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REGULAR ARTICLE

Metal free synthesis of functionalized 1-aryl isoquinolines via iodine mediated oxidative dehydrogenation and ring opening of lactam in isoindoloisoquinolinones

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Abstract. A facile and convenient method for the synthesis of substituted 2-(isoquinolin-1-yl)benzoic acids from isoindoloisoquinolinones in the presence of molecular iodine under sealed tube condition at 100°C has been developed. This methodology involves the oxidative dehydrogenation and ring opening of hydroxy lactam/methoxy lactam to furnish the 2-(isoquinolin-1-yl)benzoic acids. Some of these acids are successfully cyclized to furnish the azabenzanthrone derivatives, the potential precursors for the synthesis of menisporphine alkaloids and daurioxoisoaporphines.

Keywords. Iodine; oxidative dehydrogenation; oxoisoaporphines; 1-Azabenzanthrone; isoindoloisoquinolinones.

1. Introduction

The oxoisoaporphines constitute a small family of alkaloids that are known to occur in the rhizome of *Menispermum dauricum* DC. (Menispermaceae). The oxoisoaporphine alkaloids possess 1-azabenzanthrone (7*H*-dibenzo[*de*,*h*]quinolin-7-one) skeleton containing isoquinoline ring incorporated as part of a biaryl system in their structures (**A** in Figure 1). Derivatives of oxoisoaporphine alkaloids such as daurioxoisoaporphines exhibited cytotoxic activities against a small panel of cancer cell lines.[1] A series of 9-amino alkanamido-1-azabenzanthrone derivatives and their quaternary methiodide salts exhibited inhibitory activity against acetylcholine esterase (AChE) and butyrylcholine esterase (BuChE).[2] The 1-azabenzanthrone moiety of oxoisoaporphine alkaloids displayed DNA binding affinity with calf thymus DNA,[3] as well as cytotoxicity against tumor cell lines,[4] antiproliferative activity[5] and antiplasmodial activity.[6] Organoplatinum(II) complexes of oxoisoaporphine exhibited antitumor activity.[7]

Synthetic protocols have already been developed to accomplish the synthesis of 1-azabenzanthrone and their derivatives, which are subsequently used to synthesize oxoisoaporphine alkaloids.[6–10] Oxoisoaporphine alkaloids possess 1-azabenzanthrone skeleton which can be synthesized from the intermediates such as *o*-isoquinolin-2-yl benzoic acid (substituted or unsubstituted) or 2-(3,4-dihydroisoquinolin-1-yl) benzoic acid (substituted or unsubstituted) (Figure 2). Though the intermediates **X** and **Y** are useful for the synthesis of oxoisoaporphines or dihydrooxoisoaporphines, the methods adopted to prepare these intermediates suffered from one or more disadvantages such as high temperature, multiple steps, tedious workup, long reaction times, anhydrous conditions, low yields and difficult product purification procedures. In view of these drawbacks and our continued effort to show the synthetic potential of TfOH-mediated *6-exo-trig* cyclization of phenethylphthalimides, it has become imperative to develop a simple and efficient methodology to convert the isoindoloisoquinolinones to intermediates **X** or **Y**.

Recently, molecular iodine has attracted great attention as a catalyst for organic transformations because it is inexpensive, readily available, nonmetallic, and environmentally-benign as compared to transition metal catalysts. Further, molecular iodine has received importance in organic synthesis due to its mild Lewis acidic character. Molecular iodine has also been used in the synthesis of various heterocyclic compounds, protection and deprotection of functional groups such as alcohols and carboxylic acids, amines, phenols, iodination reactions and oxidation reactions.[11] Particularly, iodine has

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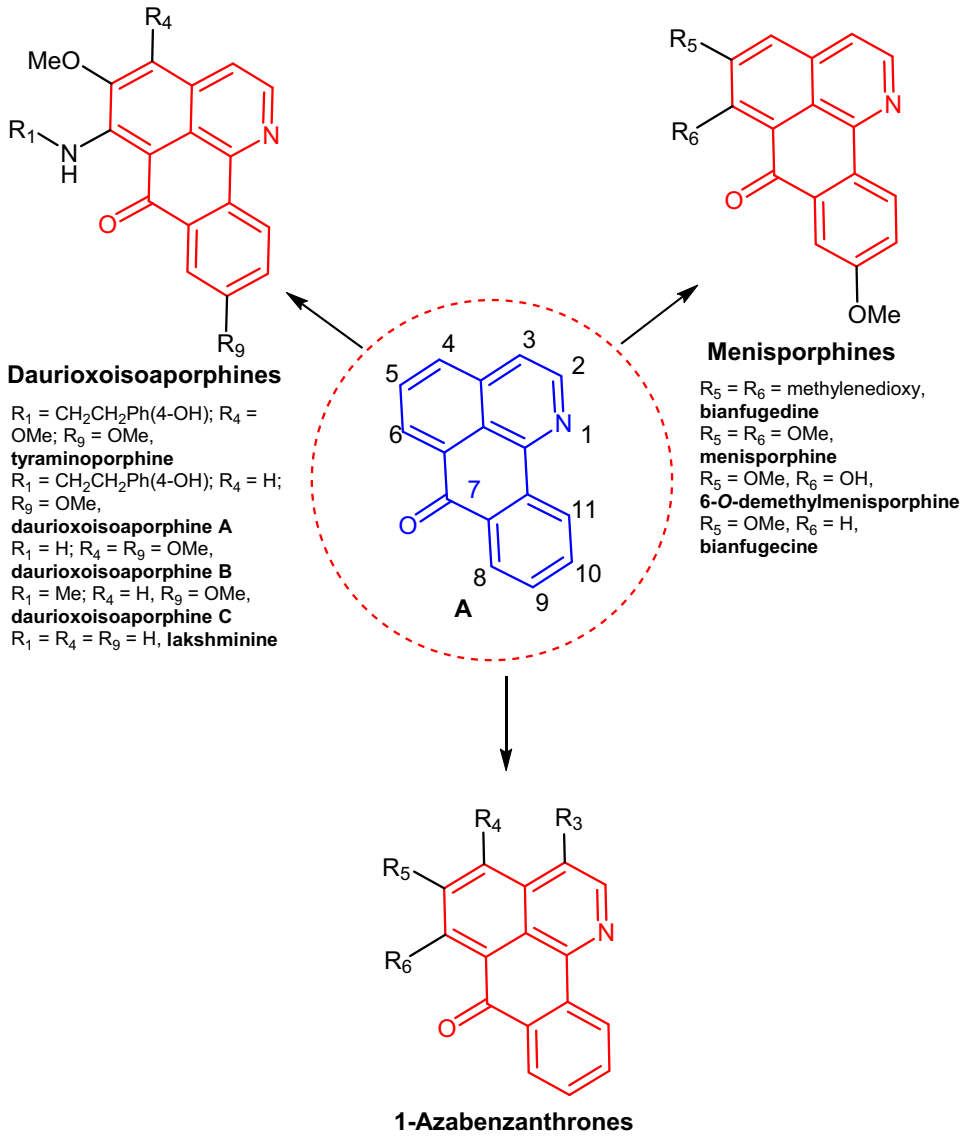


Figure 1. Structure of oxoisoaporphine, azabenzanthrones, menisporphine alkaloids.

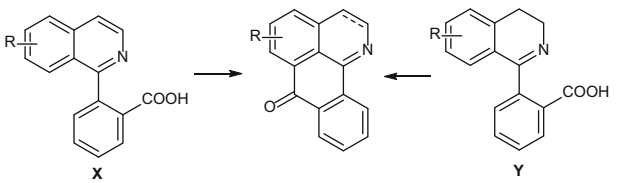
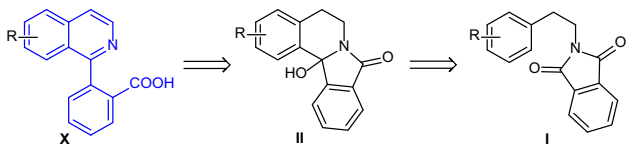


Figure 2. Synthetic routes to prepare 1-azabenzanthrone alkaloids.

been utilized for the oxidative aromatization of α, β-unsaturated cyclic compounds.[12] Similarly, oxidative aromatization of tetrahydroisoquinoline was achieved using KI and ^{t}BuOOH combination.[13] To the best of our knowledge, direct utility of molecular iodine for oxidative dehydrogenation of tetrahydroisoindoloisoquinolinone system has not been reported.

