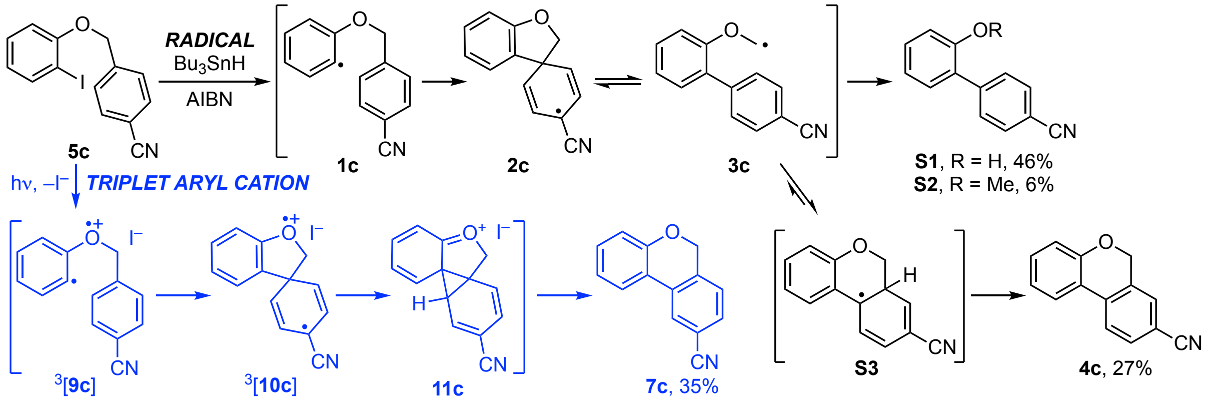
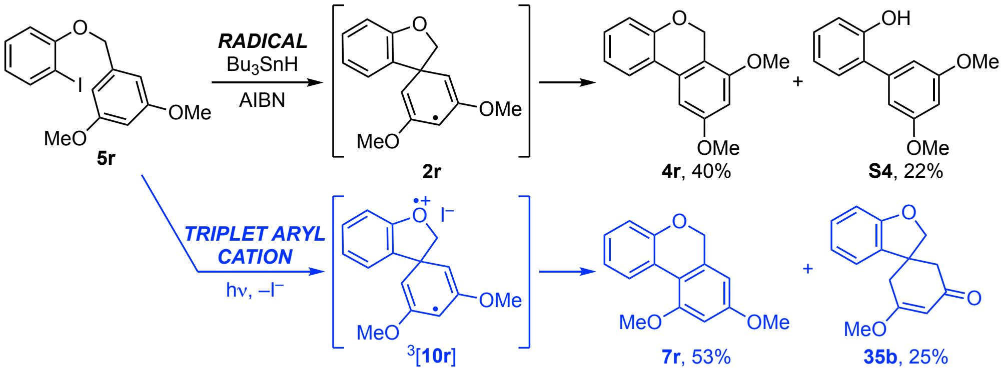
A Further Comment on the Contrasting Outcomes of Radical and Photochemical Reactions

Our proposal that these reactions proceed via the intermediacy of triplet aryl cations rather than aryl radicals centres on the contrasting outcomes observed when benzyl 2-iodoaryl ethers bearing substituents on the acceptor ring are treated under radical forming conditions and on irradiation with UVC. To that end, substrates **5c** (4-cyano, –M), **5r** (3,5-dimethoxy, +M) and **5b** (4-methyl, +I) have all been subjected to conditions that unequivocally lead to the corresponding aryl radical intermediate, and in each case the products given differ from those described herein. Thus, treatment of 4-cyanobenzyl 2-iodoaryl ether **5c** under standard tributyltin hydride-mediated radical forming conditions led to biaryls **S1** and **S2**, and 8-cyanobenzo[c]chromene **4c** (27%), implicating the intermediacy of spirocycle **2c** and its fragmentation to **3c** (Scheme S1).[1] In stark contrast, irradiation of **5c** with UVC led to the isomeric 9-cyanobenzo[c]chromene **7c** (35%), indicating that the reaction proceeded by a different pathway. The intermediacy of triplet aryl cation ^{3}[**9c**] provides an explanation for the dichotomy.



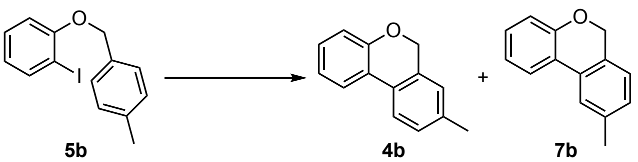
Scheme S1. Contrasting outcomes for the cyclisations of 4-cyanobenzyl 2-iodoaryl ether **5c**.

Similarly, treatment of 3,5-dimethoxybenzyl 2-iodoaryl ether **5r** under standard tributyltin hydride-mediated radical forming conditions led to biaryl **S4** (22%) and 7,9-dimethoxybenzo[c]chromene **4r** (40%) (Scheme S2).[1] In stark contrast, irradiation of **5r** with UVC led to the isomeric 8,10-dimethoxy-benzo[c]chromene **7r** (53%) and spirocycle **35b** (25%), again indicating that these reactions proceed via different intermediates.



Scheme S2. Contrasting outcomes for the cyclisations of 3,5-dimethoxybenzyl 2-iodoaryl ether **5c**.

A third, and arguably the most striking example, is provided by 2-iodoaryl 4-methylbenzyl ether **5b**.[2] Its treatment with 3 equiv. potassium *tert*-butoxide under irradiation with blue light in DMSO gave an inseparable 3.5 : 1 mixture of 8- and 9-methylbenzo[c]chromenes **4b** and **7b** in 57% yield (Scheme S3). Notably, the authors reported DFT calculations consistent with the established radical mechanism,[1] in that *ipso*-cyclisation of the aryl radical followed by rearrangement was favoured over *ortho*-cyclisation. By contrast, irradiation of **5b** with UVC light followed a different regiochemical course giving 9-methylbenzo[c]-chromene **7b** cleanly in 70% yield with no trace of its 'inseparable regioisomer' **4b** evident in the recorded ^{1}H and ^{13}C NMR spectra.



5b **4b** **7b**

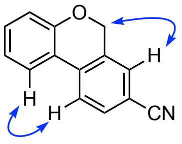
RADICAL: 3 equiv. KOtBu, blue light, DMSO 44% *inseparable* 13%

TRIPLET ARYL CATION: UVC, MeCN, continuous flow – 70%

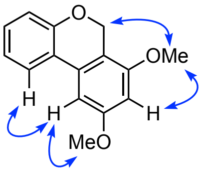
Scheme S3. Contrasting outcomes for the cyclisations of 2-iodoaryl 4-methylbenzyl ether **5b**.

Characterisation data for 8-cyano- and 7,9-dimethoxy-6*H*-benzo[c]chromenes 4c and 4r

To allow comparison of the characterisation data attained for 9-cyano-6*H*-benzo[c]chromene **7c** and 8-cyano-6*H*-benzo[c]chromene **4c**,[1] data for the latter follows [from the PhD thesis of Dr. Michael I. T. Nunn, Southampton, 2001]: **IR** ν_{max} (neat, cm^{-1}): 2226 (s), 1607 (s), 1478 (s), 1417 (m), 1247 (m), 1214 (m), 1044 (m), 1026 (m). **UV** (λ_{max}, MeOH) 319 (6210), 276 (10900), 240 (9320) nm. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.79 (1H, d, *J* = 8.5 Hz., Ar**H**), 7.75 (1H, d, *J* = 8.5 Hz, Ar**H**), 7.67 (1H, d, *J* = 7.7 Hz, Ar**H**), 7.47 (1H, s, Ar**H**), 7.35 (1H, t , *J* = 7.7 Hz, Ar**H**), 7.12 (1H, t, *J* = 7.4 Hz, Ar**H**), 7.03 (1H, d, *J* = 8.1 Hz, Ar**H**), 5.14 (2H, s, OCH_2) ppm. **GOSEY** (300 MHz, $CDCl_3$): observed enhancements are shown on the insert. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 155.3 (**C**), 134.8 (**C**), 132.3 (**C**H), 132.1 (**C**), 131.4 (**C**H), 128.3 (**C**H), 124.0 (**C**H), 122.6 (**C**H), 122.6 (**C**H), 121.3 (**C**), 118.7 (**C**), 117.8 (**C**H), 110.8 (**C**), 67.6 (**C**H_2) ppm. **LRMS** (CI): 225 ($[M+NH_4]^+$, 100 %), 207 (M^+, 62 %).

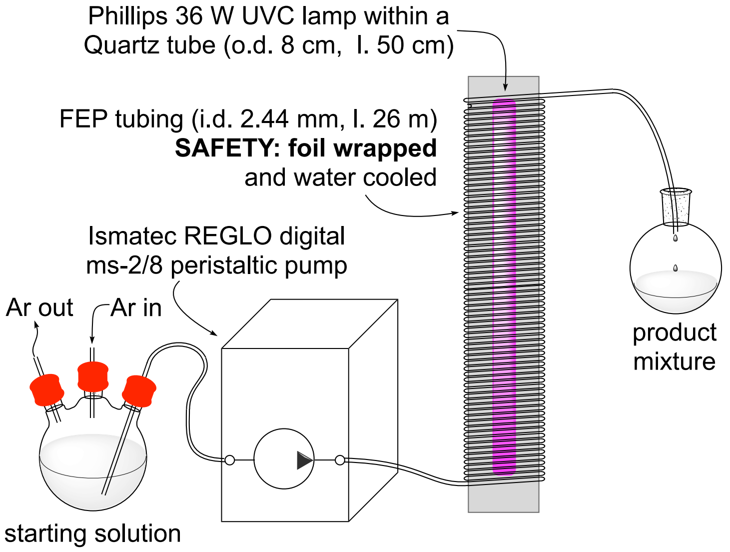


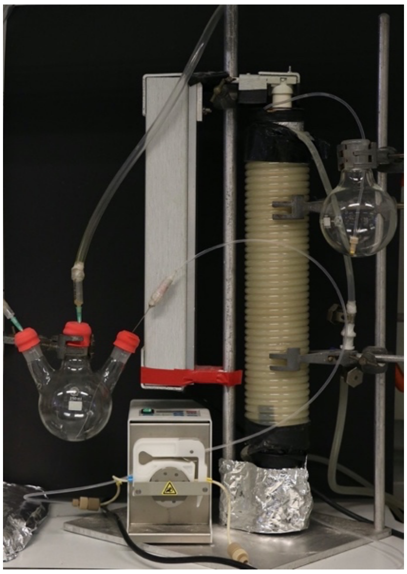
To allow comparison of the characterisation data attained for 8,10-dimethoxy-6*H*-benzo[c]chromene **7r** and 7,9-dimethoxy-6*H*-benzo[c]chromene **4r**,[1] data for the latter follows [from the PhD thesis of Dr. Michael I. T. Nunn, Southampton, 2002]: **IR** ν_{max} (neat, cm^{-1}): 1608 (s), 1571 (m), 1456 (m), 1420 (s), 1340 (m), 1276 (m), 1229 (m), 1206 (s), 1153 (s), 1096 (m), 1031 (s). **UV** (λ_{max}, MeOH) 300 (9960) 266 (11000) nm. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.68 (1H, d, *J* = 7.4 Hz, Ar**H**), 7.23 (1H, td, *J* = 7.5, 1.5 Hz., Ar**H**), 7.07 (1H, t, *J* = 7.4 Hz, Ar**H**), 7.04 (1H, d, *J* = 7.5 Hz, Ar**H**), 6.86 (1H, d, *J* = 1.8 Hz, Ar**H**), 6.43 (1H, d, *J* = 1.8 Hz, Ar**H**), 5.17 (2H, s, OCH_2), 3.92 (3H, s, OCH_3), 3.85 (3H, s, OCH_3) ppm. **GOSEY** (300 MHz, $CDCl_3$): observed enhancements are shown on the insert. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.8 (**C**), 156.2 (**C**), 155.1 (**C**), 131.8 (**C**), 129.7 (**C**H), 123.7 (**C**H), 122.9 (**C**), 121.9 (**C**H), 117.5 (**C**), 112.9 (**C**H), 98.5 (**C**H), 97.8 (**C**H), 63.2 (**C**H_2), 55.6 (2 × **C**H_3) ppm. **LRMS** (CI): 243 ($[M+H]^+$, 100 %), 227 (7%), 168 (8 %), 139 (11 %). **HRMS** (EI): Found 242.0936, $C_{15}H_{14}O_3$, M^+ requires 242.0943.



Photochemical Set-up

The reactor set-up consists of FEP tubing wound around a quartz cylinder which is then covered in a layer of aluminium foil to prevent the loss of light, and to protect the user and any observers from

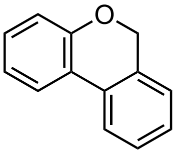




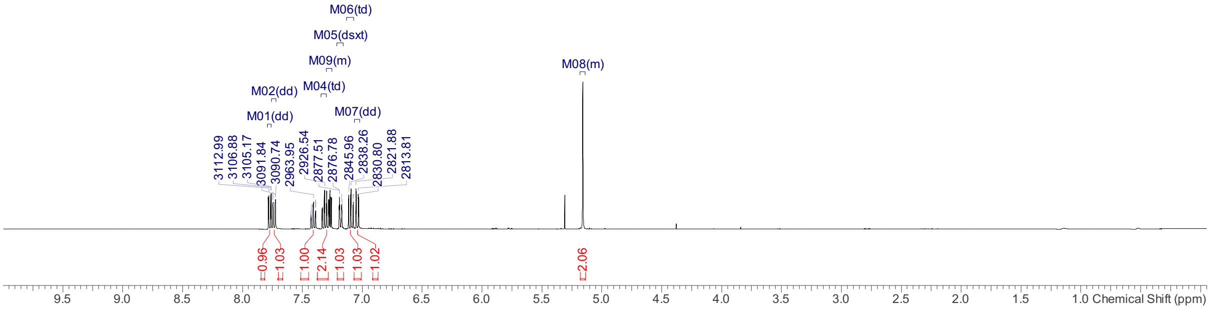
harmful UV irradiation.[3] A cooling system consisting of 10 mm diameter soft plastic condenser tubing is also wound around the reactor, with tap water running through it to remove generated heat. A 36 W Phillips UVC [254 nm] was used. The reaction solution is kept under an atmosphere of argon. A peristaltic pump connected to the FEP tubing inlet *via* a T-piece, pumps the reaction solution through the reactor. The irradiated solution leaves the reactor from an outlet at the opposite end of the reactor and is collected in a round bottomed flask.

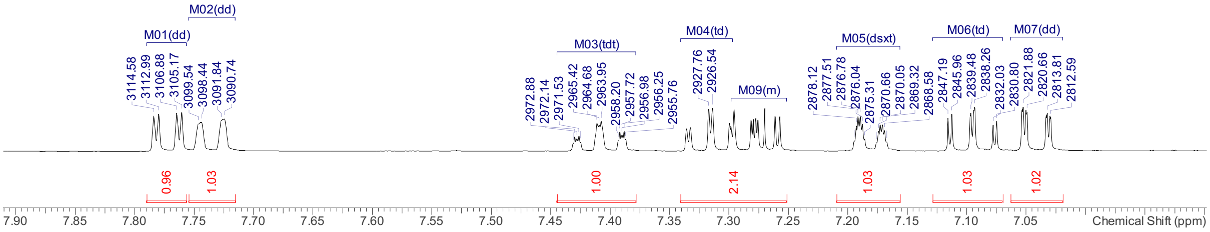
Photocyclisation Reactions

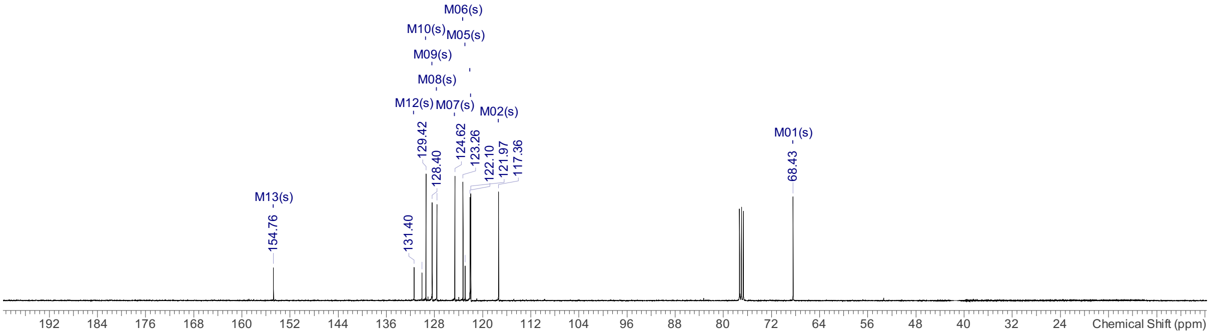
6*H*-Benzo[*c*]chromene, **7a**



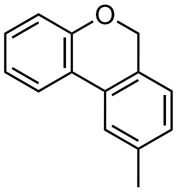
Using the flow photochemical set-up, a solution of benzyl *o*-iodophenyl ether **5a** (430 mg, 1.39 mmol) in MeCN (70 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 20% Et_2O/petrol) to afford the title compound **7a** (197 mg, 1.08 mmol, 78%) as an off-white solid. **MP**: 128 – 130 °C. **IR** ν_{max} (film, cm^{-1}): 3050 (br), 2840 (w), 1605 (m), 1485 (s), 1439 (s), 1243 (s), 1196 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (1 H, dd, *J* = 7.8, 1.7 Hz, Ar**H**), 7.74 (1 H, br d, *J* = 7.7 Hz, Ar**H**), 7.41 (1 H, app t with fine splitting, *J* = 7.6 Hz, Ar**H**), 7.32 (1 H, app td, *J* = 7.6, 1.2 Hz, Ar**H**), 7.27 (1 H, m, Ar**H**), 7.18 (1 H, d with fine splitting, *J* = 7.5, 0.7 Hz, Ar**H**), 7.10 (1 H, app td, *J* = 7.6, 1.2 Hz, Ar**H**), 7.04 (1 H, dd, *J* = 8.1, 1.2 Hz, Ar**H**), 5.16 (2 H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.8 (**C**), 131.4 (**C**), 130.1 (**C**), 129.4 (**C**H), 128.4 (**C**H), 127.6 (**C**H), 124.6 (**C**H), 123.3 (**C**H), 122.9 (**C**), 122.1 (**C**H) 122.0 (**C**H), 117.4 (**C**H), 68.4 (**C**H$_2$) ppm. **LRMS** (ESI$^+$): 183 [M+H]$^+$. **HRMS** (ESI$^+$): Found 183.0804, $C_{13}H_{11}O$ [M+H]$^+$ requires 183.0804. These data are consistent with literature reports.[4,5]



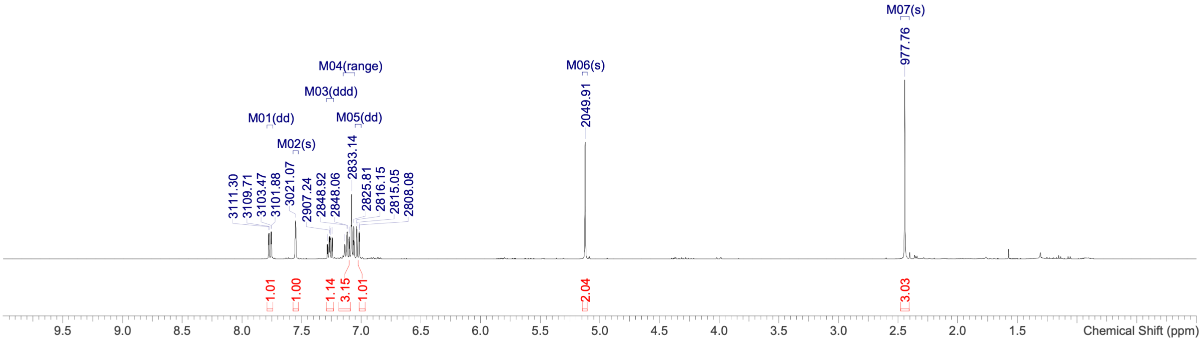


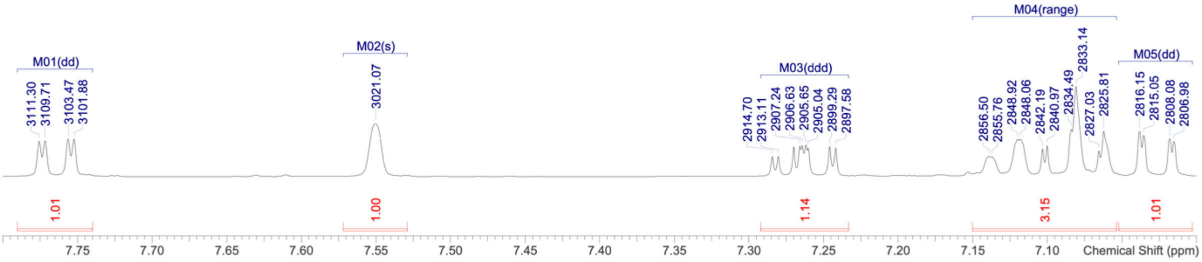


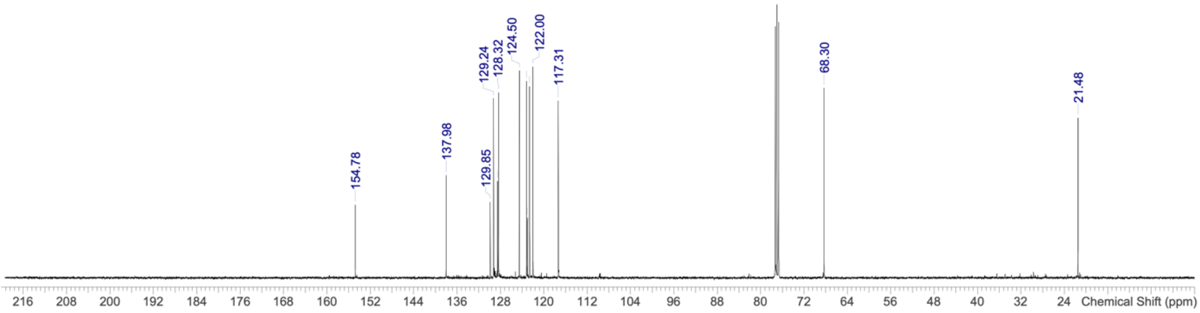
9-Methyl-6*H*-benzo[c]chromene, **7b**.



