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Catalytic hydrogenation of functionalized amides under basic and neutral conditions†

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A new, base-free high turnover number (TON) catalyst for hydrogenation of simple and functionalized amides is prepared by reacting $[Ru(\eta^3\text{-}C_3H_5)(Ph_2P(CH_2)_2NH_2)_2]BF_4$ and BH_4^- under hydrogen. The hydrogenation proceeds with C–N cleavage to form the corresponding amine and alcohol. The base-free and base-promoted hydrogenations tolerate alcohols, amines, aromatic bromides, chlorides and fluorides, ethers, certain olefins, and N-heterocyclic rings. The reaction was used to deprotect the amine groups in certain acetyl amides to form, for example, an N-heterocyclic amine containing an aryl bromide. The base-free system also selectively hydrogenates *N*-acyloxazolidinones without epimerization at the α-position, and reduced β-lactams to form the corresponding amino alcohols.

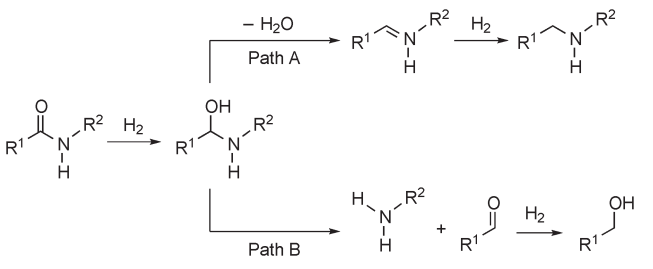
Introduction

We report an active system for the hydrogenation of simple and functionalized amides under neutral conditions with high turnover numbers (TON). The reduction of amides produces alcohols and/or amines that have biological activity and industrial applications.[1,2] Amides are the least reactive of the carboxylic acid derivatives, and their reduction requires forceful conditions or reducing agents that are oxophilic. Amide reductions are typically carried out with stoichiometric hydride reducing agents such as Al–H, B–H, or Si–H species.[3] Recently, Procter *et al.* reported a stoichiometric reduction with SmI_2 (4–8 equiv.) as reducing agent to form the amine and alcohol products of net C–N cleavage.[4] The reduction of amides proceeds through hemiaminal or related intermediates (Scheme 1).[5]

Elimination of H_2O (C–O cleavage) forms the higher amine as net product (path A). The elimination of H_2O is promoted by acid, sieves, oxophilic reagents, the presence of hydrogen on nitrogen, or by high temperatures to remove water. The majority of stoichiometric amide reductions proceed by C–O cleavage to form the higher amine. Elimination of H_2NR^2 (C–N cleavage) during amide reduction forms the corresponding lower amine and alcohol (path B). The net elimination of H_2NR^2 from the hemiaminal is promoted by basic conditions at low to moderate temperatures. The structure of the amide and catalyst will also influence the selectivity of the reduction.

The heterogeneous amide hydrogenation catalysts favor net C–O cleavage, and the more active systems use ~1 mole% catalyst at $T > 130$ °C under 30–100 atm H_2.[6] These systems tolerate certain ether functionalities, amines, and alcohols. Arene hydrogenation and bond hydrogenolysis can occur as side reactions. Recently, Cole-Hamilton *et al.* reported that a 4% Pt–4% Re/TiO_2 catalyst effects the hydrogenation of amides in flow reactors.[6n]

The homogeneous amide hydrogenation catalysts are classified into acid-promoted systems and into bifunctional-type systems that operate under neutral and basic conditions. $Ru(acac)_3$ (acacH = 2,4-pentanedione), 1,1,1-tris-(diphenylphosphinomethyl)ethane, and methanesulphonic acid form a catalyst that hydrogenates *N*-phenyl amides with predominantly C–O cleavage under acidic conditions with 1% catalyst at T = 200–220 °C under 10–40 atm H_2.[7a–d] The bifunctional homogeneous precursors include Cp*RuCl(X–N) (X = N, P),[7e–g] PNN-Ru pincer complexes (PNN = 2-(di-*tert*-butylphosphinomethyl)-6-(diethylaminomethyl)pyridine, *etc.*),[7h] and $RuCl_2(Y\text{–}N)_2$ complexes (*e.g.* Y–N = 2-((dicyclohexylphosphino)methyl)pyridine.[7k] These systems operate under neutral conditions, typically in