Hence, herein, we report an oxidative dehydrogenation and ring opening of amide group in isoindoloisoquinolinones with molecular iodine for the first time to prepare *o*-isoquinolin-2-yl benzoic acids, the potential precursors for the synthesis of oxoisoaporphine alkaloids.

A simple and efficient methodology has been developed to prepare THIQs and THBCs through activation of imide carbonyl group using Lewis acid/Brønsted acid.[14] Following this methodology, we synthesized the required starting materials in a single step from substituted phenethylphthalimides **I** for this studies. From the acquired knowledge from the synthesis of isoindoloisoquinolinones, one can visualize the precursor **X** from imide **I** *via* a C-N and C-C bond disconnections (Scheme 1).



Scheme 1. Retrosynthetic analysis of isoquinolinylbenzoic acid **X**.

2. Experimental

2.1 *General information*

Melting points reported in this paper are uncorrected and were determined using BUCHI M-560, BuchiLabortechnik AG, Switzerland. Infrared spectra were recorded on Thermo Nicolet iS10 FT-IR Spectrophotometer and are reported in frequency of absorption (cm^{-1}). Mass spectra were measured with Agilent-6530 B Q-TOF (ESI-HRMS). ^1H and ^{13}C NMR were recorded on Brucker AVANCE 400 spectrometer. NMR spectra for all the samples were measured in $CDCl_3$ or DMSO-d_6 using TMS as an internal standard. The chemical shifts are expressed in δ ppm down field from the signal of internal TMS. All solvents used in the reactions and chromatography were distilled and/or dried properly for purity using standard procedures.[16] Dry dichloroethane was obtained by distillation over calcium hydride. Column chromatography was performed on Merck silica gel 100–200 mesh and TLC analysis was facilitated using phosphomolybdic acid and $KMnO_4$ stain in addition to UV light with Merck 60 F 254 pre-coated silica plates. Starting materials were prepared from the corresponding substituted phenethylphthalimides following the existing triflic acid-mediated imide carbonyl group activation methodology.[14]

2.2 *General procedure for the synthesis of ether derivatives* ***(3a–3c, 3e–3h, 3j)***

A 20 mL-sealed tube was charged with hydroxy lactam **1** (0.4 mmol) and iodine (0.4 mmol) in dry methanol (2 mL). The tube was flushed with nitrogen gas and closed with Teflon cap. The solution was heated at 100°C for 12 h. The resulting suspension was cooled to room temperature and the solvent was removed under vacuum on rotary evaporator to dryness. Ethyl acetate (5 mL) was added with vigorous stirring and excess iodine was quenched by aqueous saturated $Na_2S_2O_3$ solution (5 mL). The organic layer was separated and aqueous layer was extracted with ethyl acetate (2 x 5 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na_2SO_4. Filtered and the solvent was removed under vacuum on rotary evaporator to dryness. The dried compound was purified through short silica gel column chromatography using hexane and ethyl acetate (90:10) as eluent to give desired products (**3a–3c**, **3e–3h, 3j**).

2.2a *12b-Methoxy-5,12b-dihydroisoindolo[1,2-a]isoquinolin-8(6H)-one* ***(3a)***: 97 mg, colorless solid, 92% yield, M.p. 127–128°C, IR (KBr, cm^{-1}): 3065, 2935, 2829, 1707, 1608, 1458, 1301, 1103, 1064, 761; ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 7.6 Hz, 1H), 7.85 (d, J = 7.2 Hz, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.30 - 7.23 (m, 2H), 7.16 (d, J = 6.8 Hz, 1H), 4.43 (ddd, J = 12.8, 6.4, 2.4 Hz, 1H), 3.43 (ddd, J = 16.0, 11.2, 4.8 Hz, 1H), 3.07 (ddd, J = 16.4, 11.2, 6.4 Hz, 1H), 2.99 (s, 3H), 2.90–2.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 144.1, 135.9, 134.9, 132.5, 132.4, 129.9, 129.4, 128.7, 127.5, 126.8, 123.8, 123.7, 90.4, 50.5, 35.2, 29.1; HRMS-ESI (m/z): $[M+H]^+$Found 266.1182 and calculated 266.1181 for $C_{17}H_{16}NO_2$.

2.2b *3-Bromo-12b-methoxy-5,12b-dihydroisoindolo[1,2-a]isoquinolin-8(6H)-one* ***(3b)***: 128 mg, colorless solid, 93% yield, M.p. 139–140°C, IR (KBr, cm^{-1}): 2928, 1707, 1610, 1440, 1378, 1109, 1014, 807, 761; ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (td, J = 7.6, 0.8 Hz, 2H), 7.70 (d, J = 8.4 Hz, 1H), 7.63 (td, J = 7.6, 1.2 Hz, 1H), 7.51 (td, J = 7.6, 1.0 Hz, 1H), 7.38 (dd, J = 8.4, 2.0 Hz, 1H),7.29 (t, J = 1.2 Hz, 1H), 4.40 (ddd, J = 8.8, 6.3, 2.6 Hz, 1H), 3.37 (ddd, J = 13.2, 11.2, 4.6 Hz, 1H), 3.06–2.97 (m, 1H), 2.96 (s, 3H), 2.82 (ddd, J = 7.2, 4.4, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 143.6, 137.1, 134.9, 132.5, 132.2, 132.1, 130.1, 129.9, 129.2, 123.9, 123.5, 122.6, 90.1, 50.5, 34.7, 28.8; HRMS-ESI (m/z): $[M+H]^+$Found 344.0308 and calculated 344.0286 for $C_{17}H_{15}BrNO_2$.

2.2c *2,3,12b-Trimethoxy-5,12b-dihydroisoindolo[1,2-a]isoquinolin-8(6H)-one* ***(3c)***: 103 mg, yellow semi solid, 76% yield, IR (KBr, cm^{-1}): 2996, 2935, 2837 1704, 1612, 1459, 1061, 1025, 758; ^1H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 7.6 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.64 (td, J = 7.6, 1.2 Hz, 1H), 7.53–7.49 (m, 1H), 7.33 (s, 1H), 6.59 (s, 1H), 4.45 (ddd, J = 12.8, 6.0, 1.6 Hz, 1H), 3.94 (s, 3H), 3.83 (s, 3H), 3.67 (td, J = 12.8, 4.4, 1H), 3.05–2.98 (m, 1H), 2.97 (s, 3H), 2.75–2.69 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 149.4, 147.9, 144.4, 132.4, 132.3, 129.8, 127.6, 127.6, 123.9, 123.3, 111.5, 110.3, 90.2, 56.2, 56.0, 50.5, 35.1, 28.8; HRMS-ESI (m/z): $[M+H]^+$Found 326.1376 and calculated 326.1392 for $C_{19}H_{20}NO_4$.

2.2d *1,4,12b-Trimethoxy-5,12b-dihydroisoindolo[1,2-a]isoquinolin-8(6H)-one* ***(3e)***: 95 mg, red semi solid, 70% yield, IR (KBr, cm^{-1}): 3084, 2945, 2833, 1701, 1602, 1475, 1262, 1070, 985, 754; ^1H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, J = 7.6 Hz, 1H), 7.83–7.80 (m, 1H), 7.55 (td, J = 7.6, 1.2 Hz, 1H), 7.48 (td, J = 7.2. 0.8 Hz, 1H), 6.81(d, J = 8.8 Hz, 1H), 6.76 (d, J = 8.8 Hz, 1H), 4.47 (ddd, J = 7.6, 6.4, 1.2 Hz, 1H), 3.96 (s, 3H), 3.74(s, 3H), 3.27-3.19 (m, 1H), 2.99 (s, 3H), 2.94-2.88 (m, 1H), 2.80–2.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 152.4, 151.6, 144.0, 132.8, 131.8, 129.8, 126.8, 126.7, 125.6, 123.2, 110.7, 110.4, 91.9, 56.1, 55.9, 50.3, 33.8, 24.1; HRMS-ESI

(m/z): $[M+H]^+$Found 326.1386 and calculated 326.1392 for $C_{19}H_{20}NO_4$.