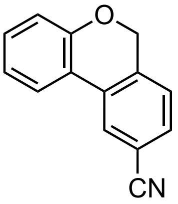
Using the flow photochemical set-up, a solution of benzyl *o*-iodoaryl ether **5b** (337 mg, 1.04 mmol) in MeCN (52 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (20 mL) were added. The aqueous phase was separated and extracted with DCM (2 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% EtOAc in petrol) to afford the title compound **7a** (143 mg, 0.73 mmol, 70%) as a white solid. **IR** ν_{max} (solid, cm^{-1}): 2841 (w), 1604 (w), 1489 (m), 1449 (s), 1243 (s), 1199 (s), 1104 (w), 1035 (m), 1009 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.55 (1 H, s, Ar**H**), 7.26 (1 H, ddd, *J* = 8.1, 7.5, 1.7 Hz, Ar**H**), 7.05 – 7.15 (3 H, m, 3 × Ar**H**), 7.03 (1 H, dd, *J* = 8.1, 1.1 Hz, Ar**H**), 5.12 (2 H, s, C**H**$_2$), 2.44 (3 H, s, C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.8 (**C**), 138.0 (**C**), 129.9 (**C**), 129.2 (**C**H), 128.5 (**C**), 128.3 (**C**H), 124.5 (**C**H), 123.2 (**C**H), 123.0 (**C**), 122.6 (**C**H), 122.0 (**C**H), 117.3 (**C**H), 68.3 (**C**H$_2$), 21.5 (**C**H$_3$) ppm. **LRMS** (ESI+): 197 ([M+H]$^+$, 100%). These data are consistent with a literature report.[5]



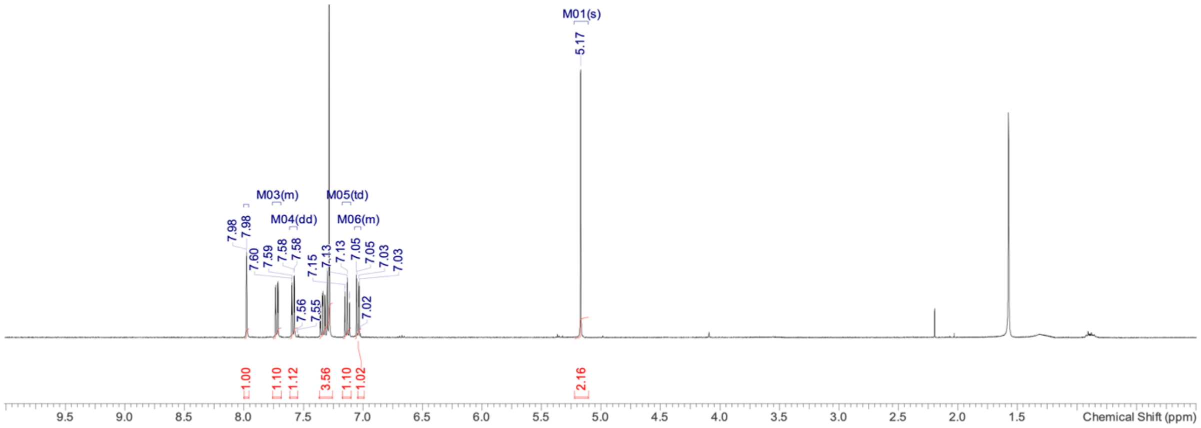


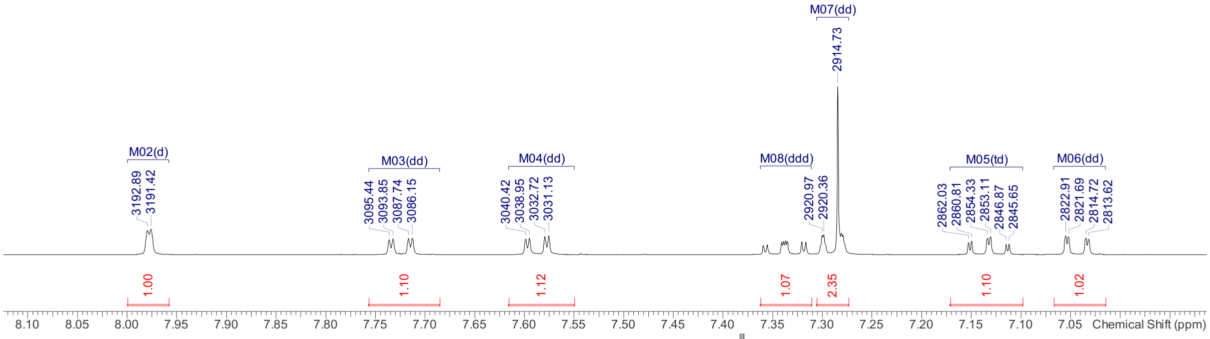


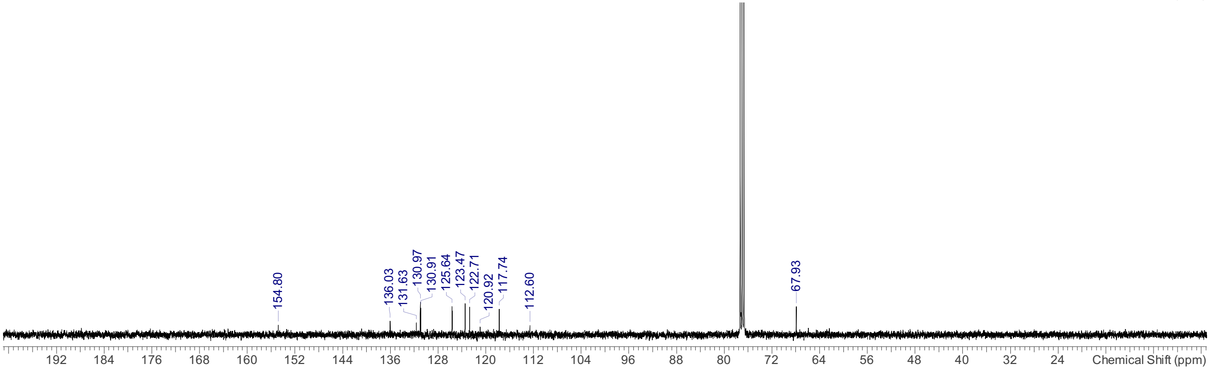
6*H*-Benzo[*c*]chromene-9-carbonitrile, **7c**.

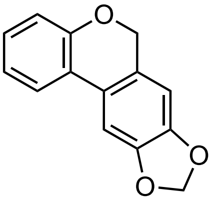


Using the flow photochemical set-up, a solution of benzyl *o*-iodoaryl ether **5c** (434 mg, 1.30 mmol) in MeCN (65 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 20% Et_2O/petrol) to afford the title compound **7c** (94 mg, 0.45 mmol, 35%) as a yellow solid. **MP**: 82 – 83 °C. **IR** ν_{max} (film, cm^{-1}): 2924 (br), 2851 (w), 2229 (s), 1607 (m), 1490 (s), 1454 (m), 1246 (s), 1200 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98 (1 H, d, *J* = 1.5 Hz, Ar**H**), 7.72 (1 H, dd, *J* = 7.7, 1.6 Hz, Ar**H**), 7.59 (1 H, dd, *J* = 7.8, 1.3 Hz, Ar**H**), 7.34 (1 H, ddd, *J* = 8.2, 7.3, 1.6 Hz, Ar**H**), 7.29 (1 H, br d, *J* = 7.7 Hz, Ar**H**), 7.13 (1 H, td, *J* = 7.6, 1.2 Hz, Ar**H**), 7.04 (1 H, dd, *J* = 8.1, 1.1 Hz, Ar**H**), 5.17 (2 H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.8 (**C**), 136.0 (**C**), 131.6 (**C**), 131.0 (**C**H), 130.9 (**C**H), 125.64 (**C**H), 125.62 (**C**H), 123.5 (**C**H), 122.7 (**C**H), 120.9 (**C**), 117.4 (**C**H) 122.0 (**C**H), 112.6 (**C**), 67.9 (**C**H$_2$) ppm. **LRMS** (EI): 207 (81%, M$^+$), 206 (100%), 177 (22%).



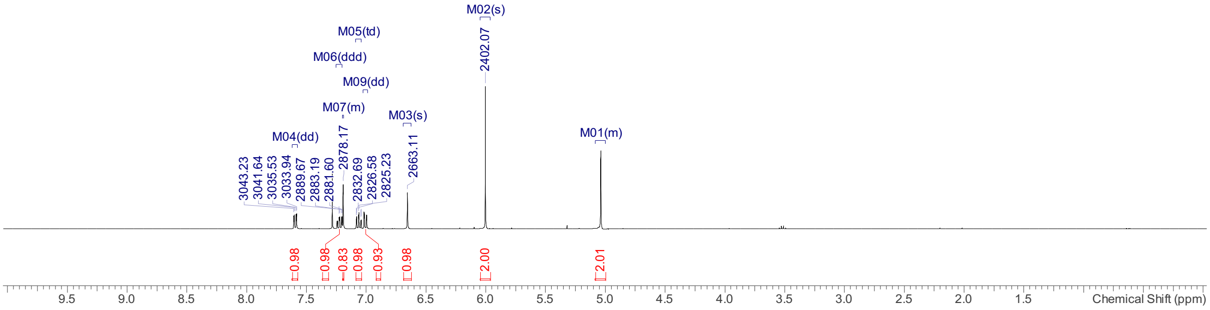


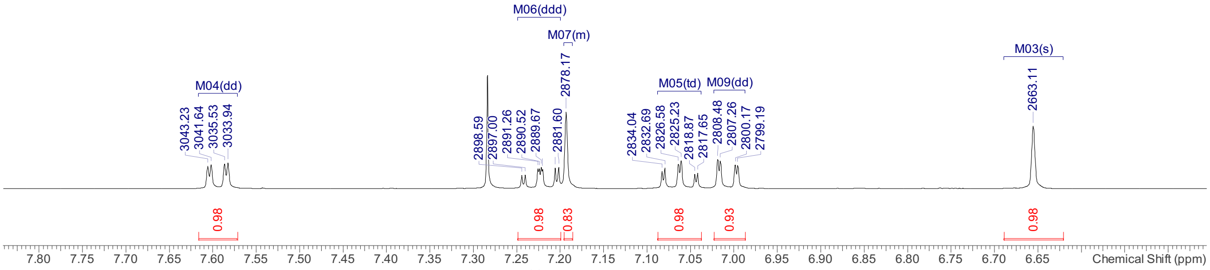


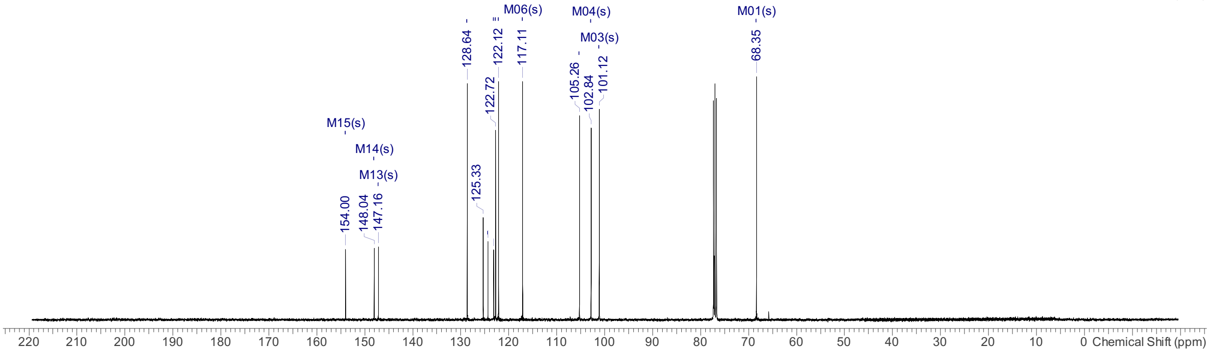


6*H*-[1,3]Dioxolo[4',5':4,5]benzo[1,2-*c*]chromene, **7d**.

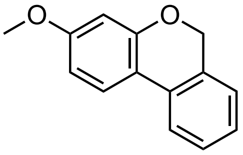
Using the flow photochemical set-up, a solution of benzyl *o*-iodoaryl ether **5d** (422 mg, 1.19 mmol) in MeCN (60 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (10 – 30% Et_2O/petrol) to afford the title compound **7d** (223 mg, 0.99 mmol, 83%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 2897 (br), 1505 (m), 1483 (s), 1458 (s), 1274 (s), 1222 (s), 1036 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.59 (1 H, dd, *J* = 7.7, 1.6 Hz, Ar**H**), 7.22 (1 H, ddd, *J* = 8.1, 7.3, 1.5 Hz, Ar**H**), 7.19 (1 H, s, Ar**H**), 7.06 (1 H, td, *J* = 7.6, 1.3 Hz, Ar**H**), 7.01 (1 H, dd, *J* = 8.1, 2.6 Hz, Ar**H**), 6.66 (2 H, s, C**H**$_2$), 6.00 (2 H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.0 (**C**), 148.0 (**C**), 147.2 (**C**), 128.6 (**C**H), 125.3 (**C**), 124.3 (**C**), 123.1 (**C**), 122.7 (**C**H), 122.1 (**C**H), 117.1 (**C**H), 105.3 (**C**H), 102.8 (**C**H), 101.1 (**C**H$_2$), 66.4 (**C**H$_2$) ppm. **LRMS** (EI): 225 (100%, [M-H]), 168 (28%), 139 (31%). **HRMS** (EI): Found 226.0616, $C_{14}H_{10}O_3$, M^+ requires 226.0624.



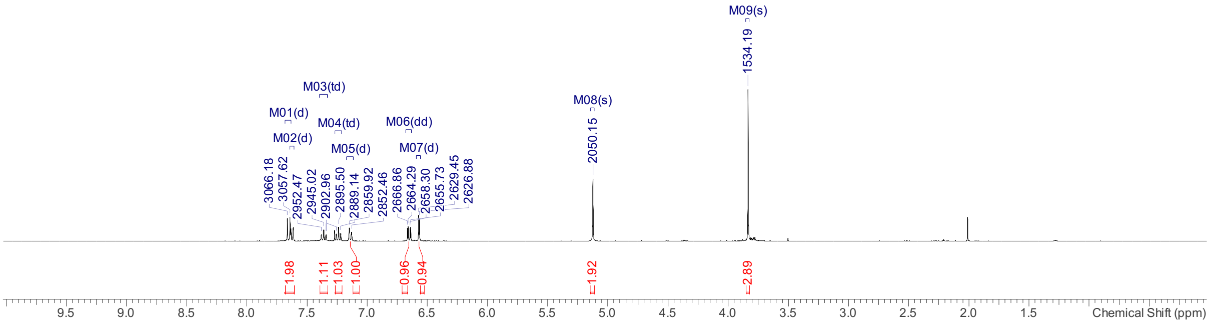


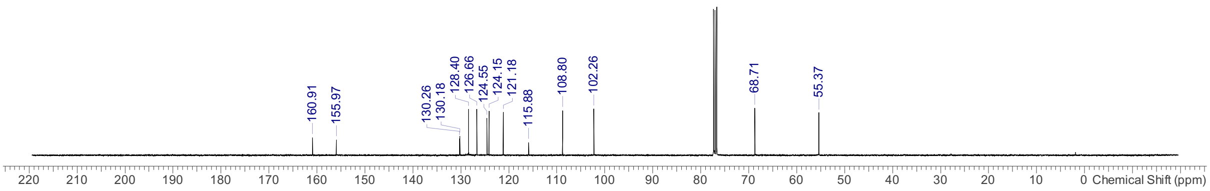


3-Methoxy-6*H*-benzo[*c*]chromene, **7e**.

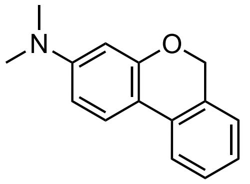


Using the flow photochemical set-up, a solution of benzyl *o*-iodoaryl ether **5e** (587 mg, 1.73 mmol) in MeCN (86 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 20% Et_2O/petrol) to afford the title compound **7e** (363 mg, 1.71 mmol, 99%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 2960 (br), 2834 (w), 1614 (s), 1483 (s), 1438 (s), 1278 (s), 1153 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.65 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.62 (1 H, d, *J* = 7.6 Hz, Ar**H**), 7.36 (1 H, td, *J* = 7.5, 0.9 Hz, Ar**H**), 7.24 (1 H, td, *J* = 7.5, 1.1 Hz, Ar**H**), 7.14 (1 H, d, *J* = 7.1 Hz, Ar**H**), 6.65 (1 H, dd, *J* = 8.6, 2.6 Hz, Ar**H**), 6.57 (1 H, d, *J* = 2.6 Hz, Ar**H**), 5.12 (2 H, s, C**H**$_2$), 3.83 (3 H, s, C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.9 (**C**), 160.0 (**C**), 130.3 (**C**), 130.2 (**C**), 128.4 (**C**H), 126.7 (**C**H), 124.6 (**C**H), 124. 2 (**C**H), 121.2 (**C**H), 115.9 (**C**), 108.8 (**C**H) 102.3 (**C**H), 68.7 (**C**H$_2$), 55.4 (**C**H$_3$) ppm. **LRMS** (ESI$^+$): 213 $[M+H]^+$. **HRMS** (ESI$^+$): Found 213.0911, $C_{14}H_{13}O_2$ $[M+H]^+$ requires 213.0910. These data are consistent with a literature report.[6]

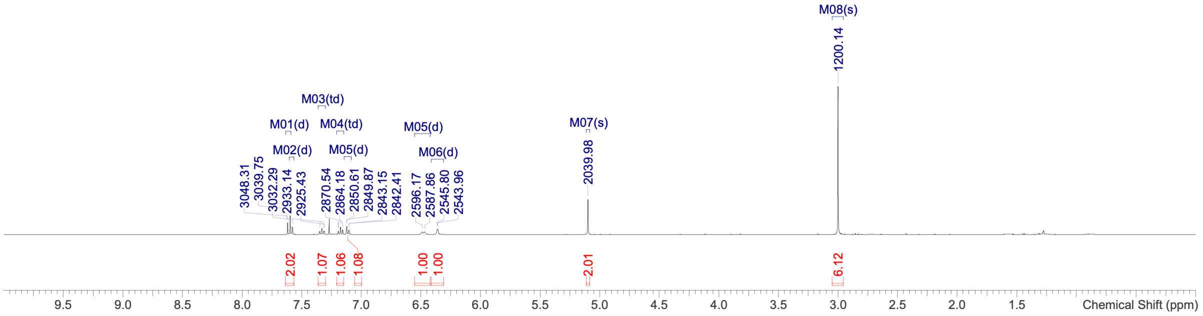


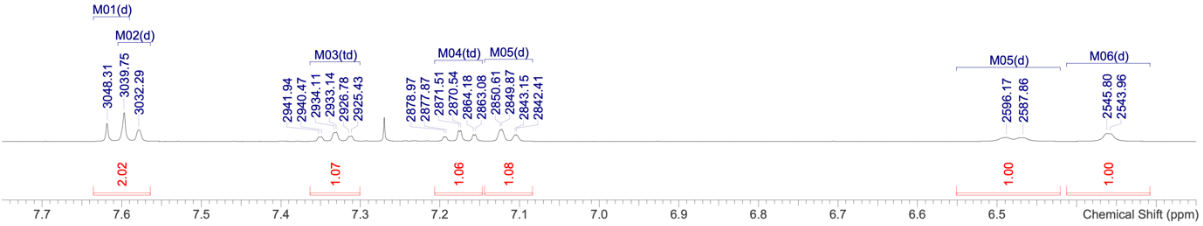


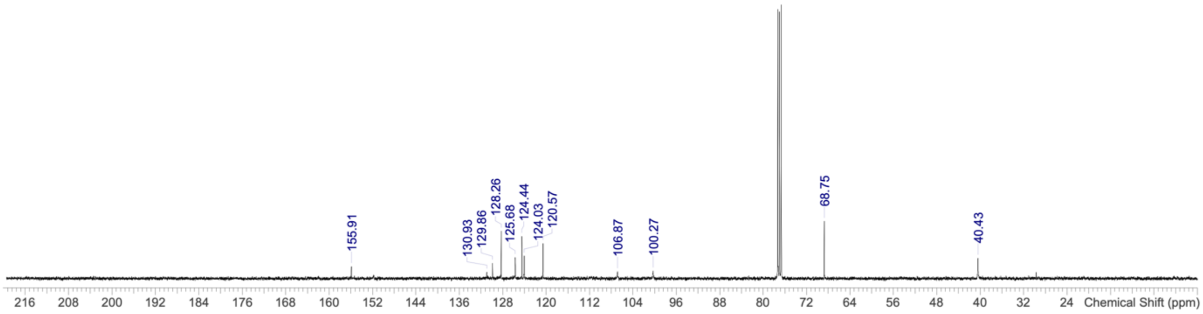
<u>*N*,*N*-Dimethyl-6*H*-benzo[c]chromen-3-amine</u>, **7f**.