Scheme 1

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THF solvent at T = 80–200 °C with 1–10 mole% catalyst under 10–50 atm H_2. The major products are the alcohol and amine resulting from C–N cleavage. The activity of some of these catalysts is promoted under basic conditions. In 2011, we reported that the cationic allyl precursor $[Ru(\eta^3\text{-}C_3H_5)(Ph_2P(CH_2)_2NH_2)_2]BF_4$ (**2**) or the neutral dichloride $RuCl_2(Ph_2P(CH_2)_2NH_2)_2$ (**3**) with base in THF hydrogenate a wide variety of simple amides with C–N cleavage and with remarkable TON's up to ~7000 (100 °C, 50 atm, 4–5 mol% base, 24 h).[8a]

There are no reports of a high TON (>300) neutral amide hydrogenation catalyst, nor of an amide hydrogenation catalyst that tolerates a wide variety of functional groups. We now report such a neutral catalyst, and we demonstrate its functional group tolerance under neutral and basic conditions. We also illustrate the utility of the system as a relatively mild, catalytic method to liberate amines by hydrogenation of the corresponding acetyl amides.

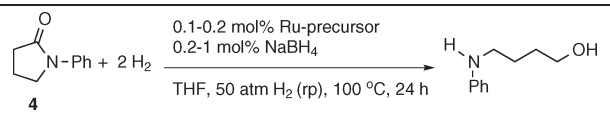
Results and discussion

Noyori[9] and others[10a–e] reported that catalysts containing BH_4^- adducts are active for ketone hydrogenations under base-free conditions.[11] For this study, we found that the cationic allyl precursor $[Ru(\eta^3\text{-}C_3H_5)(Ph_2P(CH_2)_2NH_2)_2]BF_4$ (**2**) reacts with 2 equiv. of $NaBH_4$ under H_2 in THF (~2 atm, 60 °C, 30 min) to form a base-free catalyst that hydrogenates *N*-phenylpyrrolidin-2-one (**4**) with C–N cleavage in high TON (910) (24 h, 50 atm (reaction pressure, rp), 100 °C, Table 1, entry 1). There was no evidence of C–O cleavage, despite the neutral conditions for this hydrogenation. Catalysts prepared by reacting the ruthenium precursors $[Ru((1\text{-}3;5\text{-}6\text{-}\eta)\text{-}C_8H_{11})(\eta^6\text{-anthracene})]BF_4$ (**5**)[12] or $[Ru(\eta^3\text{-}C_3H_5)(COD)(MeCN)_2]BF_4$ (COD = 1,5-cyclooctadiene) (**6**) *in situ* with $Ph_2P(CH_2)_2NH_2$ (**7**, 2 equiv.), and then with $NaBH_4$ (5 equiv.) were somewhat less active (entries 2 and 3) than the catalyst prepared from **2**. The dichloride $RuCl_2(Ph_2P(CH_2)_2NH_2)_2$ (**3**) with $NaBH_4$ was ~66% less active (entry 4). The ratio of Ru : BH_4 was increased to 1 : 5 with **5**, **6**, and **3** to accommodate any uncertainties in the amounts of *in situ* catalyst formed, as well as any potential difficulties in reducing any ligands in these precursors with BH_4^-. It is likely that the reduced activity of catalysts made from **5** and **6** results from inefficiencies inherent with utilizing two *in situ* reactions to prepare the catalyst: the reaction with **7**, followed by reaction with $NaBH_4$ and hydrogen. The relatively low reactivity of the dichloride **3** perhaps illustrates the relative ease by which the allyl group in **2** is removed by hydrogenation relative to the reduction of the chloride ligands in **3** by $NaBH_4$.

