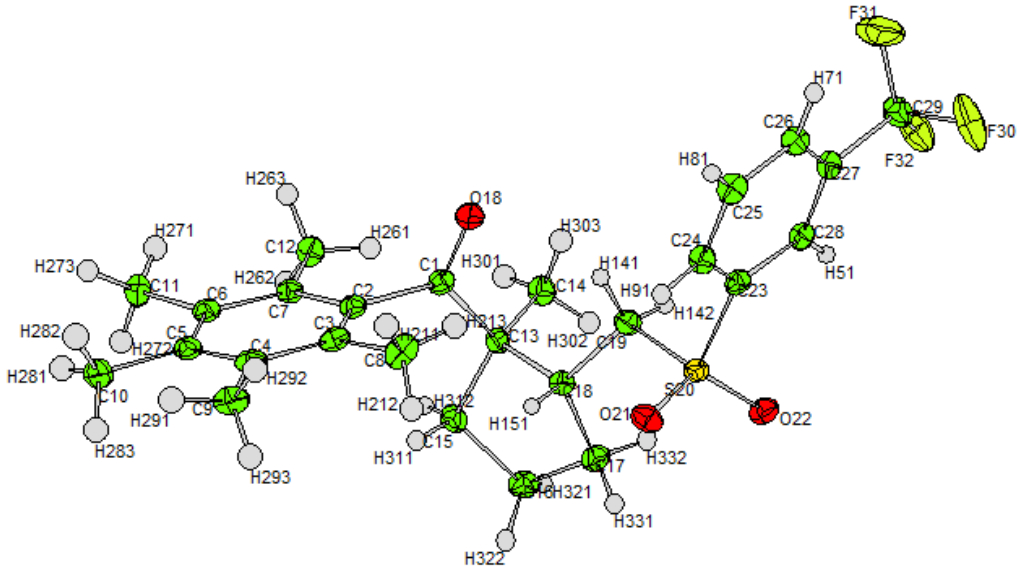
Recrystallised from $CHCl_3$/Hexane





Formula C26 H31 F3 O3 S

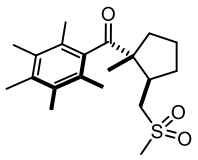
Crystal Class	monoclinic	Space Group	P 21/c
a	17.8290(1)	alpha	90
b	9.0231(1)	beta	101.6620(7)
c	14.8418(1)	gamma	90
Volume	2338.36(3)	Z	4
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.37	Mr	480.59
Mu	1.665	Temperature (K)	100
Size	0.05 × 0.30 × 0.30		
Colour	clear pale colourless	Shape	plate
Cell from	25091 Reflections	Theta range	3 to 75
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.51-0.92
Reflections measured	39759	Independent reflections	4811
Rint	0.033	Theta max	76.23
Hmin, Hmax	-22 21		
Kmin, Kmax	-11 10		
Lmin, Lmax	-18 18		
Refinement on Fsqd			
R-factor	0.040	Weighted R-factor	0.106
Max shift/su	0.0014		
Delta Rho min	-0.51	Delta Rho max	0.82
Reflections used	4811	sigma(I) limit	-3.00
Number of parameters	298	Goodness of fit	0.985

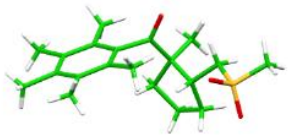


Thermal ellipsoids are drawn at the 50% probability level.

(1-Methyl-2-((methylsulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone (3g):

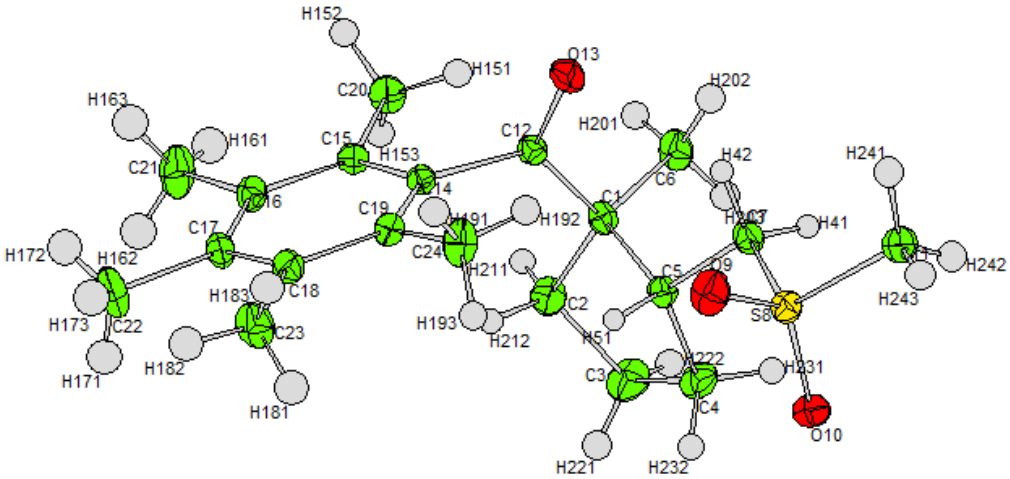
Recrystallised from $CHCl_3$/Hexane





Formula C20 H30 O3 S

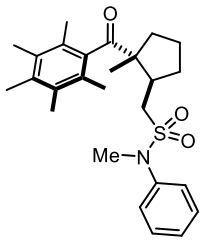
Crystal Class	orthorhombic	Space Group	P b c a
a	7.8993(1)	alpha	90
b	17.4094(1)	beta	90
c	26.6953(2)	gamma	90
Volume	3671.19(6)	Z	8
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.27	Mr	350.52
Mu	1.678	Temperature (K)	150
Size	0.10 × 0.30 × 0.40		
Colour	translucent pale colourless	Shape	plate
Cell from	55258 Reflections	Theta range	5 to 75
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.47-0.85
Reflections measured	76451	Independent reflections	3821
Rint	0.046	Theta max	76.343
Hmin, Hmax	-9 9		
Kmin, Kmax	-21 21		
Lmin, Lmax	-33 33		
Refinement on Fsqd			
R-factor	0.0372	Weighted R-factor	0.1071
Max shift/su	0.0014		
Delta Rho min	-0.45	Delta Rho max	0.35
Reflections used	3821	sigma(I) limit	-3.00
Number of parameters	217	Goodness of fit	0.9691



Thermal ellipsoids are drawn at the 50% probability level.

