DOI: 10.1002/ejoc.201300047

Synthesis of 6*H*-Isoindolo[2,1-*a*]indol-6-ones Through Wittig Reaction and Tandem Reductive Cyclization–Lactamization

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Keywords: Synthetic methods / Nitrogen heterocycles / Wittig reactions / Domino reactions / Reduction / Lactams

A convenient and efficient two-step route to 6*H*-Isoindolo[2,1-*a*]indol-6-ones has been developed starting from *o*-nitrobenzaldehydes. The methodology involves Wittig reaction followed by tandem reductive cyclization–lactamization. A series of isoindoloindolones incorporating different substituents on the indole nucleus has been prepared.

Introduction

Nitrogen-containing fused heterocyclic compounds are widely studied in chemistry and biology because of their varied biological properties and frequent natural occurrence. 6*H*-Isoindolo[2,1-*a*]indol-6-one (**1**) belongs to one such class. Although, to the best of our knowledge, this structural motif has yet to be revealed in any naturally occurring compound or metabolites, these compounds (Figure 1) are still widely studied because of their promising biological activities including anticancer, antitumor, antibacterial, and antifungal activity. For example, 2-hydroxy-8,9-dimethoxy-6*H*-isoindolo[2,1-*a*]indol-6-one (**2a**) has subnanomolar affinity for the melatonin binding site MT_3, which is a quinone reductase-2 enzyme.[1] 10-Chloro-7-[2-(diethylamino)ethylamino]-6*H*-isoindolo[2,1-*a*]indol-6-one (**2b**), 3-(diethylamino)-*N*-(6-oxo-6*H*-isoindolo[2,1-*a*]indol-2-yl)propanamide (**2c**), and 2-amino-6*H*-isoindolo[2,1-*a*]-indol-6-one (**2d**) all show DNA binding abilities and antiproliferative effects against HT-29 and L1210 cell lines.[2] They also display nonspecific topoisomerase II inhibition. 6*H*-Isoindolo[2,1-*a*]indol-6-one (**1**) is also used as a precursor for the synthesis of NorA efflux pump inhibitors.[3]

A diverse range of approaches for the synthesis of isoindoloindolones have been reported. $Pd(OAc)_2$ promoted oxidative intramolecular cyclization, reported by Itahara,[4] was extensively used as a simple procedure giving reasonable yields. Monneret et al.[2,5] synthesized isoindoloindolones using intramolecular Wittig cyclization as a key step. Estevez's group[6] developed a copper-mediated intramolecular cyclization approach using 2-(2-aminophenylethynyl)-benzoic acid esters for the synthesis of isoindoloindolones. Boussard[1] and co-workers accomplished the synthesis of

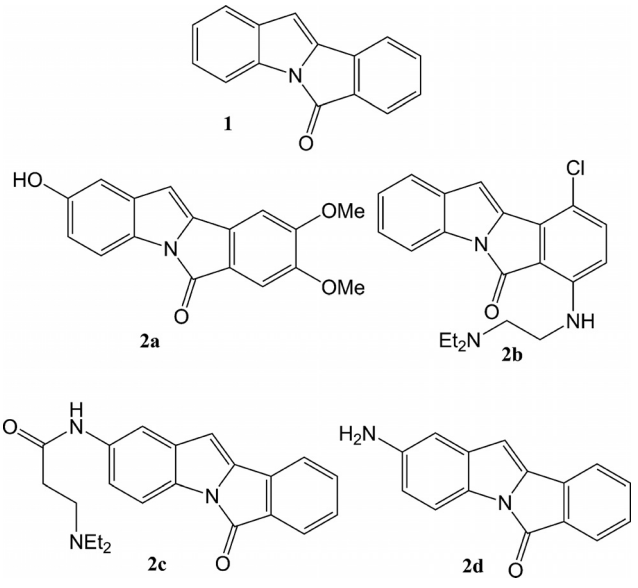

Figure 1. 6*H*-Isoindolo[2,1-*a*]indol-6-one (**1**) and similar biologically important compounds.