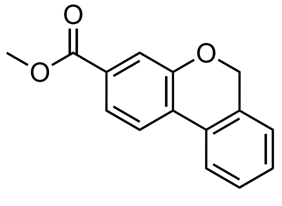
Using the flow photochemical set-up, a solution of benzyl iodoaryl ether **5f** (294 mg, 0.832 mmol) and pyridine (75 mg, 0.95 mmol) in MeCN (42 mL, 0.02 M) was irradiated for a residence time of 1 h, then concentrated *in vacuo* and purified by column chromatography (5% EtOAc in petrol) to afford the title compound **7f** (110 mg, 0.488 mmol, 59%) as a pale orange solid. **MP**: 73 – 74 °C. **IR** ν_{max} (film, cm^{-1}): 2846 (br), 1618 (s), 1522 (m), 1484 (m), 1441 (m), 1355 (m), 1242 (m), 1141 (m), 1101 (m), 1029 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.61 (1 H, br d, *J* = 8.6 Hz, Ar**H**), 7.59 (1 H, br d, *J* = 7.5 Hz, Ar**H**), 7.33 (1 H, app. td, *J* = 7.6, 1.4 Hz, Ar**H**), 7.18 (1 H, app. td, *J* = 7.4, 1.1 Hz, Ar**H**), 7.11 (1 H, br d, *J* = 7.6 Hz, Ar**H**), 6.48 (1 H, br d, *J* = 8.3 Hz, Ar**H**), 6.36 (1 H, br d, *J* = 1.8, Hz, Ar**H**), 5.10 (2 H, s, C**H**$_2$), 3.00 (6 H, s, 2 × C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.9 (**C**), 130.9 (**C**), 129.9 (**C**), 128.3 (**C**H), 125.7 (**C**H), 124.4 (**C**H), 124.0 (**C**H), 120.6 (**C**H), 106.9 (**C**H), 100.3 (**C**H), 68.8 (**C**H$_2$), 40.4 (2 × **C**H$_3$) ppm [one **C** coincident or not seen]. **LRMS** (ESI+): 226 ([M+H]$^+$, 100%), 225 (30%). **HRMS** (ESI$^+$): Found 226.1231, [M+H]$^+$ $C_{15}H_{16}NO$ requires 226.1226.



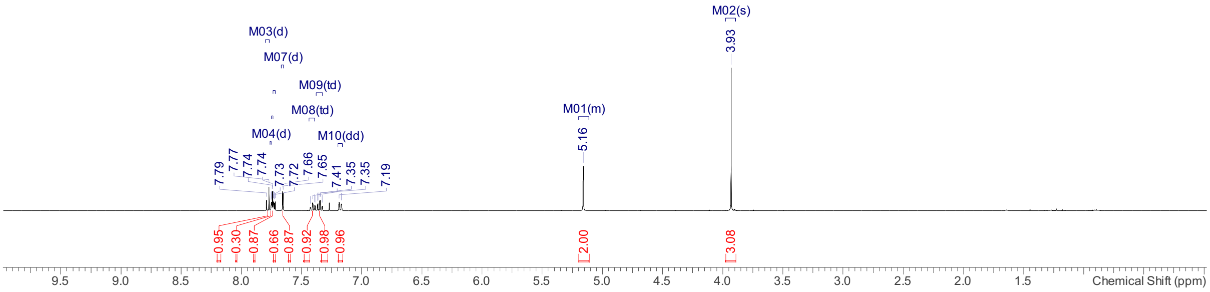


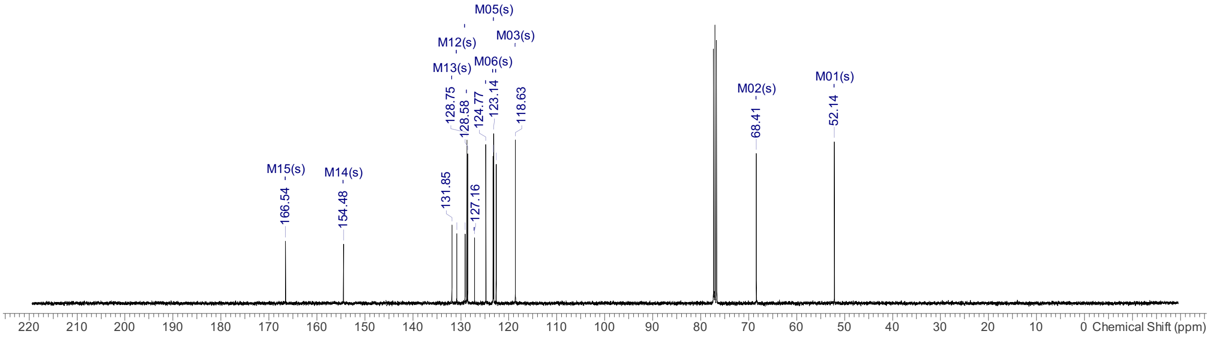


<u>Methyl 6*H*-benzo[*c*]chromene-3-carboxylate</u>, **7g**.[7]

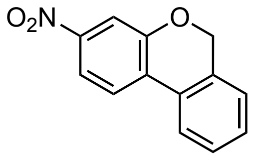


Using the flow photochemical set-up, a solution of benzyl *o*-iodoaryl ether **5g** (374 mg, 1.02 mmol) in MeCN (51 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (10 – 30% Et_2O/petrol) to afford the title compound **7g** (140 mg, 0.58 mmol, 57%) as an off-white solid. **MP**: 89 – 90 °C. **IR** ν_{max} (film, cm^{-1}): 2950 (br), 1713 (s), 1434 (m), 1414 (m), 1262 (s), 1196 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (1H, d, *J* = 8.1 Hz, Ar**H**), 7.74 - 7.70 (2H, m, 2 × Ar**H**), 7.65 (1H, d, *J* = 1.6 Hz, Ar**H**), 7.41 (1H, app td, *J* = 7.5, 1.3 Hz, Ar**H**), 7.35 (1H, app td, *J* = 7.4, 1.3 Hz, Ar**H**), 7.18 (1H, br d, *J* = 7.5 Hz, Ar**H**), 5.15 (2H, s, C**H**$_2$), 3.93 (3H, s, C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.5 (**C**), 154.5 (**C**), 131.9 (**C**), 130.9 (**C**), 129.1 (**C**), 128.8 (**C**H), 128.6 (**C**H), 127.2 (**C**), 124.8 (**C**H), 123.3 (**C**H), 123.1 (**C**H), 122.6 (**C**H), 118.5 (**C**H) 68.4 (**C**H$_2$), 52.1 (**C**H$_3$) ppm. **LRMS** (ESI$^+$): 241 [M+H]$^+$. **HRMS** (ESI$^+$): Found 241.0864, $C_{15}H_{13}O_3$ [M+H]$^+$ requires 241.0864.

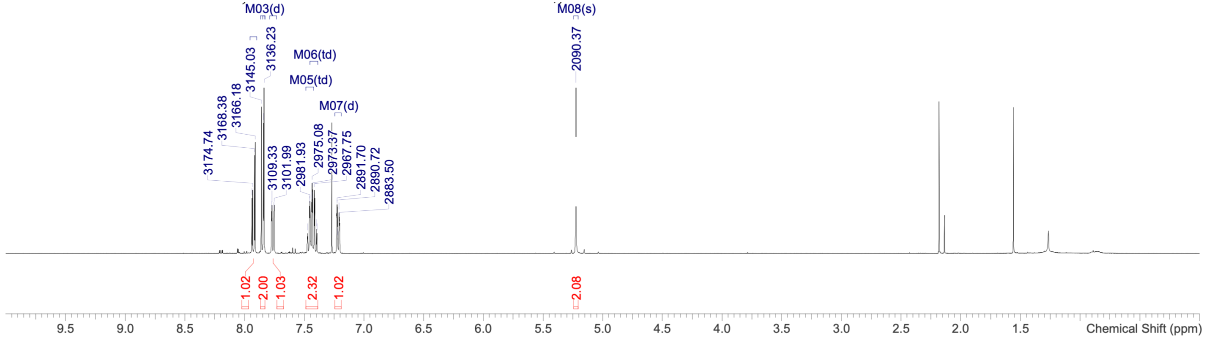


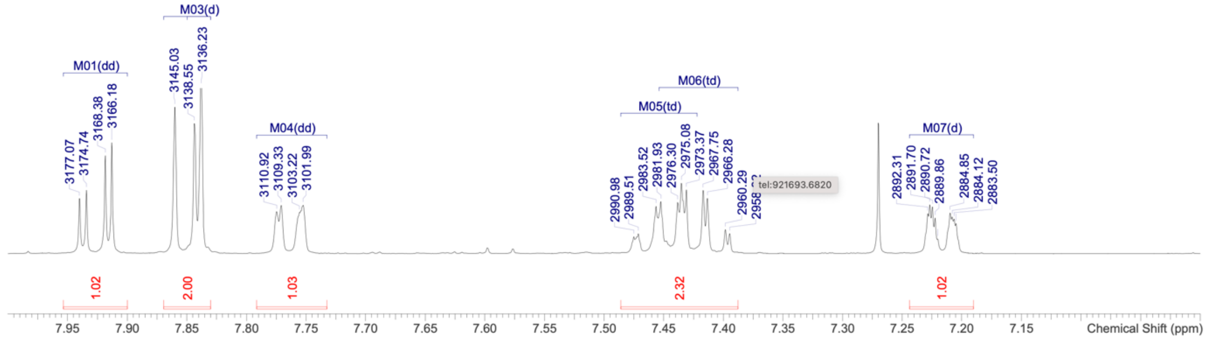


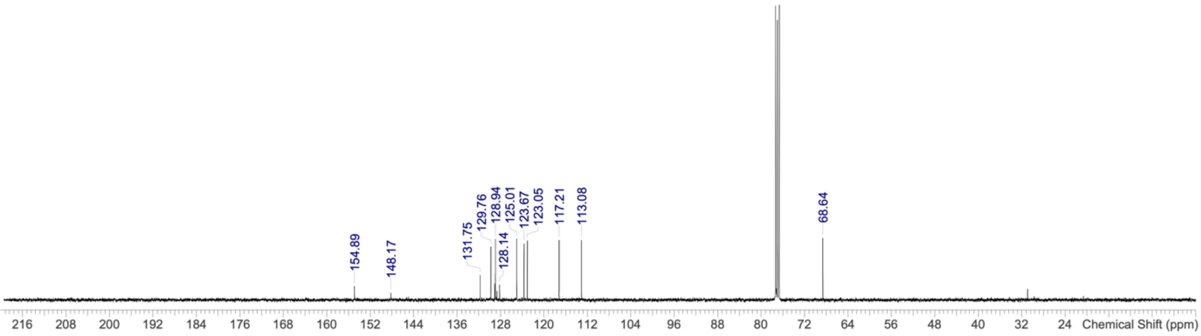
3-Nitro-6*H*-benzo[*c*]chromene, **7h**.[7]



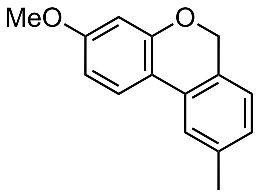
Using the flow photochemical set-up, a solution of 2-(benzyloxy)-1-iodo-4-nitrobenzene **5h** (379 mg, 1.08 mmol) in MeCN (53 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (20 mL) were added. The aqueous phase was separated and extracted with DCM (2 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the titled compound **7h** (116 mg, 0.51 mmol, 47%) as a pale yellow solid. **MP**: 120 – 121 °C. **IR** ν_{max} (film, cm^{-1}): 3086 (w), 2920 (w), 1578 (w), 1597 (w), 1518 (s), 1482 (m), 1453 (m), 1419 (m), 1342 (s), 1323 (m), 1278 (m), 1243 (m), 1202 (m), 1024 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.93 (1 H, dd, *J* = 8.6, 2.3 Hz, Ar**H**), 7.85 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.84 (1 H, d, *J* = 2.3 Hz, Ar**H**), 7.76 (1 H, br d, *J* = 7.5 Hz, Ar**H**), 7.45 (1 H, app. td, *J* = 7.5, 1.5 Hz, Ar**H**), 7.41 (1 H, app. td, *J* = 7.5, 1.5 Hz, Ar**H**), 7.19 – 7.24 (1 H, m, Ar**H**), 5.22 (2 H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.9 (**C**), 148.2 (**C**), 131.8 (**C**H), 129.8 (**C**H), 129.1 (**C**), 128.9 (**C**H), 128.1 (**C**), 125.0 (**C**H), 123.7 (**C**), 123.1 (**C**H), 117.2 (**C**H), 113.1 (**C**H), 68.6 (**C**H$_2$) ppm. **LRMS** (ESI$^+$): 228 ([M+H]$^+$, 20%), 198 (40%), 195 (100%), 167 (35%). **HRMS** (ESI$^+$): Found 250.0469, [M+Na]$^+$ $C_{13}H_9NaNO_3$ requires 250.0475.



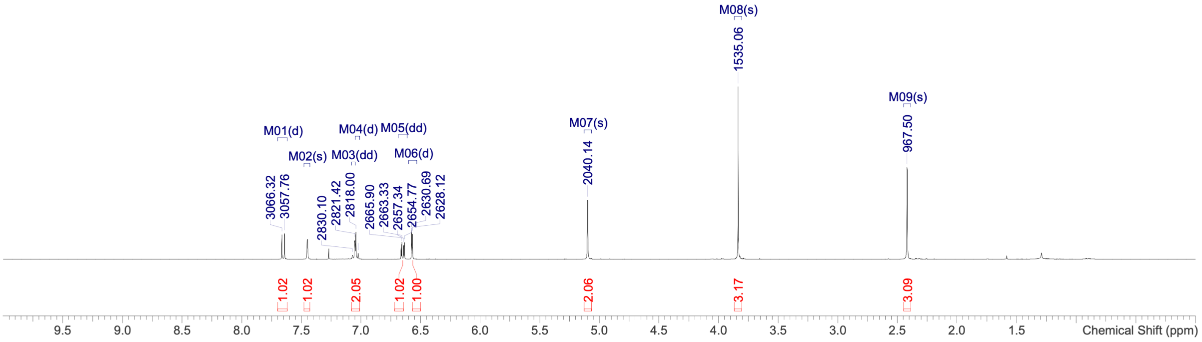


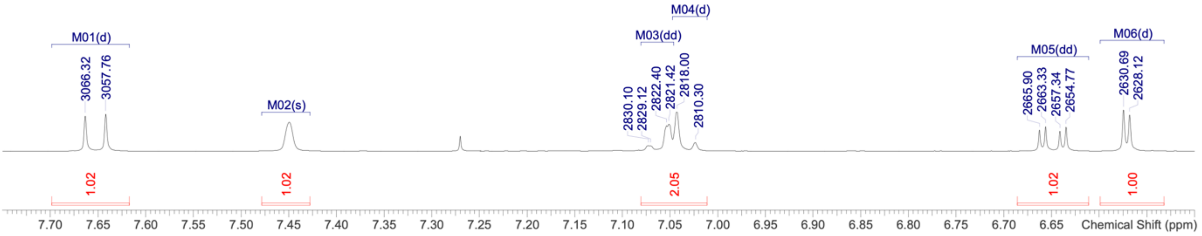


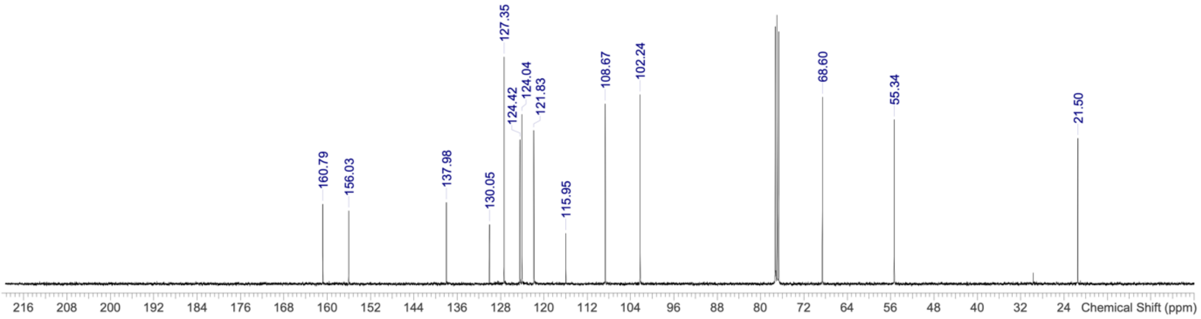
3-Methoxy-9-methyl-6*H*-benzo[*c*]chromene, **7i**.



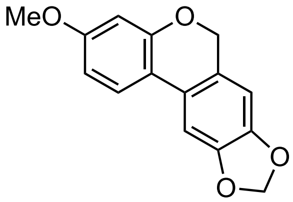
Using the flow photochemical set-up, a solution of benzyl *o*-iodoaryl ether **5i** (212 mg, 0.60 mmol) and pyridine (53 mg, 0.67 mmol) in MeCN (30 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then purified by column chromatography (5% acetone in petrol) to afford the title compound **7i** (125 mg, 0.55 mmol, 92%) as a pale orange solid. **MP**: 65 – 66 °C. **IR** ν_{max} (film, cm^{-1}): 2980 (s), 1612 (s), 1497 (m), 1462 (m), 1381 (m), 1278 (m), 1253 (m), 1142 (s), 1115 (m), 1044 (m), 1028 (m). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 7.65 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.45 (1 H, br s, Ar**H**), 7.06 (1 H, dd, *J* = 7.7, 1.0 Hz, Ar**H**), 7.03 (1 H, d, *J* = 7.7 Hz, Ar**H**), 6.65 (1 H, dd, *J* = 8.6, 2.6 Hz, Ar**H**), 6.57 (1 H, d, *J* = 2.6 Hz, Ar**H**), 5.10 (2 H, s, C**H$_2$**), 3.84 (3 H, s, OC**H**$_3$), 2.42 (3 H, s, C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 160.8 (**C**), 156.0 (**C**), 138.0 (**C**), 130.1 (**C**), 127.4 (**C**H), 124.4 (**C**H), 124.0 (**C**H), 121.8 (**C**H), 116.0 (**C**), 108.7 (**C**H), 102.2 (**C**H), 68.6 (**C**H$_2$), 55.3 (**C**H$_3$), 21.5 (**C**H$_3$) ppm [one **C** coincident or not observed] ppm. **LRMS** (ESI+): 227 ([M+H]$^+$, 60%), 199 (100%). **HRMS** (ESI+): Found 277.1068, [M+H]$^+$ $C_{15}H_{15}O_2$ requires 227.1067.



