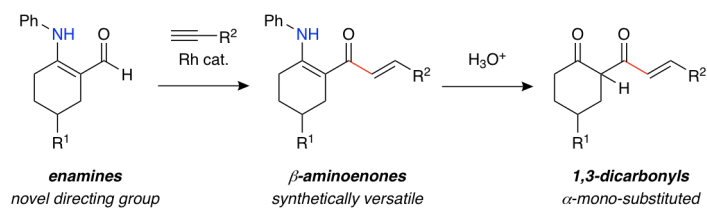


## An enamine controlling group for rhodium-catalyzed intermolecular hydroacylation

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Robert N. Straker, Michele Formica, James D. Lupton, Jingze Niu, and Michael C. Willis

*Department of Chemistry, University of Oxford, Chemistry Research Laboratory, Mansfield Road, Oxford, OX1 3TA, UK*





# An enamine controlling group for rhodium-catalyzed intermolecular hydroacylation

Robert N. Straker, Michele Formica, James D. Lupton, Jingze Niu, and Michael C. Willis\*

Department of Chemistry, University of Oxford, Chemistry Research Laboratory, Mansfield Road, Oxford, OX1 3TA, UK.

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## ABSTRACT

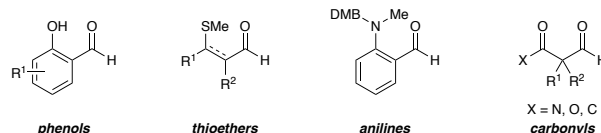
An enamine-controlled hydroacylation of alkynes using a rhodium(I)/dppe catalyst system is described. The reaction is highly selective, forming the linear enaminone products as single regioisomers in all examples. *In situ* hydrolysis of the enamine functionality generated  $\alpha$ -substituted 1,3-diketone products, and Lewis-acid mediated intramolecular conjugate addition of the hydroacylation products gave substituted hexahydroquinolones.

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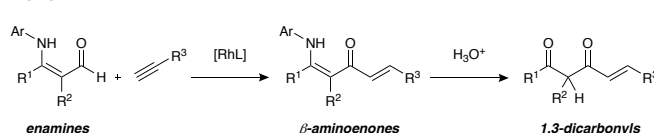
## 1. Introduction

The discovery and optimization of atom efficient processes with which to construct functionalized organic scaffolds is at the forefront of modern Organic and Medicinal Chemistry.<sup>1,2</sup> The field of hydroacylation chemistry, the formal addition of a C–H bond across a  $\pi$ -bond, has grown over the past decade to not only become a robust method for the formation of ketones, enones, and esters,<sup>3,4</sup> but also a platform for the formation of heterocycles.<sup>5–7</sup> In the majority of cases, hydroacylation requires the use of a tethered directing group on either the aldehyde or alkene/alkyne coupling partner in order to avoid reductive decarbonylation.<sup>8–17</sup> Recent methodologies have enabled the use of a variety of functionalities as directing groups (Scheme 1), including but not limited to; phenols,<sup>18–21</sup> thioethers,<sup>22–26</sup> anilines,<sup>27</sup> and most recently, carbonyl groups.<sup>28</sup> A limitation of ester and ketone-directed hydroacylation is that the inherent acidity of the  $\alpha$ -proton results in ready tautomerization under the reaction conditions, and this predominant enol form binds unproductively to the metal catalyst. This issue was alleviated by the use of  $\alpha,\alpha$ -disubstituted  $\beta$ -keto aldehydes and  $\beta$ -formyl esters, but  $\alpha$ -mono-substituted substrates could not be used. Enamines have thus far not been explored as directing groups in hydroacylation reactions, yet they have the potential not only to form synthetically useful enaminones,<sup>29–32</sup> but also to act as carbonyl surrogates which, upon hydrolysis, would provide access to otherwise inaccessible dicarbonyl hydroacylation products. Our laboratory has previously reported amine-directed hydroacylation.<sup>33</sup> In these reactions, the Lewis-basicity of the amine was tempered by virtue of its phenyl substituents. We envisaged aniline-derived enamines exhibiting similar reactivity in controlling hydroacylation, but with the potential for further functionalization.

### directing groups:



### this work:



**Scheme 1.** Directing groups in intermolecular hydroacylation, and enamine-directed alkyne hydroacylation.

## 2. Results and discussion

After a brief evaluation of amine substituents, we chose to proceed in our investigations with cyclohexene  $\beta$ -aminoenal **1a**, which, in combination with 1-octyne, was submitted to rhodium(I) catalysis with a number of *bis*-phosphine ligands of varying bite-angle and phosphine substituent (Table 1). Catalyst systems comprised of narrow bite-angle ligands dcpm, dppm and PNP(Cy) led to low conversions of aldehyde substrate after 18 hours at 55 °C, but gave high levels of regioselectivity for the linear product **2a** over the branched **3a** (Entries 1–3). Wider bite-angle ligands dcpe and dppe enhanced this selectivity and increased reactivity (Entries 4 and 5), with dppe generating the product in >20:1 rr and in 87% <sup>1</sup>H NMR yield. It was possible to isolate product **2a**, after purification on silica gel, as a single regioisomer in 73% yield, but

**Table 1.** Optimization of enamine-directed hydroacylation reaction conditions.<sup>a</sup>

Entry	Ligand	Ratio ( <b>2a</b> : <b>3a</b> ) <sup>b</sup>	Yield / % <sup>b</sup>
1	dcpm	9:1	40
2	dppm	9:1	15
3	PNP(Cy)	15:1	23
4	dcpe	>20:1	36
5	dppe	>20:1	87 (73) <sup>c</sup>
6	dppp	>20:1	53
7	DPEphos	9:1	7

dcpm, R = Cy  
dppm, R = Ph

PNP(Cy)

dcpe, R = Cy  
dppe, R = Ph

dppp

DPEphos

a. Reaction conditions: Rh(nbd)<sub>2</sub>BF<sub>4</sub> (5 mol%), ligand (5 mol%), aldehyde (0.3 mmol, 1.0 equiv.), alkyne (1.5 equiv.), acetone (0.5 M), 55 °C for 18 h. b. Yield determined by <sup>1</sup>H NMR spectroscopic analysis of the crude reaction mixture, using 1,3,5-trimethoxybenzene as internal standard. c. Isolated yield of **2a**.

it was found to hydrolyze to the 1,3-dicarbonyl product if exposed to silica for extended periods of time. Further increases to ligand bite-angle proved to be deleterious, with dppp and DPEphos both leading to reduction in reaction efficiency.

