

## Iron nitrate/TEMPO-catalyzed oxidative Passerini reaction of alcohols in air

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Dedicated to Dr. Jhillu Singh Yadav on the occasion of his 65<sup>th</sup> anniversary

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### Abstract

The oxidative three-component Passerini reaction using primary alcohols as aldehyde surrogates with ferric nitrate (Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O) and TEMPO as the catalyst system under air is described. The reaction has broad scope over all three components.

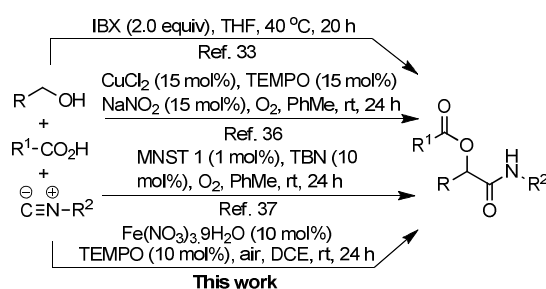
**Keywords:** Aerobic oxidation, alcohols, ferric nitrate, Passerini reaction, multicomponent reactions

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### Introduction

Multicomponent reactions (MCR) are attractive because they are generally atom and energy efficient involving multistep procedures in one-pot.<sup>1-9</sup> Amongst the MCRs, the isocyanide-based MCRs have been investigated intensively during the past two decades and many novel modifications have been developed which offer products which are building blocks for constructing important heterocyclic and medicinally important scaffolds.<sup>10-16</sup> Of particular importance in this area is the Passerini three-component (3C) reaction that involves the reaction between an aldehyde or a ketone, an isocyanide and a carboxylic acid to afford an  $\alpha$ -acyloxy amide.<sup>17-20</sup> As a consequence efforts have been directed toward developing alternatives to this important reaction.<sup>21-32</sup> However, in most of the reported 3C-Passerini reactions an aldehyde constitutes the principal starting material which limits the versatility of the reaction. In order to address this issue, the oxidative Passerini reaction involving *in situ* oxidation of alcohol to aldehyde for participating in the MCR was developed. Ngouansavanh and Zhu in their seminal work disclosed the 2-iodoxybenzoic acid (IBX)-mediated *in situ* oxidation of various primary

alcohols to aldehydes which served as the starting materials in the 3C-Passerini reaction (Scheme 1).<sup>33</sup> Subsequently, Basso *et al.*<sup>34</sup> and Li *et al.*<sup>35</sup> used this protocol for synthesizing oxazolines and developing polymers, respectively. To avoid the use of stoichiometric amount of IBX, Zhu *et al.* later developed CuCl<sub>2</sub>/TEMPO/NaNO<sub>2</sub> as a homogenous catalyst system for similar oxidative 3C-Passerini reactions.<sup>36</sup> During their study they also investigated the reaction with a FeCl<sub>3</sub>/TEMPO/NaNO<sub>2</sub> system but they found it inappropriate as the yields were inferior. Recently, Karimi and Farhangi developed magnetically recyclable TEMPO which served as an efficient heterogenous catalyst for the oxidative Passerini reaction using alcohols as the aldehyde surrogates.<sup>37</sup> More recently, Adib and co-workers accomplished the 3C-Passerini reaction using benzyl halides and tosylates as the aldehyde surrogates, but the reaction was a two-step process and limited to benzyl substrates.<sup>38</sup> Given the remarkable progress made in tandem oxidative processes,<sup>39-42</sup> we were prompted to explore the aptness of a relatively cheap and convenient catalytic system for this MCR.

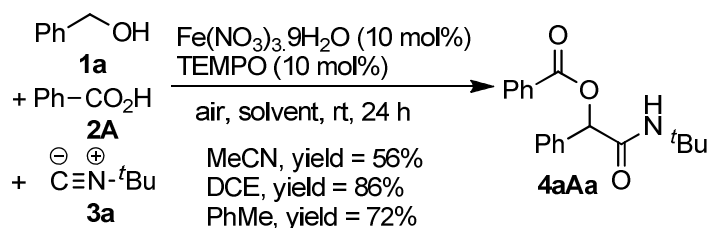


**Scheme 1.** Comparison of oxidative 3C-Passerini reaction using primary alcohols as aldehyde surrogates. (MNST: magnetic nanoparticle-supported TEMPO).

Iron-catalysed oxidative reactions are attractive because they involve the use of cheap, non-toxic and naturally abundant metal and can be carried out under aerobic conditions.<sup>43</sup> Recently, we have initiated studies exploring the potential of Fe(NO<sub>3</sub>)<sub>3</sub>.9H<sub>2</sub>O for different oxidative transformations. We have found that this homogenous catalyst is a superior option for transforming alcohols to nitriles in the presence of aqueous ammonia (30%) under air.<sup>44</sup> Subsequently we reported the suitability of this catalyst system for oxidative 3C-Ugi reaction using arylmethyl amines as the imine precursors.<sup>45</sup> In continuing studies related to the use of Fe(NO<sub>3</sub>)<sub>3</sub>.9H<sub>2</sub>O/TEMPO for oxidative reactions, we sought investigating its potential for oxidative 3C-Passerini reaction. It is worth mentioning that Fe(NO<sub>3</sub>)<sub>3</sub>.9H<sub>2</sub>O/TEMPO system has been reported to be excellent catalyst for the oxidation of alcohols to aldehydes under aerobic conditions.<sup>46,47</sup> Herein we present an update disclosing the effectiveness of Fe(NO<sub>3</sub>)<sub>3</sub>.9H<sub>2</sub>O / TEMPO as a homogenous catalyst for oxidative 3C-Passerini reaction under air.

