EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Zinc-Mediated Efficient and Selective Reduction of Carbonyl Compounds

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201700887

Link to VoR: http://dx.doi.org/10.1002/ejoc.201700887

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Zinc-Mediated Efficient and Selective Reduction of Carbonyl Compounds

Tirtha Mandal[a], Snehashish Jana[a], Jyotirmayee Dash[a]*

Dedication ((optional))

Abstract: We herein describe for the first time that an optimized combination of Zn and NH_4Cl can be used for the selective reduction of aldehydes and ketones to the corresponding alcohols. The aldehyde and keto groups are selectively reduced in the presence of azide, cyano, epoxy, ester and carbon-carbon double bond functional groups. A broad functional group compatibility, chemoselective reduction of aldehydes in the presence of ketones and selective reduction of isatins at C3 carbonyl are the highlights of the present method.

Introduction

The reduction of aldehydes and ketones is one of the fundamental transformations for the preparation of alcohols, which are used as chemical intermediates for the synthesis of natural products, pharmaceuticals, agrochemicals and functional materials.[1] Therefore, numerous reduction methods such as metal hydrides,[2] boron based reagents,[3] catalytic hydrogenation,[4] and biocatalytic reductions[5] have been reported.[1-5] However, many of these methods often generate stoichiometric amount of waste and involve long reaction times, harsh conditions (under nitrogen; in acid or alkaline conditions) and complicated operations and therefore, pose significant environmental and economic problems especially in large-scale industrial processes. Furthermore, only a few protocols are known for the chemoselective reduction of aldehydes in the presence of a keto group.[6] In this context, we planned to develop a mild and a viable process for the reduction of a wide range of aldehydes, ketones and isatins in aqueous media.

Aldehydes and ketones undergo pinacol coupling to form the corresponding diols in the presence of excess low-valent metals such as Zn−Cu couple,[7] Mg,[8] Mn,[9] Zn,[10] Sm,[11] Al,[12] V[13] and other metals. In these cases, the reduced product is formed as a minor by-product. Recently, it is reported that Mn in combination with 2,4,6-collidinium hydrochloride can chemoselectively reduce aldehydes to the alcohols, while ketones do not react under these conditions.[6c]

Among these metals, Zn has been widely used as a reducing reagent. Zinc in the presence of acetic acid is used as a reducing agent for the reduction of a range of organic functional groups. Zinc amalgam (Zn/Hg alloy) in concentrated HCl is used for the Clemmensen reduction of aldehydes and ketones to provide the corresponding hydrocarbons. Zn is known to reduce benzil and its derivatives to keto-hydroxy compounds.[14] Zn in combination with NH_4Cl has been used for the reduction of nitro and azido groups to the corresponding amines.[15] Zinc is cheap and non-toxic compared to sodium borohydride, a commonly used reagent for the reduction of aldehydes and ketones on a laboratory scale. We envisioned that Zn could be used for the reduction of aldehydes and ketones in the presence of a proton source to selectively obtain the reduced products.

Results and Discussion

We started our optimization studies using 4-methylbenzaldehyde **1a$_1$** as a model substrate to optimize the reaction conditions using different metals, proton sources at different temperatures using THF as the solvent (Table 1). The reaction did not proceed by using catalytic amount of Zn (Table 1, entry 1). Using 1 equiv of Zn, low conversion was observed along with the formation of both the desired alcohol **2a$_1$** and the pinacol product **3a$_1$** (entries 2, 3). By increasing the amount of Zn to 3 equiv as well as increasing the reaction temperature to 60 °C, the formation of **3a$_1$** was decreased but a complete conversion could not be achieved (entries 4, 5). To our delight, the reaction proceeded smoothly by using 5 equiv of Zn leading to the selective formation of **2a$_1$** (entries 9-10, 13) even at room temperature. Gratifyingly, 4-methylbenzyl alcohol **2a$_1$** was exclusively obtained in just 20 minutes by using 5 equiv of Zn in the presence of 8 M aqueous NH_4Cl (10 mL) (entry 13). When less concentrated NH_4Cl solution was used, the reaction was slow providing both the alcohol **2a$_1$** and diol **3a$_1$** (entry 9, 10). However, more concentrated NH_4Cl solution did not interfere with the outcome of the reaction. No reaction was observed by using solid NH_4Cl (entry 11). The use of aqueous NH_4Cl solution (freshly prepared) was necessary for the reaction as no reaction took place using only H_2O as the proton source (entry 12). A closely related result was also obtained using HCl (6 N) as the proton source (entry 17), but the reaction was less efficient than aq. NH_4Cl (entry 13). The reaction also proceeded in the presence of AcOH (6N), but a trace amount of diol **3a$_1$** was also formed (entry 16). When the reaction was performed using 5 equiv. of collidine.HCl as a proton source,[6c] no product was formed after 20 min at rt (entry 18). However, a complete conversion of **1a$_1$** was observed by giving longer reaction time (4 h, rt), providing alcohol **2a$_1$** as the major product along with pinacol **3a$_1$** (entry 19). The reduction of **1a$_1$** in deuteriated solvents like THF-d_8 and D_2O suggest that aq NH4Cl is the proton source (see supporting information, Table S1).

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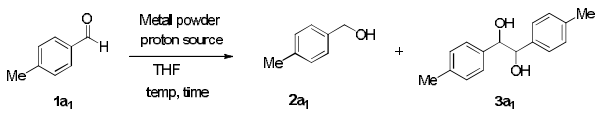
Table 1. Optimization for the reduction of aldehydes.[a]



1a$_1$ 2a$_1$ 3a$_1$

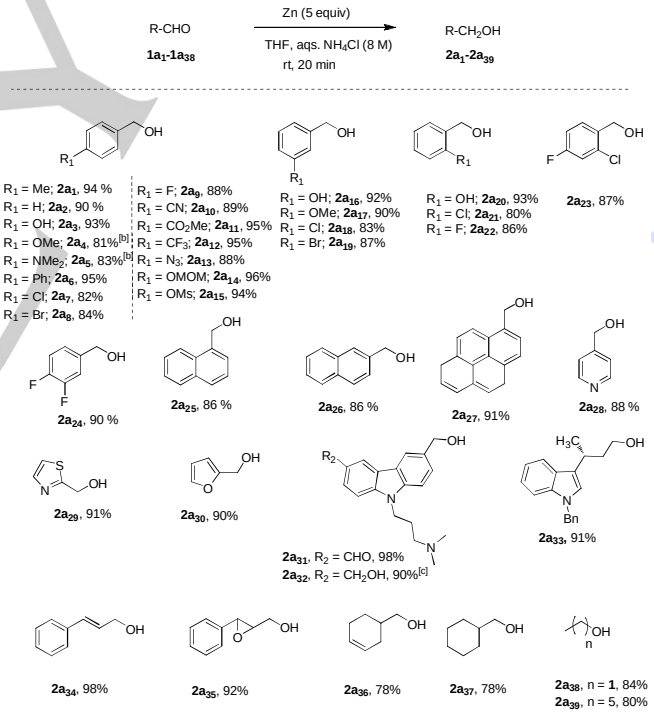
Entry	Proton source	M. (equiv.)	T (° C)	Time	Conv.(%); **2a$_1$**:**3a$_1$**[b]
1	NH_4Cl (2 M)	Zn (0.2)	rt or 60 °C[c]	6 h	No reaction
2	NH_4Cl (2 M)	Zn (1)	rt	4 h	20; 40:60
3	NH_4Cl (2 M)	Zn (1)	60 °C	4 h	25; 50:50
4	NH_4Cl (4 M)	Zn (3)	rt	3 h	80; 60:40
5	NH_4Cl (4 M)	Zn (3)	60 °C	3 h	80; 70:30
6	AcOH (4 N)	Zn (3)	rt or 60 °C[c]	3 h	90; 60:40
7	HCl (4 N)	Zn (3)	rt or 60 °C[c]	3 h	95; 70:30
8	H_2SO_4 (4 N)	Zn (3)	rt or 60 °C[c]	3 h	95; 70:30
9	NH_4Cl (4 M)	Zn (5)	rt	1 h	100; 90:10
10	NH_4Cl (4 M)	Zn (5)	60 °C	45 min	100; 90:10
11	NH_4Cl [d]	Zn (5)	rt	6 h	No reaction
12	H_2O	Zn (5)	rt	8 h	No reaction
13	NH_4Cl (8 M)	Zn (5)	rt	20 min	100; >99:1
14	AcOH (4 N)	Zn (5)	rt or 60 °C[c]	45 min	100; 90:10
15	HCl (4 N)	Zn (5)	rt or 60 °C[c]	1 h	100; 90:10
16	AcOH (6 N)	Zn (5)	rt or 60 °C[c]	30 min	100; 95:5
17	HCl (6 N)	Zn (5)	rt or 60 °C[c]	30 min	100; 95:5
18	Collidine.HCl [e]	Zn (5)	rt	20 min	No reaction
19	Collidine.HCl [e]	Zn (5)	rt	4 h	100; 80:20
20	NH_4Cl (8 M)	Fe (5)	rt	20 min	No reaction
21	NH_4Cl (8 M)	Fe (5)	60 °C	20 min	30; 50:50
22	NH_4Cl (8 M)	Mg (5)	rt or 60 °C[c]	20 min	70; 70:30
23	NH_4Cl (8 M)	Mn (5)	rt or 60 °C[c]	20 min	70; 60:40
24	NH_4Cl (8 M)	In (5)	rt or 60 °C[c]	20 min	No reaction

[a] The reactions were performed on a 1.0 mmol scale in THF (2 mL) using a proton source (10 mL); [b] The conversion and ratio of **2a$_1$** and **3a$_1$** were determined from crude NMR of the reaction mixture; [c] The outcome of reaction remain similar at 60 °C; [d] Using 5 equiv. solid NH_4Cl; [e] Using 5 equiv. Collidine.HCl

It is worth mentioning that Zn and aqueous NH_4Cl solution were added at the same time to make the reaction faster by preventing the formation of pinacol product. The other metal sources like Fe, Mn, Mg and In were found to be inefficient (Table 1, entries 20-24). The reaction with Mg and Mn provided both the reduced and the pinacol products (Table1, entries 22, 23). Then, various solvents including DMF, DMSO, MeCN, DCM, H_2O, toluene and dioxane were evaluated (entries 1−9, Table S2, S.I.). The solvent screening results showed that the highest yield of 2a$_1$ (95%) was obtained when THF was used as the solvent (Table S2, S.I.). The reaction also proceeded in dioxane, toluene and CH_3CN; but poor conversion was observed using DMSO, DMF, CH_2Cl_2 and DCE (Table S2, S.I.). No reaction took place using only water as the solvent (Table S2, S.I.). We determined the optimal reaction conditions to selectively obtain the reduced product **2a$_1$** as follows: Zn (5 equiv), 8 M NH_4Cl (10 mL) in THF (2 mL), rt, 20 min.

