A Mild Thermal and Acid Catalysed Rearrangement of *O*-Aryl Ethers into *ortho*-Hydroxy Arenes

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General Experimental

Melting points (m.p.) were measured using a Thomas-Hoover capillary tube melting point apparatus and are uncorrected.

Infra-red spectra were recorded on a Nicolet Fourier Transform Spectrometer (225 to 4400 cm⁻¹). The samples were prepared as evaporated films on sodium chloride disks. Absorption maxima (ν_{max}) are quoted in wavenumbers (cm⁻¹).

¹H and ¹³C NMR spectra were recorded on a General Electric QE-300 Spectrometer operating at ambient probe temperature using an internal deuterium lock (300 MHz for ¹H NMR and 75 MHz for ¹³C NMR). Chemical shifts are reported in parts per million (δ) at lower frequencies relative to tetramethylsilane (TMS) and are referenced internally. They are reported as; position, multiplicity and coupling constant (Hz). Standard abbreviations are used throughout (s-singlet, d-doublet, dd-doublet of doublets, t-triplet, q-quartet, m-multiplet, br-broad).

Mass spectra including chemical ionisation (C.I.) and HRMS were recorded on a VG ZAB2E or a Finnigan TSQ70 quadrupole mass spectrometer. Accurate mass measurements are correct to ± 0.001 .

The solvents used were either distilled over appropriate drying agents, or of analytical grade. All other commercially available reagents were purified as necessary following standard procedures.¹

Flash chromatography² was performed using EMD silica gel (40-63 microns). Analytical thin layer chromatography (TLC) was carried out using Merck[®] silica gel 60 F₂₅₄ plates with visualisation using either UV light or alkaline potassium permanganate.

General Experimental Methods**Method A-** *Ether formation using cesium carbonate*

The phenol (0.34 mmol, 2.0 equiv.) and Cs_2CO_3 (0.68 mmol, 4.0 equiv.) in CH_2Cl_2 (5.0 mL) were stirred at room temperature under an argon atmosphere for 10 min. The chloride (0.17 mmol, 1.0 equiv.) was added portion-wise and the solution stirred at room temperature for 15 h. Water (2.0 mL) was added and the mixture extracted with CH_2Cl_2 (3×2.0 mL). The combined organic layers were washed with water (2×2.0 mL), dried (Na_2SO_4) and concentrated under reduced pressure to yield the crude product.

Method B- *Ether formation using potassium carbonate*

A mixture of the phenol (0.78 mmol, 2.0 equiv.), the chloride (0.39 mmol, 1.0 equiv.) and K_2CO_3 (1.6 mmol, 4.0 equiv.) in acetonitrile (5.0 mL) was heated at reflux for 2 h. Water (2.0 mL) was added and the mixture extracted with EtOAc (3×2.0 mL). The combined organic layers were washed with water (2×2.0 mL), dried (Na_2SO_4) and concentrated under reduced pressure to yield the crude product.

Method C- *Ether formation using triethylamine*

Triethylamine (2.2 mmol, 1.2 equiv.) was added dropwise to a solution of the phenol (1.85 mmol, 1.0 equiv.) in CH_2Cl_2 (10.0 mL) at 0 °C under an argon atmosphere. The chloride (2.05 mmol, 1.1 equiv.) was added portion-wise and the solution stirred at 0 °C for 3 h. Water (5.0 mL) was added and the mixture extracted with CH_2Cl_2 (3×5.0 mL). The combined organic layers were washed with water (2×5.0 mL), dried (Na_2SO_4) and concentrated under reduced pressure to yield the crude product.

Method D- *Thermal rearrangement*

A mixture of the ether (0.31 mmol, 1.0 equiv.) in benzene (10 mL) was heated at reflux in a sealed tube for 15 h. The solution was concentrated under reduced pressure to yield the crude product.

Method E- Acid catalyzed rearrangement

Catalytic $\text{CF}_3\text{CO}_2\text{H}$ (1 drop) was added to a solution of the aryl ether (0.29 mmol, 1.0 equiv.) in benzene (10 mL) and the solution stirred at room temperature, under an argon atmosphere, for 15 h. Water (5.0 mL) was added and the mixture extracted with EtOAc (3×3.0 mL). The combined organic layers were washed with water (2×3.0 mL), dried (Na_2SO_4) and concentrated under reduced pressure to yield the crude product.

Experimental Details:

5-{3-[4-((S)-2-Benzylloxycarbonylamino-2-*tert*-butoxycarbonyl-ethyl)-phenoxy]-7-bromo-1-methoxymethyl-2-oxo-2,3-dihydro-1*H*-indol-3-yl}-2-((R)-1-*tert*-butoxycarbonylamino-2-methylpropyl)-oxazole-4-carboxylic acid methyl ester (6)

Cesium carbonate (130 mg, 0.4 mmol) was added to a solution of Cbz-Tyr-O^tBu (99 mg, 0.267 mmol) in toluene (1 mL) under argon at room temperature, and the resulting reaction mixture was stirred for 20 minutes. A solution of chloride **5** (78 mg, 0.133 mmol) in toluene (1 mL) was then added, and the resulting reaction mixture was stirred for 7 hours. The reaction mixture was then taken up in NH_4Cl aq. solⁿ and ethyl acetate, and extracted twice with ethyl acetate. The combined organic layers were washed with sat. brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The resulting crude was purified by flash column chromatography, eluting with 25:75 ethyl acetate:hexanes to obtain the *title compound* (91 mg, 74%) as a pale yellow foam: m.p. 64-68°C; $\nu_{\text{max}}/\text{cm}^{-1}$ 3334, 2975, 2930, 1718, 1516, 1507; δ_{H} (300 MHz, CDCl_3) 7.47 (0.5H, d, J 8.0), 7.45 (0.5H, d, J 8.0), 7.38-7.24 (6H, m), 6.93-6.89 (3H, m), 6.76 (2H, d, J 8.3), 5.45 (0.5H, d, J 10.9), 5.44 (0.5H, d, J 10.9), 5.32-5.28 (2H, m), 5.16 (1H, d, J 7.5),

5.08 (2H, s), 4.90-4.82 (1H, m), 4.47-4.40 (1H, m), 3.73 (1.5H, s), 3.71 (1.5H, s), 3.25 (1.5H, s), 3.23 (1.5H, s), 3.02-2.89 (2H, m), 2.25-2.14 (1H, m), 1.44 (4.5H, s), 1.43 (4.5H, s), 1.37 (4.5H, s), 1.35 (4.5H, s), 0.96-0.90 (6H, m); δ_{C} (75 MHz, CDCl_3) 171.6, 171.6, 170.2, 170.2, 163.9, 163.6, 161.1, 155.4, 155.2, 152.7, 151.3, 151.2, 140.8, 137.1, 136.2, 132.7, 132.6, 130.2, 129.0, 128.8, 128.5, 128.3, 128.2, 128.1, 128.0, 124.9, 124.9, 124.7, 122.1, 121.9, 103.5, 103.4, 82.3, 80.0, 77.2, 71.9, 66.8, 56.5, 55.0, 54.9, 54.2, 54.2, 52.3, 37.4, 32.9, 28.3, 27.9, 18.7, 17.9, 17.7; Found: $[\text{M}+\text{H}]^+$, 921.2876. $\text{C}_{45}\text{H}_{53}\text{N}_4\text{O}_{12}^{79}\text{Br}+\text{H}^+$ requires: $[\text{M}+\text{H}]^+$, 921.2922.