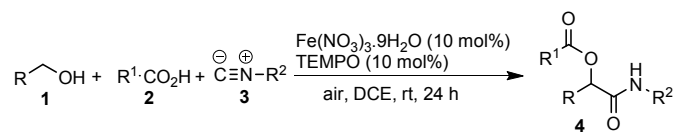
## Results and Discussion

We commenced our investigations of the oxidative 3C-Passerini reaction by treating benzyl alcohol **1a** (1.0 equiv) with benzoic acid **2A** (1.1 equiv) and tert-butylisocyanide **3a** (1.1 equiv) in the presence of Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O (10 mol%), TEMPO (10 mol%) in MeCN at room temperature under air. Although the reaction resulted in a mixture of products, we were able to isolate the α-acyloxy-amide **4aAa** in 56% yield (Scheme 2). Since Liu and Ma have reported the Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O/TEMPO-mediated oxidation of alcohols in DCE at room temperature,<sup>46-47</sup> we considered performing the same reaction in DCE. The reaction was complete in 24 h and we were pleased to observe that the isolated yield of **4aAa** enhanced to 86%. We also examined the reaction in toluene but here **4aAa** was isolated in 72% yield only.



**Scheme 2.** Result of the screening of oxidative 3C-Passerini reaction in different solvents.

With optimum conditions in hand, the scope of this iron-catalyst system for oxidative Passerini reaction was next investigated. A variety of alcohols (**1a-i**) including arylmethyl alcohols and aliphatic alcohols were found to be compatible with the protocol (Table 1). However it was observed that the yields of products (**4eAa**, **4eAb**, **4fAa**) afforded from aliphatic alcohols were moderate only (entries 11-13). Among acids, we investigated the reaction with benzoic acid (**2A**), pyridine-3-carboxylic acid (**2B**), 3-nitrobenzoic acid (**2C**), cinnamic acid, (**2D**) 3-chlorophenylacetic acid (**2E**) and discovered that all acids participated in the reaction offering the α-acyloxy-amides. Different commercially available isocyanides including *tert*-butylisocyanide (**3a**), cyclohexylisocyanide (**3b**), ethyl 2-isocyanoacetate (**3c**), 4-(2-isocyanoethyl)morpholine (**3d**) and 2,6-dimethylphenylisocyanide (**3e**) investigated in this study proved to be good substrates for the reaction, affording the products in good to excellent yields.

**Table 1.** Scope of the Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O/TEMPO-mediated oxidative 3C-Passneri reaction of alcohols<sup>a</sup>

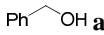
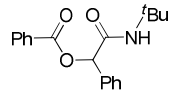
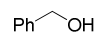
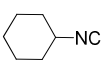
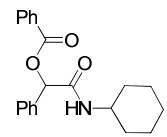
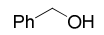
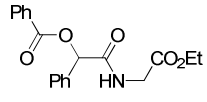
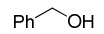
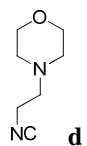
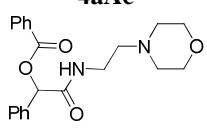
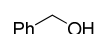
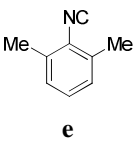
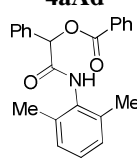
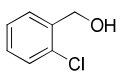
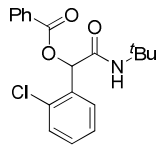
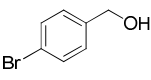
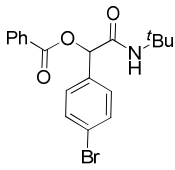
entry	alcohol (1)	acid (2)	isocyanide (3)	product (4)	yield <sup>b</sup> (%)
1		Ph-CO <sub>2</sub> H <b>A</b>	<sup>t</sup> Bu-NC <b>a</b>	 <b>4aAa</b>	86
2		Ph-CO <sub>2</sub> H <b>A</b>	 <b>b</b>	 <b>4aAb</b>	82
3		Ph-CO <sub>2</sub> H <b>A</b>	CN-CH <sub>2</sub> -CO <sub>2</sub> Et <b>c</b>	 <b>4aAc</b>	85
4		Ph-CO <sub>2</sub> H <b>A</b>	 <b>d</b>	 <b>4aAd</b>	70
5		Ph-CO <sub>2</sub> H <b>A</b>	 <b>e</b>	 <b>4aAe</b>	78
6		Ph-CO <sub>2</sub> H <b>A</b>	<sup>t</sup> Bu-NC <b>a</b>	 <b>4bAa</b>	74
7		Ph-CO <sub>2</sub> H <b>A</b>	<sup>t</sup> Bu-NC <b>a</b>	 <b>4cAa</b>	87

Table 1 (continued)

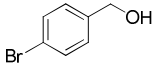
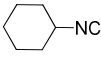
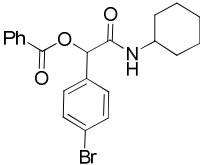
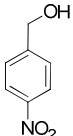
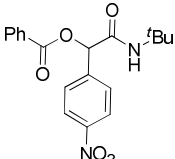
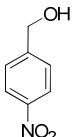
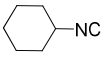
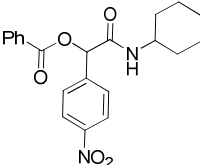
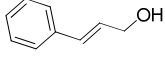
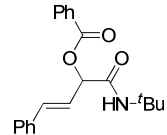
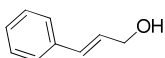
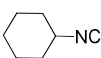
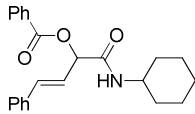
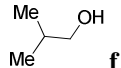
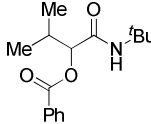
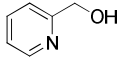
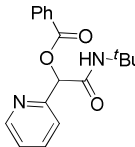
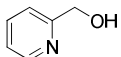
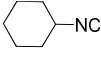
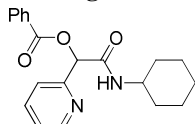
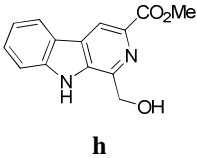
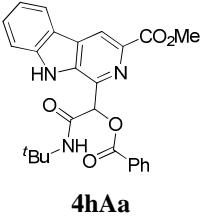
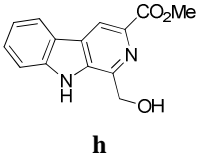