***N*-Methyl-1-(2-methyl-2-(2,3,4,5,6-pentamethylbenzoyl)cyclopentyl)-*N*-phenylmethanesulfonamide (3h):**

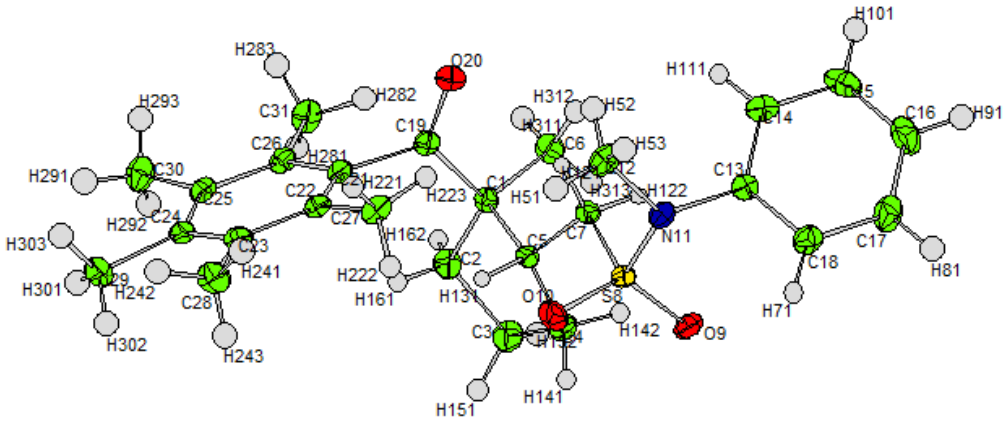
Recrystallised from $CHCl_3$/Hexane





Formula C26 H35 N O3 S

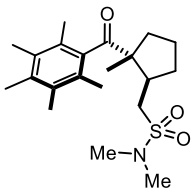
Crystal Class	triclinic	Space Group	P -1
a	8.8562(3)	alpha	74.402(3)
b	9.5977(3)	beta	78.995(3)
c	14.4886(5)	gamma	80.383(2)
Volume	1155.60(7)	Z	2
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.27	Mr	441.63
Mu	1.456	Temperature (K)	150
Size	0.40 × 0.40 × 0.40		
Colour	translucent pale colourless	Shape	cube
Cell from	13304 Reflections	Theta range	5 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.37-0.56
Reflections measured	15037	Independent reflections	4733
Rint	0.021	Theta max	73.128
Hmin, Hmax	-11 9		
Kmin, Kmax	-11 10		
Lmin, Lmax	-18 16		
Refinement on Fsqd			
R-factor	0.0383	Weighted R-factor	0.1023
Max shift/su	0.0003956		
Delta Rho min	-0.46	Delta Rho max	0.25
Reflections used	4733	sigma(I) limit	-3.00
Number of parameters	280	Goodness of fit	1.0199

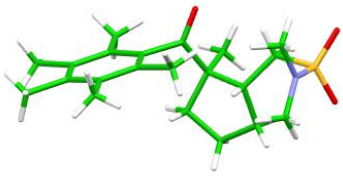


Thermal ellipsoids are drawn at the 50% probability level.

***N*,*N*-Dimethyl-1-(2-methyl-2-(2,3,4,5,6-pentamethylbenzoyl)cyclopentyl)methanesulfonamide (3i):**

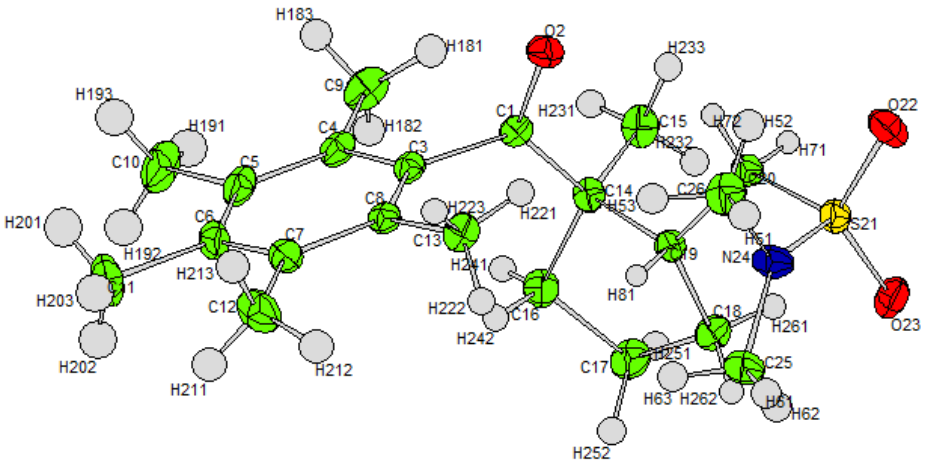
Recrystallised from $CHCl_3$/Hexane





Formula C21 H33 N O3 S

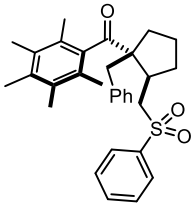
Crystal Class	triclinic	Space Group	P -1
a	6.5901(2)	alpha	110.073(4)
b	12.8809(6)	beta	97.579(3)
c	12.9173(5)	gamma	100.566(3)
Volume	989.64(8)	Z	2
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.27	Mr	379.56
Mu	1.610	Temperature (K)	150
Size	0.05 × 0.10 × 0.40		
Colour	translucent pale colourless	Shape	lath
Cell from	6877 Reflections	Theta range	4 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.57-0.92
Reflections measured	11578	Independent reflections	4073
Rint	0.031	Theta max	73.587
Hmin, Hmax	-7 8		
Kmin, Kmax	-15 16		
Lmin, Lmax	-16 15		
Refinement on Fsqd			
R-factor	0.0416	Weighted R-factor	0.1059
Max shift/su	0.0005294		
Delta Rho min	-0.42	Delta Rho max	0.39
Reflections used	4072	sigma(I) limit	-3.00
Number of parameters	235	Goodness of fit	0.9905