2a from methyl 2-[2-(5-hydroxy-2-nitrophenyl)acetyl]benzoate through Raney-nickel-mediated reduction followed by base treatment. McNab's group[7] developed a cascade approach involving sigmatropic shift–elimination–cyclization reaction of methyl 2-(indol-1-yl)benzoate by flash vacuum pyrolysis (FVP). Muthusubramanian et al.[8] prepared 6*H*-isoindolo[2,1-*a*]indol-6-one (**1**) by copper-catalyzed domino sp-sp^2 decarboxylative cross-coupling–cycloisomerization–cyclization reaction. Bao[9] and co-workers prepared a series of isoindoloindolones from *ortho-gem*-dibromovinyl aniline through one-pot sequential Cu catalyzed C–N coupling and Pd catalyzed C–H activation reaction. Griffiths et al.[10] developed a route to isoindoloindolones starting from 2-(*N*-phthaloyl)benzoic acids via β-ketophosphonates. However, many of these syntheses are either lengthy or involve complex precursors, thus, a simple, efficient, and versatile syn-

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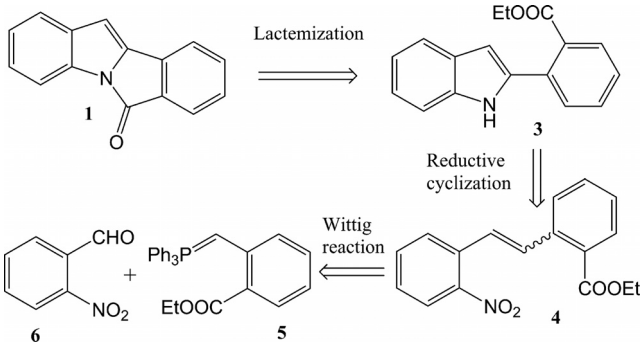
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201300047.

thetic route would increase the scope for preparing structurally similar derivatives for biological and other studies.

For several years, our group has been exploring tandem or one-pot syntheses.[11] In this context, we herein report a two-step synthesis of 6*H*-isoindolo[2,1-*a*]indol-6-one (**1**) using a Wittig reaction and tandem reductive cyclization–lactamization sequence (Scheme 1). A series of structurally similar isoindoloindolones is prepared from appropriate *o*-nitrobenzaldehydes as starting material.

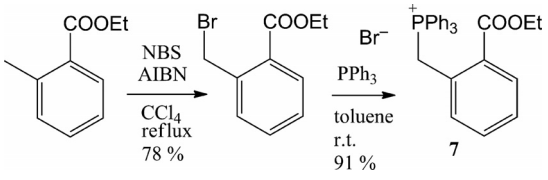
Results and Discussion

Our approach to **1** is projected in the retrosynthetic analysis shown in Scheme 1. We envisioned achieving isoindoloindolone **1** by lactamization from ethyl 2-(1*H*-indol-2-yl)benzoate (**3**), which, in turn, could be obtained from ethyl 2-(2-nitrostyryl)benzoate (**4**) through reductive cyclization. The latter compound could be obtained by Wittig reaction of phosphorane **5** and 2-nitrobenzaldehyde (**6**).



Scheme 1. Retrosynthetic scheme.

Following this strategy, we started our synthesis with the preparation of Wittig salt **7** from ethyl *o*-toluate by benzylic bromination[12] followed by addition of PPh_3 (Scheme 2). Phosphonium salt **7** was then mixed with aldehyde **6** followed by addition of base to obtain the required Wittig product **4** directly in 86% yield.



Scheme 2. Preparation of Wittig salt **7**.

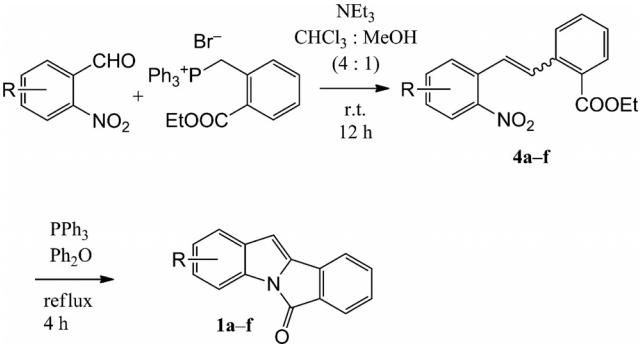
For the projected reductive cyclization step, a number of different reagent systems were tried; the results are summarized in Table 1.

Table 1. Tandem reductive cyclization–lactamization reaction.