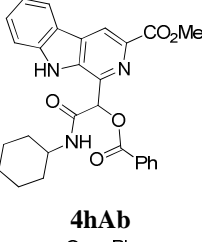


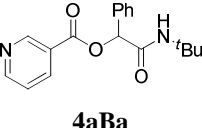



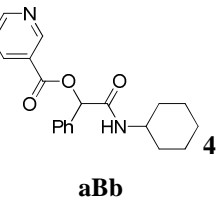

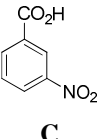

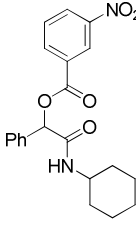

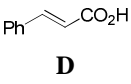

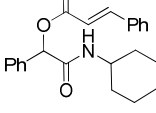

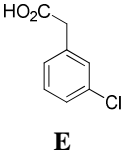
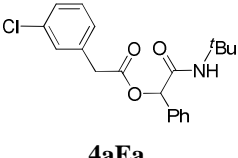
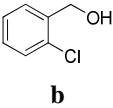
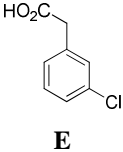
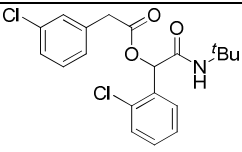
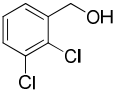
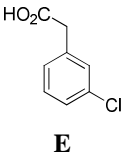
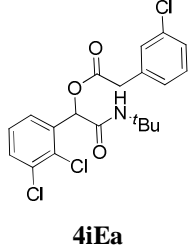
entry	alcohol (1)	acid (2)	isocyanide (3)	product (4)	yield <sup>b</sup> (%)
8	 <b>c</b>	Ph-CO <sub>2</sub> H <b>A</b>	 <b>b</b>	 <b>4cAb</b>	83
9	 <b>d</b>	Ph-CO <sub>2</sub> H <b>A</b>	<sup>t</sup> Bu-NC <b>a</b>	 <b>4dAa</b>	88
10	 <b>d</b>	Ph-CO <sub>2</sub> H <b>A</b>	 <b>b</b>	 <b>4dAb</b>	90
11	 <b>e</b>	Ph-CO <sub>2</sub> H <b>A</b>	<sup>t</sup> Bu-NC <b>a</b>	 <b>4eAa</b>	70
12	 <b>e</b>	Ph-CO <sub>2</sub> H <b>A</b>	 <b>b</b>	 <b>4eAb</b>	66
13	 <b>f</b>	Ph-CO <sub>2</sub> H <b>A</b>	<sup>t</sup> Bu-NC <b>a</b>	 <b>4fAa</b>	58
14	 <b>g</b>	Ph-CO <sub>2</sub> H <b>A</b>	<sup>t</sup> Bu-NC <b>a</b>	 <b>4gAa</b>	81
15	 <b>g</b>	Ph-CO <sub>2</sub> H <b>A</b>	 <b>b</b>	 <b>4gAb</b>	79

Table 1 (continued)

entry	alcohol (1)	acid (2)	isocyanide (3)	product (4)	yield <sup>b</sup> (%)
16		Ph-CO <sub>2</sub> H <b>A</b>	<sup>t</sup> Bu-NC <b>a</b>		92
17		Ph-CO <sub>2</sub> H <b>A</b>			85
18			<sup>t</sup> Bu-NC <b>a</b>		82
19					84
20					90
21					68
22			<sup>t</sup> Bu-NC <b>a</b>		79

**Table 1 (continued)**

entry	alcohol (1)	acid (2)	isocyanide (3)	product (4)	yield <sup>b</sup> (%)
23	 <b>b</b>	 <b>E</b>	<sup>t</sup> Bu-NC <b>a</b>	 <b>4bEa</b>	81
24	 <b>i</b>	 <b>E</b>	<sup>t</sup> Bu-NC <b>a</b>	 <b>4iEa</b>	75

<sup>a</sup> All reactions were carried out using **1** (0.1 g, 1.0 equiv), **2** (1.1 equiv), **3** (1.1 equiv), Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O (10 mol%), TEMPO (10 mol%) and DCE (5 mL), air balloon. <sup>b</sup> Isolated yields after column chromatography.

## Conclusions

In summary, we have demonstrated that the Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O/TEMPO is an effective homogenous catalyst system for oxidative 3C-Passerini reaction using air as oxidant. This catalytic system does not require any additive and the reaction has broad substrate scope across all three components. Hence this work updates the repertoire of catalytic systems for the oxidative 3C-Passerini reaction.

## Experimental Section

**General.** All experiments were monitored by analytical thin layer chromatography (TLC). TLC was performed on pre-coated silica gel plates. After elution, plate was visualized under UV illumination at 254 nm for UV active materials. Further visualization was achieved by staining with KMnO<sub>4</sub> and charring on a hot plate. The melting points were recorded on a hot stage apparatus using silicone oil. IR spectra were recorded using a FTIR spectrophotometer. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on 400 and 500 MHz spectrometers, using TMS as an internal standard (chemical shifts in δ). Peak multiplicities of NMR signals were designated as s (singlet), bs (broad singlet), d (doublet), dd (doublet of doublet), t (triplet), m (multiplet) etc. The ESI-MS were recorded on Ion Trap Mass spectrometer and the HRMS spectra were recorded as

ESI-HRMS on a Q-TOF LC-MS/MS mass spectrometer. Commercial grade reagents and solvents were used without further purification.

