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Ionic Liquid (IL) as an Effective Medium for the Highly Efficient Hydroacylation Reaction of Aldehydes with Azodicarboxylates

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Abstract: The highly efficient hydroacylation reaction of aldehydes with azodicarboxylates has been carried out in the ionic liquid,1-*n*-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide, [BMIM] [NTf_2]. The products were readily separated by extraction from the reaction medium and the ionic liquid could be recycled up to 8 times and the yields of the reactions were not affected. Compared to conventional solvents, high yields were achieved with aliphatic saturated aldehydes, and the reaction can be conducted under normal to mild conditions without the use of a catalyst.

Keywords: aldehydes; azo compounds; green chemistry; ionic liquids

Introduction

Carbon-nitrogen bond-forming reactions are without a doubt one of the most important categories of reactions in organic synthesis.[1] Efforts have been made to construct such bonds by using polar, radical, and transition metal-catalyzed reactions.[1] Over the last few decades, a very efficient reaction, which involves the use of azodicarboxylates as electrophiles, for the formation of carbon-nitrogen bonds, has been successfully used for such bond formation reactions. The efficiency of this reaction is due to the strong electron-withdrawing azodicarboxylates, which possess a vacant orbital and also serve as good nucleophilic acceptors.[1a,b] Although various types of reactions, such as the zwitterion intermediate reactions,[2] the electrophilic α-amination of carbonyl compounds,[3] the C–H activation at the α-position of amines and ethers,[4] and the ene-type reaction with olefins[5] in the presence of azodicarboxylates, have been extensively studied, the hydroacylation reaction with aldehydes has been exploited far less.[6] From the standpoint of atom economy, the hydroacylation reaction with direct functionalization of aldehydic C–H bonds to form a variety of hydrazine imides is a highly efficient synthetic methodology (Figure 1). To this end, photolytic conditions (Figure 1, method **A**) and thermal conditions (Figure 1, method **B**) have been utilized to achieve the formation of product **3**.[6] However, these

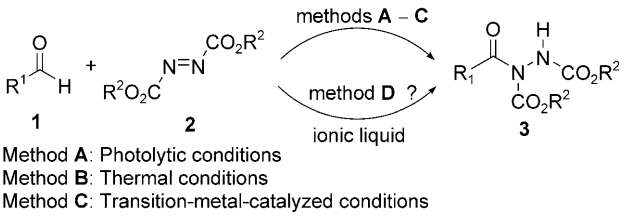


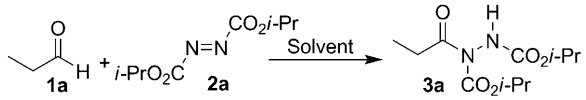
Figure 1. Hydroacylation strategy for hydrazine imides **3**.

two conditions are limited in that they often result in low yields and only a narrow scope of the substrates can be used. Recently, Lee et al. reported that a transition metal catalyst, rhodium acetate, efficiently catalyzed the hydroacylation between aliphatic saturated and unsaturated aldehydes with azodicarboxylates under mild conditions to provide the hydrazine imides **3** (Figure 1, method **C**).[7] For this method however, relatively low yields resulted when aromatic aldehydes were used as the substrates. As a result, the development of simple and efficient reaction conditions while concomitantly increasing the scope of the substrates is desirable.

One aspect of our research involves the use of room temperature ionic liquids (RTILs) for novel reactions, without metal catalysts; and we recently described that the aminohalogenation reaction of α,β-unsaturated ketones proceeded smoothly in modest to good yields and excellent regio- and stereoselectivity

in the ionic liquid [BMIM] [NTf_2].[8] During the past decade, RTILs have received considerable attention due to their ability to serve as effective reaction media for a wide variety of organic reactions and also for their use in other applications in chemistry.[9] Compared to typical organic solvents, RTILs have several intriguing properties, including their lack of measurable vapor pressure, high chemical and thermal stability, non-flammability, and high ionic conductivity;[10] these properties all serve to facilitate various chemical transformations when RTILs are used as the reaction media. Also, the high solubility of many organic and inorganic compounds in RTILs can in principle lead to enhanced rates and improved yields for reactions.[11] Furthermore, RTILs can be easily recycled, and therefore, they are recognized as potentially environmentally benign reaction media. In this paper, we wish to report the hydroacylation reaction of aldehydes and azodicarboxylates using the ionic liquid, [BMIM] [NTf_2], as solvent which resulted in high yields of product **3** (Figure 1, method **D**). Most importantly, this transformation is carried out without the use of a catalyst and is conducted under mild reaction conditions and the IL is recyclable.