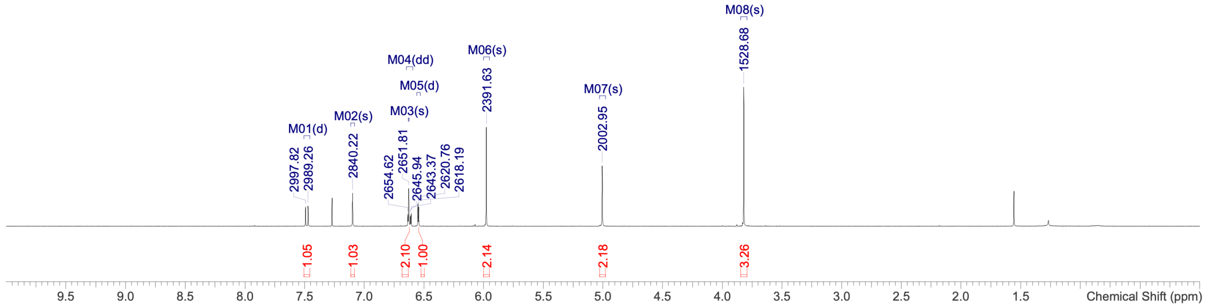


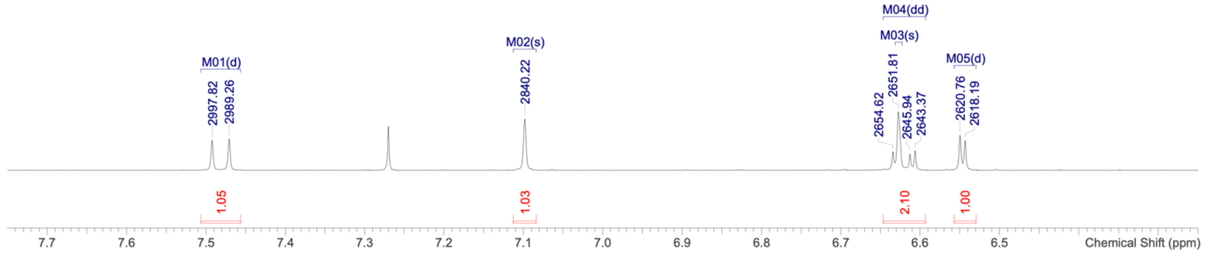


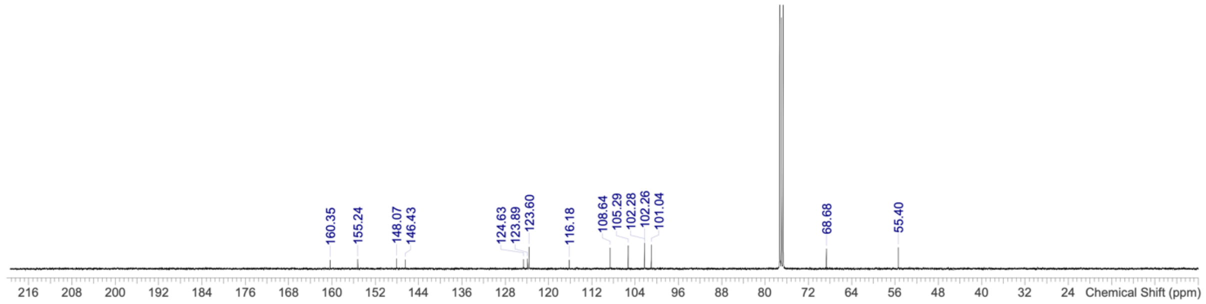
3-Methoxy-6*H*-[1,3]dioxolo[4',5':4,5]benzo[1,2-*c*]chromene, **7j**.



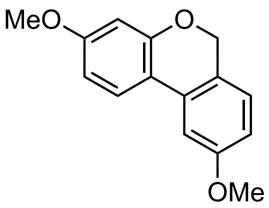
Using the flow photochemical set-up, a solution of iodoaryl ether **5j** (347 mg, 0.90 mmol) and pyridine (85 mg, 1.08 mmol) in MeCN (45 mL, 0.02 M) was irradiated for a residence time of 1 h, then concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **7j** (150 mg, 0.59 mmol, 66%) as a white solid. **MP**: 121 – 122 °C. **IR** ν_{max} (film, cm^{-1}): 2900 (br), 1612 (m), 1500 (m), 1482 (s), 1435 (m), 1363 (w), 1235 (s), 1197 (w), 1155 (m), 1130 (m), 1032 (s). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 7.48 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.10 (1 H, s, Ar**H**), 6.63 (1 H, s, Ar**H**), 6.62 (1 H, dd, *J* = 8.6, 2.6 Hz, Ar**H**), 6.55 (1 H, d, *J* = 2.6 Hz, Ar**H**), 5.98 (2 H, s, C**H$_2$**), 5.01 (2 H, s, C**H$_2$**), 3.82 (3 H, s, OC**H$_3$**) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 160.4 (**C**), 155.2 (**C**), 148.1 (**C**), 146.4 (**C**), 124.6 (**C**), 123.9 (**C**), 123.6 (**C**H), 116.2 (**C**), 108.6 (**C**H), 105.3 (**C**H), 102.28 (**C**H), 102.26 (**C**H), 101.0 (**C**H$_2$), 68.7 (**C**H$_2$), 55.4 (**C**H$_3$) ppm. **LRMS** (ESI+): 257 ([M+H]$^+$, 100%), 256 (50%). **HRMS** (ESI+): Found 257.0804, [M+H]$^+$ $C_{15}H_{13}O_4$ requires 257.0808. These data are consistent with a literature report.[8]



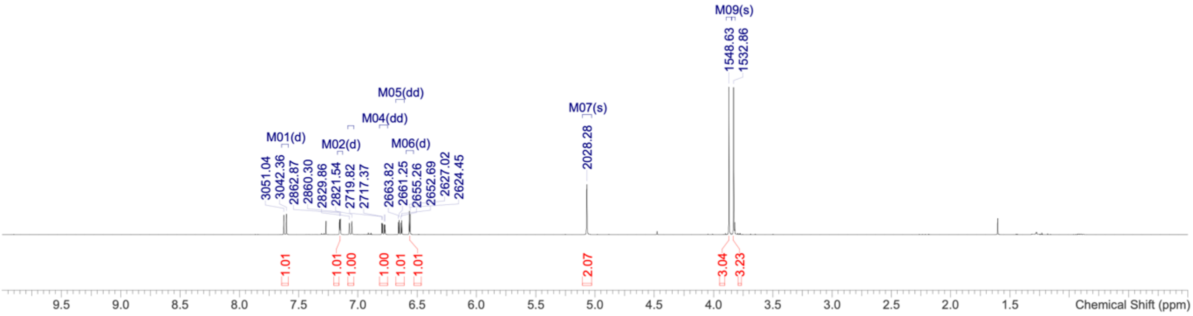


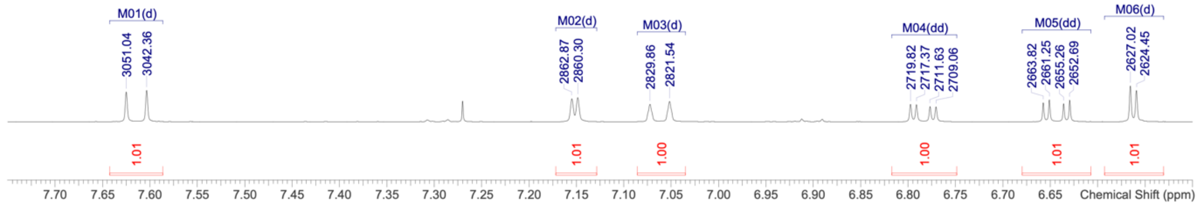


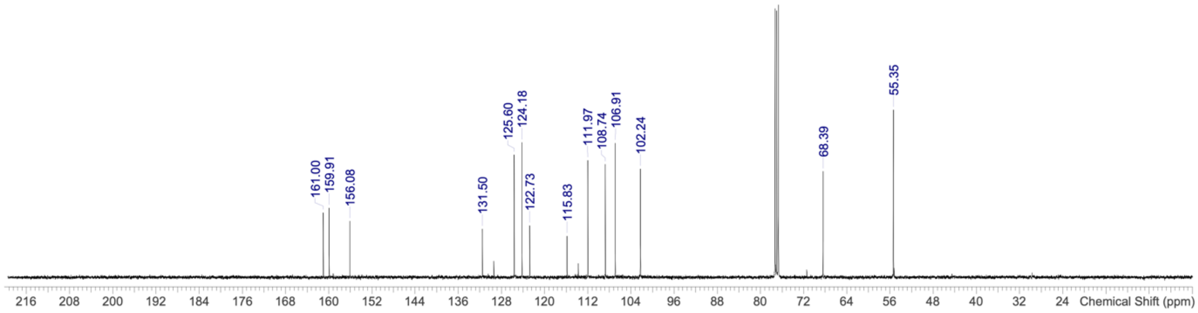
3,9-Dimethoxy-6*H*-benzo[*c*]chromene, **7k**.



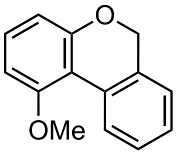
Using the flow photochemical set-up, a solution of benzyl *o*-iodoaryl ether **5k** (398 mg, 1.08 mmol) in MeCN (54 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (2 – 10% Et_2O/petrol) to afford the title compound **7k** (215 mg, 0.89 mmol, 83%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 2835 (w), 1612 (s), 1497 (s), 1458 (m), 1415 (w), 1301 (w), 1276 (m), 1191 (s), 1157 (s), 1104 (m), 1038 (m), 1022 (m). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 7.62 (1H, d, *J* = 8.7 Hz, Ar**H**), 7.15 (1H, d, *J* = 2.5 Hz, Ar**H**), 7.06 (1H, br d, *J* = 8.2 Hz, Ar**H**), 6.78 (1H, dd, *J* = 8.3, 2.5 Hz, Ar**H**), 6.64 (1H, dd, *J* = 8.6, 2.6 Hz, Ar**H**), 6.57 (1H, d, *J* = 2.6 Hz, Ar**H**), 5.07 (2H, s, C**H**$_2$), 3.87 (3H, s, OC**H**$_3$), 3.83 (3H, s, OC**H**$_3$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 161.0 (**C**), 159.9 (**C**), 156.1 (**C**), 131.5 (**C**), 125.6 (**C**H), 124.2 (**C**H), 122.7 (**C**), 115.8 (**C**), 112.0 (**C**H), 108.7 (**C**H), 106.9 (**C**H), 102.2 (**C**H), 68.4 (**C**H$_2$), 55.35 (**C**H$_3$), 55.34 (**C**H$_3$) ppm. **LRMS** (ESI$^+$): 243 ([M+H]$^+$, 100%). **HRMS** (ESI$^+$): Calculated for [M+H]$^+$ 243.1021, found: 243.1016.



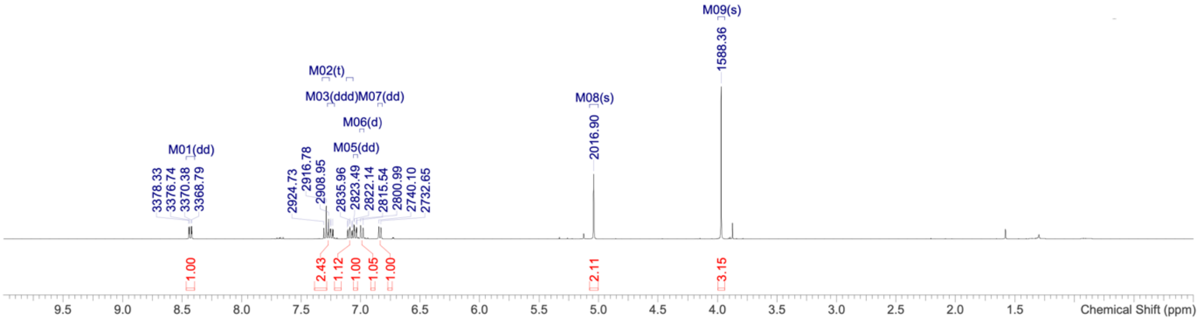


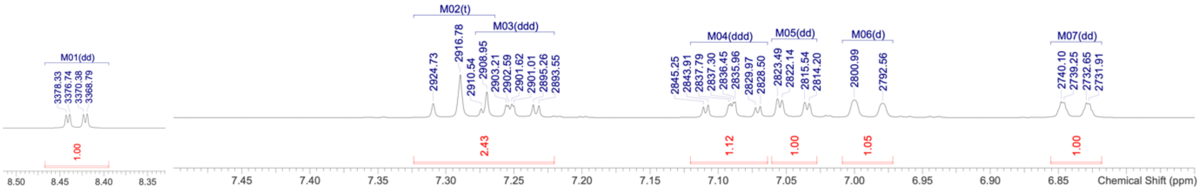


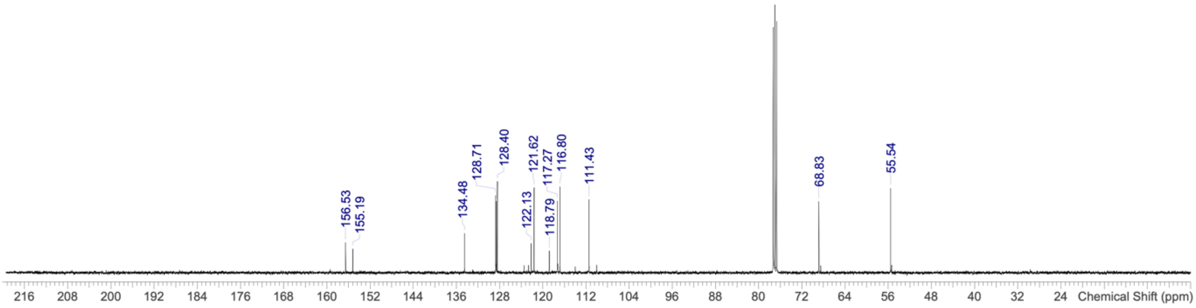
1-Methoxy-6*H*-benzo[*c*]chromene, **7l**.



Using the flow photochemical set-up, a solution of iodoaryl ether **5l** (336 mg, 0.987 mmol) in MeCN (49 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (20 mL) were added. The aqueous phase was separated and extracted with DCM (2 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **7l** (77 mg, 0.363 mmol, 37%) as a pale yellow solid. **MP**: 46 – 48 °C. **IR** ν_{max} (film, cm^{-1}): 2836 (w), 1599 (m), 1588 (m), 1496 (m), 1458 (m), 1432 (m), 1248 (m), 1236 (m), 1122 (m), 1092 (m), 1073 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.44 (1 H, dd, *J* = 8.0, 1.6 Hz, Ar**H**), 7.29 (1 H, app. t, *J* = 8.0 Hz, Ar**H**), 7.26 (1 H, app. td, *J* = 7.5, 1.7 Hz, Ar**H**), 7.07 (1 H, app td, *J* = 7.7, 1.5 Hz, Ar**H**), 7.04 (1 H, br dd, *J* = 8.0, 1.3, Ar**H**), 6.99 (1 H, br d, *J* = 8.4 Hz, Ar**H**), 6.84 (1 H, br d, *J* = 7.4 Hz, Ar**H**), 5.02 (2 H, s, C**H₂**), 3.97 (3 H, s, OC**H₃**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.9 (**C**), 156.8 (**C**), 131.9 (**C**), 129.01 (**C**H), 128.96 (**C**), 128.0 (**C**H), 126.9 (**C**H), 126.6 (**C**H), 124.3 (**C**H), 112.8 (**C**), 110.2 (**C**H), 105.1 (**C**H), 68.9 (**C**H_2), 55.6 (**C**H_3) ppm. **LRMS** (ESI+): 213 ($[M+H]^+$, 100%), 185 (50%), 153 (40%). **HRMS** (ESI+): Found 213.0912, $C_{14}H_{13}O_2$ $[M+H]^+$ requires 213.0910.

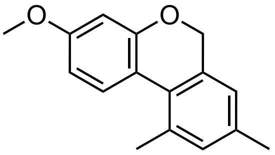




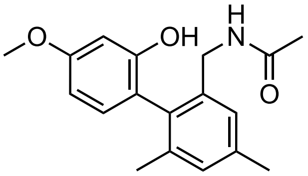


3-Methoxy-8,10-dimethyl-6*H*-benzo[*c*]chromene, **7m** and
N-((2'-hydroxy-4'-methoxy-4,6-dimethyl-[1,1'-biphenyl]-2-yl)methyl)acetamide, **12**.

Using the flow photochemical set-up, a solution of iodoaryl ether **5m** (731 mg, 1.98 mmol) in MeCN (99 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (40 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 30% acetone in petrol) to afford the title compounds:

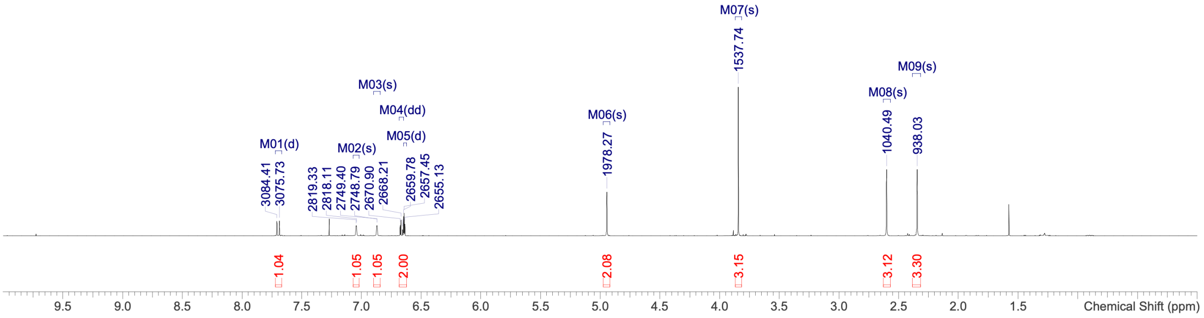


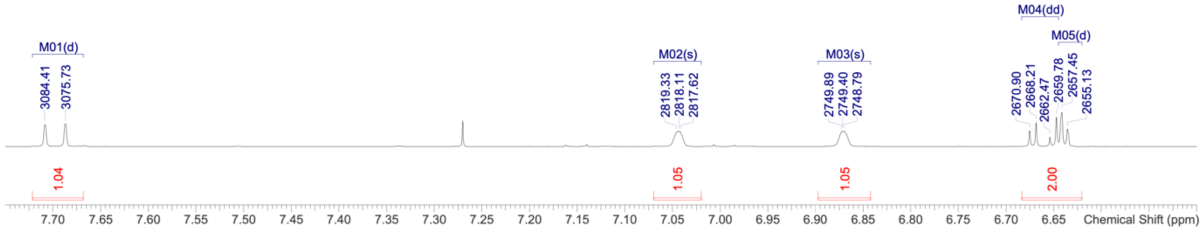
7m (154 mg, 0.64 mmol, 32%) as a pale yellow solid. **MP**: 78 – 80 °C. **IR** ν_{max} (film, cm^{-1}): 2954 (w), 2836 (w), 1617 (s), 1506 (m), 1472 (s), 1453 (m), 1439 (m), 1307 (m), 1268 (s), 1210 (m), 1193 (m), 1160 (s), 1131 (s), 1114 (m), 1041 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.70 (1 H, d, *J* = 8.7 Hz, Ar**H**), 7.04 (1 H, s with fine splitting, Ar**H**), 6.87 (1 H, s with fine splitting, Ar**H**), 6.64 (1 H, dd, *J* = 8.4, 2.7 Hz, Ar**H**), 7.70 (1 H, d, *J* = 2.3 Hz, Ar**H**), 4.94 (2 H, s, 2 × Ar**H**), 3.84 (3 H, s, OC**H**$_3$), 2.60 (3 H, s, C**H**$_3$), 2.34 (3 H, s, C**H**$_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.6 (**C**), 157.5 (**C**), 136.0 (**C**), 133.22 (**C**), 133.19 (**C**), 132.8 (**C**H), 128.4 (**C**H), 126.6 (**C**), 123.3 (**C**H), 117.5 (**C**), 107.7 (**C**H), 102.4 (**C**H), 70.0 (**C**H$_2$), 55.3 (**C**H$_3$), 23.0 (**C**H$_3$), 20.9 (**C**H$_3$) ppm. **LRMS** (ESI+): 241 ([M+H]$^+$, 100%). **HRMS** (ESI+): Found 263.1048, [M+Na]$^+$ $C_{16}H_{16}NaO_2$ requires 263.1043.