With the optimal reaction conditions in hand, the substrate scope of Zn mediated reduction of aldehydes was explored (Table 2). We found that a wide range of aldehydes regardless of the substituent position and electronic property were smoothly reduced to give the corresponding alcohols in good to excellent yields. The reduction of *p*-anisaldehyde and 4-dimethylamino benzaldehyde proceeded slowly at room temperature but they were efficiently reduced upon heating at 60 °C for 3 h to provide benzyl alcohols **2a$_4$** (81%) and **2a$_5$** (83%) respectively, in high yields; some amount of the pinacols (15 % and 12 %, respectively) were also obtained. Many functional groups such as -OH, -Cl, -Br, -F, -CN, -CO_2Me (**2a$_3$, 2a$_7$-2a$_{11}$**) were tolerated. Importantly, the aldehyde group was selectively reduced in the presence of an azido (**2a$_{13}$**) and epoxy group (**2a$_{35}$**). The labile methoxymethyl (MOM) and mesyl (Ms) groups were well tolerated under the reaction conditions (**2a$_{14}$, 2a$_{15}$**).

Table 2. Reduction of aldehydes.[a]



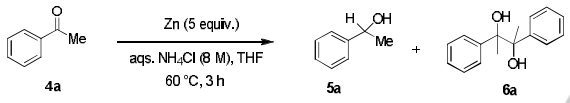
[a] The reactions were performed on a 1.0 mmol scale using Zn (5 equiv), THF (2 mL), 8 M aqs. NH_4Cl solution (10 mL) at room temperature for 20 min; [b] 60 °C for 3 h; 15% and 12% of pinacols were isolated; [c] Reaction was carried out for 45 min at rt.

The polycyclic aromatic aldehydes and heterocyclic aldehydes also furnished the corresponding benzyl alcohols (**2a$_{25}$-2a$_{27}$, 2a$_{28}$-2a$_{33}$**) in excellent yields. The carbazole dialdehyde[16] gave the reduced mono-aldehyde derivative **2a$_{31}$** in excellent yield at room temperature after 20 min. However, both the formyl groups were reduced by conducting the reaction for 45 min to provide the diol **2a$_{32}$** in excellent yield. In case of pyridine-4-aldehyde and 4-cyanobenzaldehyde, trace amounts

of the corresponding pinacols were also formed but the reduced products were easily separated by column chromatography (**2a$_{28}$ and 2a$_{10}$**). In all the other cases, no column purification was needed as the corresponding alcohols were obtained in near quantitative yields. Interestingly, the chiral indolyl aldehyde[17] underwent facile reduction to give the corresponding alcohol **2a$_{33}$** with retention in stereochemistry. The α,β-unsaturated aldehyde gave the desired alcohol **2a$_{34}$**,[6g,i] in which the *E*-stereochemistry was preserved. Aliphatic aldehydes provided their corresponding alcohols in excellent yields at room temperature but the reaction took slightly longer time with formation of trace amount of the pinacol product (**2a$_{36}$-2a$_{39}$**). Pivalaldehyde and cyclopropyl carboxaldehyde did not furnish the desired products under the optimized reaction conditions. Since excess Zn was used in the reduction, we have recovered the used Zn after completion of the reaction and reused to carry out further reactions. Zn showed diminished activity in subsequent reaction cycles (Table S3, S.I.).

We were delighted to find out that ketones although reacted slowly under the optimized reaction conditions, gave the desired alcohols **5** as the major products at 60 °C (Table 3). The reduction of ketone **4a** was inefficient using collidinium hydrochloride (entries 6,7);[6c] a low (40%) conversion of **4a** occurred after 3 h at 60 °C and a mixture of alcohol **5a** and diol **6a** were obtained by giving a longer reaction time (8 h).

Table 3. Optimisation for the reduction of ketones.[a]

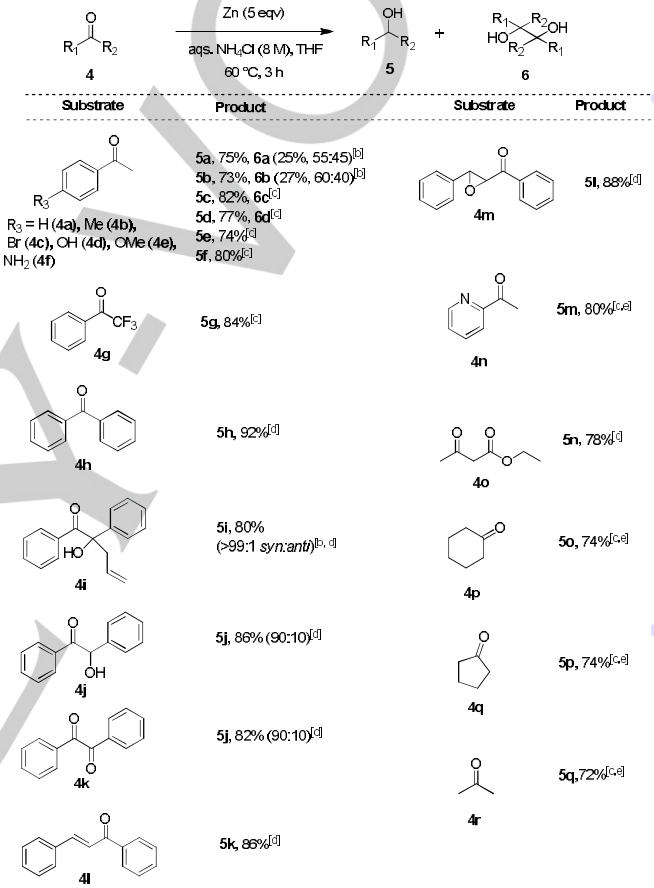


Entry	Zn (equiv.)	T (° C)	Time	Conversion (%),[b] ratio of **5a**:**6a**	**6a** (*dl*:meso)[c]
1	3	Rt	6 h	10, 50:50	Nd
2	3	60 °C	6 h	70, 60:40	50:50
3	5	Rt	4 h	40, 60:40	Nd
4	5	60 °C	3 h	100, 75:25	60:40
5	5	Rt	14 h	80, 50:50	Nd
6	5	60 °C	3 h	40, 60:40[d]	Nd
7	5	60 °C	8 h	> 99, 50:50[d]	Nd

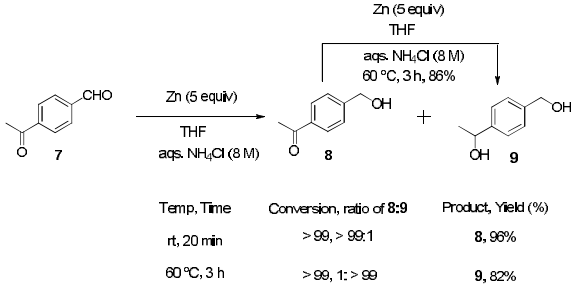
[a] The reactions were performed on a 1.0 mmol scale in solvent (2 mL); [b] The conversion and ratio (**5a**:**6a**) were determined from NMR spectra of the crude reaction mixture; [c] The *dl*:*meso* ratio was determined from the NMR spectra of isolated **6a**; [d] The reactions were performed using 5 equiv. of collidinium hydrochloride.

Aromatic ketones containing –OH, -OMe, -NH$_2$ and -Br groups were efficiently reduced to produce the corresponding secondary alcohols (**5c-5f**). Importantly, the keto group was reduced selectively in the presence of ester, double bond and epoxy groups (**5n**, **5k**, **5l**). The 2,2,2-trifluoro acetophenone derivative **4g** was reduced to afford the corresponding fluorinated secondary alcohol **5g** in high yield. It is important to note that benzophenone **4h** gave exclusively the alcohol **5h** in excellent yield (92%), better than the reported metal mediated reductions. The α-ketohydroxy derivatives **4i** and **4j** were reduced efficiently to give the desired products **5i** (*syn*:*anti* > 99:1) and **5j** (dl/meso = 90:10) respectively, in excellent yields and diastereoselectivities. Both the keto groups of benzil **4k** were reduced to provide the diol **5j** (dl/meso = 90:10). The heteroaryl **4n**, cyclic **4p-q** and acyclic **4r** aliphatic ketones were also reduced to give the corresponding reduced products by giving a slightly longer reaction time (4 h). In few cases, the pinacol products **6** were obtained as the minor products (0-27%), which could be easily separated out by column chromatography (Table 4).

Table 4. Reduction of ketones.[a]



[a] The reactions were performed on a 1.0 mmol scale using Zn (5 equiv), THF (2 mL), 8 M aqs. NH$_4$Cl solution (10 mL) at 60 °C for 3 h; [b] The *dl*:*meso* or *syn*:*anti* ratios were evaluated from the NMR spectra of isolated pinacol products; [c] ND = pinacol product was not isolated; [d] NF = pinacol product was not formed, [e] 4 h.

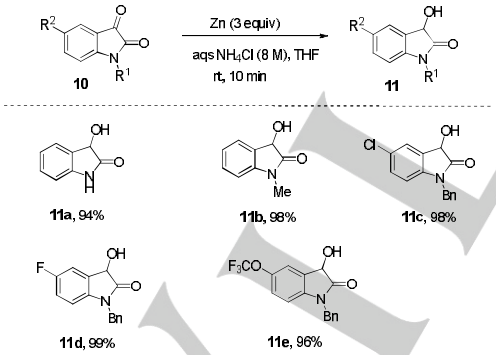


Scheme 1. Chemoselective reduction of an aldehyde in the presence of a ketone.

Next we have evaluated the chemoselectivity of the reduction process by using 4-acetylbenzaldehyde **7** (Scheme 1) as the substrate. At rt, the benzyl alcohol **8** was isolated as the sole product in 90% yield, indicating the reduction of aldehydes could be performed with excellent selectivity without concomitant reduction of the keto group. Many reducing agents would have reacted with both the functional groups providing a mixture of products.[1-5] Although a few methods have been developed for the chemoselective reduction of aldehydes in the presence of ketones,[6] the development of a practical and bench scale process is still desirable. We have established a mild protocol for chemoselective reduction of aldehydes in the presence of ketones that can be applied for large scale synthesis. By heating the aldehyde **7** at 60 °C for 3 h, both aldehyde and keto groups were reduced to provide the diol **9**, which was also obtained from the hydrogenation of **8**.

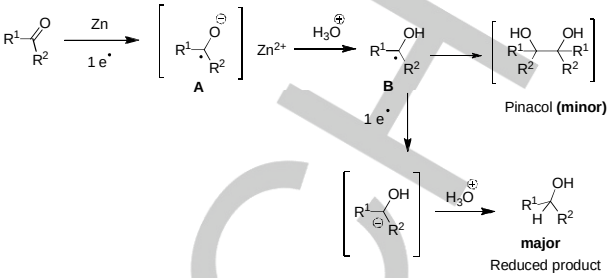
The method was also used to achieve the selective reduction of C3 carbonyl group of isatins (Table 5). Only a few methods are known for the reduction of isatins.[18] $NaBH_4$ is the commonly used reagent for the selective reduction of isatin derivatives at the C3 position, however, 5-halo substituted isatins gave the corresponding 3-hydroxy indolines in poor yields. Recently, a combination of $CeCl_3$ and $NaBH_4$ has been developed for the efficient reduction of 5-halo substituted isatins.[19] In contrary, our reaction conditions (3 equiv. Zn, aqueous 8 M NH_4Cl in THF) constitute a mild and simple alternative for the chemoselective reduction of isatins, affording the 3-hydroxy indoline derivatives **11** in near quantitative yields. The 5-halo substituted isatins were reduced efficiently under the optimized reaction conditions, affording the corresponding 3-hydroxy indolines in excellent yields without any column purification. These reactions were completed within 10 min. Moreover, these reductions could be easily performed on gram scale; the reduction of 4-methylbenzaldehyde and N-methyl isatin were carried out in 2 g scale to provide the corresponding reduced products in 90% and 94 % yields respectively.