Table 1. Optimization reaction of propionaldehyde **1a** with diisopropyl azodicarboxylate **2a**.[a]



Entry	Solvent	T [°C]	t [h]	Yield [%][b]
1	[BMIM] [BF_4]	r.t.	124	40
2	[BMIM] [PF_6]	r.t.	124	<10
3	[BMIM] [NTf_2]	r.t.	23	90
4	[BMIM] [$(C_2F_5SO_2)_2N$]	r.t.	18	92
5[c]	[BDMIM] [NTf_2]	r.t.	22	91
6[d]	[BMIM] [NTf_2]	r.t.	32	92
7[e]	[BMIM] [NTf_2]	r.t.	96	70
8	[BMIM] [NTf_2]	40	3	95
9	MeOH	r.t.	124	<10
10	MeCN	r.t.	124	<10
11	EtOAc	r.t.	124	<10

[a] Reactions were performed with a 2:1 ratio of **1a** and **2a** on a 0.5-mmol scale in 0.5 mL of ionic liquid. [BMIM] = butylmethylimidazolium.
[b] Isolated yields of pure product.
[c] [BDMIM] = 1-butyl-2,3-dimethylimidazolium.
[d] Ratio of **1a**/**2a** = 1.5:1.
[e] The ratio of **1a**/**2a** = 1:1.

Results and Discussion

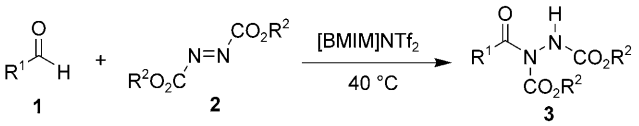
The hydroacylation reaction of propionaldehyde and diisopropyl azodicarboxylate was selected as the model for subsequent screening. As can be seen from the results summarized in Table 1, the reaction efficiency was significantly influenced by fine tuning the anion moiety of the ionic liquids, the ratio of aldehyde/azodicarboxylate, and the temperature. Among the RTILs examined as solvents, 1-*n*-butyl-3-methylimidazolium ionic liquid with the bis(trifluoromethanesulfonyl)imide as anion exhibited the highest reaction efficiency, compared to the ionic liquids with BF_4^- and PF_6^- as anions; [BMIM] [NTf_2] afforded the corresponding addition product **3a** in 90% yield at room temperature after 23 h, compared to lower yields and longer reaction times for the other ionic liquids (Table 1, entries 1–3).[12] These results indicate that the nature of the anion plays an important role in reactivity and efficiency; this could be attributed to the larger anion [NTf_2], which would result in a greater cation/anion separation, compared to other ILs with harder anions [BF_4] and [PF_6].[13] These different properties allow for a more effective interaction between the negative charge of the carbonyl oxygen and the cationic portion of the ionic liquid, compared to ILs that contain harder anions; such an interaction assists in activating the C–H bond of the aldehyde and a more effective solvent activation of the carbonyl oxygen. In order to get further insight into the role of the anion in promoting the reaction, we conducted the reaction using ionic liquid [BMIM] [$(CF_3CF_2SO_2)_2N$] as solvent,[14] which has a similar molecular composition but a larger anion comparing to [BMIM] [$(CF_3SO_2)_2N$] (Table 1, entry 4 *vs.* 3). As expected, the reaction proceeded smoothly to afford the hydroacylation product **3a** in 92% yield at room temperature for 18 h.

Recently, the effects that the cation of [BMIM]-based ionic liquids have on the electron transfer have been investigated, and it has been suggested that the acidity of the C-2 proton of the imidazolium cation plays an important role to stabilize the oxygen radical anion.[15] The question of whether the C-2 proton of the imidazolium cation also affects the hydroacylation reaction for the possible activation of the carbonyl group *via* hydrogen bonding with the C-2 proton of the imidazolium cation and thus plays a role in the reaction is a good one; but, we found that when 1-butyl-2,3-dimethylimidazolium bis(trifluoromethanesulfonyl)imide [BDMIM] [NTf_2] was used as solvent, in which the C-2 position of the imidazolium cation was substituted with a methyl group, the reaction proceeded smoothly and afforded comparable results as when [BMIM] [NTf_2] was used (Table 1, entry 3 *vs.* entry 5). This indicates that the C-2 proton of the imidazolium cation does not affect the reaction rate. Noteworthy, when the ratio of aldehyde to azodicarboxylate (**1a**/**2a**) was decreased from 2:1 to 1.5:1 and 1:1, the reaction proceeded slower and resulted in a lower yield with azodicarboxylate (**1a**/**2a**) decreasing from 2:1 to 1.5:1 and 1:1 (Table 1, entries 3, 6, and 7).