Entry	Reaction conditions	Yield (%)[a]
1	$P(OEt)_3$, reflux, 30 min	56
2	$[MoO_2Cl_2dmf_2]$ (10 mol-%), PPh_3, toluene, reflux, 12 h	51
3	PPh_3, Ph_2O, reflux, 4 h	75

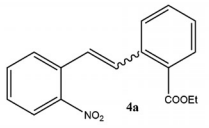
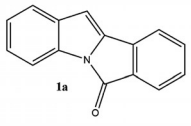
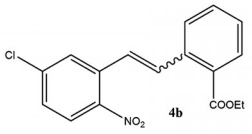
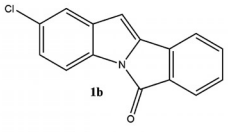
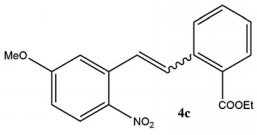
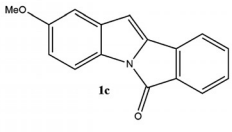
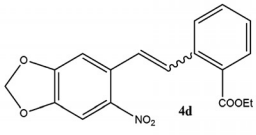
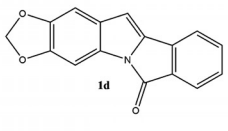
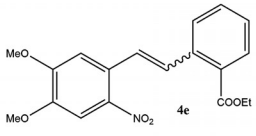
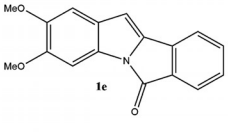
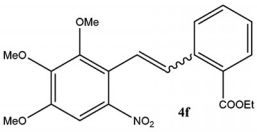
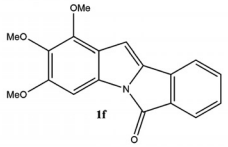
[a] Isolated yield after column chromatography.

Conducting the reaction with triethylphosphite[13] required the shortest reaction time and yielded the final product **1a** directly in 56% yield. Less encouraging results were obtained when the Mo catalyst[14] was used for the reductive cyclization. Good yields were achieved only with PPh_3 at high temperature,[15] giving the desired product **1a** in 75% yield. During this one-pot experiment, tandem re-



Scheme 3. Synthetic scheme depicting the two-step synthesis of 6*H*-isoindolo[2,1-*a*]indol-6-ones **1**.

Table 2. Synthesis of 6*H*-isoindolo[2,1-*a*]indol-6-ones (Scheme 3).

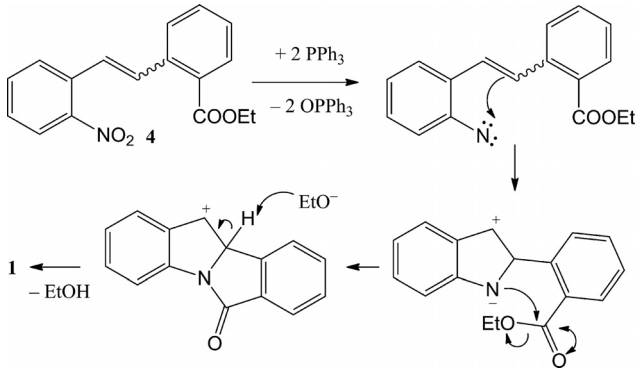
Entry	Product	Yield (%)[a]	Product	Yield (%)[a]
1	 **4a**	86[b]	 **1a**	75[b]
2	 **4b**	77	 **1b**	70
3	 **4c**	83	 **1c**	68
4	 **4d**	80	 **1d**	73
5	 **4e**	78	 **1e**	72
6	 **4f**	74	 **1f**	63

[a] Isolated yield after column chromatography. [b] Reproducible yield at 10 mmol (2 g) scale.

ductive cyclization–lactamization reaction took place. This protocol was further extended to the preparation of a series of substituted isoindoloindolones (Scheme 3).

Introduction of a halogen group on the heterocycle is known to enhance the bioactivity profile. We therefore used 5-chloro-2-nitrobenzaldehyde (**6b**) for the preparation of 2-chloro-6*H*-isoindolo[2,1-*a*]indol-6-one (**1b**). Similarly, methoxy-, dimethoxy-, methylenedioxy- and trimethoxy-substituted isoindoloindolones **1c**–**f** were also synthesized (Table 2). The efficiency of the methodology was tested on larger scale and yields were found to be reproducible even at 10 mmol (2 g) scale.