Table 5. Reduction of isatin derivatives. [a]



[a] The reactions were performed on a 1.0 mmol scale using Zn (3 equiv), THF (2 mL), aqs. NH_4Cl (8 M, 10 mL) at room temperature for 10 min.

The reduction process proceeds through a typical single electron transfer mechanism. The reduction of **1a$_1$** was inhibited in the presence of radical scavengers like TEMPO or galvinoxyl, corroborating a radical pathway (Table S4, S.I.). The electron transfer from Zn to the aldehyde and ketone functional groups generates reactive alkoxy radical intermediate (**A**), which upon protonation in the presence of aqueous NH_4Cl forms the radical intermediate **B** (Scheme 2). The intermediate **B** can undergo radical coupling to form the pinacol or it can follow another electron transfer to form the reduced alcohol. Since the pinacol product is obtained as a minor product, the electron transfer and subsequent protonation are faster than the radical coupling to provide the reduced alcohol as the major product.



Scheme 2. Proposed mechanism via SET pathway.

Conclusions

In summary, we have developed a general protocol for the reduction of different kinds of aldehydes (aliphatic, aromatic, polycyclic aromatic, heterocyclic and α,β-unsaturated) and ketones to the corresponding alcohols using an optimized amount of Zn and NH_4Cl under mild reaction conditions. The method can be used for the rapid reduction of isatins at the C3 position. The reactions proceed efficiently with excellent yields and high chemoselectivity. In most cases, the products were isolated directly without chromatographic purification. The selective reduction of aldehyde group is achieved in the presence of ketones, ester, cyano, azide, and epoxy and carbon-carbon double bond thus providing a mild, economic and attractive alternative to other reagents.

EXPERIMENTAL SECTION

General Information: All experiments were carried out under open atmosphere in flame dried flasks. Solvents were dried using standard procedures. All starting materials were obtained from commercial suppliers and used as received. Products were purified by flash chromatography on silica gel (100-200 mesh, Merck). Unless otherwise stated, yields refer to analytical pure samples. NMR spectra were recorded in $CDCl_3$ and DMSO-d_6. 1H NMR spectra were recorded at 500 MHz and 400 MHz instruments at 278 K. Data is reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constants (Hz). 13C NMR spectra were recorded on either a 100 MHz or a 125 MHz with complete proton decoupling. Chemical shifts (δ) are reported in ppm. Infrared (FTIR) spectra were recorded on a spectrophotometer with the KBr disk and KBr plate techniques for solid and liquid samples, νmax cm^{-1}.

General procedure for the reduction of aldehydes (GP-I): To a solution of aldehydes **1** (1.0 mmol, 1 equiv.) in THF (2 mL) were added Zn dust (5 mmol, 325 mg, 5 equiv.) and aqueous NH_4Cl solution (8 M, 10 mL) simultaneously. The reaction mixture was stirred at room temperature until complete conversion of starting material (as monitored by TLC), typically for 20 min. The reaction mixture was filtered through cotton into a separatory funnel and extracted with EtOAC (3 X 5 mL). The

combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated to give the corresponding alcohols **2**. In most cases, the product was sufficiently pure and no further purification was needed.

General procedure for the reduction of ketones (GP-II): To a solution of ketones **4** (1 mmol, 1 equiv.) in THF (2 mL) were added Zn dust (5 mmol, 325 mg, 5 equiv.) and aqueous NH_4Cl solution (8 M, 10 mL) simultaneously. The reaction mixture was stirred at 60 °C until complete conversion of starting material (as monitored by TLC), typically for 3-4 h. The reaction mixture was filtered through cotton into a separatory funnel and extracted with EtOAC (3 X 5 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated. The residue was purified by column chromatography on silica gel using hexanes/EtOAC as eluent (80:20-60:40) to give the corresponding secondary alcohols **5**. In some cases, the pinacol product **6** was obtained as a minor product, which was separated by using column chromatography.

General procedure for reduction of isatins (GP-III): To a solution of isatins **10** (1 mmol, 1 equiv.) in THF (2 mL) were added Zn dust (3 mmol, 195 mg, 3 equiv.) and aqueous NH_4Cl solution (8 M, 10 mL) simultaneously. The reaction mixture was stirred at room temperature until complete conversion of starting material (as monitored by TLC), typically for 10 min. The reaction mixture was filtered through cotton into a separatory funnel and extracted with EtOAC (3 X 5 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated to give the desired products **11**. The product thus obtained was sufficiently pure and no further purification was needed.

Gram scale experiments:

Preparation of 4-methylbenzyl alcohol ($2a_1$): To a solution of 4-methylbenzaldehyde **$1a_1$** (2.0 g, 16.6 mmol, 1.0 equiv.) in THF (20 mL) were added Zn dust (5.4 g, 83 mmol, 5.0 equiv.) and aqueous NH_4Cl solution (8 M, 40 mL) simultaneously. The reaction mixture was stirred at room temperature until completion of the reaction as monitored by TLC (30 min. to be specific in this case). The reaction mixture was filtered through cotton into a separatory funnel and extracted with EtOAC (3 X 20 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated to give the 4-methylbenzyl alcohol **$2a_1$** (1.8 g, 92 %) as a colorless liquid.

Preparation of 3-hydroxy-1-methylindolin-2-one (11b): To a solution of N-methyl isatin **10b** (2.0 g, 12.4 mmol, 1.0 equiv.) in THF (15 mL) were added Zn dust (2.5 g, 38.0 mmol, 3 equiv.) and aqueous NH_4Cl solution (8 M, 40 mL) simultaneously. The reaction mixture was stirred at room temperature until completion of the reaction as monitored by TLC (15 min to be specific in this case). The reaction mixture was filtered through cotton into a separatory funnel and extracted with EtOAC (3 X 20 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated to give 3-hydroxy-1-methylindolin-2-one **11b** (1.94 g, 95%) as a pale yellow solid.

Analytic data of compounds:

4-Methylbenzyl alcohol ($2a_1$):[6f] Following **GP-I**, 4-methylbenzaldehyde **$1a_1$** (120 mg, 1.0 mmol, 1.0 equiv.) afforded 4-methylbenzyl alcohol **$2a_1$** (114 mg, 94%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 2.10 (3H, s), 4.30 (2H, s), 4.96 (1H, br s), 6.94 (2H, d, *J* = 8.2 Hz), 7.04 (2H, d, *J* = 8.2 Hz); ^{13}C (125 MHz, DMSO-d_6): 20.8, 62.9, 126.6, 128.7, 135.7, 139.6; HRMS (ESI) calcd for $C_8H_{10}O[M+H]^+$: 123.0732; Found: 123.0735.

Benzyl alcohol ($2a_2$):[6f] Following **GP-I**, benzaldehyde **$1a_2$** (106 mg, 1.0 mmol, 1.0 equiv.) afforded benzyl alcohol **$2a_2$** (98 mg, 90%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): 2.90 (1H, br s), 4.65 (2H, s), 7.23-7.35 (5H, m); ^{13}C (125 MHz, $CDCl_3$): 65.1, 127.0, 127.5, 128.5, 140.9; HRMS (ESI) calcd for $C_7H_8O[M+H]^+$: 109.0575; Found: 109.0572.

4-Hydroxybenzyl alcohol ($2a_3$):[20] Following **GP-I**, 4-hydroxybenzaldehyde **$1a_3$** (122 mg, 1.0 mmol, 1.0 equiv.) afforded 4-hydroxybenzyl alcohol **$2a_3$** (116 mg, 93%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.37 (2H, s), 4.90 (1H, br s), 6.72 (2H, d, *J* = 8.4 Hz), 7.0 (2H, d, *J* = 8.4 Hz), 9.23 (1H, s); ^{13}C (100 MHz, DMSO-d_6): 62.9, 114.8, 128.1, 132.8 156.2; HRMS (ESI) calcd for $C_7H_8O_2$ $[M+H]^+$: 125.0524; Found: 125.0522.

(4-Methoxyphenyl)methanol ($2a_4$):[6f] Following **GP-II**, 4-methoxybenzaldehyde **$1a_4$** (136 mg, 1.0 mmol, 1.0 equiv.) afforded (4-methoxyphenyl)methanol **$2a_4$** (112 mg, 81%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 3.61 (3H, s), 4.31 (2H, d, *J* = 6.7 Hz), 4.94 (1H, t, *J* = 6.7 Hz), 6.76 (2H, d, *J* = 11.0 Hz), 7.12 (2H, d, *J* = 11.0 Hz); ^{13}C (125 MHz, DMSO-d_6): 54.9, 62.6, 113.5, 127.9, 134.6, 158.2; HRMS (ESI) calcd for $C_8H_{10}O_2$ $[M+H]^+$: 139.0681; Found: 139.0680.

(4-(Dimethylamino)phenyl)methanol ($2a_5$):[6j] Following **GP-II**, 4-dimethylaminobenzaldehyde **$1a_5$** (148 mg, 1.0 mmol, 1.0 equiv.) afforded methyl (4-(dimethylamino)phenyl)methanol **$2a_5$** (126 mg, 83%) as a straw yellow liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 2.88 (6H, s), 4.39 (2H, d, *J* = 5.7 Hz), 4.96 (1H, t, *J* = 5.65 Hz), 6.71 (2H, d, *J* = 8.8 Hz), 7.16 (2H, d, *J* = 8.8 Hz); ^{13}C (125 MHz, DMSO-d_6): 40.4, 63.0, 112.3, 127.9, 130.2, 149.7; HRMS (ESI) calcd for $C_9H_{13}NO[M+H]^+$: 152.0997; Found: 152.0999.

[1,1'-Biphenyl]-4-ylmethanol ($2a_6$):[6g] Following **GP-I**, [1,1'-biphenyl]-4-carbaldehyde **$1a_6$** (182 mg, 1.0 mmol, 1.0 equiv.) afforded [1,1'-biphenyl]-4-ylmethanol **$2a_6$** (87 mg, 95%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.57 (2H, d, *J* = 5.7 Hz), 5.30 (1H, t. *J* = 5.7 Hz), 7.34 (1H, t, *J* = 7.6 Hz), 7.46-7.41 (4H, m), 7.65-7.60 (4H, m); ^{13}C (100 MHz, DMSO-d_6): 62.7, 126.4, 126.6, 127.1, 127.3, 128.9, 138.7, 140.2, 141.8; HRMS (ESI) calcd for $C_{13}H_{12}O[M+H]^+$: 185.0888; Found: 185.0889.