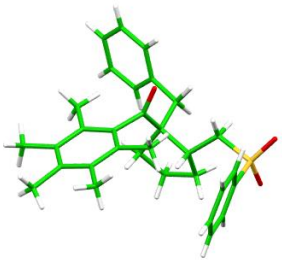


Thermal ellipsoids are drawn at the 50% probability level.

((1*S*,2*R*))-1-Benzyl-2-((phenylsulfonyl)methyl)cyclopentyl)(2,3,4,5,6-pentamethylphenyl)methanone (3l):

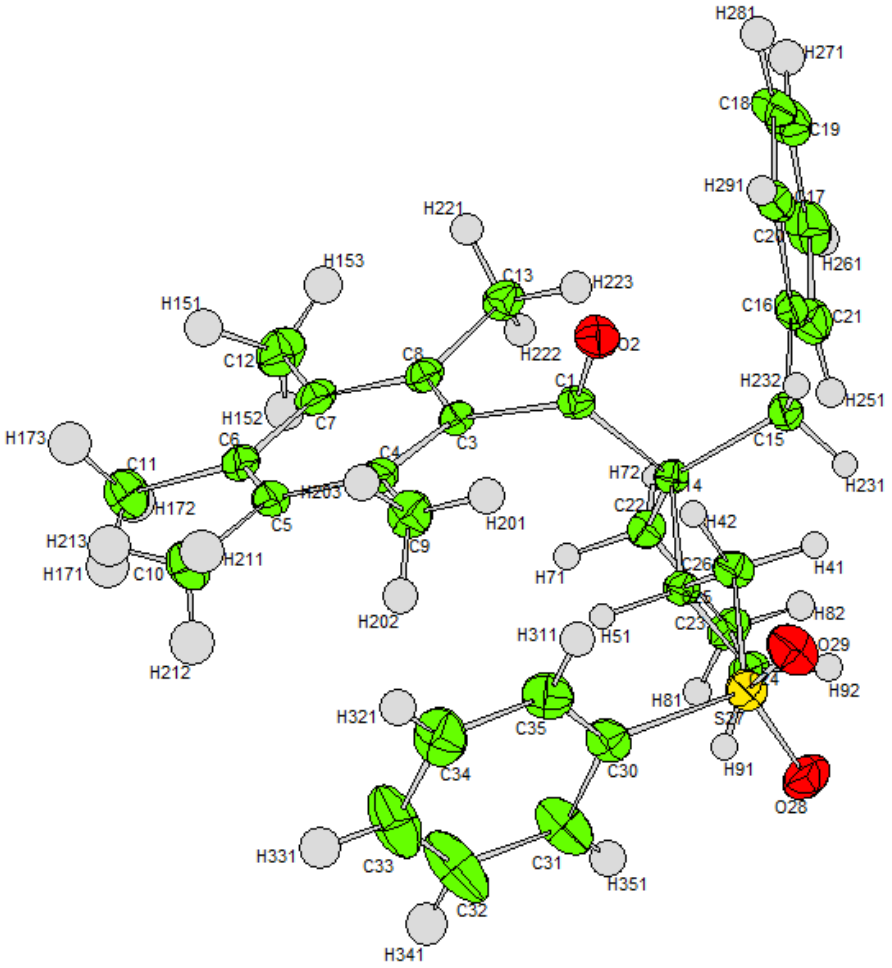
Recrystallised from $CHCl_3$/Hexane





Formula C31 H36 O3 S

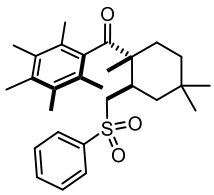
Crystal Class	triclinic	Space Group	P -1
a	10.4881(5)	alpha	60.203(6)
b	12.4032(7)	beta	74.388(5)
c	12.4500(7)	gamma	68.482(5)
Volume	1299.90(15)	Z	2
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.25	Mr	488.69
Mu	1.337	Temperature (K)	150
Size	0.20 × 0.20 × 0.20		
Colour	translucent pale colourless	Shape	irregular
Cell from	12577 Reflections	Theta range	4 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.55-0.77
Reflections measured	16552	Independent reflections	5353
Rint	0.027	Theta max	72.559
Hmin, Hmax	-12 13		
Kmin, Kmax	-15 13		
Lmin, Lmax	-15 13		
Refinement on Fsqd			
R-factor	0.0367	Weighted R-factor	0.0997
Max shift/su	0.0003719		
Delta Rho min	-0.40	Delta Rho max	0.31
Reflections used	5353	sigma(I) limit	-3.00
Number of parameters	316	Goodness of fit	0.9851

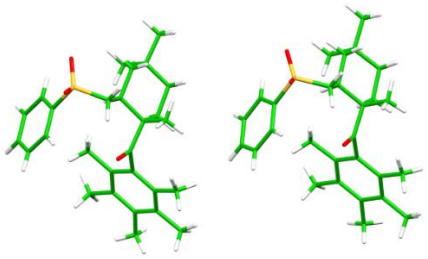


Thermal ellipsoids are drawn at the 50% probability level.

