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Iridium catalysed C-3 alkylation of oxindole with alcohols under solvent free thermal or microwave conditions

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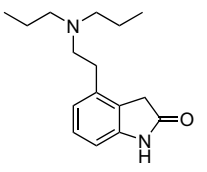
ABSTRACT

Ir-catalysed alkylation of oxindole and *N*-methyl oxindole with a range of substituted benzyl and heteroaryl alcohols under solvent free thermal or microwave conditions afforded the corresponding C-3-monoalkylated products in high to excellent yield.

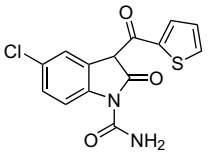
1. Introduction

Oxindole and its derivatives are of great interest due to their biological activity and presence in many compounds of pharmaceutical interest. These include the dopamine agonist Ropinirole **1** used for the treatment of Parkinson's disease, the anti-inflammatory Tenidap **2** and the anti-cancer kinase inhibitor Sunitinib **3**.[1–3] Oxindoles, specifically those with C-3 functionalisation, represent an important motif in a number of natural products.[4]

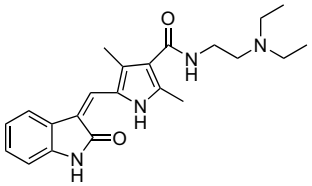
While the conventional alkylation of oxindoles has been widely reported many of these processes suffer from poor regioselectivity and yields are reduced by the formation of bis-alkylated by-products limiting their synthetic utility.[5] To increase the molecular complexity of a simple organic substrate using efficient (high atom economy), selective, high yielding and environmentally benign methods is one of the contemporary challenges for synthetic organic chemists.[6] C–C bond formation is a pivotal method for achieving this goal. Indirect functionalisation of alcohols using catalytic amounts of a metal complex and base, which generates only water as a by-product is an attractive green alternative to standard C–C bond forming reactions. These cascades are termed as redox neutral, hydrogen autotransfer or 'borrowing hydrogen' processes. We have previously reported the alkylation of active methylene and methine compounds with alcohols catalysed by iridium, rhodium and ruthenium complexes. Thus alkylation of arylacetonitriles was achieved by using rhodium[7] and more recently iridium catalysts.[8] We have also reported microwave assisted redox neutral processes for the selective monoalkylation of 1,3-dimethylbarbituric acid and *tert*-butyl cyanoacetate and by alcohols.[9,10] C-3 (methine) alkylation of indoles was also successfully carried out utilising alcohols and iridium catalysts.[11] Cho et al.



1 Ropinirole, requip™



2 Tenidap, Enablex™



3 Sunitinib, sutent™

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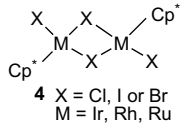
have reported the direct α-alkylation of ketones with alcohols, using a Ru catalyst, to afford saturated alcohols via α-alkylated ketones.[12] The same reaction can be performed in the presence of a sacrificial hydrogen acceptor, such as 1-dodecene, when α-alkylated ketones are obtained.[13] Alternative catalysts for the α-alkylation of ketones with alcohols include the use of the phosphine free catalyst $Ru(DMSO)_4Cl_4$[14] and palladium nanoparticles.[13] Ishi et al. reported the selective direct α-alkylation of ketones with alcohols using an Ir catalyst,[15] and Williams et al. reported indirect Wittig reactions with alcohols using $[Ir(cod)Cl]_2$[16] or a ruthenium carbene complex[17] and variants of the aldol condensation.[18] Krische et al. reported a series of Ir-catalysed C–C coupling via hydrogen autotransfer processes involving alcohols and π-unsaturated reactants (1,3-dienes, 1,2-dienes, 1,3-enynes or 1,2-diynes).[19–22] We and others reported the N-alkylation of amines with alcohols using iridium and rhodium catalysts[23] whilst Beller et al. achieved the N-alkylation of anilines with aliphatic amines using Shvo's catalyst.[24] N-acylation of amines with alcohols has been achieved from a ruthenium precursor, an *N*-heterocyclic carbene and a phosphine ligand.[25] A ruthenium pincer complex catalyst was also utilised for this transformation.[26] N-alkylation of sulfonamides with alcohols has been achieved using either a homogeneous Ru catalyst or a heterogeneous nano-Ru/Fe_3O_4 catalyst.[27,28] Aromatic heterocycles such as furans, pyrroles, indoles and quinolines have all been constructed via redox neutral processes.[29–31]

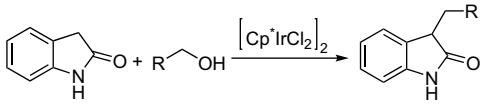
2. Results and discussion

Early extensive pioneering work by the Maitlis group[32] established simple routes to a series of halide bridged dimers **4** and highlighted their catalytic potential. Recently Fujita's group[23c–f] and others have reported applications of **4** in redox neutral processes. The alkylation of oxindole with alcohols (Scheme 1) is of interest as it provides a potential 'green' route to C-3-substituted oxindole derivatives. We initially surveyed a range of catalysts and identified the iridium chloro-bridged compound **4** [X=Cl, M=Ir(III)] as an effective catalyst for the selective C-3 alkylation of oxindole (Scheme 1).

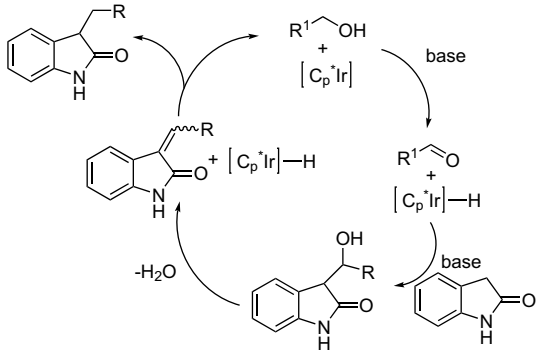
The proposed mechanism for this transformation involves dehydrogenation of the primary alcohol to generate an aldehyde and



4 X = Cl, I or Br
M = Ir, Rh, Ru

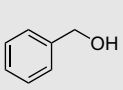
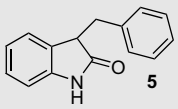
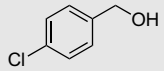
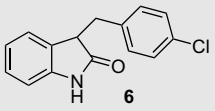
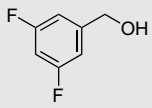
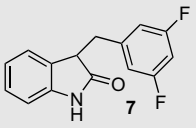
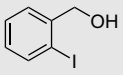
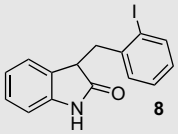
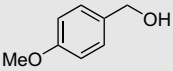
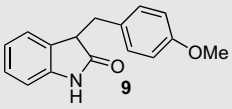
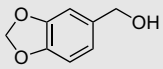
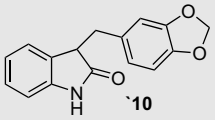
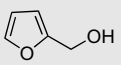
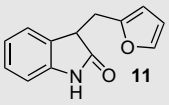
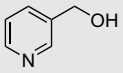
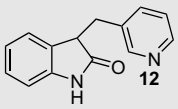
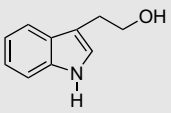
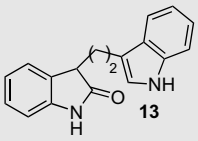
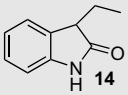
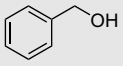
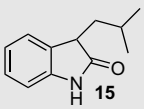
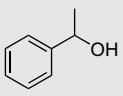
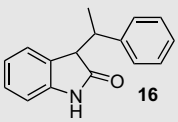
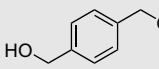
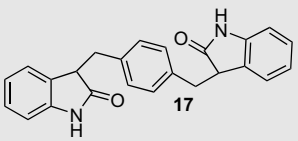


Scheme 1.



Scheme 2.

