

# Potassium Phosphate-Catalyzed Chemoselective Reduction of $\alpha$ -Keto Amides: Route to Synthesize Passerini Adducts and 3-Phenylloxindoles

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**Abstract:** A chemoselective reduction of  $\alpha$ -keto amides to biologically important  $\alpha$ -hydroxy amides (mandelamides) by polymethylhydrosiloxane (PMHS) using 5 mol% potassium phosphate ( $K_3PO_4$ ) as catalyst has been developed. This transition metal-free protocol discloses excellent chemoselectivity for the ketone reduction of  $\alpha$ -keto amides in the presence of other reducible functionalities like ketone, nitro, halides, nitrile and amide. Also, the chemoselectively re-

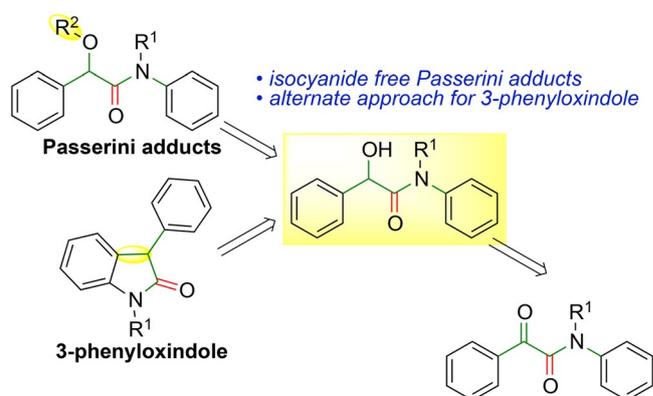
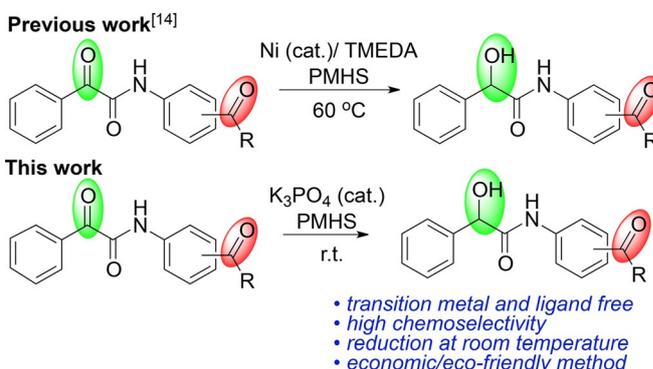
duced  $\alpha$ -hydroxy amide has been derivatized to isocyanide-free Passerini adducts. The *N*-alkyl- $\alpha$ -hydroxy amides have been successfully converted to 3-phenylloxindole derivatives by treatment with methanesulfonyl chloride and triethylamine.

**Keywords:** chemoselective reduction; metal and ligand free; Passerini adducts; 3-phenylloxindoles; phosphate catalyst

## Introduction

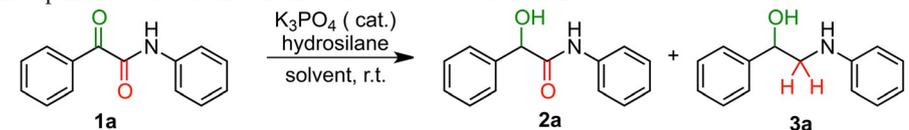
$\alpha$ -Hydroxy amides (mandelamides) are one of the most enchanting structural classes, as they exhibit medicinal and pesticidal properties.<sup>[1–3]</sup> In addition, they can act as ligands due to the existence of hydroxy and amide groups with variable coordinating abilities.<sup>[4]</sup> Altering the oxidation states of carbonyl functionalities is one of the most important transformations in organic chemistry.<sup>[5,6]</sup> Among them, reduction of carbonyl groups is always of crucial importance.<sup>[7]</sup> However, the chemoselective reduction of carbonyls over other sensitive groups at room temperature is invariably a challenging task as it is one of the key factors of modern synthetic methodologies. Until recently, the progress of most chemoselective reductions of carbonyls was based on transition metal catalysts.<sup>[8]</sup> Hence, a main goal in the carbonyl reduction is the development of new and easily available transition metal-free catalysts, which offer economic as well as ecological benefits.<sup>[9]</sup> In this context, metal-free reduction of simple carbonyls are reported with bases such as alkoxide,<sup>[10]</sup> hydroxide,<sup>[11]</sup> carbonate<sup>[12]</sup> and fluoride<sup>[13]</sup> as catalysts. However, base-catalyzed chemoselective reduction of carbonyls is not that well explored.

Recently, we developed the chemoselective reduction of  $\alpha$ -keto amides using Ni-TMEDA catalyst (Scheme 1).<sup>[14]</sup> Then, we have developed the metal-



**Scheme 1.** Chemoselective reduction of  $\alpha$ -keto amide by  $K_3PO_4$  catalyst; retrosynthetic approach towards Passerini adducts and 3-phenylloxindole via  $\alpha$ -hydroxy amide.

**Table 1.** Optimization for the chemoselective reduction of **1a**.<sup>[a]</sup>



Entry	Hydrosilane (equiv.)	Phosphate (mol%)	Solvent	Time	Yield <sup>[b]</sup> [%]	
					<b>2a</b>	<b>3a</b>
1	PMHS (2.0)	K <sub>3</sub> PO <sub>4</sub> (10 mol%)	DCM	8 h	63	18
2	PMHS (2.0)	K <sub>3</sub> PO <sub>4</sub> (10 mol%)	toluene	23 h	86	0
3	PMHS (2.0)	K <sub>3</sub> PO <sub>4</sub> (10 mol%)	THF	45 min	82	10
4	PMHS (2.0)	K <sub>3</sub> PO <sub>4</sub> (10 mol%)	MeOH	48 h	46	0
5	PMHS (2.0)	K <sub>3</sub> PO <sub>4</sub> (10 mol%)	1,4-dioxane	45 min	91	trace
<b>6</b>	<b>PMHS (2.0)</b>	<b>K<sub>3</sub>PO<sub>4</sub> (5 mol%)</b>	<b>1,4-dioxane</b>	<b>2 h</b>	<b>97</b>	<b>0</b>
7	(EtO) <sub>3</sub> SiH (2.0)	K <sub>3</sub> PO <sub>4</sub> (5 mol%)	1,4-dioxane	48 h	48	0
8	Cl(CH <sub>3</sub> ) <sub>2</sub> SiH (2.0)	K <sub>3</sub> PO <sub>4</sub> (5 mol%)	1,4-dioxane	48 h	29	0
9	Cl <sub>2</sub> (CH <sub>3</sub> )SiH (2.0)	K <sub>3</sub> PO <sub>4</sub> (5 mol%)	1,4-dioxane	48 h	35	0
10	Ph <sub>3</sub> SiH (2.0)	K <sub>3</sub> PO <sub>4</sub> (5 mol%)	1,4-dioxane	48 h	55	0
11	Ph <sub>2</sub> SiH <sub>2</sub> (2.0)	K <sub>3</sub> PO <sub>4</sub> (5 mol%)	1,4-dioxane	3 h	58	0
12	TMDSO (2.0)	K <sub>3</sub> PO <sub>4</sub> (5 mol%)	1,4-dioxane	27 h	92	0
13	PMHS (2.0)	K <sub>2</sub> HPO <sub>4</sub> (5 mol%)	1,4-dioxane	24 h	0	0
14	PMHS (2.0)	KH <sub>2</sub> PO <sub>4</sub> (5 mol%)	1,4-dioxane	24 h	0	0
15	PMHS (2.0)	Na <sub>2</sub> HPO <sub>4</sub> (5 mol%)	1,4-dioxane	24 h	0	0
16	PMHS (2.0)	NaH <sub>2</sub> PO <sub>4</sub> (5 mol%)	1,4-dioxane	24 h	0	0
17 <sup>[c]</sup>	PMHS (2.0)	none	1,4-dioxane	24 h	0	0
18	PMHS (2.0)	K <sub>3</sub> PO <sub>4</sub> (5 mol%)	2-MeTHF	3 h	63	11

<sup>[a]</sup> Reaction conditions: 0.5 mmol of **1a** in 1.5 mL of solvent.