(2,3,4,5,6-Pentamethylphenyl)(1,4,4-trimethyl-2-((phenylsulfonyl)methyl)cyclohexyl)methanone (3p):

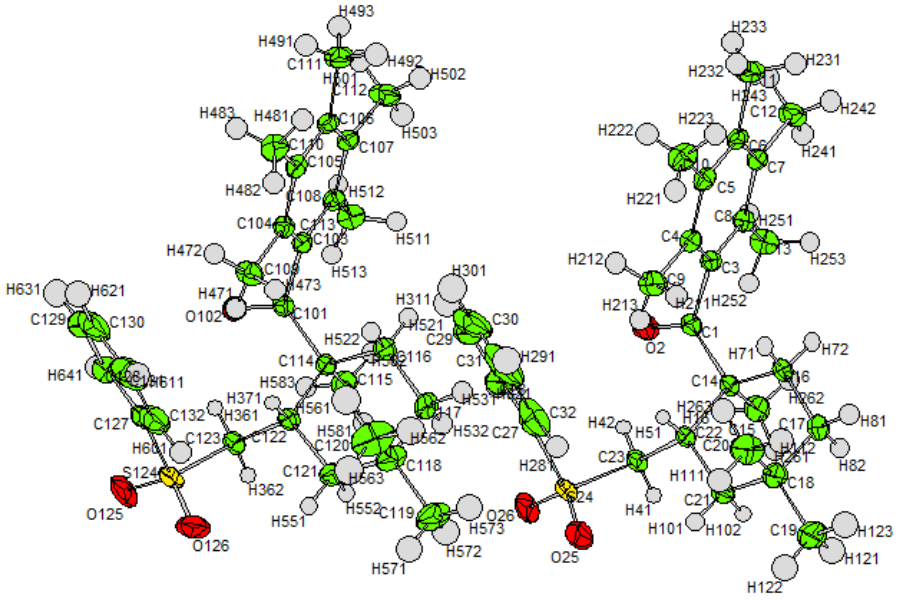
Recrystallised from $CHCl_3$/Hexane/MTBE





Formula C28 H38 O3 S

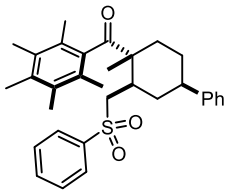
Crystal Class	monoclinic	Space Group	P 21/c
a	21.3312(2)	alpha	90
b	12.6039(1)	beta	115.7155(10)
c	20.5534(2)	gamma	90
Volume	4978.62(9)	Z	8
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.21	Mr	454.67
Mu	1.354	Temperature (K)	150
Size	0.20 × 0.20 × 0.20		
Colour	translucent pale colourless	Shape	cube
Cell from	50850 Reflections	Theta range	4 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.62-0.76
Reflections measured	93581	Independent reflections	10329
Rint	0.041	Theta max	74.644
Hmin, Hmax	-26 26		
Kmin, Kmax	-15 15		
Lmin, Lmax	-25 25		
Refinement on Fsqd			
R-factor	0.0442	Weighted R-factor	0.1168
Max shift/su	0.0008559		
Delta Rho min	-0.45	Delta Rho max	0.34
Reflections used	10329	sigma(I) limit	-3.00
Number of parameters	577	Goodness of fit	0.9766

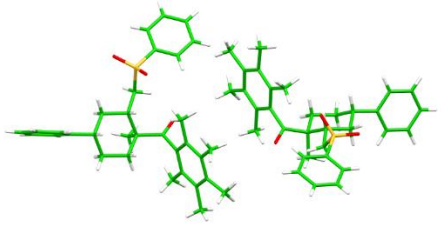


Thermal ellipsoids are drawn at the 50% probability level.

(1-Methyl-4-phenyl-2-((phenylsulfonyl)methyl)cyclohexyl)(2,3,4,5,6-pentamethylphenyl)methanone (3q):

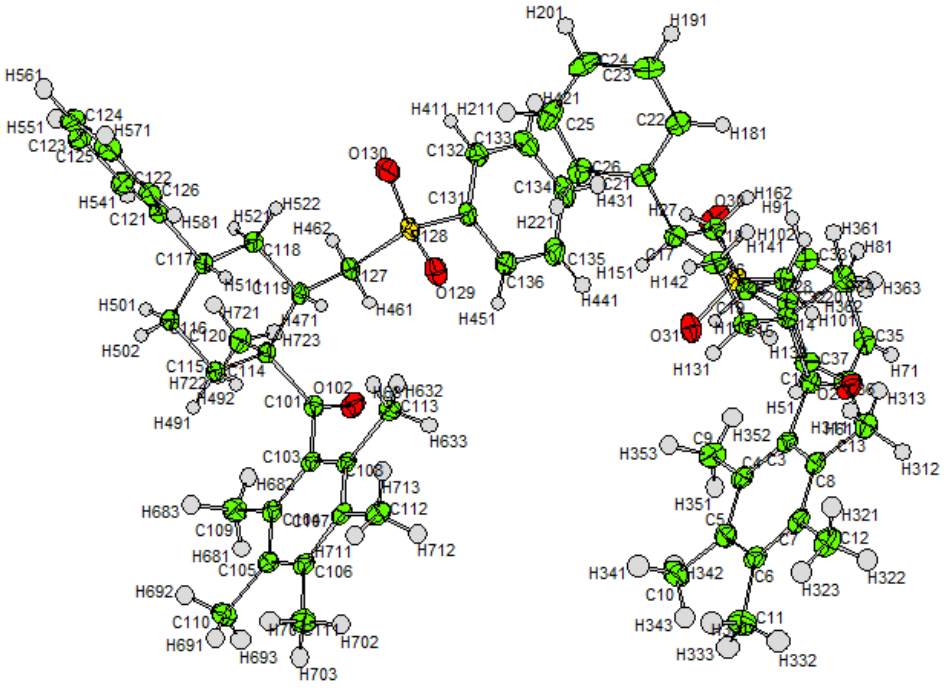
Recrystallised from $CHCl_3$/Hexane/MeOH