With an efficient catalytic manifold for enamine-directed hydroacylation in hand, we applied the optimized conditions to β-aminoenal **1a** in reaction with various alkynes (Table 2). Pleasingly, more sterically encumbered aliphatic alkynes were well tolerated; cyclohexyl and *tert*-butyl substituted alkynes delivered the desired enone products **2b** and **2d** in 77% and 85% yield respectively. In order to demonstrate the practicability of this methodology, reaction of **1a** with 3,3-dimethyl-1-butyne was performed on a 4 mmol scale, using only 2.5 mol% catalyst, which gave product **2d** in 87% yield (0.99 g) after 18 hours at room temperature. Primary alkyl halides and silyl ether functionalities remained intact, with the corresponding products **2e** and **2f** isolated in high yields. It was found that hydroacylation of aryl alkynes was not possible under the reaction conditions, and that the aldehyde starting material could be cleanly recovered from reactions with both electron-rich and electron-poor phenyl-substituted alkynes. However, phenyl-substituted aliphatic alkyne underwent the desired hydroacylation, generating the product **2g** in 46% yield, and phthalimide product **2i** could also be obtained in moderate yield. We next examined variation of the aldehyde component in reaction with 1-octyne. Deviation of ring size to 5- or 7-membered rings resulted in complete loss of reactivity, which is likely due to a subtle electronic effect of the cyclohexene β-aminoenal, which is disrupted by changes in geometry. Likewise, substitution to the cyclohexene ring was unfavorable and only tolerated at the 4-position. Reaction of **1b-c** required 10 mol% catalyst loading, but nevertheless delivered products **2j-l** in good yields. Complete linear regioselectivity (>20:1 rr) was observed in all cases, and low yielding examples were only as a result of incomplete consumption of aldehyde starting material.

**Table 2.** Scope of β-Aminoenal hydroacylation.<sup>a</sup>

<b>2a</b> , 73%	<b>2b</b> , 77%	<b>2c</b> , 53%
<b>2d</b> , 85% (4 mmol, 2.5 mol% cat., 87%) <sup>b</sup>	<b>2e</b> , 63%	<b>2f</b> , 83%
<b>2g</b> , 46%	<b>2h</b> , 62%	<b>2i</b> , 50%
<b>2j</b> , 71% <sup>c</sup>	<b>2k</b> , 74% <sup>c</sup>	<b>2l</b> , 66% <sup>c</sup>

a. Reaction conditions: Rh(nbd)<sub>2</sub>BF<sub>4</sub> (5 mol%), dppe (5 mol%), aldehyde (0.3 mmol, 1.0 equiv.), alkyne (1.5 equiv.), acetone (0.5 M), 55 °C for 18 h. b. Performed with 4 mmol of aldehyde, using 2.5 mol% catalyst. c. 10 mol% catalyst was used.

Having developed the enamine-directed hydroacylation methodology and applied it to a number of combinations of aldehydes and alkynes, we next turned our attention to isolating the hydrolyzed enamine products from a one-pot hydroacylation/hydrolysis process (Table 3). It was found that direct addition of aqueous hydrochloric acid to the reaction vessel, following successful hydroacylation, facilitated rapid enamine hydrolysis (*ca* 2 hours). The α-mono-substituted 1,3-dicarbonyl products **4a-h** were generated in good to excellent yields and were

**Table 3.** Tandem enamine-directed hydroacylation/hydrolysis.<sup>a</sup>

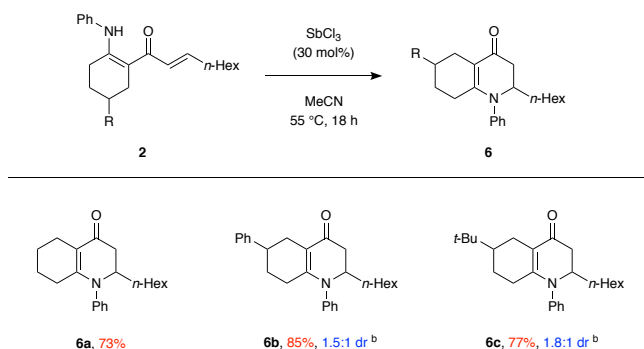
<b>4a</b> , 56%	<b>4b</b> , 66%	<b>4d</b> , 88%
<b>4e</b> , 70%	<b>4g</b> , 49%	<b>4h</b> , 73%

a. Reaction conditions: Rh(nbd)<sub>2</sub>BF<sub>4</sub> (5 mol%), dppe (5 mol%), aldehyde (0.3 mmol, 1.0 equiv.), alkyne (1.5 equiv.), acetone (0.5 M), 55 °C for 18 h, then aq. HCl (2 M, 0.6 mL).

indeed found to exist entirely as the enol tautomer (**5**), as was observed by  $^1\text{H}$  NMR spectroscopy in  $\text{CDCl}_3$ , and confirmed by HMBC analysis.

Finally, we investigated the possibility of further utilizing the enamine functionality in a Lewis acid-catalyzed aza-conjugate addition process,<sup>34</sup> in order to construct functionalized hexahydroquinolinones (Table 4). Pleasingly, using catalytic antimony(III) trichloride in acetonitrile for 18 hours at 55 °C, the isolated hydroacylation products (**2**) underwent the desired intramolecular cyclisation to generate bicyclic products **6a-c** in high yields. In the case of **6b** and **6c**, which bore substituents on the cyclohexene ring, low diastereoselectivity was observed in the conjugate addition (1.5:1 dr and 1.8:1 dr respectively). This was perhaps due to the planarity of the enamine preventing effective chirality relay in the formation of the new stereocentre.