5-{3-[5-((S)-2-Benzyloxycarbonylamino-2-*tert*-butoxycarbonyl-ethyl)-2-hydroxy-phenyl]-7-bromo-1-methoxymethyl-2-oxo-2,3-dihydro-1*H*-indol-3-yl}-2-((R)-1-*tert*-butoxycarbonylamino-2-methylpropyl)-oxazole-4-carboxylic acid methyl ester (7)

A solution of **6** (134 mg, 0.145 mmol) in benzene (5 ml) was heated at reflux for 2 hours, then was allowed to cool to room temperature and concentrated *in vacuo*. The resulting crude was purified by flash column chromatography, eluting with 25:75 ethyl acetate:hexanes, then was further purified by flash column chromatography, eluting with 2:98 methanol:dichloromethane to obtain the *title compound* (108 mg, 81%) as a yellow foam: m.p. 85-90°C; $\nu_{\text{max}}/\text{cm}^{-1}$ 3337, 2976, 1716, 1653, 1647, 1601, 1577, 1558, 1539, 1506; δ_{H} (300 MHz, CDCl_3) 9.05 (0.5H, s), 8.89 (0.5H, s), 7.55 (0.5H, d, *J*8.7), 7.50 (0.5H, d, *J*8.3), 7.36-7.33 (5H, m), 7.12-6.81 (4H, m), 6.60 (0.5H, s), 6.48 (0.5H, s), 5.64-5.58 (1H, m), 5.46-5.41 (1H, m), 5.34 (0.5H, d, *J*9.0), 5.25-5.20 (0.5H, m), 5.13 (2H, s), 5.13-4.98 (1H, m), 4.68-4.59 (1H, m), 4.50-4.46 (0.5H, m), 4.37-4.31 (0.5H, m), 3.75 (1.5H, s), 3.72 (1.5H, s), 3.33 (1.5H, s), 3.33 (1.5H, s), 2.96-2.84 (2H, m), 2.09-1.97 (1H, m), 1.41 (9H, s), 1.33 (9H, s), 0.88-0.83 (6H, m); δ_{C} (75 MHz, CDCl_3) 178.6, 178.5,

170.2, 169.8, 163.3, 162.3, 161.2, 161.2, 155.6, 155.5, 155.2, 155.0, 154.9, 153.6, 139.5, 136.1, 135.5, 135.4, 131.9, 131.6, 129.8, 128.5, 128.3, 128.0, 127.9, 127.8, 125.4, 125.0, 125.0, 122.7, 122.4, 120.1, 104.2, 103.9, 81.9, 79.7, 77.1, 72.4, 72.3, 66.6, 56.5, 56.1, 55.9, 55.8, 54.8, 54.6, 54.5, 53.9, 53.7, 52.2, 52.1, 37.7, 37.0, 33.0, 32.8, 28.0, 27.7, 27.7, 18.2, 17.9, 17.7, 17.5; Found: $[M+H]^+$, 921.2915. $C_{45}H_{53}N_4O_{12}^{79}Br+H^+$ requires: $[M+H]^+$, 921.2922.

5-(7-Bromo-3-chloro-2-oxo-2,3-dihydro-1H-indol-3-yl)-2-((S)-1-tert-butoxycarbonylamino-2-methylpropyl)-oxazole-4-carboxylic acid methyl ester (8)

A solution of the tertiary alcohol (150 mg, 0.29 mmol, 1.0 equiv.) and pyridine (227 mg, 2.87 mmol, 10.0 equiv.) in ether (3.0 mL) was stirred at 0 °C for 15 min. Thionyl chloride (136 mg, 1.15 mmol, 4.0 equiv.) was added and the solution stirred for 30 min. Water (2.0 mL) was added and the solution concentrated under reduced pressure. The residue was washed with sat. aqueous bicarbonate solution (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organics were washed with brine (25 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification by column chromatography (SiO_2 ; 50 % EtOAc:hexanes) gave the *title compound* (90 mg, 40 %) as a yellow foam: $\nu_{max}(CHCl_3)/cm^{-1}$ 3282, 2973, 1747, 1715, 1699, 1616, 1506, 1472, 1367, 1218, 1126, 910, 734; δ_H (300 MHz, $CDCl_3$) 8.57 (1H, d, J 18 Hz, NH), 7.43 (1H, d, J 8.0 Hz), 7.15 (1H, dd, J 7.5 and 7.5 Hz), 6.89-6.97 (1H, m), 5.29-5.36 (1H, m), 4.86-4.93 (1H, m), 3.71 (3H, s), 2.21-2.30 (1H, m), 1.44 (9H, s), 0.89-1.00 (6H, m); δ_C (75 MHz, $CDCl_3$) 170.5, 164.1, 163.9, 160.7, 155.1, 155.0, 149.3, 149.2, 139.9, 133.4, 129.4, 129.3, 128.2, 128.1, 124.5, 123.0, 103.3, 80.0, 58.0, 54.1, 52.1, 32.9, 32.7, 28.1, 27.3, 20.8, 18.5, 17.8,

17.7; m/z (C.I.) 452, 486, 488, 542 (100 %, $M + H^+$); HRMS (Found: MH^+ , 542.0667.

$C_{22}H_{26}N_3O_6ClBr$ requires 542.0693.

5-{3-[4-((S)-2-Benzyloxycarbonylamino-2-*tert*-butoxycarbonyl-ethyl)-phenoxy]-7-bromo-2-oxo-2,3-dihydro-1*H*-indol-3-yl}-2-((R)-1-*tert*-butoxycarbonylamino-2-methylpropyl)-oxazole-4-carboxylic acid (9)

Tertiary chloride **8** (10 mg, 0.018 mmol, 1.0 equiv.) and the phenol (18 mg, 0.043 mmol, 2.0 equiv.) were treated according to **Method A**. Purification by column chromatography (SiO_2 ; 50 % EtOAc:hexanes) gave the *title compound* (12 mg, 75 %) as a colourless oil: $\nu_{max}(CHCl_3)/cm^{-1}$ 3282, 2976, 1723, 1716, 1506, 1472, 1367, 1214, 1165, 734; δ_H (300 MHz, $CDCl_3$) 7.64 (1H, s), 7.25-7.38 (7H, m), 6.81-6.95 (4H, m), 5.30 (2H, s), 5.13 (2H, s), 5.00-5.40 (1H, m), 4.80-4.90 (1H, m), 4.40-4.50 (1H, m), 3.75 (3H, s), 2.96-3.00 (2H, m), 2.05-2.15 (1H, m), 1.44 (9H, s), 1.35 (9H, s), 0.86-0.99 (6H, m); δ_C (75 MHz, $CDCl_3$) 1705., 164.1, 163.9, 160.7, 155.1, 155.0, 149.3, 149.2, 139.9, 133.4, 129.4, 129.3, 128.2, 128.1, 124.5, 123.0, 103.3, 80.0, 58.0, 54.1, 52.1, 32.9, 32.7, 28.1, 27.3, 20.8, 18.5, 17.8, 17.7; m/z (C.I.) 777, 821, 877 (100 %, $M + H^+$); HRMS (Found: MH^+ , 876.2593. $C_{43}H_{49}N_4O_{11}Br$ requires 876.2581).

5-{3-[5-((S)-2-Benzoyloxycarbonylamino-2-*tert*-butoxycarbonyl-ethyl)-2-hydroxyphenyl]-7-bromo-2-oxo-2,3-dihydro-1*H*-indol-3-yl}-2-((R)-1-*tert*-butoxycarbonylamino-2-methylpropyl)-oxazole-4-carboxylic acid methyl ester (10)

O-Arylether **9** (12 mg, 0.014 mmol, 1.0 equiv.) in deuterated chloroform (1.0 mL) was heated in a sealed tube at 80 °C for 12 h. Purification by column chromatography (SiO₂; 50 % EtOAc:hexanes) gave the *title compound* (12 mg, 100 %) as a colourless oil: $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 3306, 3232, 2974, 1715, 1701, 1157, 733; $\delta_{\text{H}}(300 \text{ MHz, CDCl}_3)$ 8.91 (1H, s, brs), 7.88 (1H, d, *J* 9.0 Hz), 7.21-7.47 (8H, m), 6.50-7.10 (3H, m), 5.30-5.36 (1H, m), 5.00-5.24 (2H, m), 4.32-4.70 (2H, m), 3.70 (3H, s), 2.81-3.02 (2H, m), 2.01-2.08 (1H, m), 1.32 (9H, s), 1.28 (9H, s), 0.70-0.88 (6H, m); *m/z* (C.I.) 876 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 876.2593. C₄₃H₄₉N₄O₁₁Br requires 876.2581).