Upon raising the temperature from room temperature to 40 °C, the reaction rate was dramatically increased with slightly improved yield, which gave the best optimal performance for the hydroacylation reaction (Table 1, entry 8). Conventional organic solvents, such as MeOH, CH_3CN, and EtOAc, which do not exhibit similar properties as IL, resulted in poor yields (Table 1, entries 9–11).

Encouraged by these results, we next probed the scope of this hydroacylation reaction with a variety of aldehydes and azodicarboxylates (Table 2). All reactions were carried out simply by mixing the reactants in a one-pot operation system in the ionic liquid, [BMIM] [NTf_2] at 40 °C affording the corresponding hydroacylation products **3b**–**3r**. Typically, different substituents on the aliphatic aldehydes significantly influence the reaction rates and chemical yields. For example, the aliphatic saturated aldehydes **1b–e**, with either linear or branched substituents when used in the reaction with diisopropyl azodicarboxylate, afforded the desired products **3b–e** in excellent chemical yields (Table 2, etries 1–4). It was also observed that the substitution pattern of aliphatic saturated aldehyde influences the reaction rate. For example, in the case of 3-phenylpropionaldehyde, when a phenyl group is present at the γ-position of propionaldehyde, relatively low reaction rate and chemical yield were observed (Table 2, entry 5). The aliphatic aldehydes **1g** and **h** with unsaturation either at the terminal or internal position also provided the desired products **3g** and **3h**, respectively, but in low yields (Table 2, entries 6 and 7). In these two examples, the low yields might be due to an ene-type reaction to generate the bisazodicarboxylates;[16] the same phenomenon was also observed by Lee's research group using the catalyst, rhodium acetate.[7a] Those aromatic aldehydes, which contain H and Cl were also good substrates for this reaction and afforded the hydroacylation products in good yield, although the reaction rate was relatively slower (Table 2, entries 8 and 9). On the other hand, aromatic aldehydes with electron-donoting OMe and electron-withdrawing NO_2 groups gave poor yields (Table 2, entries 10 and 11). To broaden the scope of the reaction, a wide range of azodicarboxylates **2b–f**, including azodicarboxylates containing phenyl groups substituted with electron-withdrawing and electron-donating groups were used in the reaction with propionaldehyde (Table 2, entries 12–16). In general, hydrogen and other substituents on the phenyl ring influenced the reaction rate and yield. For example, substrates with the phenyl ring substituted with H, Cl, and NO_2 groups gave the desired products 3**n–p** in 85–94% yields (Table 2, entries 13–15); whereas, when the phenyl ring contains the electron-donating group OMe, a very poor yield with long reaction time resulted (Table 2, entry 16). In order to further confirm the structure of the hydroacylation product, the reaction of cyclopentanecarbaldehyde **1m** and **2d** was investigated and gave the hydroacylation product **3r** (Table 2, entry 17). The structure of **3r** was unambiguously determined by an X-ray diffraction study (Figure 2).[17]

Table 2. Hydroacylation reaction of aldehydes with azobicarboxylates.