2.2e *2,3,4,12b-Tetramethoxy-5,12b-dihydroisoindolo [1,2-a]isoquinolin-8(6H)-one* ***(3f)***: 94 mg, yellow semi solid, 66% yield, IR (KBr, cm^{-1}): 2941, 2836, 1702, 1606, 1459, 1112, 1040, 747; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, J = 13.2, 7.6 Hz, 2H), 7.63 (td, J = 7.6, 0.8 Hz, 1H), 7.51 (td, J = 7.6, 0.8 Hz, 1H), 7.18 (s, 1H), 4.45 (ddd, J = 8.0, 6.0, 2.0 Hz, 1H), 3.92 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 3.32–3.25 (m, 1H), 2.96 (s, 3H), 2.93–2.87 (m, 1H), 2.84–2.71 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 152.2, 151.1, 144.1, 142.5, 132.4, 132.3, 130.9, 129.9, 123.9, 123.4, 122.0, 106.6, 90.1, 60.8, 60.6, 56.2, 50.4, 34.6, 22.9; HRMS-ESI (m/z): $[M+H]^+$Found 356.1501 and calculated 356.1498 for $C_{20}H_{22}NO_5$.

2.2f *12b-Methoxy-3-methyl-5,12b-dihydroisoindolo [1,2-a]isoquinolin-8(6H)-one (***3g***)*: 75 mg, colorless solid, 67% yield, M.p. 134–137°C, IR (KBr, cm^{-1}): 2930, 2817, 1702, 1611, 1457, 1380, 1102, 1057, 755; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.6 Hz, 1H), 7.83 (dt, J = 7.6, 0.8 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.63 (td, J = 7.6, 1.2 Hz, 1H), 7.50 (td, J = 7.2, 0.8 Hz, 1H), 7.09 (d, J = 8.0 Hz, 1H), 6.97 (s, 1H), 4.41 (ddd, J = 12.8, 6.0, 1.8 Hz, 1H), 3.40 (ddd, J = 16.0, 11.2, 4.4 Hz, 1H), 3.07–2.98 (m, 1H), 2.97 (s, 3H), 2.82 (ddd, J = 16.0, 4.4, 2.4 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 144.2, 138.6, 134.7, 133.0, 132.4, 132.3, 129.9, 129.8, 127.7, 127.4, 123.8, 123.6, 90.4, 50.5, 35.1, 29.1, 21.1; HRMS-ESI (m/z): $[M+H]^+$Found 280.1371 and calculated 280.1338 for $C_{18}H_{18}NO_2$.

2.2g *11,12b-Dimethoxy-5,12b-dihydroisoindolo[1,2 -a]isoquinolin-8(6H)-one* ***(3h)***: 46 mg, colorless solid, 39% yield, M.p. 159–161°C, IR (KBr, cm^{-1}): 2934, 2834, 1699, 1610, 1449, 1105, 1062, 765; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (dd, J = 8.0, 2.0 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.39 (d, J = 2.0 Hz, 1H), 7.30 - 7.22 (m, 2H), 7.16 (d, J = 6.8 Hz, 1H), 7.08 (dd, J = 8.4, 2.0 Hz, 1H) 4.39 (ddd, J = 8.8, 6.0, 2.4 Hz, 1H), 3.93 (s, 3H), 3.40 (ddd, J = 12.4, 11.2, 4.8 Hz, 1H), 3.09–3.03 (m 1H), 3.01 (s, 3H), 2.85 (ddd, J = 11.2, 4.4, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 163.4, 146.3, 135.9, 135.1, 129.4, 128.6, 127.3, 126.8, 125.2, 125.0, 115.5, 109.4, 90.1, 55.9, 50.5, 35.3, 29.0; HRMS-ESI (m/z): $[M+H]^+$Found 296.1277 and calculated 296.1287 for $C_{18}H_{18}NO_3$.

2.2h *12b-Methoxy-5,12b-dihydro-[1,3]dioxolo[4,5-g] isoindolo[1,2-a]isoquinolin-8(6H)-one* ***(3j)***: 83 mg, light yellow semi solid, 67% yield, IR (KBr, cm^{-1}): 2935, 2893, 1703, 1621, 1480, 1039, 760; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, J = 7.6, 3.6 Hz, 2H), 7.64 (td, J = 7.6, 0.8 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.31 (s, 1H), 6.58 (s, 1H), 5.91 (dd, J = 13.6, 1.2 Hz, 2H), 4.40 (ddd, J = 8.4, 6.0, 2.4 Hz, 1H), 3.36 (ddd, J = 12.8, 11.6, 4.4 Hz, 1H), 3.01-2.93 (m 1H), 2.96 (s, 3H), 2.73 (ddd, J = 6.8, 4.4, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 147.9, 146.7, 144.2, 132.4, 132.3, 129.9, 129.0, 128.9, 123.9, 123.5, 108.9, 107.4, 101.3, 90.4, 50.5, 35.1, 29.3; HRMS-ESI (m/z): $[M+H]^+$Found 310.1087 and calculated 310.1079 for $C_{18}H_{16}NO_3$.

2.3 *General procedure for the synthesis of 2-(isoquinolin-1-yl)benzoic acid/ ester derivatives* ***(2a-2i/ 4a, 4c, 4e, 4h)***

A 20 mL-sealed tube was charged with corresponding substrate **1** or **3** (0.2 mmol) and iodine (1 equiv.) in dry 1,2-dichloroethane (2 mL). The tube was flushed with nitrogen gas and closed with Teflon cap. The solution was heated at 100°C for 12 h. The resulting suspension was cooled to room temperature and ethyl acetate (5 mL) was added with vigorous stirring and stirring was continued for 1 h. Excess iodine was quenched by saturated aqueous $Na_2S_2O_3$ solution (5 mL). The organic layer was separated and aqueous layer was extracted with ethyl acetate (2 x 5 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na_2SO_4. Filtered and the solvent was removed under vacuum on rotary evaporator to dryness. The dried compound was purified through short silica gel column chromatography using methanol as eluent to give desired product **2** and hexane and ethyl acetate (90:10) as eluent to give desired product **4**.

2.3a *2-(Isoquinolin-1-yl)benzoic acid* ***(2a)***: 46 mg, colorless solid, 92% yield, M.p. 245–246°C, IR (KBr, cm^{-1}): 3425, 1685, 1594, 1385, 1260, 762; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.48 (d, J = 6.0 Hz, 1H), 8.01–7.98 (m, 2H), 7.80 (d, J = 5.6 Hz, 1H), 7.76–7.72 (m, 1H), 7.68 (td, J = 7.6, 1.6 Hz, 1H), 7.61 (td, J = 7.6, 1.6 Hz, 1H), 7.58–7.53 (m, 2H), 7.42 (dd, J = 7.6, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.8, 160.7, 141.6, 139.9, 135.5, 132.1, 131.4, 130.7, 130.0, 129.8, 128.4, 127.4, 126.9, 126.7, 126.3, 119.7; HRMS-ESI (m/z): $[M+H]^+$ Found 250.0862 and calculated 250.0868 for $C_{16}H_{12}NO_2$.

2.3b *2-(6-Bromoisoquinolin-1-yl)benzoic acid* ***(2b)***: 41 mg, colorless solid, 62% yield, M.p. 278–281°C, IR (KBr, cm^{-1}): 3401, 2831, 2725, 1706, 1594, 1375, 1119, 770; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.53 (d, J = 5.6 Hz, 1H), 8.17–8.16 (m, 1H), 8.01 (dd, J = 8.0, 1.6 Hz, 1H), 7.81 – 7.79 (m, 1H), 7.72 (td, J = 7.6, 1.6 Hz, 1H), 7.65 (td, J = 7.6, 1.6 Hz, 1H), 7.57 (d, J = 1.6 Hz, 2H), 7.45 (dd, J = 7.6, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.7, 160.9, 142.8, 139.5, 136.4, 134.8, 132.0, 131.5, 130.7, 129.9, 128.8, 128.7, 128.0, 125.6, 125.2, 119.0; HRMS-ESI (m/z): $[M+H]^+$ Found 327.9974 and calculated 327.9973 for $C_{16}H_{11}BrNO_2$.