Formula C32 H38 O3 S

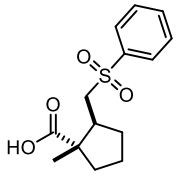
Crystal Class	triclinic	Space Group	P -1
a	8.7976(1)	alpha	108.163(2)
b	15.5963(4)	beta	98.2579(15)
c	20.6782(4)	gamma	92.4685(16)
Volume	2656.27(10)	Z	4
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.26	Mr	502.72
Mu	1.323	Temperature (K)	150
Size	0.20 × 0.20 × 0.60		
Colour	translucent pale colourless	Shape	needle
Cell from	26991 Reflections	Theta range	4 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.48-0.77
Reflections measured	36853	Independent reflections	10940
Rint	0.030	Theta max	73.919
Hmin, Hmax	-11 8		
Kmin, Kmax	-19 19		
Lmin, Lmax	-25 25		
Refinement on Fsqd			
R-factor	0.0394	Weighted R-factor	0.1036
Max shift/su	0.0006249		
Delta Rho min	-0.41	Delta Rho max	0.40
Reflections used	10940	sigma(I) limit	-3.00
Number of parameters	649	Goodness of fit	0.9868



Thermal ellipsoids are drawn at the 50% probability level.

(1*SR*,2*SR*)-1-Methyl-2-((phenylsulfonyl)methyl)cyclopentane-1-carboxylic acid (5):

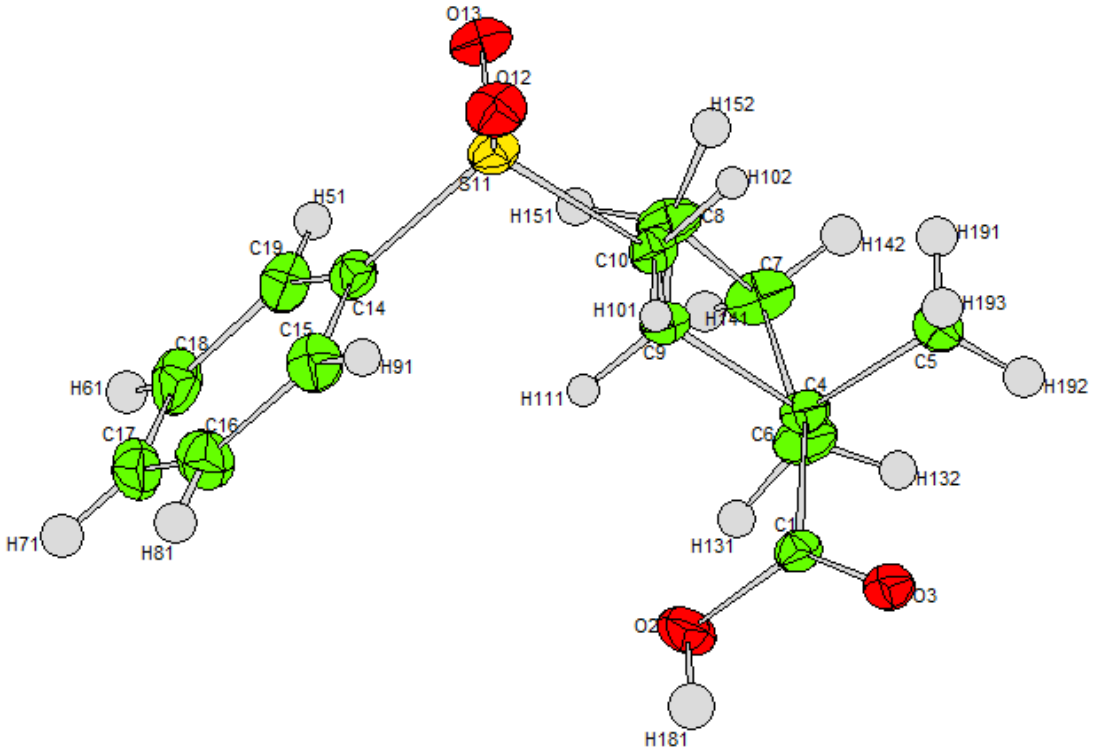
Recrystallised from CH_2Cl_2/EtOAc





Formula C14 H18 O4 S

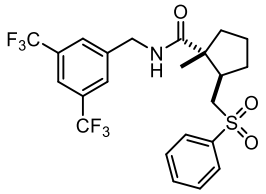
Crystal Class	monoclinic	Space Group	P 21/c
a	10.0128(1)	alpha	90
b	13.9422(1)	beta	114.9904(11)
c	10.8501(1)	gamma	90
Volume	1372.87(2)	Z	4
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.37	Mr	282.36
Mu	2.172	Temperature (K)	150
Size	0.20 × 0.20 × 0.20		
Colour	pale light colourless	Shape	irregular
Cell from	23076 Reflections	Theta range	5 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.47-0.65
Reflections measured	29135	Independent reflections	2871
Rint	0.021	Theta max	76.183
Hmin, Hmax	-12 12		
Kmin, Kmax	-17 17		
Lmin, Lmax	-13 13		
Refinement on Fsqd			
R-factor	0.0274	Weighted R-factor	0.0765
Max shift/su	0.0005886		
Delta Rho min	-0.36	Delta Rho max	0.28
Reflections used	2871	sigma(I) limit	-3.00
Number of parameters	176	Goodness of fit	0.9772

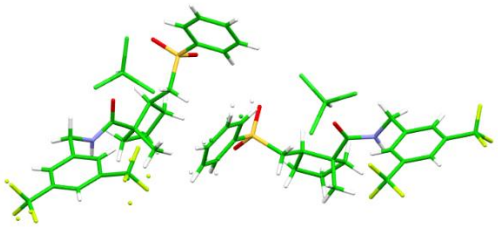


Thermal ellipsoids are drawn at the 50% probability level.