Entry	R^1	R^2	t [h]	Product	Yield [%][a]
1	**1b** *n*-C_4H_9	**2a** *i*-Pr	6	**3b**	98
2	**1c** $(CH_3)_2CHCH_2$	**2a** *i*-Pr	5	**3c**	98
3	**1d** $(CH_3)_2CH$	**2a** *i*-Pr	1	**3d**	99
4	**1e** Cyclohexyl	**2a** *i*-Pr	9	**3e**	99
5	**1f** $PhCH_2CH_2$	**2a** *i*-Pr	48	**3f**	88
6	**1g** (*cis*) *n*-C_5H_{11}-CH=$CHCH_2CH_2$	**2a** *i*-Pr	48	**3g**	43
7	**1h** CH_2=$CHCH_2(CH_3)_2C$	**2a** *i*-Pr	48	**3h**	40
8	**1i** Ph	**2a** *i*-Pr	120	**3i**	80
9	**1j** 4-Cl-C_6H_4	**2a** *i*-Pr	168	**3j**	69
10	**1k** 4-MeO-C_6H_4	**2a** *i*-Pr	168	**3k**	<10
11	**1l** 4-NO_2-C_6H_4	**2a** *i*-Pr	168	**3l**	<10
12	**1a** CH_3CH_2	**2b** Et	1.5	**3m**	94
13	**1a** CH_3CH_2	**2c** Bn	20	**3n**	89
14	**1a** CH_3CH_2	**2d** 4-$ClC_6H_4CH_2$	20	**3o**	94
15	**1a** CH_3CH_2	**2e** 4-$NO_2C_6H_4CH_2$	24	**3p**	85
16	**1a** CH_3CH_2	**2f** 4-$MeOC_6H_4CH_2$	168	**3q**	<10
17	**1m** Cyclopentyl	**2d** 4-$ClC_6H_4CH_2$	2	**3r**	98

[a] Isolated yields of pure product after column chromatography.

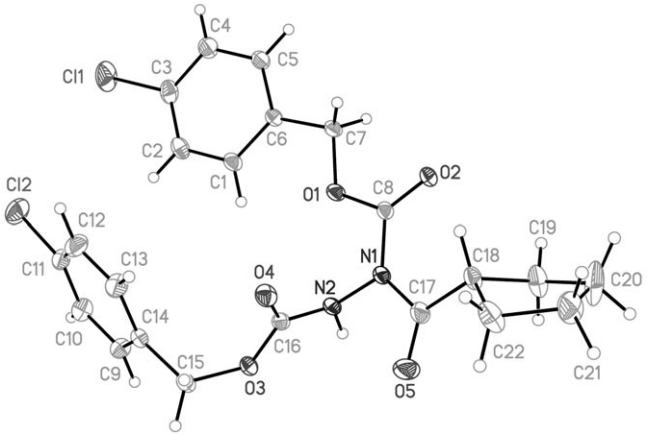
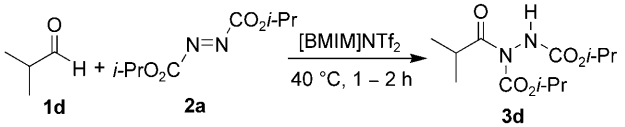


Figure 2. X-ray crystal structure of **3r**.

We chose the hydroacylation reaction of isobutyraldehyde **1d** and diisopropyl azodicarboxylate **2a** under optimized reaction conditions to examine the recyclability of ionic liquid [BMIM] [NTf_2]. When the first cycle of the reaction was completed, the reaction mixture was extracted with ether four times. The ether solution was combined, concentrated, and purified by flash chromatography to afford the product **3d**. The ether insoluble ionic liquid [BMIM] [NTf_2] was recovered and dried under vacuum for 1 h and reused for the next cycle of the reaction. The ionic liquid can be recycled for another 7 times without significant loss of chemical yield and the ionic liquid (Table 3).

It was described in previous studies that the hydroacylation of aldehydes with azodicarboxylate considered to proceed by a radical intermediate mechanism.[6,7a] We assume that the hydroacylation reaction in an ionic liquid may still proceed *via* a radical mechanism, and that the ionic liquid plays an important role in stabilizing the radical transition intermediate through an ionic solvation effect and facilitating the addition of the acyl radical intermediate to azodicarboxylate to form the hydroacylation product.

Table 3. Recycling studies of hydroacylation reaction of isobutyraldehyde **1d** and diisopropyl azodicarboxylate **2a** in the ionic liquid [BMIM] [NTf_2].



Cycle	Yield [%][a]	Cycle	Yield [%][a]
1	99	5	98
2	95	6	96
3	97	7	96
4	96	8	97

[a] Isolated yields of pure product after column chromatography.

Conclusions

In conclusion, we have developed an efficient hydroacylation reaction of aldehydes with azodicarboxylates in the ionic liquid [BMIM] [NTf_2], the reaction can be conducted under convenient and mild conditions without the special protection of inert gases as well as in the absence of metal catalysts. The products can be readily separated by extraction due to the solubility characteristics of the ionic liquid, and the ionic liquid can be efficiently recycled 8 times without any significant loss of the chemical yield.