2.3c *2-(6,7-Dimethoxyisoquinolin-1-yl)benzoic acid* ***(2c)***: 46 mg, colorless solid, 75% yield, M.p. 220–221°C, IR (KBr, cm^{-1}): 3450, 2925, 2834, 1689, 1565, 1481, 1417, 1384, 1278, 772; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.24 (d, J = 6.0 Hz, 1H), 7.88 (dd, J = 5.6, 3.2 Hz, 1H), 7.52 (d, J = 5.6 Hz, 1H), 7.42 (dd, J = 5.2, 3.2 Hz, 2H), 7.29 (s,

1H), 7.22 (dd, J = 5.6, 3.2 Hz, 1H), 6.95 (s, 1H), 3.90 (s, 3H), 3.62 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.8, 160.5, 152.0, 149.0, 140.7, 140.3, 138.9, 132.1, 130.1, 129.1, 128.1, 127.3, 123.0, 117.9, 105.8, 105.0, 55.7, 55.2; HRMS-ESI (m/z): $[M+H]^+$ Found 310.1073 and calculated 310.1079 for $C_{18}H_{16}NO_4$.

2.3d *2-(6,8-Dimethoxyisoquinolin-1-yl)benzoic acid **(2d)***: 40 mg, colorless solid, 65% yield, M.p. 198–200°C, IR (KBr, cm^{-1}): 3457, 3008, 2934, 2854, 1701, 1668, 1615, 1586, 1413, 1158, 760; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, J = 5.2 Hz, 1H), 7.99 (d, J = 7.2 Hz, 1H), 7.52–7.46 (m, 2H), 7.42 (t, J = 7.2 Hz, 1H), 7.19 (d, J = 7.6 Hz, 1H), 6.71 (d, J = 2.4 Hz, 1H), 6.41 (d, J = 2.0 Hz, 1H), 3.93 (s, 3H), 3.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.7, 159.4, 158.6, 152.7, 140.3, 132.3, 130.4, 130.1, 130.0, 129.3, 127.4, 124.3, 119.5, 115.9, 100.2, 97.8, 55.7, 55.6; HRMS-ESI (m/z): $[M+H]^+$ Found 310.1075 and calculated 310.1079 for $C_{18}H_{16}NO_4$.

2.3e *2-(5,8-Dimethoxyisoquinolin-1-yl)benzoic acid **(2e)***: 28 mg, yellow solid, 45% yield, M.p. 211–213°C, IR (KBr, cm^{-1}): 3449, 3005, 2940, 2843, 1671, 1577, 1417, 1384, 1122, 768; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.45 (d, J =5.6 Hz, 1H), 7.94–7.89 (m, 2H), 7.56 (td, J = 7.2, 1.2 Hz, 1 H), 7.47 (td, J = 7.2, 1.6 Hz, 1H), 7.19 (dd, J = 7.2, 0.8 Hz, 1H), 7.10 (d, J = 8.8 Hz, 1H), 6.87 (d, J = 8.8 Hz, 1H), 3.95 (s, 3H), 3.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.7, 149.8, 147.8, 145.8, 141.5, 137.2, 130.6, 130.0, 129.5, 129.0, 128.7, 126.8, 119.3, 113.1, 108.3, 107.0, 56.0, 55.7; HRMS-ESI (m/z): $[M+H]^+$ Found 310.1089 and calculated 310.1079 for $C_{18}H_{16}NO_4$.

2.3f *2-(5,6,7-Trimethoxyisoquinolin-1-yl)benzoic acid **(2f)***: 32 mg, colorless semi solid, 51% yield, IR (KBr, cm^{-1}): 3425, 3002, 2945, 2851, 1682, 1586, 1510, 1420, 1160, 670; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.36–8.28 (m, 1H), 7.89–7.85 (m, 1H), 7.50–7.40 (m, 3H), 7.19 (t, J = 2.4 Hz, 1H), 6.83–6.71 (m, 1H), 3.96 (s, 3H), 3.87 (s, 3H), 3.84 (s, 3H); HRMS-ESI (m/z): $[M+H]^+$Found 340.1186 and calculated 340.1185 for $C_{19}H_{18}NO_5$.

2.3g *2-(6-Methylisoquinolin-1-yl)benzoic acid (**2g**)*: 28 mg, colorless solid, 53% yield, M.p. 232–233°C, IR (KBr, cm^{-1}): 3416, 2925, 2850, 1682, 1589, 1468, 1385, 704; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.50–8.25 (m, 2H), 8.07–7.91 (m, 1H), 7.66–7.56 (m, 1H), 7.44–7.36 (m, 3H), 7.15–6.98 (m, 1H), 6.89–6.49 (m, 1H), 1.77 (s, 3H); HRMS-ESI (m/z): $[M+H]^+$ Found 264.1028 and calculated 264.1025 for $C_{17}H_{14}NO_2$.

2.3h *2-(Isoquinolin-1-yl)-4-methoxybenzoic acid **(2h)***: 42mg, colorless semi solid, 76% yield, IR (KBr, cm^{-1}): 3399, 3058, 2934, 1696, 1603, 1451, 1233, 1027, 754; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.47 (d, J = 6.0 Hz, 1H), 8.01 (t, J = 8.8 Hz, 2H), 7.80 (d, J = 5.6 Hz, 1H), 7.75–7.71 (m, 1H), 7.54–7.53 (m, 2H), 7.17 (dd, J = 8.8, 2.4 Hz, 1H), 6.90 (d, J = 2.4 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.1, 161.7, 160.9, 142.6, 141.6, 135.5, 132.4, 130.1, 127.5, 126.9, 126.4, 123.6, 119.9, 116.1, 113.9, 55.7; HRMS-ESI (m/z): $[M+H]^+$Found 280.0957 and calculated 280.0974 for $C_{17}H_{14}NO_3$.

2.3i *2-(Benzo[g]isoquinolin-1-yl)benzoic acid **(2i)***: 25 mg, red solid, 41% yield, M.p. 244–245°C, IR (KBr, cm^{-1}): 3425, 2846, 2781, 1722, 1600, 1460, 1290, 813; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.52 (d, J = 5.2 Hz, 1H), 8.05 - 8.01 (m, 2H), 7.94 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.79 (d, J = 5.2 Hz, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.54–7.42 (m, 3H), 7.17–7.13 (m, 1H) 6.91 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.4, 160.9, 144.7, 143.2, 137.6, 136.3, 133.8, 133.4, 132.1, 130.9, 130.8, 129.7, 129.3, 128.2, 127.5, 127.1, 126.7, 126.1, 123.9, 120.6; HRMS-ESI (m/z): $[M+H]^+$ Found 300.1026 and calculated 300.1025 for $C_{20}H_{14}NO_2$.

2.3j *Methyl 2-(isoquinolin-1-yl)benzoate **(4a)***: 28 mg, colorless semi solid, 53% yield, IR (KBr, cm^{-1}): 3056, 2942, 2849, 1723, 1569, 1441, 1285, 1081, 760; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, J = 5.6 Hz, 1H), 8.12 (dd, J = 8.0, 1.6 Hz, 1H), 7.88 (d, J =8.4 Hz, 1H), 7.68–7.61 (m, 4H), 7.57 (td, J = 7.6, 1.2 Hz, 1H), 7.50 (td, J = 7.6, 1.2 Hz, 1H), 7.46–7.44 (m, 1H), 3.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 161.1, 141.8, 140.8, 136.1, 132.0, 130.9, 130.8, 130.5, 130.1, 128.6, 127.5, 127.3, 127.0, 126.8, 120.1, 51.9; HRMS-ESI (m/z): $[M+Na]^+$Found 286.0833 and calculated 286.0844 for $C_{17}H_{13}NNaO_2$.

