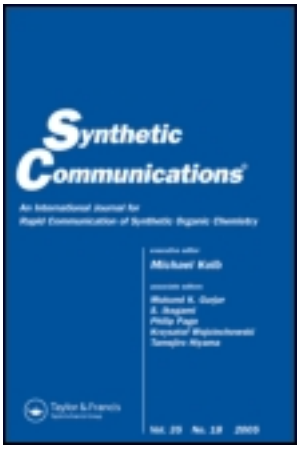

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Pankaj Gupta [a b], Abdul Rouf [a], Bhahwal A. Shah [a], Debaraj Mukherjee [a] & Subhash C. Taneja [a]

[a] Indian Institute of Integrative Medicine (CSIR), Jammu, India

[b] Department of Chemistry, Govt. Degree College, Kathua, J & K, India

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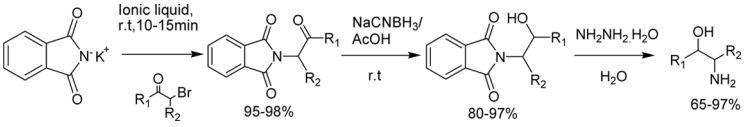
EFFICIENT PREPARATION OF BIOLOGICALLY IMPORTANT 1,2-AMINO ALCOHOLS

Pankaj Gupta,[1,2] Abdul Rouf,[1] Bhahwal A. Shah,[1] Debaraj Mukherjee,[1] and Subhash C. Taneja[1]

[1]*Indian Institute of Integrative Medicine (CSIR), Jammu, India*
[2]*Department of Chemistry, Govt. Degree College, Kathua, J & K, India*

GRAPHICAL ABSTRACT



Abstract *An efficient three-step methodology developed for the preparation of 1,2-amino alcohols. In the first step a rapid coupling between bromoketones and potassium phthalimide in ionic liquid produced α-phthalimido ketones in quantitative yields, which is followed by a facile reduction using $NaCNBH_3$ in acetic acid to give corresponding phthalimido alcohols and finally effecting hydrazinolysis in water at 60°C to yield biologically important 1,2-amino alcohols.*

Keywords β-Amino alcohols; hydrazinolysis; ionic liquid; $NaCNBH_3$; α-phthalimidoketones

INTRODUCTION

The β-amino alcohol moiety is a widespread structural motif in natural and synthetic biologically active molecules.[1] This can also be used as versatile chiral building block and chiral catalyst or ligand in a variety of asymmetric synthesis, such as enantioselective dialkylzinc addition to aldehydes[2] and in Henry reactions.[3] In view of their high requirements in organic synthesis, numerous methods have been reported for their preparation. Prominent among them are epoxide ring opening with an amine in the presence of catalysts,[4,5] selective reduction of oxazolidinones,[6] and intermolecular Pd-catalyzed aminoacetoxylation of alkenes with phthalimide.[7] The amino ketone reduction strategy is undoubtedly more attractive than epoxide ring opening, because it avoids the handling of the transition-metal catalysts.

The selective reduction of protected amino ketone derivatives is preferred because of their good stability.[8] However, their precursors (amino ketones) are difficult to isolate as free amines because of the formation of Schiff bases. One way of

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Address correspondence to Subhash C. Taneja, Indian Institute of Integrative Medicne (CSIR), Canal Road, Jammu 180001, India. E-mail: sctaneja@iiim.ac.in

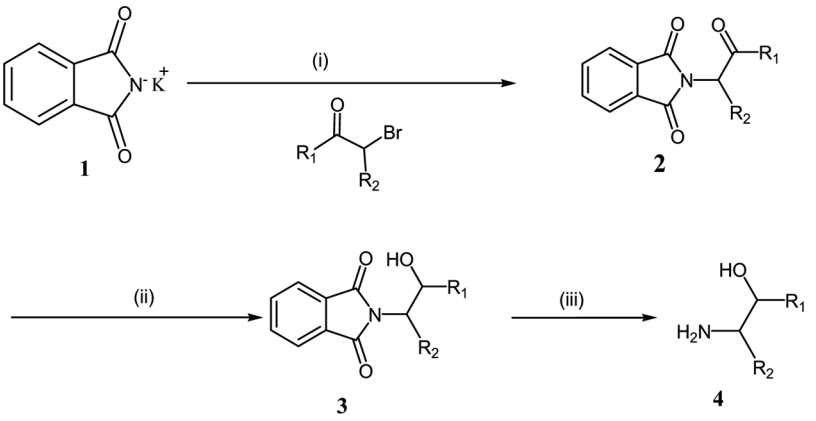
overcoming the difficulty of isolation is to protect the amino alcohols with a suitable protecting group such as phthalimide, which is a comparatively stable. Moreover, the phthalimide analogs are reported to have anti-inflammatory,[9] analgesic,[10] anticonvulsant,[11] herbicidal,[12] and insecticidal[13] activities.

Most of the methodologies used for the reduction of α-phthalimido ketones suffer from the formation of side products because of the labile phthalimide moiety. The hydride attack on the phthaloyl moiety leads to the formation of major side products during sodium borohydride reduction.[14] However, transition-metal catalysts at higher temperature and pressure may be used for this purpose.[15]

RESULTS AND DISCUSSION

Our three-step strategy for the preparation of 1,2-amino alcohols was initiated with the preparation of α-phthalimido ketones via coupling of α-bromoketones and potassium phthalimide in dimethylformamide (DMF) (Scheme 1).[15] The methodology required longer duration (~12 h) and the final yields in our hands varied between 70 and 85%. Therefore, the present strategy also envisaged the development of a more efficient method for preparation of α-phthalimido ketones. The improved methodology involves the coupling of bromoketones with potassium phthalimide in an ionic liquid (1-butyl-3-methylimidazoliumtetrafluoroborate) [bmim]PF4.[16]

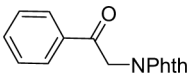
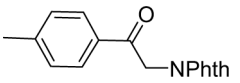
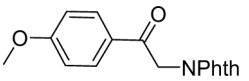
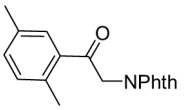
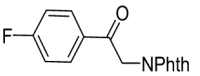
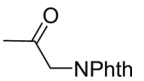
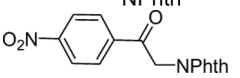
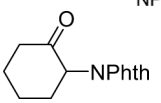
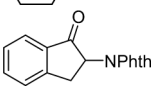
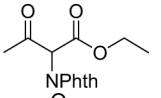
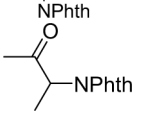
In this method the coupling reaction was completed within 10–15 min of stirring at room temperature (Scheme 1), and the product **2** was easily extracted in tetrehydrofuran (THF) in almost quantitative yield. The ionic liquid after washing and drying under vacuum could be reused for the reaction up to four to five cycles without any loss in activity (Table 1). The coupling reaction thus demonstrated the



a) R_1 = Phenyl, R_2 = H; b) R_1 = p-methyl-Phenyl, R_2 = H; c) R_1 = p-methoxy-Phenyl, R_2 = H; d) R_1 = 2,5-dimethyl-Phenyl, R_2 = H; e) R_1 = p-Fluoro-Phenyl, R_2 = H; f) R_1 = methyl, R_2 = H; g) R_1 = p-nitro-Phenyl, R_2 = H; h) $R_1 + R_2$ = -$CH_2CH_2CH_2CH_2$-; i) $R_1 + R_2$ = $C_6H_4CH_2$; j) R_1 = Me, R_2 = $COOCH_2CH_3$; k) R_1 = Me, R_2 = Me.