A probable mechanism[16] for product formation in the tandem reductive cyclization–lactamization reaction is depicted in Scheme 4.



Scheme 4. Proposed mechanism.

Conclusions

We have developed a simple and efficient two-step method for the synthesis of 6*H*-isoindolo[2,1-*a*]indol-6-one derivatives **1** through Wittig reaction and tandem reductive cyclization–lactamization. The versatility of this method has been demonstrated by the synthesis of a series of structurally related isoindoloindolones.

Experimental Section

General: Commercial reagents were purchased from Sigma–Aldrich and used without further purification. Solvents were distilled prior to use. Reactions were monitored by thin-layer chromatography (TLC Silica gel 60 F_{254} purchased from Merck). Column chromatography was performed on silica gel (60–120 mesh). ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded with a Bruker 400 instrument using $CDCl_3$ or DMSO as solvent and TMS as internal standard. HRMS were recorded with a MicroMass ES-QTOF. IR spectra were recorded with a Shimatzu FTIR instrument. Melting points are recorded with a Thiele apparatus and are uncorrected. Elemental analyses were performed with an Elementar CHNS instrument.

General Procedure for the Synthesis of Ethyl 2-(2-Nitrostyryl)benzoates 4a–f: *o*-Nitrobenzaldehyde **6a**–**f** (2 mmol) and [2-(ethoxycarbonyl)benzyl]triphenylphosphonium bromide (**7**; 1.012 g, 2.8 mmol) were dissolved in chloroform/methanol (8:2, 20 mL) and stirred at room temperature. Triethylamine (0.202 g, 3.2 mmol) was added slowly with stirring and the mixture was stirred at room temperature for 12 h. On completion of the reaction (monitored with TLC), solvent was removed under reduced pressure and water (20 mL) was added. The mixture was extracted in EtOAc (3 × 15 mL) and the combined organic layers were washed with brine (10 mL), dried with anhyd. Na_2SO_4, concentrated under reduced pressure, and purified by flash chromatography (EtOAc/hexanes, 20%).

Ethyl 2-(2-Nitrostyryl)benzoate (4a): Pale-yellow solid; m.p. 87–88 °C.[17] IR (KBr): $\tilde{\nu}$ = 1344, 1522, 1712, 2990, 3080 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (t, J = 7.2 Hz, 3 H), 4.34 (q, J = 7.2 Hz, 2 H), 6.85–6.95 (m, 3 H), 7.11–7.20 (m, 5 H), 7.90 (d, J = 8.0 Hz, 1 H), 7.95 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.34 (CH_3), 61.16 (CH_2), 124.49 (CH), 126.16 (CH), 127.39 (CH), 127.81 (CH), 129.69 (Cq), 130.52 (CH), 131.40 (CH), 131.87 (CH), 132.79 (CH), 132.85 (CH), 132.91 (CH), 133.31 (Cq), 138.34 (Cq), 148.34 (Cq), 166.94 (Cq) ppm.

Ethyl 2-(5-Chloro-2-nitrostyryl)benzoate (4b): Pale-yellow solid; m.p. 68–69 °C. IR (KBr): $\tilde{\nu}$ = 1344, 1520, 1711, 2982, 3063 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (t, J = 7.2 Hz, 3 H), 4.33 (q, J = 7.2 Hz, 2 H), 6.82–6.91 (m, 3 H), 7.17–7.26 (m, 4 H), 7.90–7.95 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.31 (CH_3), 61.23 (CH_2), 124.92 (CH), 126.01 (CH), 127.79 (CH), 127.92 (CH), 129.68 (Cq), 130.72 (CH), 131.11 (CH), 132.03 (CH), 132.47 (CH), 133.91 (CH), 135.13 (Cq), 137.67 (Cq), 139.08 (Cq), 146.57 (Cq), 166.77 (Cq) ppm. HRMS: m/z calcd. for $C_{17}H_{14}ClNO_4Na$ [M + Na]$^+$ 354.0509; found 354.0509. $C_{17}H_{14}ClNO_4$ (331.75): calcd. C 61.55, H 4.25, N 4.22; found C 61.73, H 4.17, N 4.36.