2.3k *Methyl 2-(6,7-dimethoxyisoquinolin-1-yl)benzoate **(4c)***: 27 mg, colorless semi solid, 42% yield, IR (KBr, cm^{-1}): 3017, 2926, 2853, 1724, 1617, 1504, 1425, 1270, 1127, 1027, 762; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, J = 5.6 Hz, 1H), 8.08 (dd, J = 7.6, 1.2 Hz, 1H), 7.67 (td, J = 7.6, 1.2 Hz, 1H), 7.62 – 7.48 (m, 3H), 7.13 (s, 1H), 6.87 (s, 1H), 4.04 (s, 3H), 3.77 (s, 3H), 3.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 158.3, 152.8, 150.2, 140.9, 140.7, 133.1, 132.1, 131.1, 130.9, 130.4, 128.6, 123.2, 119.0, 105.1, 104.8, 56.2, 55.9, 52.0; HRMS-ESI (m/z): $[M+H]^+$Found 324.1233 and calculated 342.1236 for $C_{19}H_{18}NO_4$.

2.3l *Methyl 2-(5,8-dimethoxyisoquinolin-1-yl)benzoate **(4e)***: 28 mg, colorless solid, 46% yield, M.p. 159–160°C, IR (KBr, cm^{-1}): 3067, 2944, 2840, 1723, 1616, 1563, 1452, 1259, 1114, 778, 762; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, J = 6.0 Hz, 1H), 8.06-8.02 (m, 2H), 7.56 (td, J = 7.2, 1.2 Hz, 1H), 7.44 (td, J = 7.6, 1.2 Hz, 1H), 7.32 (dd, J = 7.6, 1.2 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 3.98 (s, 3H), 3.43 (s, 3H), 3.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 158.6, 150.3, 148.7, 146.1, 141.8, 131.4, 130.2, 129.5, 129.3, 129.1, 127.0, 120.1, 114.0, 107.7, 106.4, 56.0, 55.8, 51.7; HRMS-ESI (m/z): $[M+H]^+$Found 324.1233 and calculated 342.1236 for $C_{19}H_{18}NO_4$.

2.3m *Methyl 2-(isoquinolin-1-yl)-4-methoxybenzoate **(4h)***: 36 mg, colorless semi solid, 61% yield, IR (KBr, cm^{-1}): 2929, 2851, 1717, 1603, 1429, 1271, 1123, 1031, 828; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, J = 5.6 Hz, 1H), 8.05 (d, J = 8.8 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.61–7.56 (m, 2H), 7.54–7.51 (m, 1H), 7.41–7.37 (m, 1H), 7.00 (dd, J = 78.8, 2.4 Hz, 1H), 6.90 (d, J = 2.8 Hz, 1H), 3.80 (s, 3H), 3.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 162.5, 161.3, 143.2, 141.8, 136.0, 132.8, 130.1, 127.6, 127.3, 127.0, 126.8, 122.6, 120.1, 115.9, 114.4, 55.7, 51.7; HRMS-ESI (m/z): $[M+H]^+$Found 294.1114 and calculated 294.1130 for $C_{18}H_{16}NO_3$.

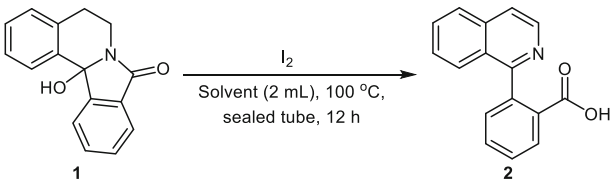
2.4 *Synthesis of 1-azabenzanthrone **(A)***

2-(Isoquinolin-1-yl)benzoic acid **2a** (100 mg, 0.4 mmol) was poured slowly into concentrated sulfuric acid (2 mL) at 90°C. The mixture was stirred and heated at 230–240°C for 2 h. After being cooled, the solution was poured onto crushed ice. Sodium hydroxide was added until pH = 3 was obtained and the resultant precipitate was filtered off and washed in turn with dilute aqueous sodium hydroxide and water to give the crude product, which was extracted with acetic acid. The extract was condensed under reduced pressure and the resultant precipitate was washed off, dried to give the product 7H-dibenzo[de,h]quinolin-7-one **A** as light yellow solid. 51 mg, 55% yield, M.p. 182–184°C (lit.[8] 181–183°C), IR (KBr, cm^{-1}): 3055, 2924, 2849, 1657, 1586, 1434, 1361, 1288, 796, 699; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (dd, J = 7.6, 0.8 Hz, 1H), 8.78 (d, J = 5.6 Hz, 1H), 8.66 (dd, J = 7.2, 1.2 Hz, 1H), 8.42 (dd, J = 7.8, 1.2 Hz, 1H), 8.15 (dd, J = 8.4, 0.8 Hz, 1H), 7.93-7.89 (m, 1H), 7.81 (td, J = 8.0, 1.2 Hz, 1H), 7.75 (d, J = 5.6 Hz, 1H), 7.65 (td, J = 8.0, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.4, 148.8, 144.1, 136.8, 135.2, 134.1, 133.4, 132.4, 130.6, 130.4, 129.9, 129.1, 127.6, 125.3, 122.9, 121.0; HRMS-ESI (m/z): $[M+H]^+$Found 232.0770 and calculated 232.0762 for $C_{16}H_{10}NO$.

2.5 *Synthesis of 3-bromo-1-azabenzanthrone **(B)***

To the solution of 1-azabenzanthrone **A** (40 mg, 17.3 mmol) in CH_3CN (2.5 mL) was added drop wise with stirring to a solution of 0.5 M Br_2 in CH_3CN (3.0 mL, 1.54 mmol). The mixture was heated at 80°C for 24 h. The solvent and excess reagent were removed by evaporation under reduced pressure and the residue was chromatographed on silica gel, eluting with CH_2Cl_2, to afford 3-bromo-1-aza-benzo[de]anthracen-7-one **B** as yellow solid. 18 mg, 34% yield, M.p. 254–256°C (lit.[17] 256°C), IR (KBr, cm^{-1}): 3064, 2921, 2854, 1665, 1594, 1559, 1472, 1388, 1278, 793; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91 (s, 1H), 8.81 (d, J = 8.0 Hz, 1H), 8.70 (dd, J = 7.6, 0.8 Hz, 1H), 8.47 (dd, J = 8.4, 0.8 Hz, 1H), 8.39 (dd, J = 8.0, 0.8 Hz, 1H), 8.00 (dd, J = 8.4, 7.6 Hz, 1H), 7.82–7.78 (m, 1H), 7.68–7.64 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.0, 148.1, 145.8, 136.3, 134.4, 134.2, 132.7, 132.0, 131.7, 130.8, 129.4, 127.8, 125.5, 120.2, 117.3, 116.1; HRMS-ESI (m/z): $[M+H]^+$Found 309.9874 and calculated 309.9868 for $C_{16}H_9BrNO$.

Table 1. Optimization of the reaction conditions[a].



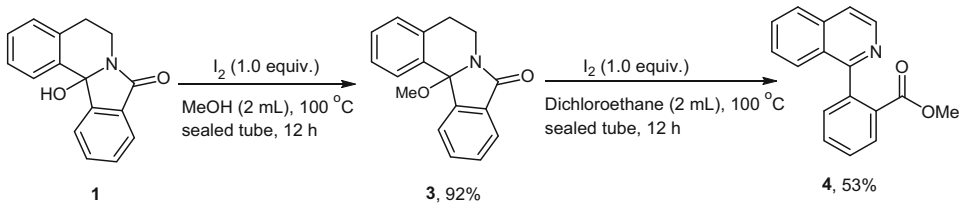
1 2

Entry	I_2 (equiv.)	Solvent	Yield[b]
1[c]	1.0	Dichloroethane	28%
2[d]	1.0	Dichloroethane	32%
3[e]	1.0	Dichloroethane	41%
4[f]	1.0	Dichloroethane	38%
5	0.2	Dichloroethane	-
6	0.4	Dichloroethane	-
7	0.6	Dichloroethane	10%
8	0.8	Dichloroethane	15%
9	1.0	Dichloroethane	92%
10	2.0	Dichloroethane	70%
11[g]	2.0	Dichloroethane	53%
12[h]	2.0	Dichloroethane	80%
13	1.0	Toluene	87%
14	1.0	Tetrachloroethane	89%
15	1.0	Acetonitrile	-
16	1.0	DMF	-
17	1.0	DMSO	-

[a]Conditions: **1** (0.2 mmol) and iodine were used in solvent (2 mL) for 12 h in sealed tube. [b]Isolated yield. [c]Nitrogen atmosphere without sealed tube. [d]Oxygen atmosphere without sealed tube. [e]Nitrogen atmosphere in closed reaction tube. [f]Oxygen atmosphere in closed reaction tube. [g]In sealed tube for 5 h. [h]In sealed tube for 8 h.