Scheme 1. Synthesis of 1,2-amino alcohols; Reagents and conditions: (i) ionic liquid [bmim]BF_4, rt, 10–15 min, >95%; (ii) method A: Pd/C hydrogenation, 40–50 psi; method B: $NaCNBH_3$ in acetic acid; method C: $NaCNBH_3$ in methanol at pH 4 (3 N HCl in MeOH); (iii) $NH_2NH_2{\cdot}H_2O$, H_2O, 60 °C.

Table 1. Coupling reaction using ionic liquid

Entry	Product **2** (reaction 1)	Y(%)/T (min)
a		95/15
b		97/12
c		96/13
d		97/15
e		98/12
f		95/15
g		97/13
h		95/14
i		96/15
j		95/14
k		96/14
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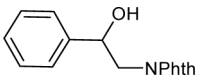
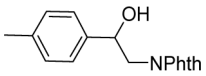
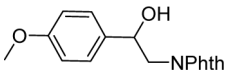
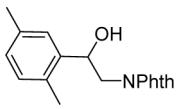
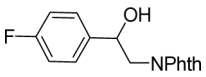
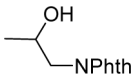
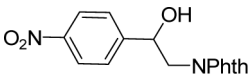
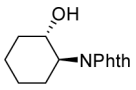
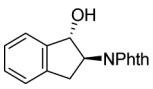
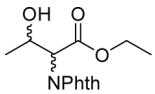
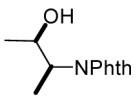
Notes. Phth, phthalimide; T (min), time in minutes; Y (%), isolated yield in %.

importance of ionic liquids as reusable reaction media for the rapid chemical transformations at ambient temperature.[17]

In the next step of reduction of carbonyl function, α-phthalimido ketones (2) were subjected to hydrogenation under Pd/C and hydrogen gas at high pressure (method A). However, this method was more applicable to the reduction of the carbonyl function in an activated aromatic ring only, whereas carbonyl compounds with deactivated aromatic rings including aliphatic ketones gave lower yields after

Table 2. Reaction conditions for the selective reduction of α-phthalimido ketones

		Method A		Method B		Method C	
Entry	Product (**3**) reaction 2	T (h)	Y (%)	T (h)	Y (%)	T (h)	Y (%)
a		10	95	24	95	60	ND
b		40	85	24	95	60	ND
c		48	90	24	96	60	ND
d		70	10	24	97	60	ND
e		70	10	24	96	60	ND
f		70	ND	24	92	60	85
g		12	ND	48	88	60	ND
h[a]		70	ND	36	90	60	75
i[a]		12	80	48	85	60	ND
j[b]		70	ND	48	80	60	ND
k[c]		70	ND	36	96	60	65

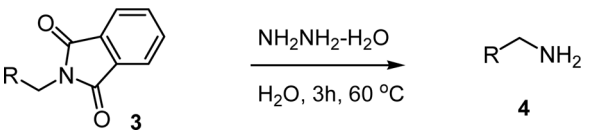
Notes. Phth, phthalimide; T (h), time in hours; Y (%), isolated yield in %; ND, not detected. The structures of the products were established from their spectral (^{1}H, ^{13}C NMR, and MS) and analytical data.

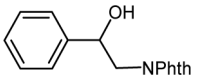
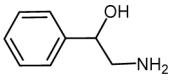
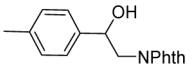
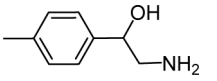
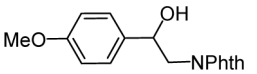
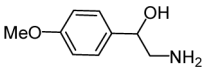
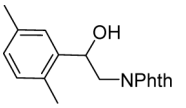
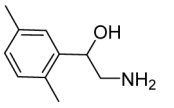
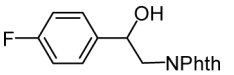
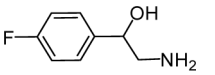
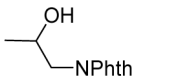
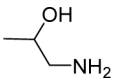
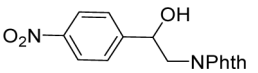
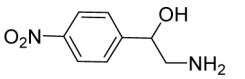
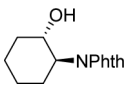
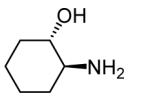
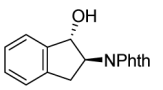
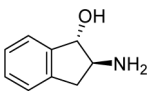
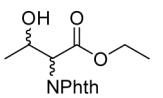
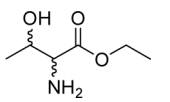
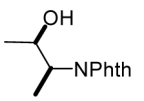
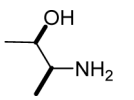
[a] *anti*/*syn* = > 99 (using NMR).

[b] *anti*/*syn* = 43:57.

[c] *anti*/*syn* = 1:1.

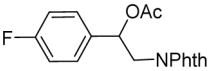
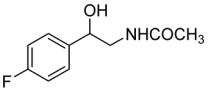
Table 3. Deprotection of phthalimides **3** to amines **4** by hydrazine hydrate



Entry	Substrate (**3**)	Product (**4**)	Time (h)	Yield (%)
a			3	97
b			3	95
c			3	90
d			3	93
e			3	95
f			3	40
g			3	95
h			3	65
i			3	96
j			3	60
k			3	55

(*Continued*)

Table 3. Continued

Entry	Substrate (**3**)	Product (**4**)	Time (h)	Yield (%)
1			3	94

2-eq. of hydrazine hydrate was used and yield mentioned was isolated yield; structures of the final products were confirmed by spectroscopic analysis.

a long reaction time. These problems were eliminated by opting for more effective reduction procedure using acetic acid and $NaCNBH_3$ for the reduction of α-phthalimido ketones (Table 2).

Earlier $NaCNBH_3$–acetic acid[18] and $NaCNBH_3$–TMSCl[19] combinations have been used to convert acyl to alkyl derivatives. In the present study it has been demonstrated that among other reducing agents used for α-phthalimido ketones, $NaCNBH_3$ in acetic acid (method B) (also a chemoselective reducing agent)[20] was found to be the most effective, whereas other mild reducing agents such as $NaBH_4$ and $Pd/C\text{-}H_2$ were not so successful. We also attempted to use the mild reducing system such as $NaCNBH_3$ in MeOH at pH 4, which gave lower yields of secondary alcohols yet proved to be highly chemoselective as it could reduce only a nonenolizable aliphatic carbonyl after a longer reaction time (2–3 days, method C), leaving aromatic ketones or enolizable ketones intact. Another interesting observation made during the use of method B was high diastereoselectivity (*anti*, 99%) of products in the case of cyclic amino alcohol intermediates (entries **3h** and **3i,** Table 2). However, poor diastereoselectivity was recorded during reduction of acyclic molecules (entries **3j** and **3k,** Table 2).

Despite the beneficial properties of phthalimide protection, removal of the phthaloyl group can often be problematic. Literature study revealed that generally deprotection of N-substituted phthalimides can be effected at elevated temperatures using large access of hydrazine hydrate,[21] butylamine,[22] hydroxylamine[23] or diamine[24] as amine bases in protic solvents. Over the years, many experimental procedures for phthalimido deprotection have been documented with different *N*-alkylphthalimide substrates, with variations in the molar proportions of amine bases, solvent, reaction temperature, time, and workup procedures (i.e., acid/alkaline conditions).[25]

Recently, interest has been emerging in organic reactions in water because of water's natural abundance and its environmental friendliness, using it as a sole reaction medium. Indeed, industry prefers to use water as a solvent rather than hazardous organic solvents, and therefore deprotection of N-substituted phthalimides under greener condition is desirable.