Table 1
Alkylation of oxindole with alcohols[a]

Entry	Alcohol	Product	Yield[b] (%)
1		 **5**	94 (90)
2		 **6**	83 (76)
3		 **7**	80 (77)
4		 **8**	70[c] (76)[d]
5		 **9**	91 (95)
6		 **10**	99 (93)
7		 **11**	98 (94)
8		 **12**	90 (96)
9		 **13**	81 (87)
10		 **14**	89 (78)
11		 **15**	71 (76)
12		 **16**	82[c] (74)[d] dr 2:1
13		 **17**	79[c,e] (76)[e] dr 2:1

[a] The reaction was carried out at 110 °C for 15 h under solvent free conditions with oxindole (1 mmol), alcohol (3 mmol), $[IrCp^*Cl_2]_2$ (2.5 mol %) and KOH (20 mol %).
[b] Isolated yield.
[c] Reaction time 24 h.
[d] Reaction time 60 min, MWI. Numbers in parentheses are isolated yields obtained using MWI, 110 °C, 20 min.
[e] Toluene (10 mmol) added to the mixture.

metal hydride species. Knoevenagel type condensation occurs followed by hydrogenation of the double bond by the in situ formed metal hydride to give the product (Scheme 2).

Further optimisation showed that the reaction could be achieved under essentially solvent free conditions and identified potassium hydroxide as the base of choice. Initially we carried out the alkylation reaction of oxindole (1 mmol) with benzyl alcohol (1.5 mmol), KOH (15–20 mol %) and $[Cp^*IrCl_2]_2$ (2.5 mol %) at 110 °C for 15 h, which afforded the monoalkylated product **5** in 94% yield (Table 1, entry 1). Microwave irradiation (MWI) could be used to achieve a significant rate enhancement. Thus the alkylation of oxindole with benzyl alcohol at 110 °C for 20 min under microwave irradiation afforded **5** in 90% yield.

Benzyl alcohols substituted with electron-withdrawing or donating groups and aliphatic, primary and secondary alcohols were readily alkylated to afford the corresponding 3-substituted oxindole derivatives **5**–**17** in high yield (Table 1, entries 2–13). The reaction was not significantly affected by either the location or the electronic nature of the substituent on the aryl ring. Under the optimised conditions all the additional functional groups (F, Cl, I) were stable. The reaction of tryptol afforded the alkylated product **13** (Table 1, entry 9) in 81% yield. The heteroaromatic furfuryl alcohol and 3-pyridyl methanol were alkylated to the corresponding C-3 substituted oxindole derivatives (Table 1 entries 7 and 8) in excellent yield. During all these reactions clean C-3 regioselectivity was observed with none of the *N*-alkylated oxindole derivatives. Interestingly with a slight variation in reaction conditions 1,4-dibenzyl alcohol was successfully bis-alkylated to **17** in 79% yield (dr 2:1) (Table 1, entry 13). All the above reactions (Table 1) were also successfully carried out using microwave irradiation (110 °C, 20 min) in high yield.

Next we explored the alkylation of the commercially available substituted oxindoles **18a**,**b** with alcohols using microwave irradiation (Table 2, entries 1–6). Substitution was readily tolerated (Cl, Br) on the aromatic ring. Once again high yields were achieved for the regioselective C-3 alkylation of substituted oxindole by benzyl, heteroaryl and aliphatic alcohols (Table 2, entries 1–6).

Finally we studied the alkylation of *N*-methyl oxindole with a small range of alcohols under thermal conditions. High yields were achieved using benzyl, heteroaryl and aliphatic alcohols (Table 3, entries 1–6).

3. Conclusion

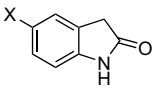
In conclusion oxindole and substituted oxindoles were successfully alkylated with a range of substituted benzyl, heteroaryl and aliphatic alcohols to afford the corresponding C-3 alkylated products in high yield.

4. Experimental

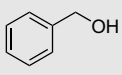
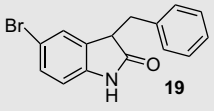
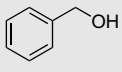
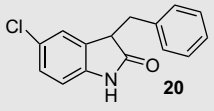
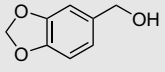
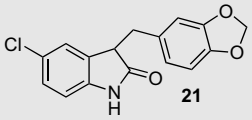
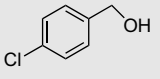
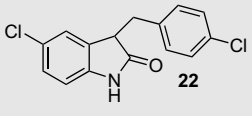
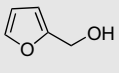
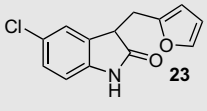
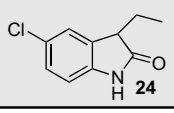
4.1. General

Unless otherwise noted all reagents were obtained from commercial suppliers and used without further purification. Chromatography columns were prepared using Fisher Chemicals 60A 35–70 micron silica gel. Nuclear magnetic resonance spectra were recorded using Bruker DPX300 and DPX500 MHz spectrometers. Chemical shifts are reported in parts per million (δ) downfield relative to the internal reference tetramethylsilane. Unless otherwise specified NMR spectra were recorded in deuterochloroform at room temperature. Abbreviations used: Ar=aromatic, d=doublet,

Table 2
Alkylation of **18a–b** with alcohols[a]

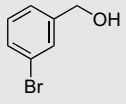
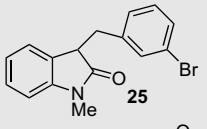
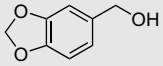
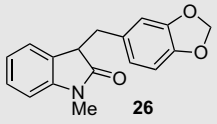
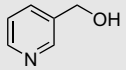
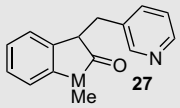
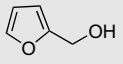
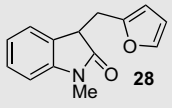
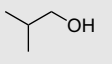
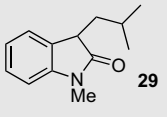
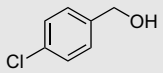
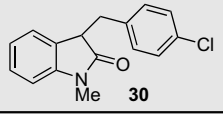


18 a. X = Br
b. X = Cl

Entry	18	Alcohol	Product	Yield[b] (%)
1	**18a**		 **19**	82
2	**18b**		 **20**	75
3	**18b**		 **21**	65
4	**18b**		 **22**	75
5	**18b**		 **23**	76
6	**18b**		 **24**	81[c]

[a] Oxindole (1.1 mmol), alcohol (3 mmol), $[IrCp^*Cl_2]_2$ (2.5 mol %), KOH (20 mol %), N_2 (1 atm), 110 °C, 20 min, MWI.
[b] Isolated yield.
[c] Ethanol (8 mmol) was used.

Table 3
Alkylation of *N*-methyl oxindole with alcohols[a]

Entry	Alcohol	Product	Yield[b] (%)
1		 **25**	64
2		 **26**	76
3		 **27**	84
4		 **28**	87
5		 **29**	81
6		 **30**	97

[a] The reaction was carried out at 110 °C for 15 h under solvent free conditions with oxindole (1 mmol), alcohol (3 mmol), $[IrCp^*Cl_2]_2$ (2.5 mol %) and KOH (20 mol %).
[b] Isolated yield.

dd=doublet of doublets, dq=doublet of quartets, dt=doublet of triplets, m=multiplet, q=quartet, s=singlet, t=triplet. Mass spectra were recorded using a micromass ZMD 2000 spectrometer employing the electrospray (ES+) ionisation technique. Accurate molecular masses were obtained from Walters LCT or GCT or Bruker MicroTof spectrometers. Infrared spectra were recorded using a Perkin–Elmer FT-IR spectrometer. IR spectra of liquids were recorded as thin films on sodium chloride plates. IR spectra of solids were recorded using the 'golden gate' apparatus. Petrol refers the fraction of petroleum ether with bp 40–60 °C and ether refers to diethylether. Accurate masses refer to ^{35}Cl and ^{79}Br isotopes.

4.2. General procedure for the alkylation of oxindoles with alcohols

4.2.1. General procedure A

The oxindole (1.0 mmol), $[Cp^*IrCl_2]_2$ (0.020 g, 2.5 mol%), KOH (0.011 g, 0.2 mmol) and the alcohol (3.0 mmol) were combined in a thick walled glass tube. The tube was sealed with a rubber septum, purged with nitrogen and magnetically stirred at 110 °C for 15 h then allowed to cool to room temperature. The reaction mixture was analysed by ^{1}H NMR and thereafter purified by chromatography.

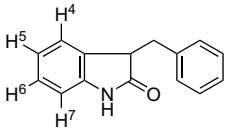
4.2.2. General procedure B

Alkylation of oxindoles with alcohols with MWI. As for general procedure A but with microwave heating for 20 min at 110 °C.