**Table 4.** Lewis acid-mediated aza-conjugate addition.<sup>a</sup>



a. Reaction conditions:  $\beta$ -aminoenone (0.2 mmol, 1.0 equiv.),  $\text{SbCl}_3$  (30 mol%), MeCN (0.3 M), 55 °C for 18 h. b. Diastereomeric ratio determined by  $^1\text{H}$  NMR spectroscopic analysis of the crude reaction mixture.

### 3. Conclusions

We have demonstrated enamines as efficient directing groups for intermolecular hydroacylation of alkynes. Using a rhodium(I)/dppe catalyst system, the enaminone products were generated as single regioisomers (>20:1 rr), and isolated in moderate to high yields. These products could alternatively be hydrolyzed *in situ* to access the corresponding 1,3-dicarbonyl products, previously inaccessible using carbonyl-directed hydroacylation, or cyclized *via* intramolecular aza-conjugate addition to generate synthetically attractive hetero-bicyclic systems.

## 4. Experimental

### 4.1. General information

All reactions were performed under argon using standard Schlenk techniques.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were obtained on a Bruker AVIII400 (400 MHz) spectrometer using the residual solvent signal as an internal standard ( $\text{CDCl}_3$ :  $\delta_{\text{H}} = 7.26$  ppm,  $\delta_{\text{C}} = 77.16$  ppm). All coupling constants ( $J$  values) were reported in Hertz (Hz). Multiplicities were reported as follows: s, singlet; d, doublet; t, triplet; q, quartet; quin., quintet; m, multiplet. High-resolution mass spectrometry (HRMS) measurements were recorded on a Bruker Daltonics microTOF (ESI) spectrometer. Infrared spectra were recorded as thin films on a Bruker Tensor 27 FT-IR spectrometer. Flash chromatography was carried out using matrix 60 silica. All alkynes were distilled prior to use. Acetone was dried over Drierite<sup>TM</sup> overnight, distilled at atmospheric pressure, and degassed with argon prior to use.

### 4.2. Rhodium-catalyzed $\beta$ -aminoenal hydroacylation

#### 4.2.1. General procedure; 0.3 mmol scale

A 10 mL microwave vial containing  $[\text{Rh}(\text{nbd})_2]\text{BF}_4$  (5 mol%) and dppe (5 mol%) was placed under vacuum (0.05 mbar) and back-filled with argon. This vacuum cycle was repeated three times. The mixture was dissolved in acetone (0.5 mL), and hydrogen bubbled through the solution for 1 min. The solvent was then removed by purging the vial with argon. The air and moisture sensitive catalyst residue was dissolved in acetone (0.6 mL), and the solution added to an argon-filled 10 mL microwave vial containing aldehyde (0.3 mmol, 1.0 equiv.) and alkyne (0.45 mmol, 1.5 equiv.). The solution was stirred at 55 °C for 18 h, after which time the reaction mixture was concentrated in vacuo. The crude material was purified by flash column chromatography.

#### 4.2.2. General procedure; 4 mmol scale

A 10 mL microwave vial containing  $[\text{Rh}(\text{nbd})_2]\text{BF}_4$  (2.5 mol%) and dppe (2.5 mol%) was placed under vacuum (0.05 mbar) and back-filled with argon. This vacuum cycle was repeated three times. The mixture was dissolved in acetone (2.0 mL), and hydrogen bubbled through the solution for 2 min. The solvent was then removed by purging the vial with argon. The air and moisture sensitive catalyst residue was dissolved in acetone (4.0 mL), and the solution added to an argon-filled 25 mL round-bottom flask containing a stirred solution of aldehyde (4.00 mmol, 1.0 equiv.) and alkyne (6.00 mmol, 1.5 equiv.) in acetone (4.0 mL). The solution was stirred at 55 °C for 18 h, after which time the reaction mixture was concentrated in vacuo. The crude material was purified by flash column chromatography.

#### 4.2.3. (*E*)-1-(2-(Phenylamino)cyclohex-1-en-1-yl)non-2-en-1-one, (**2a**)

Yellow oil, 73% yield.  $R_f$  0.28 (petroleum ether /  $\text{Et}_2\text{O}$  (95:5)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2927, 2856, 1575, 1499, 1206, 1169, 751, 698;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.75 (1H, s), 7.31 (2H, d,  $J = 8.0$  Hz), 7.14 (1H, t,  $J = 7.5$  Hz), 7.10 (2H, d,  $J = 7.5$  Hz), 6.85 (1H, dt,  $J = 15.0$  and 7.0 Hz), 6.58 (1H, d,  $J = 15.0$  Hz), 2.55 (2H, t,  $J = 6.5$  Hz), 2.42 (2H, t,  $J = 6.0$  Hz), 2.23 (2H, qd,  $J = 7.0$  and 1.0 Hz), 1.72-1.66 (2H, m), 1.62-1.56 (2H, m), 1.51-1.43 (2H, m), 1.37-1.23 (6H, m), 0.89 (3H, t,  $J = 7.0$  Hz);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.4, 160.8, 144.2, 139.3, 129.0, 127.2, 125.4, 125.1, 102.1, 32.9, 31.8, 29.1, 28.8, 28.6, 25.5, 23.2, 22.7, 21.9, 14.2; HRMS (ESI<sup>+</sup>) calc. for  $\text{C}_{21}\text{H}_{30}\text{NO}$   $[\text{M}+\text{H}]^+$  312.2322, found 312.2321.