The present improved methodology involves stirring phthalimido derivatives **3** in water at moderately elevated temperature (60 °C) in the presence of 2 equivalent of hydrazine hydrate (Table 3). The products **4a–l** are easily isolated in 99% purity (NMR) simply by ethyl acetate extraction without any further column purification. The comparatively poor yields of **4f, 4h, 4j**, and **4k** can be attributed to the loss of

some free amino alcohols in the aqueous phase during workup. It is worth mentioning that during hydrazinolysis of compound **3l**, the initially formed free amine got acetylated probably because of in situ O-Ac to N-Ac migration[26] under basic conditions. The formation of N-acetyl derivative (**4l**) was confirmed by spectroscopic analysis.

CONCLUSIONS

In conclusion, an efficient three-step methodology for the preparation of 1,2-amino alcohols in good yields has been demonstrated that involved a rapid coupling between bromoketones and potassium phthalimide, followed by selective reduction using $NaCNBH_3$–acetic acid, and finally efficient removal of phthalimido protection in water at 60 °C.

EXPERIMENTAL

^{1}H NMR spectra in $CDCl_3$ were recorded on Bruker 200-MHz spectrometers with tetramethylsilane (TMS) as the internal standard. Chemical shifts were expressed in parts per million (δ ppm). Reagents and solvents used were mostly laboratory reagent (LR) grade. Silica gel–coated aluminum plates coated on alumina from M/s Merck were used for thin-layer chromatography (TLC). Mass Spectra (MS) were recorded on Jeol MSD-300 and Bruker Esquire 3000 GC-mass spectrometers. Infrared (IR) was recorded on a Fourier transform (FT)–IR Bruker (270-30) spectrophotometer. Melting points were determined on a Buchi B-542 apparatus by the open capillary method and are uncorrected.

α-Phthalimido Ketones

A mixture of potassium phthalimide (1.1 mmol) and bromo ketone (1 mmol) in a 10-mL conical flask was added to 1 mL ionic liquid [1-butyl-3-methylimidazolium tetrafluoroborate], and the resulting reaction mixture was stirred at room temperature for 10–15 min. The reaction mixture was extracted from the ionic liquid phase with tetrahydrofuran (THF) (2×5 mL). The organic layer was concentrated and evaporated under reduced pressure. The residue was purified by column chromatography to obtain the corresponding product. The ionic liquid left in the flask was further washed with ethylacetate, dried under vacuum, and reused in four to five subsequent reactions without loss in activity.

2-(2-Oxo-2-phenyl-ethyl)-isoindole-1,3-dione (2a) ($C_{16}H_{11}NO_3$). Pale yellow crystals; mp 168–170 °C; IR (KBr) cm^{-1}: 1419.8, 1914.1, 1962.3. ^{1}H NMR, δ: 5.14 (s, 2H, C*H*$_2$), 7.51–7.56 (m, 3H, Ar*H*), 7.74–7.78 (m, 2H, Ar*H*), 7.91–7.93 (m, 2H, Ar*H*), 8.00 (d, $J = 7.10$ Hz, 2H, Ar*H*). ^{13}C NMR, δ: 44.3, 123.6, 127.9, 128.2, 132.1, 133.9, 134.1, 134.5, 167.1, 191.1. ESI-MS (*m*/*z*): 265. Anal. calc. for $C_{16}H_{11}NO_3$: C, 72.45; H, 4.18; N, 5.28. Found: C, 72.48; H, 4.17; N, 5.26.

2-(2-Oxo-2-*p*-tolyl-ethyl)-isoindole-1,3-dione (2b) ($C_{17}H_{13}NO_3$). Yellow crystals; mp 184–186 °C. IR (KBr) cm^{-1}: 1416.7, 1689.4, 1725.4, 1775.5. ^{1}H NMR, δ: 2.44 (s, 3H, C*H*$_3$), 5.11 (s, 2H, C*H*$_2$), 7.26–7.33 (m, 2H, Ar*H*), 7.74–7.79

(m, 2H, Ar*H*), 7.86–7.93 (m, 4H, Ar*H*); ^{13}CNMR, δ: 20.8, 43.1, 123.5, 125.7, 128.2, 133.2, 134.1, 134.6, 145.0, 167.9, 187.4. ESI-MS (*m/z*): 279. Anal. calc. for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.13; H, 4.67; N, 5.06.

2-[2-(4-Methoxyphenyl)-2-oxo-ethyl]-isoindole-1,3-dione (2c) ($C_{17}H_{13}NO_4$). Pale yellow crystals; mp 164–168 °C; IR (KBr) cm^{-1}: 1420.7, 1600.2, 1716.3, 1773.5. ^{1}H NMR, δ: 3.90 (s, 3H, OC*H*$_3$), 5.08 (s, 2H, C*H*$_2$), 6.97 (d, $J = 8.9$ Hz, 2H, Ar*H*), 7.76–7.78 (m, 2H, Ar*H*), 7.86–7.93 (m, 2H, Ar*H*), 7.99 (d, $J = 8.9$ Hz, 2H, Ar*H*). ^{13}C NMR, δ: 42.9, 54.6, 113.1, 120.3, 125.5, 128.0, 132.7, 133.1, 163.8, 187.2. ESI-MS (*m/z*): 295. Anal. calc. for $C_{17}H_{13}NO_4$: C, 69.15; H, 4.44; N, 4.74. Found: C, 69.18; H, 4.47; N, 4.76.

2-[2-(2,5-Dimethyl-phenyl)-2-oxo-ethyl]-isoindole-1,3-dione (2d) ($C_{18}H_{15}NO_3$). White crystals, mp 145–147 °C; IR (KBr) cm^{-1}: 1419.7, 1687.4, 1716.5, 1769.1, 2927.4, 2960.7, 3030.8. ^{1}H NMR, δ: 2.39 (s, 3H, C*H*$_3$), 2.46 (s, 3H, C*H*$_3$), 5.01 (s, 2H, C*H*$_2$), 7.15–7.27 (m, 2H, Ar*H*), 7.61 (s, 1H, Ar*H*), 7.72–7.78(m, 2H, Ar*H*), 7.85–7.96 (m, 2H, Ar*H*). ^{13}C NMR, δ: 21.1, 21.2, 45.8, 124.7, 130.5, 133.6, 134.6, 135.5, 135.7, 136.9, 137.8, 169.4, 195.6. ESI-MS (*m/z*): 293. Anal. calc. for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.73; H, 5.17; N, 4.79.

2-[2-(4-Fluoro-phenyl)-2-oxo-ethyl]-isoindole-1,3-dione (2e) ($C_{16}H_{10}FNO_3$). White crystals; mp 114–116 °C. IR (KBr) cm^{-1}: 1419.9, 1510.8, 1692.9, 1716.2, 1775.5, 2945.4. ^{1}H NMR, δ: 5.04 (s, 2H, C*H*$_2$), 7.16–7.26 (m, 2H, Ar*H*), 7.74–7.78 (m, 2H, Ar*H*), 7.87–7.93 (m, 2H, Ar*H*). 8.02–8.09 (m, 2H, Ar*H*). ^{13}C NMR, δ: 44.4, 116.3, 116.5, 116.7, 124.0, 131.2, 132.6, 134.6, 168.2, 189.9. ESI-MS (*m/z*): 283. Anal. calc. for $C_{16}H_{10}FNO_3$: C, 67.84; H, 3.56; N, 4.94. Found: C, 67.83; H, 3.57; N, 4.96.