7-Bromo-3-chloro-3-phenyl-1,3-dihydroindol-2-one (11)

A solution of 7-bromo-3-hydroxy-3-phenyl-1,3-dihydroindol-2-one³ (0.28 g, 0.92 mmol, 1.0 equiv.) and pyridine (0.74 mL, 9.2 mmol, 10 equiv.) in diethyl ether (10 mL) was stirred at 0 °C under an argon atmosphere for 15 min. Thionyl chloride (0.27 mL, 3.6 mmol, 4.0 equiv.) was added dropwise and the solution stirred at 0 °C for 30 min. Water (5.0 mL) was added and the mixture extracted with EtOAc (4 × 5.0 mL). The combined organic layers were washed with water (2 × 5.0 mL), dried (Na₂SO₄) and concentrated

under reduced pressure to yield the crude product. Recrystallisation from hot EtOAc:hexane yielded the *title compound* (0.20 g, 67 %) as yellow needles: m.p. 186-187 °C; R_f (1:1 hexane:EtOAc) 0.45; $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 3300 (NH), 3090 (CH), 1732 (C=O); $\delta_{\text{H}}(300 \text{ MHz}, \text{CDCl}_3)$ 7.30-7.48 (4H, m), 7.50-7.55 (3H, m), 7.05 (1H, t, J 7.7 Hz); $\delta_{\text{C}}(75 \text{ MHz}, \text{CDCl}_3)$ 172.4, 132.8, 129.7, 129.4, 129.0, 128.7, 128.5, 128.1, 127.5, 127.1, 124.9, 124.6; m/z (C.I.) 324 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 321.9634. $\text{C}_{14}\text{H}_{10}\text{NOClBr}$ requires 321.9624).

7-Bromo-3-phenyl-3-*p*-tolxyloxy-1,3-dihydroindol-2-one (12)

7-bromo-3-chloro-3-phenyl-1,3-dihydroindol-2-one **11** (0.20 g, 0.62 mmol, 1.0 equiv.) and *p*-cresol (0.13 mL, 1.24 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by recrystallisation from hexane:EtOAc to afford the *title compound* (0.16 g, 67 %) as orange needles: m.p. 153-154 °C; R_f (1:1 hexane:EtOAc) 0.50; $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 3210 (NH), 3088 (CH), 1732 (C=O); $\delta_{\text{H}}(300 \text{ MHz}, \text{CDCl}_3)$ 7.80 (1H, brs), 7.50-7.55 (2H, m), 7.35-7.45 (4H, m), 7.24 (1H, d, J 7.6 Hz), 7.02 (1H, t, J 7.6 Hz), 6.90 (2H, d, J 8.4 Hz), 6.78 (2H, d, J 8.4 Hz), 2.20 (3H, s); $\delta_{\text{C}}(75 \text{ MHz}, \text{CDCl}_3)$ 174.7, 152.8, 140.0, 137.8, 133.1, 132.7, 129.9, 129.5, 128.7, 128.4, 126.2, 125.3, 124.2, 120.4, 103.4, 20.5; m/z (C.I.) 395 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: M^+ , 394.0429. $\text{C}_{21}\text{H}_{16}\text{NO}_2\text{Br}$ requires 394.0443).

7-Bromo-3-(2-hydroxy-5-methylphenyl)-3-phenyl-1,3-dihydroindol-2-one (13)

7-Bromo-3-phenyl-3-*p*-tolylloxy-1,3-dihydroindol-2-one **12** (45 mg, 0.1 mmol) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO₂; 100 % CH₂Cl₂) to afford the *title compound* (37 mg, 82 %) as a white solid: m.p. 202-203 °C; *R*_f(100 % CH₂Cl₂) 0.40; ν_{max} (CHCl₃)/cm⁻¹ 3214 (OH, NH), 3075 (CH), 1699 (C=O); δ_{H} (300 MHz, CDCl₃) 8.50 (1H, brs), 8.30 (1H, brs), 7.42 (1H, dd, *J* 8.5 and 3.0 Hz), 7.24-7.38 (3H, m), 7.00-7.17 (5H, m), 6.90 (1H, d, *J* 8.1 Hz), 6.70 (1H, s), 2.20 (3H, s); δ_{C} (75 MHz, CDCl₃) 181.5, 154.2, 139.5, 138.7, 134.1, 131.2, 130.8, 129.4, 129.3, 128.9, 127.8, 126.5, 126.1, 124.6, 124.4, 120.0, 103.7, 64.0, 30.9, 20.7; *m/z* (C.I.) 395 (100 %, *M* + *H*⁺); HRMS (Found: *M*⁺, 394.0444. C₂₁H₁₆NO₂Br requires 394.0443).

3-Chloro-3-phenyl-1,3-dihydroindol-2-one (**14**)⁴

A solution of 3-hydroxy-3-phenyl-1,3-dihydroindol-2-one⁴ (6.32 g, 28.1 mmol, 1.0 equiv.) and pyridine (22.7 mL, 281 mmol, 10 equiv.) in diethyl ether (200 mL) was stirred at 0 °C under an argon atmosphere for 15 min. Thionyl chloride (8.20 mL, 112 mmol, 4.0 equiv.) was added dropwise and the solution stirred at 0 °C for 30 min. Water (50 mL) was added and the mixture extracted with EtOAc (4 × 50 mL). The combined organic layers were washed with water (2 × 50 mL), dried (Na₂SO₄) and concentrated under reduced pressure to yield the crude product. Recrystallisation from hot EtOAc:hexane yielded the *title compound* (3.60 g, 55 %) as needles. Data was consistent with that already reported: m.p. 145-146 °C (lit.⁴ 145-146 °C); *R*_f(1:1 hexane:EtOAc) 0.60; δ_{H} (300 MHz, CDCl₃) 8.40 (1H, brs), 7.55 (2H, dd, *J* 4.3 and 2.8 Hz), 7.26-7.40 (5H, m), 7.18 (1H, t *J* 7.4 Hz), 6.98 (1H, d, *J* 7.7 Hz); *m/z* (C.I.) 244 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 244.0448. C₁₄H₁₀NOCl requires 244.0451).

3-Phenoxy-3-phenyl-1,3-dihydroindol-2-one (15a)

3-Chloro-3-phenyl-1,3-dihydroindol-2-one **14** (0.10 g, 0.41 mmol, 1.0 equiv.) and phenol (80 mg, 0.82 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by flash column chromatography (SiO₂; 100 % CH₂Cl₂) to afford the *title compound* (88 mg, 73 %) as a white solid: m.p. 159-160 °C; *R*_f(100 % CH₂Cl₂) 0.45; ν_{max} (CHCl₃)/cm⁻¹ 3254 (NH), 3064 (CH), 1716 (C=O); δ_{H} (300 MHz, CDCl₃) 8.80 (1H, brs), 7.55 (2H, dd, *J* 4.0 and 2.7 Hz), 7.38-7.40 (3H, m), 7.24-7.30 (2H, m), 7.06-7.13 (3H, m), 6.86-7.05 (4H, m); δ_{C} (75 MHz, CDCl₃) 176.5, 155.3, 140.7, 138.3, 138.2, 130.1, 128.9, 128.5, 128.4, 126.3, 126.2, 126.1, 123.1, 123.0, 119.9, 110.6, 84.8; *m/z* (C.I.) 302 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 302.1182. C₂₀H₁₆NO₂ requires 302.1181).