#### 4.2.4. (*E*)-3-Cyclohexyl-1-(2-(phenylamino)cyclohex-1-en-1-yl)prop-2-en-1-one, (**2b**)

Yellow oil, 77% yield.  $R_f$  0.24 (petroleum ether /  $\text{Et}_2\text{O}$  (95:5)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2923, 2850, 1572, 1499, 1163, 963, 752, 697;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.78 (1H, s), 7.30 (2H, t,  $J = 8.0$  Hz), 7.14 (1H, t,  $J = 7.5$  Hz), 7.09 (2H, d,  $J = 7.5$  Hz), 6.81 (1H, dd,  $J = 15.5$  and 7.0 Hz), 6.54 (1H, dd,  $J = 15.5$  and 1.0 Hz), 2.54 (2H, t,  $J = 6.5$  Hz), 2.41 (2H, t,  $J = 6.0$  Hz), 2.20-2.14 (1H, m), 1.80-1.66 (7H, m), 1.61-1.55 (2H, m), 1.36-1.13 (5H, m);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.6, 160.7, 149.2, 139.3, 129.0, 125.4, 125.1, 124.6, 102.3, 41.1, 32.4, 28.6, 26.2, 26.0, 25.5, 23.2, 21.9; HRMS (ESI<sup>+</sup>) calc. for  $\text{C}_{21}\text{H}_{28}\text{NO}$   $[\text{M}+\text{H}]^+$  310.2165, found 310.2165.

#### 4.2.5. (*E*)-3-Cyclopentyl-1-(2-(phenylamino)cyclohex-1-en-1-yl)prop-2-en-1-one, (**2c**)

Yellow oil, 53%.  $R_f$  0.33 (petroleum ether /  $\text{Et}_2\text{O}$  (90:10)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2939, 1574, 1295, 1254, 1208, 698;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.78 (1H, s), 7.30 (2H, t,  $J = 8.0$  Hz), 7.15-7.08 (3H, m), 6.84 (1H, dd,  $J = 15.0$  and 8.5 Hz), 6.56 (1H, d,  $J = 15.0$  Hz), 2.68-2.58 (1H, m), 2.54 (2H, t,  $J = 6.5$  Hz), 2.41 (2H, t,

$J = 6.5$  Hz), 1.87-1.80 (2H, m), 1.74-1.64 (4H, m), 1.63-1.55 (4H, m), 1.48-1.39 (2H, m);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.4, 160.7, 148.4, 139.3, 129.0, 125.3, 125.2, 125.1, 102.2, 43.5, 33.0, 28.6, 25.5, 25.4, 23.2, 21.9; HRMS ( $\text{ESI}^+$ ) calc. for  $\text{C}_{20}\text{H}_{26}\text{NO}$   $[\text{M}+\text{H}]^+$  296.2009, found 296.2022.

#### 4.2.6. (E)-4,4-Dimethyl-1-(2-(phenylamino)cyclohex-1-en-1-yl)pent-2-en-1-one, (2d)

Yellow oil, 85% yield.  $R_f$  0.30 (petroleum ether /  $\text{Et}_2\text{O}$  (95:5)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2958, 1576, 1499, 1301, 1270, 1215, 1168;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.79 (1H, s), 7.31 (2H, t,  $J = 8.0$  Hz), 7.14 (1H, t,  $J = 7.5$  Hz), 7.10 (2H, d,  $J = 7.5$  Hz), 6.87 (1H, d,  $J = 15.5$  Hz), 6.49 (1H, d,  $J = 15.5$  Hz), 2.56 (2H, t,  $J = 6.5$  Hz), 2.42 (2H, t,  $J = 6.0$  Hz), 1.73-1.66 (2H, m), 1.63-1.56 (2H, m), 1.11 (9H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.7, 160.7, 154.1, 139.3, 129.0, 125.4, 125.1, 122.1, 102.4, 33.9, 29.2, 28.6, 25.5, 23.2, 21.9; HRMS ( $\text{ESI}^+$ ) calc. for  $\text{C}_{19}\text{H}_{26}\text{NO}$   $[\text{M}+\text{H}]^+$  284.2009, found 284.2007.

#### 4.2.7. (E)-6-Chloro-1-(2-(phenylamino)cyclohex-1-en-1-yl)hex-2-en-1-one, (2e)

Yellow oil, 63% yield.  $R_f$  0.28 (petroleum ether /  $\text{Et}_2\text{O}$  (90:10)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2935, 1572, 1498, 1434, 1293, 1264, 1213, 1179, 750, 698;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.77 (1H, s), 7.31 (2H, t,  $J = 8.0$  Hz), 7.16 (1H, t,  $J = 7.5$  Hz), 7.10 (2H, d,  $J = 7.5$  Hz), 6.78 (1H, dt,  $J = 15.0$  and 7.0 Hz), 6.64 (1H, d,  $J = 15.0$  Hz), 3.57 (2H, t,  $J = 6.5$  Hz), 2.54 (2H, t,  $J = 6.5$  Hz), 2.43-2.38 (4H, m), 1.99-1.92 (2H, m), 1.72-1.66 (2H, m), 1.62-1.56 (2H, m);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  187.7, 161.3, 141.3, 139.1, 129.0, 128.5, 125.5, 125.3, 102.0, 44.4, 31.4, 29.8, 28.6, 25.4, 23.2, 21.8; HRMS ( $\text{ESI}^+$ ) calc. for  $\text{C}_{18}\text{H}_{23}^{35}\text{ClNO}$   $[\text{M}+\text{H}]^+$  304.1463, found 304.1463.

#### 4.2.8. (E)-6-((tert-Butyldimethylsilyl)oxy)-1-(2-(phenylamino)cyclohex-1-en-1-yl)hex-2-en-1-one, (2f)

Yellow oil, 83% yield.  $R_f$  0.33 (petroleum ether /  $\text{Et}_2\text{O}$  (90:10)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2929, 2856, 1573, 1499, 1210, 1167, 1097, 834;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.76 (1H, s), 7.30 (2H, t,  $J = 8.0$  Hz), 7.14 (1H, t,  $J = 7.5$  Hz), 7.10 (2H, d,  $J = 8.0$  Hz), 6.85 (1H, dt,  $J = 15.0$  and 7.0 Hz), 6.60 (1H, d,  $J = 15.0$  Hz), 3.65 (2H, t,  $J = 6.0$  Hz), 2.54 (2H, t,  $J = 6.5$  Hz), 2.41 (2H, t,  $J = 6.5$  Hz), 2.30 (2H, q,  $J = 7.0$  Hz), 1.73-1.66 (4H, m), 1.61-1.55 (2H, m), 0.90 (9H, s), 0.06 (6H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.1, 160.9, 143.4, 139.2, 129.0, 127.4, 125.4, 125.1, 102.0, 62.5, 31.8, 29.2, 28.6, 26.1, 25.5, 23.2, 21.9, 18.4, -5.2; HRMS ( $\text{ESI}^+$ ) calc. for  $\text{C}_{24}\text{H}_{38}\text{NO}_2\text{Si}$   $[\text{M}+\text{H}]^+$  400.2666, found 400.2676.