<sup>[b]</sup> Isolated yield.

<sup>[c]</sup> In the absence of K<sub>3</sub>PO<sub>4</sub>.

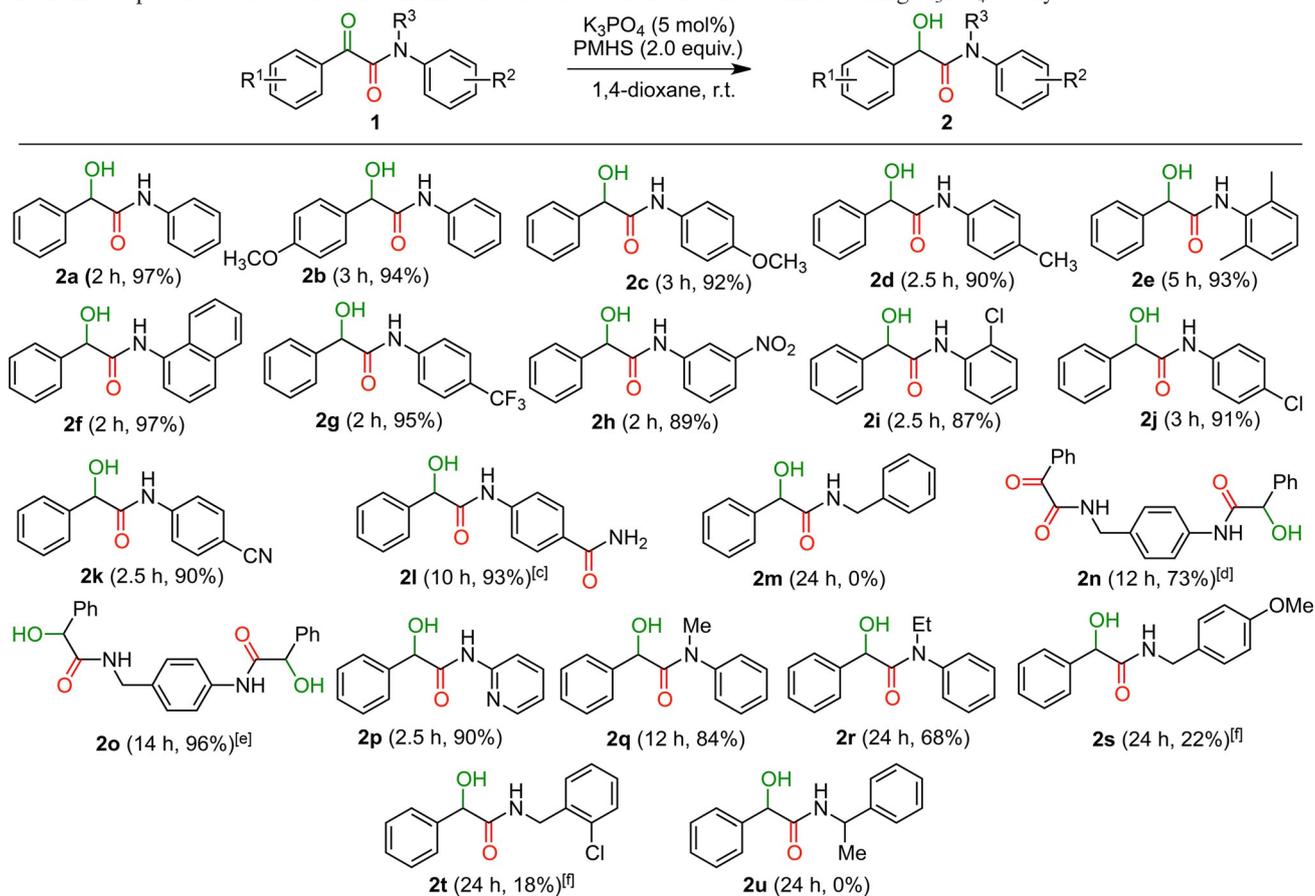
free chemoselective reduction of  $\alpha$ -keto amides using TBAF as catalyst.<sup>[15]</sup> Although efficient catalytic systems for the reduction of  $\alpha$ -keto amides have been developed, our focus is shifted towards the development of more efficient catalytic systems to overcome the shortcomings such as need of inert atmosphere, loss of chemoselectivity and use of expensive Ph<sub>3</sub>SiH which gives high molecular weight by-products, etc. As part of our research towards developing metal-free organic transformations,<sup>[16]</sup> herein we report a mild, efficient and economic chemoselective reduction of the keto group of  $\alpha$ -keto amides in the presence of reducible functional groups using K<sub>3</sub>PO<sub>4</sub> as catalyst (Scheme 1). To show the utility of mandelamide, a retrosynthetic approach towards highly important Passerini adducts and 3-phenyloxindoles from  $\alpha$ -keto amides is given. Albeit K<sub>3</sub>PO<sub>4</sub> is an inexpensive base, it is typically used in stoichiometric quanti-

ties for organic transformations.<sup>[17]</sup> Only a handful examples are known for its catalytic activity.<sup>[18]</sup>

## Results and Discussion

The initial optimization for the chemoselective reduction was carried out with 2-oxo-*N*-2-diphenylacetamide **1a** as model substrate, using 2 equivalents of low cost, non-toxic, air-stable and eco-friendly polymethylhydrosiloxane (PMHS)<sup>[19]</sup> as reducing agent and 10 mol% of K<sub>3</sub>PO<sub>4</sub> as catalyst at room temperature in dichloromethane. The reaction yielded 63% of the selective reduction product  $\alpha$ -hydroxy amide **2a** and 18% of complete reduction (both keto and amide groups) product *N*-phenylphenylethanolamine **3a** in 8 h (Table 1, entry 1). Use of a non-polar hydrocarbon solvent, for instance, toluene gave exclusively **2a** in

**Table 2.** Scope of substrates for the chemoselective reduction of  $\alpha$ -keto amides using  $K_3PO_4$  catalyst.<sup>[a,b]</sup>



<sup>[a]</sup> Reaction conditions: 0.5 mmol of **1** in 1.5 mL of 1,4-dioxane.

<sup>[b]</sup> Isolated yield.

<sup>[c]</sup> 10 mol% of  $K_3PO_4$  was used and reaction was carried out at 60 °C.

<sup>[d]</sup> 21% of **2o** was isolated along with **2n**.

<sup>[e]</sup> 10 mol% of  $K_3PO_4$  and 5.0 equiv. of PMHS were used.

<sup>[f]</sup> 20 mol% of  $K_3PO_4$  and 4 equiv. of PMHS were used at 60 °C.

23 h with 86% isolated yield (entry 2). When the solvent was altered to THF, a drastic upturn in the reactivity was observed but the selectivity got diminished as it yielded 82% of **2a** along with 10% of **3a** in 45 min (entry 3). The polar protic solvent methanol provided only 46% of **2a** even after two days (entry 4). When 1,4-dioxane was used, the reaction was completed in 45 min with 91% of **2a** and a trace amount of **3a** (entry 5). From this study of solvent effects, it is understood that polar aprotic solvents are appropriate for this transformation.

Next, the amount of catalyst loading was reduced to 5 mol% and the reaction was performed in 1,4-dioxane. It yielded exclusively the selective reduction product **2a** with 97% yield in 2 h (entry 6). However, the derivative of THF such as 2-methyl-THF a “greener” solvent furnished 63% of **2a** and 11% of **3a** (entry 18). In order to understand the chemoselectivity, various hydrosilanes were examined and the results

are summarized in Table 1. The silanes  $(EtO)_3SiH$ ,  $ClSi(CH_3)_2H$ ,  $Cl_2(CH_3)SiH$  and  $Ph_3SiH$  did not afford complete conversion of starting material **1a** to  $\alpha$ -hydroxy amide **2a** even after 48 h (entries 7–10). When  $Ph_2SiH_2$  was used, 58% of **2a** was isolated along with unidentified side products (entry 11). In the case of tetramethyldisiloxane (TMDSO), 92% of **2a** was isolated (entry 12). It is important to mention that screening of other phosphate bases such as  $K_2HPO_4$ ,  $KH_2PO_4$ ,  $Na_2HPO_4$  and  $NaH_2PO_4$  did not afford **2a** (entries 13–16). As anticipated, there was no reaction in the absence of  $K_3PO_4$  (entry 17).