Ethyl 2-(5-Methoxy-2-nitrostyryl)benzoate (4c): Yellow oil. IR (neat): $\tilde{\nu}$ = 1335, 1525, 1711, 2982, 3062 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.2 Hz, 3 H), 3.36 (s, 3 H), 4.28 (q, J = 7.2 Hz, 2 H), 6.33 (s, 1 H), 6.62 (d, J = 9.2 Hz, 1 H), 6.83 (d, J = 8.4 Hz, 1 H), 6.90 (d, J = 12.0 Hz, 1 H), 7.09–7.15 (m, 3 H), 7.83 (d, J = 7.6 Hz, 1 H), 7.94 (d, J = 9.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.28 (CH_3), 55.52 (CH_3), 61.12 (CH_2), 113.80 (CH), 116.69 (CH), 127.10 (CH), 127.28 (CH), 127.33 (Cq), 129.74 (Cq), 130.31 (CH), 131.24 (CH), 131.89 (CH), 132.24 (CH), 136.08 (CH), 138.27 (Cq), 141.20 (Cq), 162.66 (Cq), 166.91 (Cq) ppm. HRMS: m/z calcd. for $C_{18}H_{17}NO_5Na$ [M + Na]$^+$ 350.1004; found 350.1004.

Ethyl 2-[2-(6-Nitrobenzo[*d*][1,3]dioxol-5-yl)vinyl]benzoate (4d): Yellow solid; m.p. 123–124 °C. IR (KBr): $\tilde{\nu}$ = 1321, 1518, 1712, 2982, 3125 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (t, J = 7.2 Hz, 3 H), 4.32 (q, J = 7.2 Hz, 2 H), 5.92 (s, 2 H), 6.31 (s, 1 H), 6.84–6.91 (m, 2 H), 7.10 (d, J = 12.4 Hz, 1 H), 7.10–7.16 (m, 2 H), 7.51 (s, 1 H), 7.91 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.31 (CH_3), 61.16 (CH_2), 102.80 (CH_2), 105.16 (CH), 111.19 (CH), 126.98 (CH), 127.42 (CH), 129.62 (Cq), 130.53 (CH), 130.68 (Cq), 131.35 (CH), 131.78 (CH), 131.99 (CH), 138.29 (Cq), 142.26 (Cq), 147.05 (Cq), 151.47 (Cq), 166.97 (Cq) ppm. HRMS: m/z calcd. for $C_{18}H_{15}NO_6Na$ [M + Na]$^+$ 364.0797; found 364.0806.

Ethyl 2-(4,5-Dimethoxy-2-nitrostyryl)benzoate (4e): Yellow solid; m.p. 56–57 °C. IR (KBr): $\tilde{\nu}$ = 1345, 1530, 1709, 2990, 3075 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (t, J = 7.2 Hz, 3 H), 3.32 (s, 3 H), 3.84 (s, 3 H), 4.33 (q, J = 7.2 Hz, 2 H), 6.31 (s, 1 H), 6.89 (d, J = 8.4 Hz, 1 H), 7.01 (d, J = 12.0 Hz, 1 H), 7.14–7.19 (m, 3 H), 7.57 (s, 1 H), 7.88 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.29 (CH_3), 54.87 (CH_3), 55.21 (CH_3), 60.16 (CH_2), 106.30 (CH), 113.18 (CH), 126.25 (CH), 126.36 (CH), 127.11 (Cq), 128.80 (Cq), 129.17 (CH), 130.43 (CH), 130.79 (CH),

130.93 (CH), 137.71 (Cq), 139.46 (Cq), 146.72 (Cq), 151.40 (Cq), 166.08 (Cq) ppm. HRMS: *m*/*z* calcd. for $C_{19}H_{19}NO_6Na$ [M + Na]$^+$ 380.1110; found 380.1111.