Experimental Section

General Remarks

All reactions were performed in oven-dried vials. All commercially available reagents were purchased from Aldrich and used without further purification. Flash chromatography was performed using silica gel (Merck 60, 230–400 mesh).

Typical Procedure for the Hydroacylation Reaction in Ionic Liquid [BMIM] [NTf_2]

To a stirred solution of aldehyde **1** (1.0 mmol) in ionic liquid [BMIM] [NTf_2] (0.5 mL) was added azodicarboxylate **2** (0.5 mmol). The reaction was stirred at 40 °C for the time as indicated in Table 1 and Table 2. The reaction mixture was extracted with ether for four times (5 mL × 4). The ether solution was combined, concentrated, and purified by flash chromatography on silica gel (hexane:ethyl acetate = 4:1) to afford the product diisopropyl 1-acylhydrazine-1,2-dicarboxylate **3**. The ether insoluble ionic liquid [BMIM] [NTf_2] was recovered and dried under vacuum for 1 h and reused for the next cycle of reaction.

Hydroacylation Product 3a:[7a] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.70 (br, 1H, N*H*), 5.10–4.92 [m, 2H, $(CH_3)_2CHO$], 2.98–2.87 (m, 2H, CH_3CH_2), 1.32 [d, J = 7.2 Hz, 6H, $(CH_3)_2CHO$], 1.27 [br, 6H, $(CH_3)_2CHO$], 1.17 (t, J = 7.2 Hz, 3H, CH_3CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.6, 155.1, 152.6, 72.1, 70.3, 30.5, 21.8, 21.7, 8.8.

Hydroacylation Product 3b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.72 (br, 1H, N*H*), 5.10–4.92 [m, 2H, $(CH_3)_2CH$], 2.86–2.85 (m, 2H, $CH_3CH_2CH_2CH_2$), 1.65 (m, 2H, $CH_3CH_2CH_2CH_2$), 1.43–1.34 (m, 2H, $CH_3CH_2CH_2CH_2$), 1.32 [d, J = 7.2 Hz, 6H, $(CH_3)_2CH$], 1.28 [br, 6H, $(CH_3)_2CH$], 0.93 (t, J = 7.2 Hz, 3H, $CH_3CH_2CH_2CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.9, 155.1, 152.6, 72.0, 70.3, 36.7, 26.8, 26.7, 22.2, 21.8, 21.6, 13.8, 13.6; HR-MS: m/z = 289.1769, calcd. for $C_{13}H_{24}N_2O_5$ $(M+H)^+$: 289.1763.

Hydroacylation Product 3c: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.72 (br, 1H, N*H*), 5.09–4.92 [m, 2H, $(CH_3)_2CHO$], 2.80 [br, 2H, $(CH_3)_2CHCH_2$], 2.25–2.13 [m, 1H, $(CH_3)_2CHCH_2$], 1.32 [d, J = 6.0 Hz, 6H, $(CH_3)_2CHO$], 1.28 [br, 6H, $(CH_3)_2CHO$], 0.98 [d, J = 6.8 Hz, 6H, $(CH_3)_2CHCH_2$]; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.1, 155.1, 152.6, 72.0, 70.3, 45.5, 25.4, 25.2, 22.4, 22.3, 21.8, 21.6; HR-MS: m/z = 311.1590, calcd. for $C_{13}H_{24}N_2O_5$ $(M+Na)^+$: 311.1577.

Hydroacylation Product 3d: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.77$ (br, 1H, N*H*), 5.10–4.92 [m, 2H, $(CH_3)_2CHO$], 3.70–3.57 [m, 1H, $(CH_3)_2CH$], 1.32 [d, $J = 6.4$ Hz, 6H, $(CH_3)_2CHO$], 1.28 [br, 6H, $(CH_3)_2CHO$], 1.20 [d, $J = 6.4$ Hz, 6H, $(CH_3)_2CH$]; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 178.2$, 155.2, 152.5, 72.0, 70.2, 34.2, 21.8, 21.6, 19.2, 18.8; HR-MS: $m/z = 297.1436$, calcd. for $C_{13}H_{24}N_2O_5$ $(M+Na)^+$: 297.1421.