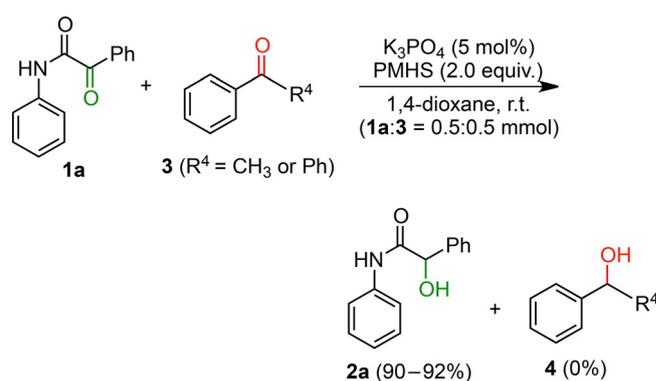
With the optimized conditions in hand (Table 1, entry 6), the scope of the chemoselective reduction protocol was investigated with several  $\alpha$ -keto amides and the results are summarized in Table 2. Both electron-releasing and electron-withdrawing groups attached to either side of the  $\alpha$ -keto amide furnished the corresponding  $\alpha$ -hydroxy amides in good to excel-

lent yield. It is vital to mention that other sensitive functional groups prone to reduction such as nitro (**2h**), chloro (**2i** and **2j**) and nitrile (**2k**) were unaffected under the reaction conditions. The 1-naphthylamine-derived  $\alpha$ -keto amide yielded 97% of the respective  $\alpha$ -hydroxy amide (**2f**).

The methodology worked well for the reduction of  $\alpha$ -keto amide bearing an amide group *para* to the anilide ring to the  $\alpha$ -hydroxy amide (**2l**) in 93% yield without affecting both amide groups using 10 mol% of  $K_3PO_4$  at 60 °C. This is due to the insoluble nature of the  $\alpha$ -keto amide at room temperature. Importantly,  $\alpha$ -keto benzylamide failed to render the mandelamide (**2m**). Hence, to distinguish the chemoselective ketone reduction of  $\alpha$ -keto anilide over  $\alpha$ -keto benzylamide, the 4-(aminomethyl)aniline derived di- $\alpha$ -keto amide was examined under the defined conditions. Interestingly, both mono keto reduced  $\alpha$ -hydroxy amide (**2n**) and the diketo reduced di- $\alpha$ -hydroxy amide (**2o**) were isolated in 73% and 21% yield, respectively. In addition, a set of conditions was achieved to attain only di- $\alpha$ -hydroxyamide (**2o**) in 96% yield by increasing the catalyst amount to 10 mol% and PMHS to 5 equivalents. A 2-pyridyl group bearing  $\alpha$ -keto amide rendered the corresponding product (**2p**) in excellent yield. *N*-Substituted  $\alpha$ -keto amides furnished the mandelamide analogues (**2q** and **2r**) in moderate to good yield. In addition, a few substituted  $\alpha$ -keto benzylamides were examined under the optimized conditions. None of them gave the corresponding products. But trace amounts of products (**2s** and **2t**) were identified when the amount of  $K_3PO_4$  was increased to 20 mol% and PMHS to 4 equivalents. Reactions at 60 °C with 20 mol% of  $K_3PO_4$  and 4 equivalents of PMHS resulted in 22% of **2s** and 18% of **2t**. Further increases in temperature did not improve the reaction yield. The  $\alpha$ -keto amides derived from benzylamine and 1-phenylethanamine did not afford the reduced products (**2m** and **2u**) even if  $K_3PO_4$ , PMHS and temperature were increased. Also, the aliphatic amines derived  $\alpha$ -keto amides did not yield the corresponding mandelamides.

To show the utility of this protocol, an intermolecular competitive reduction experiment between  $\alpha$ -ketoamide (**1a**) and simple ketones (**3**) like acetophenone or benzophenone was carried out under the defined conditions. The chemoselectivity of these reduction reactions was perfect and  $\alpha$ -hydroxy amide (**2a**) was obtained as the exclusive product along with **3** as intact starting materials (Scheme 2). This displays that the reaction is mild and precise for the chemoselective reduction of  $\alpha$ -keto amides.

The usefulness of the competitive experiment was further studied with the  $\alpha$ -keto amides (**5a–5c**) bearing isolated ketones under the defined conditions. The keto functionality of  $\alpha$ -keto amides got reduced to the corresponding  $\alpha$ -hydroxy amides (**6a–6c**) exclu-

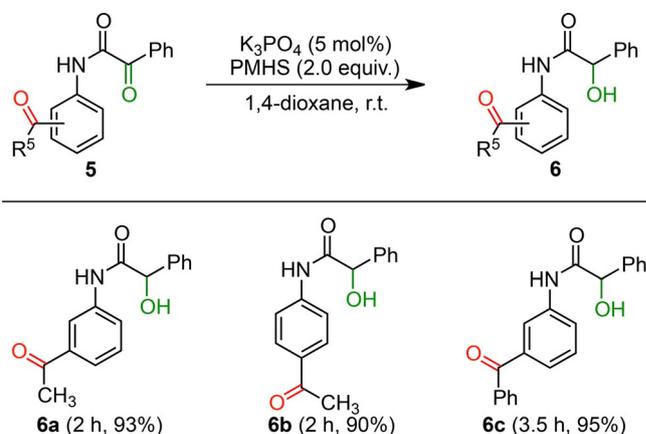


**Scheme 2.** Intermolecular competitive reduction experiments between **1a** and simple ketones.

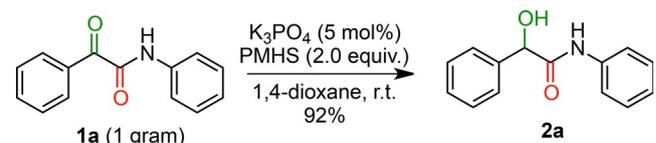
sively without affecting the isolated ketones (Scheme 3).

To examine the scalability of the metal free transformation, the chemoselective reduction of 2-oxo-*N*-2-diphenylacetamide **1a** was performed by employing 1 gram (4.4 mmol) of **1a** under the standard reaction conditions. This transformation proceeded well to afford  $\alpha$ -hydroxy amide **2a** in 92% yield (Scheme 4).

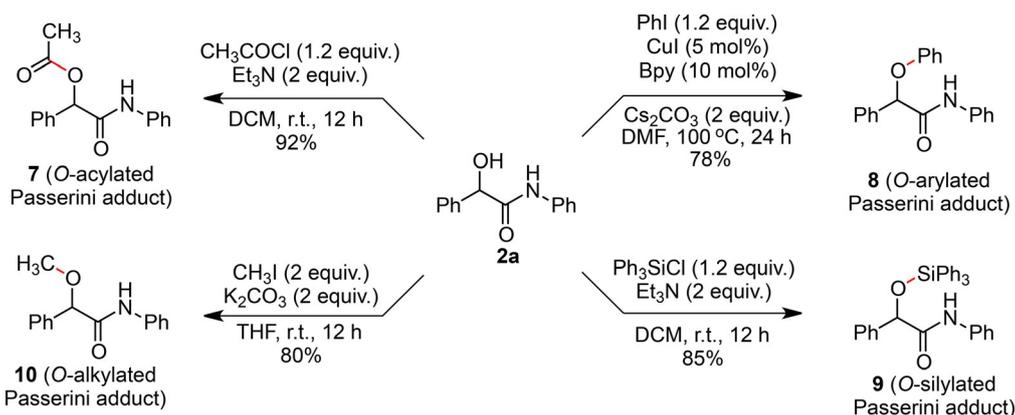
The  $\alpha$ -hydroxy amide **2a** was successfully converted to synthetically and biologically important *O*-acylated (**7**), arylated (**8**), silylated (**9**) and alkylated (**10**) Passerini adducts,<sup>[20a]</sup> respectively. Although it involves two more steps, noxious, bad smelling and expensive isocyanides<sup>[20b]</sup> can be avoided through this pathway



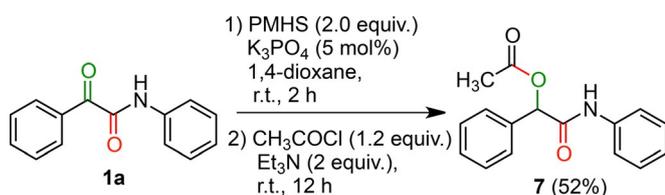
**Scheme 3.** Chemoselective reduction of  $\alpha$ -keto amide versus simple ketone. Reaction conditions: 0.5 mmol of **5** in 1.5 mL of 1,4-dioxane; isolated yields given.