4-Chlorobenzyl alcohol ($2a_7$):[6b] Following **GP-I**, 4-chlorobenzaldehyde **$1a_7$** (140 mg, 1.0 mmol, 1.0 equiv.) afforded 4-chlorobenzyl alcohol **$2a_7$** (116 mg, 82%) as a straw yellow liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.35 (2H, d, *J* = 5.6 Hz), 5.17 (1H, t, *J* = 6.4 Hz), 7.15 (2H, d, *J* = 8.2 Hz), 7.48 (2H, d, *J* = 8.8 Hz); ^{13}C (125 MHz, DMSO-d_6): 62.1, 119.5, 128.5, 130.8, 141.8; HRMS (ESI) calcd for $C_7H_7ClO[M+H]^+$: 143.0185; Found: 143.0183.

4-Bromobenzyl alcohol ($2a_8$):[6h] Following **GP-I**, 4-bromobenzaldehyde **$1a_8$** (184 mg, 1.0 mmol, 1.0 equiv.) afforded 4-bromobenzyl alcohol **$2a_8$** (158 mg, 84%) as a straw yellow liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.45 (2H, d, *J* = 5.7 Hz), 5.27 (1H, t, *J* = 6.3 Hz), 7.25 (2H, d, *J* = 8.2 Hz), 7.48 (2H, d, *J* = 8.8 Hz); ^{13}C (125 MHz, DMSO-d_6): 62.2, 119.6, 128.6, 130.9,

141.9; HRMS (ESI) calcd for $C_7H_7BrO[M+H]^+$: 186.9680; Found: 186.9678.

4-Fluorobenzyl alcohol ($2a_9$):[6g] Following **GP-I**, 4-flurobenzaldehyde **$1a_9$** (124 mg, 1.0 mmol, 1.0 equiv.) afforded 4-flurobenzyl alcohol **$2a_9$** (110 mg, 88%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.37 (2H, d, *J* = 5.6 Hz), 5.13 (1H, t, *J* = 5.6 Hz), 7.0-7.10 (2H, m), 7.24 (2H, dd, *J* = 6.3, 2.5 Hz); ^{13}C (125 MHz, DMSO-d_6): 62.2, 114.6, 114.8, 128.3, 128.4, 138.6, 138.7, 160.2, 162.1; HRMS (ESI) calcd for $C_7H_7FO[M+H]^+$: 127.0481; Found: 127.0479.

4-Cyanobenzyl alcohol ($2a_{10}$):[6h] Following **GP-I**, 4-cyanobenzaldehyde **$1a_{10}$** (130 mg, 1.0 mmol, 1.0 equiv.) afforded 4-cyanobenzyl alcohol **$2a_{10}$** (118 mg, 89%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.52 (2H, d, *J* = 5.0 Hz), 5.38 (1H, t, *J* = 5.9 Hz), 7.44 (2H, d, *J* = 7.5 Hz), 7.71 (2H, d, *J* = 7.5 Hz); ^{13}C (125 MHz, DMSO-d_6): 62.2, 109.3, 119.0, 126.9, 132.0, 148.5; HRMS (ESI) calcd for C_8H_7NO $[M+H]^+$: 134.0528; Found: 134.0526.

Methyl 4-(hydroxymethyl)benzoate ($2a_{11}$):[6f] Following **GP-I**, Methyl 4-formylbenzoate **$1a_{11}$** (164 mg, 1.0 mmol, 1.0 equiv.) afforded methyl 4-(hydroxymethyl)benzoate **$2a_{11}$** (158 mg, 95%) . ^{1}H NMR (500 MHz, DMSO-d_6): 3.80 (3H, s), 4.53 (2H, d, *J* = 7.4 Hz), 5.30 (1H, t, *J* = 7.7 Hz), 7.42 (2H, d, *J* = 9.8 Hz), 7.88 (2H, d, *J* = 9.8 Hz); ^{13}C (125 MHz, DMSO-d_6): 51.9, 62.4, 126.2, 126.3, 129.0, 148.3, 166.2; HRMS (ESI) calcd for $C_9H_{10}O_3$ $[M+H]^+$: 167.0630; Found: 167.06329.

(4-(Trifluoromethyl)phenyl)methanol ($2a_{12}$):[6h] Following **GP-I**, 4-trifluoromethyl benzaldehyde **$1a_{12}$** (174 mg, 1.0 mmol, 1.0 equiv.) afforded 4-(trifluoromethyl)phenyl)methanol **$2a_{12}$** (168 mg, 95%). ^{1}H NMR (500 MHz, DMSO-d_6): 4.62 (2H, d, *J* = 5.0 Hz), 5.48 (1H, t, *J* = 5.7 Hz), 7.55 (2H, d, *J* = 8.2 Hz), 7.68 (2H, d, *J* = 8.2 Hz); ^{13}C (100 MHz, DMSO-d_6): 62.3,123.1, 124.9, 125.9, 126.9, 127.3, 127.7, 147.5; HRMS (ESI) calcd for $C_8H_7F_3O[M+H]^+$: 177.0449; Found: 177.0449.

(4-Azidophenyl)methanol ($2a_{13}$):[21] Following **GP-I**, 4-azidobenzaldehyde **$1a_{13}$** (146 mg, 1.0 mmol, 1.0 equiv.) afforded (4-azidophenyl)methanol **$2a_{13}$** (134 mg, 90%) as a straw yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6): 4.47 (2H, d, *J* = 5.9 Hz), 5.22 (1H, t, *J* = 5.9 Hz), 7.06 (2H, d, *J* = 8.3 Hz), 7.25 (2H, d, *J* = 8.3 Hz); ^{13}C (100 MHz, DMSO-d_6): 62.3, 118.7, 128.1, 137.6, 139.6; HRMS (ESI) calcd for $C_7H_7N_3O$ $[M+H]^+$: 150.0589; Found: 150.0588.

(4-(methoxymethoxy)phenyl)methanol ($2a_{14}$): Following **GP-I**, 4-(methoxymethoxy)benzaldehyde**$1a_{14}$** (166 mg, 1.0 mmol, 1.0 equiv.) afforded (4-(methoxymethoxy)phenyl)methanol **$2a_{14}$** (164 mg, 96%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): 3.46 (3H, s), 4.56 (2H, s), 5.15 (2H, s), 7.00 (2H, d, *J* = 8.8 Hz), 7.25 (2H, d, *J* = 8.3 Hz); ^{13}C (100 MHz, $CDCl_3$): 55.9, 64.6, 94.5, 116.7, 128.5, 134.7, 156.7; HRMS (ESI) calcd for $C_9H_{12}O_3$ $[M+H]^+$: 169.0786; Found: 169.0784.

4-(hydroxymethyl)phenyl methanesulfonate ($2a_{15}$): Following **GP-I**, 4-formylphenyl methanesulfonate **$1a_{15}$** (200 mg, 1.0 mmol, 1.0 equiv.) afforded 4-(hydroxymethyl)phenyl methanesulfonate **$2a_{15}$** (190 mg, 94%) as a pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): 3.12 (3H, s), 4.65 (2H, s), 7.27-7.23 (2H, m), 7.41-7.36 (2H, m); ^{13}C (100 MHz, $CDCl_3$): 37.4, 64.2, 122.1, 128.5, 140.4, 148.5; HRMS (ESI) calcd for $C_8H_{10}O_4S$ $[M+H]^+$: 203.0300; Found: 203.0301.

3-Hydroxybenzyl alcohol ($2a_{16}$):[20] Following **GP-I**, 3-hydroxybenzaldehyde **$1a_{16}$** (122 mg, 1.0 mmol, 1.0 equiv.) afforded 3-hydroxybenzyl alcohol **$2a_{16}$** (114 mg, 92%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.42 (2H, d, *J* = 5.1 Hz), 5.10 (1H, t, *J* = 5.7 Hz), 6.62 (1H, dd, *J* = 1.9, 5.7 Hz), 6.72 (1H, d, *J* = 7.6 Hz), 6.76 (1H, s), 7.10 (1H, t, *J* = 8.0 Hz), 9.27 (1H, s); ^{13}C (100 MHz, DMSO-d_6): 63.0, 113.4, 113.6, 117.1, 129.1, 144.1, 157.3; HRMS (ESI) calcd for $C_7H_8O_2$ $[M+H]^+$: 125.0524; Found: 125.0524.

(3-Methoxyphenyl)methanol ($2a_{17}$):[6f] Following **GP-I**, 3-methoxybenzaldehyde **$1a_{17}$** (136 mg, 1.0 mmol, 1.0 equiv.) afforded (3-methoxyphenyl)methanol **$2a_{17}$** (124 mg, 90%) as a colourless liquid. ^{1}H NMR (400 MHz, DMSO-d_6): 3.72 (3H, d, *J* = 2. Hz), 4.48 (2H, d, *J* = 5.5 Hz), 5.19 (1H, t, *J* = 6.1 Hz), 6.76 (1H d, *J* = 10.3 Hz), 6.90 (2H, s), 7.21 (1H, t, *J* = 7.3 Hz); ^{13}C (100 MHz, DMSO-d_6): 54.9, 62.8, 111.8, 112.1, 118.5, 129.1, 144.3, 159.3; HRMS (ESI) calcd for $C_8H_{10}O_2$ $[M+H]^+$: 139.0681; Found: 139.0680.

3-Chlorobenzyl alcohol ($2a_{18}$):[6b] Following **GP-I**, 3-chlorobenzaldehyde **$1a_{18}$** (140 mg, 1.0 mmol, 1.0 equiv.) afforded 3-chloro benzyl alcohol **$2a_{18}$** (118 mg, 83%) as a straw yellow liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.50 (2H, d, *J* = 1.9 Hz), 5.40-5.35 (1H, m), 7.24 (2H, d, *J* = 7.6 Hz), 7.33-7.30 (1H, m), 7.35 (1H, s); ^{13}C (100 MHz, DMSO-d_6): 62.3, 125.0, 126.2, 126.6, 130.0, 133.0, 145.3; HRMS (ESI) calcd for $C_7H_7ClO[M+H]^+$: 143.0185; Found: 143.0183.

3-Bromobenzyl alcohol ($2a_{19}$):[6f] Following **GP-I**, 3-bromobenzaldehyde **$1a_{19}$** (184 mg, 1.0 mmol, 1.0 equiv.) afforded 3-bromobenzyl alcohol **$2a_{19}$** (162 mg, 87%) as a straw yellow liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.51 (2H, d, *J* = 5.7 Hz), 5.38 (1H, t, *J* = 5.7 Hz), 7.32-7.36 (2H, m), 7.41 (1H, d, *J* = 7.6 Hz), 7.52 (1H, s); ^{13}C (100 MHz, DMSO-d_6): 62.2, 121.6, 125.3, 129.1, 129.5, 130.3, 145.5; HRMS (ESI) calcd for $C_7H_7BrO[M+H]^+$: 186.9680; Found: 186.9678.