**General procedure for the oxidative 3C-Passerini reaction as exemplified for the formation of 4aAa.** To a flask charged with DCE (5 mL) were added benzyl alcohol **1a** (0.1 g, 0.92 mmol), benzoic acid **2A** (0.124 g, 1.02 mmol) and *tert*-butylisocyanide **3a** (115  $\mu$ L, 1.02 mmol) at room temperature under air (maintained by air balloon). Thereafter, Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O (0.037 g, 0.092 mmol) and TEMPO (0.014 g, 0.092 mmol) were added and the mixture was stirred at room temperature for 24 h. After completion of reaction (as monitored by TLC), the solvent was evaporated and the residue was extracted with EtOAc (15 mL x 2) and water (25 mL). The organic layers were pooled, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated to obtain the crude product. Purification of the crude material via column chromatography over silica gel using hexanes/EtOAc (80:20, v/v) as eluent furnished **4aAa** as a white solid (0.247 g, 86%).

**2-(*tert*-Butylamino)-2-oxo-1-phenylethyl benzoate (4aAa).**<sup>48</sup> Yield. 86% (0.248 g from 0.1 g); a white solid, mp 152-154 °C; R<sub>f</sub> = 0.62 (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 774, 1088, 1216, 1425, 1556, 1638, 1750, 3151 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) = 1.29 (s, 9H), 5.92 (s, 1H), 6.15 (s, 1H), 7.26-7.34 (m, 3H), 7.39-7.46 (m, 4H), 7.51-7.55 (m, 1H), 8.01-8.02 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) = 28.8, 51.7, 76.2, 127.6, 128.5, 128.8, 128.9, 129.0, 129.9, 133.7, 136.1, 165.1, 167.6. MS (ESI+):  $m/z$  = 312.4. ESI-HR-MS calculated for C<sub>19</sub>H<sub>21</sub>NO<sub>3</sub> [MH]<sup>+</sup>: 312.1600, found: 312.1597.

**2-(Cyclohexylamino)-2-oxo-1-phenylethyl benzoate (4aAb).**<sup>48</sup> Yield. 82% (0.256 g from 0.1 g); a white solid, mp 138-140 °C; R<sub>f</sub> = 0.62 (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 665, 1145, 1254, 1440, 1479, 1567, 1658, 1759, 3092 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) = 1.07-1.57 (m, 4H), 1.24-1.35 (m, 2H), 1.51-1.63 (m, 2H), 1.80-1.88 (m, 2H), 3.71-3.81 (m, 1H), 5.96 (d,  $J$  = 7.4 Hz, 1H), 6.23 (s, 1H), 7.26-7.35 (m, 3H), 7.37-7.76 (m, 7H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) = 24.8, 25.6, 33.0, 33.1, 48.4, 76.1, 127.5, 128.8, 128.9, 129.1, 129.5, 129.9, 133.7, 135.9, 165.1, 167.5. MS (ESI+):  $m/z$  = 338.3. ESI-HR-MS calculated for C<sub>21</sub>H<sub>23</sub>NO<sub>3</sub> [MH]<sup>+</sup>: 338.1756, found: 338.1751.

**2-[(2-Ethoxy-2-oxoethyl)amino]-2-oxo-1-phenylethyl benzoate (4aAc).**<sup>49</sup> Yield. 85% (0.268 g from 0.1 g); a white solid, mp 100-102 °C; R<sub>f</sub> = 0.62 (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 1158, 1273, 1421, 1565, 1648, 1758, 3246 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) = 1.28 (t,  $J$  = 7.2 Hz, 3H), 4.08 (dd,  $J_1$  = 5.1 Hz,  $J_2$  = 5.3 Hz, 2H), 4.22 (q,  $J$  = 7.2 Hz, 2H), 6.41 (s, 1H), 6.94 (s, 1H), 7.38-7.44 (m, 3H), 7.47-7.51 (m, 2H), 7.58-7.64 (m, 3H), 8.14 (dd,  $J_1$  = 1.4 Hz,  $J_2$  = 0.7 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) = 14.2, 41.4, 61.8, 75.9, 127.6, 128.8, 128.9, 129.2, 130.0, 133.8, 135.4, 165.0, 168.7, 169.6. MS (ESI+):  $m/z$  = 342.3. ESI-HR-MS calculated for C<sub>19</sub>H<sub>19</sub>NO<sub>5</sub> [MH]<sup>+</sup>: 342.1341, found: 342.1345.

**2-[(2-Morpholinoethyl)amino]-2-oxo-1-phenylethyl benzoate (4aAd).** Yield. 70% (0.239 g from 0.1 g); a white solid, mp 86-88 °C; R<sub>f</sub> = 0.62 (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 669, 769, 1163, 1254, 1430, 1653, 1758, 3065 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) = 2.39-2.42 (m, 2H), 2.56 (t,  $J$  = 6.1 Hz, 4H), 3.31-3.36 (m, 2H), 3.51 (dd,  $J_1$  = 6.3 Hz,  $J_2$  = 6.3 Hz, 4H), 7.01 (bs, 2H), 7.33-7.46 (m, 6H), 7.73-7.76 (m, 4H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$



(ppm) = 28.8, 51.7, 76.2, 121.9, 123.5, 128.6, 129.5, 130.1, 133.6, 137.3, 149.2, 155.6, 165.2, 165.9. MS (ESI+):  $m/z$  = 369.2. ESI-HR-MS calculated for  $C_{21}H_{24}N_2O_4$   $[MH]^+$ : 369.1814, found: 369.1819.

**2-[(2,6-Dimethylphenyl)amino]-2-oxo-1-phenylethyl benzoate (4aAe).** Yield. 78% (0.259 g from 0.1 g); a white solid, mp 146-148 °C;  $R_f$  = 0.62 (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 669, 769, 1084, 1216, 1402, 1638, 1751, 3151  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 2.04 (s, 6H), 6.39 (s, 1H), 6.94-7.05 (m, 4H), 7.33-7.44 (m, 6H), 7.53-7.61 (m, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 18.3, 76.5, 127.3, 127.7, 128.3, 128.8, 129.0, 129.2, 129.3, 130.0, 132.8, 133.8, 135.4, 135.6, 165.3, 166.9. MS (ESI+):  $m/z$  = 360.3. ESI-HR-MS calculated for  $C_{23}H_{21}NO_3$   $[MH]^+$ : 360.1600, found: 360.1605.