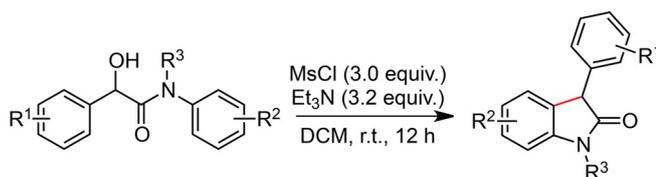
**Scheme 4.** Gram-scale synthesis of **2a**.



**Scheme 5.** Derivatization of **2a** to isocyanide-free Passerini adducts



**Scheme 6.** Isocyanide-free one-pot synthesis of *O*-acylated Passerini adduct **7**



**2q**: R<sup>1</sup>, R<sup>2</sup> = H; R<sup>3</sup> = Me

**2r**: R<sup>1</sup>, R<sup>2</sup> = H; R<sup>3</sup> = Et

**11q**: R<sup>1</sup>, R<sup>2</sup> = H; R<sup>3</sup> = Me, 76%

**11r**: R<sup>1</sup>, R<sup>2</sup> = H; R<sup>3</sup> = Et, 71%

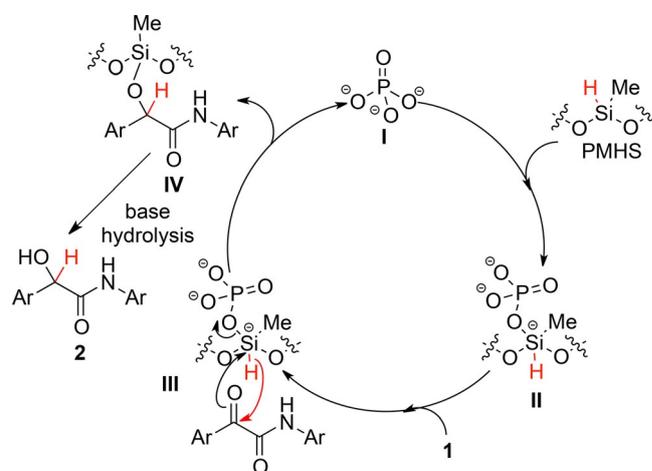
**Scheme 7.** Synthesis of *N*-alkyl-3-phenyloxindoles from mandelamides

in short reaction times and good to excellent yields (Scheme 5).

We also succeeded to synthesize the *O*-acylated Passerini adduct (**7**) by a one-pot synthesis involving reduction of **1a** followed by acylation using acetyl chloride in 52% isolated yield (Scheme 6).

The *N*-alkyl- $\alpha$ -hydroxy amides (**2q** and **2r**) were further converted in good yield to highly important *N*-alkyl-3-phenyloxindoles<sup>[21]</sup> (**11q** and **11r**) by treatment with methanesulfonyl chloride and triethylamine (Scheme 7). Although several ways are possible to synthesize 3-phenyloxindoles,<sup>[22]</sup> this method represents one of the most easily accomplished ways to access them.

Based on the base-catalyzed, hydrosilane-mediated reductions,<sup>[10–13]</sup> a plausible mechanism for this phos-



**Scheme 8.** Plausible mechanism for phosphate-catalyzed chemoselective reduction of  $\alpha$ -keto amides.

phate-promoted chemoselective reduction of  $\alpha$ -keto amides using PMHS has been proposed (Scheme 8). Initially, phosphate anion **I** may interact with PMHS to give hypervalent silyl-phosphate ester **II**.<sup>[23]</sup> This further reacts with  $\alpha$ -keto amide **1** via the transfer of hydride to activated ketone to form *O*-silyl ether **IV** by discharging the phosphate ion **I**. Hydrolysis of **IV** provides  $\alpha$ -hydroxy amide **2**. However, detailed mechanistic studies and further applications of this chemoselective reduction are in progress.

## Conclusions

In summary, we have established a mild, efficient, transition metal- and ligand-free chemoselective reduction of  $\alpha$ -keto amides to  $\alpha$ -hydroxy amides by inexpensive, air stable and eco-friendly PMHS using K<sub>3</sub>PO<sub>4</sub> as catalyst at room temperature. The metal-free protocol has several advantages including cost-effectiveness, short reaction time, high yield and room

temperature reaction. More importantly, the other reducible functionalities such as ketone, nitro, halides, nitrile and amide are well tolerated. To show the importance of this methodology, several Passerini adducts have been synthesized from  $\alpha$ -hydroxy amides by avoiding harmful isocyanides. Also, *N*-alkyl- $\alpha$ -hydroxy amides have been easily converted to 3-phenyl-indole derivatives in a single step process.

## Experimental Section

### General Considerations

Hydrosilanes and  $K_3PO_4$  were purchased from Sigma-Aldrich and Alfa Aesar chemical companies, respectively. Thin-layer chromatography (TLC) was performed using Merck silica gel 60 F254 pre-coated plates (0.25 mm) and visualized by UV fluorescence quenching. Silica gel for column chromatography (100–200 mesh) was purchased from SRL India.  $^1H$  and  $^{13}C$  NMR spectra were recorded on a Bruker 400 or 500 MHz instrument.  $^1H$  NMR spectra are reported relative to residual  $CHCl_3$  ( $\delta=7.26$  ppm) or  $DMSO-d_6$  ( $\delta=2.50$  ppm).  $^{13}C$  NMR are reported relative to  $CDCl_3$  ( $\delta=77.16$  ppm) or  $DMSO-d_6$  ( $\delta=39.52$  ppm). FT-IR spectra were recorded on a JASCO spectrometer and are reported in frequency of absorption ( $cm^{-1}$ ). High resolution mass spectra (HR-MS) were recorded on Q-ToF Micro mass spectrometer.

### General Experimental Procedure for Synthesis of $\alpha$ -Keto Amides

Thionyl chloride (4 mmol) was added dropwise to a stirred mixture of benzoylformic acid (2 mmol) and  $Et_3N$  (4 mmol) in  $CH_2Cl_2$  (10 mL) at  $0^\circ C$  under a nitrogen atmosphere. The stirring was continued for 20 min and then a suspension of the corresponding amine (2 mmol) in  $CH_2Cl_2$  (10 mL) was added slowly to the reaction mixture at  $0^\circ C$  under a nitrogen atmosphere. The stirring was continued at room temperature and the completion of the reaction was monitored by TLC. The organic layer was washed with water for two times, then a saturated aqueous solution of  $NaHCO_3$  (20 mL) was slowly added to the reaction mixture. The organic layer was separated, washed with water ( $3 \times 15$  mL) and evaporated under reduced pressure. The solid residue was purified by silica gel column chromatography.