2-(2-Oxo-propyl)-isoindole-1,3-dione (2f) ($C_{11}H_9NO_3$). White solid; mp 122–124 °C. IR (KBr) cm^{-1}: 1415.1, 1467.8, 1726.1, 1773.3, 2940.6, 3064.4. ^{1}H NMR, δ: 2.27 (s, 3H, C*H*$_3$), 4.50 (s, 2H, C*H*$_2$), 7.72–7.78 (m, 2H, Ar*H*), 7.84–7.90 (m, 2H, Ar*H*); ^{13}C NMR, δ: 27.5, 47.7, 123.6, 132.5, 134.2, 168.0, 203.7. ESI-MS (*m/z*): 203. Anal. calc. for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.03; H, 4.47; N, 6.91.

2-(2-(4-Nitro-phenyl)-2-oxo-ethyl]-isoindole-1,3-dione (2g) ($C_{16}H_{10}N_2O_5$). Pale yellow solid; mp 234–236 °C; IR (neat) cm^{-1}: 1419.7, 1526.0, 1699.4, 1718.2, 2337.5, 2361.8, 2965.2. ^{1}H NMR, δ: 5.17 (s, 2H, C*H*$_2$), 7.78–7.82 (m, 2H, Ar*H*), 7.91–7.96 (m, 2H, Ar*H*), 8.20 (d, $J = 8.9$ Hz, 2H, Ar*H*), 8.40 (d, $J = 8.9$ Hz, 2H, Ar*H*). ^{13}C NMR, δ: 44.6, 123.9, 124.4, 129.5, 132.2, 134.7, 138.9, 151.0, 168.1, 190.4. ESI-MS (*m/z*): 310. Anal. calc. for $C_{16}H_{10}N_2O_5$: C, 61.94; H, 3.25; N, 9.03. Found: C, 61.97; H, 3.24; N, 9.05.

2-(2-Oxo-cyclohexyl)-isoindole-1,3-dione (2h) ($C_{14}H_{13}NO_3$). White solid; mp 165–167 °C; IR (KBr) cm^{-1}: 1466.2, 1612.7, 1717.6, 1765.2, 2952.6. ^{1}H NMR, δ: 1.80–188 (m, 2H, C*H*$_2$), 2.04–2.23 (m, 2H, C*H*$_2$), 2.25–2.28 (m, 2H, C*H*$_2$), 2.63–2.69 (m, 2H, C*H*$_2$), 4.80 (dd, $J = 6.3$ Hz & 12.9 Hz, 1H, C*H*N), 7.26–7.76 (m, 2H, Ar*H*), 7.81–7.87 (m, 2H, Ar*H*). ^{13}C NMR, δ: 25.2, 26.2, 30.9, 41.4, 58.1, 123.9, 132.4, 134.4, 168.3, 203.2. ESI-MS (*m/z*): 243. Anal. calc. for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.13; H, 5.37; N, 5.73.

2-(1-Oxo-indan-2-yl)-isoindole-1,3-dione (2i) ($C_{17}H_{11}NO_3$). Reddish brown solid; mp 191 °C; IR (neat) cm^{-1}: 1468.1, 1611.9, 1714.5, 1777.8, 2925.9, 3030.2. ^1H NMR, δ: 3.41 (dd, $J = 5.9$ Hz & 16.5 Hz, 1H, C*H*), 3.61 (dd, $J = 8.4$ Hz & 16.6 Hz, 1H, C*H*), 5.09 (dd, $J = 6.0$ Hz & 8.4 Hz, 1H, C*H*N), 7.41–7.52 (m, 2H, Ar*H*), 7.64–788 (m, 6H, Ar*H*). ^{13}C NMR, δ: 32.0, 53.8, 123.7, 124.7, 126.8, 128.2, 132.3, 134.4, 135.8. 151.1, 167.7, 200.2. ESI-MS (*m*/*z*): 277. Anal. calc. for $C_{11}H_9NO_3$: C, 73.64; H, 4.00; N, 5.05. Found: C, 73.63; H, 4.03; N, 5.02.

2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3-oxo-butyric acid ethyl ester (2j) ($C_{14}H_{13}NO_5$). (Keto/enol = 18:82) white solid, mp 94–96 °C; IR (KBr) cm^{-1}: 1427.3, 1468.7, 1626.7, 1656.1, 1722.1, 1787.9, 2931.3, 2984.7. ^1H NMR, δ: 1.16 (t, $J = 7.1$ Hz, 3H, CH_3), 1.96 (s, 3H, COCH_3), 4.19 (q, $J = 7.1$ Hz, 2H, OCH_2), 7.75–7.83 (m, 2H, Ar*H*), 7.88–7.95 (m, 2H, Ar*H*). ^{13}C NMR, δ: 14.5, 18.5, 61.8, 97.1, 124.2, 132.2, 134.7, 168.1, 169.8, 177.3. ESI-MS (*m*/*z*): 275. Anal. calc. for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 61.07; H, 4.74; N, 5.08.

2-(1-Methyl-2-oxo-propyl)-isoindole-1,3-dione (2k) ($C_{12}H_{11}NO_3$). Yellow crystals; mp 77–79 °C; IR (KBr) cm^{-1}: 1467.8, 1714.1, 1776.9, 2942.6, 2994.9. ^1H NMR, δ: 1.65 (d, $J = 7.3$ Hz, CH_3), 2.21 (s, 3H, COCH_3), 4.82 (q, $J = 7.3$ Hz, 1H, C*H*N), 7.72–7.80 (m, 2H, Ar*H*), 7.84–7.90 (m, 2H, Ar*H*). ^{13}C NMR, δ: 14.6, 26.6, 55.1, 123.5, 132.3, 133.5, 134.5, 169.1. ESI-MS (*m*/*z*): 217. Anal. calc. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.33; H, 5.14; N, 6.43.

Hydrogenation of protected amino ketones (2a, 2b, 2c, 2d). Hydrogen gas was purged thoroughly in a solution of α-phthalimide ketones (1 mmol) and Pd/C (10%) (catalytic amount) in anhydrous ethanol (10 mL). The final hydrogen pressure was adjusted to 40–70 psi, and the reaction mixture was shaken at room temperature. After a certain time the hydrogen pressure was released and the solvent was removed after filtration to get the product, which was purified through a silica-gel column.

$NaCNBH_3$ Reduction of Protected Amino Ketones (2a–k)

General method a ($NaCNBH_3$ in MeOH). $NaCNBH_3$(2.0 equivalents) was added at 0 °C to a solution of α-phthalimido ketones (1 mmol) in methanol (15 mL). A trace of bromocresol green was also added to monitor the reaction. The solution immediately turned blue when 3 N HCl in methanol was added dropwise to restore the yellow color while stirring continued for 60 h at room temperature. The contents were concentrated under reduced pressure, and the residue was extracted with diethyl ether. The combined extracts were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The product was purified on a silica-gel column.

General method b ($NaCNBH_3$ in acetic acid). $NaCNBH_3$(2 mmol) was added at room temperature to a solution of α-phthalimido ketones in acetic acid (1 mmol in 15 mL). After the completion of the reaction as indicated by TLC, the reaction was quenched by saturated $NaHCO_3$ solution and extracted with ethyl acetate. The combined extracts were washed with water, dried over anhydrous sodium

sulfate, and concentrated under reduced pressure. The product was purified on a silica-gel column.