**2-(tert-Butylamino)-1-(2-chlorophenyl)-2-oxoethyl benzoate (4bAa).** Yield. 74% (0.179 g from 0.1 g); a white solid, mp 170-172 °C;  $R_f$  = 0.61 (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 677, 1098, 1267, 1472, 1530, 1661, 1754, 3052  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.29 (s, 9H), 5.96 (s, 1H), 6.45 (s, 1H), 7.22-7.27 (m, 2H), 7.34-7.36 (m, 1H), 7.39 (t,  $J$  = 7.8 Hz, 2H), 7.51-7.58 (m, 2H), 8.02 (t,  $J$  = 7.2 Hz, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 28.8, 51.9, 73.4, 127.4, 128.7, 129.4, 130.0, 130.1, 130.3, 133.6, 133.7, 133.9, 165.3, 166.6. MS (ESI+):  $m/z$  = 346.1. ESI-HR-MS calculated for  $C_{19}H_{20}ClNO_3$   $[MH]^+$ : 346.1210, found: 346.1206.

**1-(4-Bromophenyl)-2-(tert-butylamino)-2-oxoethyl benzoate (4cAa).**<sup>50</sup> Yield. 87% (0.181 g from 0.1 g); a white solid, mp 160-162 °C;  $R_f$  = 0.60 (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 698, 1265, 1436, 1540, 1658, 1759, 3098  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.29 (s, 9H), 5.96 (s, 1H), 6.09 (s, 1H), 7.33 (d,  $J$  = 8.3 Hz, 2H), 7.39-7.46 (m, 4H), 7.55 (t,  $J$  = 7.4 Hz, 1H), 8.00 (d,  $J$  = 7.5 Hz, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 28.8, 51.8, 75.5, 123.2, 128.9, 129.2, 129.3, 129.9, 132.0, 133.9, 135.2, 164.9, 167.0. MS (ESI+):  $m/z$  = 390.1. ESI-HR-MS calculated for  $C_{19}H_{20}BrNO_3$   $[MH]^+$ : 390.0705, found: 390.0707.

**1-(4-Bromophenyl)-2-(cyclohexylamino)-2-oxoethyl benzoate (4cAb).** Yield. 83% (0.185 g from 0.1 g); a white solid, mp 118-120 °C;  $R_f$  = 0.60 (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 690, 1203, 1267, 1438, 1543, 1655, 1760, 3089  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.11-1.28 (m, 3H), 1.34-1.44 (m, 2H), 1.68-1.74 (m, 3H), 1.91-1.97 (m, 2H), 3.79-3.87 (m, 1H), 6.09 (d,  $J$  = 7.5 Hz, 1H), 6.27 (s, 1H), 7.43 (d,  $J$  = 8.4 Hz, 2H), 7.49-7.55 (m, 4H), 7.65 (t,  $J$  = 7.4 Hz, 1H), 8.09 (d,  $J$  = 7.3 Hz, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 24.8, 25.5, 32.9, 33.1, 48.5, 75.3, 123.3, 128.9, 129.2, 129.9, 132.0, 133.9, 134.9, 164.9, 166.9. MS (ESI+):  $m/z$  = 416.1. ESI-HR-MS calculated for  $C_{21}H_{22}BrNO_3$   $[MH]^+$ : 416.0861, found: 416.0864.

**2-(tert-Butylamino)-1-(4-nitrophenyl)-2-oxoethyl benzoate (4dAa).** Yield. 88% (0.205 g from 0.1 g); a white solid, mp 198-200 °C;  $R_f$  = 0.62 (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 771, 1161, 1267, 1462, 1646, 1756, 3151  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.31 (s, 9H), 6.08 (s, 1H), 6.22 (s, 1H), 7.45 (t,  $J$  = 7.9 Hz, 2H), 7.59 (t,  $J$  = 7.5 Hz, 1H), 7.63 (s, 1H); 7.66 (s, 1H), 8.01 (d,  $J$  = 1.3 Hz, 1H), 8.03 (s, 1H), 8.16 (s, 1H), 8.18 (d,  $J$  = 1.8 Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 28.8, 52.0, 75.0, 124.0, 128.2, 128.8, 129.0, 129.9, 134.2, 143.0, 148.2,

164.6, 166.2. MS (ESI+):  $m/z = 357.1$ . ESI-HR-MS calculated for  $C_{19}H_{20}N_2O_5$   $[MH]^+$ : 357.1450, found: 357.1454.

**2-(Cyclohexylamino)-1-(4-nitrophenyl)-2-oxoethyl benzoate (4dAb).**<sup>3</sup> Yield. 90% (0.225 g from 0.1 g); a white solid, mp 216-218 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 670, 1143, 1266, 1430, 1528, 1656, 1752, 3098  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.05-1.19 (m, 3H), 1.25-1.34 (m, 2H), 1.53-1.65 (m, 3H), 1.85 (d,  $J = 10.8$  Hz, 2H), 3.69-3.79 (m, 1H), 6.12 (d,  $J = 7.7$  Hz, 1H), 6.31 (s, 1H), 7.46 (t,  $J = 7.8$  Hz, 2H), 7.59 (t,  $J = 7.4$  Hz, 1H); 7.65 (s, 1H), 7.67 (s, 1H); 8.02 (d,  $J = 1.3$  Hz, 1H), 8.04 (s, 1H), 8.16 (s, 1H), 8.18 (s, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 24.8, 25.5, 33.0, 33.0, 48.6, 74.9, 124.0, 128.2, 128.8, 129.0, 129.9, 134.2, 142.8, 148.3, 164.7, 166.2. MS (ESI+):  $m/z = 383.2$ . ESI-HR-MS calculated for  $C_{21}H_{22}N_2O_5$   $[MH]^+$ : 383.1607, found: 383.1601.