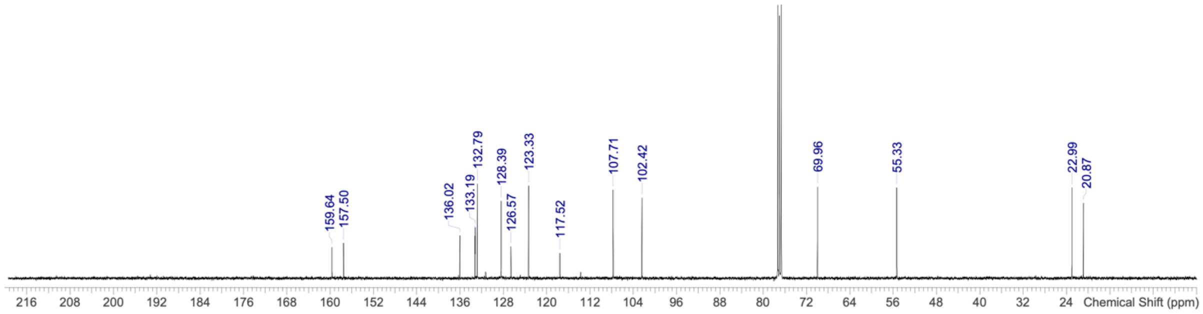


12 (100 mg, 0.33 mmol, 17%) as a pale yellow solid. MP**:** 98 – 100 °C. **IR** ν_{max} (film, cm^{-1}): 3285 (br), 3001 (w), 2922 (w), 1646 (s), 1613 (s), 1523 (m), 1466 (m), 1426 (m), 1290 (m), 1202 (m), 1163 (m), 1123 (w), 1042 (w). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.11 (1 H, br s, Ar**H**), 7.07 (1 H, br s, Ar**H**), 6.89 (1 H, d, *J* = 8.2 Hz, Ar**H**), 6.60 (1 H, d, *J* = 2.5 Hz, Ar**H**), 6.57 (1 H, dd, *J* = 8.3, 2.5 Hz, Ar**H**), 5.76 (1 H, br s, N**H**), 5.70 (1 H, br s, O**H**), 4.13 (1 H, dd, *J* = 14.6, 6.3 Hz, CH**H**), 4.07 (1 H, dd, *J* = 14.7, 5.4 Hz, C**H**H), 3.83 (3 H, s, OC**H**$_3$), 2.35 (3 H, s, C**H**$_3$), 2.01 (3 H, s, C**H**$_3$), 1.91 (3 H, s, C**H**$_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.9 (**C**), 160.6 (**C**), 153.8 (**C**), 138.6 (**C**), 138.4 (**C**), 138.1 (**C**), 131.9 (**C**), 130.7 (**C**H), 130.4 (**C**H), 127.1 (**C**H), 118.2 (**C**), 107.1 (**C**H), 101.7 (**C**H), 55.3 (**C**H$_3$), 42.2 (**C**H$_2$), 23.2 (**C**H$_3$), 21.1 (**C**H$_3$), 20.1 (**C**H$_3$) ppm. **LRMS** (ESI+): 322 ([M+Na]$^+$, 20%), 300 ([M+H]$^+$, 100%). **HRMS** (ESI+): Found 322.1410, [M+Na]$^+$ $C_{18}H_{21}NNaO_3$ requires 322.1414.

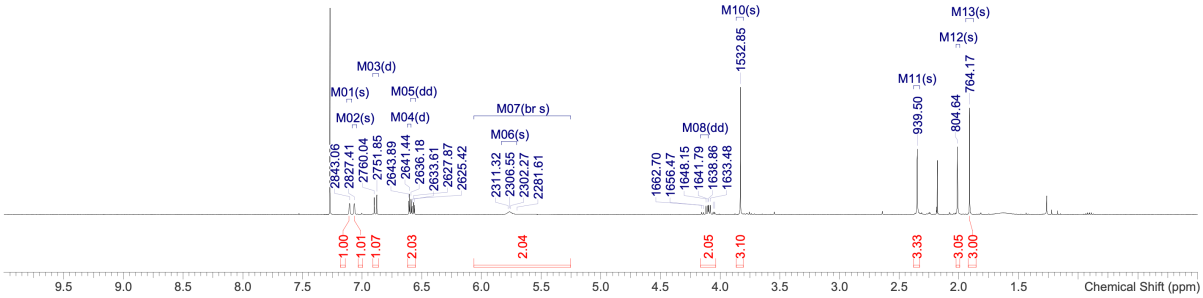
NMR spectra for **7m**

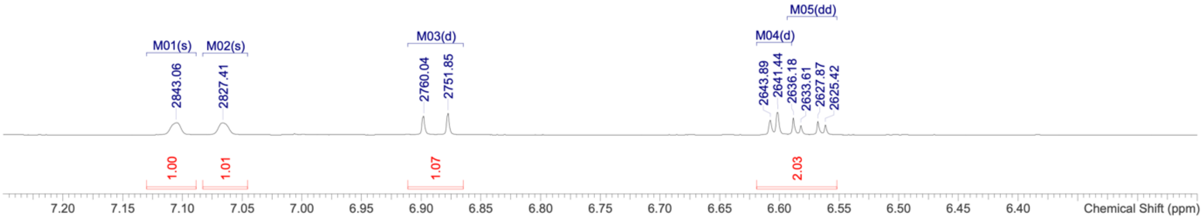


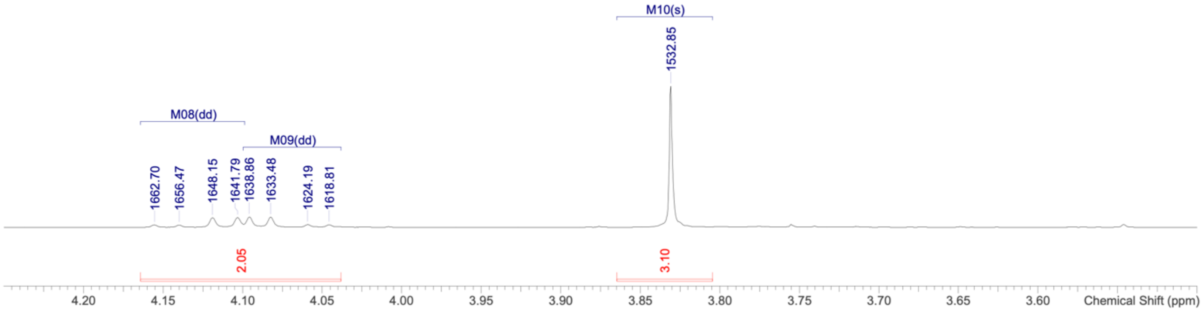


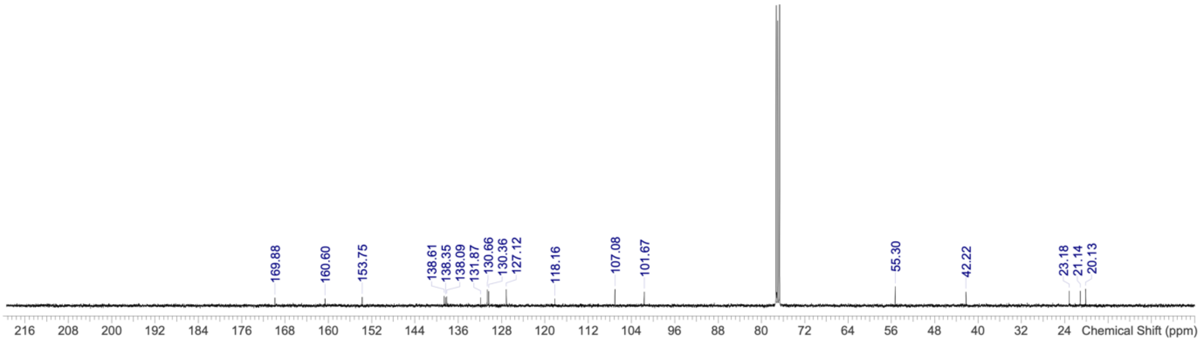


NMR spectra for **12**



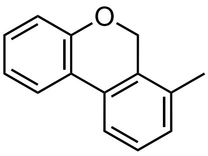




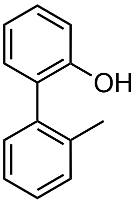


7-Methyl-6*H*-benzo[*c*]chromene, **7o** and 2'-methyl-[1,1'-biphenyl]-2-ol, **33b**.

Using the flow photochemical set-up, a solution of benzyl *o*-iodoaryl ether **5o** (401 mg, 1.23 mmol) in MeCN (56 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (20 mL) were added. The aqueous phase was separated and extracted with DCM (2 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% EtOAc in petrol) to afford respectively the titled compounds:

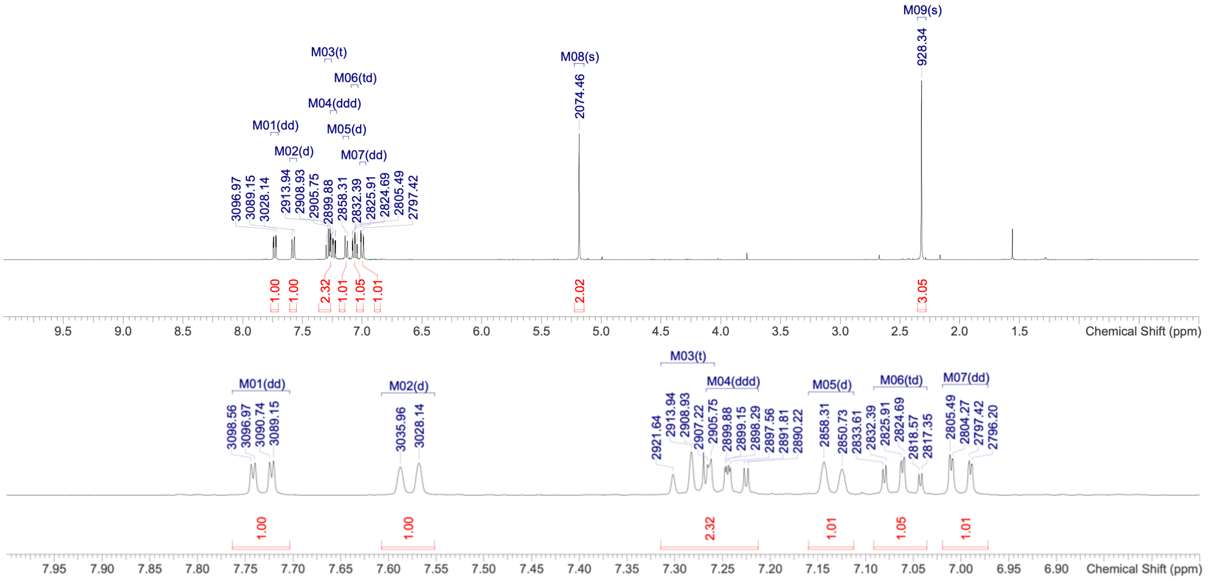


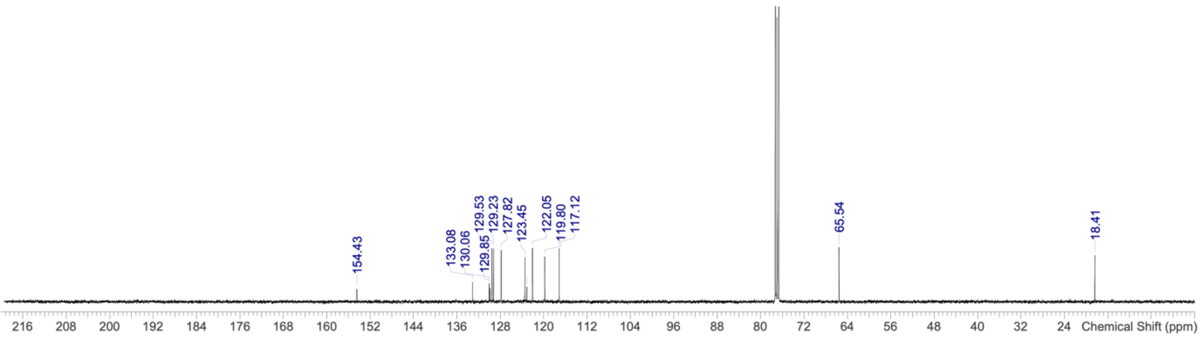
7o (92 mg, 0.469 mmol, 38%) as a yellow solid. **IR** ν_{max} (film, cm^{-1}): 1598 (m), 1497 (w), 1452 (m), 1423 (m), 1295 (w), 1249 (m), 1225 (m), 1197 (m), 1040 (m), 1017 (m). ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.73 (1 H, dd, J = 7.8, 1.6 Hz, ArH), 7.58 (1 H, br d, J = 7.8 Hz, ArH), 7.28 (1 H, t, J = 7.7 Hz, ArH), 7.24 (1 H, ddd, J = 8.1, 7.3, 1.6 Hz, ArH), 7.13 (1 H, br d, J = 7.6 Hz, ArH), 7.06 (1 H, app. td, J = 7.5, 1.2 Hz, ArH), 7.00 (1 H, dd, J = 8.1, 1.2 Hz, ArH), 5.18 (2 H, s, CH_2), 2.32 (3 H, s, CH_3). ^{13}**C NMR** (100 MHz, $CDCl_3$) δ 154.4 (**C**), 133.1 (**C**), 130.1 (**C**), 129.9 (**C**), 129.5 (**C**H), 129.2 (**C**H), 127.8 (**C**H), 123.5 (**C**H), 123.1 (**C**), 122.1 (**C**H), 119.8 (**C**H), 117.1 (**C**H), 65.5 (**C**H_2), 18.4 (**C**H_3) ppm. **LRMS** (EI): 196 ([M]$^+$, 100%). These data are consistent with a literature report.[9]



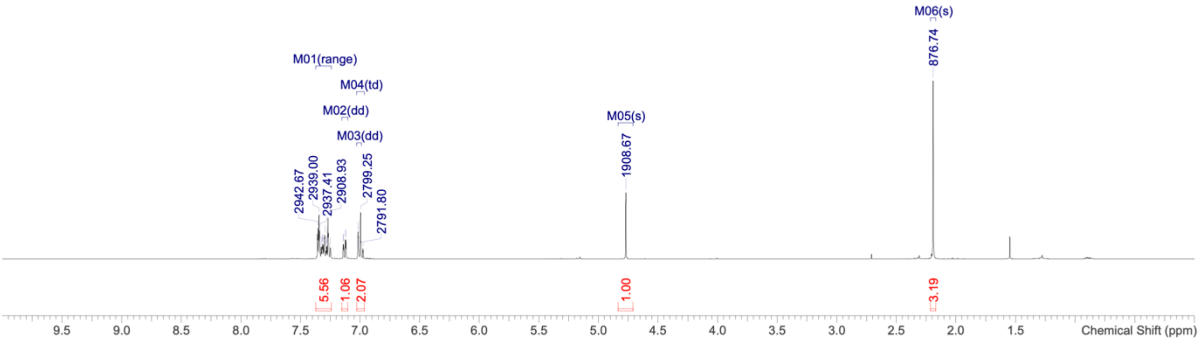
33b (45 mg, 0.244 mmol, 20%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 3503 (br), 1578 (w), 1497 (w), 1478 (s), 1445 (m), 1338 (m), 1222 (m), 1184 (br). ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.24 – 7.37 (5 H, m, 5 × Ar**H**), 7.13 (1 H, dd, *J* = 7.5, 1.7 Hz, Ar**H**), 7.01 (1 H, dd, *J* = 8.6, 1.2 Hz, Ar**H**), 6.99 (1 H, app. td, *J* = 7.5, 1.7 Hz, Ar**H**), 4.77 (1 H, s, O**H**), 2.19 (3 H, s, C**H**$_3$). ^{13}**C NMR** (100 MHz, $CDCl_3$) δ 152.5 (**C**), 137.4 (**C**), 135.7 (**C**), 130.7 (**C**H), 130.5 (**C**H), 130.1 (**C**H), 129.1 (**C**H), 128.5 (**C**H), 127.70 (**C**), 126.5 (**C**H), 120.4 (**C**H), 115.3 (**C**H), 19.7 (**C**H_3) ppm. **LRMS** (EI): 184 ([M]$^+$, 100%). These data are consistent with a literature report.[10]

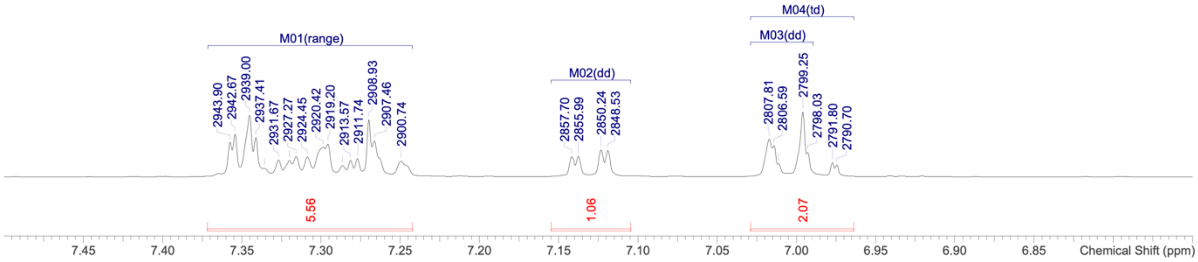
NMR spectra for **7o**.

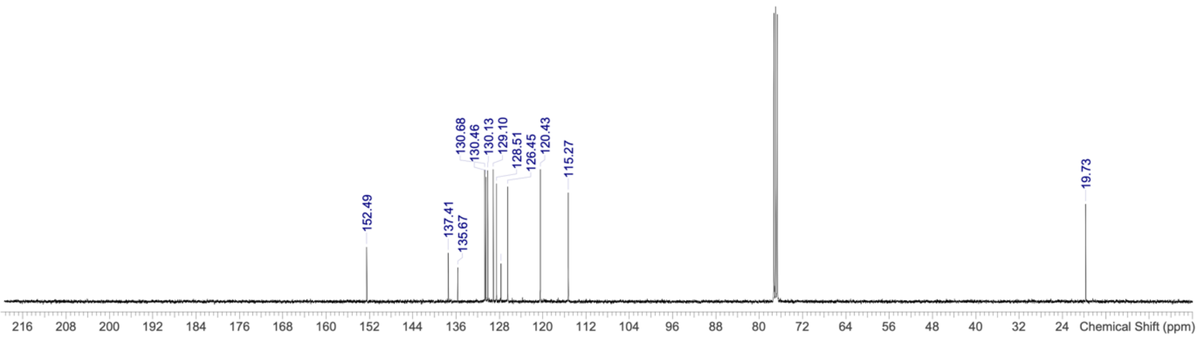




NMR spectra for **33b**.