Ethyl 2-(4,5,6-Trimethoxy-2-nitrostyryl)benzoate (4f): Yellow solid; m.p. 45–46 °C. IR (KBr): $\tilde{\nu}$ = 1344, 1527, 1710, 2950, 3060 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (t, J = 7.2 Hz, 3 H), 3.82 (s, 3 H), 3.86 (s, 3 H), 3.90 (s, 3 H), 4.30 (q, J = 7.2 Hz, 2 H), 6.93 (d, J = 16.0 Hz, 1 H), 7.20 (s, 1 H), 7.28 (t, J = 8.0 Hz, 1 H), 7.45 (t, J = 8.0 Hz, 1 H), 7.66 (d, J = 8.0 Hz, 1 H), 7.84 (s, 1 H), 7.86 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.31 (CH_3), 56.36 (CH_3), 61.05 (CH_2), 61.16 (CH_3), 61.22 (CH_3), 104.08 (CH), 121.21 (Cq), 121.50 (CH), 127.38 (CH), 127.60 (CH), 129.24 (Cq), 130.43 (CH), 132.15 (CH), 133.81 (CH), 139.11 (Cq), 144.51 (Cq), 146.85 (Cq), 151.99 (Cq), 152.46 (Cq), 167.23 (Cq) ppm. HRMS: *m*/*z* calcd. for $C_{20}H_{21}NO_7Na$ [M + Na]$^+$ 410.1216; found 410.1215.

General Procedure for the Synthesis of 6*H*-Isoindolo[2,1-*a*]indol-6-ones 1a–f: A mixture of ethyl 2-(2-nitrostyryl)benzoate **4a**–**f** (1 mmol) and triphenylphosphane (576 mg, 2.2 mmol) was heated to reflux in diphenyl ether (10 mL) for 4 h. After cooling, the mixture was purified by chromatography (silica gel; hexanes then EtOAc/hexanes 10%) to afford the isoindolo-indolones **1a**–**f**.

6*H*-Isoindolo[2,1-*a*]indol-6-one (1a): Yellow solid; m.p. 153–154 °C (ref.[7] 153–154 °C). IR (KBr): $\tilde{\nu}$ = 1444, 1725, 3057 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.54 (s, 1 H), 7.08 (t, J = 8.0 Hz, 1 H), 7.21 (t, J = 8.0 Hz, 1 H), 7.27 (m, 1 H), 7.36 (d, J = 8.0 Hz, 1 H), 7.44 (m, 2 H), 7.67 (d, J = 7.6 Hz, 1 H), 7.80 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 103.54 (CH), 113.34 (CH), 121.26 (CH), 122.30 (CH), 123.90 (CH), 125.29 (CH), 126.33 (CH), 128.81 (CH), 133.59 (Cq), 133.72 (CH), 133.86 (Cq), 134.52 (Cq), 134.66 (Cq), 138.83 (Cq), 162.67 (Cq) ppm. $C_{15}H_9NO$ (219.24): calcd. C 82.18, H 4.14, N 6.39; found C 82.39, H 4.34, N 6.73.

2-Chloro-6*H*-isoindolo[2,1-*a*]indol-6-one (1b): Yellow solid; m.p. 160–162 °C. IR (KBr): $\tilde{\nu}$ = 1440, 1728, 3059 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.48 (s, 1 H), 7.15 (d, J = 7.6 Hz, 1 H), 7.28–7.31 (m, 1 H), 7.34 (s, 1 H), 7.45–7.46 (m, 2 H), 7.68–7.73 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 102.56 (CH), 114.05 (CH), 121.50 (CH), 121.96 (CH), 125.47 (CH), 126.31 (CH), 129.24 (CH), 129.36 (Cq), 131.87 (Cq), 133.64 (Cq), 133.96 (CH), 134.36 (Cq), 135.70 (Cq), 140.08 (Cq), 162.44 (Cq) ppm. HRMS: *m*/*z* calcd. for $C_{15}H_8ClNOH$ [M + H]$^+$ 254.0373; found 254.0370.

2-Methoxy-6*H*-isoindolo[2,1-*a*]indol-6-one (1c): Yellow solid; m.p. 160–161 °C (ref.[5] 165–166 °C). IR (KBr): $\tilde{\nu}$ = 1440, 1724, 3057 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.72 (s, 3 H), 6.37 (s, 1 H), 6.75 (d, J = 8.0 Hz, 1 H), 6.79 (s, 1 H), 7.20 (d, J = 8.0 Hz, 1 H), 7.32–7.37 (m, 2 H), 7.58–7.63 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.69 (CH_3), 103.40 (CH), 105.86 (CH), 113.77 (CH), 113.94 (CH), 121.07 (CH), 125.09 (CH), 128.21 (Cq), 128.71 (CH), 133.50 (CH), 133.9 (Cq), 134.59 (Cq), 135.49 (Cq), 139.66 (Cq), 156.69 (Cq), 162.30 (Cq) ppm. HRMS: *m*/*z* calcd. for $C_{16}H_{11}NO_2Na$ [M + Na]$^+$ 272.0687; found 272.0687. $C_{16}H_{11}NO_2$ (249.27): calcd. C 77.10, H 4.45, N 5.62; found C 77.40, H 4.40, N 5.99.