Table 2 shows the results for the base-free hydrogenations of representative simple amides with **2** (0.1 mol%) and $NaBH_4$ (B/Ru = 2, 100 °C, 50 atm (rp), 24 h, THF). For comparison, we include the yields reported previously for the same hydrogenations carried out with excess base (4 mol% $KN[Si(CH_3)_3]_2$).[8a] The *N*-diphenyl (entry 1), *N*-phenyl-*N*-methyl (entry 2), and *N*-phenyl acetamides (entry 3) were all hydrogenated in high TON (800–1000) with both catalyst systems. Interestingly, the 2° *N*-phenyl acetamide (entry 3) was slightly more reactive with the base-free catalyst than with the base-promoted catalyst. The same order of activity occurs with *N*,*N*-diphenyl benzamide as substrate (entry 6). We believe that under basic conditions, 2° amides are deprotonated at nitrogen to form strongly coordinating amidate anions that partially hinder the catalyst. The hydrogenations with BH_4^- are less susceptible to this type of inhibition. The morpholino acetamide (8d) was smoothly hydrogenated under base-free and basic conditions (entry 4), and the stable *N*,*N*-dimethylacetamide (8e), was hydrogenated with appreciable TON (240, entry 5) with the base-free catalyst. The base-promoted system was more active (TON = 500). Taken together, the hydrogenations of the *N*-phenyl, *N*-alkyl, and secondary acetamides in Table 1 demonstrate that these hydrogenations offer a relatively mild, efficient, and environmentally benign alternative to the stoichiometric methods used to liberate amines that were protected as acetamides.[14]

Table 3 shows the results from the base-free and base-promoted hydrogenations of functionalized amides. Generally, the system with added base was more active for these

Table 1 Base-free hydrogenation of **4** by various Ru-precursors

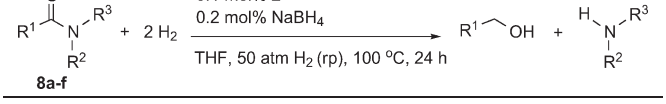


4

Entry	Catalyst	Ru : $NaBH_4$	% conv[a]	TON
1[b]	**2**	1 : 2	91	913
2[c]	**5**	1 : 5	71	710
3[c]	**6**	1 : 5	66	660
4[d]	**3**	1 : 5	76	378

[a] Determined by ^1H NMR spectroscopy. [b] **2** was reacted with $NaBH_4$ for 20 min under ~2 atm H_2 at 60 °C. [c] **5** or **6** were reacted with 2 equiv. **7** (under Ar for 30 min), then with $NaBH_4$ under ~2 atm H_2 for 20 min at 60 °C. [d] **3** was reacted with $NaBH_4$ for 20 min under ~2 atm H_2 at 60 °C. rp = reaction pressure.

Table 2 Base-free hydrogenation of simple amides[a,b]

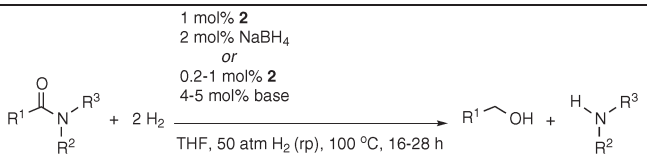


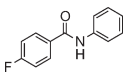
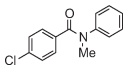
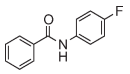
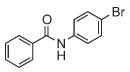
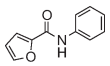
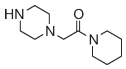
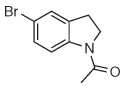
8a-f

Entry	Sub	R^1	R^2	R^3	% conv[c]	TON
1	8a	Me	Ph	Ph	100(100)	1000
2	8b	Me	Ph	Me	93(100)	930
3	8c	Me	Ph	H	80(70)	800
4	8d	Me	$-C_4H_8O-$[f]		96(100)	960
5	8e[d]	Me	Me	Me	24(50)	240
6	8f[e]	Ph	Ph	H	71(50)	710

[a] **2** reacted with $NaBH_4$ for 20 min under ~2 atm H_2 at 60 °C. [8a–e] = 2.5 M in THF. [b] In parenthesis are the results for the base-assisted hydrogenation using 0.1 mol% **2** and 4 mol% $KN[Si(CH_3)_3]_2$. [c] Determined using ^1H NMR spectroscopy. [d] Anthracene used as internal standard. [e] [8f] = 2 M in THF. [f] $-CH_2CH_2OCH_2CH_2-$.