4.2.3. General procedure C

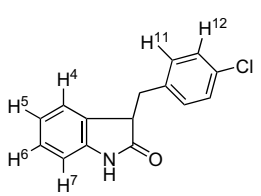
N-Methyl oxindole with alcohols under thermal conditions. As for general procedure A, but employing *N*-methyl oxindole (0.147 g, 1.0 mmol).

4.3. 3-Benzylindolin-2-one (5)



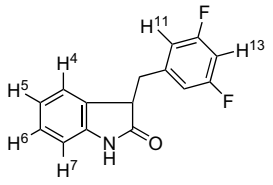
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and benzyl alcohol (0.324 g, 3.0 mmol). Chromatography eluting with 1:1 v/v petrol–ether followed by crystallisation from DCM and hexane gave the product (0.210 g, 94%) by general procedure A and (0.201 g, 90%) by general procedure B as a colourless solid. Mp 129.0–130.0 °C (lit.[33] mp 129.0–131.0 °C); δ_H (500 MHz, $CDCl_3$); 7.27–7.20 (m, 3H, 3×ArH), 7.19–7.14 (m, 3H, 3×ArH), 6.89 (t, 1H, *J* 7.7, H^5), 6.83 (d, 1H, *J* 7.7, H^4), 6.74 (d, 1H, *J* 7.7, H^7), 3.75 (dd, 1H, *J* 9.4, 4.7, CH), 3.50 (dd, 1H, *J* 13.7, 4.7, CH*H*), 2.94 (dd, 1H, *J* 13.7, 9.4, C*H*H); ν_{max} (film)/cm^{-1} 1707 (CO), 1621, 1470, 1338, 1230; HRMS [ES+] found M+Na 246.0885. $C_{15}H_{13}NONa$ requires 246.0889.

4.4. 3-(4-Chlorobenzyl)indolin-2-one (6)



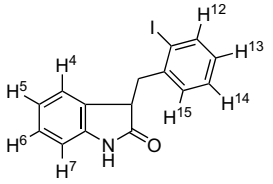
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and 4-chlorobenzyl alcohol (0.426 g, 3.0 mmol). Chromatography eluting with 1:1 v/v ether–petrol followed by crystallisation from DCM and hexane gave the product (0.213 g, 83%) by general procedure A and (0.195 g, 76%) by general procedure B as colourless needles. Mp 140.0–142.0 °C (Found: C, 69.85; H, 4.80; N, 5.45; Cl, 13.75. $C_{15}H_{12}NClO$ requires: C, 69.91; H, 4.69; N, 5.43; Cl, 13.76%); δ_H (500 MHz, $CDCl_3$); 8.25 (br s, 1H, NH), 7.19 (d, 2H, *J* 8.5, H^{11}), 7.18 (t, 1H, *J* 7.7, H^6), 7.08 (d, 2H, *J* 8.5, H^{12} and H$^{12'}$), 6.94 (t, 1H, *J* 7.7, H^5), 6.85 (d, 1H, *J* 7.7, H^4), 6.81 (d, 1H, *J* 7.7, H^7), 3.73 (dd, 1H, *J* 4.7, 8.3, CH), 3.41 (dd, 1H, *J* 4.7, 13.7, C*H*H), 3.01 (dd, 1H, *J* 8.3, 13.7 CH*H*); δ_C (75 MHz, $CDCl_3$); 179.39 (CO), 141.71 (ArC), 136.41 (ArC), 132.94 (ArC), 131.22 (ArCH), 128.91 (ArC), 128.85 (ArCH), 128.57 (ArCH), 125.12 (ArCH), 122.61 (ArCH), 110.16 (ArCH), 47.70 (CH), 36.22 (CH_2); ν_{max}/cm^{-1} (film) 1709 (CO), 1621, 1492, 1471, 1338; HRMS [ES+] found M+1 258.0680. $C_{15}H_{13}NO^{35}Cl$ requires 258.0680.

4.5. 3-(3,5-Difluorobenzyl)indolin-2-one (7)



Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and 3,5-difluorobenzyl alcohol (0.432 g, 3.0 mmol). Chromatography eluting with 1:1 v/v ether and petrol followed by crystallisation from DCM and hexane gave the product (0.207 g, 80%) by general procedure A and (0.199 g, 77%) by general procedure B as pale yellow prisms. Mp 105.0–106.0 °C (Found: C, 69.35; H, 4.25; N, 5.20; F, 14.55. $C_{15}H_{11}NF_2O$ requires: C, 69.49; H, 4.28; N, 5.40; F, 14.66%); δ_H (500 MHz, $CDCl_3$); 8.88 (br s, 1H, NH), 7.20 (t, 1H, *J* 7.7, H^6), 6.99 (t, 1H, *J* 7.7, H^5), 6.86 (d, 1H, *J* 7.7, H^4), 6.86 (d, 1H, *J* 7.7, H^7), 6.73–6.68 (m, 2H, H^{11}), 6.65 (tt, 1H, $^3J_{HF}$ 9.0, 2.1, H^{13}), 3.74 (dd, 1H, *J* 4.7, 8.6, CH), 3.42 (dd, 1H, *J* 4.7, 13.7, CH*H*), 3.00 (dd, 1H, *J* 8.6, 13.7 C*H*H); δ_C (75 MHz, $CDCl_3$); 179.59 (CO), 163.19 (dd, $^1J_{CF}$ 248.3, $^3J_{CF}$ 12.7, 2×ArCF), 141.98 (t, $^3J_{CF}$ 9.2, ArC), 141.81 (ArC), 128.79 (ArCH), 128.58 (ArC), 124.94 (ArCH), 122.78 (ArCH), 112.67 (dd, $^2J_{CF}$ 16.7 and $^4J_{CF}$ 7.5, ArCH$^{11'}$), 110.44 (ArCH), 102.74 (t, $^2J_{CF}$ 25.3, ArCH^{13}), 47.41 (CH), 36.52 (CH_2); ν_{max}/cm^{-1} (film) 1712 (CO), 1624, 1596, 1471, 1339, 1225, 1118, 752; HRMS [ES+] found M+1 260.0878. $C_{15}H_{12}NF_2O$ requires 260.0881.

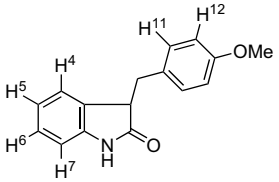
4.6. 3-(2-Iodobenzyl)-indolin-2-one (8)



Prepared by general procedure A with heating for 24 h and general procedure B with heating for 1 h from oxindole (0.133 g, 1.0 mmol) and 2-iodobenzyl alcohol (0.702 g, 3.0 mmol). Chromatography eluting with 1:1 v/v petrol–ether followed by crystallisation of the residue gave the product (0.244 g, 70%) by general procedure A and (0.265 g, 76%) by general procedure B as colourless microprisms. Mp 148.0–149.0 °C (Found: C, 51.30; H, 3.35; N, 4.25; I, 36.60. $C_{15}H_{12}NOI$ requires: C, 51.60; H, 3.46; N, 4.01; I, 36.34%); δ_H (500 MHz, $CDCl_3$); 7.90 (dd, 1H, *J* 7.7, 0.9, H^{12}), 7.79 (br s, 1H, NH), 7.31 (dt, 1H, *J* 0.9, 7.7, H^{14}), 7.24 (dd, 1H, *J* 1.7, 7.7, H^{15}), 7.19 (t, 1H, *J* 7.7, H^6), 6.99 (dt, 1H, *J* 7.7, 1.7, H^{13}), 6.88 (t, 1H, *J* 7.7, H^5), 6.88 (d, 1H, *J* 7.7, H^4), 6.63 (d, 1H, *J* 7.7, H^7), 3.92 (dd, 1H, *J* 5.6, 9.8, CH), 3.56 (dd, 1H, *J* 5.6, 14.1, C*H*H), 3.00 (dd, 1H, *J* 9.8, 14.1, CH*H*); δ_C (75 MHz, $CDCl_3$); 178.62 (CO), 141.06 (ArC), 140.60 (ArC), 139.82 (ArCH), 131.31 (ArCH), 128.73 (ArCH), 128.59 (ArC), 128.17 (ArCH),

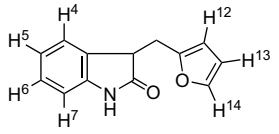
128.04 (ArCH), 125.29 (ArCH), 122.05 (ArCH), 109.48 (ArCH), 100.98 (ArC), 45.22 (CH), 41.78 (CH_2); ν_{max}/cm^{-1} (film) 1707 (CO), 1620, 1470, 1338, 1230; HRMS [ES+] found M+1 350.0026. $C_{15}H_{13}NOI$ requires 350.0036.