### General Experimental Procedure for Chemoselective Reduction of $\alpha$ -Keto Amides using $K_3PO_4$ Catalyst

A mixture of  $K_3PO_4$  (0.05 mmol) and  $\alpha$ -keto amide (0.5 mmol) in 1.5 mL of distilled 1,4-dioxane was taken in an oven-dried reaction tube. The reaction mixture was stirred at room temperature for 10 min. Then PMHS (1.0 mmol) was added to the reaction mixture. After that, the reaction tube was closed with a glass stopper and the resulting reaction mixture was stirred vigorously at room temperature. The progress of the reaction was monitored by TLC. After complete disappearance of substrate, 10 mL of 2N aqueous NaOH solution was added to the reaction and the resulting mixture was stirred for 10 min. The reaction

mixture was extracted with ethyl acetate ( $2 \times 10$  mL). The combined organic layers were washed with brine, dried over anhydrous  $MgSO_4$ , filtered off and the solvent was removed under reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent: hexanes-ethyl acetate, 80:20) to obtain the pure  $\alpha$ -hydroxyamide.

**2-Hydroxy-*N*,2-diphenylacetamide (2a):**<sup>[24]</sup> Colourless solid; mp  $151$ – $152^\circ C$  (Lit.<sup>[24]</sup> mp  $150$ – $151^\circ C$ );  $R_f=0.54$  (hexanes:ethyl acetate, 80:20 v/v);  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta=8.18$  (bs, 1H), 7.43–7.56 (m, 4H), 7.28–7.42 (m, 5H), 7.12 (t,  $J=7.0$  Hz, 1H), 5.17 (s, 1H);  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta=170.1$ , 139.1, 137.2, 129.2, 129.1, 129.0, 127.0, 124.9, 120.0, 74.9; IR (KBr):  $\nu=3302$ , 1685, 1653, 1648,  $1077\text{ cm}^{-1}$ ; HR-MS:  $m/z=250.0852$  [ $M+Na$ ]<sup>+</sup>, calcd. for  $C_{14}H_{13}NO_2Na$ ; 250.0844.

**2-Hydroxy-2-(4-methoxyphenyl)-*N*-phenylacetamide (2b):**<sup>[14]</sup> Colourless solid; mp  $95$ – $96^\circ C$  (Lit.<sup>[14]</sup> mp  $94$ – $95^\circ C$ );  $R_f=0.32$  (hexanes:ethyl acetate, 80:20 v/v);  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta=8.24$  (bs, 1H), 7.51 (d,  $J=7.5$  Hz, 2H), 7.36 (d,  $J=8.5$  Hz, 2H), 7.30 (t,  $J=7.5$  Hz, 2H), 7.11 (t,  $J=7.5$  Hz, 1H), 6.89 (d,  $J=8.5$  Hz, 2H), 5.09 (s, 1H), 3.79 (s, 3H);  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta=170.5$ , 160.1, 137.2, 131.3, 129.2, 128.4, 124.8, 119.9, 114.5, 74.4, 55.4; IR (KBr):  $\nu=3366$ , 1670, 1598, 1534, 1444,  $1077\text{ cm}^{-1}$ ; HR-MS:  $m/z=280.0939$  [ $M+Na$ ]<sup>+</sup>, calcd. for  $C_{15}H_{15}NO_3Na$ ; 280.0950.

**2-Hydroxy-*N*-(4-methoxyphenyl)-2-phenylacetamide (2c):**<sup>[25]</sup> Colourless solid; mp  $153$ – $154^\circ C$  (Lit.<sup>[25]</sup> mp  $153$ – $154^\circ C$ );  $R_f=0.34$  (hexanes:ethyl acetate, 80:20 v/v);  $^1H$  NMR (400 MHz,  $DMSO-d_6$ ):  $\delta=9.78$  (s, 1H), 7.59 (dd,  $J=7.2$ , 2.0 Hz, 2H), 7.50 (d,  $J=7.2$  Hz, 2H) 7.25–7.39 (m, 3H), 6.86 (d,  $J=6.8$  Hz, 2H), 6.38 (d,  $J=4.8$  Hz, 1H), 5.07 (d,  $J=4.4$  Hz, 1H), 3.70 (s, 3H);  $^{13}C$  NMR (100 MHz,  $DMSO-d_6$ ):  $\delta=170.7$ , 155.4, 141.0, 131.7, 128.1, 127.6, 126.6, 121.2, 113.7, 73.9, 55.1; IR (KBr):  $\nu=3651$ , 1647, 1559, 1540, 1534,  $1090\text{ cm}^{-1}$ ; HR-MS:  $m/z=280.0945$  [ $M+Na$ ]<sup>+</sup>, calcd. for  $C_{15}H_{15}NO_3Na$ ; 280.0950.

**2-Hydroxy-2-phenyl-*N*-*p*-tolylacetamide (2d):**<sup>[26]</sup> Colourless solid; mp  $167$ – $168^\circ C$  (Lit.<sup>[26]</sup> mp  $169$ – $170^\circ C$ );  $R_f=0.44$  (hexanes:ethyl acetate, 70:30 v/v);  $^1H$  NMR (400 MHz,  $DMSO-d_6$ ):  $\delta=9.80$  (bs, 1H), 7.57 (d,  $J=8.4$  Hz, 2H), 7.50 (d,  $J=7.2$  Hz, 2H), 7.25–7.39 (m, 3H), 7.08 (d,  $J=8.4$  Hz, 2H), 6.39 (d,  $J=4.4$  Hz, 1H), 5.08 (d,  $J=4.8$  Hz, 1H), 2.23 (s, 3H);  $^{13}C$  NMR (100 MHz,  $DMSO-d_6$ ):  $\delta=170.9$ , 140.9, 136.0, 132.4, 129.0, 128.1, 127.6, 126.6, 119.7, 74.0, 20.4; IR (KBr):  $\nu=3412$ , 1522, 1437,  $1364\text{ cm}^{-1}$ ; HR-MS:  $m/z=264.0989$  [ $M+Na$ ]<sup>+</sup>, calcd. for  $C_{15}H_{15}N_1O_2Na$ ; 264.1000.

***N*-(2,6-Dimethylphenyl)-2-hydroxy-2-phenylacetamide (2e):** Colourless solid; mp  $140$ – $141^\circ C$ ;  $R_f=0.48$  (hexanes:ethyl acetate, 70:30 v/v);  $^1H$  NMR (400 MHz,  $DMSO-d_6$ ):  $\delta=9.36$  (s, 1H), 7.60 (m, 2H), 7.26–7.41 (m, 3H), 6.99–7.06 (m, 3H), 6.33 (d,  $J=4.8$  Hz, 1H), 5.12 (d,  $J=4.8$  Hz, 1H), 2.02 (s, 6H);  $^{13}C$  NMR (100 MHz,  $DMSO-d_6$ ):  $\delta=170.9$ , 141.3, 135.4, 134.7, 127.9, 127.5, 127.4, 126.6, 126.4, 74.0, 17.9; IR (KBr):  $\nu=3447$ , 1684, 1653, 1559, 1507,  $1364\text{ cm}^{-1}$ .

**2-Hydroxy-*N*-(naphthalen-1-yl)-2-phenylacetamide (2f):** Colourless solid; mp  $113$ – $114^\circ C$ ;  $R_f=0.55$  (hexanes:ethyl acetate, 90:10 v/v);  $^1H$  NMR (400 MHz,  $DMSO-d_6$ ):  $\delta=10.06$  (bs, 1H), 7.83–7.99 (m, 2H), 7.78 (d,  $J=8.4$  Hz, 1H), 7.62 (t,  $J=8.4$  Hz, 3H), 7.45–7.57 (m, 3H), 7.29–7.45 (m, 3H), 6.57 (d,  $J=3.6$  Hz, 1H), 5.28 (d,  $J=4.0$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $DMSO-d_6$ ):  $\delta=171.1$ , 143.0, 133.7,

133.0, 128.2, 128.1, 127.9, 127.7, 126.7, 126.1, 126.0, 125.6, 122.2, 121.7, 74.0; IR (KBr):  $\nu$  = 3409, 3005, 1659, 1541, 1499, 1436, 1092  $\text{cm}^{-1}$ ; HR-MS:  $m/z$  = 300.0990  $[\text{M} + \text{Na}]^+$ , calcd. for  $\text{C}_{18}\text{H}_{15}\text{N}_1\text{O}_2\text{Na}_1$ : 300.1000.