3-Phenyl-3-*p*-tolylloxy-1,3-dihydroindol-2-one (15b)

3-chloro-3-phenyl-1,3-dihydroindol-2-one **14** (0.10 g, 0.41 mmol, 1.0 equiv.) and *p*-cresol (0.10 mL, 0.82 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by flash column chromatography (SiO₂; 100 % CH₂Cl₂) to afford the *title compound* (0.10 g, 76 %) as a white solid: m.p. 140-141 °C; *R*_f(100 % CH₂Cl₂) 0.45; ν_{max} (CHCl₃)/cm⁻¹ 3243 (NH), 2976 (CH), 1724 (C=O); δ_{H} (300 MHz, CDCl₃) 8.45 (1H, brs), 7.55 (2H, dd, *J* 4.3 and 2.5 Hz), 7.25-7.40 (5H, m), 7.52 (1H, t, *J* 8.5 Hz), 6.85 (3H, m), 6.78 (2H, d, *J* 7.9 Hz), 2.18 (3H, s); δ_{C} (75 MHz, CDCl₃) 176.5, 153.0, 140.8, 138.4, 132.6, 130.0, 129.4, 128.6, 128.4, 128.3, 126.4, 126.2, 123.0, 120.1, 110.5, 85.0, 20.4; *m/z* (C.I.) 316 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 316.1332. C₂₁H₁₈NO₂ requires 316.1338).

3-(4-Isopropylphenoxy)-3-phenyl-1,3-dihydroindol-2-one (15c)

3-Chloro-3-phenyl-1,3-dihydroindol-2-one **14** (0.10 g, 0.41 mmol, 1.0 equiv.) and 4-isopropylphenol (0.11 g, 0.82 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by flash column chromatography (SiO₂; 1:1 hexane :EtOAc) to afford the *title compound* (89 mg, 64 %) as a white solid: m.p. 171-172 °C; *R*_f(1:1 hexane:EtOAc) 0.65; ν_{max} (CHCl₃)/cm⁻¹ 3231 (NH), 2963 (CH), 1728 (C=O); δ_{H} (300 MHz, CDCl₃) 8.20 (1H, brs), 7.52-7.55 (2H, m), 7.26-7.40 (5H, m), 7.08 (1H, t, *J* 7.4 Hz), 6.90 (2H, d, *J* 8.6 Hz), 6.86 (1H, d, *J* 7.6 Hz), 6.78 (2H, d, *J* 8.6 Hz), 2.75 (1H, sept, *J* 6.8 Hz), 1.18 (6H, d, *J* 6.8 Hz); δ_{C} (75 MHz, CDCl₃) 176.4, 153.5, 143.6, 140.8, 138.7, 130.2, 128.9, 128.6, 128.5, 126.9, 126.6, 126.4, 123.3, 119.9, 110.6, 84.9, 33.2, 23.9; *m/z* (C.I.) 344 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 344.1651. C₂₃H₂₂NO₂ requires 344.1650).

3-(4-Nitrophenoxy)-3-phenyl-1,3-dihydroindol-2-one (15d)

3-Chloro-3-phenyl-1,3-dihydroindol-2-one **14** (0.10 g, 0.41 mmol, 1.1 equiv.) and 4-nitrophenol (50 mg, 0.37 mmol, 1.0 equiv.) were treated according to **Method C**. The crude product was purified by recrystallisation from hexane:EtOAc to afford the *title compound* (0.11 g, 79 %) as yellow needles: m.p. 199-200 °C; *R*_f(100 % CH₂Cl₂) 0.60; ν_{max} (CHCl₃)/cm⁻¹ 3258 (NH), 3064 (CH), 1732 (C=O); δ_{H} (300 MHz, CDCl₃) 8.50 (1H, brs), 8.04 (2H, d, *J* 7.0 Hz), 7.20-7.51 (7H, m), 7.14 (1H, t, *J* 7.4 Hz), 7.08 (1H, d, *J* 7.4 Hz), 6.92 (2H, d, *J* 7.0 Hz); δ_{C} (75 MHz, CDCl₃) 175.0, 160.6, 142.5, 140.4, 137.2, 130.8, 129.0, 128.6, 127.2, 126.0, 125.9, 125.3, 123.7, 118.4, 110.9, 84.7; *m/z* (C.I.) 347 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 347.1033. C₂₀H₁₅N₂O₄ requires 347.1032).

3-(4-Chlorophenoxy)-3-phenyl-1,3-dihydroindol-2-one (15e)

3-chloro-3-phenyl-1,3-dihydroindol-2-one **14** (0.10 g, 0.41 mmol, 1.0 equiv.) and 4-chlorophenol (0.11 g, 0.82 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by flash column chromatography (SiO₂; 5:1 hexane:EtOAc) to afford the *title compound* (0.11 g, 76 %) as a white solid: m.p. 157-158 °C; *R*_f(5:1 hexane:EtOAc) 0.45; $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 3242 (NH), 3025 (CH), 1724 (C=O); δ_{H} (300 MHz, CDCl₃) 8.33 (1H, brs), 7.50-7.54 (2H, m), 7.25-7.41 (6H, m), 7.08 (2H, d, *J* 8.8 Hz), 6.88 (1H, d, *J* 7.7 Hz), 6.84 (2H, d, *J* 8.8 Hz); δ_{C} (75 MHz, CDCl₃) 175.9, 154.0, 140.9, 138.1, 130.6, 129.1, 128.9, 128.7, 128.6, 128.2, 126.6, 126.4, 123.5, 121.9, 110.7, 85.4; *m/z* (C.I.) 336 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 336.0792. C₂₀H₁₅N₂O₂Cl requires 336.0791).

3-(4-Acetylphenoxy)-3-phenyl-1,3-dihydroindol-2-one (15f)

3-chloro-3-phenyl-1,3-dihydroindol-2-one **14** (0.10 g, 0.41 mmol, 1.0 equiv.) and 4-hydroxyacetophenone (0.11 g, 0.82 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by flash column chromatography (SiO₂; 2:1 hexane:EtOAc) to afford the *title compound* (0.11 g, 78 %) as a white solid: m.p. 152-153 °C; *R*_f(2:1 hexane:EtOAc) 0.50; $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 3250 (NH), 3060 (CH), 1720 (C=O), 1673 (C=O); δ_{H} (300 MHz, CDCl₃) 9.15 (1H, brs), 7.72 (2H, d, *J* 8.6 Hz), 7.49-7.53 (2H,

m), 7.23-7.38 (6H, m), 7.05 (1H, t, J 7.2 Hz), 6.88 (2H, d, J 8.6 Hz), 2.45 (3H, s); δ_{C} (75 MHz, CDCl_3) 196.8, 176.1, 159.7, 140.8, 137.9, 131.9, 130.6, 130.2, 128.9, 128.7, 128.0, 126.3, 126.1, 123.6, 118.5, 111.1, 84.7, 30.9, 26.3; m/z (C.I.) 344 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 344.1285. $\text{C}_{22}\text{H}_{18}\text{NO}_3$ requires 344.1287).

3-Phenyl-3-*o*-tolylloxy-1,3-dihydroindol-2-one (15h)

3-chloro-3-phenyl-1,3-dihydroindol-2-one **14** (0.10 g, 0.41 mmol, 1.0 equiv.) and *o*-cresol (0.10 mL, 0.82 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by flash column chromatography (SiO_2 ; 100 % CH_2Cl_2) to afford the *title compound* (0.10 g, 74 %) as a white solid: m.p. 164-165 °C; R_f (100 % CH_2Cl_2) 0.55; ν_{max} (CHCl_3)/ cm^{-1} 3242 (NH), 3056 (CH), 1720 (C=O); δ_{H} (300 MHz, CDCl_3) 8.85 (1H, brs), 7.56 (2H, dd, J 4.3 and 2.3 Hz), 7.38 (3H, m), 7.30 (1H, d, J 8.1 Hz), 7.12 (2H, m), 7.02 (1H, d, J 7.8 Hz), 6.92 (1H, d, J 7.8 Hz), 6.82 (2H, m), 6.50 (1H, m), 2.38 (3H, s); δ_{C} (75 MHz, CDCl_3) 176.9, 154.1, 140.9, 138.9, 130.9, 130.3, 129.6, 129.0, 128.6, 128.5, 126.5, 126.3, 125.9, 123.4, 122.4, 115.9, 110.8, 84.3, 17.1; m/z (C.I.) 316 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 316.1339. $\text{C}_{21}\text{H}_{18}\text{NO}_2$ requires 316.1338).