#### 4.2.9. (E)-5-Phenyl-1-(2-(phenylamino)cyclohex-1-en-1-yl)pent-2-en-1-one, (2g)

Yellow oil, 46%.  $R_f$  0.18 (petroleum ether /  $\text{Et}_2\text{O}$  (90:10)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2955, 1573, 1207, 1171, 689;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.75 (1H, s), 7.34-7.28 (4H, m), 7.23-7.19 (3H, m), 7.16 (1H, t,  $J = 7.5$  Hz), 7.11 (2H, d,  $J = 8.0$  Hz), 6.90 (1H, dt,  $J = 15.0$  and 7.0 Hz), 6.60 (1H, d,  $J = 15.0$  Hz), 2.81 (2H, dd,  $J = 8.0$  and 7.5 Hz), 2.57 (2H, q,  $J = 7.0$  Hz), 2.50 (2H, t,  $J = 6.5$  Hz), 2.42 (2H, t,  $J = 6.5$  Hz), 1.72-1.66 (2H, m), 1.62-1.56 (2H, m);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.1, 161.0, 142.6, 141.5, 139.3, 129.0, 128.5, 128.5, 127.9, 126.1, 125.5, 125.2, 102.1, 35.1, 34.7, 28.6, 25.5, 23.2, 21.9; HRMS ( $\text{ESI}^+$ ) calc. for  $\text{C}_{23}\text{H}_{26}\text{NO}$   $[\text{M}+\text{H}]^+$  332.2009, found 332.2004.

#### 4.2.10. (E)-4-Cyclohexyl-1-(2-(phenylamino)cyclohex-1-en-1-yl)but-2-en-1-one, (2h)

Yellow oil, 62% yield.  $R_f$  0.37 (petroleum ether /  $\text{Et}_2\text{O}$  (90:10)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2921, 2850, 1573, 1499, 1435, 1266,

1214, 1167;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.76 (1H, s), 7.31 (2H, t,  $J = 8.0$  Hz), 7.14 (1H, t,  $J = 8.0$  Hz), 7.10 (2H, d,  $J = 8.0$  Hz), 6.84 (1H, dt,  $J = 15.0$  and 7.5 Hz), 6.56 (1H, d,  $J = 15.0$  Hz), 2.54 (2H, t,  $J = 6.5$  Hz), 2.42 (2H, t,  $J = 6.5$  Hz), 2.13 (2H, t,  $J = 7.5$  Hz), 1.77-1.56 (9H, m), 1.49-1.37 (1H, m), 1.28-1.10 (3H, m), 0.95 (2H, m);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.2, 160.8, 142.9, 139.3, 129.0, 128.2, 125.4, 125.1, 102.1, 40.9, 37.8, 33.4, 28.6, 26.6, 26.4, 25.5, 23.2, 21.9; HRMS ( $\text{ESI}^+$ ) calc. for  $\text{C}_{22}\text{H}_{30}\text{NO}$   $[\text{M}+\text{H}]^+$  324.2322, found 324.2321.

#### 4.2.11. (E)-2-(7-Oxo-7-(2-(phenylamino)cyclohex-1-en-1-yl)hept-5-en-1-yl)isoindoline-1,3-dione, (2i)

Yellow oil, 50% yield.  $R_f$  0.26 (petroleum ether /  $\text{EtOAc}$  (80:20)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2980, 2936, 1711, 1574, 1396, 1170, 720;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.73 (1H, s), 7.84-7.79 (2H, m), 7.71-7.67 (2H, m), 7.29 (2H, d,  $J = 8.0$  Hz), 7.14-7.07 (3H, m), 6.78 (1H, dt,  $J = 15.0$  and 7.0 Hz), 6.57 (1H, d,  $J = 15.0$  Hz), 3.69 (2H, t,  $J = 7.5$  Hz), 2.51 (2H, t,  $J = 6.0$  Hz), 2.39 (2H, t,  $J = 6.0$  Hz), 2.28 (2H, q,  $J = 7.0$  Hz), 1.76-1.63 (4H, m), 1.59-1.49 (4H, m);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.0, 168.4, 160.9, 143.0, 139.2, 133.9, 132.2, 129.0, 127.7, 125.4, 125.1, 123.2, 102.1, 37.8, 32.3, 28.5, 28.2, 26.0, 25.4, 23.2, 21.8; HRMS ( $\text{ESI}^+$ ) calc. for  $\text{C}_{27}\text{H}_{29}\text{N}_2\text{O}_3$   $[\text{M}+\text{H}]^+$  429.2173, found 429.2162.