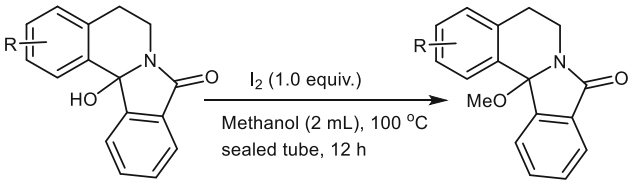
2.6 *Synthesis of 5-methoxy-6-hydroxy-1-azabenzanthrone* **(C)**

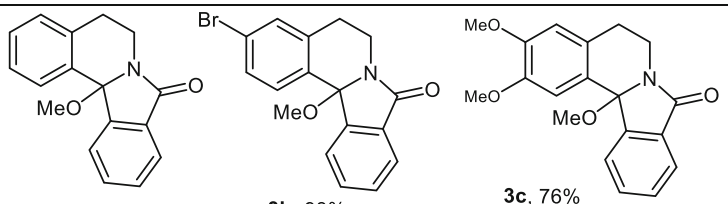
The substrate 2-(6,7-dimethoxyisoquinolin-1-yl)benzoic acid **2c** (45 mg, 0.11 mmol) in polyphosphoric acid washeated at 130°C for 2 h. The reaction mixture was cooled to room temperature, the mixture was poured into ice water, made alkaline with 10% aqueous NH_4OH solution, and extracted with CH_2Cl_2 (5 x 5 mL), The organic extracts were washed with water, dried over Na_2SO_4 and solvent was removed by evaporation under reduced pressure and the residue was chromatographed on silica gel, eluting with CH_2Cl_2, to afford 6-hydroxy-5-methoxy-1-aza-benzo[de]anthracen-7-one **C** as yellow solid. 23 mg, 57% yield, M.p. 233–235°*C* (lit.[17] 233–234°C), IR (KBr, cm^{-1}): 3398, 2926, 2843, 1726, 1624, 1574, 1489, 1276, 1090, 927, 753; ^{1}H NMR (400 MHz, $CDCl_3$): δ 16.05 (s, 1H), 9.09 (d, J = 8.0 Hz, 1H), 8.81 (d, J = 5.2 Hz, 1H), 8.57 (dd, J = 8.0, 1.2 Hz, 1H), 7.92 (td, J = 8.0, 1.2 Hz, 1H), 7.76–7.72 (m, 1H), 7.68 (d, J = 5.6 Hz, 1H) 7.35 (s, 1H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.1, 164.7, 153.1, 144.2, 143.7, 139.4, 134.2, 131.1, 130.4, 129.7,

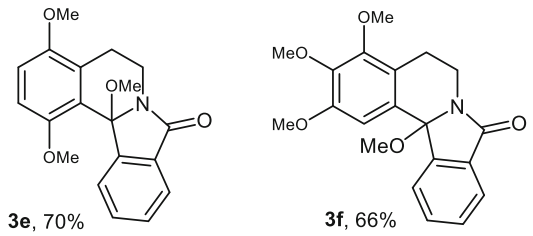


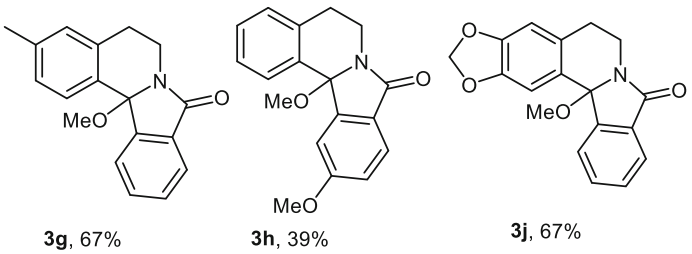
Scheme 2. Synthesis of methyl 2-(isoquinolin-1-yl)benzoate **4**.

Table 2. Iodine mediated etherification of substituted isoindoloisoquinolinones[a].









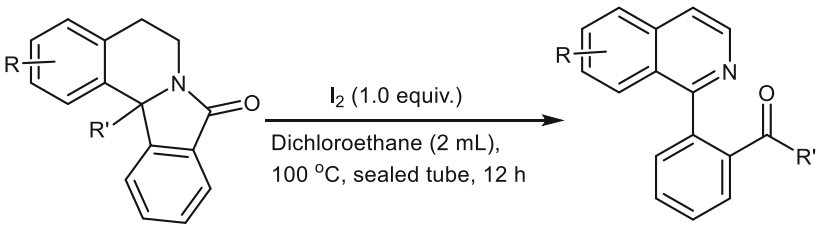
[a]Conditions: In all reactions, 0.4 mmol of **1** was used.

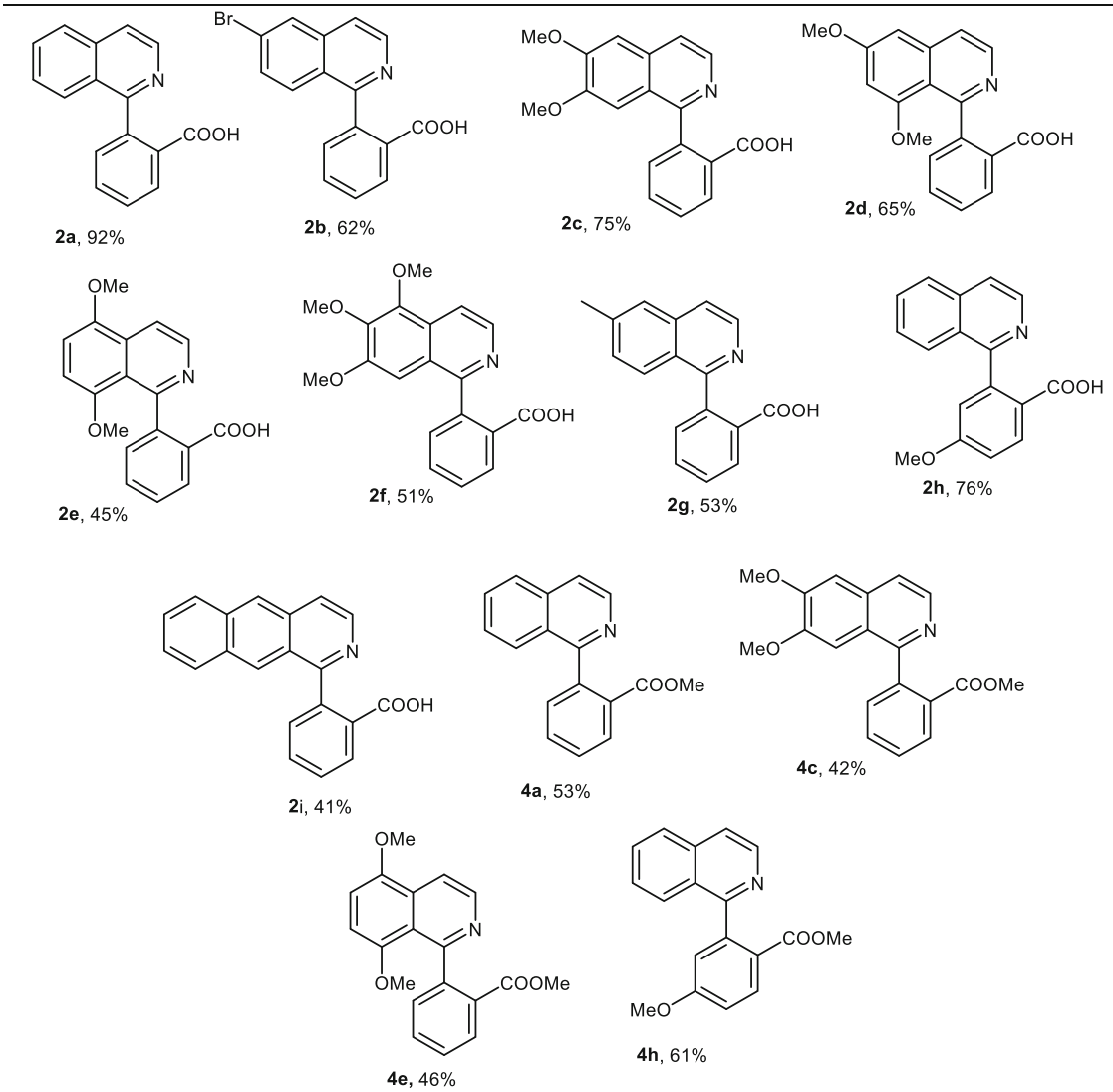
126.6, 125.4, 120.7, 114.2, 112.1, 108.8, 56.5; HRMS-ESI (m/z): $[M+H]^+$Found 278.0820 and calculated 278.0817 for $C_{17}H_{12}NO_3$.