(1*RS*,2*RS*)-*N*-(3,5-Bis(trifluoromethyl)benzyl)-1-methyl-2-((phenylsulfonyl)methyl)cyclopentane-1-carboxamide (8):

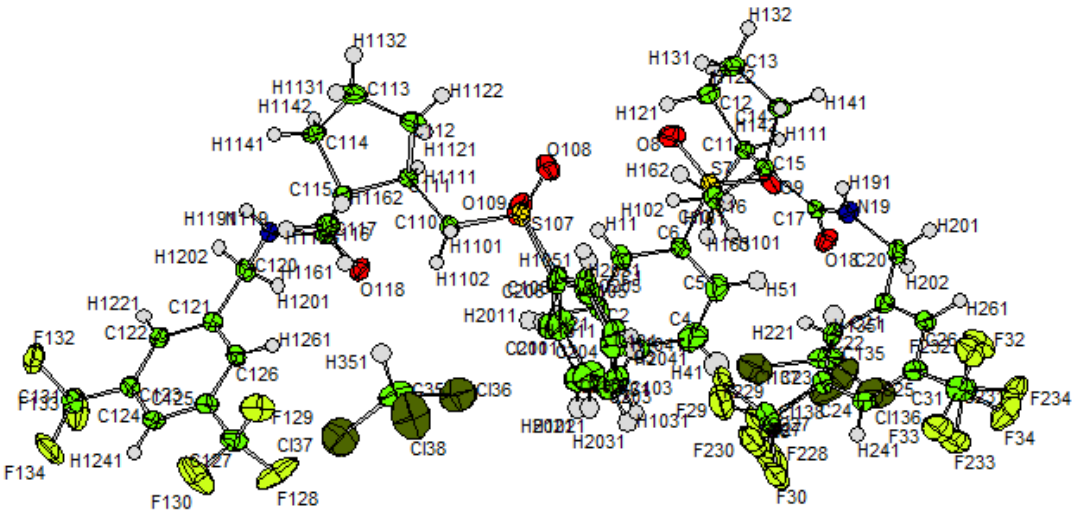
Recrystallised from CH_2Cl_2/EtOAc





Formula C23 H23 F6 N O3 S, C H Cl3

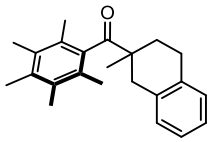
Crystal Class	monoclinic	Space Group	P 21/c
a	9.9278(1)	alpha	90
b	27.1253(2)	beta	90.7049(8)
c	20.2583(2)	gamma	90
Volume	5455.04(9)	Z	8
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.53	Mr	626.87
Mu	4.390	Temperature (K)	150
Size	0.20 × 0.40 × 0.80		
Colour	translucent pale colourless	Shape	lath
Cell from	62340 Reflections	Theta range	4 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.04-0.42
Reflections measured	128032	Independent reflections	11382
Rint	0.070	Theta max	74.751
Hmin, Hmax	-12 12		
Kmin, Kmax	-34 34		
Lmin, Lmax	-22 25		
Refinement on Fsqd			
R-factor	0.0604	Weighted R-factor	0.1449
Max shift/su	0.0049594		
Delta Rho min	-0.88	Delta Rho max	0.96
Reflections used	11382	sigma(I) limit	-3.00
Number of parameters	814	Goodness of fit	1.0031

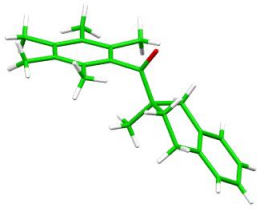


Thermal ellipsoids are drawn at the 50% probability level.

(2-Methyl-1,2,3,4-tetrahydronaphthalen-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone (13a):

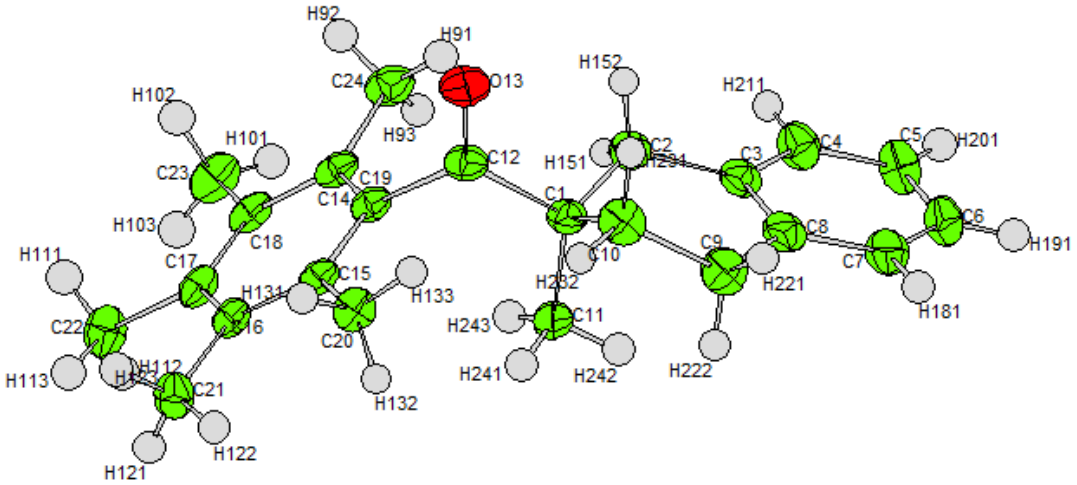
Recrystallised from MeOH





Formula C23 H28 O

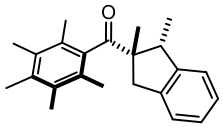
Crystal Class	monoclinic	Space Group	P 21/n
a	6.2088(1)	alpha	90
b	12.5108(3)	beta	93.915(2)
c	23.2538(5)	gamma	90
Volume	1802.07(7)	Z	4
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.18	Mr	320.47
Mu	0.531	Temperature (K)	150
Size	0.20 × 0.20 × 0.60		
Colour	translucent pale colourless	Shape	needle
Cell from	7166 Reflections	Theta range	4 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.49-0.90
Reflections measured	11817	Independent reflections	3732
Rint	0.027	Theta max	73.883
Hmin, Hmax	-7 7		
Kmin, Kmax	-15 13		
Lmin, Lmax	-29 26		
Refinement on Fsqd			
R-factor	0.0472	Weighted R-factor	0.1219
Max shift/su	0.0068597		
Delta Rho min	-0.17	Delta Rho max	0.27
Reflections used	3728	sigma(I) limit	-3.00
Number of parameters	217	Goodness of fit	0.9798