#### 4.2.12. (E)-1-(5-Methoxy-2-(phenylamino)cyclohex-1-en-1-yl)non-2-en-1-one, (2j)

Yellow oil, 71% yield.  $R_f$  0.29 (petroleum ether /  $\text{EtOAc}$  (90:10)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2926, 1576, 1499, 1203, 1102, 780, 759, 694;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.68 (1H, s), 7.31 (2H, t,  $J = 8.0$  Hz), 7.16 (1H, t,  $J = 8.0$  Hz), 7.10 (2H, d,  $J = 8.0$  Hz), 6.86 (1H, dt,  $J = 15.0$  and 7.0 Hz), 6.55 (1H, dt,  $J = 15.0$  and 1.5 Hz), 3.58-3.52 (1H, m), 3.41 (3H, s), 2.86 (1H, dd,  $J = 15.0$  and 5.0 Hz), 2.62-2.52 (2H, m), 2.45-2.37 (1H, m), 2.23 (2H, qd,  $J = 7.0$  and 1.5 Hz), 1.88-1.81 (1H, m), 1.70-1.62 (1H, m), 1.50-1.43 (2H, m), 1.37-1.24 (6H, m), 0.89 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.3, 159.8, 144.7, 139.2, 129.1, 127.0, 125.4, 125.3, 99.3, 75.3, 56.1, 32.9, 31.8, 31.3, 29.0, 28.7, 26.0, 25.5, 22.7, 14.2; HRMS ( $\text{ESI}^+$ ) calc. for  $\text{C}_{22}\text{H}_{32}\text{NO}_2$   $[\text{M}+\text{H}]^+$  342.2428, found 342.2435.

#### 4.2.13. (E)-1-(4-(Phenylamino)-1,2,5,6-tetrahydro-[1,1'-biphenyl]-3-yl)non-2-en-1-one, (2k)

Yellow oil, 56% yield.  $R_f$  0.28 (petroleum ether /  $\text{Et}_2\text{O}$  (90:10)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2980, 2927, 2349, 1573, 672, 665;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.77 (1H, s), 7.37-7.23 (7H, m), 7.19-7.13 (3H, m), 6.88 (1H, dt,  $J = 15.0$  and 7.0 Hz), 6.55 (1H, d,  $J = 15.0$  Hz), 2.94-2.80 (2H, m), 2.67-2.52 (3H, m), 2.20 (2H, q,  $J = 7.0$  Hz), 2.00-1.93 (1H, m), 1.82-1.71 (1H, m), 1.48-1.41 (2H, m), 1.35-1.22 (6H, m), 0.87 (3H, t,  $J = 7.0$  Hz);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.2, 160.1, 146.4, 144.7, 139.3, 129.1, 128.6, 127.1, 127.0, 126.5, 125.5, 125.3, 102.0, 40.9, 34.5, 32.9, 31.8, 29.0, 28.9, 28.7, 28.3, 22.7, 14.2; HRMS ( $\text{ESI}^+$ ) calc. for  $\text{C}_{27}\text{H}_{34}\text{NO}$   $[\text{M}+\text{H}]^+$  388.2635, found 388.2635.

#### 4.2.14. (E)-1-(5-(tert-Butyl)-2-(phenylamino)cyclohex-1-en-1-yl)non-2-en-1-one, (2l)

Yellow oil, 43% yield.  $R_f$  0.36 (petroleum ether /  $\text{Et}_2\text{O}$  (90:10)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2980, 2971, 1578, 1393, 1170, 967;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  13.71 (1H, s), 7.30 (2H, d,  $J = 7.5$  Hz), 7.16-7.08 (3H, m), 6.87 (1H, dt,  $J = 15.5$  and 7.0 Hz), 6.59 (1H, d,  $J = 15.5$  Hz), 2.62 (1H, dd,  $J = 14.5$  and 5.0 Hz), 2.53-2.41 (2H, m), 2.29-2.18 (3H, m), 1.85-1.78 (1H, m), 1.52-1.45 (2H, m), 1.39-1.26 (7H, m), 1.16-1.05 (1H, m), 0.94 (9H, s), 0.89 (3H, t,  $J = 7.0$  Hz);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  188.5, 160.6, 144.3, 139.4, 129.0, 127.1, 125.2, 125.0, 102.3, 44.8, 32.9, 32.6, 31.8,

29.8, 29.1, 28.8, 27.4, 27.0, 23.1, 22.8, 14.2; HRMS (ESI<sup>+</sup>) calc. for C<sub>25</sub>H<sub>38</sub>NO [M+H]<sup>+</sup> 368.2948, found 368.2971.

### 4.3. Tandem hydroacylation / enamine hydrolysis

#### 4.3.1. General procedure

Following completion of the β-aminoenal hydroacylation, HCl (aq. 2 M, 0.6 mL) was added and the reaction mixture stirred vigorously for a further 2 h. Upon consumption of the hydroacylation product, as seen by TLC, the biphasic mixture was partitioned between water (20 mL) and CH<sub>2</sub>Cl<sub>2</sub> (20 mL). The aqueous layer was separated and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 20 mL). The combined organic extracts were dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography.

#### 4.3.2. (E)-2-(Non-2-enoyl)cyclohexan-1-one, (4a)

Colourless oil, 56% yield. R<sub>f</sub> 0.39 (petroleum ether / Et<sub>2</sub>O (95:5)); IR (thin film, ν<sub>max</sub>/cm<sup>-1</sup>) 2927, 2855, 1646, 1539, 1456, 1412, 1304, 990, 669; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 16.75 (1H, s), 6.96 (1H, dt, *J* = 15.5 and 7.0 Hz), 6.30 (1H, d, *J* = 15.5 Hz), 2.43-2.36 (4H, m), 2.24 (2H, qd, *J* = 7.5 and 1.0 Hz), 1.74-1.65 (4H, m), 1.49-1.42 (2H, m), 1.35-1.23 (6H, m), 0.87 (3H, t, *J* = 7.0 Hz); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 191.8, 182.4, 146.9, 123.0, 106.3, 33.8, 33.2, 31.8, 29.0, 28.5, 23.9, 23.1, 22.7, 21.9, 14.2; HRMS (ESI<sup>+</sup>) calc. for C<sub>15</sub>H<sub>25</sub>O<sub>2</sub> [M+H]<sup>+</sup> 237.1849, found 237.1810.