**(E)-1-(tert-Butylamino)-1-oxo-4-phenylbut-3-en-2-yl benzoate (4eAa).** Yield. 70% (0.176 g from 0.1 g); a white solid, mp 138-140 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 1145, 1263, 1430, 1476, 1587, 1654, 1755, 3251  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.31 (s, 9H), 5.83 (dd,  $J_1 = 1.3$  Hz,  $J_2 = 1.3$  Hz, 1H), 5.88 (s, 1H), 6.34 (dd,  $J_1 = 6.7$  Hz,  $J_2 = 6.7$  Hz, 1H), 6.73 (d,  $J = 15.9$  Hz, 1H), 7.17-7.27 (m, 3H), 7.33-7.35 (m, 2H), 7.43 (t,  $J = 7.8$  Hz, 2H), 7.53-7.57 (m, 1H), 8.03 (t,  $J = 1.4$  Hz, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 28.8, 51.7, 75.2, 123.0, 127.0, 128.5, 128.7, 128.8, 129.5, 129.9, 133.8, 134.7, 135.9, 165.1, 167.3. MS (ESI+):  $m/z = 338.7$ . ESI-HR-MS calculated for  $C_{21}H_{23}NO_3$   $[MH]^+$ : 338.1756, found: 338.1755.

**(E)-1-(Cyclohexylamino)-1-oxo-4-phenylbut-3-en-2-yl benzoate (4eAb).** Yield. 66% (0.179 g from 0.1 g); a white solid, mp 178-180 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 656, 1145, 1223, 1440, 1473, 1554, 1641, 1754, 3098  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.16-1.23 (m, 3H), 1.35-1.43 (m, 2H), 1.61-1.74 (m, 3H), 1.93-1.99 (m, 2H), 3.82-3.90 (m, 1H), 6.01 (dd,  $J_1 = 1.0$  Hz,  $J_2 = 1.0$  Hz, 1H), 6.05 (d,  $J = 7.8$  Hz, 1H), 6.44 (dd,  $J_1 = 6.7$  Hz,  $J_2 = 6.6$  Hz, 1H), 6.84 (d,  $J = 15.9$  Hz, 1H), 7.27-7.36 (m, 3H), 7.43 (d,  $J = 7.1$  Hz, 2H), 7.52 (t,  $J = 7.8$  Hz, 2H), 7.65 (t,  $J = 7.5$  Hz, 1H), 8.13 (d,  $J = 1.2$  Hz, 1H), 8.15 (s, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 24.9, 25.6, 33.1, 33.2, 48.4, 75.0, 122.9, 127.0, 128.5, 128.7, 128.8, 129.5, 129.9, 133.8, 134.7, 135.9, 165.1, 167.3. MS (ESI+):  $m/z = 364.2$ . ESI-HR-MS calculated for  $C_{23}H_{25}NO_3$   $[MH]^+$ : 364.1913, found: 364.1918.

**1-(tert-Butylamino)-3-methyl-1-oxobutan-2-yl benzoate (4fAa).** Yield. 58 % (0.217 g from 0.1 g); a white solid, mp 140-142 °C;  $R_f = 0.65$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 778, 1241, 1432, 1476, 1587, 1654, 1759, 3256  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.01 (d,  $J = 6.9$  Hz, 3H), 1.05 (d,  $J = 6.8$  Hz, 3H), 1.35 (s, 9H), 2.42-2.48 (m, 1H), 5.20 (d,  $J = 4.2$  Hz, 1H), 5.84 (s, 1H), 7.50 (t,  $J = 7.9$  Hz, 2H), 7.64 (t,  $J = 7.5$  Hz, 1H), 8.08-8.09 (m, 2H)  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 17.0, 19.1, 28.8, 30.9, 51.4, 78.8, 128.8, 129.6, 129.8, 133.7, 165.5, 168.5. MS (ESI+):  $m/z = 278.1$ . ESI-HR-MS calculated for  $C_{16}H_{23}NO_3$   $[MH]^+$ : 278.1756, found: 278.1759.

**2-(tert-Butylamino)-2-oxo-1-(pyridin-2-yl)ethyl benzoate (4gAa).** Yield. 81% (0.232 g from 0.1 g); a white solid, mp 102-104 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 656, 1056, 1162, 1216, 1428, 1583, 1662, 1743, 3151  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) =

1.34 (s, 9H), 6.29 (s, 1H), 6.84 (s, 1H), 7.27 (dd,  $J_1 = 6.2$  Hz,  $J_2 = 1.5$  Hz, 1H), 7.46 (dd,  $J_1 = 1.2$  Hz,  $J_2 = 6.7$  Hz, 2H), 7.57-7.61 (m, 1H), 7.65 (d,  $J = 7.8$  Hz, 1H), 7.74 (t,  $J = 7.7$  Hz, 1H), 8.17 (d,  $J = 8.3$  Hz, 2H), 8.58 (dd,  $J_1 = 2.2$  Hz,  $J_2 = 0.7$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 28.8, 51.7, 76.2, 121.9, 123.5, 128.6, 129.5, 130.1, 133.6, 137.3, 149.2, 155.6, 165.2, 165.9. MS (ESI+):  $m/z = 313.3$ . ESI-HR-MS calculated for  $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_3$   $[\text{MH}]^+$ : 313.1552, found: 313.1557.