**2-Hydroxy-2-phenyl-*N*-[4-(trifluoromethyl)phenyl]acetamide (2g):** Colourless solid; mp 175–176 °C;  $R_f$  = 0.40 (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  = 10.31 (bs, 1H), 7.94 (d,  $J$  = 8.4 Hz, 2H), 7.65 (d,  $J$  = 8.4 Hz, 2H), 7.52 (d,  $J$  = 7.2 Hz, 2H), 7.26–7.41 (m, 3H), 6.53 (d,  $J$  = 4.4 Hz, 1H), 5.14 (d,  $J$  = 4.0 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  = 171.8, 142.1, 140.5, 134.4, 128.1, 127.9, 127.7, 126.6, 125.9 (q,  $J$  = 4.0 Hz,  $\text{CF}_3$ ), 119.7, 74.1; IR (KBr):  $\nu$  = 3293, 1657, 1601, 1557, 1543, 1116  $\text{cm}^{-1}$ ; HR-MS:  $m/z$  = 318.0705  $[\text{M} + \text{Na}]^+$ , calcd. for  $\text{C}_{15}\text{H}_{12}\text{N}_1\text{O}_2\text{F}_3\text{Na}_1$ : 318.0718.

**2-Hydroxy-*N*-(3-nitrophenyl)-2-phenylacetamide (2h):** Colourless solid; mp 142–143 °C;  $R_f$  = 0.42 (hexanes:ethyl acetate, 70:30 v/v);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  = 10.49 (bs, 1H), 8.76 (s, 1H), 8.12 (d,  $J$  = 7.6 Hz, 1H), 7.91 (dd,  $J$  = 8.2, 1.4 Hz, 1H), 7.48–7.63 (m, 3H), 7.20–7.40 (m, 3H), 6.58 (d,  $J$  = 4.4 Hz, 1H), 5.16 (d,  $J$  = 4.0 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  = 172.1, 147.9, 140.5, 139.8, 130.0, 128.2, 127.8, 126.6, 125.9, 118.1, 113.9, 74.1; IR (KBr):  $\nu$  = 3292, 1653, 1647, 1595, 1507, 1062  $\text{cm}^{-1}$ ; HR-MS:  $m/z$  = 273.0887  $[\text{M} + \text{H}]^+$ , calcd. for  $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}_4$ : 273.0875.

***N*-(4-Chlorophenyl)-2-hydroxy-2-phenylacetamide (2i):** Colourless solid; mp 97–98 °C;  $R_f$  = 0.36 (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  = 9.64 (s, 1H), 8.09 (dd,  $J$  = 8.2, 1.4 Hz, 1H), 7.46–7.55 (m, 3H), 7.29–7.40 (m, 4H), 7.12–7.19 (m, 1H), 6.93 (d,  $J$  = 4.4 Hz, 1H), 5.18 (d,  $J$  = 4.4 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  = 170.8, 140.4, 134.1, 129.3, 128.2, 127.83, 127.8, 126.7, 125.5, 123.8, 122.2, 73.6; IR (KBr):  $\nu$  = 3235, 1666, 1614, 1604, 1556, 1072  $\text{cm}^{-1}$ .

***N*-(4-Chlorophenyl)-2-hydroxy-2-phenylacetamide (2j):**<sup>[27]</sup> Colourless solid; mp 159–160 °C (Lit.<sup>[27]</sup> mp 161–164 °C);  $R_f$  = 0.54 (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  = 10.08 (s, 1H), 7.75 (dd,  $J$  = 6.8, 2.0 Hz, 2H), 7.51 (d,  $J$  = 7.2 Hz, 2H), 7.39–7.26 (m, 5H), 6.48 (d,  $J$  = 4.8 Hz, 1H), 5.10 (d,  $J$  = 4.8 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  = 171.4, 140.7, 137.5, 128.5, 128.1, 127.7, 127.1, 126.6, 121.3, 74.0; IR (KBr):  $\nu$  = 3298, 1696, 1684, 1653, 1522, 1065  $\text{cm}^{-1}$ ; HR-MS:  $m/z$  = 284.0460  $[\text{M} + \text{Na}]^+$ , calcd. for  $\text{C}_{14}\text{H}_{12}\text{N}_1\text{O}_2\text{Cl}_1\text{Na}_1$ : 284.0454.

***N*-(4-Cyanophenyl)-2-hydroxy-2-phenylacetamide (2k):**<sup>[14]</sup> Colourless solid; mp 131–132 °C (Lit.<sup>[14]</sup> mp 130–131 °C);  $R_f$  = 0.38 (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  = 10.36 (s, 1H), 7.93 (d,  $J$  = 8.8 Hz, 2H), 7.75 (d,  $J$  = 8.8 Hz, 2H), 7.51 (d,  $J$  = 7.2 Hz, 2H), 7.26–7.41 (m, 3H), 6.55 (d,  $J$  = 4.4 Hz, 1H), 5.15 (d,  $J$  = 4.4 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  = 172.1, 142.8, 140.4, 133.1, 128.2, 127.8, 126.6, 119.8, 118.99, 105.3, 74.1; IR (KBr):  $\nu$  = 3670, 1946, 1675, 1653, 1603, 1559  $\text{cm}^{-1}$ .

**4-(2-Hydroxy-2-phenylacetamido)benzamide (2l):** Colourless solid; mp 161–162 °C;  $R_f$  = 0.32 (hexanes:ethyl acetate, 70:30 v/v);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  = 10.12 (s, 1H), 7.70–7.95 (m, 5H), 7.52 (d,  $J$  = 6.8 Hz, 2H), 7.16–7.44 (m, 4H), 6.48 (s, 1H), 5.13 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  = 171.5, 167.3, 141.1, 140.6, 129.1, 128.2, 128.1, 127.7, 126.6, 118.8, 70.0; IR (KBr):  $\nu$  = 3361, 1653, 1623, 1596, 1522  $\text{cm}^{-1}$ .

**2-Hydroxy-*N*-[4-(2-oxo-2-phenylacetamido)methyl]phenyl]-2-phenylacetamide (2n):** Colourless solid; mp 176–177 °C;  $R_f$  = 0.38 (hexanes:ethyl acetate, 70:30 v/v);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  = 9.91 (s, 1H), 9.38 (t,  $J$  = 6.0 Hz, 1H), 7.95–7.99 (m, 2H), 7.64–7.75 (m, 3H), 7.54–7.61 (m, 2H), 7.49–7.53 (m, 2H), 7.32–7.38 (m, 2H), 7.24–7.31 (m, 3H), 6.42 (d,  $J$  = 4.4 Hz, 1H), 5.10 (d,  $J$  = 4.4 Hz, 1H), 4.40 (d,  $J$  = 6.0 Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  = 190.3, 171.1, 164.9, 140.8, 137.5, 134.6, 133.6, 132.9, 129.7, 129.0, 128.1, 127.8, 127.6, 126.6, 119.8, 74.0, 41.5; IR (KBr):  $\nu$  = 3567, 3537, 3058, 1793, 1711, 1612, 1090, 1074  $\text{cm}^{-1}$ ; HR-MS:  $m/z$  = 411.1313  $[\text{M} + \text{Na}]^+$ , calcd. for  $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_4\text{Na}_1$ : 411.1321.

**2-Hydroxy-*N*-[4-(2-hydroxy-2-phenylacetamido)benzyl]-2-phenylacetamide (2o):** Colourless solid; mp 191–192 °C;  $R_f$  = 0.32 (hexanes:ethyl acetate, 60:40 v/v);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  = 9.86 (s, 1H), 8.46 (t,  $J$  = 6.2 Hz, 1H), 7.58 (dd,  $J$  = 7.0, 2.0 Hz, 2H), 7.53–7.47 (m, 2H), 7.39–7.44 (m, 2H), 7.23–7.38 (m, 6H), 7.11 (d,  $J$  = 8.8 Hz, 2H), 6.41 (d,  $J$  = 4.8 Hz, 1H), 6.17 (d,  $J$  = 4.8 Hz, 1H), 5.08 (d,  $J$  = 4.8 Hz, 1H), 4.95 (d,  $J$  = 4.8 Hz, 1H), 4.21 (dd,  $J$  = 6.0, 2.8 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  = 172.2, 171.0, 141.3, 140.9, 137.1, 134.7, 128.1, 127.9, 127.6, 127.4, 126.6, 126.5, 119.6, 74.0, 73.6, 41.3; IR (KBr):  $\nu$  = 3552, 3546, 1706, 1700, 1653, 1647, 1636, 1363, 1228  $\text{cm}^{-1}$ ; HR-MS:  $m/z$  = 411.1470  $[\text{M} + \text{Na}]^+$ , calcd. for  $\text{C}_{23}\text{H}_{22}\text{N}_2\text{O}_4\text{Na}_1$ : 413.1477.