2-Hydroxybenzyl alcohol ($2a_{20}$):[6k] Following **GP-I**, 2-hydroxybenzaldehyde **$1a_{20}$** (122 mg, 1.0 mmol, 1.0 equiv.) afforded 2-hydroxy benzyl alcohol **$2a_{20}$** (116 mg, 93%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.45 (2H, s), 4.93 (1H, br s), 6.79 (2H, t, *J* = 10.8 Hz), 7.02-7.05 (1H, m), 7.28 (1H, d, *J* = 6.7 Hz), 9.28 (1H, s); ^{13}C (100 MHz, DMSO-d_6): 58.3, 114.5, 118.6, 127.2, 127.3, 128.5, 154.1; HRMS (ESI) calcd for $C_7H_8O_2$ $[M+H]^+$: 125.0524; Found: 125.0523.

2-Chlorobenzyl alcohol ($2a_{21}$):[6b] Following **GP-I**, 2-chlorobenzaldehyde **$1a_{21}$** (140 mg, 1.0 mmol, 1.0 equiv.) afforded 2-chlorobenzyl alcohol **$2a_{21}$**(114 mg, 80%) as a straw yellow liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.50 (2H, d, *J* = 5.65 Hz), 5.35 (1H, t, *J* = 5.65Hz), 7.16-7.12 (1H, m), 7.26-7.21 (2H, m), 7.47 (1H, d, *J* = 7.55 Hz); ^{13}C (100 MHz, DMSO-d_6): 60.5, 127.1, 128.2, 128.3, 128.8, 131.2, 139.6HRMS (ESI) calcd for $C_7H_7ClO[M+H]^+$: 143.0185; Found: 143.0183.

2-Fluorobenzyl alcohol ($2a_{22}$):[6g] Following **GP-I**, 2-flurobenzaldehyde **$1a_{22}$** (124 mg, 1.0 mmol, 1.0 equiv.) afforded 2-fluorobenzyl alcohol **$2a_{22}$** (108 mg, 86%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.55 (2H, d, *J* = 5.7 Hz), 5.32-5.29 (1H, m), 7.13-7.09 (1H, m), 7.18-7.15 (1H, m), 7.30-7.26 (1H, m), 7.48-7.45 (1H, m); ^{13}C (125 MHz, DMSO-d_6): 56.7, 56.8, 114.7, 114.9, 124.2, 124.3, 128.7, 128.8, 129.1, 129.2, 129.2, 129.2, 158.5, 160.9; HRMS (ESI) calcd for $C_7H_7FO[M+H]^+$: 127.0481; Found: 127.0479.

2-Chloro-4-fluorobenzyl alcohol (2a$_{23}$):[22] Following **GP-I**, 2-chloro-4-flurobenzaldehyde **1a$_{23}$** (158 mg, 1.0 mmol, 1.0 equiv.) afforded 2-chloro-4-fluorobenzyl alcohol **2a$_{23}$** (140 mg, 87%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d$_6$): 4.53 (2H, d, *J* = 5.0 Hz), 5.39 (1H, t, *J* = 5.7 Hz), 7.32-7.25 (2H, m), 7.48 (1H, t, *J* = 8.2 Hz); ^{13}C (125 MHz, DMSO-d$_6$): 56.4, 56.4, 115.3, 115.6, 124.5, 128.4, 128.5, 130.2, 130.3, 132.1, 132.2, 158.3, 160.8; HRMS (ESI) calcd for $C_7H_6FClO[M+H]^+$: 161.5733; Found: 161.5734.

3,4-Difluorobenzyl alcohol (2a$_{24}$):[23] Following **GP-I**, 3,4-diflurobenzaldehyde **1a$_{24}$** (142 mg, 1.0 mmol, 1.0 equiv.) afforded 3,4-difluorobenzyl alcohol **2a$_{24}$** (128 mg, 90%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d$_6$): 4.46 (2H, d, *J* = 6.3 Hz), 5.39 (1H, t, *J* = 6.3 Hz), 7.13-7.11 (1H, m), 7.40-7.37 (2H, m); ^{13}C (100 MHz, DMSO-d$_6$): 61.8, 115.1, 115.3, 116.9,117.1, 122.8, 122.8, 122.8, 122.9, 140.4, 140.5, 140.6, 147.1, 147.2, 148.2, 148.3, 149.5, 149.6, 150.6, 150.7; HRMS (ESI) calcd for $C_7H_6F_2O[M+H]^+$: 145.0387; Found: 145.0389.

1-Naphthalenemethanol (2a$_{25}$):[6j] Following **GP-I**, α-napthaldehyde **1a$_{25}$** (156 mg, 1.0 mmol, 1.0 equiv.) afforded 1-naphthalenemethanol **2a$_{25}$** (136 mg, 86%) as a colorless liquid. ^{1}H NMR (400 MHz, DMSO-d$_6$): 4.94 (2H, d, *J* = 4.2 Hz), 5.30 (1H, br s), 7.39-7.54 (4H, m), 7.75 (1H, d, *J* = 7.9 Hz), 7.85 (1H, d, *J* = 8.6 Hz), 8.04 (1H, d, *J* = 7.3 Hz); ^{13}C (100 MHz, DMSO-d$_6$): 61.2, 123.7, 124.2, 125.4, 125.6, 125.9, 127.3, 128.3, 130.7, 133.2, 137.8; HRMS (ESI) calcd for $C_{11}H_{10}O[M+H]^+$: 159.0732; Found: 159.0730

2-Naphthalenemethanol (2a$_{26}$):[6d] Following **GP-I**, 2–naphthaldehyde **1a$_{26}$** (156 mg, 0.50 mmol, 1.0 equiv.) afforded 2-naphthalenemethanol **2a$_{26}$** (136 mg, 86%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d$_6$): 5.65 (2H, d, *J* = 5.7 Hz), 5.37 (1H, t, *J* = 5.7 Hz), 7.38-7.44 (3H, m), 7.78-7.82 (4H, m);^{13}C (100 MHz, DMSO-d$_6$): 63.2, 124.4, 125.4, 125.5, 126.1, 127.6, 127.7, 132.3, 133.1, 140.3; HRMS (ESI) calcd for $C_{11}H_{10}O[M+H]^+$: 159.0732; Found: 159.0731.

(4,8-Dihydropyren-1-yl)methanol (2a$_{27}$):[24] Following **GP-I**, pyrenecarbaldehyde **1a$_{27}$** (232 mg, 1.0 mmol, 1.0 equiv.) afforded (4,8-dihydropyren-1-yl)methanol **2a$_{27}$** (212 mg, 91%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d$_6$): 1.98 (1H, br s), 5.39 (2H, s), 7.99-8.05 (4H, m), 8.14 (2H, t, *J* = 7.6 Hz), 8.20 (2H, t, *J* = 6.7 Hz), 8.36 (1H, d, *J* = 9.2 Hz); ^{13}C (100 MHz, DMSO-d$_6$): 63.9, 123.3, 124.9, 125.1, 125.2, 125.5, 126.2, 126.3, 127.7, 128.1, 129.1, 131.1, 131.5, 130.9, 131.6, 134.3; HRMS (ESI) calcd for $C_{17}H_{14}O[M+H]^+$: 235.1045; Found: 235.1048.

Pyridine-4-ylmethanol (2a$_{28}$):[6k] Following **GP-I**, pyridine-4-carbaldehyde **1a$_{28}$** (106 mg, 1.0 mmol, 1.0 equiv.) afforded pyridine-4-ylmethanol **2a$_{28}$** (96 mg, 88%) as a colorless liquid. ^{1}H NMR (400 MHz, DMSO-d$_6$): 4.48 (2H, d, *J* = 6.1 Hz), 5.38 (1H, t, *J* = 6.1 Hz), 7.27 (2H, d, *J* = 4.9 Hz), 8.46 (2H, d, *J* = 4.9 Hz); ^{13}C (100 MHz, DMSO-d$_6$): 61.4, 121.1, 149.3, 151.5; HRMS (ESI) calcd for $C_6H_7NO[M+H]^+$: 110.0528; Found: 110.0526.

Thiazol-2-ylmethanol (2a$_{29}$):[25] Following **GP-I**, thiazole-2-carbaldehyde **1a$_{29}$** (112 mg, 1.0 mmol, 1.0 equiv.) afforded thiazol-2-ylmethanol **2a$_{29}$** (104 mg, 91%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d$_6$): 4.64 (2H, d, *J* = 5.9 Hz), 5.9 (1H, t, *J* = 5.9 Hz), 7.55 (1H, d, *J* = 3.4 Hz), 8 (1H, d, *J* = 3.4 Hz); ^{13}C (100 MHz, DMSO-d$_6$): 60.9, 119.5, 142.3, 173.7; HRMS (ESI) calcd for $C_4H_5NOS[M+H]^+$: 116.0092; Found: 116.0090.

Furan-2-ylmethanol (2a$_{30}$):[6b] Following **GP-I**, furan-2-carbaldehyde **1a$_{30}$** (96 mg, 1.0 mmol, 1.0 equiv.) afforded furan-2-ylmethanol **2a$_{30}$** (88 mg, 90%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d$_6$): 4.64 (2H, d, *J* = 5.9 Hz), 5.9 (1H, t, *J* = 5.9 Hz), 7.55 (1H, d, *J* = 3.4 Hz), 8 (1H, d, *J* = 3.4 Hz); ^{13}C (100 MHz, DMSO-d$_6$): 55.7, 106.9, 110.3, 142.1, 155.5; HRMS (ESI) calcd for $C_5H_6O_2[M+H]^+$: 99.0368; Found: 99.0367.

9-(3-(Dimethylamino)propyl)-6-(hydroxymethyl)-9H-carbazole-3-carbaldehyde (2a$_{31}$): Following **GP-I**, 9-(3-(dimethylamino)propyl)-9H-carbazole-3,6-dicarbaldehyde **1a$_{31}$** (308 mg, 1.0 mmol, 1.0 equiv.) afforded 9-(3-(dimethylamino)propyl)-6-(hydroxymethyl)-9H-carbazole-3-carbaldehyde **2a$_{31}$** (304 mg, 98%) as a pale yellow liquid. ^{1}H NMR (400 MHz, DMSO-d$_6$): 1.92 (2H, t, *J* = 6.8 Hz), 2.12 (6H, s) 2.19 (2H, t, *J* = 6.7 Hz), 4.80 (2H, t, *J* = 6.7 Hz), 4.68 (2H, s), 5.22 (1H, br s), 7.51 (1H, d, *J* = 8.4 Hz), 7.66 (2H, d, *J* = 8.4 Hz), 7.76 (1H, d, *J* = 8.4 Hz), 7.98 (1H,d, *J* = 10.1 Hz), 8.21 (1H, s), 8.74(1H, s), 10.06 (1H, s); ^{13}C (100 MHz, DMSO-d$_6$): 26.3, 40.5, 45.0, 55.8, 63.3, 109.7, 109.8, 118.1, 122.0, 122.2, 124.1, 126.0, 126.2, 128.2, 134.6, 140.0, 143.8, 191.8; HRMS (ESI) calcd for $C_{19}H_{22}N_2O_2[M+H]^+$: 311.1681; Found: 311.1682.