4.7. 3-(4-Methoxybenzyl)indolin-2-one (9)



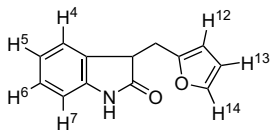
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and 4-methoxybenzyl alcohol (0.414 g, 3.0 mmol). Chromatography eluting with 1:1 v/v petrol–ether followed by crystallisation from DCM and hexane gave the product (0.229 g, 91%) by general procedure A and (0.240 g, 95%) by general procedure B as colourless microneedles. Mp 114.0–115.0 °C (Found: C, 75.70; H, 5.95; N, 5.45: $C_{16}H_{15}NO_2$ requires: C, 75.87; H, 5.97; N, 5.53%); δ_H (500 MHz, $CDCl_3$); 9.16 (br s, 1H, NH), 7.15 (t, 1H, *J* 7.5, ArH), 7.07 (d, 2H, *J* 8.6, H^{11}), 6.90 (t, 1H, *J* 7.5, ArH), 6.85 (d, 1H, *J* 7.7, H^7), 6.78 (d, 1H, *J* 7.7, H^4), 6.76 (d, 2H, *J* 8.6, H^{12}), 3.75 (s, 3H, CH_3), 3.70 (dd, 1H, *J* 4.7, 9.0, CH), 3.41 (dd, 1H, *J* 4.7, 13.7, C*H*H), 2.90 (dd, 1H, *J* 9.0, 13.7, CH*H*); δ_C (75 MHz, $CDCl_3$); 180.48 (CO), 158.74 (ArC), 142.04 (ArC), 130.82 (ArCH), 130.17 (ArC), 129.53 (ArC), 128.34 (ArCH), 125.22 (ArCH), 122.39 (ArCH), 114.12 (ArCH), 110.24 (ArCH), 55.58 (CH_3), 48.23 (CH), 36.17 (CH_2); ν_{max}/cm^{-1} (film) 1708 (CO), 1619, 1513, 1471, 1248, 1178, 1035, 828; HRMS [ES+] found M+1 254.1171. $C_{16}H_{16}NO_2$ requires 254.1176.

4.8. 3-(Benzo[*d*][1,3]dioxol-5-ylmethyl)indolin-2-one (10)



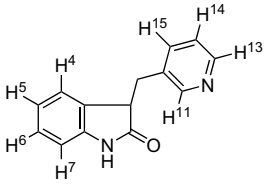
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and 3,4-methylenedioxybenzyl alcohol (0.456 g, 3.0 mmol). Chromatography eluting with 1:1 v/v ether–petrol followed by crystallisation from DCM and hexane gave the product (0.264 g, 99%) by general procedure A and (0.248 g, 93%) by general procedure B as a colourless amorphous solid. Mp 138–139.0 °C (lit.[34] mp 138.0–139.0); δ_H (500 MHz, $CDCl_3$); 8.60 (1H, br s, NH), 7.15 (t, 1H, *J* 7.7, H^6), 6.93 (t, 1H, *J* 7.7, H^5), 6.85 (d, 1H, *J* 7.7, H^4), 6.83 (d, 1H, *J* 8.1, H^{14}), 6.68 (d, 1H, *J* 7.7, H^7), 6.67 (d, 1H, *J* 1.3, H^{11}), 6.60 (dd, 1H, *J* 1.3, 8.1 H^{15}), 5.91 (s, 2H, OCH_2O), 3.69 (dd, 1H, *J* 4.7, 9.0, CH), 3.39 (dd, 1H, *J* 4.7, 13.7, CH*H*), 2.89 (dd, 1H, *J* 9.0, 13.7, C*H*H); ν_{max}/cm^{-1} (film) 1708 (CO), 1620, 1502, 1489, 1470, 1444; HRMS [ES+] found M+Na 290.0775. $C_{16}H_{13}NO_3Na$ requires 290.0788.

4.9. 3-(Furan-2-ylmethyl)indolin-2-one (11)



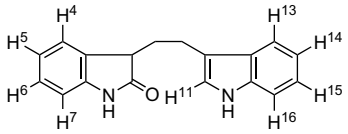
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and furfuryl alcohol (0.294 g, 3.0 mmol). Chromatography eluting with 1:1 v/v ether–petrol followed by crystallisation from DCM and hexane gave the product (0.209 g, 98%) by general procedure A and (0.200 g, 94%) by general procedure B as colourless needles. Mp 150.0–152.0 °C (Found: C, 73.00; H, 5.25; N, 6.65. $C_{13}H_{11}NO_2$ requires: C, 73.23; H, 5.20; N, 6.57%); δ_H (500 MHz, $CDCl_3$); 8.75 (br s, 1H, NH), 7.34 (d, 1H, *J* 1.3, H^{14}), 7.19 (t, 1H, *J* 7.7, H^6), 6.94 (t, 1H, *J* 7.7, H^5), 6.89 (d, 1H, *J* 7.7, H^4), 6.79 (d, 1H, *J* 7.7, H^7), 6.29 (dd, 1H, *J* 3.4, 1.3, H^{13}), 6.03 (d, 1H, *J* 3.4, H^{12}), 3.81 (dd, 1H, 9.4, 4.7), 3.47 (dd, 1H, *J* 4.7, 15.0, CH*H*), 2.99 (dd, 1H, *J* 9.4, 15.0, C*H*H); δ_C (75 MHz, $CDCl_3$); 179.80 (CO), 152.32 (ArC), 141.98 (ArCH), 141.78 (ArH), 129.16 (ArH), 128.52 (ArCH), 125.10 (ArCH), 122.69 (ArCH), 110.78 (ArCH), 110.16 (ArCH), 107.74 (ArCH), 45.57 (CH), 29.47 (CH_2); ν_{max}/cm^{-1} (film) 1702 (CO), 1619, 1506, 1470, 1343, 1231; HRMS [ES+] found M+1 214.0862. $C_{13}H_{12}NO_2$ requires 214.0863.

4.10. 3-(Pyridin-3-ylmethyl)indolin-2-one (12)



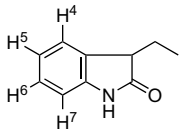
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and pyridine 3-methanol (0.327 g, 3.0 mmol). Chromatography eluting with 95:5 v/v DCM–methanol gave the product (0.202 g, 90%) by general procedure A and (0.215 g, 96%) by general procedure B as a colourless solid. Mp 140.0–142.0 °C (lit.[35] mp 139.0–141.0 °C); δ_H (500 MHz, C_6D_6); 8.44 (d, 1H, *J* 1.7, H^{11}), 8.35 (dd, 1H, *J* 1.3, 4.7, H^{13}), 8.26 (br s, 1H, NH), 7.05 (ddd, 1H, *J* 1.3, 1.7, 7.7, H^{15}), 6.88 (t, 1H, *J* 7.7, H^6), 6.70 (t, 1H, *J* 7.7, H^5), 6.60 (dd, 1H, *J* 4.7, 7.7 H^{14}), 6.57 (d, 1H, *J* 7.7, H^4), 6.35 (d, 1H, *J* 7.7, H^7), 3.25 (dd, 1H *J* 5.1, 7.7, CH), 2.95 (dd, 1H, *J* 5.1, 13.7, C*H*H), 2.78 (dd, 1H, *J* 7.7, 13.7, CH*H*); ν_{max}/cm^{-1} (film) 1704 (CO), 1622, 1471, 1426, 1338; HRMS [ES+] found M+1 225.1021. $C_{14}H_{13}N_2O$ requires 225.1022.