2-(2-Hydroxy-2-phenyl-ethyl)-isoindole-1,3-dione (3a) ($C_{16}H_{13}NO_3$). White solid; mp 161–163 °C; IR (KBr) cm^{-1}: 1420.9, 1457.7, 1695.4, 1768.6, 2899.6, 3460.8. ^{1}H NMR, δ: 3.88–4.02 (m, 2H, CH_2), 5.01 (dd, $J = 4.2$ Hz, 3.3 Hz, 1H, C*H*), 7.1–7.3 (m, 5H, Ar*H*), 7.73–7.77 (m, 2H, Ar*H*), 7.84–7.86 (m, 2H, Ar*H*). ^{13}C NMR, δ: 45.8, 72.6, 123.4, 123.5, 125.9, 127.8, 128.5, 128.9, 131.9, 134.0, 134.1, 141.1, 168.8. ESI-MS (*m/z*): 267. Anal. calc. for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90; N, 5.24. Found: C, 71.92; H, 4.93; N, 5.25.

2-[2-Hydroxy-2-*p*-tolyl-ethyl)-isoindole-1,3-dione (3b) ($C_{17}H_{15}NO_3$). Pale yellow solid; mp 139–141 °C; IR (KBr) cm^{-1}: 1420.5, 1605.7, 1690.1, 1716.4, 1775.7, 2920.4, 3476.4. ^{1}H NMR, δ: 2.39 (s, 3H, CH_3), 2.85 (brs, 1H, *OH*), 3.98 (m, 2H, CH_2), 5.05 (m, 1H, C*H*), 7.02 (d, $J = 8$ Hz, 2H, Ar*H*), 7.42 (d, $J = 8$ Hz, 2H, Ar*H*), 7.75–7.82 (m, 2H, Ar*H*), 7.84–7.93 (m, 2H, Ar*H*). ^{13}C NMR, δ: 21.2, 45.4, 72.3, 123.3, 125.9, 129.3, 131.9, 134.1, 137.9, 138.2, 168.8. ESI-MS (*m/z*): 281. Anal. calc. for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.56; H, 5.36; N, 4.99.

2-[2-Hydroxy-2-(4-methoxy-phenyl)-ethyl]-isoindole-1,3-dione (3c) ($C_{17}H_{15}NO_4$). White solid; mp 164–166 °C; IR (KBr) cm^{-1}: 1462.6, 1514.1, 1692.0, 2923.7, 3445.2. ^{1}H NMR, δ: 2.84 (brs, 1H, *OH*), 3.83 (s, 3H, OCH_3), 3.88–4.10 (m, 2H, CH_2), 5.02–5.10 (m, 1H, C*H*), 6.90–6.95 (m, 2H, Ar*H*), 7.39–7.43 (m, 2H, Ar*H*), 7.74–7.78 (m, 2H, Ar*H*), 7.86–7.96 (m, 2H, Ar*H*). ^{13}C NMR, δ: 45.7, 55.3, 72.1, 114.1, 122.6, 127.2, 131.2, 133.3, 134.2, 159.5, 168.8. ESI-MS (*m/z*): 297. Anal. calc. for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.69; H, 5.07; N, 4.72.

2-[2-(2,5-Dimethyl-phenyl)-2-hydroxy-ethyl]-isoindole-1,3-dione (3d) ($C_{18}H_{17}NO_3$). White solid; mp 127–129 °C; IR (KBr) cm^{-1}: 1422.8, 1709.3, 1771.9, 2925.5, 3433.5. ^{1}H NMR, δ: 2.43 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 3.90–3.94 (m, 2H, CH_2), 5.21 (dd, $J = 3.7$ Hz & 7.8 Hz, 1H, C*H*OH), 7.06–7.08 (m, 2H, Ar*H*), 7.22 (s, 1H, Ar*H*), 7.64–7.80 (m, 2H, Ar*H*), 7.87–7.93 (m, 2H, Ar*H*). ^{13}C NMR, δ: 18.7, 21.2, 45.1, 70.1, 123.7, 123.7, 126.1, 128.8, 130.7, 133.6, 134.4, 135.6, 140.2, 169.4. ESI-MS (*m/z*): 295. Anal. calc. for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.70. Found: C, 73.23; H, 5.84; N, 4.71.

2-[2-(4-Fluoro-phenyl)-2-hydroxy)-ethyl]-isoindole-1,3-dione (3e) ($C_{16}H_{12}FNO_3$). White solid; mp 162–164 °C; IR (KBr) cm^{-1}: 1510.4, 1609.9, 1692.4, 1709.4, 2930.7, 3420.3. ^{1}H NMR, δ: 3.03 (brs, 1H, *OH*), 3.94–3.99 (m, 2H, CH_2), 5.04–5.07 (m, 1H, C*H*), 7.04 (t, $J = 8.7$ Hz, 2H, Ar*H*), 7.39–7.46 (m, 2H, Ar*H*), 7.71–7.76 (m, 2H, Ar*H*), 7.81–7.88 (m, 2H, Ar*H*). ^{13}C NMR, δ: 44.6, 71.0, 114.3, 114.7, 119.5, 125.5, 126.5, 129.9, 133.2, 135.0, 165.0. ESI-MS (*m/z*): 285. Anal. calc. for $C_{16}H_{12}FNO_3$: C, 67.36; H, 4.24; N, 4.91. Found: C, 67.38; H, 4.22; N, 4.90.

2-(2-Hydroxy)-propyl-isoindole-1,3-dione (3f) ($C_{11}H_{11}NO_3$). White solid; mp 89–91 °C; IR (KBr) cm^{-1}: 1424.2, 1611.2, 1718.1, 1767.4, 2928.6, 2964.7, 3422.4, 3484.2. ^{1}H NMR, δ: 1.25 (d, $J = 6.4$ Hz, 3H, CH_3), 3.74–3.78 (m, 2H, CH_2), 4.12–4.17 (m, 1H, C*H*OH), 7.72–7.78 (m, 2H, Ar*H*), 7.83–7.89 (m, 2H,

Ar*H*). ^{13}C NMR, δ: 20.3, 44.9, 65.7, 122.4, 130.5, 132.4, 168.0. ESI-MS (*m*/*z*): 205. Anal. calc. for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.38; H, 5.42; N, 6.84.

2-[2-Hydroxy-2-(4-nitro-phenyl)-ethyl]-isoindole-1,3-dione (3g) ($C_{16}H_{12}N_2O_5$). Pale yellow solid, mp 166–168 °C; IR (KBr) cm^{-1}: 1401.7, 1518.2, 1687.4, 1706.6, 2922.7, 3382.0. ^{1}H NMR, δ: 3.86 (dd, $J = 4.5$ Hz & 14.1 Hz, 1H, C*H*N), 4.01 (dd, $J = 8.0$ Hz & 14.1 Hz, 1H, C*H*N), 5.16–5.20 (m, 1H, C*H*OH), 7.67 (d, $J = 8.6$ Hz, 2H, Ar*H*), 7.72–7.79 (m, 2H, Ar*H*), 7.81–7.88 (m, 2H, Ar*H*), 8.20 (d, $J = 8.7$ Hz, 2H, Ar*H*). ^{13}C NMR, δ: 45.7, 71.1, 123.7, 123.9, 127.4, 132.2, 134.5, 148.1, 150.2, 168.5. ESI-MS (*m*/*z*): 312. Anal. calc. for $C_{16}H_{12}N_2O_5$: C, 61.54; H, 3.87; N, 8.97. Found: C, 61.53; H, 3.85; N, 8.95.