(9-(3-(dimethylamino)propyl)-9H-carbazole-3,6-diyl)dimethanol (2a$_{32}$): Following **GP-I**, 9-(3-(dimethylamino)propyl)-9H-carbazole-3,6-dicarbaldehyde **1a$_{31}$** (308 mg, 1.0 mmol, 1.0 equiv.) afforded (9-(3-(dimethylamino)propyl)-9H-carbazole-3,6-diyl)dimethanol **2a$_{32}$** (294 mg, 90%) as a pale yellow liquid. ^{1}H NMR (400 MHz, DMSO-d$_6$): 1.92 (2H, t, *J* = 6.8 Hz), 2.15 (6H, s), 2.19 (2H, t, *J* = 6.8 Hz), 4.42 (2H, t, *J* = 6.4 Hz), 4.75 (4H, d, *J* = 3.0 Hz), 5.27 (2H, br s), 7.48 (2H, d, *J* = 9.3 Hz), 7.57 (2H, d, *J* = 8.3 Hz), 8.15 (2H, s); ^{13}C (100 MHz, DMSO-d$_6$): 26.5, 39.3, 45.0, 56.0, 63.6, 108.7, 118.4, 121.9, 125.0, 126.2, 132.9, 139.6; HRMS (ESI) calcd for $C_{19}H_{24}N_2O_2[M+H]^+$: 313.1838; Found: 313.1838.

(*R*)-3-(1-benzyl-1H-indol-3-yl)butan-1-ol (2a$_{33}$): Following **GP-I**, (*R*)-3-(1-benzyl-1H-indol-3-yl)butanal **1a$_{32}$** (276 mg, 1.0 mmol, 1.0 equiv.) afforded (*R*)-3-(1-benzyl-1H-indol-3-yl)butan-1-ol **2a$_{33}$** (256 mg, 92%) as a brown liquid. ^{1}H NMR (500 MHz, $CDCl_3$): 1.40 (3H, d, *J* = 6.7 Hz), 1.96-1.92 (1H, m), 2.08-2.03 (1H, m), 3.26-3.22 (1H, m), 3.70-3.66 (2H, m), 5.28 (2H, s), 6.92 (1H, s), 7.13-7.10 (3H, m), 7.17 (1H, t, *J* = 6.7 Hz), 7.31-7.25 (4H, m), 7.68 (1H, d, *J* = 8.4 Hz); ^{13}C (125 MHz, $CDCl_3$): 22.0, 27.9, 40.6, 50.0, 61.8, 109.9, 119.0, 119.7, 121.1, 121.9, 124.5, 126.8, 127.5, 127.7, 128.9, 137.1, 137.9; HRMS (ESI) calcd for $C_{19}H_{21}NO[M+H]^+$: 280.1623; Found: 280.1622.

***Trans*-cinnamyl alcohol (2a$_{34}$):**[6f] Following **GP-I**, *trans*-cinnamaldehyde **1a$_{33}$** (132 mg, 1.0 mmol, 1.0 equiv.) afforded *trans*-cinnamyl alcohol **2a$_{34}$** (130 mg, 98%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d$_6$): 4.06-4.09 (2H, m), 4.82 (1H, t, *J* = 5.5 Hz), 6.30-6.36 (1H, m), 6.51 (1H, d, *J* = 15.8 Hz), 7.18 (1H, t, *J* = 7.32 Hz), 7.28 (2H, t, *J* = 7.3 Hz), 7.37 (2H, d, *J* = 7.3 Hz); ^{13}C (100 MHz, DMSO-d$_6$): 61.4, 126.0, 127.1, 128.4, 128.3, 130.7, 136.9; HRMS (ESI) calcd for $C_9H_{10}O[M+H]^+$: 135.0732; Found: 135.0736.

(3-phenyloxiran-2-yl)methanol (2a$_{35}$):[6f] Following **GP-I**, 3-phenyloxirane-2-carbaldehyde **1a$_{34}$** (148 mg, 1.0 mmol, 1.0 equiv.) afforded (3-phenyloxiran-2-yl)methanol **2a$_{35}$** (140 mg, 92%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): 2.67 (1H, br s), 3.23-3.21 (1H, m), 3.76 (1H, d, *J* = 11.2 Hz), 3.91 (1H, d, *J* = 2.0 Hz), 4.02 (1H, d, *J* = 12.7 Hz), 7.36-7.25 (5H, m); ^{13}C (100 MHz, $CDCl_3$): 55.8, 61.4, 62.7, 125.8, 128.4, 128.6, 136.7;

HRMS (ESI) calcd for $C_9H_{10}O_2[M+H]^+$: 151.0681; Found: 151.0680.

Cyclohex-3-en-1-ylmethanol (2a$_{36}$):[26] Following **GP-I**, 3-cyclohexenecarbaxaldehyde **1a$_{35}$** (110 mg, 1.0 mmol, 1.0 equiv.) afforded cyclohex-3-en-1-ylmethanol **2a$_{36}$** (88 mg, 78%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): 1.23-1.15 (1H, m), 1.70-1.62 (2H, m), 1.78-1.75 (1H, m), 2.06-1.98 (3H, m), 3.34-3.29 (2H, m), 4.52 (1H, t, *J* = 5.0 Hz), 5.66 (2H, s); ^{13}C(100 MHz, $CDCl_3$): 24.3, 25.1, 27.9, 36.1, 65.8, 126.3, 126.9; HRMS (ESI) calcd for $C_7H_{12}O[M+H]^+$: 113.1045; Found: 113.1044.

Cyclohexylmethanol (2a$_{37}$):[6f] Following **GP-I**, cyclohexanecarbaxaldehyde **1a$_{36}$** (112 mg, 1.0 mmol, 1.0 equiv.) afforded cyclohexylmethanol **2a$_{37}$** (88 mg, 78%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): 0.87-0.95 (2H, m), 1.11-1.28 (3H, m), 1.43-1.50 (1H, m), 1.65-1.75 (5H, m), 2.0 (1H, t, *J* = 11.4 Hz), 3.40 (2H, d, *J* = 3.3 Hz); ^{13}C(100 MHz, $CDCl_3$): 26.1, 26.8, 29.8, 40.7, 68.9; HRMS (ESI) calcd for $C_7H_{14}O[M+H]^+$: 115.1045; Found: 115.1042.

Ethanol (2a$_{38}$): Following **GP-I**, acetaldehyde **1a$_{37}$** (44 mg, 1.0 mmol, 1.0 equiv.) afforded ethanol **2a$_{38}$** (38 mg, 84%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): 0.85 (3H, t, *J* = 6.9 Hz), 3.28-3.33 (2H, m), 4.60 (1H, t, *J* = 4.4 Hz); ^{13}C (125 MHz, $CDCl_3$): 17.5, 57.1; HRMS (ESI) calcd for $C_2H_6O[M+H]^+$: 47.0419; Found: 47.0416.

Hexan-1-ol (2a$_{39}$):[6b] Following **GP-I**, hexanal **1a$_{38}$** (100 mg, 1.0 mmol, 1.0 equiv.) afforded hexanol **2a$_{39}$** (82 mg, 80%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 0.87-0.85 (3H, m), 1.30-1.22 (6H, m), 1.43-1.37 (2H, m), 3.39-3.35 (2H, m), 4.31 (1H, t, *J* = 5.7 Hz); ^{13}C (100 MHz, DMSO-d_6): 13.8, 22.1, 25.2, 31.2, 32.5, 60.7; HRMS (ESI) calcd for $C_6H_{14}O[M+H]^+$: 103.1045; Found: 103.1039.

1-Phenylethanol (5a):[6e] Following **GP-II**, acetophenone **4a** (120 mg, 1.0 mmol, 1.0 equiv.) afforded 1-phenylethanol **5a** (92 mg, 75%) as a colorless liquid. ^{1}H NMR (400 MHz, DMSO-d_6): 1.29 (3H, d, *J* = 6.7 Hz), 4..70 (1H, t, *J* = 4.9 Hz), 5.12 (1H, d, *J* = 3.6 Hz), 7.16 (1H, t, *J* = 6.7 Hz), 7.33-7.25 (4H, m); ^{13}C (100 MHz, DMSO-d_6): 25.9, 68.2, 125.3, 126.5, 127.9, 147.4; HRMS (ESI) calcd for $C_8H_{10}O[M+H]^+$: 123.0732; Found: 123.0730.

1-(*p*-Tolyl)ethanol (5b):[27] Following **GP-II**, 4-methylacetophenone **4b** (134 mg, 1.0 mmol, 1.0 equiv.) afforded 1-(*p*-tolyl)ethanol **5b** (100 mg, 73%) as a pale yellow liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 1.20 (3H, t, *J* = 3.8 Hz), 2.15 (3H, s), 4.55-4.59 (1H, m), 4.95 (1H, d, *J* = 4.4 Hz), 6.97 (2H, d, *J* = 7.6 Hz), 7.10 (2H, d, *J* = 7.6 Hz); ^{13}C (100 MHz, DMSO-d_6): 20.6, 25.9, 67.9, 125.2, 128.5, 135.4, 143.4; HRMS (ESI) calcd for $C_9H_{12}O[M+H]^+$: 137.0888; Found: 137.0884.

1-(4-Bromophenyl)ethanol (5c):[6d] Following **GP-II**, 4-bromoacetophenone **4c** (200 mg, 1.0 mmol, 1.0 equiv.) afforded 1-(4-bromophenyl)ethanol **5c** (164 mg, 82%) as a straw yellow liquid. ^{1}H NMR (400 MHz, DMSO-d_6): 1.22 (3H, d, *J* = 6.7 Hz), 4.62-4.65 (1H, m), 5.16 (1H, d, *J* = 4.3 Hz), 7.22 (2H, d, *J* = 8.5 Hz), 7.41 (2H, dd, *J* = 1.8, 6.9 Hz); ^{13}C (100 MHz, DMSO-d_6): 25.7, 67.4, 119.3, 127.5, 130.8, 146.7; HRMS (ESI) calcd for $C_8H_9BrO[M+H]^+$: 200.9837; Found: 200.9834.

4-(1-Hydroxyethyl)phenol (5d):[28] Following **GP-II**, 4-hydroxyacetophenone **4d** (136 mg, 1.0 mmol, 1.0 equiv.) afforded 4-(1-hydroxyethyl)phenol **5d** (106 mg, 77%) as a colorless liquid. ^{1}H NMR (400 MHz, DMSO-d_6): 1.21 (3H, d, *J* = 6.1 Hz), 4.52-4.56 (1H, m), 4.85 (1H, d, *J* = 3.6 Hz), 6.63 (2H, dd, *J* = 1.8, 6.7 Hz), 7.06 (2H, t, *J* = 7.9 Hz), 9.12 (1H, s); ^{13}C (125 MHz, DMSO-d_6): 25.9, 67.7, 114.6, 126.4, 137.6, 159.9; HRMS (ESI) calcd for $C_8H_{10}O_2[M+H]^+$: 139.0681; Found: 139.0679.