4.11. 3-(2-(1*H*-Indol-3-yl)ethyl)indolin-2-one (13)



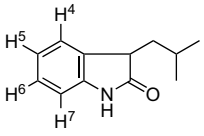
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and tryptophol (0.483 g, 3.0 mmol). Chromatography eluting with 1:1 v/v petrol–ether gave the product (0.224 g, 81%) by general procedure A and (0.240 g, 87%) by general procedure B as a colourless solid. Mp 80.0–82.0 °C; δ_H (500 MHz, $CDCl_3$); 8.47 (br s, 1H, NH), 7.97 (br s, 1H, NH), 7.58 (d, 1H, *J* 7.3, H^{13}), 7.33 (d, 1H, *J* 7.7, H^4), 7.28 (d, 1H, *J* 7.3, H^{16}), 7.22 (t, 1H, *J* 7.7, H^6), 7.17 (t, 1H, *J* 7.3, H^{15}), 7.09 (t, 1H, *J* 7.7, H^5), 7.05 (t, 1H, *J* 7.3, H^{14}), 6.99 (d, 1H, *J* 1.7, H^{11}), 6.89 (d, 1H, *J* 7.7, H^7), 3.58 (t, 1H, *J* 6.0, CH), 2.98–2.90 (m, 1H, CHCH*H*), 2.87–2.80 (m, 1H, CHC*H*H), 2.41–2.34 (m, 2H, $CHCH_2CH_2$); δ_C (75 MHz, $CDCl_3$); 180.82 (CO), 142.01 (ArC), 136.71 (ArC), 130.15 (ArC), 128.30 (ArCH), 127.80 (ArC), 124.58 (ArCH), 122.77 (ArCH), 122.38 (ArCH), 121.98 (ArCH), 119.66 (ArCH), 119.29 (ArCH), 115.84 (ArC), 111.50 (ArCH), 110.13 (ArCH), 46.00 (CH), 31.52 (CH_2), 21.81 (CH_2); ν_{max}/cm^{-1} (film) 1699, 1620, 1470, 741; HRMS [ES+] found M+Na 299.1148. $C_{18}H_{16}N_2ONa$ requires 299.1155.

4.12. 3-Ethylindolin-2-one (14)



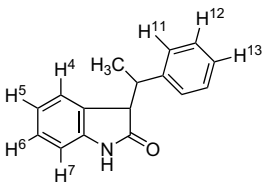
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and ethanol (1.0 mL). Chromatography eluting with 1:1 v/v ether–petrol followed by crystallisation from DCM and hexane gave the product (0.142 g, 89%) by general procedure A and (0.126 g, 78%) by general procedure B as colourless microprisms. Mp 99.0–101.0 °C (lit.[36] mp 104.0 °C); δ_H (500 MHz, $CDCl_3$); 8.16 (br s, 1H, NH), 7.23 (d, 1H, *J* 7.7, H^4), 7.22 (t, 1H, *J* 7.7, H^6), 7.04 (t, 1H, *J* 7.7, H^5), 6.88 (1H, d, *J* 7.7, H^7), 3.46 (1H, t, *J* 5.8, CH), 2.04 (m, 2H, CH_2), 0.93 (t, 3H, *J* 7.5, CH_3); δ_C (75 MHz, $CDCl_3$); 180.13 (CO), 141.61 (ArC), 129.50 (ArC), 127.82 (ArCH), 124.16 (ArCH), 122.27 (ArCH), 109.52 (ArCH), 47.04 (CH), 23.59 (CH_2), 9.99 (CH_3); ν_{max}/cm^{-1} (film) 1708 (CO), 1621, 1471, 1338, 1220; HRMS [ES+] found M+1 162.0918. $C_{10}H_{12}NO$ requires 162.0913.

4.13. 3-Isobutylindolin-2-one (15)



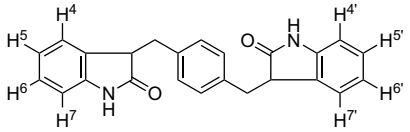
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and 2-methyl propanol (1.0 mL). Chromatography eluting with 1:1 v/v ether–petrol followed by crystallisation of the residue from DCM and hexane gave the product (0.135 g, 71%) by general procedure A and (0.148 g, 76%) by general procedure B as colourless prisms. Mp 96.0–97.0 °C (Found: C, 75.95; H, 8.05; N, 7.35. $C_{12}H_{15}NO$ requires: C, 76.16; H, 7.99; N, 7.40%); δ_H (500 MHz, $CDCl_3$); 8.51 (br s, 1H, NH), 7.22 (m, 2H, H^6 and H^7), 7.01 (t, 1H, *J* 7.7, H^5), 6.90 (d, 1H, *J* 7.7, H^4), 3.48 (t, 1H, *J* 7.3, H^3), 2.09–2.01 (m, 1H, CH_3CHCH_3), 1.90–1.84 (m, 1H, C*H*H), 1.73–1.67 (m, 1H, CH*H*), 1.01 (d, 3H, *J* 6.4, CH_3), 0.96 (d, 3H, *J* 6.4, CH_3); δ_C (75 MHz, $CDCl_3$); 181.28 (CO), 141.73 (ArC), 130.71 (ArC), 128.15 (ArCH), 124.80 (ArCH), 122.53 (ArCH), 110.07 (ArCH), 44.66 (CH), 40.36 (CH_2), 25.73 (CH), 23.33 (CH_3), 22.54 (CH_3); ν_{max}/cm^{-1} (film) 1705, 1620, 1471, 1332, 1230, 1102, 1018, 749, 668; HRMS [EI+] found M+1 190.1233. $C_{12}H_{16}NO$ requires 190.1226.

4.14. 3-(1-Phenylethyl)indolin-2-one (16)



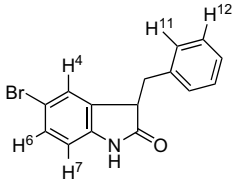
Prepared by general procedures A and B from oxindole (0.133 g, 1.0 mmol) and 1-phenyl ethanol (0.366 g, 3.0 mmol). Chromatography eluting with 1:1 v/v petrol–ether followed by crystallisation from DCM–hexane gave the product (0.237 g, 82%) by general procedure A and (214 g, 74%) by general procedure B as a colourless solid. ^1H NMR showed that the product was a 2:1 mixture of diastereoisomers; δ_H (500 MHz, $CDCl_3$); 8.49 (br s, 1H, ^{MAJ}NH), 8.14 (br s, 1H, ^{MIN}NH), 7.42–7.30 (m, 7H, 7×ArH), 7.24–7.18 (m, 4H, 2×^{MIN}ArH and 2×^{MAJ}ArH), 7.14–7.09 (m, 2H, ^{MIN}ArH and ^{MAJ}ArH), 7.00 (t, 1H, *J* 7.5, $^{MIN}H^5$), 6.93–6.88 (m, 2H, $^{MAJ}H^5$ and $^{MAJ}H^7$), 6.79 (d, 1H, *J* 8.1, $^{MIN}H^4$), 6.57 (d, 1H, *J* 7.3, $^{MAJ}H^4$), 1.69 (d, 3H, *J* 7.3, $^{MIN}CH_3$), 1.25 (d, 3H, *J* 8.6, $^{MAJ}CH_3$); δ_C (75 MHz, $CDCl_3$); 179.53 (CO), 179.131 (CO), 143.15, 142.51, 142.25, 141.99, 128.75, 128.5, 128.38, 128.35, 128.27, 127.37, 127.13, 127.08, 125.57, 122.30, 122.30, 122.27, 109.85, 53.32, 52.76, 42.26, 39.93, 19.64, 13.93; ν_{max}/cm^{-1} (solid) 1705 (CO), 1620, 1470, 1339, 1227, 1020, 751, 699; HRMS [ES+] found M+1 238.1226. $C_{16}H_{16}NO$ requires 238.1226.