Hydroacylation Product 3e:[7a] ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.75$ (br, 1H, N*H*), 5.06–4.86 [m, 2H, $(CH_3)_2CHO$], 3.37–3.27 (m, 1H, cyclohexyl-*CH*), 1.97–1.82 (m, 2H, cyclohexyl-CH_2), 1.80–1.57 (m, 3H, cyclohexyl-CH_2), 1.48–1.35 (m, 2H, cyclohexyl-CH_2), 1.27 [d, $J = 6.4$ Hz, 6H, $(CH_3)_2CHO$], 1.25–1.10 [m, 9H, $(CH_3)_2CHO$ and cyclohexyl-CH_2]; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 181.1$, 152.6, 72.0, 70.2, 44.0, 42.8, 29.4, 28.8, 25.8, 25.7, 25.6, 25.3, 21.8, 21.6.

Hydroacylation Product 3f:[7a] ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.30$–7.13 (m, 5H, Ar*H*), 6.71 (br, 1H, N*H*), 5.06–4.88 [m, 2H, $(CH_3)_2CHO$], 3.21 (t, $J = 8.0$ Hz, 2H, $PhCH_2CH_2$), 2.97 (t, $J = 8.0$ Hz, 2H, $PhCH_2CH_2$), 1.28 [d, $J = 6.0$ Hz, 6H, $(CH_3)_2CHO$], 1.25 [br, 6H, $(CH_3)_2CHO$]; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 172.9$, 155.0, 152.5, 140.6, 128.4, 126.1, 72.1, 70.3, 38.6, 30.6, 21.8, 21.6.

Hydroacylation Product 3g:[7a] ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.68$ (br, 1H, N*H*), 5.44–5.27 (m, 2H, $CH_2CH{=}CHCH_2$), 5.06–4.87 [m, 2H, $(CH_3)_2CHO$], 2.90 (br, 2H, $CHCH_2CH_2CO$), 2.35 (q, $J = 7.2$ Hz, 2H, $CHCH_2CH_2CO$), 2.00 (q, $J = 6.8$ Hz, 2H, n-$C_4H_9CH_2CH$), 1.36–1.10 [m, 18H, $(CH_3)_2CHO$ and $CH_3(CH_2)_3CH_2$], 0.84 [t, $J = 6.4$ Hz, 3H, $CH_3(CH_2)_2CH_2$]; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 173.2$, 155.0, 152.6, 131.4, 127.4, 72.0, 70.3, 37.0, 31.4, 29.2, 27.1, 22.5, 22.4, 21.8, 21.6, 14.0.

Hydroacylation Product 3h:[7a] ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.58$ (br, 1H, N*H*), 5.80–5.66 (m, 1H, $CH_2{=}CH$), 5.08–4.90 [m, 4H, $CH_2{=}CH$ and $(CH_3)_2CHO$], 2.42 (d, $J = 7.2$ Hz, 2H, $CH_2{=}CHCH_2$), 1.32–1.16 8 [m, 18H, $(CH_3)_2C$ and $(CH_3)_2CHO$]; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 178.6$, 155.6, 153.2, 134.2, 117.9, 72.2, 70.6, 45.5, 44.7, 25.2, 22.0, 21.9, 21.8, 21.7.

Hydroacylation Product 3i:[7a] ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.65$ (br, 2H, Ar*H*), 7.48 (t, $J = 7.2$ Hz, 1H, Ar*H*), 7.38 (t, $J = 7.6$ Hz, 2H, Ar*H*), 7.03 (br, 1H, N*H*), 5.04–4.93 [m, 1H, $(CH_3)_2CHO$], 4.90–4.80 [m, 1H, $(CH_3)_2CHO$], 1.26 [t, $J = 6.4$ Hz, 6H, $(CH_3)_2CHO$], 1.03 [t, $J = 6.4$ Hz, 6H, $(CH_3)_2CHO$]; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.2$, 155.2, 152.8, 135.2, 131.8, 128.0, 72.4, 70.8, 70.6, 70.4, 22.0, 21.8, 21.6, 21.2.

Hydroacylation Product 3j:[7a] ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.65$ (d, $J = 7.2$ Hz, 2H, Ar*H*), 7.39 (d, $J = 8.4$ Hz, 2H, Ar*H*), 7.25 (br, 1H, N*H*), 5.10–4.85 [m, 2H, $(CH_3)_2CHO$], 1.28 [d, $J = 6.0$ Hz, 6H, $(CH_3)_2CHO$], 1.12 [d, $J = 6.0$ Hz, 6H, $(CH_3)_2CHO$]; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.2$, 155.3, 152.8, 138.3, 133.6, 129.8, 128.6, 72.8, 70.8, 22.0, 21.4.