1-(4-Methoxyphenyl)ethanol (5e):[6e] Following **GP-II**, 4-methoxyacetophenone **4e** (150 mg, 1.0 mmol, 1.0 equiv.) afforded 1-(4-methoxyphenyl)ethanol **5e** (112 mg, 74%) as a colorless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 1.23 (3H, d, *J* = 5.9 Hz), 3.65 (3H, d, *J* = 10.0 Hz), 4.60 (1H, d, *J* = 3.4 Hz), 4.94 (1H, d, *J* = 2.5 Hz), 6.78 (2H, t, *J* = 5.0 Hz), 7.17 (2H, t, *J* = 5.0 Hz); ^{13}C (100 MHz, DMSO-d_6): 25.9, 55.0, 67.7, 113.3, 126.4, 139.4, 158.0;HRMS (ESI) calcd for $C_9H_{12}O_2[M+H]^+$: 153.0837; Found: 153.0834.

1-(4-aminophenyl)ethanol (5f):[6e] Following **GP-II**, 4-aminoacetophenone **4f** (135 mg, 1.0 mmol, 1.0 equiv.) afforded 1-(4-aminophenyl)ethanol **5f** (114 mg, 80%) as a deep brown liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 1.26 (3H, d, *J* = 5.9 Hz), 4.57-4.52 (1H, m), 4.79 (1H, d, *J* = 2.5 Hz), 4.87 (2H, br s), 6.50 (2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.4 Hz); ^{13}C (125 MHz, DMSO-d_6): 25.8, 67.9, 113.5, 126.0, 134.6, 147.2; HRMS (ESI) calcd for $C_8H_{11}NO$ $[M+H]^+$: 138.0841; Found: 138.0843.

2,2,2-trifluoro-1-phenylethanol (5g):[6e] Following **GP-II**, 2,2,2-trifluoro acetophenone **4g** (174 mg, 1.0 mmol, 1.0 equiv.) afforded 2,2,2-trifluoro-1-phenylethanol **5g** (152 mg, 84%) as a colorless liquid. ^{1}H NMR (400 MHz, DMSO-d_6): 5.17 (1H, q, *J* = 7.3 Hz), 7.44-7.38 (3H, m), 7.54 (2H, d, *J* = 6.7 Hz); ^{13}C (100 MHz, DMSO-d_6): 70.4, 70.7, 71.0, 71.3, 123.8, 126.7, 127.7, 128.3, 128.9, 136.1; HRMS (ESI) calcd for $C_8H_7F_3O[M+H]^+$: 177.0449; Found: 177.0450.

Diphenylmethanol (5h):[6j] Following **GP-II**, benzophenone **4h** (182 mg, 1.0 mmol, 1.0 equiv.) afforded diphenylmethanol **5f** (175 mg, 95%) as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6): 5.64 (1H, d, *J* = 6.9 Hz), 5.81 (1H, d, *J* = 3.8 Hz), 7.15-7.12 (2H, m), 7.25-7.22 (2H, m), 7.31 (4H, d, *J* = 6.9 Hz); ^{13}C (100 MHz, DMSO-d_6): 74.2, 126.2, 126.6, 128.0, 145.7; HRMS (ESI) calcd for $C_{13}H_{12}O[M+H]^+$: 185.0888; Found: 185.0886.

1,2-Diphenylpent-4-ene-1,2-diol (5i):[29] Following **GP-II**, **4i** (252 mg, 1.0 mmol, 1.0 equiv.) afforded 1,2-diphenylpent-4-ene-1,2-diol **5g** (204 mg, 80%) as a white solid. ^{1}H NMR of *syn* isomer (400 MHz, $CDCl_3$): 2.53 (2H, br s), 2.76 (1H, dd, *J* = 4.9, 9.2 Hz), 2.94 (1H, dd, *J* = 5.5, 8.7 Hz), 4.79 (1H, s), 5.09 (1H, d, *J* = 10.3 Hz), 5.17 (1H, d, *J* = 17.1 Hz), 5.63-5.52 (1H, m), 6.99 (2H, dd, *J* = 1.2, 6.1 Hz), 7.21-7.12 (8H, m); ^{13}C of *syn* isomer (100 MHz, $CDCl_3$): 42.7, 78.5, 80.6, 119.9, 126.7, 127.0, 127.6, 127.7, 127.9, 128.8, 133.5, 139.5, 141.7;HRMS (ESI) calcd for $C_{17}H_{18}O_2$ $[M+H]^+$: 255.1307; Found: 255.1309.

1,2-Diphenylethane-1,2–diol (5j):[10c] Following **GP-II**, 2-hydroxy-1,2-diphenylethanone **4j** (212 mg, 1.0 mmol, 1.0 equiv.) afforded 1,2-diphenylethane-1,2 –diol **5j** (184 mg, 86%) as a white solid.^{1}H NMR of *dl* isomer (500 MHz, DMSO-d_6): 4.57 (2H, d, *J* = 1.3 Hz), 5.19 (2H, d, *J* = 1.2 Hz), 7.24-7.18 (10H, m); ^{13}C *dl* isomer (100 MHz, DMSO-d_6): 76.9, 126.5, 127.2, 127.3, 143.2; HRMS (ESI) calcd for $C_{14}H_{14}O_2$ $[M+H]^+$: 215.0994; Found: 215.0991.

1,2-Diphenylethane-1,2–diol (5j):[10c] Following **GP-II**, benzil **4k** (210 mg, 1.0 mmol, 1.0 equiv.) afforded 1,2-diphenylethane-1,2-diol **5j** (176 mg, 82%) as a white solid.

(*E*)-1,3-diphenylprop-2-en-1-ol (5k): Following **GP-II**, (*E*)-chalcone **4l** (208 mg, 1.0 mmol, 1.0 equiv.) afforded (*E*)-1,3-diphenylprop-2-en-1-ol **5k** (194 mg, 86%) as a white solid.^{1}H NMR (400 MHz, DMSO-d_6): 5.25 (1H, t, *J* = 5.5 Hz), 5.62 (1H, d, *J* = 4.2 Hz), 6.39 (1H, dd, *J* = 6.1, 9.8 Hz), 6.63 (1H, d, *J* = 15.9 Hz), 7.24 (2H, dd, *J* = 7.9, 8.0 Hz), 7.36-7.29 (4H, m), 7.41 (4H, t, *J* = 6.70 Hz); ^{13}C (100 MHz, DMSO-d_6): 73.1, 126.1, 126.2, 126.8, 126.7, 128.1, 128.5, 133.6, 136.6, 144.4; HRMS (ESI) calcd for $C_{15}H_{14}O$ $[M+H]^+$: 211.1045; Found: 211.1044.

Phenyl(3-phenyloxiran-2-yl)methanol (5l): Following **GP-II**, phenyl(3-phenyloxiran-2-yl)methanone **4m** (224 mg, 1.0 mmol, 1.0 equiv.) afforded phenyl(3-phenyloxiran-2-yl)methanol **5l** (208 mg, 88%) as a colourless liquid. ^{1}H NMR (500 MHz, DMSO-d_6): 2.66 (1H, br s), 3.31-3.29 (1H, m), 4.01 (1H, d, *J* = 2.0 Hz), 4.72 (1H, s), 7.25 (2H, d, *J* = 7.3 Hz), 7.35-7.29 (4H, m), 7.38 (2H, t, *J* = 6.9 Hz), 7.43 (2H, t, *J* = 7.4 Hz) ; ^{13}C (100 MHz, DMSO-d_6): 57.0, 65.8, 73.5, 125.9, 126.3, 126.7, 128.4, 128.5, 128.7, 128.9, 136.5, 140.3; HRMS (ESI) calcd for $C_{15}H_{14}O_2$ $[M+H]^+$: 227.0994; Found: 227.0993.

1-(Pyridin-2-yl)ethanol (5m):[27] Following **GP-II**, 2-acetylpyridine **4n** (120 mg, 1.0 mmol, 1.0 equiv.) afforded 1-(pyridin-2-yl)ethanol **5m** (98 mg, 80%) as a pale yellow liquid. ^{1}H NMR (400 MHz, DMSO-d_6): 1.44 (3H, d, *J* = 6.7 Hz), 4.85-4.79 (1H, m), 5.46 (1H, d, *J* = 4.3 Hz), 7.31-7.28 (1H, m), 7.60 (1H, d, *J* = 7.9 Hz), 7.86-7.82 (1H, m), 8.55-8.54 (1H, m); ^{13}C (100 MHz, DMSO-d_6): 24.2, 69.4, 119.3, 121.8, 136.6, 148.2, 165.6; HRMS (ESI) calcd for $C_7H_9NO[M+H]^+$: 124.0684; Found: 124.0680.

Ethyl 3-hydroxybutanoate (5n): Following **GP-II**, ethyl 3-oxobutanoate **4o** (130 mg, 1.0 mmol, 1.0 equiv.) afforded ethyl 3-hydroxybutanoate **5n** (104 mg, 74%) as a colorless liquid. ^{1}H NMR (400 MHz, DMSO-d_6): 1.00 (3H, d, *J* = 6.1 Hz), 1.09 (3H, t, *J* = 6.7 Hz), 2.25 (2H, t, *J* = 7.9 Hz), 3.49 (1H, s), 3.98-3.90 (2H, m), 4.63 (1H, d, *J* = 4.9 Hz); ^{13}C (125 MHz, DMSO-d_6): 14.1, 22.3, 43.9, 59.6, 63.4, 171.1; HRMS (ESI) calcd for $C_6H_{12}O_3[M+H]^+$: 133.0786; Found: 133.0788.

Cyclohexanol (5o):[6e] Following **GP-II**, cyclohexanone **4p** (98 mg, 1.0 mmol, 1.0 equiv.) afforded cyclohexanol **5o** (74 mg, 74%) as a colorless liquid.^{1}H NMR (500 MHz, $CDCl_3$): 0.97-1.11 (5H, m), 1.35 (1H, t, *J* = 4.2 Hz), 1.55 (2H, s), 1.70 (2H, s), 3.37 (1H, s), 3.74 (1H, br s); ^{13}C (125 MHz, $CDCl_3$): 24.0, 25.3, 35.1, 69.6; HRMS (ESI) calcd for $C_6H_{12}O[M+H]^+$: 101.0888; Found: 101.0883.

Cyclopentanol (5p):[30] Following **GP-II**, cyclopentanone **4q** (84 mg, 1.0 mmol, 1.0 equiv.) afforded cyclopentanol **5p** (64 mg, 74%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): 1.46-1.50 (4H, m), 1.66 (4H, t, *J* = 1.9 Hz), 2.89-3.04 (1H, m), 4.19 (1H, br s); ^{13}C (100 MHz, $CDCl_3$): 23.2, 35.3, 73.6; HRMS (ESI) calcd for $C_5H_{10}O[M+H]^+$: 87.0732; Found: 87.0728.