**2-(Cyclohexylamino)-2-oxo-1-(pyridin-2-yl)ethyl benzoate (4gAb)**. Yield. 79% (0.245 g from 0.1 g); a white solid, mp 126-128 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{\text{max}}$ : 673, 789, 1186, 1263, 1422, 1556, 1640, 1752, 3241  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 1.11-1.35 (m, 5H); 1.54-1.86 (m, 5H); 3.68-3.73 (m, 1H), 7.18-7.28 (m, 2H); 7.37-7.54 (m, 4H); 7.67-7.77 (m, 1H); 8.01 (dd,  $J_1 = 0.7$  Hz,  $J_2 = 1.4$  Hz, 2H), 8.47 (d,  $J = 5.1$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 24.6, 26.1, 33.5, 51.7, 76.2, 121.8, 123.5, 128.6, 129.5, 130.1, 133.6, 137.3, 149.2, 155.6, 165.2, 165.9. MS (ESI+):  $m/z = 339.5$ . ESI-HR-MS calculated for  $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_3$   $[\text{MH}]^+$ : 339.1709, found: 339.1713.

**Methyl 1-(1-(benzoyloxy)-2-(tert-butylamino)-2-oxoethyl)-9H-pyrido[3,4-b]indole-3-carboxylate (4hAa)**. Yield. 92% (0.165 g from 0.1 g); a white solid, mp 88-90 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{\text{max}}$ : 1265, 1123, 1284, 1146, 1285, 1432, 1567, 1638, 1757, 3321  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 1.24 (s, 9H), 3.97 (s, 3H), 6.43 (s, 1H), 6.76 (s, 1H), 7.32 (t,  $J = 7.2$  Hz, 3H), 7.47 (t,  $J = 6.8$  Hz, 1H), 7.56 (t,  $J = 7.0$  Hz, 2H), 7.98 (d,  $J = 7.25$ , 2H), 8.14 (d,  $J = 7.8$  Hz, 1H), 8.85 (s, 1H), 10.33 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 28.6, 52.4, 52.8, 78.8, 112.8, 118.8, 121.1, 121.5, 121.9, 128.6, 129.3, 129.4, 130.1, 130.6, 133.6, 136.4, 136.6, 137.6, 141.4, 165.5, 166.4, 167.0. MS (ESI+):  $m/z = 460.2$ . ESI-HR-MS calculated for  $\text{C}_{26}\text{H}_{25}\text{N}_3\text{O}_5$   $[\text{MH}]^+$ : 460.1872, found: 460.1869.

**Methyl 1-(1-(benzoyloxy)-2-(cyclohexylamino)-2-oxoethyl)-9H-pyrido[3,4-b]indole-3-carboxylate (4hAb)**. Yield. 85% (0.161 g from 0.1 g); a white solid, mp 144-146 °C;  $R_f = 0.28$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{\text{max}}$ : 1260, 1147, 1284, 1356, 1432, 1567, 1639, 1759, 3322  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 0.93-1.31 (m, 6H), 1.58-1.65 (m, 2H), 1.97 (s, 2H), 3.66-3.68 (m, 1H), 3.97 (s, 3H), 6.47 (s, 1H), 6.75 (d,  $J = 7.3$  Hz, 1H), 7.28-7.36 (m, 3H), 7.49 (t,  $J = 7.5$  Hz, 1H), 7.55 (d,  $J = 3.6$  Hz, 2H), 7.99 (d,  $J = 7.5$  Hz, 2H), 8.13 (d,  $J = 7.8$  Hz, 1H), 8.84 (s, 1H), 10.26 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 24.8, 25.5, 32.5, 32.7, 49.3, 52.8, 78.5, 112.7, 118.8, 121.1, 121.5, 121.9, 128.6, 129.3, 129.4, 130.1, 130.6, 133.6, 136.4, 136.7, 137.4, 141.3, 165.6, 166.4, 166.9. MS (ESI+):  $m/z = 486.3$ . ESI-HR-MS calculated for  $\text{C}_{28}\text{H}_{27}\text{N}_3\text{O}_5$   $[\text{MH}]^+$ : 486.2029, found: 486.2024.

**2-(tert-Butylamino)-2-oxo-1-phenylethyl nicotinate (4aBa)**. Yield. 82% (0.352 g from 0.1 g); a white solid, mp 92-94 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{\text{max}}$ : 1142, 1236, 1452, 1647, 1748, 3151  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 1.34 (s, 9H), 6.32 (s, 1H), 6.93 (s, 1H), 7.24-7.27 (m, 1H), 7.45 (t,  $J = 7.8$  Hz, 2H), 7.55-7.59 (m, 1H), 7.66 (d,  $J = 7.8$  Hz, 1H), 7.71-7.76 (m, 1H), 8.16 (t,  $J = 7.1$  Hz, 2H), 8.58 (d,  $J = 4.3$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 28.5, 51.4, 76.1, 121.6, 123.3, 128.4, 129.2, 129.8, 133.3, 137.1, 148.9, 155.2,

165.0, 165.8. MS (ESI+):  $m/z = 313.1$ . ESI-HR-MS calculated for  $C_{18}H_{20}N_2O_3$   $[MH]^+$ : 313.1552, found: 313.1555.

**2-(Cyclohexylamino)-2-oxo-1-phenylethyl nicotinate (4aBb)**. Yield. 84% (0.263 g from 0.1 g); a white solid, mp 104-106 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 1123, 1257, 1450, 1640, 1753, 3252  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.11-1.21 (m, 3H), 1.31-1.38 (m, 3H), 1.59-1.71 (m, 2H), 1.89-1.96 (m, 2H), 3.79-3.86 (m, 1H), 6.08 (d,  $J = 7.7$  Hz, 1H), 6.29 (s, 1H), 7.38-7.45 (m, 5H), 8.10 (d,  $J = 7.4$  Hz, 1H), 8.36 (d,  $J = 7.9$  Hz, 1H), 8.81 (dd,  $J_1 = 1.4$  Hz,  $J_2 = 1.2$  Hz, 1H), 9.29 (d,  $J = 1.2$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 24.8, 25.5, 32.9, 48.5, 76.4, 123.6, 127.6, 128.7, 128.8, 128.9, 129.3, 137.5, 150.9, 154.0, 164.1, 166.9. MS (ESI+):  $m/z = 339.7$ . ESI-HR-MS calculated for  $C_{20}H_{22}N_2O_3$   $[MH]^+$ : 339.1709, found: 339.1712.