Table 3 Base-free[a] *vs.* base-assisted[b] hydrogenation of functionalized amides



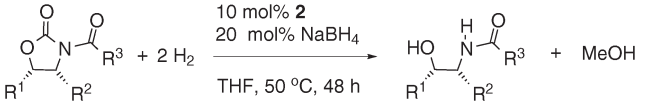
Entry	Sub	t (t)[c]	% conv		TON	
			Base-free	Base-assisted	Base-free	Base-assisted
1		24(24)	34	89[d]	34	442
2		24(21)	0	50[e]	0	50
3		19(28)	69	100[f,g]	69	500
4		nd(24)	nd	100	nd	100
5		16(24)	32	88[d]	32	438
6		nd(24)	nd	100[d,g]	nd	500
7		24(24)	5	86	5	86
8		24(24) nd(24)	100 nd	100 100[h]	100 nd	500 500

[a] 2 (1 mol%) reacted with $NaBH_4$ (2 mol%) for 20 min under ~2 atm H_2 at 60 °C. [amide] = 0.25 M in THF. nd = not determined. [b] 2 (1 mol%) reacted with KO*t*-Bu (4 mol%). [Amide] = 0.25 M in THF. [c] Time for base-assisted hydrogenations denoted in parenthesis. [d] Ru : KO*t*-Bu : amide 1 : 20 : 500. [e] Ru : KO*t*-Bu : amide 1 : 5 : 100. [f] Proceeded with 8% C–O cleavage. [g] Ferrocene used as internal standard. [h] Reaction performed at 10 atm H_2 pressure.

substrates. The functional groups that tolerated the base-promoted hydrogenation with good TON (400–500) include arene rings, aromatic fluorides (entries 1 and 3), and bromides (entry 4). The halide can reside on the acyl group (entries 1 and 2), or in the amine of the amide (entries 3 and 4). Interestingly, and for reasons unknown at this time, the base-assisted hydrogenation of the *N*-(4-fluorophenyl)benzamide (entry 3) proceeded quantitatively (TON = 500) with 92% net C–N cleavage and ~8% net C–O cleavage. The aromatic chloride (entry 2) was less reactive than the fluorides and bromides. Importantly, furans are not hydrogenated and do not hinder catalysis (entries 5 and 6, TON = 400–500), demonstrating that amides can be selectively hydrogenated in the presence of furans. Amides containing 2° N-heterocycles can also be hydrogenated, albeit with lower, but useful TON (86, entry 7). The halogenated heterocyclic amine 5-bromoindoline was deprotected by the neutral and base-promoted hydrogenations of 1-acetyl-5-bromoindoline (entry 8). Significantly, the base-promoted hydrogenation of this substrate (entry 8) was carried out under 10 atm *reaction pressure* to give 500 turnovers in 24 hours, demonstrating that this catalytic system is active towards certain amides under lower pressures. The hydrogenation also tolerates ethers (see Table 2, entry 4), as well as alcohols and amines as these are the products of the hydrogenation.