3-(4-Hydroxy-3,5-dimethylphenyl)-3-phenyl-1,3-dihydroindol-2-one (16)

2,6-dimethylphenol (50 mg, 0.42 mmol, 2.0 equiv.) and Cs_2CO_3 (0.26 g, 0.82 mmol, 4.0 equiv.) in toluene (5.0 mL) were stirred at room temperature under an argon atmosphere for 20 min. 3-Chloro-3-phenyl-1,3-dihydroindol-2-one **14** (50 mg, 0.21 mmol, 1.0 equiv.) in toluene (2.0 mL) was added dropwise and the solution stirred at reflux for 18 h. Water

(2.0 mL) was added and the mixture extracted with CH₂Cl₂ (3 × 2.0 mL). The combined organic layers were washed with water (2 × 2.0 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO₂; 100 % CH₂Cl₂) to afford the *title compound* (40 mg, 59 %) as a white solid: m.p. 161-162 °C; *R*_f(100 % CH₂Cl₂) 0.70; *v*_{max}(CHCl₃)/cm⁻¹ 3056 (NH, OH), 2928 (CH), 1716 (C=O); *δ*_H(300 MHz, CDCl₃) 7.24-7.32 (9H, m), 7.10 (1H, t *J* 7.7 Hz), 6.92 (1H, d, *J* 7.7 Hz), 6.86 (2H, s), 2.20 (6H, s); *δ*_C(75 MHz, CDCl₃) 177.8, 156.2, 143.0, 142.0, 136.8, 133.2, 130.7, 128.8, 128.4, 128.3, 128.2, 127.2, 126.0, 122.8, 108.4, 62.0, 59.6, 26.7, 16.2; *m/z* (C.I.) 330 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 330.1864. C₂₂H₁₉NO₂ requires 330.1897).

3-(2-Hydroxyphenyl)-3-phenyl-1,3-dihydroindol-2-one (17a)⁵

3-Phenoxy-3-phenyl-1,3-dihydroindol-2-one **15a** (88 mg, 0.29 mmol) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO₂; 2:1 hexane:EtOAc) to afford the *title compound* (65 mg, 75 %) as a white solid: m.p. 181-182 °C; *R*_f(1:1 hexane:EtOAc) 0.65; *v*_{max}(CHCl₃)/cm⁻¹ 3258 (NH, OH), 3056 (CH), 1689 (C=O); *δ*_H(300 MHz, CDCl₃) 9.06 (1H, brs), 8.42 (1H, brs), 7.25-7.30 (6H, m), 7.10-7.17 (3H, m), 7.00-7.05 (3H, m), 6.85 (1H, t, *J* 7.8 Hz); *δ*_C(75 MHz, CDCl₃) 182.7, 156.6, 139.8, 138.8, 132.6, 129.9, 128.9, 128.7, 128.4, 128.3, 127.4, 127.2, 126.2, 124.7, 123.3, 119.8, 110.7, 60.2; *m/z* (C.I.) 302 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 302.1177. C₂₀H₁₆NO₂ requires 302.1181).

3-(2-Hydroxy-5-methylphenyl)-3-phenyl-1,3-dihydroindol-2-one (17b)

3-Phenyl-3-*p*-tolxyloxy-1,3-dihydroindol-2-one **15b** (98 mg, 0.31 mmol) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO₂; 2:1 hexane:EtOAc) to afford the *title compound* (64 mg, 68 %) as a white solid: m.p. 205-206 °C; *R*_f(1:1 hexane:EtOAc) 0.60; ν_{max} (CHCl₃)/cm⁻¹ 3238 (NH, OH), 2950 (CH), 1698 (C=O); δ_{H} (300 MHz, CDCl₃) 8.95 (1H, brs), 8.85 (1H, brs), 7.10-7.29 (9H, m), 7.10 (1H, d, *J* 8.2 Hz), 6.95 (1H, d, *J* 8.2 Hz), 6.80 (1H, s), 2.18 (3H, s); δ_{C} (75 MHz, CDCl₃) 183.0, 154.4, 140.1, 139.1, 132.9, 130.6, 129.5, 129.2, 128.9, 128.5, 127.5, 127.4, 124.8, 123.4, 119.9, 110.8, 62.7, 29.2, 20.7; *m/z* (C.I.) 316 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 316.1346. C₂₁H₁₈NO₂ requires 316.1338).

3-(2-Hydroxy-5-isopropylphenyl)-3-phenyl-1,3-dihydroindol-2-one (17c)

3-(4-Isopropylphenoxy)-3-phenyl-1,3-dihydroindol-2-one **15c** (89 mg, 0.26 mmol) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO₂; 2:1 hexane:EtOAc) to afford the *title compound* (56 mg, 63 %) as a white solid: m.p. 177-178 °C; *R*_f(1:1 hexane:EtOAc) 0.60; ν_{max} (CHCl₃)/cm⁻¹ 3254 (NH, OH), 2959 (CH), 1704 (C=O); δ_{H} (300 MHz, CDCl₃) 8.90 (1H, brs), 8.10 (1H, brs), 7.22-7.34 (5H, m), 7.12-7.16 (4H, m), 7.04 (1H, d, *J* 8.2 Hz), 6.94 (1H, d, *J* 8.2 Hz), 6.85 (1H, s), 2.75 (1H, sept, *J* 6.8 Hz), 1.15 (6H, d, *J* 6.8 Hz); δ_{C} (75 MHz, CDCl₃) 182.7, 154.6, 140.4, 140.3, 138.9, 132.9, 128.9, 128.5, 127.7, 127.5, 127.4, 127.2, 126.4, 124.5,

123.3, 119.9, 110.7, 62.8, 60.4, 33.3, 24.3, 23.9; m/z (C.I.) 344 (100 %, $M + H^+$); HRMS (Found: MH^+ , 344.1645. $C_{23}H_{22}NO_2$ requires 344.1650).

3-(2-Hydroxy-5-nitrophenyl)-3-phenyl-1,3-dihydroindol-2-one (17d)

3-(4-Nitrophenoxy)-3-phenyl-1,3-dihydroindol-2-one **15d** (0.10 g, 0.29 mmol) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO_2 ; 3:1 hexane:EtOAc) to afford the *title compound* (58 mg, 73 %) as a white solid: m.p. 196-197 °C; R_f (3:1 hexane:EtOAc) 0.45; $\nu_{max}(CHCl_3)/cm^{-1}$ 3277 (NH, OH), 2916 (CH), 1716 (C=O); δ_H (300 MHz, $CDCl_3$) 10.30 (1H, brs), 8.20 (1H, dd, J 8.8 and 1.9 Hz), 8.08 (1H, s), 7.22-7.40 (4H, m), 7.06-7.18 (6H, m); δ_C (75 MHz, $CDCl_3$) 178.8, 140.4, 139.8, 131.9, 129.9, 129.3, 129.2, 128.9, 128.7, 128.6, 128.4, 126.2, 125.4, 125.2, 125.1, 123.6, 110.3, 29.7; m/z (C.I.) 347 (100 %, $M + H^+$); HRMS (Found: MH^+ , 347.1031. $C_{20}H_{15}N_2O_4$ requires 347.1032).

3-(5-Chloro-2-hydroxyphenyl)-3-phenyl-1,3-dihydroindol-2-one (17e)

3-(4-Chlorophenoxy)-3-phenyl-1,3-dihydroindol-2-one **15e** (0.10 g, 0.29 mmol) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO_2 ; 3:1 hexane:EtOAc) to afford the *title compound* (71 mg, 71 %) as a white solid: m.p. 170-171 °C; R_f (3:1 hexane:EtOAc) 0.45; $\nu_{max}(CHCl_3)/cm^{-1}$ 3394 (NH), 3211 (OH), 2815 (CH), 1693 (C=O); δ_H (300 MHz, $CDCl_3$) 9.30 (1H, brs), 8.75

(1H, brs), 7.21-7.50 (6H, m), 7.12-7.18 (3H, m), 7.15 (2H, m), 7.20 (1H, d, J 7.6 Hz); δ_{C} (75 MHz, CDCl_3) 182.5, 171.2, 155.6, 139.4, 138.9, 132.2, 129.9, 129.0, 128.9, 127.8, 127.2, 126.7, 126.3, 124.9, 123.9, 121.4, 111.0, 62.5, 60.4, 14.2; m/z (C.I.) 336 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 336.0787. $\text{C}_{20}\text{H}_{15}\text{NO}_2\text{Cl}$ requires 336.0791).