3. Results and Discussion

For preliminary studies, the compound **1** was chosen as a model substrate. To exploit the oxidizing ability of iodine, the isoindoloisoquinolinone derivative **1** was treated with 1.0 equivalent of I_2 at room temperature in 1,2-dichloroethane. Even after 24 h, the substrate **1** failed to generate the expected product **2**. Performing the reaction at 60°C for 12 h as well as 24 h with 1.0 equivalent of I_2 failed to furnish the product **2**. Quite interestingly, the product **2** was obtained in 28% and 32% yield, respectively, when the experiments were carried out at 100°C under N_2 as well as O_2 atmosphere. On the other hand, when the reactions were performed in a closed vessel at 100°C under N_2 as well as O_2 atmosphere for 12 h, the yields of the product **2** increased to 41% and 38%, respectively (Table 1, entries 3, 4). These

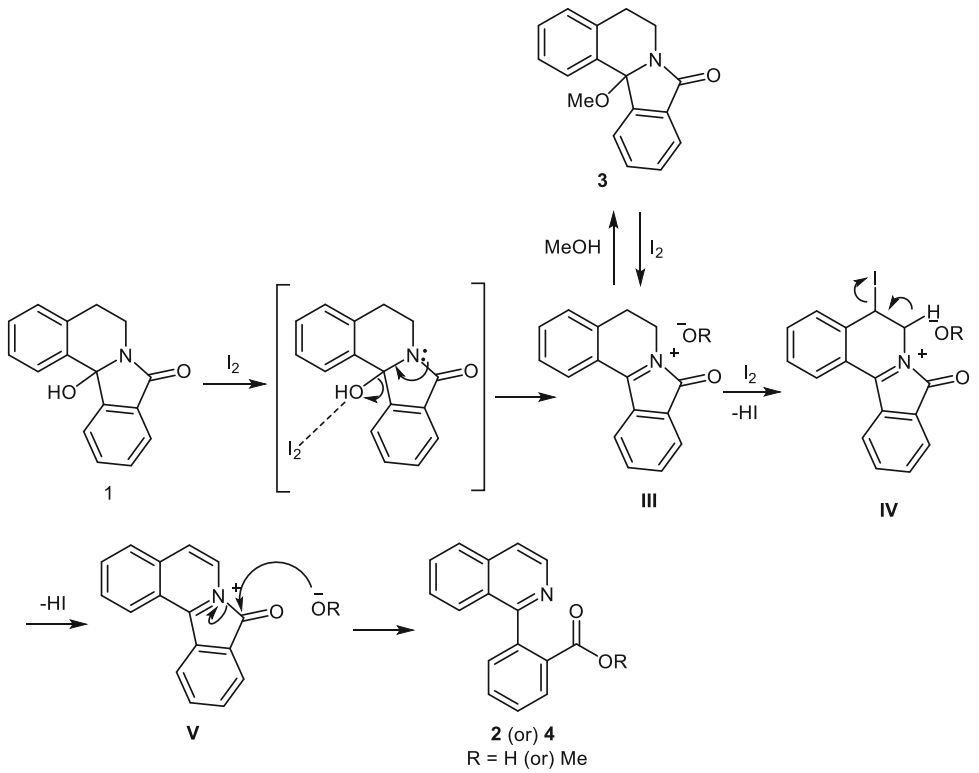
Table 3. Iodine mediated oxidative dehydrogenation of substituted isoindoloisoquinolinones[a].





[a]Conditions: In all reactions 0.2 mmol of **1** or **3** was used.

experiments prompted us to carry out this reaction in a sealed tube. Therefore, the compound **1** was first treated with 20 mol% of I_2 in 1,2-dichloroethane at 100°C in a sealed tube which failed to generate the expected product **2** (Table 1, entry 5). Increasing the amount of iodine to 40 mol% was also not fruitful (Table 1, entry 6). The compound **2** was obtained in 10% and 15% yields when the reaction was carried out with 60 mol% and 80 mol% of I_2, respectively (Table 1, entries 7, 8). Later, the reaction was carried out with 1.0 equivalent of iodine, which afforded the desired product **2** in 92% yield (Table 1, entry 9). Increasing the amount of iodine from 1.0 to 2.0 equivalents too decreased the yield from 92% to 70% (Table 1, entry 10). Decreasing the time from 12



Scheme 3. Plausible mechanism for the formation of **3** and **2** (or) **4**.

h to 5 h as well as to 8 h with 2.0 equivalents of iodine gave the product **2** in 53% and 80% yield, respectively (Table 1, entries 11, 12). Based on these observations it is concluded that, 1.0 equivalent of iodine is suitable for obtaining the desired product **2** in good yield.

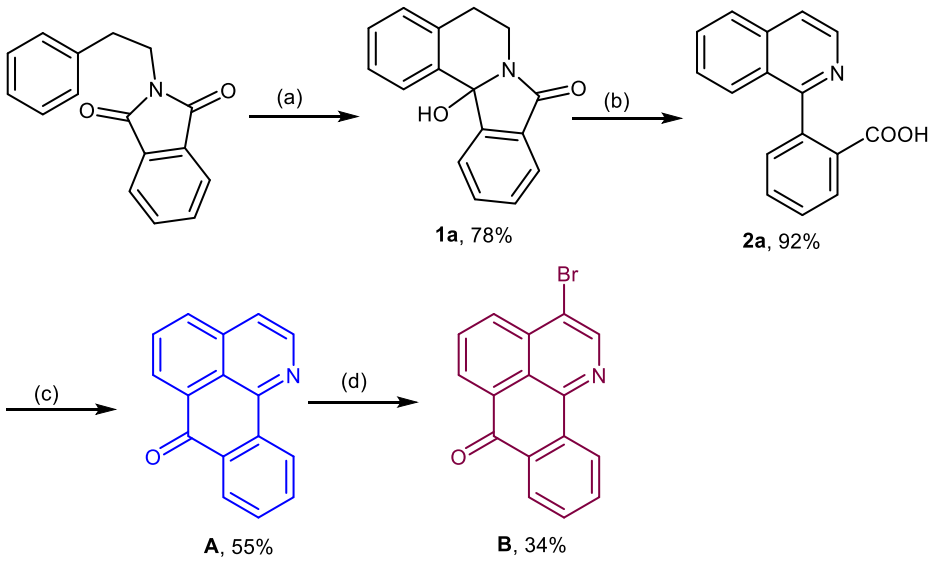
With 1.0 equivalent of I_2, experiments were carried out in different solvents such as toluene, tetrachloroethane, acetonitrile, DMF and DMSO at 100°C in sealed tube. In the case of nonpolar solvents such as toluene and tetrachloroethane, the compound **2** was obtained in 87% and 89% yield, respectively (Table 1, entries 13, 14). The solvents such as CH_3CN, DMF and DMSO failed to produce **2** (Table 1, entries 15–17). From these systematic observations, the optimized condition for the conversion of **1** to **2** was found to be 1.0 equivalent of iodine in 1,2-dichloroethane at 100°C in a sealed tube for 12 h (Table 1).

With optimized reaction condition in methanol in lieu of 1,2-dichloroethane, the compound **1** failed to furnish the product **2**; instead, ether **3** was produced in 92% yield. Subsequently, when this compound **3** was subjected to the oxidative dehydrogenation condition using I_2, the ester **4** was generated in 53% yield (Scheme 2).