N-Acyloxazolidinones are typically harder to reduce than amides. We prepared the diastereomerically pure (2-benzyl)-propanamide oxazolidinones **9a** and **9b** by benzylation of the parent enolates.[13] Hydrogenation of **9a** and **9b** under base-free conditions with 10 mol% Ru proceeded with quantitative reduction of the endocyclic C–N bond to furnish only the corresponding hydroxyl amides and methanol (Table 4) The diastereomeric ratio of the product was (>99 : 1) for both these hydrogenations, showing epimerization did not occur. Steric crowding around the exocyclic amide bond likely drives the preference for hydrogenation of the oxazolidinone

Table 4 Base-free hydrogenation of *N*-acyloxazolidinones



Entry	Sub	R^1	R^2	R^3	% conv[a]	TON[a]
1[b]	**9a**	Ph	Me	CMe(H)Bn	100	10
2[b]	**9b**	H	iPr	CMe(H)Bn	100	10

[a] Determined using ^1H NMR spectroscopy. [b] 2 (10 mol%) reacted with $NaBH_4$ (20 mol%) for 10 min under ~2 atm H_2 at 60 °C. Reaction conditions: 50 atm H_2 (rp) at 50 °C for 24 h. [**9a** or **9b**] = 25 mM in THF. dr of **9a** or **9b** = 99 : 1.

carbonyl. In contrast, the hydrogenation of **9a** with **2** in the presence of base (10 mol% **2**, 20 mol% KO*t*-Bu) also occurred with near exclusive endocyclic C–N cleavage, but the products consisted of a mixture of diasteromeric hydroxyl amides resulting from base-catalyzed epimerization of the (2-benzyl)propanamide group. These results demonstrate that the base-free hydrogenation will preserve the stereochemistry at enolizable carbon centers. Ikariya and coworkers reported that hydrogenation of **9a** using 3 mol% Cp*RuCl($Ph_2P(CH_2)_2NH_2$) and KO*t*-Bu (Ru : base = 1 : 1) under 30 atm H_2 at 80 °C for 20 h in 2-PrOH proceeding exclusively with exocyclic C–N cleavage resulting from hydrogenation of the acyl carbonyl.[7e] We believe the active catalyst generated from **2** and BH_4^- is more susceptible to steric crowding than the catalyst Cp*RuH($Ph_2P(CH_2)_2NH_2$) described by Ikariya and coworkers.

Control experiments were performed to investigate the identity of the active catalyst. The use of Ru black as catalyst resulted only in the hydrogenation of the arene ring in **5**. It is therefore unlikely that Ru nanoparticles are the active catalyst in these amide hydrogenations. In control NMR experiments, we found that **2** reacts with 2 equiv. of $NaBH_4$ after 30 min at 60 °C under ~2 atm H_2 to form in 95% yield *trans*-Ru(H)(BH_4)($Ph_2P(CH_2)_2NH_2$)$_2$. Propylene and remaining $NaBH_4$ were also present. The *trans*-H–Ru–BH_4 complex was identified using ^{1}H, ^{1}H{^{31}P}, ^{31}P{^{1}H}, ^{11}B, ^{1}H–^{15}N HSQC, gTOCSY, and gCOSY NMR experiments. Based upon this observation, we propose that the catalyst generated under base-free conditions is *trans*-Ru(H)$_2$($Ph_2P(CH_2)_2NH_2$)$_2$, made from *trans*-Ru(H)(BH_4)($Ph_2P(CH_2)_2NH_2$)$_2$.[9b]

Conclusions

The new base-free catalyst system and the base-promoted catalyst system hydrogenate a synthetically useful variety of functionalized and heterocyclic amides. The absolute configurations are preserved at stereogenic carbon centers in groups attached to nitrogen, and in groups alpha to the carbonyl group under base-free conditions. Certain olefins tolerate the hydrogenation, and the system is a catalytic, clean method to deprotect amines from acetyl amides.

Experimental section

General procedures used to synthesize ruthenium precursors

[Ru(η^3-C_3H_5)($Ph_2P(CH_2)_2NH_2$)$_2$]BF_4 (**2**) was prepared according to our original procedure.[8a] ^{31}P{^{1}H} NMR – (201.643 MHz, CD_2Cl_2, 27 °C): δ 48.5 (*minor*, s), 51.9 (*major*, d, $^2J_{P-P}$ = 29.6 Hz), 69.9 (*major*, d, $^2J_{P-P}$ = 30.2 Hz).