3-(5-Acetyl-2-hydroxyphenyl)-3-phenyl-1,3-dihydroindol-2-one (17f)

3-(4-Acetylphenoxy)-3-phenyl-1,3-dihydroindol-2-one **15f** (0.11 g, 0.32 mmol) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO_2 ; 2:1 hexane:EtOAc) to afford the *title compound* (75 mg, 68 %) as a white solid: m.p. 164-165 °C; R_f (2:1 hexane:EtOAc) 0.65; $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 3250 (NH, OH), 2928 (CH), 1720 (C=O), 1681 (C=O); δ_{H} (300 MHz, CDCl_3) 9.87 (1H, brs), 8.10 (1H, brs), 7.89 (1H, dd, J 8.2 and 1.9 Hz), 7.80 (1H, d, J 1.9 Hz), 7.26-7.34 (4H, m), 7.15 (1H, d, J 6.7 Hz), 7.05-7.12 (5H, m), 2.45 (3H, s); δ_{C} (75 MHz, CDCl_3) 196.6, 182.4, 161.7, 139.5, 138.8, 132.1, 131.2, 130.1, 126.7, 129.1, 128.9, 127.9, 127.3, 126.2, 124.8, 123.9, 120.0, 111.0, 96.4, 62.7, 26.2; m/z (C.I.) 344 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 344.1286. $\text{C}_{22}\text{H}_{18}\text{NO}_3$ requires 344.1287).

3-(2-Hydroxy-5-methoxyphenyl)-3-phenyl-1,3-dihydroindol-2-one (17g)

3-chloro-3-phenyl-1,3-dihydroindol-2-one **14** (0.12 g, 0.49 mmol, 1.0 equiv.) and *p*-methoxyphenol (0.12 g, 0.99 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by flash column chromatography (SiO_2 ; 3:1 hexane:EtOAc) to

afford the *title compound* (70 mg, 50 %) as a white solid: m.p. 148-149 °C; R_f (1:1 hexane:EtOAc) 0.55; $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 3254 (NH, OH), 2928 (CH), 1712 (C=O); δ_{H} (300 MHz, CDCl_3) 9.16 (1H, brs), 8.78 (1H, brs), 7.10-7.38 (9H, m), 6.98 (1H, t, J 7.6 Hz), 6.82 (1H, d, J 7.6 Hz), 6.62 (1H, s), 3.70 (3H, s); δ_{C} (75 MHz, CDCl_3) 182.9, 171.2, 153.1, 150.4, 139.9, 132.7, 128.9, 128.6, 127.6, 127.1, 126.4, 126.2, 123.5, 120.5, 115.9, 114.1, 111.0, 62.7, 55.6, 14.2; m/z (C.I.) 332 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 332.1293. $\text{C}_{21}\text{H}_{18}\text{NO}_3$ requires 332.1287).

3-(2-Hydroxy-3-methylphenyl)-3-phenyl-1,3-dihydroindo-2-one (17h)

3-Phenyl-3-*o*-tolxyloxy-1,3-dihydroindol-2-one **15h** (96 mg, 0.30 mmol) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO_2 ; 100 % CH_2Cl_2) to afford the *title compound* (91 mg, 85 %) as a white solid: m.p. 178-179 °C; R_f (100 % CH_2Cl_2) 0.50; $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 3262 (NH, OH), 3056 (CH), 1700 (C=O); δ_{H} (300 MHz, CDCl_3) 9.04 (1H, brs), 8.24 (1H, brs), 7.20-7.34 (4H, m), 7.05-7.19 (5H, m), 7.00 (1H, d, J 7.6 Hz), 6.85 (1H, dd, J 7.9 and 1.3 Hz), 6.74 (1H, t, J 7.6 Hz), 2.25 (3H, s); δ_{C} (75 MHz, CDCl_3) 182.9, 154.9, 140.2, 138.9, 133.2, 131.5, 128.9, 128.4, 127.6, 127.5, 126.9, 126.3, 124.6, 123.4, 119.4, 110.7, 62.8, 16.5; m/z (C.I.) 316 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 316.1337. $\text{C}_{21}\text{H}_{18}\text{NO}_2$ requires 316.1338).

3-(2-Hydroxy-3-methoxyphenyl)-3-phenyl-1,3-dihydroindol-2-one (17i)

3-Chloro-1-methyl-3-phenyl-1,3-dihydroindol-2-one **14** (0.10 g, 0.41 mmol, 1.0 equiv.) and guaiacol (0.09 mL, 0.82 mmol, 2.0 equiv.) were treated according to **Method A**. The

crude product was purified by flash column chromatography (SiO₂; 100 % CH₂Cl₂) to afford the *title compound* (65 mg, 55 %) as a white solid: m.p. 176-177 °C; *R*_f(100 % CH₂Cl₂) 0.40; ν_{max} (CHCl₃)/cm⁻¹ 3262 (OH, NH), 2932 (CH), 1704 (C=O); δ_{H} (300 MHz, CDCl₃) 8.95 (1H, brs), 7.60 (2H, dd, *J* 7.9 and 1.9 Hz), 7.30-7.39 (3H, m), 7.25 (1H, t, *J* 7.8 Hz), 7.14 (1H, d, *J* 8.0 Hz), 6.85-6.94 (4H, m), 6.75 (1H, d, *J* 8.0 Hz), 6.8 (1H, t, *J* 7.8 Hz), 3.70 (3H, s); δ_{C} (75 MHz, CDCl₃) 177.3, 152.1, 145.0, 141.3, 138.9, 130.0, 128.4, 126.7, 126.4, 124.3, 122.6, 120.9, 120.4, 112.1, 110.3, 85.6, 60.4, 55.4; *m/z* (C.I.) 332 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 332.1285. C₂₁H₁₈NO₃ requires 332.1287).

3-(4-Hydroxyphenyl)-3-phenyl-1,3-dihydroindol-2-one (18a)⁵

3-Phenoxy-3-phenyl-1,3-dihydroindol-2-one **15a** (90 mg, 0.29 mmol) was treated according to **Method E**. The crude product was purified by recrystallisation from hexane:EtOAc to afford the *title compound* (65 mg, 73 %) as a white solid: m.p. 195-196 °C; *R*_f(1:1 hexane:EtOAc) 0.75; ν_{max} (CHCl₃)/cm⁻¹ 3363 (OH), 3258 (NH), 3025 (CH), 1697 (C=O); δ_{H} (300 MHz, CDCl₃) 9.20 (1H, brs), 8.00 (1H, brs), 7.10-7.33 (8H, m), 7.15 (2H, d, *J* 8.6 Hz), 6.94 (1H, d, *J* 7.8 Hz), 6.75 (2H, d, *J* 8.6 Hz); δ_{C} (75 MHz, CDCl₃) 179.8, 154.9, 141.8, 139.8, 138.8, 133.5, 129.8, 128.5, 128.3, 128.2, 127.3, 126.3, 122.9, 115.3, 110.1, 62.2, 60.4; *m/z* (C.I.) 302 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 302.1181. C₂₀H₁₆NO₂ requires 302.1181).