**2-(Cyclohexylamino)-2-oxo-1-phenylethyl 3-nitrobenzoate (4aCb)**. Yield. 90% (0.318 g from 0.1 g); a white solid, mp 182-184 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 669, 769, 1084, 1216, 1440, 1551, 1638, 1739, 3151  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.02-1.18 (m, 6H), 1.55-1.64 (m, 2H), 1.78-1.89 (m, 2H), 3.73-3.80 (m, 1H), 5.73 (d,  $J = 7.2$  Hz, 1H), 6.21 (s, 1H); 7.33-7.38 (m, 3H), 7.46-7.48 (m, 2H), 7.57-7.63 (m, 1H), 8.34-8.39 (m, 2H), 8.83 (d,  $J = 1.5$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 24.9, 25.6, 33.0, 33.1, 48.3, 75.6, 116.9, 127.6, 128.4, 128.8, 129.0, 129.1, 130.9, 134.1, 136.0, 146.7, 165.3, 167.5 MS (ESI+):  $m/z = 383.4$ . ESI-HR-MS calculated for  $C_{21}H_{22}N_2O_5$   $[MH]^+$ : 383.1607, found: 383.1612.

**2-(Cyclohexylamino)-2-oxo-1-phenylethyl cinnamate (4aDb)**. Yield. 68% (0.228 g from 0.1 g); a white solid, mp 166-168 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 960, 1126, 1430, 1469, 1521, 1649, 1743, 3089  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.08-1.13 (m, 3H), 1.25-1.31 (m, 2H), 1.53-1.59 (m, 3H), 1.86 (bs, 2H), 3.74-3.76 (m, 1H), 5.99 (s, 1H), 6.13 (s, 1H), 6.47 (dd,  $J_1 = 3.8$  Hz,  $J_2 = 3.8$  Hz, 1H), 7.29-7.34 (m, 5H), 7.41-7.48 (m, 5H), 7.69 (dd,  $J_1 = 3.6$  Hz,  $J_2 = 3.8$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 24.3, 24.4, 25.0, 32.1, 48.0, 76.2, 124.3, 127.1, 127.2, 128.3, 128.5, 129.5, 131.0, 135.0, 135.2, 147.8, 163.1, 166.6 MS (ESI+):  $m/z = 364.4$ . ESI-HR-MS calculated for  $C_{23}H_{25}NO_3$   $[MH]^+$ : 364.1913, found: 364.1918.

**2-(tert-Butylamino)-2-oxo-1-phenylethyl 2-(3-chlorophenyl)acetate (4aEa)**. Yield. 79% (0.263 g from 0.1 g); a white solid, mp 166-168 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 696, 1134, 1269, 1438, 1568, 1640, 1753, 3080  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.26 (s, 9H), 3.88 (s, 2H), 5.88 (s, 1H), 5.99 (s, 1H), 7.26-7.28 (m, 4H), 7.29-7.32 (m, 5H);  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 28.6, 40.9, 51.9, 73.4, 127.8, 129.6, 129.9, 130.1, 130.2, 130.4, 133.5, 133.7, 134.7, 166.5, 169.3. MS (ESI+):  $m/z = 360.2$ . ESI-HR-MS calculated for  $C_{20}H_{22}ClNO_3$   $[MH]^+$ : 360.1366, found: 360.1363.

**2-(tert-Butylamino)-1-(2-chlorophenyl)-2-oxoethyl 2-(3-chlorophenyl)acetate (4bEa)**. Yield. 81% (0.224 g from 0.1 g); a white solid, mp 94-96 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 1110, 1205, 1430, 1489, 1532, 1654, 1764, 3320  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.19 (s, 9H), 3.65 (s, 2H), 5.67 (s, 1H), 6.21 (s, 1H); 7.11-7.13 (m, 1H), 7.19-7.22 (m, 4H), 7.24 (s, 1H), 7.31-7.36 (m, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 28.6, 40.9, 51.8,

73.3, 127.4, 127.7, 127.8, 129.6, 129.9, 130.1, 130.1, 130.3, 133.5, 133.6, 134.6, 135.3, 166.4, 169.2. MS (ESI+):  $m/z = 394.4$ . ESI-HR-MS calculated for  $C_{20}H_{21}Cl_2NO_3$   $[MH]^+$ : 394.0977, found: 394.0980.

**2-(tert-Butylamino)-1-(2,3-dichlorophenyl)-2-oxoethyl 2-(3-chlorophenyl)acetate (4iEa).** Yield. 75% (0.182 g from 0.1 g); a white solid, mp 122-124 °C;  $R_f = 0.62$  (hexanes: EtOAc, 6:4, v/v); IR (KBr)  $\nu_{max}$ : 711, 1084, 1454, 1495, 1560, 1657, 1740, 3091  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 1.26 (s, 9H), 3.70 (s, 2H), 5.85 (s, 1H), 6.28 (s, 1H), 7.15-7.21 (m, 2H), 7.26 (d,  $J = 0.6$  Hz, 1H); 7.27 (s, 1H), 7.29-7.32 (m, 2H), 7.43 (dd,  $J_1 = 1.5$  Hz,  $J_2 = 1.5$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  (ppm) = 28.4, 40.7, 51.8, 73.5, 127.6, 127.6, 127.7, 128.0, 129.4, 130.1, 131.0, 132.1, 133.7, 134.6, 135.1, 135.7, 165.9, 169.0. MS (ESI+):  $m/z = 428.4$ . ESI-HR-MS calculated for  $C_{20}H_{20}Cl_3NO_3$   $[MH]^+$ : 428.0587, found: 428.0591.

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