$RuCl_2(Ph_2P(CH_2)_2NH_2)_2$ (**3**) was prepared according to a procedure reported by Morris and coworkers.[15]

^{31}P{^{1}H} NMR – (161.839 MHz, CD_2Cl_2, 27 °C): δ 55.4 (*trans*, d, $^2J_{P-P}$ = 32.0 Hz), 61.8 (*cis*, s), 66.8 (*trans*, d, $^2J_{P-P}$ = 32.0 Hz).

[Ru((1-3;5-6-η)-C_8H_{11})(η^6-anthracene)]BF_4 (**5**) was prepared[16] *via* a modification of a procedure reported by Komiya and coworkers.[12]

Catalyst preparation

General procedure for base-assisted hydrogenations using 2 and KO*t*-Bu. **2** (6.80–13.8 mg, 10.0–20.0 μmol) and KO*t*-Bu (9.00–44.8 mg, 80.0–400 μmol, 4.00–5.00 mol%) were weighed out into two respective NMR tubes in a glove box. Freshly distilled THF (1.0 mL) was then added by cannula under Ar pressure into the tube containing **2**. This yellow solution was then cannulated into the NMR tube containing KO*t*-Bu under ~2 atm H_2 pressure. It was then heated at 60 °C for 20 min with occasional mixing. This mixture turned orange/red during this time and was then used for the base-assisted amide hydrogenations described in the next section (method A or B).

General procedure for base-free hydrogenations using 2 or 3 and $NaBH_4$. **2** or **3** (13.8 mg **2** or 12.6 mg **3**, 20.0 μmol respectively) and $NaBH_4$ (1.50 mg, 2.00 equiv. based on **2**, 40.0 μmol, or 3.80 mg, 5.00 equiv. based on **3**, 100 μmol) were weighed out into two respective NMR tubes in a glove box. THF (1.0 mL) was then added by cannula under Ar pressure into the NMR tube containing the Ru-precursor at room temperature. This solution (or mixture) was then transferred by cannula using ~2 atm H_2 pressure into the NMR tube containing $NaBH_4$ at room temperature. The mixture was then heated at 60 °C for 20 min under ~2 atm H_2 with periodic mixing. The mixture turned orange/brown during this time and was then used for the base-free amide hydrogenations described in the next section (method A or B).

General procedure for base-free hydrogenations using *in situ* prepared catalysts derived from 5 or 6, 2 equiv. $Ph_2P(CH_2)_2NH_2$ and 5 equiv. $NaBH_4$. **5** or **6** (8.4 mg, 20 μmol **5** or 9.7 mg, 20 μmol **6**) and $NaBH_4$ (3.8 mg, 0.10 mmol, 5.0 equiv. based on Ru) were weighed out into two respective NMR tubes in a glove box. THF (1.0 mL) was then added by cannula under Ar pressure to the NMR tube containing the Ru-precursor at room temperature. $Ph_2P(CH_2)_2NH_2$ (7.8 μL, 40 μmol, 2.0 equiv. based on Ru) was then added to the THF solution of Ru-precursors. The contents of the NMR tube were then heated at 60 °C for 0.5 h under Ar with periodic mixing. This solution was then transferred by cannula under ~2 atm H_2 pressure at room temperature into the NMR tube containing the 5.0 equiv. $NaBH_4$. The mixture was then heated at 60 °C for 20 min with periodic shaking. The mixture turned orange/brown during this time and was then used for the base-free amide hydrogenation described in the next section (method A).

General procedures for hydrogenation

Method A: solid amides. The amide (2.0–20 mmol, 100–1000 equiv.) was added to a stainless steel autoclave equipped with a magnetic stir bar. The autoclave was then purged with H_2 for 10 min at room temperature. 4.0–5.0 mL of THF was then added to the autoclave using a gas tight syringe. The catalyst–$NaBH_4$ or catalyst–base mixture, prepared above, was then added by cannula under H_2 pressure followed by a 2.0–4.0 mL THF wash. The autoclave was then pressurized to 50 atm H_2. The reaction mixture was stirred at

50–100 °C for 23 h. The autoclave was then allowed to cool over the course of 1 h before venting at room temperature. The percent conversions were determined by ^{1}H NMR spectroscopy.