Hydroacylation Product 3m: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.89$ (br, 1H, N*H*), 4.25 (q, $J = 7.2$ Hz, 2H, CH_3CH_2O), 4.17 (q, $J = 7.2$ Hz, 2H, CH_3CH_2O), 2.87 (q, $J = 6.8$ Hz, 2H, CH_3CH_2), 1.29 (t, $J = 6.8$ Hz, 3H, CH_3CH_2O), 1.24 (br, 3H, CH_3CH_2O), 1.12 (t, $J = 7.2$ Hz, 3H, CH_3CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.6$, 155.6, 153.1, 63.8, 62.4, 30.4, 14.3, 14.0, 8.8, 8.7; HR-MS: $m/z = 255.0962$, calcd. for $C_{13}H_{24}N_2O_5$ $(M+Na)^+$: 255.0951.

Hydroacylation Product 3n: White solid, mp 110–112 °C (ethyl acetate-hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.34$ (br, 10H, Ar*H*), 6.86 (br, 1H, N*H*), 5.23 (s, 2H, $PhCH_2$), 5.17 (s, 2H, $PhCH_2$), 2.29 (br, 2H, CH_3CH_2), 1.16 (t, $J = 7.2$ Hz, 3H, CH_3CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.4$, 155.4, 153.0, 135.4, 134.7, 128.8, 128.6, 128.4, 128.1, 69.1, 68.1, 30.5, 8.7; anal. calcd. for $C_{19}H_{20}N_2O_5$: C 64.04, H 5.66, N 7.86; found: C 64.22, H 5.68, N 7.72.

Hydroacylation Product 3o: White solid, mp 100–101 °C (ethyl acetate-hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.20$–7.05 (m, 8H, Ar*H*), 6.91 (br, 1H, N*H*), 5.16 (s, 2H, 4-$ClPhCH_2$), 5.10 (s, 2H, 4-$ClPhCH_2$), 2.89 (br, 2H, CH_3CH_2), 1.13 (t, $J = 7.2$ Hz, 3H, CH_3CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.3$, 155.2, 152.9, 134.6, 134.4, 133.8, 133.1, 129.5, 128.4, 128.8, 128.6, 68.3, 67.2, 30.5, 8.7; anal. calcd. for $C_{19}H_{18}Cl_2N_2O_5$: C 53.66, H 4.27, N 6.59; found: C 53.74, H 4.25, N 6.57.

Hydroacylation Product 3q: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.21$ (d, $J = 8.4$ Hz, 4H, Ar*H*), 7.51 (d, $J = 8.4$ Hz, 4H, Ar*H*), 7.02 (br, 1H, N*H*), 5.35 (s, 2H, 4-NO_2PhCH_2), 5.31 (s, 2H, 4-NO_2PhCH_2), 2.94 (br, 2H, CH_3CH_2), 1.18 (t, $J = 7.2$ Hz, 3H, CH_3CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.2$, 155.2, 152.8, 147.9, 147.8, 142.5, 141.9, 128.2, 128.1, 127.0, 123.9, 123.8, 123.7, 67.5, 66.6, 30.5, 8.7; anal. calcd. for $C_{19}H_{18}N_4O_9$: C 51.12, H 4.06, N 12.55; found: C 51.34, H 4.14, N 12.34.

Hydroacylation Product 3r: White solid, mp 97–98 °C (ethyl acetate-hexane); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.40$–7.18 (m, 8H, Ar*H*), 6.83 (br, 1H, N*H*), 5.17 (s, 2H, 4-$ClPhCH_2$), 5.11 (s, 2H, 4-$ClPhCH_2$), 3.76–3.60 (m, 1H, cyclopentyl-*CH*), 2.00–1.50 (m, 8H, cyclopentyl-CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 176.9$, 155.3, 152.8, 134.6, 134.4, 133.8, 133.2, 129.5, 128.9, 128.8, 68.3, 67.2, 44.6, 30.2, 25.9; anal. calcd. for $C_{22}H_{22}Cl_2N_2O_5$: C 56.78, H 4.77, N 6.02; found: C 56.85, H 4.75, N 5.99.

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