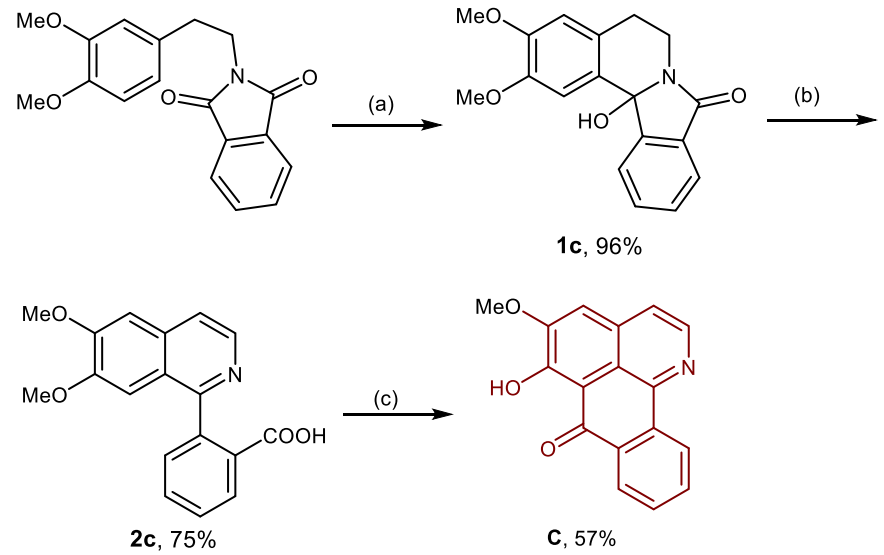
This observation supports the involvement of internal nucleophile either HO^- or MeO^- present in the substrate **1** or **3** is responsible for the formation of acid **2** or ester **4**. To prove this, when the substrate **1** was treated with iodine in the presence of external π-nucleophile, *i.e.*, anisole, the reaction furnished only acid **2** in 86% yield.

To further generalize this etherification reaction, different types of methoxy/methyl/bromo substituted isoindoloisoquinolinones (**1a–1c, 1e–1h, 1j**) were treated with iodine under the optimized etherification conditions. As illustrated in Table 2, for example, unsubstituted **1a**, 3,4-dimethoxy **1c**, 2,5-dimethoxy **1e** and 2,3,4-trimethoxy **1f** isoindoloisoquinolinone derivatives successfully furnished the corresponding ethers **3a**, **3c**, **3e** and **3f** in moderate to good yields. Similarly, the 3-bromo derivative **1b** also produced the ether **3b** in 93% yield. In addition, 3-methyl derivative **1g** and methylenedioxy derivative **1j** also delivered the corresponding ether, **3g** and **3j** in moderate yield. The derivative **1h** also delivered the corresponding ether **3h** in 39% yield.

With the optimized reaction conditions in hand, we then evaluated the scope of the oxidative dehydrogenation and ring opening of lactam using a series of isoindoloisoquinolinone derivatives (**1a–1i**) and the results are summarized in Table 3. All the substrates underwent oxidative dehydrogenation and ring opening reactions smoothly and delivered the corresponding products **2a–2i**. For example, unsubstituted **1a**, 3-bromo **1b**, 3,4-dimethoxy **1c** and 3,5-dimethoxy **1d** derivatives delivered products **2a–2c** in moderate to good yields.



a) TfOH, CH_2Cl_2, 0 °C-rt, 1 h, aq. $NaHCO_3$,1 h; b) I_2, dichloroethane, sealed tube, 100 °C, 12 h; c) H_2SO_4 , 90 °C, 1 h then 220 °C, 2 h; d) Br_2, CH_3CN, 80 °C, 24 h.



a) TfOH, CH_2Cl_2, 0 °C-rt, 30 min, aq. $NaHCO_3$,1 h; b) I_2, dichloroethane, sealed tube, 100 °C, 12 h; c) PPA, 130 °C, 3 h.

Scheme 4. Synthesis of 1-azabenzanthrone **A,** 3-bromo-1-azabenzanthrone **B** and 5-methoxy-6-hydroxy-1-azabenzanthrone **C**.

Further, 2,5-dimethoxy **1e**, **1h** and naphthyl **1i** derivatives under standard conditions afforded the products **2e**, **2h** and **2i** in 45%, 76% and 41% yields, respectively. Formation of these products was characterized by IR, NMR and HRMS analysis, except 2,3,4-trimethoxy **1f**, 3-methyl **1g** derivatives. Though the reactions were clean, the spectral analysis after column chromatography or recrystallization, especially ^{13}C NMR, of the products obtained from **1f** and **1g**, were not clear. This may be due to the inherent poor stability of these molecules. But the products were confirmed by IR, ^1H NMR and mass spectrometry.

To overcome this problem, the compounds **1f** and **1g** were subjected to etherification followed by oxidative cleavage conditions. Etherification of the compounds **1f** and **1g** underwent smoothly and afforded the products **3f** and **3g** in 66% and 67% yields, respectively. Oxidative dehydrogenation and ring opening reaction

of these ethers **3f** and **3g** furnished the ester products **4f** and **4g**. Unfortunately, again the isolation of these products has become difficult due to the instability of products. Oxidative dehydrogenation and ring opening strategy has been extended to ethers such as **3a**, **3c, 3e** and **3h** (Table 3). Under the optimized conditions, these substrates furnished the expected products **4a**, **4c**, **4e** and**4h** in 42**–**61% yields.

The formation of ether **3** from alcohol **1** may be explained through the Lewis acidic nature of iodine. Coordination of iodine with oxygen lone pair in –OH group may facilitate the formation of condensed cyclic *N*-acyliminium ion which on further reaction with methanol might have generated the corresponding ether **3** (Scheme 3). The formation of **2** or **4** may follow the similar mechanism until the formation of condensed cyclic *N*-acyliminium ion **III** from either **1** or **3** in presence of I_2. In the absence of nucleophilic solvent methanol, the condensed cyclic *N*-acyliminium ion **III** may have possibly undergone benzylic iodination to **IV,** followed by dehydroiodination through 1,4-elimination, which may lead to the formation of highly electrophilic isoquinolium imide **V**. The electrophilic carbonyl group in **V** might have accepted the available nucleophiles HO^- or MeO^- generated in the reaction to deliver the ring opened products either **2** or **4** (Scheme 3).

To show the utility of this protocol, we intended to synthesize azabenzanthrones and analogue of menisporphine. Accordingly, 1-azabenzanthrone **A** from phenethylphthalimide was synthesized in 3 steps with 40% overall yield (Scheme 4). Bromination of 1-azabenzanthrone successfully furnished 3-bromo-1-azabenzanthrone **B** in 34% yield. 5-Methoxy-6-hydroxy-1-azabenzanthrone **C**, which is an analogue of 6-*O*-demethyl menisporphine, was successfully synthesized from 3,4-dimethoxy phenethylphthalimide in 3 steps with 41% overall yield (Scheme 4). Compound **C** is a potential precursor for the synthesis of Lakshminine, an alkaloid extracted from a basic fraction of woody vines (collected from two bush-ropes) of *Sciadotenia toxifera*.[15]

4. Conclusions

In conclusion, we have developed a simple methodology for the synthesis of functionalized 1-aryl isoquinolines which are useful intermediates for the synthesis of 1-azabenzanthrone derivatives. In addition, we have synthesized 1-azabenzanthrone **A**, 3-bromo-1-azabenzanthrone **B** and 5-methoxy-6-hydroxy-1-azab enzanthrone **C**. 5-Methoxy-6-hydroxy-1-azabenzanthrone **C**, can be utilized for the synthesis of Lakshminine. This method could be utilized for the synthesis of analogues of menisporphine alkaloids and 1-aryl-1,2,3,4-tetrahydroisoquinolines.

Supplementary Information (SI)

^1H and ^{13}C NMR spectra of the ethers **3a–3c, 3e–3h, 3j**, acids/esters **2a–2i/ 4a, 4c, 4e, 4h** and compounds **A**, **B**, **C** are provided in Supplementary Information which is available at www.ias.ac.in/chemsci.

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