4.15. 1,4-Bis(3-methylindolin-2-one) benzene (17)



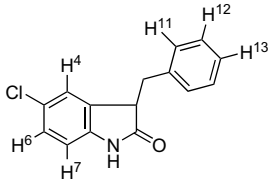
Prepared by general procedures A and B from oxindole (0.146 g, 1.1 mmol) and 1,4-dibenzyl alcohol (0.069 g, 0.5 mmol) but with the addition of toluene (1.0 mL). Chromatography eluting with 19:1 v/v DCM–methanol gave the product (0.145 g, 79%) as a pale yellow solid as a 2:1 mixture of diastereoisomers. δ_H (500 MHz, DMSO-d_6); 10.24 (br s, 2H, NH_2^{MAJ}), 10.23 (br s, 2H, NH_2^{MIN}), 7.05–6.99 (m, 2H), 6.93 (s, 4H, 4×PhH^{MAJ}), 6.92 (s, 4H, 4×PhH^{MIN}), 6.74–6.64 (m, 4H), 6.57–6.52 (m, 2H), 3.69 (m, 2H, 2×CH), 3.23–3.17 (m, 2H, 2×C*H*H), 2.78–2.70 (m, 2H, 2×CH*H*); δ_C (75 MHz, DMSO-d_6); 178.46 (CO), 142.96 (ArC), 136.39 (ArC), 136.34 (ArC), 129.29 (ArCH), 129.22 (ArC), 127.86 (ArCH), 124.65 (ArCH), 121.18 (ArCH), 109.38 (ArCH), 46.82 (CH), 35.40 (CH_2); ν_{max}/cm^{-1} (solid) 1702 (CO), 1764, 1615, 1468, 1336, 1230, 1017, 959; HRMS [ES+] found M+Na 391.1413. $C_{24}H_{20}N_2O_2Na$ requires 391.1417.

4.16. 3-Benzyl-5-bromo-indolin-2-one (19)



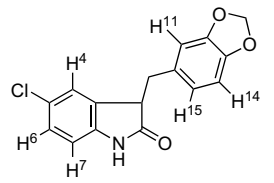
Prepared by general procedure B from 5-bromo oxindole (0.212 g, 1.0 mmol) and benzyl alcohol (0.324 g, 3.0 mmol). Chromatography eluting with 1:1 v/v ether–petrol followed by crystallisation from DCM and hexane gave the product (0.248 g, 82%) as colourless prisms. Mp 138.0–140.0 °C (Found: C, 59.85; H, 4.00; N, 4.65; Br, 26.15. $C_{15}H_{12}BrNO$ requires: C, 59.62; H, 4.00; N, 4.64; Cl, 26.44%); δ_H (500 MHz, $CDCl_3$); 8.68 (br s, 1H, NH), 7.32–7.14 (m, 6H, 6×ArH), 6.86 (s, 1H, H^4), 6.72 (d, 1H, *J* 8.1, H^6), 3.73 (dd, 1H, *J* 4.5, 8.8, CH), 3.45 (dd, 1H, *J* 4.5, 13.7, C*H*H), 2.95 (dd, 1H, *J* 8.8, 13.7, CH*H*); δ_C (75 MHz, $CDCl_3$); 179.45 (CO), 140.81 (ArC), 137.52 (ArC), 131.41 (ArC), 131.29 (ArCH), 129.78 (2×ArCH), 128.91 (2×ArCH), 128.44 (ArCH), 127.39 (ArCH), 115.14 (ArC), 111.54 (ArCH), 48.02 (CH), 36.85 (CH_2); ν_{max}/cm^{-1} (film) 1709 (CO), 1616, 1473, 1313, 1228, 1117, 812, 698; HRMS [ES+] found M−1 300.0029. $C_{15}H_{11}BrNO$ requires 300.0030.

4.17. 3-Benzyl-5-chloro-indolin-2-one (20)



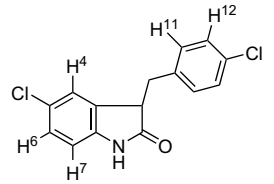
Prepared by general procedure B from 5-chloro oxindole (0.167 g, 1.0 mmol) and benzyl alcohol (0.324 g, 3.0 mmol). Chromatography eluting with 1:1 v/v petrol–ether followed by crystallisation from DCM and hexane gave the product (0.193 g, 75%) as colourless plates. Mp 115.0–116.0 °C (Found: C, 69.70; H, 4.55; N, 5.40; Cl, 13.65%. $C_{15}H_{12}ClNO$ requires: C, 69.91; H, 4.69; N, 5.43; Cl, 13.76%); δ_H (500 MHz, $CDCl_3$); 8.71 (1H, br s, NH), 7.29–7.21 (3H, m), 7.18–7.13 (3H, m), 6.76 (1H, d, *J* 8.6, H^7), 6.73 (1H, s, H^4), 3.74 (1H, dd, *J* 4.7, 9.0, CH), 3.46 (1H, dd, *J* 4.7, 13.7, C*H*H), 2.96 (1H, dd, *J* 9.0, 13.7, CH*H*); δ_C (75 MHz, $CDCl_3$); 179.18 (CO), 139.91 (ArC), 137.13 (ArC), 130.59 (ArC), 129.34 (ArCH), 128.49 (ArCH), 127.97 (ArCH), 127.41 (ArC), 126.95 (ArCH), 125.23 (ArCH), 110.61 (ArCH), 47.66 (CH), 36.42 (CH_2); ν_{max}/cm^{-1} (film) 1710 (CO), 1619, 1476, 1454,1313.

4.18. 3-(Piperonyl)-5-chloro-indolin-2-one (21)



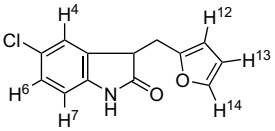
Prepared by general procedure B from 5-chloro oxindole (0.167 g, 1.0 mmol) and 3,4-methylenedioxybenzyl alcohol (0.456 g, 3.0 mmol). Chromatography eluting 1:1 v/v petrol–ether followed by crystallisation from DCM and hexane gave the product (0.196 g, 65%) as colourless microneedles. Mp 159.0–160.0 °C (Found: C, 63.75; H, 3.95; N, 4.60; Cl, 11.75. $C_{16}H_{12}NO_3Cl$ requires: C, 63.69; H, 4.01; N, 4.64; Cl, 11.75%); δ_H (500 MHz, $CDCl_3$); 8.54 (1H, br s, NH), 7.16 (1, dd, *J* 1.7, 8.1, H^6), 6.83 (1H, d, *J* 1.7, H^4), 6.76 (1H, d, *J* 8.1, H^7), 6.69 (1H, d, *J* 8.1, H^{14}), 6.66 (1H, d, *J* 1.3, H^{11}), 6.58 (1H, dd, *J* 1.3, 7.7, H^{15}), 5.92 (1H, d, *J* 2.1, OCH_2O), 3.68 (1H, dd, *J* 4.7, 8.6, CH), 3.35 (1H, dd, *J* 4.7, 13.7, C*H*H), 2.91 (1H, dd, *J* 8.6, 13.7, CH*H*); δ_C (75 MHz, $CDCl_3$); 179.35 (CO), 148.09 (ArC), 146.88 (ArC), 140.30 (ArC), 131.16 (ArCH), 130.95 (ArC), 128.42 (ArCH), 127.87 (ArC), 125.60 (ArCH), 122.97 (ArCH), 111.03 (ArCH), 109.87 (ArCH), 108.56 (ArCH), 101.38 (OCH_2O), 48.16 (CH), 36.52 (CH_2); ν_{max}/cm^{-1} (film) 1710 (CO), 1618, 1502, 1478, 1443; HRMS [ES+] found M+Cl 324.0391. $C_{16}H_{12}NClO_3Na$ requires 324.0398.

4.19. 3-(4-Chlorobenzyl)-5-chloro-indolin-2-one (22)



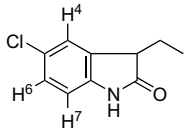
Prepared by general procedure B from 5-chloro oxindole (0.167 g, 1.0 mmol) and 4-chlorobenzyl alcohol (0.426 g, 3.0 mmol). Chromatography eluting with 1:1 v/v petrol–ether followed by crystallisation from DCM and hexane gave the product (0.219 g, 75%) as colourless needles. Mp 157.5–158.5 °C (Found: C, 61.50; H, 3.70; N, 4.80; Cl, 24.10. $C_{15}H_{11}Cl_2NO_2$ requires: C, 61.67; H, 3.79; N, 4.79; Cl, 24.27%); δ_H (500 MHz, $CDCl_3$); 8.91 (1H, br s, NH), 7.21 (2H, d, *J* 8.3, H^{12}), 7.16 (1H, dd, *J* 1.7, 8.6, H^6), 7.06 (2H, d, *J* 8.3, H^{11}), 6.87 (1H, d, *J* 1.7, H^4), 6.75 (1H, d, *J* 8.6, H^7), 3.72 (1H, dd, *J* 4.7, 8.1, CH), 3.45 (1H, dd, *J* 4.7, 13.7, CH*H*), 3.03 (1H, dd, *J* 8.1, 13.7, C*H*H); δ_C (75 MHz, $CDCl_3$); 178.81 (CO), 139.91 (ArC), 135.37 (ArC), 132.79 (ArC), 130.70 (ArCH), 130.19 (ArC), 128.57 (ArCH), 128.19 (ArC), 127.58 (ArCH), 125.00 (ArCH), 110.76 (ArCH), 47.46 (CH), 36.58 (CH_2); ν_{max}/cm^{-1} (film) 1712 (CO), 1619, 1489, 1478, 1439; HRMS [ES−] found M−1 290.0136. $C_{15}H_{10}NCl_2O$ requires 290.0145.