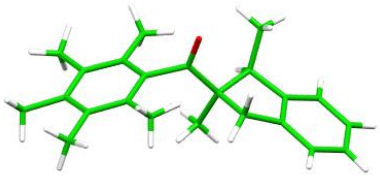


Thermal ellipsoids are drawn at the 50% probability level.

((1*RS*,2*SR*)-1,2-dimethyl-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone (17):

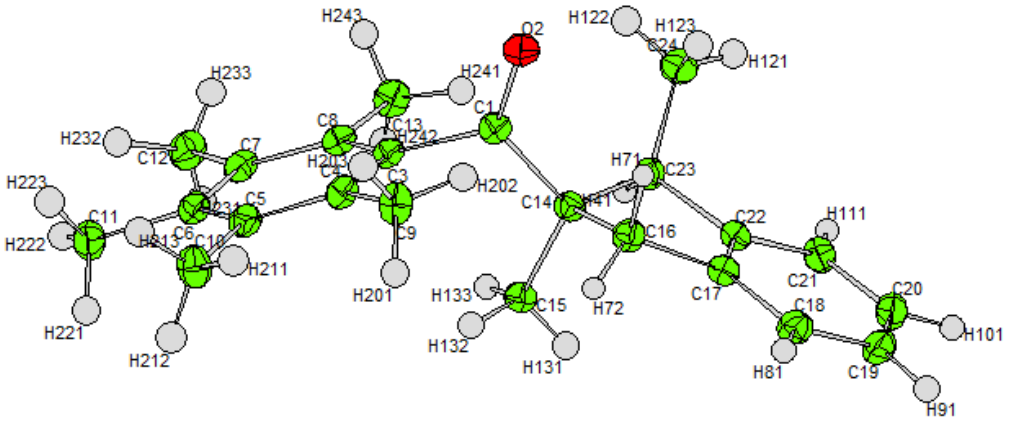
Recrystallised from $CHCl_3$/Hexane





Formula C23 H28 O

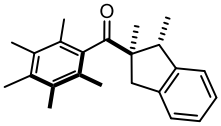
Crystal Class	monoclinic	Space Group	P 21/n
a	6.9236(1)	alpha	90
b	10.2877(1)	beta	97.5344(5)
c	25.5860(1)	gamma	90
Volume	1372.87(2)	Z	4
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.18	Mr	320.47
Mu	0.529	Temperature (K)	100
Size	0.10 × 0.10 × 0.30		
Colour	clear pale colourless	Shape	needle
Cell from	32088 Reflections	Theta range	3 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.84-0.95
Reflections measured	43267	Independent reflections	3738
Rint	0.020	Theta max	73.824
Hmin, Hmax	-8 8		
Kmin, Kmax	-10 12		
Lmin, Lmax	-31 32		
Refinement on Fsqd			
R-factor	0.0438	Weighted R-factor	0.1151
Max shift/su	0.0005622		
Delta Rho min	-0.23	Delta Rho max	0.25
Reflections used	3738	sigma(I) limit	-3.00
Number of parameters	217	Goodness of fit	0.9799

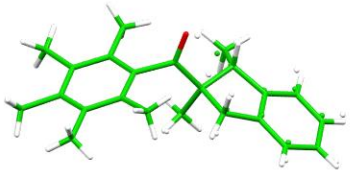


Thermal ellipsoids are drawn at the 50% probability level.

((1*RS*,2*RS*)-1,2-dimethyl-2,3-dihydro-1*H*-inden-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone (18):

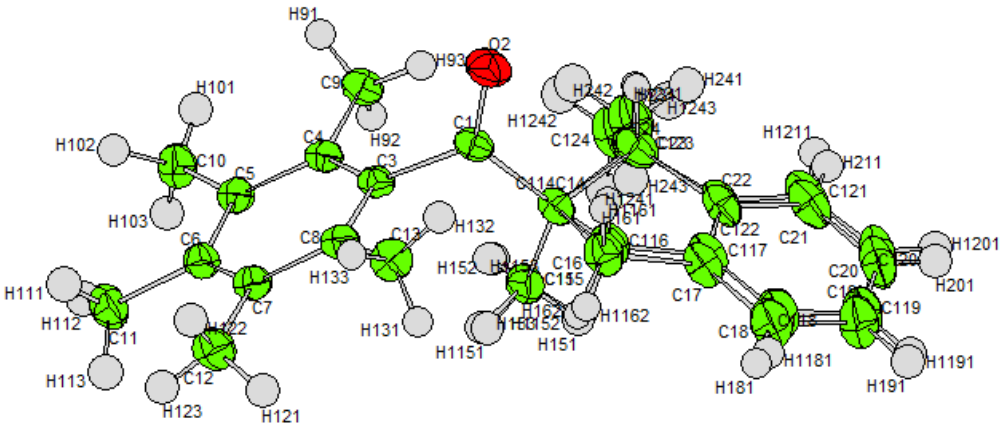
Recrystallised from $CHCl_3$/Hexane





Formula C23 H28 O

Crystal Class	monoclinic	Space Group	P 1 21/n 1
a	6.4087(1)	alpha	90
b	12.2607(2)	beta	95.8532(14)
c	23.2559(3)	gamma	90
Volume	1817.81(5)	Z	4
Radiation type	Cu K\a	Wavelength	1.54184
Dx	1.17	Mr	320.47
Mu	0.526	Temperature (K)	150
Size	0.10 × 0.20 × 0.50		
Colour	translucent light colourless	Shape	lath
Cell from	17081 Reflections	Theta range	4 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.48-0.99
Reflections measured	35895	Independent reflections	3775
Rint	0.048	Theta max	74.612
Hmin, Hmax	-7 7		
Kmin, Kmax	-15 15		
Lmin, Lmax	-29 29		
Refinement on Fsqd			
R-factor	0.0684	Weighted R-factor	0.1775
Max shift/su	0.0039498		
Delta Rho min	-0.27	Delta Rho max	0.58
Reflections used	3775	sigma(I) limit	-3.00
Number of parameters	244	Goodness of fit	0.9677