6*H*-(1,3)Dioxo(4,5-*f*)isoindolo[2,1-*a*]indol-6-one (1d): Orange solid; m.p. 201–202 °C. IR (KBr): $\tilde{\nu}$ = 1468, 1724, 3057 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.91 (s, 2 H), 6.38 (s, 1 H), 6.75 (s, 1 H), 7.20 (t, J = 7.4 Hz, 1 H), 7.31 (s, 1 H), 7.34 (d, J = 7.6 Hz, 1 H), 7.38 (t, J = 7.6 Hz, 1 H), 7.63 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 95.36 (CH), 101.36 (CH_2), 101.54 (CH), 103.88 (CH), 120.51 (CH), 125.28 (CH), 128.10 (CH), 128.23 (Cq), 128.80 (Cq), 133.35 (Cq), 133.77 (CH), 135.14 (Cq), 137.79 (Cq), 145.11 (Cq), 147.42 (Cq), 162.66 (Cq) ppm. HRMS: *m*/*z* calcd. for $C_{16}H_9NO_3Na$ [M + Na]$^+$ 286.0480; found 286.0480.

2,3-Dimethoxy-6*H*-isoindolo[2,1-*a*]indol-6-one (1e): Light-brown solid; m.p. 168–169 °C (ref.[9] 160–161 °C). IR (KBr): $\tilde{\nu}$ = 1445, 1724, 3055 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 3 H), 3.89 (s, 3 H), 6.39 (s, 1 H), 6.82 (s, 1 H), 7.19–7.20 (m, 1 H), 7.32–7.38 (m, 3 H), 7.61 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.23 (CH_3), 55.33 (CH_3), 96.01 (CH), 102.71 (CH), 103.29 (CH), 119.49 (CH), 124.19 (CH), 125.75 (Cq), 127.02 (CH), 127.20 (Cq), 132.47 (Cq), 132.66 (CH), 134.10 (Cq), 136.56 (Cq), 145.83 (Cq), 148.36 (Cq), 161.73 (Cq) ppm. HRMS: *m*/*z* calcd. for $C_{17}H_{13}NO_3Na$ [M + Na]$^+$ 302.0793; found 302.0792.

1,2,3-Trimethoxy-6*H*-isoindolo[2,1-*a*]indol-6-one (1f): Brown solid; m.p. 156–158 °C. IR (KBr): $\tilde{\nu}$ = 1437, 1724, 3061 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.78 (s, 3 H), 3.85 (s, 3 H), 3.98 (s, 3 H), 6.55 (s, 1 H), 7.09 (s, 1 H), 7.17–7.19 (m, 1 H), 7.33–7.37 (m, 2 H), 7.61 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.48 (CH_3), 61.13 (CH_3), 61.34 (CH_3), 92.76 (CH), 101.45 (CH), 120.53 (Cq), 120.60 (CH), 125.25 (CH), 128.10 (CH), 130.46 (Cq), 133.40 (Cq), 133.71 (CH), 134.83 (Cq), 136.58 (Cq), 138.26 (Cq), 147.20 (Cq), 154.09 (Cq), 162.75 (Cq) ppm. HRMS: *m*/*z* calcd. for $C_{18}H_{15}NO_4Na$ [M + Na]$^+$ 332.0899; found 332.0895.

Supporting Information (see footnote on the first page of this article): Spectral data of all the products are given.

Acknowledgments

The authors are thankful to the Department of Science and Technology (DST), New Delhi and the Council for Scientific and Industrial Research (CSIR), New Delhi for financial support, and IISc (Bangalore) for use of the HRMS facility. H. K. K. acknowledges CSIR (New Delhi) for the award of a NET Senior Research Fellowship.

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Received: January 11, 2013
Published Online: May 23, 2013