#### 4.3.3. (E)-2-(3-Cyclohexylacryloyl)cyclohexan-1-one, (4b)

Colourless oil, 66% yield. R<sub>f</sub> 0.35 (petroleum ether / Et<sub>2</sub>O (95:5)); IR (thin film, ν<sub>max</sub>/cm<sup>-1</sup>) 2924, 2851, 1640, 1559, 1447, 1410, 1301, 1168, 963; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 16.75 (1H, s), 6.90 (1H, dd, *J* = 15.5 and 7.0 Hz), 6.25 (1H, d, *J* = 15.5 Hz), 2.43-2.40 (2H, m), 2.38-2.35 (2H, m), 2.21-2.12 (1H, m), 1.78-1.65 (9H, m), 1.35-1.11 (5H, m); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 191.6, 182.8, 151.7, 120.5, 106.5, 41.3, 33.7, 32.1, 26.1, 25.9, 23.9, 23.1, 21.9; HRMS (ESI<sup>+</sup>) calc. for C<sub>15</sub>H<sub>22</sub>O<sub>2</sub> [M+H]<sup>+</sup> 235.1693, found 235.1701.

#### 4.3.4. (E)-2-(4,4-Dimethylpent-2-enoyl)cyclohexan-1-one, (4d)

Colourless oil, 88% yield. R<sub>f</sub> 0.36 (petroleum ether / Et<sub>2</sub>O (95:5)); IR (thin film, ν<sub>max</sub>/cm<sup>-1</sup>) 2953, 2866, 1639, 1561, 1460, 1410, 1309, 1270, 1168, 979; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 16.75 (1H, s), 6.96 (1H, d, *J* = 15.5 Hz), 6.20 (1H, d, *J* = 15.5 Hz), 2.43-2.41 (2H, m), 2.38-2.35 (2H, m), 1.73-1.66 (4H, m), 1.08 (9H, s); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 191.3, 183.1, 156.4, 118.1, 106.6, 34.2, 33.7, 28.9, 23.9, 23.1, 21.8; HRMS (ESI<sup>+</sup>) calc. for C<sub>13</sub>H<sub>21</sub>O<sub>2</sub> [M+H]<sup>+</sup> 209.1536, found 209.1548.

#### 4.3.5. (E)-2-(6-Chlorohex-2-enoyl)cyclohexan-1-one, (4e)

Colourless oil, 70% yield. R<sub>f</sub> 0.17 (petroleum ether / Et<sub>2</sub>O (95:5)); IR (thin film, ν<sub>max</sub>/cm<sup>-1</sup>) 2938, 2865, 1712, 1645, 1561, 1446, 1410, 1299, 1168, 969; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 16.65 (1H, s), 6.88 (1H, dt, *J* = 15.5 and 7.0 Hz), 6.36 (1H, d, *J* = 15.5 Hz), 3.55 (2H, t, *J* = 6.5 Hz), 2.45-2.35 (6H, m), 1.98-1.91 (2H, m), 1.74-1.66 (4H, m); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 192.6, 181.4, 143.9, 124.2, 106.5, 44.2, 33.9, 31.1, 30.1, 23.8, 23.1, 21.8; HRMS (ESI<sup>+</sup>) calc. for C<sub>12</sub>H<sub>18</sub><sup>15</sup>ClO<sub>2</sub> [M+H]<sup>+</sup> 229.0990, found 229.0993.

#### 4.3.6. (E)-2-(5-Phenylpent-2-enoyl)cyclohexan-1-one, (4g)

Colourless oil, 49% yield. R<sub>f</sub> 0.27 (petroleum ether / Et<sub>2</sub>O (95:5)); IR (thin film, ν<sub>max</sub>/cm<sup>-1</sup>) 3061, 3027, 2935, 2858, 1644, 1560, 1496, 1452, 1409, 1303, 1168, 967; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 16.71 (1H, s), 7.30 (2H, t, *J* = 8.0 Hz), 7.22-7.19 (3H,

m), 7.00 (1H, dt, *J* = 15.5 and 7.0 Hz), 6.32 (1H, d, *J* = 15.5 Hz), 2.80 (2H, t, *J* = 8.0 Hz), 2.58 (2H, q, *J* = 7.5 Hz), 2.40-2.37 (4H, m), 1.75-1.66 (4H, m); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 192.2, 181.8, 145.1, 141.1, 128.6, 128.5, 126.2, 123.6, 106.4, 34.8 (2C), 33.9, 23.8, 23.1, 21.8; HRMS (ESI<sup>+</sup>) calc. for C<sub>17</sub>H<sub>21</sub>O<sub>2</sub> [M+H]<sup>+</sup> 257.1536, found 257.1542.

#### 4.3.7. (E)-2-(4-cyclohexylbut-2-enoyl)cyclohexan-1-one, (4h)

Colourless oil, 73% yield. R<sub>f</sub> 0.45 (petroleum ether / Et<sub>2</sub>O (90:10)); IR (thin film, ν<sub>max</sub>/cm<sup>-1</sup>) 2922, 2850, 1643, 1562, 1447, 1410, 1230, 1168, 1006, 977; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 16.73 (1H, s), 6.94 (1H, dt, *J* = 15.5 and 7.5 Hz), 6.27 (1H, d, *J* = 15.5 Hz), 2.42-2.35 (4H, m), 2.13 (2H, t, *J* = 7.0 Hz), 1.71-1.61 (9H, m), 1.48-1.36 (1H, m), 1.27-1.08 (3H, m), 0.97-0.87 (2H, m); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 191.8, 182.2, 145.6, 124.0, 106.2, 41.1, 37.7, 33.8, 33.3, 26.5, 26.3, 23.9, 23.1, 21.9; HRMS (ESI<sup>+</sup>) calc. for C<sub>16</sub>H<sub>25</sub>O<sub>2</sub> [M+H]<sup>+</sup> 249.1849, found 249.1849.

### 4.4. Aza-conjugate addition

#### 4.4.1. General procedure

To an argon-filled vial containing β-aminoenone (0.200 mmol, 1.0 equiv.) and antimony(III) trichloride (0.060 mmol, 30 mol%) was added MeCN (0.3 M), and the reaction mixture stirred for 18 hours at 55 °C. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography.