Thermal ellipsoids are drawn at the 50% probability level.

8. References

1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J., *Organometallics* **1996,** *15* (5), 1518-1520.
2. Cosier, J.; Glazer, A. M., *J. Appl. Cryst.* **1986,** *19*, 105-107.
3. Palatinus, L.; Chapuis, G., *J. Appl. Cryst.* **2007,** *40*, 786-790.
4. Cooper, R. I. T., A. L.; Watkin, D. J., *J. Appl. Cryst.* **2010,** *43*, 1100-1107.
5. Parois, P.; Cooper, R. I.; Thompson, A. L., *Chem. Cent. J.* **2015,** *9* (1), 30.
6. Frost, J. R.; Cheong, C. B.; Akhtar, W. M.; Caputo, D. F. J.; Christensen, K. E.; Stevenson, N. G.; Donohoe, T. J., *Tetrahedron* **2021,** *86*, 132051.
7. Chen, S.; Li, Y.; Wang, M.; Jiang, X., *Green Chem.* **2020,** *22* (2), 322-326.
8. Ozaki, T.; Yorimitsu, H.; Perry, G. J. P., *Chem. Eur. J.* **2021,** *27* (62), 15387-15391.
9. Yang, C.; Jin, Q.; Zhang, H.; Liao, J.; Zhu, J.; Yu, B.; Deng, J., *Green Chem.* **2009,** *11* (9), 1401-1405.
10. Zhou, G.; Ting, P.; Aslanian, R.; Piwinski, J. J., *Org. Lett.* **2008,** *10* (12), 2517-2520.
11. Barton, P. J. C., D. S.; Davies, C. D.; Hargreaves, R. B.; Pease, J. E.; Rankine, M. T.; Chemical Compounds. WO2004011410A1, 2004.
12. Frost, J. R.; Cheong, C. B.; Akhtar, W. M.; Caputo, D. F.; Stevenson, N. G.; Donohoe, T. J., *J. Am. Chem. Soc.* **2015,** *137* (50), 15664-7.
13. Frost, J. R.; Cheong, C. B.; Akhtar, W. M.; Caputo, D. F. J.; Stevenson, N. G.; Donohoe, T. J., *J. Am. Chem. Soc.* **2015,** *137* (50), 15664-15667.
14. Zheng, T.; Narayan, R. S.; Schomaker, J. M.; Borhan, B., *J. Am. Chem. Soc.* **2005,** *127* (19), 6946-6947.
15. Masuda, Y.; Ito, M.; Murakami, M., *Chem. Lett.* **2021,** *50* (5), 1030-1033.
16. Yuan, G.; Liu, J.; Yu, S.; Wang, X.; Bian, Q.; Wang, M.; Zhong, J., *Synlett* **2021,** *33* (01), 80-83.
17. Akhtar, W. M.; Armstrong, R. J.; Frost, J. R.; Stevenson, N. G.; Donohoe, T. J., *J. Am. Chem. Soc.* **2018,** *140* (38), 11916-11920.
18. Mitachi, K.; Aleiwi, B. A.; Schneider, C. M.; Siricilla, S.; Kurosu, M., *J. Am. Chem. Soc.* **2016,** *138* (39), 12975-12980.
19. Akhtar, W. M.; Armstrong, R. J.; Frost, J. R.; Stevenson, N. G.; Donohoe, T. J., *J. Am. Chem. Soc.* **2018,** *140* (38), 11916-11920.
20. Kiprof, P.; Li, J.; Renish, C. L.; Kalombo, E. K.; Young, V. G., *J Organomet Chem* **2001,** *620* (1-2), 113-118.
21. Lerch, S.; Fritsch, S.; Strassner, T., *Beilstein J. Org. Chem.* **2023,** *19*, 212-216.
22. Gündemir-Durmaz, T.; Schmid, F.; El Baz, Y.; Häusser, A.; Schneider, C.; Bilitewski, U.; Rauhut, G.; Garnier, D.; Baro, A.; Laschat, S., *Org. Biomol. Chem.* **2016,** *14* (35), 8261-8269.
23. Moser, D.; Jana, K.; Sparr, C., *Angew. Chem. Int. Ed. Engl.* **2023,** *62* (39), e202309053.
24. Santoso, H.; Casana, M. I.; Donner, C. D., *Org. Biomol. Chem.* **2014,** *12* (1), 171-176.
25. Chen, L.-Y.; Li, J., *J. Org. Chem.* **2023,** *88* (14), 10252-10256.
26. Vlaar, T.; Mampuys, P.; Helliwell, M.; Maes, B. U. W.; Orru, R. V. A.; Ruijter, E., *J. Org. Chem.* **2013,** *78* (13), 6735-6745.
27. Zhuang, Z.; Herron, A. N.; Liu, S.; Yu, J.-Q., *J. Am. Chem. Soc.* **2021,** *143* (2), 687-692.
28. Ramachary, D. B.; Mondal, R.; Venkaiah, C., *Eur. J. Org. Chem* **2010,** *2010* (17), 3205-3210.