2-(2-Hydroxy-cyclohexyl)-isoindole-1,3-dione (3h) ($C_{14}H_{15}NO_3$). White solid; mp 90–92 °C; IR (KBr) cm^{-1}: 1450.8, 1467.3, 1653.1, 1707.1, 1772.1, 2862.3, 2937.9, 3447.8. ^{1}H NMR, δ: 1.21–1.42 (m, 4H, CH_2's), 1.68–1.83 (m, 2H, CH_2), 2.13–2.24 (m, 2H, CH_2), 3.97 (ddd, $J = 3.7$, 10.1 & 12.4 Hz, C*H*N), 4.26–4.37 (m, 1H, C*H*OH), 7.67–7.74 (m, 2H, Ar*H*), 7.78–7.85 (m, 2H, Ar*H*). ^{13}C NMR, δ: 24.2, 25.1, 28.6, 34.6, 57.1, 68.6, 122.7, 131.7, 133.8, 169.5. ESI-MS (*m*/*z*): 245. Anal. calc. for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.59; H, 6.15; N, 5.73.

2-(1-Hydroxy-indan-2-yl)-isoindole-1,3-dione (3i) ($C_{17}H_{13}NO_3$). Yellow solid; mp 217–219 °C; IR (KBr) cm^{-1}: 1468.3, 1711.6, 1771.1, 2854.1, 2925.9, 3491.4. ^{1}H NMR, δ: 3.12–3.24 (m, 1H, CH_2), 3.95–4.08 (m, 1H, CH_2), 5.11–5.18 (m, 2H, C*H*OH & C*H*N), 7.29–7.31 (m, 3H, Ar*H*), 7.49–7.53 (m, 1H, Ar*H*), 7.72–7.76 (m, 2H, Ar*H*), 7.84–7.88 (m, 2H, Ar*H*). ^{13}C NMR, δ: 32.7, 52.9, 76.2, 123.4, 124.9, 125.6, 127.5, 129.4, 131.9, 134.2, 140.2, 142.5, 169.6. ESI-MS (*m*/*z*): 279. Anal. calc. for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.13; H, 4.65; N, 5.03.

2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-butyric acid ethyl ester (3j) ($C_{14}H_{15}NO_5$). ***syn-isomer***. mp 58–60 °C; IR (KBr) cm^{-1}: 1468.2, 1717.4, 1775.14, 2934.8, 2981.9, 3451.2. ^{1}H NMR, δ: 1.21–1.32 (m, 6H, CH_3's), 4.28 (q, $J = 7.1$ Hz, 2H, OCH_2), 4.65–4.69 (m, 1H, C*H*OH), 4.99 (d, $J = 4.1$ Hz, 1H, C*H*N), 7.78–7.82 (m, 2H, Ar*H*), 7.89–7.95 (m, 2H, Ar*H*). ^{13}C NMR, δ: 14.5, 20.6, 59.7, 62.6, 67.1, 124.3, 130.8, 134.9, 167.7, 168.8. ESI-MS (*m*/*z*): 277. Anal. calc. for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found C, 60.63; H, 5.44; N, 5.01.

anti-isomer. oil; IR (KBr) cm^{-1}: 1468.2, 1717.4, 1775.14, 2934.8, 2981.9, 3451.2. ^{1}H NMR, δ: 1.21 (t, $J = 7.1$ Hz, 3H, CH_3CH$_2$), 1.28 (d, $J = 6.4$ Hz, 3H, CH_3CHOH), 4.28 (q, $J = 7.1$ Hz, 2H, OCH_2), 4.51–4.58 (m, 1H, C*H*OH), 4.71 (d, $J = 6.5$ Hz, 1H, C*H*N), 7.77–7.80 (m, 2H, Ar*H*), 7.88–7.91 (m, 2H, Ar*H*). ^{13}C NMR, δ: 13.7, 19.3, 57.3, 61.9, 66.2, 123.5, 133.2, 134.5, 167.5, 168.5. ESI-MS (*m*/*z*): 277. Anal. calc. for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.63; H, 5.44; N, 5.01.

2-(2-Hydroxy-1-methyl-propyl)-isoindole-1,3-dione (3k) ($C_{12}H_{13}NO_3$). Semisolid; IR (KBr) cm^{-1}: 1467.7, 1614.1, 1707.0, 1773.7, 2935.2, 2977.4, 3446.7. ^{1}H NMR, δ: 1.20–1.27 (m, 3H, CH_3CHOH), 1.41–1.48 (m, 3H, CH_3CHN), 4.14 (m, 2H, C*H*OH & C*H*N), 7.28–7.78 (m, 2H, Ar*H*), 7.82–7.87 (m, 2H, Ar*H*). ^{13}C

NMR, δ: 12.6, 15.9, 53.5, 69.2, 123.4, 133.2, 134.5, 170.5. ESI-MS (*m/z*): 219. Anal. calc. for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.73; H, 5.95; N, 6.36.

Hydrazinolysis of 2-Phthalimidoalcohols

Hydrazine hydrate (3 eq.) was added to a suspension of 2-phthalimidoalcohols (1 mmol) in water (5 mL), and the resulting mixture was stirred at 60 °C for 3 h. After the completion of the reaction as indicated by TLC, the reaction mixture was saturated with NaCl and extracted with ethyl acetate (3 × 20 mL). The combined extracts were washed with water, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to get amino alcohols (**4a–l**).

2-Amino-1-phenylethanol (4a) ($C_8H_{11}NO$). White solid; mp 56–58 °C; IR (KBr) cm^{-1}: 1061.5, 1402.4, 1579.5, 2868.3, 3030.0, 3358.5. ^{1}H NMR, δ: 2.67 (dd, $J = 12.9$, 7.7 Hz, 1H), 2.80 (dd, $J = 12.9$, 4.0 Hz, 1H), 4.52 (dd, $J = 7.7$, 4.0 Hz, 1H), 7.13–7.17 (m, 5H); ^{13}C NMR, δ: 49.3, 74.3, 125.9, 127.4, 127.5, 128.4, 128.5, 142.8; ESI-MS (*m/z*): 137. Anal. calc. for $C_8H_{11}NO$ C, 70.08; H, 8.08; N, 10.21. Found: C, 70.15; H, 8.11; N, 10.30.

2-Amino-1-(4-methylphenyl)ethanol (4b) ($C_9H_{13}NO$). Semisolid; IR (KBr) cm^{-1}: 1071.9, 1405.3, 1459.1, 2854.3, 2955.5, 3362.5; ^{1}H NMR, (CD_3OD) δ: 2.32 (s, 3H, C*H*$_3$), 2.75–2.80 (m, 1H, C*H*HNH$_2$), 2.89–2.92 (m, 1H, CH*H*NH$_2$), 4.55–4.58 (m, 1H, C*H*OH), 7.13 (d, $J = 7.6$ Hz, 2H, Ar*H*), 7.21 (d, $J = 7.6$ Hz, 2H, Ar*H*); ^{13}C NMR (CD_3OD) δ: 20.7, 48.0, 72.9, 124.7, 128.1, 137.3, 139.2; ESI-MS (*m/z*): 151. Anal. calc. for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.45; H, 8.71; N, 9.29.

2-Amino-1-(4-methoxyphenyl)ethanol (4c) ($C_9H_{13}NO_2$). White solid; mp 70 °C; IR (KBr) cm^{-1}: 1032.6, 1248.2, 1513.5, 2929.0, 3299.2; ^{1}H NMR, δ: 2.73 (dd, $J = 12.5$, 8.1 Hz, 1H, C*H*HNH$_2$), 2.87 (dd, $J = 12.5$, 4.0 Hz, 1H, CH*H*NH$_2$), 3.79 (s, 3H, OC*H*$_3$), 6.85 (d, $J = 8.4$ Hz, 2H, Ar*H*), 7.23 (d, $J = 8.4$ Hz, 2H, Ar*H*); ^{13}C NMR, δ: 49.2, 55.3, 72.7, 113.8, 127.4, 135.1, 159.1; ESI-MS (*m/z*): 167. Anal. calc. for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.61; H, 7.97, N, 8.44.