Method B: liquid amide or *N*-acyloxazolidinones (9a and 9b). The atmosphere of a stainless steel autoclave was purged with H_2 for 10 min at room temperature. A solution of the amide or *N*-acyloxazolidinone (0.2–20 mmol, 10–1000 equiv.) in THF (1.0 mL), prepared under Ar, was then added by a cannula under H_2 pressure followed by a 4.0 mL THF wash. The catalyst–$NaBH_4$ mixture, prepared above, was then added by cannula under H_2 pressure followed by a 2.0 mL THF wash. The autoclave was then pressurized to 50 atm H_2. The reaction mixture was stirred at 50–100 °C for 23–47 h. The autoclave was then allowed to cool over the course of 1 h before venting at room temperature. The percent conversions were determined by ^{1}H NMR spectroscopy.

Spectroscopic identification of products

All hydrogenation products except **9a** and **9b** are known.

9a: ^{1}H NMR (599. 926 MHz, $CDCl_3$, 27 °C): δ 0.71 (3H, d, J = 7.0 Hz, CH_3), 0.78 (3H, d, J = 6.5 Hz, CH_3), 1.21 (3H, d, J = 6.0 Hz, CH_3), 1.73 (1H, m, CH), 2.53 (1H, m, CH), 2.70 (1H, m, CH), 2.95 (1H, m, CH), 3.23 (1H, bs, OH), 3.60 (3H, m, 3 CH), 5.72 (1H, bs, NH), 7.17–7.26 (5H, m, 5 aromatic CH). ^{13}C{^{1}H} NMR (175.969 MHz, $CDCl_3$, 27 °C): δ 17.9 (*C*H), 18.5 (*C*H), 19.2 (*C*H), 28.6 (*C*H), 40.4 (*C*H), 43.9 (*C*HNH), 56.9 (aromatic), 63.6 (CHOH), 126.2 (aromatic), 128.3 (aromatic), 128.8 (aromatic), 139.7 (aromatic), 176.5 (*C*═O). ^{1}H–^{15}N HSQC (498.117 MHz, $CDCl_3$, 27 °C): δ 123. HRMS (ESI$^+$) m/z calculated for $C_{15}H_{24}NO_2$ $(M + H)^+$: 250.18. Found: 250.1802. Difference (ppm): 0.75. **9a** is not stable for prolonged periods in solution.

9b: ^{1}H NMR (599. 926 MHz, $CDCl_3$, 27 °C): δ 0.79 (3H, d, J = 7.2 Hz, CH_3), 1.21 (3H, d, J = 6.6 Hz, CH_3), 2.43 (1H, sex, J = 6.6 Hz, CH), 2.70 (1H, dd, J = 6.6 Hz, CH), 2.93 (1H, dd, J = 8.4 Hz, CH), 3.91 (1H, bs, OH), 4.19 (1H, m, CH), 4.75 (1H, bs, NH), 5.38 (1H, d, J = 7.8 Hz, CH), 7.15–7.33 (10H, m, 10 aromatic CH). ^{13}C{^{1}H} NMR (150.868 MHz, $CDCl_3$, 27 °C): δ 14.5 (*C*H), 17.7 (*C*H), 40.5 (*C*H), 43.8 (*C*H), 50.9 (*C*HNH), 76.7 (*C*HOH), 126.3 (aromatic), 126.4 (aromatic), 127.4 (aromatic), 128.0 (aromatic), 128.4 (aromatic), 128.9 (aromatic), 139.7 (aromatic), 140.7 (aromatic), 176.4 (*C*═O). ^{1}H–^{15}N HSQC (599.925 MHz, $CDCl_3$, 27 °C): δ 127. HRMS (ESI$^+$) m/z calculated for $C_{19}H_{23}NO_2$ $(M + Na)^+$: 320.1621. Found: 320.1621. Difference (ppm): 0.01.

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