**2-Hydroxy-2-phenyl-*N*-(pyridin-2-yl)acetamide (2p):** Colourless solid; mp 119–120 °C;  $R_f$  = 0.38 (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  = 9.95 (s, 1H), 8.30–8.35 (m, 1H), 8.03 (dt,  $J$  = 8.4, 0.8 Hz, 1H), 7.75–7.82 (m, 1H), 7.48–7.54 (m, 2H), 7.25–7.39 (m, 3H), 7.09–7.16 (m, 1H), 6.52 (d,  $J$  = 5.2 Hz, 1H), 5.23 (d,  $J$  = 5.2 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  = 171.4, 151.0, 148.1, 140.4, 138.4, 128.1, 127.7, 126.6, 119.9, 113.1, 73.3; IR (KBr):  $\nu$  = 3358, 1671, 1577, 1517, 1507, 1436, 1304  $\text{cm}^{-1}$ ; HR-MS:  $m/z$  = 251.0791  $[\text{M} + \text{Na}]^+$ , calcd. for  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_2\text{Na}_1$ : 251.0796.

**2-Hydroxy-*N*-methyl-*N*,2-diphenylacetamide (2q):**<sup>[14]</sup> Colourless solid; mp 89–90 °C (Lit.<sup>[14]</sup> mp 89–90 °C);  $R_f$  = 0.40 (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.08–7.35 (m, 6H), 6.70–6.90 (m, 4H), 5.00 (s, 1H), 3.30 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 173.0, 141.6, 139.4, 129.7, 128.5, 128.2, 128.1, 127.4, 71.8, 38.4; IR (KBr):  $\nu$  = 3422, 1648, 1605, 1594, 1496, 1369, 1085  $\text{cm}^{-1}$ .

***N*-Ethyl-2-hydroxy-*N*,2-diphenylacetamide (2r):** Oily liquid;  $R_f$  = 0.44 (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.10–7.34 (m, 6H), 6.69–6.85 (m, 4H), 4.92 (s, 1H), 3.87–4.00 (m, 1H), 3.52–3.64 (m, 1H) 3.35 (bs, 1H), 1.12 (t,  $J$  = 7.2 Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 172.4, 139.9, 139.6, 129.5, 129.2, 128.5, 128.4, 128.1, 127.5, 71.9, 45.5, 12.9; IR (neat):  $\nu$  = 3421, 3063, 1652, 1595, 1454, 1380, 1092  $\text{cm}^{-1}$ .

**2-Hydroxy-*N*-(4-methoxybenzyl)-2-phenylacetamide (2s):** Colourless solid; mp 141–142 °C;  $R_f$  = 0.36 (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.32–7.45 (m, 5H), 7.11 (d,  $J$  = 7.6 Hz, 2H), 6.83 (d,  $J$  = 7.6 Hz, 2H), 6.43 (bs, 1H), 5.06 (s, 1H), 4.37 (d,  $J$  = 6.8 Hz, 2H), 3.78 (s, 3H), 2.38 (bs, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 172.1, 159.2, 139.5, 129.9, 129.2, 129.1, 128.9, 127.0, 114.2, 74.4, 55.4, 43.3; IR (KBr):  $\nu$  = 3220, 2965, 1712, 1635, 1540, 1459, 1065  $\text{cm}^{-1}$ .

***N*-(2-Chlorobenzyl)-2-hydroxy-2-phenylacetamide (2t):** Colourless solid; mp 124–125 °C;  $R_f=0.43$  (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta=7.31$ –7.40 (m, 6H), 7.15–7.25 (m, 3H), 6.80 (bs, 1H), 5.02 (s, 1H), 4.49 (d,  $J=6.0$  Hz, 2H), 2.96 (bs, 1H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta=172.4$ , 139.4, 135.2, 133.7, 130.0, 129.7, 129.2, 129.0, 128.8, 127.2, 126.9, 74.3, 41.6; IR (KBr):  $\nu=3230$ , 3058, 1682, 1605, 1510, 1468, 1050  $\text{cm}^{-1}$ .

***N*-(3-Acetylphenyl)-2-hydroxy-2-phenylacetamide (6a):**<sup>[14]</sup> Pale yellow solid; mp 116–117 °C (Lit.<sup>[14]</sup> mp 118–119 °C);  $R_f=0.38$  (hexanes:ethyl acetate, 70:30 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta=10.14$  (s, 1H), 8.32 (t,  $J=1.8$  Hz, 1H), 7.94–8.01 (m, 1H), 7.62–7.68 (m, 1H), 7.50–7.56 (m, 2H), 7.44 (t,  $J=8.0$  Hz, 1H), 7.33–7.40 (m, 2H), 7.26–7.32 (m, 1H), 6.47 (d,  $J=4.8$  Hz, 1H), 5.13 (d,  $J=4.4$  Hz, 1H), 2.54 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta=197.7$ , 171.6, 140.7, 138.9, 137.3, 129.0, 128.1, 127.7, 126.6, 124.2, 123.4, 119.2, 74.1, 26.7; IR (KBr):  $\nu=3308$ , 1653, 1591, 1559, 1540, 1490, 1062  $\text{cm}^{-1}$ .

***N*-(4-Acetylphenyl)-2-hydroxy-2-phenylacetamide (6b):**<sup>[14]</sup> Colourless solid; mp 149–150 °C (Lit.<sup>[14]</sup> mp 148–149 °C);  $R_f=0.39$  (hexanes:ethyl acetate, 70:30 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta=10.77$  (s, 1H), 8.34–8.48 (m, 4H), 8.04 (d,  $J=8.0$  Hz, 2H), 7.87 (t,  $J=7.4$  Hz, 2H), 7.78–7.84 (m, 1H), 7.02 (d,  $J=4.4$  Hz, 1H), 5.66 (d,  $J=4.4$  Hz, 1H), 3.03 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta=196.6$ , 171.8, 142.9, 140.5, 132.0, 129.3, 128.2, 127.7, 126.6, 119.0, 74.1, 26.4; IR(KBr):  $\nu=3285$ , 1674, 1657, 1598, 1543, 1183  $\text{cm}^{-1}$ .

***N*-(3-Benzoylphenyl)-2-hydroxy-2-phenylacetamide (6c):**<sup>[14]</sup> Colourless solid; mp 124–125 °C (Lit.<sup>[14]</sup> mp 126–127 °C);  $R_f=0.35$  (hexanes:ethyl acetate, 70:30 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta=8.52$  (s, 1H), 7.89–7.96 (m, 1H), 7.74–7.85 (m, 3H), 7.58 (tt,  $J=7.4$ , 1.2 Hz, 1H), 7.43–7.51 (m, 5H), 7.32–7.43 (m, 4H), 5.17 (d,  $J=3.6$  Hz, 1H), 3.76 (d,  $J=3.6$  Hz, 1H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta=196.5$ , 170.5, 138.9, 138.5, 137.5, 137.3, 132.9, 130.2, 129.2, 129.1, 129.0, 128.5, 126.9, 126.4, 123.9, 121.1, 74.8; IR (KBr):  $\nu=3335$ , 3307, 1696, 1654, 1542, 1106, 1028  $\text{cm}^{-1}$ .