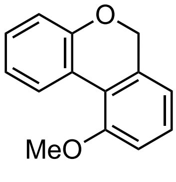






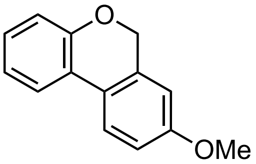
10-Methoxy-6*H*-benzo[*c*]chromene, **7q'**; 8-methoxy-6*H*-benzo[*c*]chromene, **7q** and 2*H*-spiro[benzofuran-3,1'-cyclohexan]-3'-en-5'-one, **35a**

Using the flow photochemical set-up, a solution of iodoaryl ether **7q** (367 mg, 1.08 mmol) in MeCN (51 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (20 mL) were added. The aqueous phase was separated and extracted with DCM (2 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% EtOAc in petrol) to afford respectively the title compounds:

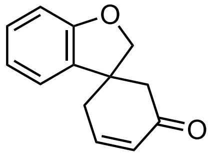


7q' (26 mg, 0.123 mmol, 12%) as a white solid: **IR** ν_{max} (film, cm^{-1}): 1457 (m), 1433 (m), 1269 (s), 1238 (s), 1078 (m), 1044 (m), 1022 (w), 1010 (w). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.43 (1 H, dd, *J* = 8.0, 1.6 Hz, Ar**H**), 7.29 (1 H, t, *J* = 8.0 Hz, Ar**H**), 7.25 (1 H, ddd, *J* = 8.1, 7.5, 1.7 Hz, Ar**H**), 7.09 (1 H, ddd, *J* = 7.9, 7.5, 1.4 Hz, Ar**H**), 7.04 (1 H, dd, *J* = 8.0, 1.3 Hz, Ar**H**), 6.99 (1 H, d, *J* = 8.4 Hz, Ar**H**), 6.84 (1 H, d with fine splitting, *J* = 7.4 Hz, Ar**H**), 5.04 (2 H, s, C**H**$_2$), 3.97 (3H, s, OC**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.5 (**C**), 155.2 (**C**), 134.5 (**C**), 128.7 (**C**H), 128.6 (**C**H), 128.4 (**C**H), 122.1 (**C**), 121.6 (**C**H), 118.8 (**C**), 117.3 (**C**H), 116.8

(**C**H), 111.4 (**C**H), 68.8 (**C**H$_2$), 55.5 (**C**H$_3$). **LRMS** (ESI$^+$): 213 ([M+H], 100%). These data are largely consistent with those extracted from an isomeric mixture.[9]

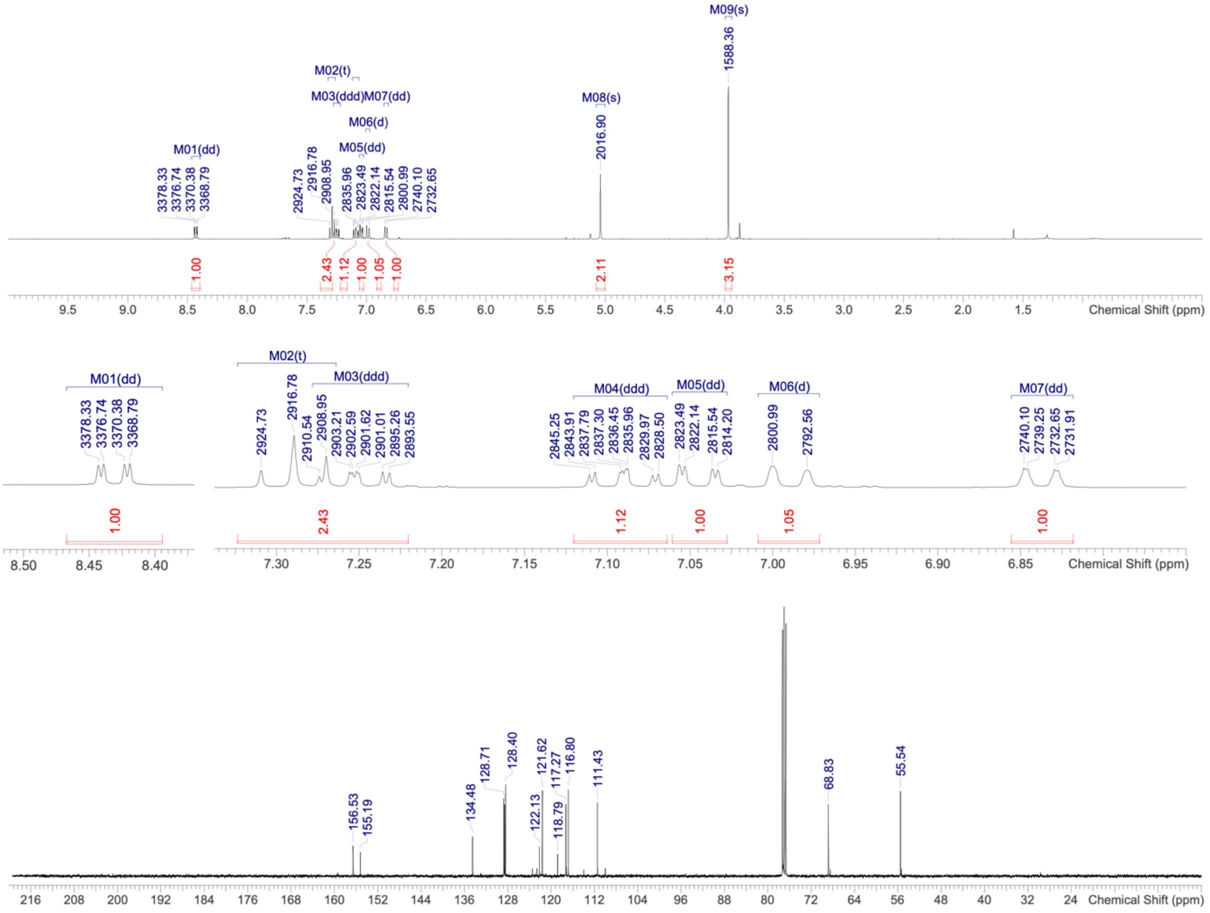


7q (82 mg, 0.387 mmol, 36%) as a white solid. **IR** ν$_{max}$ (film, cm^{-1}): 1611 (m), 1509 (m), 1481 (s), 1460 (m), 1426 (m), 1279 (s), 1229 (m), 1250 (m), 1158 (m), 1040 (s), 1019 (s). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 7.68 (1 H, dd, *J* = 7.7, 1.6 Hz, Ar**H**)7.64 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.21 (1 H, app. td, *J* = 7.7, 1.5 Hz, Ar**H**), 7.06 (1 H, app. td, *J* = 7.6, 1.2 Hz, Ar**H**), 7.00 (1 H, brdd, *J* = 8.1, 1.1 Hz, Ar**H**), 6.93 (1 H, dd, *J* = 8.6, 2.6 Hz, Ar**H**), 6.71 (1 H, d, *J* = 2.7 Hz, Ar**H**), 5.11 (2 H, s, C**H**$_2$), 3.85 (3 H, s, OC**H**$_3$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 159.4 (**C**), 153.9 (**C**), 133.0 (**C**), 128.4 (**C**H), 123.4 (**C**H), 123.0 (**C**), 122.9 (**C**), 122.6 (**C**H), 122.1 (**C**H), 117.2 (**C**H), 114.0 (**C**H), 110.0 (**C**H), 68.5 (**C**H$_2$), 55.3 (**C**H$_3$) ppm. **LRMS** (ESI$^+$): 213 ([M+H]$^+$, 100%).[9]

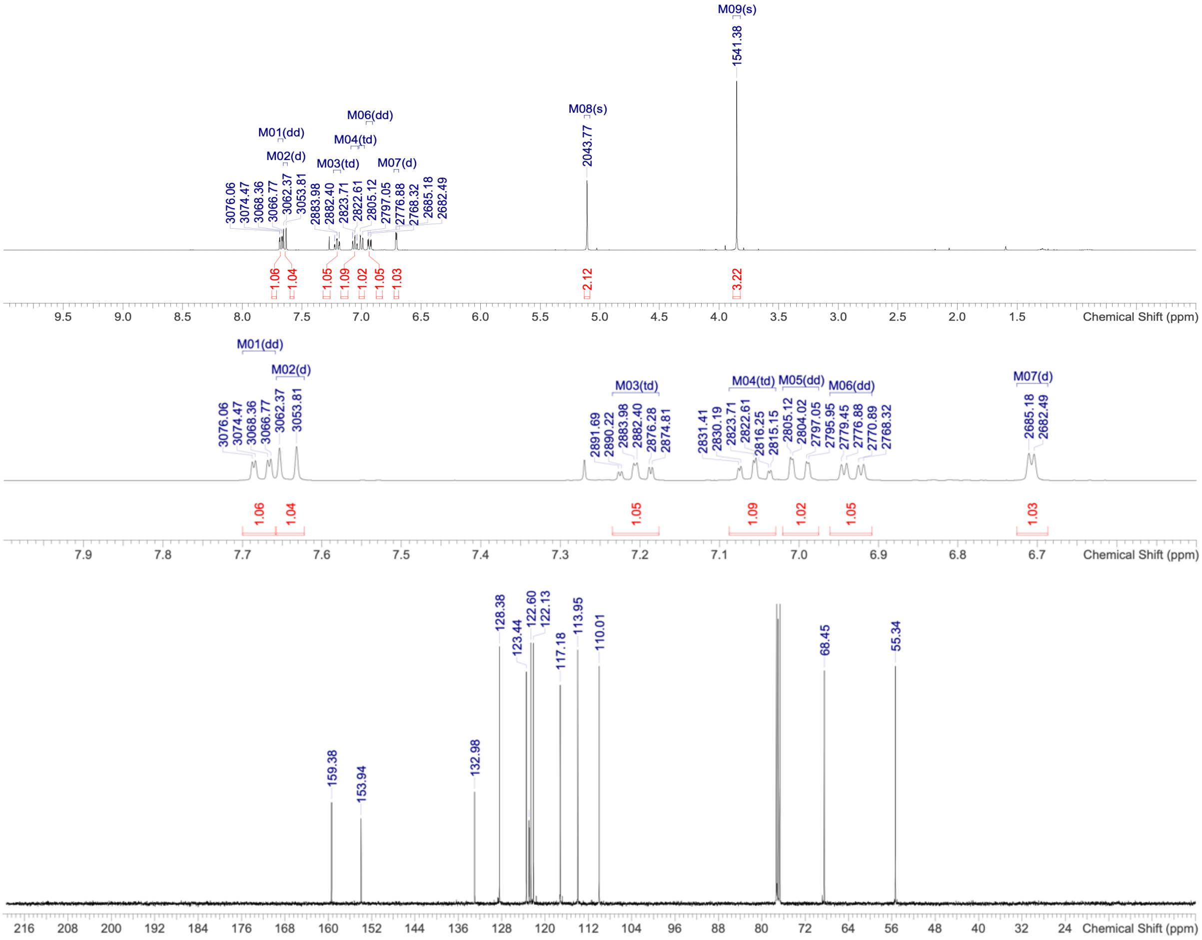


35a (43 mg, 0.178 mmol, 21%) as a pale yellow oil. **IR** ν$_{max}$ (film, cm^{-1}): 1678 (s), 1598 (w), 1480 (s), 1459 (m), 1384 (w), 1229 (m). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 7.20 (1 H, app. td, *J* = 7.8, 1.4 Hz, Ar**H**), 7.17 (1 H, br d, *J* = 7.5 Hz, Ar**H**), 7.02 (1 H, ddd, *J* = 10.2, 4.9, 3.2 Hz, C**H**), 6.91 (1 H, app. td, *J* = 7.5, 0.8 Hz, Ar**H**), 6.85 (1 H, d, *J* = 7.9 Hz, Ar**H**), 6.20 (1 H, dt, *J* = 10.2, 1.9 Hz, C**H**), 4.36 (1 H, d, *J* = 8.9 Hz, C**H**H), 4.29 (1 H, d, *J* = 9.1 Hz, CH**H**), 2.86 (1 H, d, *J* = 16.4 Hz, C**H**H), 2.77 (1 H, dt, *J* = 19.1, 2.8 Hz, C**H**H), 2.68 (1 H, br d, *J* = 15.5 Hz, CH**H**), 2.66 (1 H, ddt, *J* = 19.0, 5.0, 1.4 Hz, CH**H**). **^{13}C NMR** (100 MHz, CDCl$_3$) δ 197.2 (**C**), 159.3 (**C**), 147.7 (**C**H), 132.1 (**C**), 130.4 (**C**H), 129.3 (**C**H), 122.8 (**C**H), 120.9 (**C**H), 110.4 (**C**H), 81.8 (**C**H$_2$), 47.9 (**C**H$_2$), 47.6 (**C**), 37.2 (**C**H$_2$) ppm. **LRMS** (ESI+): 201 ([M+H]$^+$, 100%). **HRMS** (ESI$^+$): Found 201.0909, [M+H]$^+$ $C_{13}H_{13}O_2$ requires 201.0910.

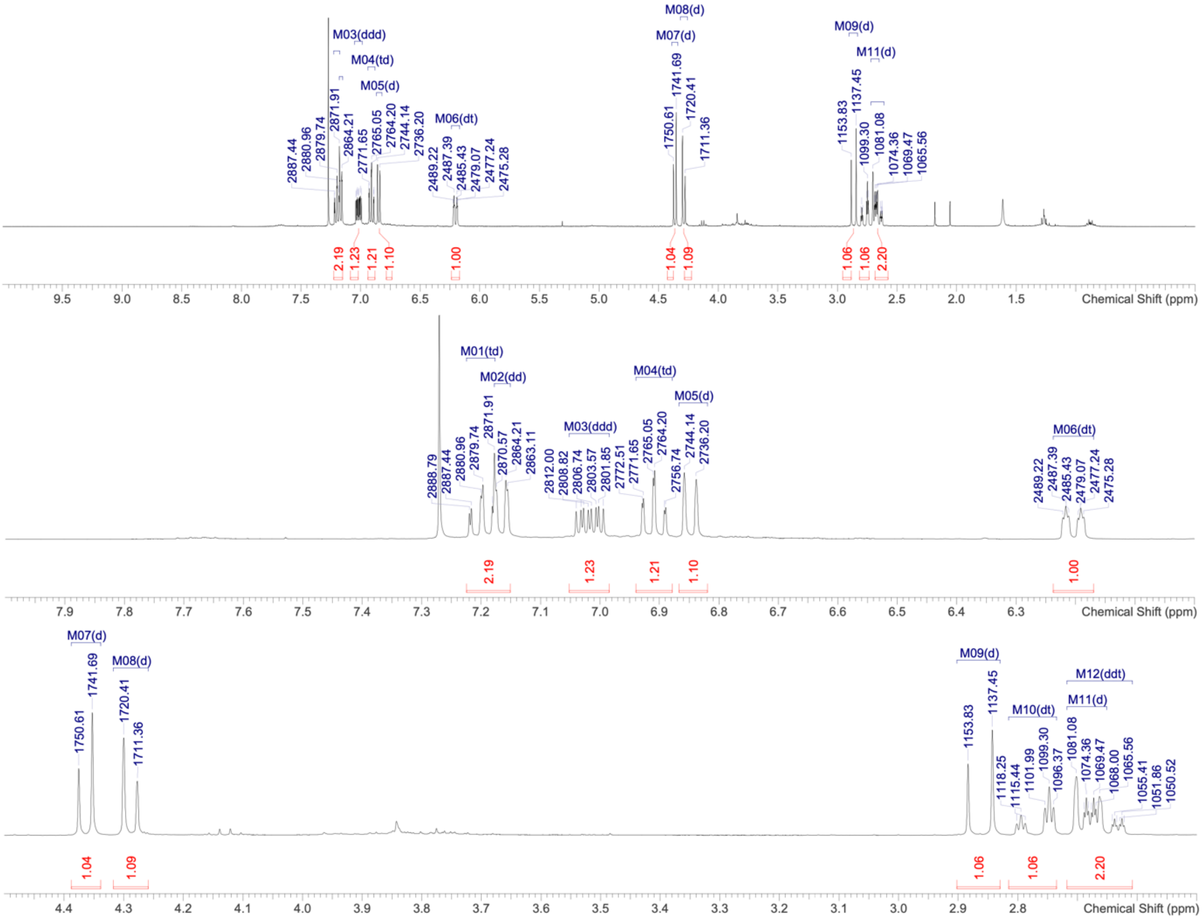
NMR data for **7q'**.

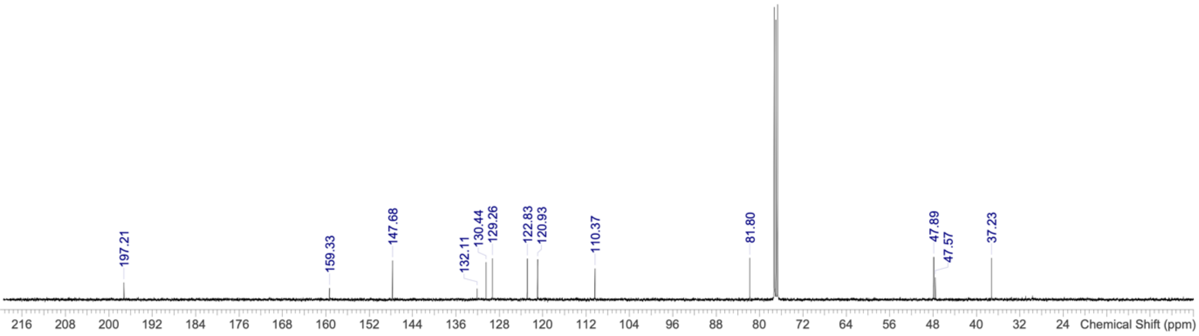


NMR data for **7q**.



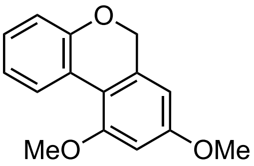
NMR data for **35a**.



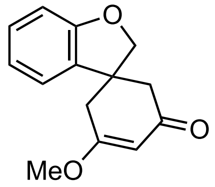


8,10-Dimethoxy-6*H*-benzo[*c*]chromene, **7r** and 3'-methoxy-2*H*-spiro[benzofuran-3,1'-cyclohexan]-3'-en-5'-one, **35b**

Using the flow photochemical set-up, a solution of 1-((2-iodophenoxy)methyl)-3,5-dimethoxybenzene **5r** (391 mg, 1.06 mmol) in MeCN (53 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (20 mL) were added. The aqueous phase was separated and extracted with DCM (2 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 40% ethyl acetate in petrol) to afford respectively the titled compounds:

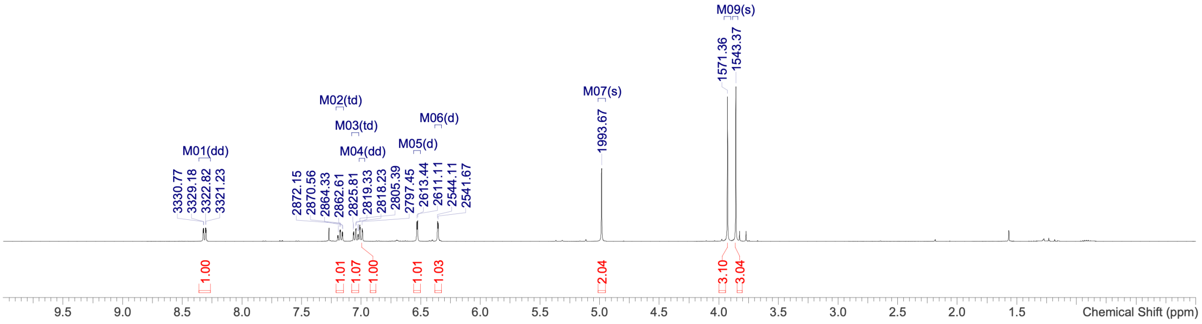


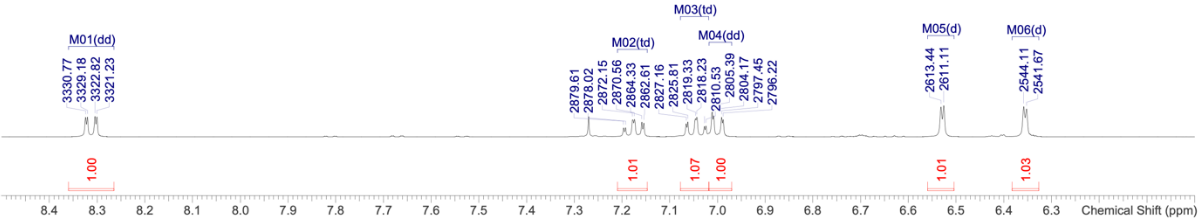
7r (137 mg, 0.565 mmol, 53%) as a white solid. **MP** 109 – 111 °C. **IR** ν_{max} (solid, cm^{-1}): 1608 (s), 1460 (s), 1420 (m), 1335 (s), 1298 (w), 1231 (s), 1156 (s), 1087 (m), 1046 (m), 1025 (m). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 8.31 (1 H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.18 (1 H, app. td, *J* = 7.7, 1.7 Hz, ArH), 7.04 (1 H, app. td, *J* = 7.6, 1.4 Hz, ArH), 7.00 (1 H, dd, *J* = 8.0, 1.2 Hz, ArH), 6.53 (1 H, d, *J* = 2.3 Hz, ArH), 6.36 (1 H, d, *J* = 2.4 Hz, ArH), 4.98 (2 H, s, CH$_2$), 3.93 (3 H, s, OCH$_3$), 3.86 (3 H, s, OCH$_3$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 160.0 (**C**), 157.9 (**C**), 154.4 (**C**), 135.4 (**C**), 127.7 (**C**H), 127.6 (**C**H), 122.3 (**C**), 121.7 (**C**H), 116.6 (**C**H), 112.0 (**C**), 101.6 (**C**H), 98.8 (**C**H), 69.1 (**C**H$_2$), 55.5 (**C**H$_3$), 55.4 (**C**H$_3$). **LRMS** (ESI$^+$): 243 ([M+H]$^+$, 50%), 242 (100%). **HRMS** (ESI$^+$): Found 243.1012, [M+H]$^+$ $C_{15}H_{15}O_3$ requires 243.1016.