#### 4.4.2. 2-Hexyl-1-phenyl-2,3,5,6,7,8-hexahydroquinolin-4(1H)-one, (6a)

Colourless oil, 73%. R<sub>f</sub> 0.18 (petroleum ether / EtOAc (80:20)); IR (thin film, ν<sub>max</sub>/cm<sup>-1</sup>) 2927, 2856, 1634, 1561, 1491, 1419, 1285, 1190, 1166; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 7.38 (2H, t, *J* = 8.0 Hz), 7.29 (1H, t, *J* = 7.5 Hz), 7.13 (2H, t, *J* = 8.0 Hz), 3.72-3.66 (1H, m), 2.84 (1H, dd, *J* = 16.5 and 6.0 Hz), 2.43 (1H, dd, *J* = 16.5 and 6.0 Hz), 2.41-2.27 (2H, m), 2.00-1.85 (2H, m), 1.72-1.46 (6H, m), 1.34-1.08 (8H, m), 0.82 (3H, t, *J* = 7.0 Hz); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 191.0, 158.0, 144.0, 129.4, 128.5, 127.2, 108.4, 61.2, 40.0, 31.8, 30.6, 30.1, 29.2, 25.8, 22.7, 22.6, 22.3, 21.8, 14.1; HRMS (ESI<sup>+</sup>) calc. for C<sub>21</sub>H<sub>30</sub>NO [M+H]<sup>+</sup> 312.2322, found 312.2321.

#### 4.4.3. 2-Hexyl-1,6-diphenyl-2,3,5,6,7,8-hexahydroquinolin-4(1H)-one, (6b)

Colourless oil, isolated as an inseparable mixture of diastereomers (1.4:1 dr). 85% yield. R<sub>f</sub> 0.20 (petroleum ether / EtOAc (80:20)); IR (thin film, ν<sub>max</sub>/cm<sup>-1</sup>) 3028, 2926, 2856, 1632, 1561, 1491, 1453, 1419, 1181; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 7.35-7.30 (4H, m), 7.25-7.13 (6H, m), 7.25-7.13 (10H, m), 3.71-3.62 (2H, m), 2.91-2.61 (6H, m), 2.44-2.38 (2H, m), 2.32-2.11 (3H, m), 2.05-1.91 (3H, m), 1.82-1.39 (8H, m), 1.26-1.02 (16H, m), 0.78-0.74 (6H, m); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 191.1, 190.4, 158.3, 156.6, 146.2, 145.9, 144.0, 143.6, 129.5, 128.6, 128.3, 128.3, 127.4, 126.9, 126.1, 108.4, 107.4, 61.3, 61.0, 40.5, 39.7, 39.5, 39.3, 31.7, 31.7, 31.6, 30.4, 30.1, 29.5<sub>3</sub>, 29.5<sub>0</sub>, 29.4<sub>2</sub>, 29.3<sub>7</sub>, 29.2, 25.8, 25.5, 22.6, 14.1; HRMS (ESI<sup>+</sup>) calc. for C<sub>27</sub>H<sub>34</sub>NO [M+H]<sup>+</sup> 388.2635, found 388.2643.

#### 4.4.4. 6-(tert-Butyl)-2-hexyl-1-phenyl-2,3,5,6,7,8-hexahydroquinolin-4(1H)-one, (6c)

Diastereomer 1: Colourless oil, 47% yield. R<sub>f</sub> 0.40 (petroleum ether / EtOAc (80:20)); IR (thin film, ν<sub>max</sub>/cm<sup>-1</sup>) 2929, 2860, 1638, 1571, 1491, 1421, 1364, 1281, 1178; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 7.37 (2H, d, *J* = 8.0 Hz), 7.28 (1H, t, *J* = 8.0 Hz), 7.11 (2H, d, *J* = 8.0 Hz), 3.74 (1H, m), 2.71 (1H, dd, *J* = 16.0 and 5.0 Hz), 2.65-2.60 (1H, m), 2.43 (1H, dd, *J* = 16.0 and 10.0 Hz), 2.02-1.86 (3H,



m), 1.73-1.68 (1H, m), 1.55-1.39 (2H, m), 1.32-1.05 (10H, m), 0.87 (9H, s), 0.82 (3H, t,  $J = 7.0$  Hz);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  191.8, 159.4, 143.7, 129.4, 128.2, 127.2, 109.4, 60.9, 44.2, 40.9, 32.5, 32.2, 31.8, 31.6, 29.2, 27.4, 25.5, 24.1, 23.4, 22.6, 14.1; HRMS (ESI<sup>+</sup>) calc. for  $\text{C}_{25}\text{H}_{38}\text{NO}$   $[\text{M}+\text{H}]^+$  368.2948, found 368.2957.

Diastereomer 2: Colourless oil, 31% yield.  $R_f$  0.23 (petroleum ether / EtOAc (80:20)); IR (thin film,  $\nu_{\text{max}}/\text{cm}^{-1}$ ) 2930, 2858, 1633, 1565, 1491, 1420, 1379, 1232, 1183;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  7.39 (2H, d,  $J = 8.0$  Hz), 7.29 (1H, t,  $J = 8.0$  Hz), 7.14 (2H, d,  $J = 8.0$  Hz), 3.71-3.65 (1H, m), 2.94 (1H, dd,  $J = 16.5$  and  $6.5$  Hz), 2.62 (1H, dd,  $J = 16.0$  and  $4.5$  Hz), 2.46 (1H, dd,  $J = 16.5$  and  $3.5$  Hz), 2.11-1.68 (5H, m), 1.60-1.52 (1H, m), 1.34-0.98 (10H, m), 0.88 (9H, s), 0.82 (3H, t,  $J = 7.0$  Hz);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  190.7, 157.1, 144.3, 129.4, 128.7, 127.2, 107.8, 61.4, 44.2, 39.5, 32.5, 31.8, 31.4, 29.3, 29.2, 27.4, 25.9, 23.8, 23.4, 22.7, 14.2; HRMS (ESI<sup>+</sup>) calc. for  $\text{C}_{25}\text{H}_{38}\text{NO}$   $[\text{M}+\text{H}]^+$  368.2948, found 368.2956.

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## Appendix A. Supplementary data

Supplementary data relating to this article may be found at.

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