### Experimental Procedure for *O*-Acylation of $\alpha$ -Hydroxy Amides

Acetyl chloride (0.6 mmol) was added dropwise to a stirred mixture of  $\alpha$ -hydroxy amide (0.5 mmol) and  $\text{Et}_3\text{N}$  (1 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (1.5 mL) at 0 °C under a nitrogen atmosphere. The stirring was continued for 12 h at room temperature and the completion of reaction was monitored by TLC. The organic layer was washed with water for two times, then a saturated aqueous solution of  $\text{NaHCO}_3$  (10 mL) was slowly added to the reaction mixture. The organic layer was separated, washed with water (3  $\times$  10 mL), dried over  $\text{MgSO}_4$  and evaporated under reduced pressure. The solid residue was purified by silica gel column chromatography.

**2-Oxo-1-phenyl-2-(phenylamino)ethyl acetate (7):** Colourless solid; mp 118–119 °C;  $R_f=0.52$  (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta=7.86$  (bs, 1H), 7.46–7.56 (m, 4H), 7.35–7.43 (m, 3H), 7.31 (t,  $J=8.0$  Hz, 2H), 7.13 (t,  $J=7.4$  Hz, 1H), 6.20 (s, 1H), 2.24 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta=169.3$ , 166.5, 137.0, 135.3, 129.4, 129.2, 129.1, 127.6, 125.1, 120.2, 75.9, 21.2; IR (KBr):  $\nu=3327$ , 1749, 1685, 1681, 1432, 1031  $\text{cm}^{-1}$ .

### Experimental Procedure for *O*-Arylation of $\alpha$ -Hydroxy Amides

To an oven-dried reaction tube,  $\alpha$ -hydroxy amide (0.5 mmol), phenyl iodide (0.6 mmol),  $\text{CuI}$  (0.025 mmol), 1,2-bipyridine (0.05 mmol), and  $\text{Cs}_2\text{CO}_3$  (1.0 mmol) were added and the reaction tube was evacuated and refilled with nitrogen. Then dry DMF (1.5 mL) was added and the reaction mixture was stirred at 100 °C under a nitrogen atmosphere for 24 h. The completion of reaction was monitored by TLC. After the completion of reaction, the reaction mixture was extracted three times with ethylacetate water mixture and the combined organic layer was dried over  $\text{MgSO}_4$  and evaporated under reduced pressure. The solid residue was purified by silica gel column chromatography.

**2-Phenoxy-*N*,2-diphenylacetamide (8):** Colourless solid; mp 124–125 °C;  $R_f=0.58$  (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta=8.44$  (bs, 1H), 7.54–7.63 (m, 4H), 7.27–7.43 (m, 7H), 7.09–7.16 (m, 1H), 7.00–7.06 (m, 3H), 5.65 (s, 1H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta=167.9$ , 156.8, 137.2, 136.3, 130.0, 129.2, 128.9, 128.8, 126.7, 124.9, 122.8, 120.2, 116.2, 80.9; IR (KBr):  $\nu=3284$ , 1685, 1676, 1599, 1055  $\text{cm}^{-1}$ .

### Experimental Procedure for *O*-Silylation of $\alpha$ -Hydroxy Amides

Triphenylsilyl chloride (0.6 mmol) was added dropwise to a stirred mixture of  $\alpha$ -hydroxy amide (0.5 mmol) and  $\text{Et}_3\text{N}$  (1 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (1.5 mL) at 0 °C under a nitrogen atmosphere. The stirring was continued for 12 h in room temperature and the completion of reaction was monitored by TLC. The organic layer was washed with water for two times then a saturated aqueous solution of  $\text{NaHCO}_3$  (10 mL) was slowly added to the reaction mixture. The organic layer was dried over  $\text{MgSO}_4$  and evaporated under reduced pressure. The solid residue was purified by silica gel column chromatography.

***N*,2-Diphenyl-2-[(triphenylsilyloxy)acetamide (9):** Colourless semi-solid;  $R_f=0.60$  (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta=8.76$  (bs, 1H), 7.62–7.67 (m, 2H), 7.54–7.60 (m, 6H), 7.44–7.50 (m, 3H), 7.34–7.43 (m, 9H), 7.24–7.32 (m, 4H), 7.06–7.13 (m, 1H), 5.36 (s, 1H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta=169.6$ , 138.9, 137.3, 135.6, 135.5, 135.4, 135.1, 132.8, 130.8, 130.3, 129.1, 128.6, 128.44, 128.41, 128.38, 128.34, 128.30, 128.28, 128.1, 126.8, 124.6, 119.7; IR (neat):  $\nu=3393$ , 1653, 1647, 1601, 1091, 1067  $\text{cm}^{-1}$ .

### Experimental Procedure for *O*-Methylation of $\alpha$ -Hydroxy Amides

Methyl iodide (1.0 mmol) was added dropwise to a stirred mixture of  $\alpha$ -hydroxy amide (0.5 mmol) and  $\text{K}_2\text{CO}_3$  (1.0 mmol) in dry THF (1.5 mL) at room temperature under a nitrogen atmosphere. The stirring was continued for 12 h and the completion of reaction was monitored by TLC. After the completion of reaction, the reaction mixture was extracted three times with an ethyl acetate/water mixture and the combined organic layer was dried over  $\text{MgSO}_4$  and evaporated under reduced pressure. The residue was purified by silica gel column chromatography.

**2-Methoxy-N,2-diphenylacetamide (10):** Colourless solid; mp 102–103 °C;  $R_f=0.56$  (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta=8.56$  (bs, 1H), 7.56–7.63 (m, 2H), 7.44–7.49 (m, 2H), 7.29–7.42 (m, 5H), 7.08–7.15 (m, 1H), 4.74 (s, 1H), 3.46 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta=168.6, 137.4, 136.7, 129.1, 128.8, 128.7, 127.2, 124.5, 119.8, 84.0, 57.5$ ; IR (KBr):  $\nu=3232, 1666, 1660, 1651, 1600, 1066\text{ cm}^{-1}$ .

### General Experimental Procedure for Synthesis of N-Alkyl-3-phenyloxindoles

Methanesulfonyl chloride (1.5 mmol) was slowly added dropwise to a stirred mixture of N-alkyl- $\alpha$ -hydroxy amide (0.5 mmol) and  $\text{Et}_3\text{N}$  (1.6 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (1.5 mL) at room temperature under a nitrogen atmosphere. The stirring was continued for 12 h in room temperature and the completion of reaction was monitored by TLC. The organic layer was washed with water for two times then a saturated aqueous solution of  $\text{NaHCO}_3$  (10 mL) was slowly added to the reaction mixture. The organic layer was separated, washed with water ( $3 \times 10$  mL), dried over  $\text{MgSO}_4$  and evaporated under reduced pressure. The residue was purified by silica gel column chromatography.

**1-Methyl-3-phenylindolin-2-one (11r):** Colourless solid; mp 118–119 °C;  $R_f=0.35$  (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta=7.27$ – $7.37$  (m, 4H), 7.15–7.23 (m, 3H), 7.07 (td,  $J=7.5, 0.8$  Hz, 1H); 6.90 (d,  $J=7.6$  Hz, 1H), 4.61 (s, 1H), 3.26 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta=176.1, 144.7, 136.8, 129.0, 128.6, 127.7, 125.2, 122.9, 108.3, 52.2, 26.6$ ; IR (KBr):  $\nu=1694, 1609, 1496, 1364, 1347, 1124, 1087\text{ cm}^{-1}$ .

**1-Ethyl-3-phenylindolin-2-one (11s):** Colourless solid; mp 96–97 °C;  $R_f=0.38$  (hexanes:ethyl acetate, 80:20 v/v);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta=7.27$ – $7.36$  (m, 4H), 7.14–7.22 (m, 3H), 7.05 (td,  $J=7.4, 0.8$  Hz, 1H); 6.92 (d,  $J=8.0$  Hz, 1H), 4.59 (s, 1H), 3.81 (q,  $J=7.2$  Hz, 2H), 1.30 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta=175.8, 143.7, 137.0, 129.4, 129.0, 128.5, 128.4, 128.6, 125.4, 122.6, 108.4, 52.2, 35.0, 12.8$ ; IR (KBr):  $\nu=1711, 1612, 1489, 1353, 1225, 1090\text{ cm}^{-1}$ .

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