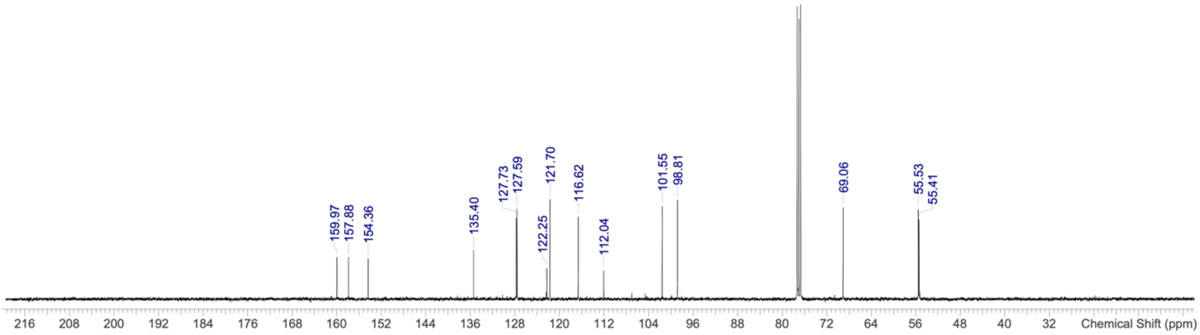


35b (50 mg, 0.217 mmol, 21%) as a white solid. **MP** 69 – 70 °C. **IR** ν_{max} (solid, cm^{-1}): 1652 (s), 1602 (s), 1480 (m), 1459 (m), 1375 (s), 1219 (s). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 7.20 (1 H, ddd, *J* = 8.0, 7.5, 1.3 Hz, ArH), 7.17 (1 H, dd, *J* = 7.6, 0.9 Hz, ArH), 6.91 (1 H, app. td, *J* = 7.5, 1.0 Hz, ArH), 6.84 (1 H, br d, *J* = 8.1 Hz, ArH), 5.52 (1 H, d, *J* = 1.2 Hz, CH), 4.37 (1 H, d, *J* = 9.1 Hz, CHH), 4.30 (1 H, dd, *J* = 9.1, 0.6 Hz, CHH), 3.76 (3 H, s, OCH$_3$), 2.85 (1 H, d, *J* = 17.5 Hz, CHH), 2.77 (1 H, d, *J* = 16.5 Hz, CHH), 2.63 (1 H, dd, *J* = 17.4, 1.6 Hz, CHH), 2.61 (1 H, dd, *J* = 16.6, 1.4 Hz, CHH) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 196.8 (**C**), 176.0 (**C**), 159.4 (**C**), 131.6 (**C**), 129.3 (**C**H), 122.8 (**C**H), 121.0 (**C**H), 110.4 (**C**H), 102.6 (**C**H), 81.7 (**C**H$_2$), 56.1 (**C**H$_3$), 47.0 (**C**H$_2$), 46.3 (**C**), 40.1 (**C**H$_2$). **LRMS** (ESI$^+$): 231 ([M+H]$^+$, 100%). **HRMS** (ESI$^+$): Found 231.1019, [M+H]$^+$ $C_{14}H_{15}O_3$ requires 231.1016.

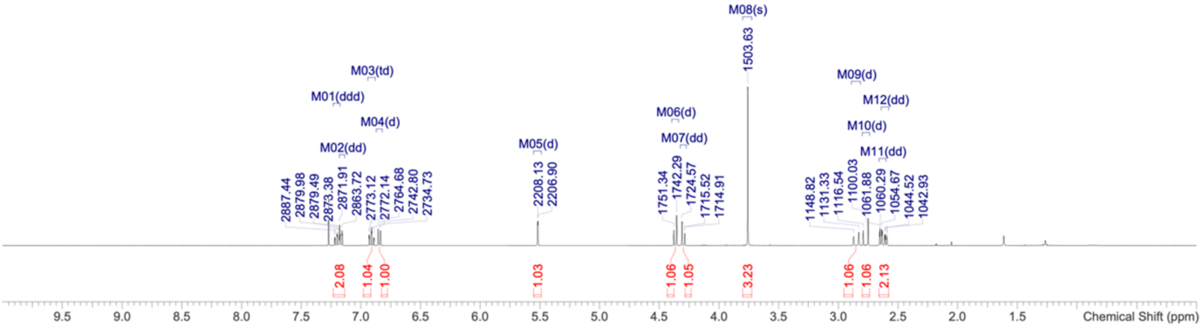
NMR spectra for **7r**.

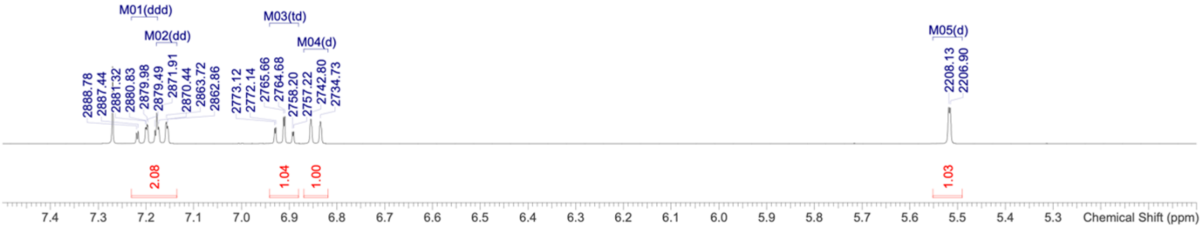


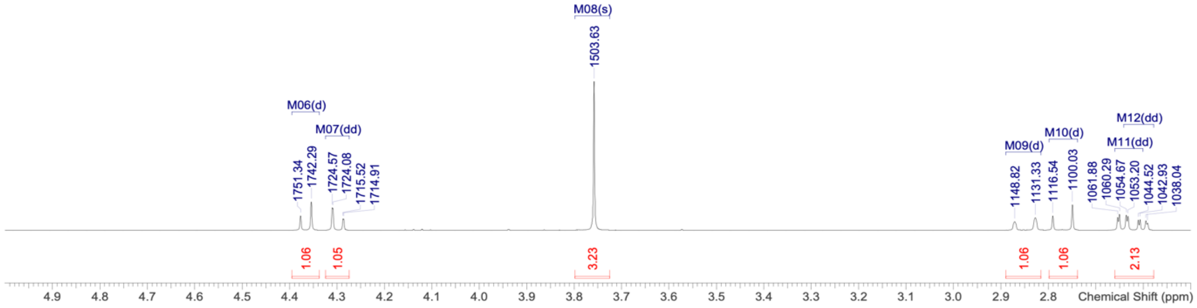


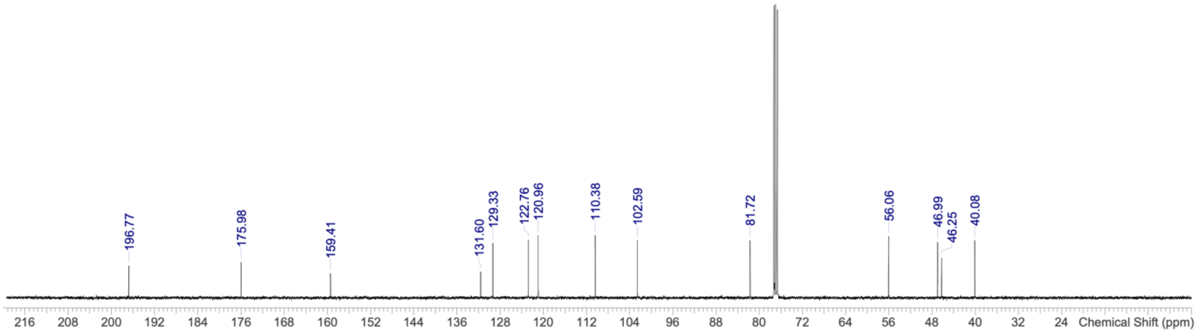


NMR spectra for **35b**.



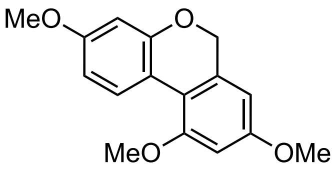




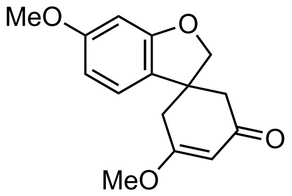


3,8,10-Trimethoxy-6*H*-benzo[*c*]chromene, **7s** and
3',6-dimethoxy-2*H*-spiro[benzofuran-3,1'-cyclohexan]-3'-en-5'-one, **35c**.

Using the flow photochemical set-up, a solution of iodoaryl ether **5s** (426 mg, 1.06 mmol) in MeCN (53 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (20 mL) were added. The aqueous phase was separated and extracted with DCM (4 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 10% acetone in petrol) to afford the title compounds:

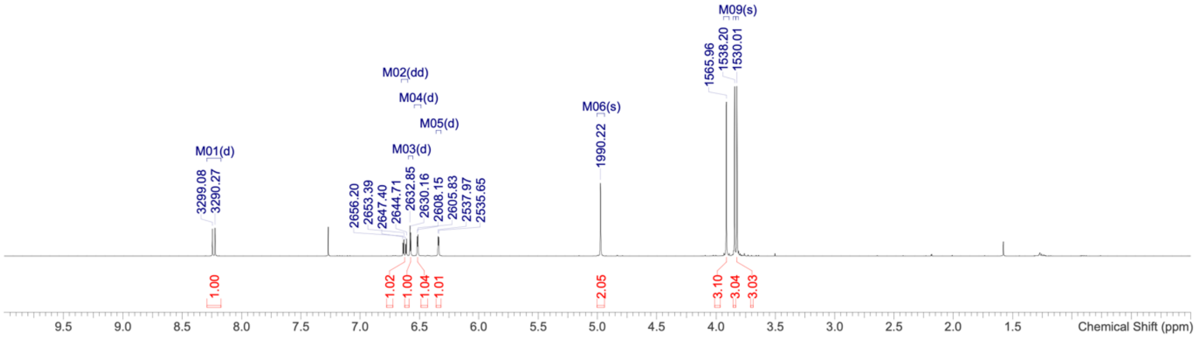


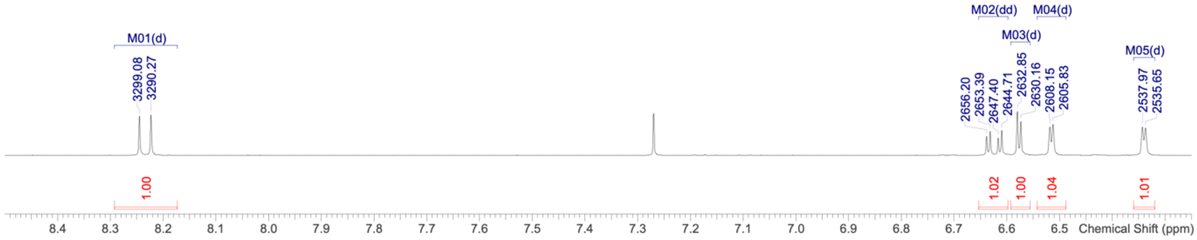
7s (132 mg, 0.49 mmol, 46%) as an off-white solid: **MP**: 87 – 88 °C. **IR** ν_{max} (film, cm^{-1}): 2836 (w), 1612 (s), 1565 (m), 1480 (s), 1459(s), 1336 (m), 1268 (s), 1212 (m), 1156 (s), 1062 (m), 1039 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.23 (1 H, d, *J* = 8.8 Hz, Ar**H**), 6.62 (1 H, dd, *J* = 8.7, 2.8 Hz, Ar**H**), 6.58 (1 H, d, *J* = 2.7 Hz, Ar**H**), 6.52 (1 H, d, *J* = 2.3 Hz, Ar**H**), 6.34 (1 H, d, *J* = 2.3 Hz, Ar**H**), 4.97 (2 H, s, C**H**$_2$), 3.91 (3 H, s, OC**H**$_3$), 3.84 (3 H, s, OC**H**$_3$), 3.82 (3 H, s, OC**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.3 (**C**), 159.2 (**C**), 157.2 (**C**), 155.6 (**C**), 134.0 (**C**), 128.6 (**C**H), 115.1 (**C**), 112.3 (**C**), 107.8 (**C**H), 102.1 (**C**H), 101.5 (**C**H), 98.8 (**C**H), 69.3 (**C**H$_2$), 55.5 (**C**H$_3$), 55.4 (**C**H$_3$), 55.3 (**C**H$_3$). **LRMS** (ESI+): 273 ([M+H]$^+$, 100 %), 258 (40%). **HRMS** (ESI+): Found 273.1124, [M+H]$^+$ $C_{16}H_{17}O_4$ requires 273.1121.

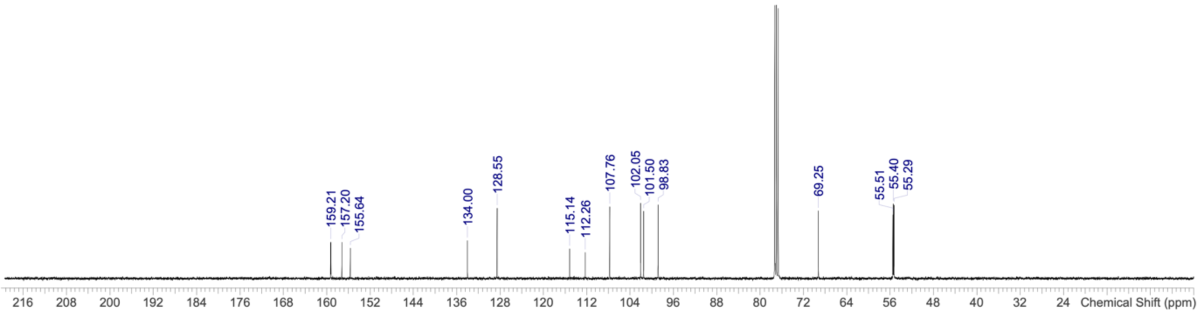


35b (69 mg, 0.27 mmol, 25%) as a pale oil. **IR** ν_{max} (film, cm^{-1}): 2943 (br), 1653 (m), 1604 (s), 1498 (m), 1446 (w), 1376 (m), 1282 (w), 1223 (s), 1147 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.03 (1 H, d, *J* = 8.2 Hz, Ar**H**), 6.45 (1 H, dd, *J* = 8.3, 2.3 Hz, Ar**H**), 6.42 (1 H, d, *J* = 2.2 Hz, Ar**H**), 5.50 (1 H, s, C**H**), 4.37 (1 H, d, *J* = 9.1 Hz, C**H**H), 4.30 (1 H, d, *J* = 9.1 Hz, CH**H**), 3.78 (3 H, s, OC**H**$_3$), 3.75 (3 H, s, OC**H**$_3$), 2.81 (1 H, d, *J* = 17.1 Hz, C**H**H), 2.73 (1 H, d, *J* = 16.5 Hz, CH**H**), 2.60 (1 H, dd, *J* = 17.1, 1.2 Hz, C**H**H), 2.58 (1 H, dd, *J* = 16.5, 1.3 Hz, CH**H**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.0 (**C**), 176.1 (**C**), 161.2 (**C**), 160.8 (**C**), 123.8 (**C**), 122.9 (**C**H), 106.7 (**C**H), 102.6 (**C**H), 96.7 (**C**H), 82.5 (**C**H$_2$), 56.0 (**C**H$_3$), 55.5 (**C**H$_3$), 47.3 (**C**H$_2$), 45.8 (**C**), 40.4 (**C**H$_2$) ppm. **LRMS** (ESI+): 261 ([M+H]$^+$, 100 %), 229 (50%). **HRMS** (ESI+): Found 261.1126, [M+H]$^+$ $C_{15}H_{17}O_4$ requires 261.1121.

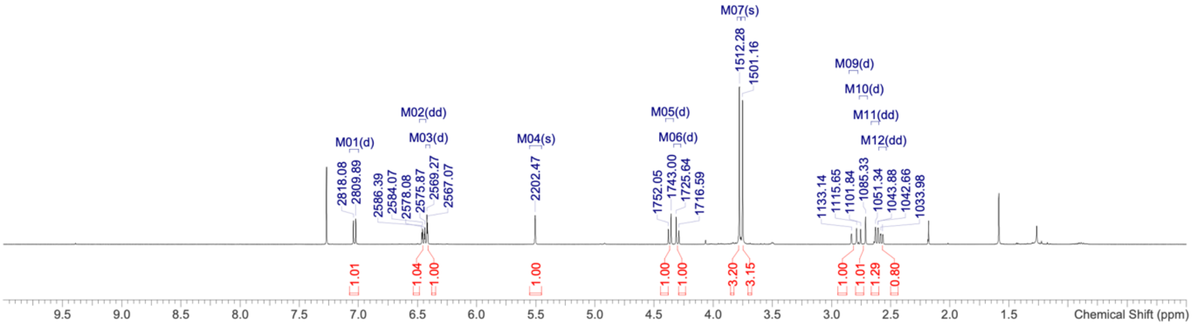
NMR data for **7s**.

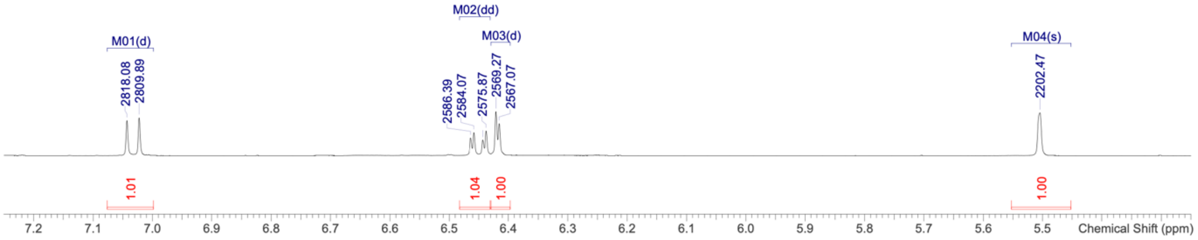


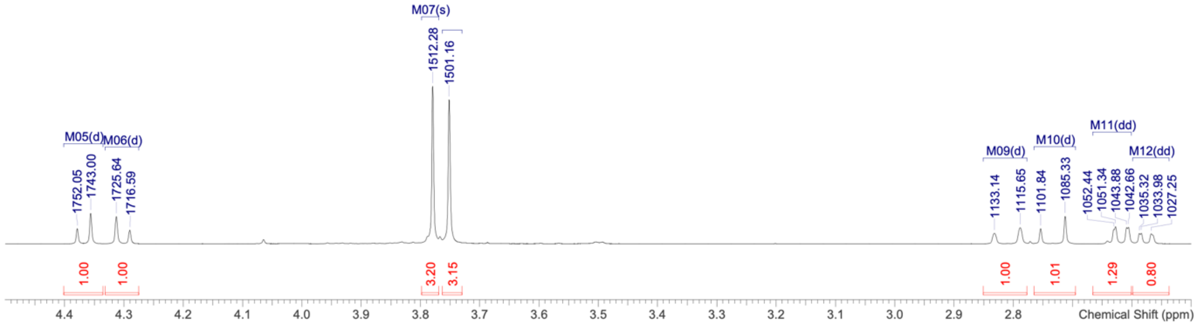


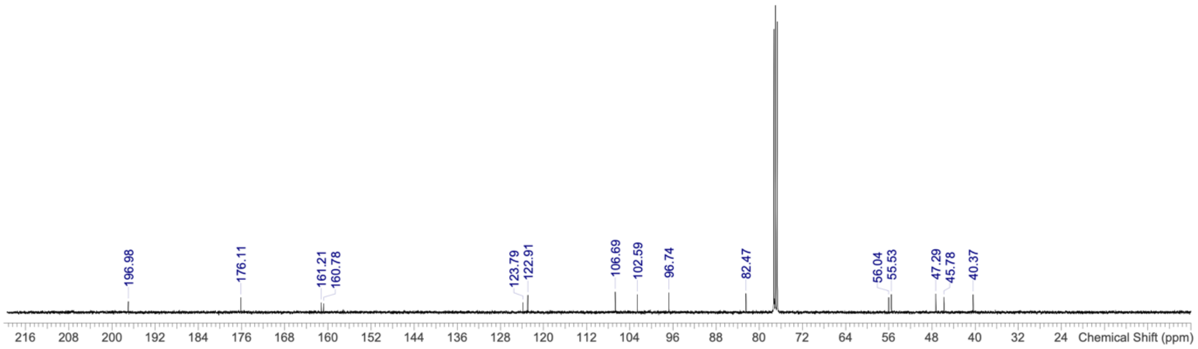


NMR data for **35b**.

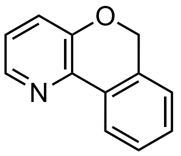






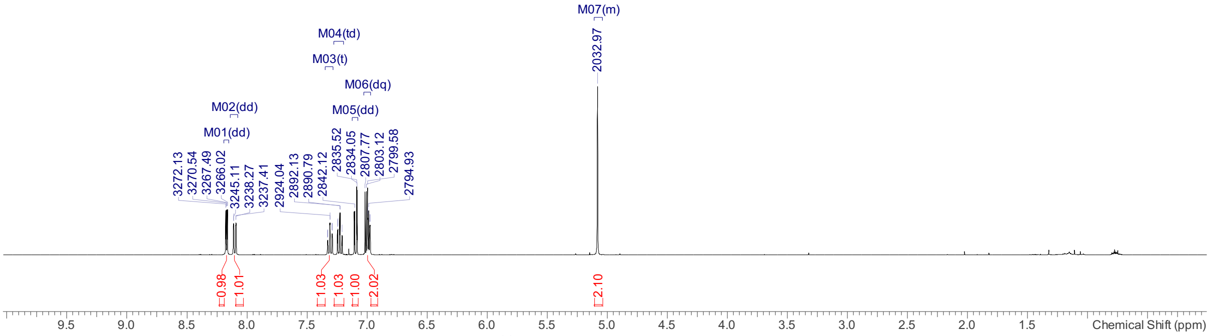


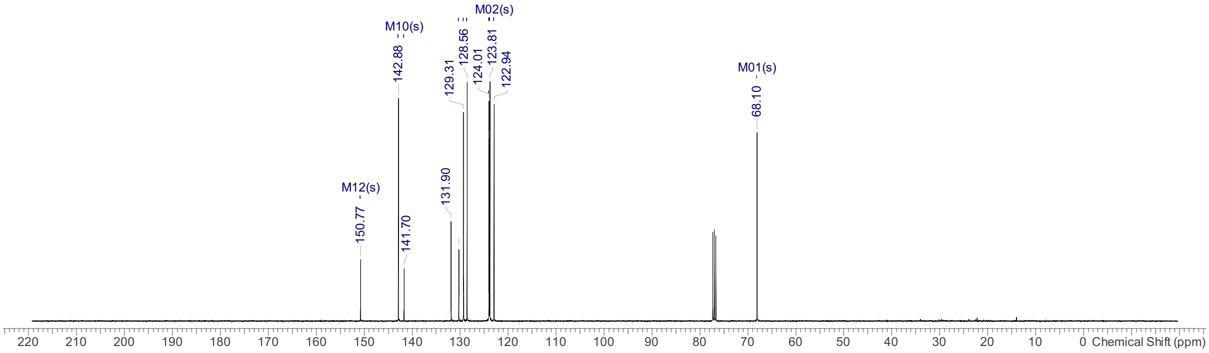
6*H*-Isochromeno[4,3-*b*]pyridine, **16a**.