4.20. 3-Furfuryl-5-chloro-indolin-2-one (23)



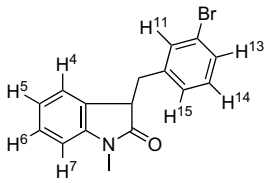
Prepared by general procedure B from 5-chloro oxindole (0.167 g, 1.0 mmol) and furfuryl alcohol (0.294 g, 3.0 mmol). Chromatography eluting with 1:1 v/v ether–petrol-ether followed by crystallisation from DCM and hexane gave the product (0.188 g, 76%) as colourless microneedles. Mp 150.5–152.5 °C (Found: C, 62.75; H, 4.00; N, 5.60; Cl, 14.30. $C_{13}H_{10}ClNO_2$ requires: C, 63.04; H, 4.07; N, 5.66; Cl, 14.31%); δ_H (500 MHz, $CDCl_3$); 9.09 (br s, 1H, NH), 7.34 (d, 1H, *J* 1.5, H^4), 7.17 (1H, dd, *J* 1.5, 8.3, H^6), 6.82 (d, 1H, *J* 8.3, H^7), 6.77 (d, 1H, *J* 1.7, H^{14}), 6.30 (dd, 1H, *J* 1.7, 3.0, H^{13}), 6.06 (d, 1H, *J* 3.0, H^{12}), 3.80 (dd, 1H, *J* 4.7, 9.4, CH), 3.45 (dd, 1H, *J* 4.7, 15.0, CH*H*), 2.99 (1H, dd, *J* 9.4, 15.0, C*H*H); δ_C (75 MHz, $CDCl_3$); 179.54 (CO), 151.71 (ArC), 142.18 (ArCH), 140.36 (ArC), 130.80 (ArC), 128.53 (ArCH), 128.07 (ArC), 125.54 (ArCH), 111.16 (ArCH), 110.90 (ArCH), 108.01 (ArCH), 45.79 (CH), 29.27 (CH_2); ν_{max}/cm^{-1} (film) 1712 (CO), 1619, 1478, 1442, 1316; HRMS [ES+] found M+1 248.0472. $C_{13}H_{11}NO_2Cl$ requires 248.0473.

4.21. 3-Ethyl-5-chloro-indolin-2-one (24)



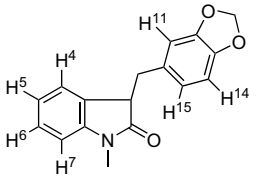
Prepared by general procedure B from 5-chloro oxindole (0.167 g, 1.0 mmol) and ethanol (1.0 mL). Chromatography eluting with 1:1 v/v petrol–ether followed by crystallisation from DCM and hexane gave the product (0.158 g, 81%) as colourless prisms. Mp 128.0–129.0 °C (Found: C, 61.20; H, 5.05; N, 7.25; Cl, 17.95. $C_{10}H_{10}ClNO$ requires: C, 61.39; H, 5.15; N, 7.16; Cl, 18.12%); δ_H (500 MHz, $CDCl_3$); δ 9.45 (1H, br s, NH), 7.21 (1H, s, H^4), 7.19 (1H, d, *J* 8.1, H^6), 7.85 (1H, d, *J* 8.1, H^7), 3.47 (1H, t, *J* 5.6, CH), 2.03 (2H, dq, *J* 5.6, 7.5, CH_2), 0.92 (3H, t, *J* 7.5, CH_3); δ_C (75 MHz, $CDCl_3$); δ 180.66 (CO), 140.47 (ArC), 131.22 (ArC), 127.84 (ArCH), 127.64 (ArC), 124.48 (ArCH), 110.77 (ArCH), 47.40 (CH), 23.44 (CH_2), 9.91 (CH_3); ν_{max}/cm^{-1} (film) 1709 (CO), 1620, 1479, 1458, 1313, 1220, 1172, 813; HRMS [ES+] found M+Na 218.0340. $C_{10}H_{10}NONa$ requires 218.0343.

4.22. 3-(3-Bromobenzyl)-1-methylindolin-2-one (25)



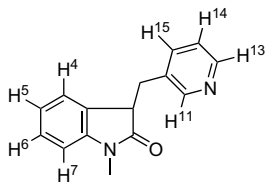
Prepared by general procedure C from *N*-methyl oxindole (0.147 g, 1.0 mmol) and 3-bromobenzyl alcohol (0.280 g, 1.5 mmol). Chromatography eluting with 1:1 v/v petrol–ether gave the product (0.202 g, 64%) as a colourless solid. Mp 108.0–109.0 °C (Found: C, 60.55; H, 4.45; N, 4.35; Br, 25.05. $C_{16}H_{14}BrNO$ requires: C, 60.78; H, 4.46; N, 4.43; Br, 25.27%); δ_H (500 MHz, $CDCl_3$); 7.34 (d, 1H, *J* 7.3, H^4), 7.31 (s, 1H, H^{11}), 7.24 (t, 1H, *J* 7.6, H^6), 7.14–7.07 (m, 2H, H^{13} and H^{14}), 6.95 (appar t, 1H, *J* 7.5, H^5), 6.79 (d, 1H, *J* 7.5, H^{15}), 6.76 (d, 1H, *J* 7.6, H^7), 3.69 (dd, 1H, *J* 3.8, 9.2, CH), 3.43 (dd, 1H, *J* 3.8, 13.7, C*H*H), 3.16 (s, 3H, CH_3), 2.88 (dd, 1H, *J* 9.2, 13.7, CH*H*); δ_C (75 MHz, $CDCl_3$); 176.66 (CO), 144.16 (ArC), 140.25 (ArC) 132.35 (ArCH), 129.79 (ArCH), 128.16 (ArCH), 128.06 (ArCH), 127.88 (ArC), 124.38 (ArCH), 122.27 (ArC), 122.19 (ArCH), 108.06 (ArCH), 46.73 (CH), 36.36 (CH_2), 26.15 (CH_3); ν_{max}/cm^{-1} (film) 2925, 1708 (CO), 1612, 1567, 1470, 1375, 1087, 750; HRMS [ES+] found M+1 316.0336. $C_{16}H_{15}BrNO$ requires 316.2001.

4.23. 3-(Benzo[*d*][1,3]dioxol-5-ylmethyl)-1-methylindolin-2-one (26)



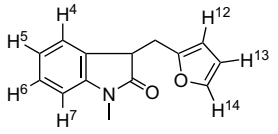
Prepared by general procedure C from *N*-methyl oxindole (0.147 g, 1.0 mmol) and 3,4-methylenedioxy benzyl alcohol (0.228 g, 1.5 mmol). Chromatography eluting with 1:1 v/v petrol–ether gave the product (0.213 g, 76%) as a pale yellow oil; δ_H (500 MHz, $CDCl_3$); 7.22 (t, 1H, *J* 7.5, H^5), 6.93 (appar t, 1H, *J* 7.5, H^6), 6.81 (d, 1H, *J* 7.5, H^4), 6.76 (d, 1H, *J* 7.5, H^7), 6.68 (d, 1H, *J* 7.3, H^{14}), 6.66 (s, 1H, H^{11}), 6.59 (d, 1H, *J* 7.3, H^{15}), 5.90 (d, 2H, *J* 1.7, OCH_2O), 3.64 (dd, 1H, *J* 4.3, 9.2, CH), 3.39 (dd, 1H, *J* 4.3, 13.7, C*H*H), 3.16 (s, 3H, CH_3), 2.81 (dd, 1H, *J* 9.2, 13.7, CH*H*); δ_C (75 MHz, $CDCl_3$); 177.36 (CO), 147.92 (ArC), 146.63 (ArC), 144.60 (ArC), 132.06 (ArC), 128.70 (ArC), 128.38 (ArCH), 124.93 (ArCH), 122.93 (ArCH) 122.50 (ArCH), 110.01 (ArCH), 108.43 (ArCH), 108.36 (ArCH), 101.28 (CH_2), 47.59 (CH), 36.89 (CH_2), 26.56 (CH_3); ν_{max} (film)/cm^{-1} 1709 (CO), 1612, 1490, 1470, 1443, 1376; HRMS [ES+] found M+1 282.1135. $C_{17}H_{16}NO_3$ requires 282.1125.