2-Amino-1-(2,5-dimethyl-phenyl)ethanol (4d) ($C_{10}H_{15}NO$). Semi solid; IR (KBr) cm^{-1}: 1404.0, 2845.3, 2920.0, 3412.2. ^{1}H NMR, δ: 2.43 (s, 3H, C*H*$_3$), 2.49 (s, 3H, C*H*$_3$), 3.01–3.60 (m, 2H, C*H*$_2$), 4.60 (dd, 1H, C*H*OH), 7.06–7.08 (m, 2H, Ar*H*), 7.10 (s, 1H, Ar*H*). ^{13}C NMR, δ: 18.4, 23.2, 48.1, 70.1, 127.7, 128.9, 129.1, 132.7, 134.4, 139.5. ESI-MS (*m/z*): 165. Anal. calc. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.67; H, 9.20; N, 8.51.

2-Amino-1-(4-fluorophenyl)ethanol (4e) ($C_8H_{10}FNO$). Semi solid; IR (KBr) cm^{-1}: 1501.5, 1603.6, 2878.0, 2998.8, 3357.1. ^{1}H NMR, δ: 2.76 (dd, $J = 7.8$, 12.7 Hz, 1H, CH*H*NH$_2$), 2.98 (dd, $J = 3.9$, 12.7 Hz, 1H, C*H*HNH$_2$), 4.61 (dd, $J = 3.9$, 7.8 Hz, 1H, C*H*OH), 7.90–7.16 (m, 2H, Ar*H*), 7.31–7.38 (m, 2H, Ar*H*); ^{13}C NMR, δ: 49.5, 73.2, 113.9, 114.3, 127.1, 127.6, 139.9, 163.1; ESI-MS (*m/z*): 155. Anal. calc. for $C_8H_{10}FNO$: C, 61.92; H, 6.50; N, 9.03. Found: C, 61.87; H, 6.59; N, 9.12.

1-Amino-2-propanol (4f) (C_3H_9NO). Clear to light yellow liquid; mp 1.4 °C; IR (KBr) cm^{-1}: 1423.6, 2913.1, 3395.0. ^1H NMR, δ: 1.16 (d, $J = 6.3$ Hz, 3H, CH_3). 2.44 (dd, $J = 8.1$, 12.7 Hz, 1H), 2.65 (dd, $J = 2.65$, 12.7 Hz, 1H), 2.55–3.65 (m, 1H). ^{13}C NMR, δ: 20.8, 54.9, 71.7. ESI-MS (m/z): 75. Anal. calc. for C_3H_9NO: C, 47.97; H, 12.08; N,18.65. Found: C, 47.88; H, 12.10; N, 18.73.

2-Amino-1-(p-nitrophenyl)ethanol (4g) ($C_8H_{10}N_2O_3$). Semisolid; IR (KBr) cm^{-1}: 1398.5, 1510.3, 2901.0, 3250.2, 3360.3. ^1H NMR, δ: 2.6–2.9 (m, 2H, CH_2), 4.7 (t, $J = 4.2$, C*H*OH), 7.5–7.6 (d, 2H, Ar*H*), 8.1–8.2 (d, 2H, Ar*H*). ^{13}C NMR, δ: 48.8, 72.9, 123.6, 126.6, 147.4, 149.9. ESI-MS (m/z): 182. Anal. calc. for $C_8H_{10}N_2O_3$: C, 52.74; H, 5.53; N, 15.38. Found: C, 52.82; H, 5.64; N, 15.42.

2-Amino-1-cyclohexanol (4h) ($C_6H_{13}NO$). White solid; mp 87 °C; IR (KBr) cm^{-1}: 1074.8, 1499.7, 2857.6, 3283.3; ^1H NMR, δ: 1.23–1.46 (m, 2H, CH_2), 1.65–2.12 (m, 6H, CH_2's), 2.38–2.46 (m, 1H, C*H*NH_2), 3.10–3.15 (m, 1H, C*H*OH); ^{13}C NMR, δ: 24.8, 25.0, 33.9, 34.3, 56.9, 75.6; ESI-MS (m/z): 115. Anal. calc. for $C_6H_{13}NO$: C, 62.37; H, 11.38; N, 12.16. Found: C, 62.26; H, 11.44; N, 12.21.

2-Amino-1-indanol (4i) ($C_9H_{11}NO$). White to off-white crystal; mp 160–161 °C; IR (KBr) cm^{-1}: 1070, 1490, 1570, 2400–3400. ^1H NMR, δ: 2.60 (dd, $J = 15.3$, 8.0 Hz, 1H, CH_2), 3.22 (dd, $J = 15.3$, 8.0 Hz, 1H, CH_2), 3.47 (dt, $J = 8.0$, 6.5 Hz, 1H, C*H*N,) 4.79 (d, 6.5 Hz, 1H, C*H*OH), 7.15–7.60 (m, 4H). ^{13}C NMR, δ: 38.8, 62.9, 82.2, 123.6,124.7, 126.9, 128.1, 139.5, 143.3. ESI-MS (m/z): 149. Anal. calc. for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.40; H, 7.55; N, 9.43.

Ethyl-2-amino-3-hydroxybutanoate (4j) ($C_6H_{13}NO_3$). Semisolid; IR (KBr) cm^{-1}: 1421.0, 1685.4, 2895.2, 2907.0, 3385.6. ^1H NMR, δ: 1.21-1.32 (m, 6H, CH_3's), 3.90 (m, 1H, C*H*N), 4.13 (m, 1H, C*H*OH), 4.21 (q, $J = 7.1$ Hz, 2H, OCH_2). ^{13}C NMR, δ: 14.5, 20.0, 57.7, 61.6, 65.1, 168.7. ESI-MS (m/z): 147. Anal. calc. for $C_6H_{13}NO_3$: C, 48.97; H, 8.90; N, 9.52. Found: C, 48.89; H, 8.99; N, 9.59.

3-Amino-2-butanol (4k) ($C_4H_{11}NO$). Semisolid; IR (KBr) cm^{-1}: 1216, 1458, 1609, 2854, 2924, 3396. ^1H NMR, δ: 1.09 (d, $J = 6.6$ Hz, 3H, CH_3CHN), 1.12 (d, $J = 6.9$ Hz, 3H, CH_3CHOH), 3.26 (m, 1H, C*H*N), 3.7 (m, 1H, C*H*OH). ^{13}C NMR, δ: 17.6, 18.9, 54.5, 67.8. ESI-MS (m/z): 89. Anal. calc. for $C_4H_{11}NO$: C, 53.90; H, 12.44; N, 15.71. Found: C, 53.88; H, 12.53; N, 15.79.

2-Acetamido-1-(4-fluorophenyl)ethanol (4l) ($C_{10}H_{12}FNO_2$). Semisolid; IR (KBr) cm^{-1}: 1222.7, 1403.1, 1642.1, 2925.5, 3285.9. ^1H NMR, δ: 1.97 (s, 3H), 3.24–3.33 (m, 1H), 3.55–3.65 (m, 1H), 4.77–4.82 (dd, $J = 7.8$, 3.2 Hz, 1H), 6.97–7.06 (m, 2H), 7.26–7.35 (m, 2H); ^{13}C NMR. δ: 23.1, 47.6, 73.0, 115.2, 127.4, 137.6, 161.4, 171.7. ESI-MS (m/z): 197. Anal. calc. for $C_{10}H_{12}FNO_2$: C, 60.90; H, 6.13; N, 7.10. Found: C, 60.88; H, 6.22; N, 7.17.