3-(4-Hydroxy-3-methylphenyl)-3-phenyl-1,3-dihydroindol-2-one (18b)

3-Phenyl-3-*o*-tolxyloxy-1,3-dihydroindol-2-one **15h** (90 mg, 0.29 mmol) was treated according to **Method E**. The crude product was purified by recrystallisation from hexane:EtOAc to afford the *title compound* (65 mg, 73%) as a white solid: m.p. 142-143 °C; R_f (100 % CH₂Cl₂) 0.45; $\nu_{\max}$ (CHCl₃)/cm⁻¹ 3366 (OH), 3258 (NH), 3060 (CH), 1700 (C=O); δ_H (300 MHz, CDCl₃) 8.50 (1H, brs), 7.20-7.29 (7H, m), 7.05 (1H, d, *J* 8.3 Hz), 7.02 (1H, s), 6.92 (2H, t, *J* 7.5 Hz), 6.65 (1H, d, *J* 8.3 Hz), 2.18 (3H, s); δ_C (75 MHz, CDCl₃) 178.6, 154.5, 142.5, 141.3, 133.7, 131.8, 130.2, 128.2, 128.0, 127.9, 126.8, 126.4, 125.9, 123.5, 121.8, 114.3, 109.8, 61.4, 30.6, 16.1; m/z (C.I.) 316 (100 %, $M + H^+$); HRMS (Found: MH^+ , 316.1335. C₂₁H₁₈NO₂ requires 316.1338).

3-(4-Hydroxy-3-methoxyphenyl)-3-phenyl-1,3-dihydroindol-2-one (18c)

3-(2-Hydroxy-3-methoxyphenyl)-3-phenyl-1,3-dihydroindol-2-one **17h** (65 mg, 0.19 mmol, 1.0 equiv.) was treated according to **Method E**. The crude product was purified by flash column chromatography (SiO₂; 100 % CH₂Cl₂) to afford the *title compound* (48 mg, 74 %) as a white solid: m.p. 190-191 °C; R_f (100 % CH₂Cl₂) 0.45; $\nu_{\max}$ (CHCl₃)/cm⁻¹ 3258 (OH, NH), 2928 (CH), 1700 (C=O); δ_H (300 MHz, CDCl₃) 8.48 (1H, brs), 7.40-7.55 (7H, m), 7.27 (1H, d, *J* 7.2 Hz), 7.16 (1H, d, *J* 7.6 Hz), 7.08 (1H, d, *J* 1.9 Hz), 7.02 (1H, d, *J* 8.3 Hz), 6.95 (1H, dd, *J* 8.3 and 1.9 Hz), 3.80 (3H, s); δ_C (75 MHz, CDCl₃) 178.4, 147.2, 145.9, 142.5, 141.3, 135.5, 132.1, 128.3, 128.1, 127.9, 126.8, 125.9, 121.8, 120.7, 115.1, 112.7, 109.9, 61.6, 55.6, 30.6; m/z (C.I.) 332 (100 %, $M + H^+$); HRMS (Found: MH^+ , 332.1288. C₂₁H₁₈NO₃ requires 332.1287).

3-Chloro-1-methyl-3-phenyl-1,3-dihydroindol-2-one (19)⁶

A solution of 3-hydroxy-1-methyl-3-phenyl-1,3-dihydroindol-2-one⁷ (2.30 g, 9.6 mmol, 1.0 equiv.) and pyridine (7.76 mL, 96 mmol, 10 equiv.) in diethyl ether (100 mL) was stirred at 0 °C under an argon atmosphere for 15 min. Thionyl chloride (2.80 mL, 38.4 mmol, 4.0 equiv.) was added dropwise and the solution stirred at 0 °C for 30 min. Water (20 mL) was added and the mixture extracted with EtOAc (4 × 20 mL). The combined organic layers were washed with water (2 × 20 mL), dried (Na₂SO₄) and concentrated under reduced pressure to yield the crude product. Recrystallisation from hot EtOAc:hexane yielded the *title compound* (1.82 g, 74 %) as needles: m.p. 105-106 °C (lit.⁶ 108-109 °C); *R*_f(1:1 hexane:EtOAc) 0.65; *v*_{max}(CHCl₃)/cm⁻¹ 3055 (CH), 1732 (C=O); *δ*_H(300 MHz, CDCl₃) 7.54-7.58 (2H, m), 7.35-7.45 (5H, m), 7.20 (1H, d, *J* 7.2 Hz), 6.90 (1H, d, *J* 7.2 Hz), 3.28 (3H, s); *δ*_C(75 MHz, CDCl₃) 173.2, 142.6, 136.4, 130.2, 128.7, 128.3, 127.3, 125.8, 123.4, 108.7, 26.7; *m/z* (C.I.) 259 (100 %, *M* + *H*⁺); HRMS (Found: *MH*⁺, 258.0677. C₁₅H₁₃NOC1 requires 258.0686).

1-Methyl-3-(4-nitrophenoxy)-3-phenyl-1,3-dihydroindol-2-one (20c)

3-Chloro-1-methyl-3-phenyl-1,3-dihydroindol-2-one **19** (0.10 g, 0.39 mmol, 1.0 equiv.) and *p*-nitrophenol (0.10 g, 0.78 mmol, 2.0 equiv.) were treated according to **Method B**. The crude product was purified by recrystallisation from hexane:EtOAc to afford the *title compound* (82 mg, 60 %) as needles: m.p. 163-164 °C; *R*_f(1:1 hexane:EtOAc) 0.45; *v*_{max}(CHCl₃)/cm⁻¹ 3064 (CH), 1728 (C=O); *δ*_H(300 MHz, CDCl₃) 8.05 (2H, d, *J* 7.8 Hz),

7.26-7.48 (7H, m), 7.18 (1H, t, J 7.5 Hz), 7.00 (1H, d, J 7.8 Hz), 6.85 (2H, d, J 7.8 Hz), 3.25 (3H, s); δ_{C} (75 MHz, CDCl_3) 173.4, 160.9, 143.6, 142.8, 137.5, 131.0, 129.2, 128.7, 127.1, 126.4, 126.1, 125.9, 125.4, 123.8, 118.8, 115.6, 109.2, 84.8, 26.7; m/z (C.I.) 361 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 361.1188. $\text{C}_{21}\text{H}_{17}\text{N}_2\text{O}_4$ requires 361.1188).

1-Methyl-3-(2-nitrophenoxy)-3-phenyl-1,3-dihydroindol-2-one (20e)

3-Chloro-1-methyl-3-phenyl-1,3-dihydroindol-2-one **19** (0.35 g, 1.36 mmol, 1.0 equiv.) and 2-nitrophenol (0.38 g, 2.72 mmol, 2.0 equiv.) were treated according to **Method B**. The crude product was purified by flash column chromatography (SiO_2 ; 100 % CH_2Cl_2) to afford the *title compound* (0.35 g, 72 %) as a pale yellow solid: m.p. 142-143 °C; R_{f} (100 % CH_2Cl_2) 0.60; ν_{max} (CHCl_3)/ cm^{-1} 2935 (CH), 1728 (C=O); δ_{H} (300 MHz, CDCl_3) 7.70 (1H, d, J 7.7 Hz), 7.52 (2H, dd, J 7.4 and 2.3 Hz), 7.20-7.42 (6H, m), 7.00-7.09 (2H, m), 6.95 (1H, d, J 7.8 Hz), 6.75 (1H, d, J 8.4 Hz), 3.30 (3H, s); δ_{C} (75 MHz, CDCl_3) 173.4, 143.5, 133.1, 130.7, 128.7, 128.6, 128.5, 127.8, 127.5, 127.1, 126.2, 125.7, 125.5, 125.1, 123.6, 123.1, 122.6, 119.7, 108.8, 85.6, 26.5; m/z (C.I.) 361 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 361.1185. $\text{C}_{21}\text{H}_{17}\text{N}_2\text{O}_4$ requires 361.1188).

3-(2-Hydroxyphenyl)-1-methyl-3-phenyl-1,3-dihydroindol-2-one (21a)

3-Chloro-1-methyl-3-phenyl-1,3-dihydroindol-2-one **19** (0.10 g, 0.39 mmol, 1.0 equiv.) and phenol (0.10 g, 0.78 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by recrystallisation from hexane:EtOAc to afford the *title compound* (75 mg, 63 %) as needles: m.p. 226-227 °C; R_{f} (1:1 hexane:EtOAc) 0.60; ν_{max} (CHCl_3)/ cm^{-1}

3339 (OH), 3064 (CH), 1681 (C=O); δ_{H} (300 MHz, CDCl_3) 7.23-7.34 (7H, m), 7.08 (3H, m), 6.90 (1H, d, J 7.9 Hz), 6.75 (2H, dd, J 7.9 and 1.7 Hz), 5.15 (1H, brs), 3.30 (3H, s); δ_{C} (75 MHz, CDCl_3) 177.9, 154.9, 142.9, 142.1, 133.7, 133.2, 129.8, 128.4, 128.3, 128.2, 127.2, 125.9, 122.8, 115.3, 108.5, 61.9, 26.7; m/z (C.I.) 316 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 316.1339. $\text{C}_{21}\text{H}_{18}\text{NO}_2$ requires 316.1338).