4.24. 1-Methyl-3-(pyridin-3-ylmethyl)indolin-2-one (27)



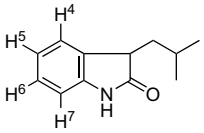
Prepared by general procedure C from *N*-methyl oxindole (0.147 g, 1.0 mmol) and pyridine 3-methanol (0.163 g, 1.5 mmol). Chromatography eluting with 19:1 v/v DCM–methanol followed by crystallisation from DCM and hexane gave the product (0.200 g, 84%) as colourless needles. Mp 107.0–108.0 °C; δ_H (500 MHz, $CDCl_3$); 8.43 (d, 1H, *J* 3.4, H^{13}), 8.34 (s, 1H, H^{11}), 7.47 (d, 1H, *J* 7.7, H^{15}), 7.23 (t, 1H, *J* 7.5, H^6), 7.15 (dd, 1H, *J* 7.5, 3.4, H^{14}), 6.97 (t, 1H, *J* 7.5, H^5), 6.91 (d, 1H, *J* 7.5, H^4), 6.73 (d, 1H, *J* 7.7, H^7), 3.73 (dd, 1H, *J* 4.5, 7.5 CH), 3.41 (dd, 1H, *J* 4.5, 14.1 C*H*H), 3.12 (s, 3H, CH_3), 3.06 (dd, 1H, *J* 7.5, 14.1 CH*H*); δ_C (75 MHz, $CDCl_3$); 176.86 (CO), 151.06 (ArCH), 148.57 (ArCH), 144.59 (ArC), 137.26 (ArCH), 133.43 (ArC), 128.73 (ArCH), 127.88 (ArC), 124.64 (ArCH), 123.54 (ArCH), 122.77 (ArCH), 108.56 (ArCH), 47.00 (CH), 34.14 (CH_2), 26.53 (CH_3); ν_{max} (film)/cm^{-1} 1709 (CO), 1612, 1493, 1469, 1424, 1375, 1126, 1088; HRMS [ES+] found M+1 239.1186. $C_{15}H_{15}N_2O$ requires 239.1186.

4.25. 3-(Furan-2-ylmethyl)-1-methylindolin-2-one (28)



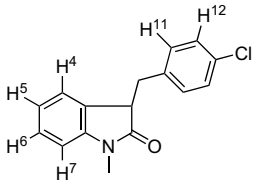
Prepared by general procedure C from *N*-methyl oxindole (0.147 g, 1.0 mmol) and furfuryl alcohol (0.147 g, 1.5 mmol). Chromatography eluting with 1:1 v/v petrol–ether gave the product (0.185 g, 75%) as a colourless oil. δ_H (500 MHz, $CDCl_3$); 7.34 (s, 1H, H^{14}), 7.25 (appar t, 1H, *J* 7.3, H^6), 6.96 (appar t, 1H, *J* 7.3, H^5), 6.80 (d, 1H, *J* 6.8, H^4), 6.42 (d, 1H, *J* 6.4, H^7), 6.28 (s, 1H, H^{13}), 6.01 (s, 1H, H^{12}), 3.77 (dd, 1H, *J* 3.9, 9.6, CH), 3.47 (dd, 1H, *J* 3.9, 15.0, C*H*H), 3.20 (s, 3H, CH_3), 2.90 (dd, 1H, *J* 9.6, 15.0, CH*H*); δ_C (75 MHz, $CDCl_3$); 177.14 (CO), 152.52 (ArC), 144.55 (ArC), 141.91 (ArCH), 128.59 (ArC), 128.50 (ArCH), 124.81 (ArCH), 122.71 (ArCH), 110.77 (ArCH), 108.35 (ArCH), 107.66 (ArCH), 45.06 (CH), 29.66 (CH_2), 26.65 (CH_3); ν_{max} (film)/cm^{-1} 1710 (CO), 1612, 1493, 1469, 1376, 1350; HRMS [ES+] found M+1 228.1020. $C_{14}H_{14}NO_2$ requires 228.1019.

4.26. 3-*iso*-Butyl-1-methylindolin-2-one (29)



Prepared by general procedure C from *N*-methyl oxindole (0.147 g, 1.0 mmol) and 2-methyl propanol (1.0 mL). Chromatography eluting with 1:1 v/v ether–petrol gave the product (0.165 g, 81%) as a colourless oil. δ_H (500 MHz, $CDCl_3$); 7.27 (t, 1H, *J* 7.7, H^6), 7.24 (d, 1H, *J* 7.7, H^4), 7.04 (t, 1H, *J* 7.7, H^5), 6.82 (d, 1H, *J* 7.7, H^7), 3.44 (t, 1H, *J* 7.3), 3.20 (s, 3H, NCH_3), 2.10–1.99 (m, 1H, CH), 1.85 (ddd, 1H, *J* 6.0, 7.9, 14.1, C*H*H), 1.64 (ddd, 1H, *J* 6.8, 8.1, 14.1, CH*H*) 1.00 (d, 3H, *J* 6.4, CH_3), 0.94 (d, 3H, *J* 6.4, CH_3); δ_C (75 MHz, $CDCl_3$); 178.35 (CO), 144.17 (ArC), 129.70 (ArC), 127.73 (ArCH), 124.05 (ArCH), 122.11 (ArCH), 107.93 (ArCH), 43.70 (CH), 40.06 (CH_2), 26.14 (CH_3), 25.29 (CH), 22.90 (CH_3), 22.10 (CH_3); ν_{max} (film)/cm^{-1} 3054, 2956, 2869, 1712 (CO), 1613, 1494; HRMS [ES+] found M+Na 226.1202. $C_{13}H_{17}NONa$ requires 226.2763.

4.27. 3-(4-Chlorobenzyl)-1-methylindolin-2-one (30)



Prepared by general procedure C from *N*-methyl oxindole (0.147 g, 1.0 mmol) and 4-chlorobenzyl alcohol (0.213 g, 1.5 mmol).

Chromatography eluting with 1:1 v/v petrol–ether gave the product (0.264 g, 97%) as colourless prisms. Mp 115.0–116.0 °C (Found: C, 70.55; H, 5.15; N, 5.15; Cl, 13.05. $C_{16}H_{14}ClNO$ requires: C, 70.72; H, 5.19; N, 5.15; Cl, 13.05%); δ_H (500 MHz, $CDCl_3$); 7.23 (t, 1H, *J* 7.7, H^5), 7.19 (d, 2H, *J* 8.1, H^{12}), 7.06 (d, 2H, *J* 8.1, H^{11}), 6.94 (t, 1H, *J* 7.5, H^6), 6.84 (d, 1H, *J* 7.3, H^4), 6.74 (d, 1H, *J* 8.1, H^7), 3.69 (dd, 1H, *J* 4.7, 8.6, CH), 3.41 (dd, 1H, *J* 4.7, 13.7, C*H*H), 3.14 (s, 3H, CH_3), 2.95 (dd, 1H, *J* 8.55, 13.7, CH*H*); δ_C (75 MHz, $CDCl_3$); 177.12 (CO), 144.64 (ArC), 136.62 (ArC), 132.87 (ArC), 131.16 (ArCH), 128.76 (ArCH), 128.53 (ArCH), 128.35 (ArC), 124.73 (ArCH), 122.55 (ArCH), 108.45 (ArCH), 47.28 (CH), 36.40 (CH_2), 26.51 (CH_3); ν_{max}/cm^{-1} (film) 2925, 1704 (CO), 1610, 1490, 1467, 1373, 1346, 1086; HRMS [ES+] found M+1 272.0841. $C_{16}H_{15}ClNO$ requires 272.0837.

Acknowledgements

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