Propan-2-ol (5q): Following **GP-II**, acetone **4r** (60 mg, 0.50 mmol, 1.0 equiv.) afforded Propan-2-ol **5q** (44 mg, 72%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): 1.0-1.05 (6H, m), 3.31-3.68 (1H, m), 3.83 (1H, br s); ^{13}C (100 MHz, $CDCl_3$): 25.0, 63.7; HRMS (ESI) calcd for C_3H_8O $[M+H]^+$: 61.0575; Found: 61.0574.

2,3-Diphenylbutane-2,3-diol (6a):[9] Following **GP-II**, acetophenone **4a** (120 mg, 1.0 mmol, 1.0 equiv.) afforded 2,3-diphenylbutane-2,3-diol **6a** (54 mg, 23%) as a white solid. ^{1}H NMR (*dl/meso, 60:40* ratio) (500 MHz, $CDCl_3$): 1.49 (6H, s), 1.57 (6H, s), 2.33 (2H, s), 2.64 (2H, s), 7.17-7.25 (20H, m); ^{13}C (*dl/meso, 60:40* ratio) (100 MHz, $CDCl_3$): 25.1, 25.2, 78.7, 78.9, 127.5, 127.4, 127.3, 127.2, 127.1, 127.0, 143.6, 143.9; HRMS (ESI) calcd for $C_{16}H_{18}O_2[M+H]^+$: 243.1207; Found: 243.1205.

2,3-Di-p-tolylbutane-2,3-diol (6b):[9] Following **GP-II**, 4-methylacetophenone **4b** (134 mg, 1.0 mmol, 1.0 equiv.) afforded 2,3-di-p-tolylbutane-2,3-diol **6b** (70 mg, 26%) as a white solid. ^{1}H NMR (*dl/meso, 60:40* ratio) (500 MHz, $CDCl_3$): 1.46 (6H, s), 1.53 (6H, s), 2.32 (12H, d, *J* = 6.7 Hz), 2.23 (2H, br s), 2.58 (2H, br s), 7.09-7.04 (14H, m), 7.14 (2H, d, *J* = 7.6 Hz); ^{13}C (*dl/meso, 60:40* ratio) (100 MHz, $CDCl_3$): 21.0, 21.1, 25.2, 25.4, 78.7, 78.9, 127.0, 127.4, 128.0, 128.1, 136.5, 136.7, 140.7, 141.1; HRMS (ESI) calcd for $C_{18}H_{22}O_2$ $[M+H]^+$: 271.1620; Found: 271.1618.

1-(4-(Hydroxymethyl)phenyl)ethanone (8):[6h] Following **GP-I**, 4-acetylbenzaldehyde **7** (148 mg, 1.0 mmol, 1.0 equiv.) afforded 1-(4-(hydroxymethyl)phenyl)ethanone **8** (144 mg, 96%) as a colorless liquid. ^{1}H NMR (300 MHz, DMSO-d_6): 2.52 (3H, s) 4.53 (2H, d, *J* = 5.9 Hz), 5.32 (1H, t, *J* = 5.9 Hz), 7.41 (2H, d, *J* = 8.1 Hz), 7.87 (2H, dd, *J* = 1.8, 4.4 Hz); ^{13}C (125 MHz, DMSO-d_6): 26.7, 62.5, 126.3, 128.2, 135.5, 148.2, 197.6; HRMS (ESI) calcd for $C_9H_{10}O_2$ $[M+H]^+$: 151.0681; Found: 151.0684

1-(4-(Hydroxymethyl)phenyl)ethanol (9):[31] Following **GP-II**, 4-acetylbenzaldehyde **7** (148 mg, 1.0 mmol, 1.0 equiv.) afforded 1-(4-(hydroxymethyl)phenyl)ethanol **9** (124 mg, 82%) as a brown liquid. ^{1}H NMR (400 MHz, DMSO-d_6): 1.13 (3H, d, *J* = 6.1 Hz), 4.29 (2H, d, *J* = 5.9 Hz), 4.49-4.51 (1H, m), 4.92-4.96 (2H, m), 7.08 (4H, dd, *J* = 8.0, 7.9 Hz); ^{13}C (100 MHz, DMSO-d_6): 26.1, 63.0, 68.1, 125.1, 126.3, 140.8, 145.9; HRMS (ESI) calcd for $C_9H_{12}O_2$ $[M+H]^+$: 153.0837; Found: 153.0835.

1-(4-(Hydroxymethyl)phenyl)ethanol (9):[31] Following **GP-II**, 1-(4-(hydroxymethyl)phenyl)ethanone **8** (150 mg, 1.0 mmol, 1.0 equiv.) afforded 1-(4-(hydroxymethyl)phenyl)ethanol **9** (130 mg, 86%) as a brown liquid.

3-Hydroxyindolin-2-one (11a):[18b] Following **GP-III**, isatin **10a** (148 mg, 1.0 mmol, 1.0 equiv.) afforded 3-hydroxyindolin-2-one **11a** (140 mg, 94%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): 3.18(1H, br s), 5.08 (1H, s), 6.86 (1H, d, *J* = 7.6 Hz), 7.09 (1H, t, *J* = 7.5 Hz), 7.28 (1H, d, *J* = 7.6 Hz), 7.44 (1H, d, *J* = 6.9 Hz); ^{13}C (100 MHz, $CDCl_3$): 70.3, 110.4, 123.5, 125.8, 130.2, 138.8, 141.1, 178.4; HRMS (ESI) calcd for $C_8H_7NO_2$ $[M+H]^+$: 150.0477; Found: 150.0467.

3-Hydroxy-1-methylindolin-2-one (11b):[18b] Following **GP-III**, N-methyl isatin **10b** (160 mg, 1.0 mmol, 1.0 equiv.) afforded 3-hydroxy-1-methylindolin-2-one **11b** (160 mg, 98%) as a pale yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6): 2.98 (3H, s), 4.80 (1H, d, *J* = 7.6 Hz), 6.15 (1H, d, *J* = 7.1 Hz), 6.84 (1H, d, *J* = 7.6 Hz), 6.95 (1H, t, *J* = 6.7 Hz), 7.25-7.19 (2H, m); ^{13}C (100 MHz, DMSO-d_6): 25.7, 68.7, 108.3, 122.1, 124.4, 128.5, 129.0, 143.7, 175.9; HRMS (ESI) calcd for $C_9H_9NO_2$ $[M+H]^+$: 164.0633; Found: 164.0631.

1-Benzyl-5-chloro-3-hydroxyindolin-2-one (11c): Following **GP-III**, 5-chloro-N-benzyl isatin **10c** (270 mg, 1.0 mmol, 1.0 equiv.) afforded 1-benzyl-5-chloro-3-hydroxyindolin-2-one **11c** (268 mg, 98%) as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6): 4.80 (2H, s), 5.05 (1H, d, *J* = 7.6 Hz), 6.48 (1H, d, *J* = 7.6 Hz), 6.79 (1H, d, *J* = 7.5 Hz), 7.28-7.16 (6H, m), 7.33 (1H, s); ^{13}C (125 MHz, DMSO-d_6): 42.6, 68.7, 110.5, 124.2, 126.6, 126.9, 127.2, 127.4, 128.7, 130.8, 135.9, 141.5, 175.8; HRMS (ESI) calcd for $C_{15}H_{12}ClNO_2$ $[M+H]^+$: 274.0557; Found: 274.0564.

1-Benzyl-5-fluoro-3-hydroxyindoline-2-one (11d): Following **GP-III**, 5-fluoro-N-benzyl isatin **10d** (254 mg, 1.0 mmol, 1.0 equiv.) afforded 1-benzyl-5-fluoro-3-hydroxyindolin-2-one **11d** (254 mg, 99%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): 4.79 (2H, dd, *J* = 15.2, 15.3 Hz), 5.23 (1H, s), 5.59 (1H, br s), 6.56 (1H, dd, *J* = 4.9, 3.7 Hz), 6.83 (1H, t, *J* = 9.1 Hz), 7.27-7.15 (6H, m); ^{13}C (125 MHz, $CDCl_3$): 44.0, 69.9, 110.1, 110.2, 113.3, 113.5, 115.6, 115.8, 117.0, 117.2, 127.0, 127.3, 127.7, 127.9, 128.8, 128.9, 129.1, 129.2, 134.5, 135.0, 138.6, 139.4, 158.4, 160.8, 177.6; HRMS (ESI) calcd for $C_{15}H_{10}FNO_2$ $[M+H]^+$: 258.0696; Found: 258.0698.

1-benzyl-5-(trifluoromethoxy)-3-hydroxyindoline-2-one (11e): Following **GP-III**, 5-trifluoromethoxy-N-benzyl isatin **10e** (320 mg, 1.0 mmol, 1.0 equiv.) afforded 1-benzyl-5-trifluoromethoxy-3-hydroxyindolin-2-one **11e** (310 mg, 96%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): 4.62 (1H, s), 4.79 (2H, dd, *J* = 15.8, 15.1 Hz), 5.12 (1H, s), 6.61 (1H, d, *J* = 8.4 Hz), 7.00 (1H, d, *J* = 8.4 Hz), 7.29-7.18 (6H, m); ^{13}C (125 MHz, $CDCl_3$): 44.2, 69.8, 110.2, 119.4, 123.0, 124.1, 127.2, 127.4, 127.8, 127.9, 128.2, 128.6, 128.7, 129.0, 129.1, 134.4, 134.9, 141.0, 141.6, 142.2, 145.4, 177.2; HRMS (ESI) calcd for $C_{16}H_{10}F_3NO_3$ $[M+H]^+$: 324.0613; Found: 324.0603.

Radical quenching experiment: To a stirring solution of 4-methylbenzaldehyde **1a$_1$** (1.0 mmol) in THF was added Zn dust (5.0 mmol), aqueous NH_4Cl solution (8 M) and TEMPO or Galvinoxyl (1 mmol) at the same time. The reaction mixture was stirred at room temperature for 30 min. No product formation was observed.

Acknowledgements ((optional))

We thank DST India for research funding. JD thanks DST for a SwarnaJayanti fellowship. TM and SJ thank CSIR-India for research fellowships.

Keywords: Aldehyde · Chemoselective · Isatin · Ketone · Reduction · Zn

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Layout 1:

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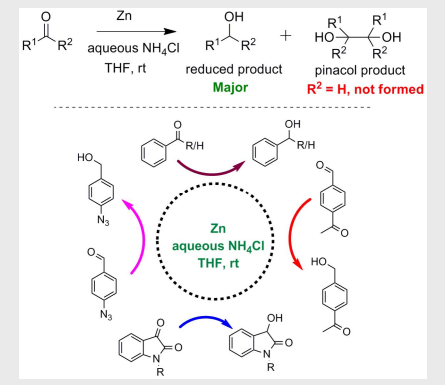
Simple yet unknown! Aldehydes and ketones can be easily reduced to the corresponding alcohols using Zn/NH_4Cl, which is used for pinacol coupling reactions. Chemoselective reduction of aldehydes in the presence of ketones is achieved. Isatins can be efficiently reduced at the C3 position.



Chemoselective reduction of carbonyl compounds*

*Tirtha Mandal, Snehasish Jana and Jyotirmayee Dash**

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Zinc-Mediated Efficient and Selective Reduction of Carbonyl Compounds