3-(2-Hydroxy-5-methylphenyl)-1-methyl-3-phenyl-1,3-dihydroindol-2-one (21b)

3-Chloro-1-methyl-3-phenyl-1,3-dihydroindol-2-one **19** (0.10 g, 0.39 mmol, 1.0 equiv.) and *p*-cresol (0.10 mL, 0.78 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by recrystallisation from hexane:EtOAc to afford the *title compound* (70 mg, 68 %) as needles: m.p. 164-165 °C; R_{f} (1:1 hexane:EtOAc) 0.50; $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 3277 (OH), 3056 (CH), 1681 (C=O); δ_{H} (300 MHz, CDCl_3) 9.25 (1H, brs), 7.07-7.36 (9H, m), 7.05 (1H, d, J 8.1 Hz), 6.95 (1H, d, J 8.1 Hz), 6.80 (1H, s), 3.40 (3H, s), 2.20 (3H, s); δ_{C} (75 MHz, CDCl_3) 180.9, 154.7, 142.1, 140.5, 132.4, 130.5, 129.3, 128.9, 128.8, 128.5, 127.4, 127.1, 126.3, 124.8, 123.5, 120.1, 109.3, 62.4, 26.8, 20.7; m/z (C.I.) 330 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 330.1494. $\text{C}_{22}\text{H}_{20}\text{NO}_2$ requires 330.1494).

3-(2-Hydroxy-5-nitrophenyl)- 1-methyl-3-phenyl-1,3-dihydroindol-2-one (21c)

1-Methyl-3-(4-nitrophenoxy)-3-phenyl-1,3-dihydroindol-2-one **20c** (82 mg, 0.23 mmol) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO₂; 100 % CH₂Cl₂) to afford the *title compound* (54 mg, 67 %) as a white solid: m.p. 225-226 °C; *R*_f(100 % CH₂Cl₂) 0.45; ν_{max} (CHCl₃)/cm⁻¹ 3168 (OH), 2928 (CH), 1681 (C=O); δ_{H} (300 MHz, CDCl₃) 10.75 (1H, brs), 8.18 (1H, dd, *J* 8.8 and 2.7), 8.08 (1H, s), 7.42-7.45 (2H, m), 7.18-7.30 (5H, m), 7.02-7.08 (3H, m), 3.26 (3H, s); δ_{C} (75 MHz, CDCl₃) 180.2, 163.5, 141.8, 140.7, 139.1, 130.9, 129.4, 129.2, 128.0, 126.9, 126.1, 125.4, 124.5, 120.5, 109.9, 62.2, 30.9, 27.1; *m/z* (C.I.) 361 (100 %, *M* + *H*⁺); HRMS (Found: *M*⁺, 361.1190. C₂₁H₁₇N₂O₄ requires 361.1188).

3-(2-Hydroxy-3-methylphenyl)-1-methyl-3-phenyl-1,3-dihydroindol-2-one (21d)

3-Chloro-1-methyl-3-phenyl-1,3-dihydroindol-2-one **19** (0.10 g, 0.39 mmol, 1.0 equiv.) and *o*-cresol (0.10 mL, 0.78 mmol, 2.0 equiv.) were treated according to **Method A**. The crude product was purified by flash column chromatography (SiO₂; 100 % CH₂Cl₂) to afford the *title compound* (73 mg, 57 %) as needles: m.p. 157-158 °C; *R*_f(100 % CH₂Cl₂) 0.55; ν_{max} (CHCl₃)/cm⁻¹ 3374 (OH), 3056 (CH), 1712 (C=O); δ_{H} (300 MHz, CDCl₃) 9.50 (1H, brs), 7.50 (1H, m), 7.36-7.43 (2H, m), 7.05-7.27 (7H, m), 6.95 (1H, d, *J* 7.6 Hz), 6.80 (1H, dd, *J* 7.6 and 3.2 Hz), 3.25 (3H, s), 2.38 (3H, s); δ_{C} (75 MHz, CDCl₃) 180.9, 174.5, 155.2, 154.2, 143.9, 142.0, 140.5, 139.1, 127.4, 127.2, 126.7, 126.4, 126.3, 125.7,

123.4, 122.5, 116.1, 108.7, 26.6, 17.2 ; m/z (C.I.) 330 (100 %, $M + H^+$); HRMS (Found: MH^+ , 330.1490. $C_{22}H_{20}NO_2$ requires 330.1494).

3-(2-Hydroxy-3-nitrophenyl)-1-methyl-3-phenyl-1,3-dihydroindol-2-one (21e)

1-Methyl-3-(2-nitrophenoxy)-3-phenyl-1,3-dihydroindol-2-one **20e** (0.15 g, 0.42 mmol, 1.0 equiv.) was treated according to **Method D**. The crude product was purified by flash column chromatography (SiO_2 ; 100 % CH_2Cl_2) to afford the *title compound* (0.12 g, 77 %) as a pale yellow solid: m.p. 191-192 °C; R_f (100 % CH_2Cl_2) 0.65; $\nu_{max}(CHCl_3)/cm^{-1}$ 3260 (OH), 2929 (CH), 1708 (C=O); δ_H (300 MHz, $CDCl_3$) 10.58 (1H, brs), 7.95 (1H, dd, J 7.8 and 2.3 Hz), 7.62 (1H, dd, J 7.8 and 2.3 Hz), 7.10-7.39 (9H, m), 6.90 (1H, d, J 7.8 Hz), 3.36 (3H, s); δ_C (75 MHz, $CDCl_3$) 176.5, 154.3, 142.7, 140.8, 138.2, 133.9, 132.8, 131.4, 128.7, 128.6, 128.5, 127.7, 127.5, 125.6, 124.1, 123.1, 120.1, 108.8, 61.1, 26.6; m/z (C.I.) 361 (100 %, $M + H^+$); HRMS (Found: MH^+ , 361.1182. $C_{21}H_{17}N_2O_4$ requires 361.1188).

3-(4-Hydroxy-3-nitrophenyl)-1-methyl-3-phenyl-1,3-dihydroindol-2-one (22)

1-Methyl-3-(2-nitrophenoxy)-3-phenyl-1,3-dihydroindol-2-one **20e** (0.15 g, 0.42 mmol, 1.0 equiv.) was treated according to **Method E**. The crude product was purified by flash column chromatography (SiO_2 ; 100 % CH_2Cl_2) to afford the *title compound* (90 mg, 60 %) as a pale yellow solid: m.p. 200-201 °C; R_f (100 % CH_2Cl_2) 0.55; $\nu_{max}(CHCl_3)/cm^{-1}$

3384 (OH), 2929 (CH), 1711 (C=O); δ_{H} (300 MHz, CDCl_3) 7.05-7.39 (10H, m), 7.10 (1H, t, J 7.8 Hz), 6.90 (1H, t, J 7.8 Hz), 3.80 (1H, brs), 3.28 (3H, s); δ_{C} (75 MHz, CDCl_3) 171.5, 143.4, 140.1, 131.6, 129.7, 128.5, 128.4, 128.3, 128.2, 127.9, 126.3, 125.3, 124.9, 123.5, 108.6, 77.9, 53.0, 26.4; m/z (C.I.) 361 (100 %, $\text{M} + \text{H}^+$); HRMS (Found: MH^+ , 361.1182. $\text{C}_{21}\text{H}_{17}\text{N}_2\text{O}_4$ requires 361.1188).

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