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REFERENCES

1. Ager, D. J.; Prakash, I.; Schaad, D. R. 1,2-Amino alcohols and their heterocyclic derivatives as chiral auxiliaries in asymmetric synthesis. *Chem. Rev.* **1996**, *96*, 835–875.
2. Pu, L.; Yu, H.-B. Catalytic asymmetric organozinc additions to carbonyl compounds. *Chem. Rev.* **2001**, *101*, 757–824.
3. Palomo, C.; Oiarbide, M.; Laso, A. Enantioslective Hanry reactions under dual Lewis acid / amine catalysis using chiral alcohol ligands. *Angew. Chem. Int. Ed.* **2005**, *44*, 3881–3884.
4. Cepanec, I.; Litvic, M.; Mikuldas, H.; Bartolincic, A.; Vinkovic, V. Calcium trifluoromethanesulfonate–catalysed aminolysis of epoxides. *Tetrahedron* **2003**, *59*, 2435–2439.
5. Bradley, D.; Williams, G.; Lawton, M. Aluminium triflate: An efficient recyclable Lewis acid catalyst for the aminolysis of epoxides. *Tetrahedron Lett.* **2006**, *47*, 6557–6560.
6. Reddy, G. V.; Rao, G. V.; Iyengar, D. S. Selective reductions of oxazolidinones: New protocol for diastereoselective synthesis of vicinal amino alcohols. *Tetrahedron Lett.* **1999**, *40*, 2653–2656.
7. Liu, G.; Stahl, S. S. Highly regioselective Pd-catalyzed intermolecular aminoacetoxylation of alkenes and evidence for *cis*-aminopalladation and S_N2 C−O bond formation. *J. Am. Chem. Soc.* **2006**, *128*, 7179–7181.
8. Fujisawa, T.; Hayashi, H.; Kishioka, Y. Enantioselective synthesis of optically pure amino alcohol derivatives by yeast reduction. *Chem. Lett.* **1987**, 129–132.
9. (a) Machado, A. L.; Lima, L. M.; Araujo, J. X. Jr.; Fraga, C. A. M.; Koatzc, V. L. G.; Barreiro, E. J. Design, synthesis, and anti-inflammatory activity of novel phthalimide derivatives, structurally related to thalidomide. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1169–1172; (b) Collin, X.; Robert, J.; Wielgosz, G.; Le Baut, G.; Bobin-Dubigeon, C.; Grimaud, N.; Petit, J. New anti-inflammatory *N*-pyridinyl(alkyl)phthalimides acting as tumour necrosis factor-α production inhibitors. *Eur. J. Med. Chem.* **2001**, *36*, 639–649.
10. Antunes, R.; Batista, H.; Srivastava, R. M.; Thomas, G.; Araujo, C. C. New phthalimide derivatives with potent analgesic activity, II. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3071–3076.
11. Abdel-Hafez, A. A. Synthesis and anticonvulsant evaluation of N-substituted-isoindolinedione derivatives. *Arch. Pharm. Res.* **2004**, *27*, 495–501.
12. Kawagushi, S.; Ikeda, O. Jpn. Pat. Appl. JP2001328911, 2001.
13. Ebihara, K.; Oora, T.; Nakaya, M.; Shiraishi, S.; Yasui, N. Jpn. Pat. Appl. JP08245585, 1996.
14. (a) Bartovic, A.; Decroix, B.; Netchitailo, P. Synthesis of 1,2-oxazaheterocycles containing an isoindolone moiety from *N*-hydroxyphthalimide. *J. Heterocycl. Chem.* **2000**, *37*, 827–830; (b) Speckamp, W. N.; Moolenaar, M. J. New developments in the chemistry of *N*-acyliminium ions and related intermediates. *Tetrahedron* **2000**, *56*, 3817–3857.
15. Lei, A.; Wu, S.; He, M.; Zhang, X. Highly enantioselective asymmetric hydrogenation of α-phthalimide ketone: An efficient entry to enantiomerically pure amino alcohols. *J. Am. Chem. Soc.* **2004**, *126*, 1626–1627.
16. Gupta, P.; Shah, B. A.; Parshad, R.; Qazi, G. N.; Taneja, S. C. A facile approach towards enantiomerically pure masked β-amino alcohols. *Green Chem.* **2007**, *9*, 1120–1125.
17. (a) Sheldon, R. Catalytic reactions in ionic liquids. *J. Chem. Soc., Chem. Commun.* **2001**, 2399–2407; (b) Peng, J.; Deng, Y. Ionic liquids–catalyzed Biginelli reaction under solvent-free conditions. *Tetrahedron Lett.* **2001**, *42*, 5917–5919.
18. Nutaitis, C. F.; Schultz, A.; Obaza, J. R.; Smith, F. X. Reduction of isopropylidene acylmalonates, 5-acylbarbituric acids, and 3-acyl-4-hydroxycoumarins to the corresponding alkyl derivatives by sodium cyanoborohydride-acetic acid. *J. Org. Chem.* **1980**, *45*, 4606–4608.
19. Vernon, G. S. B.; Panayiotis, C. M. Reductive, selective deoxygenation of acylbenzo[b]-furans, aromatic aldehydes, and ketones with $NaBH_3CN$-TMSCl. *Tetrahedron Lett.* **1998**, *39*, 7059–7062.

20. Christian, V. S.; Ellen, V. M.; Yves, E.; Bart, V.; Wim, H. Synthesis of highly functionalised spiro-indoles by a halogen atom transfer radical cyclization. *Chem. Comm.* **2005**, 4827–4829.
21. Bundle, D. R.; Josephson, S. Artificial carbohydrate antigens: Synthesis of rhamnose disaccharides common to *Shigella flexneri O*-antigen determinants. *Can. J. Chem.* **1979**, *57*, 662–668.
22. Durette, P. L.; Meitzner, E. P.; Shen, T. Y. Bacterial cell wall constituents, II: Synthesis of *O*-(*N*-acetyl-β-muramyl-*L*-alanyl-*D*-isoglutamine)-(1→4)-*N*-acetyl-*D*-glucosamine. *Tetrahedron Lett.* **1979**, *20*, 4013–4016.
23. Madsen, R.; Udodong, W. E. Studies related to synthesis of glycophosphatidylinositol membrane-bound protein anchors, 6: Convergent assembly of subunits. *J. Am. Chem. Soc.* **1995**, *117*, 1554–1565.
24. Kanie, O.; Crawley, S. C.; Palcic, M. M.; Hindsgaul, O. Acceptor-substrate recognition by *N*-acetylglucosaminyltransferase V: Critical role of the 4″-hydroxyl group in β-D-Glc*p*NAc-(1 → 2)-α-D-Man*p*(1 → 6)-β-D-Glc*p*-OR. *Carbohydr. Res.* **1993**, *243*, 139–164.
25. Arffin, A.; Khan, M. N.; Lan, L. C.; May, F. Y.; Yun, C. S. Suggested improved method for the Ing–Manske and related reactions for the second step of Gabriel synthesis of primary amines. *Synth. Commun.* **2004**, *34*, 4439–4445.
26. Torre, O.; Gotor-Fernandez, V.; Gotor, V. Lipase-catalyzed resolution of chiral 1,3-amino alcohols: Application in the asymmetric synthesis of (*S*)-dapoxetine. *Tetrahedron: Asymmetry* **2006**, *17*, 860–866.