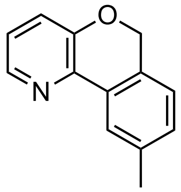
Using the flow photochemical set-up, a solution of benzyl 2-iodopyrid-3-yl ether **15a** (361 mg, 1.16 mmol) in MeCN (60 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (20 – 40% Et_2O/petrol) to afford the title compound **16a** (187 mg, 1.02 mmol, 88%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 3053 (br), 2852 (br), 1585 (m), 1424 (s), 1248 (s), 1187 (s), 1100 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.17 (1H, dd, *J* = 4.6, 1.5

Hz, Ar**H**), 8.10 (1H, dd, *J* = 7.6, 1.0 Hz, Ar**H**), 7.31 (1H, app. t, *J* = 7.5 Hz, Ar**H**), 7.23 (1H, td, *J* = 7.5, 1.3 Hz, Ar**H**), 7.10 (1H, dd, *J* = 8.1, 1.6 Hz, Ar**H**), 7.09 (1H, dd, *J* = 8.2, 4.7 Hz, Ar**H**), 6.99 (1H, br d, *J* = 7.5 Hz, Ar**H**), 5.08 (2H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 150.8 (**C**), 142.9 (**C**H), 141.7 (**C**), 131.9 (**C**), 130.3 (**C**), 129.3 (**C**H), 128.6 (**C**H), 124.0 (**C**H), 123.8 (**C**H), 122.9 (**C**H), 68.1 (**C**H$_2$) ppm. **LRMS** (ESI$^+$): 184 [M+H]$^+$. **HRMS** (ESI$^+$): Found 184.0758, C$_{12}$H$_{10}$NO [M+H]$^+$ requires 184.0757.

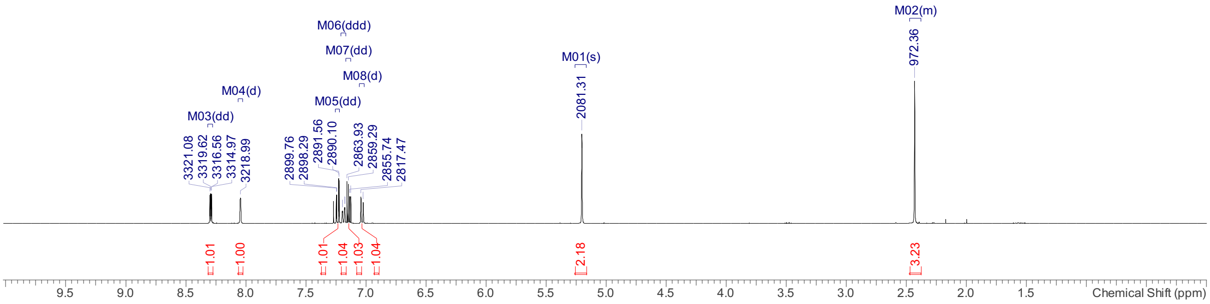


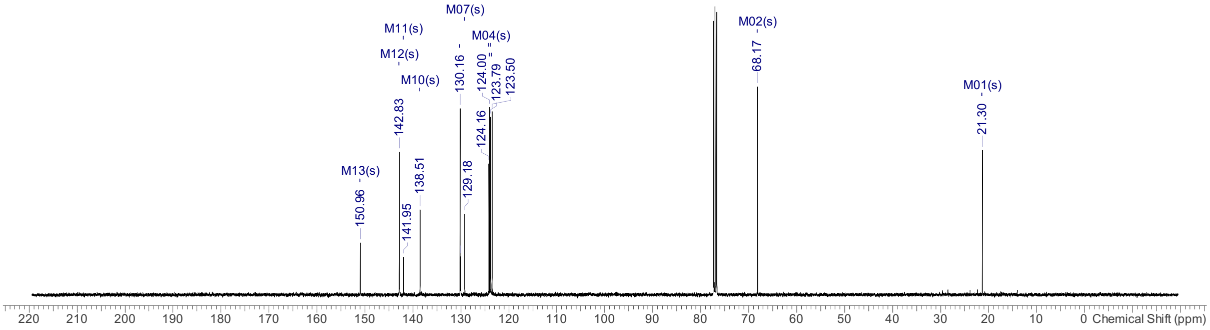


9-Methyl-6*H*-isochromeno[4,3-*b*]pyridine, **16b**.

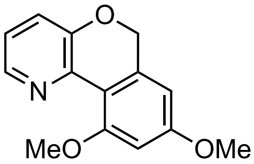


Using the flow photochemical set-up, a solution of benzyl 2-iodopyrid-3-yl ether **15b** (393 mg, 1.21 mmol) in MeCN (60 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. Na$_2$S$_2$O$_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over MgSO$_4$, concentrated *in vacuo* and purified by column chromatography (30 – 50% EtOAc/petrol) to afford the title compound **16b** (152 mg, 0.77 mmol, 64%) as a yellow oil. **IR** ν$_{max}$ (film, cm^{-1}): 3055 (br), 2920 (br), 1457 (s), 1401 (s), 1250 (s), 1200 (m). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 8.29 (1H, dd, *J* = 4.7, 1.5 Hz, Ar**H**), 8.05 (1H, br s, Ar**H**), 7.24 (1H, d, *J* = 8.2, 1.5 Hz, Ar**H**), 7.19 (1H, ddd, *J* = 7.7, 1.7, 0.6 Hz, Ar**H**), 7.14 (1H, dd, *J* = 8.1, 4.7 Hz, Ar**H**), 7.03 (1H, d, *J* = 7.6 Hz, Ar**H**), 5.20 (2H, s, C**H**$_2$), 2.43 (3H, s, C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 151.0 (**C**), 142.8 (**C**H), 142.0 (**C**), 138.5 (**C**), 130.2 (**C**H), 130.1 (**C**), 129.2 (**C**), 124.2 (**C**), 124.2 (**C**H), 124.0 (**C**H), 123.8 (**C**H), 123.5 (**C**H), 68.2 (**C**H$_2$), 21.3 (**C**H$_3$) ppm. **LRMS** (ESI$^+$): 198 [M+H]$^+$. **HRMS** (ESI$^+$): Found 198.0917, C$_{13}$H$_{12}$NO [M+H]$^+$ requires 198.0913.

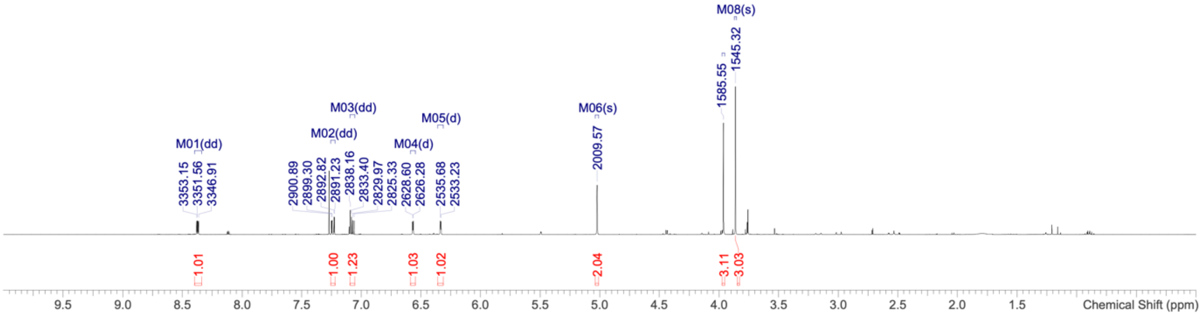


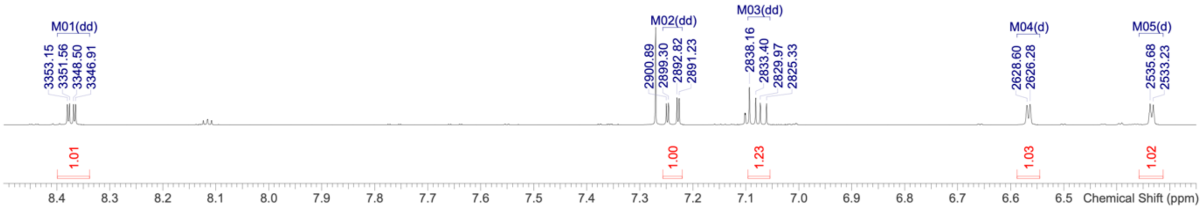


8,10-Dimethoxy-6*H*-isochromeno[4,3-*b*]pyridine, **16c**.

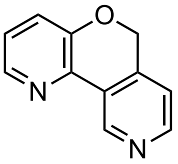


Using the flow photochemical set-up, a solution iodopyridyl ether **15c** (607 mg, 1.64 mmol) in MeCN (117 mL, 0.014 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then acetone (30 mL), sat. $NaHCO_3$ (20 mL), EtOAc (60 mL) and water (20 mL) were added. The aqueous phase was separated and extracted with DCM (4 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (60 – 80% EtOAc in petrol) to afford the title compound **16c** (186 mg, 0.77 mmol, 47%, ~95% purity with sample deteriorating on standing in $CDCl_3$) as an orange oil. **IR** ν_{max} (film, cm^{-1}): 1605 (s), 1431 (m), 1451 (m), 1418 (s), 1336 (m), 1253 (m), 1228 (m), 1160 (m), 1089 (w), 1066 (w), 1023 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.37 (1 H, dd, *J* = 4.7, 1.6 Hz, Ar**H**), 7.24 (1 H, dd, *J* = 8.1, 1.6 Hz, Ar**H**), 7.08 (1 H, dd, *J* = 8.1, 4.7 Hz, Ar**H**), 6.57 (1 H, d, *J* = 2.3 Hz, Ar**H**), 6.33 (1 H, d with fine splitting, *J* = 2.5 Hz, Ar**H**), 5.02 (2 H, s with fine splitting, C**H$_2$**), 3.96 (3 H, s, OC**H$_3$**), 3.96 (3 H, s, OC**H$_3$**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.3 (**C**), 158.8 (**C**), 150.8 (**C**), 143.1 (**C**), 142.8 (**C**H), 137.1 (**C**), 123.5 (**C**H), 122.0 (**C**H), 112.3 (**C**), 101.4 (**C**H), 99.4 (**C**H), 69.2 (**C**H$_2$), 56.4 (**C**H$_3$), 55.4 (**C**H$_3$) ppm. **LRMS** (ESI+): 244 ([M+H]$^+$, 100%). **HRMS** (ESI+): Found 244.0972, [M+H]$^+$ $C_{14}H_{14}NO_3$ requires 244.0968.

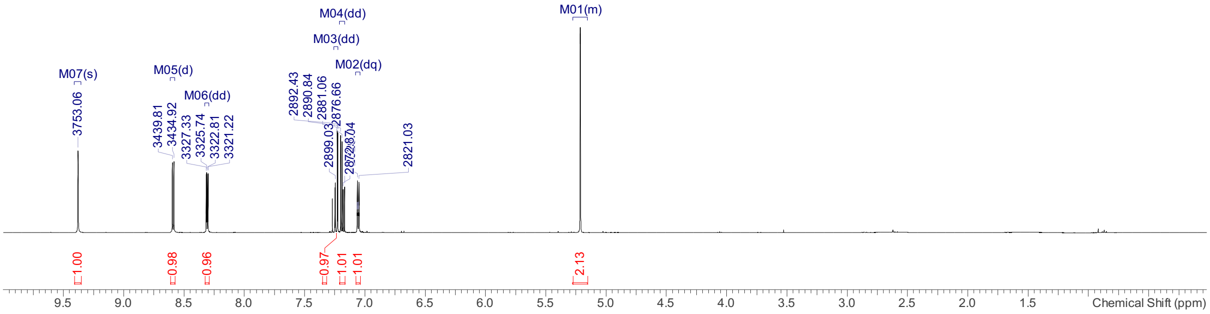


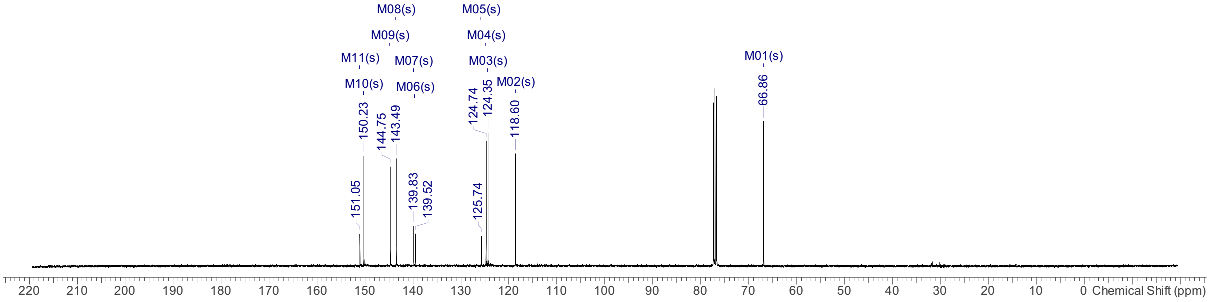


6*H*-Pyrano[3,2-*b*:4,5-*c*′]dipyridine, **16d**.

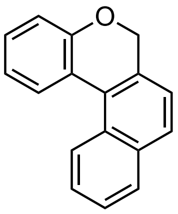


Using the flow photochemical set-up, a solution of 2-iodopyrid-3-yl ether **15d** (378 mg, 1.21 mmol) in MeCN (60 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (30 – 60% EtOAc/petrol) to afford the title compound **16d** (131 mg, 0.71 mmol, 59%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 3400 (br), 3056 (br), 1603 (m), 1458 (s), 1401 (s), 1267 (m), 1193 (m), 1023 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.38 (1H, s, Ar**H**), 8.59 (1H, d, *J* = 4.9 Hz, Ar**H**), 8.31 (1H, d, *J* = 4.5, 1.6 Hz, Ar**H**), 7.24 (1H, dd, *J* = 8.2, 1.6 Hz, Ar**H**), 7.18 (1H, dd, *J* = 8.4, 4.4 Hz, Ar**H**), 7.06 (1H, br d, *J* = 5.0 Hz, Ar**H**), 5.21 (2H, s, C**H$_2$**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.1 (**C**), 150.2 (**C**H), 144.8 (**C**H), 143.5 (**C**H), 139.8 (**C**), 139.5 (**C**), 125.7 (**C**), 124.7 (**C**H), 124.4 (**C**H), 118.6 (**C**H), 66.9 (**C**H_2) ppm. **LRMS** (ESI^+): 185 $[M+H]^+$. **HRMS** (ESI^+): Found 185.0713, $C_{11}H_9N_2O$ $[M+H]^+$ requires 185.0709.

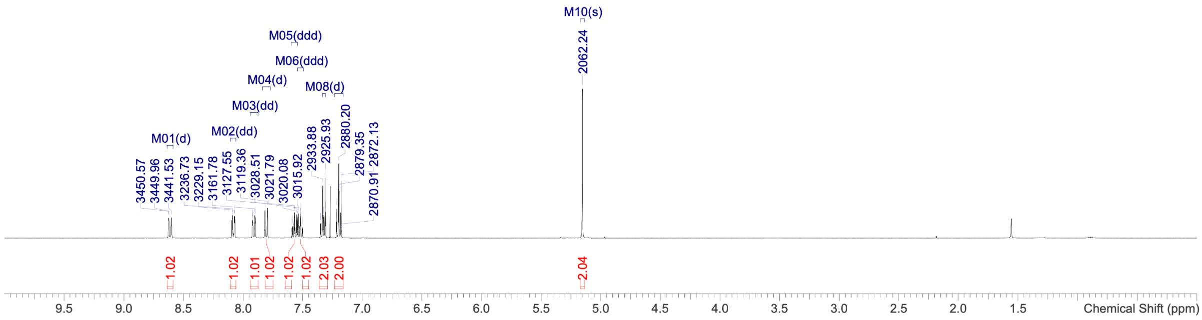


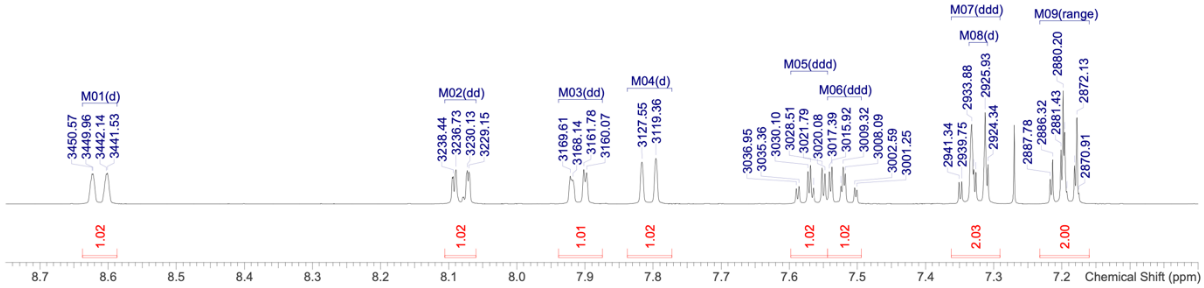


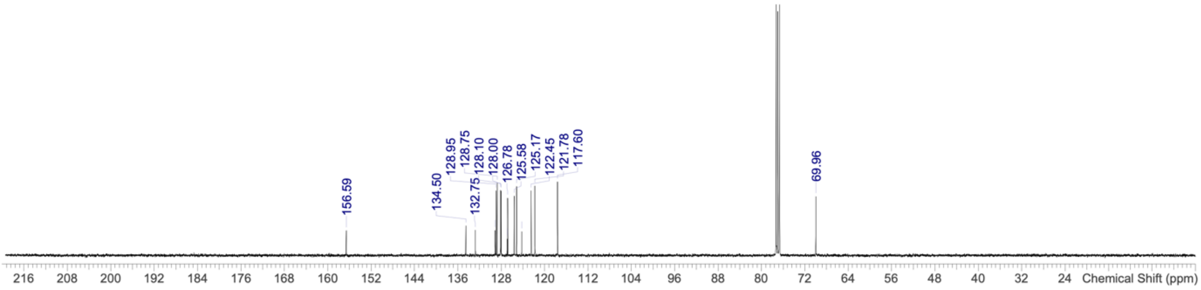
<u>6*H*-Naphtho[2,1-*c*]chromene</u>, **18**.



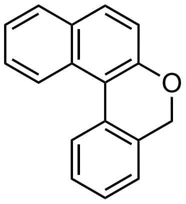
Using the flow photochemical set-up, a solution of 2-iodophenyl ether **17** (500 mg, 1.39 mmol) in MeCN (70 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (2.5% acetone in petrol) to afford the title compound **18** (178 mg, 0.764 mmol, 55%) as a white solid. **IR** ν_{max} (film, cm^{-1}): 2971 (br), 2901 (br), 1484 (m), 1389 (w), 1243 (s), 1195 (w), 1034 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.61 (1 H, br d, *J* = 8.4 Hz, Ar**H**), 8.08 (1 H, dd, *J* = 8.0, 1.3 Hz, Ar**H**), 7.91 (1 H, dd, *J* = 8.0, 1.6 Hz, Ar**H**), 7.81 (1 H, br d, *J* = 8.2 Hz, Ar**H**), 7.57 (1 H, ddd, *J* = 8.4, 6.8, 1.6 Hz, Ar**H**), 7.52 (1 H, ddd, *J* = 8.1, 6.8, 1.4 Hz, Ar**H**), 7.33 (1 H, ddd, *J* = 8.3, 7.1, 1.8 Hz, Ar**H**), 7.32 (1 H, d, *J* = 8.0 Hz, Ar**H**), 7.16 – 7.23 (2 H, m, 2 × Ar**H**), 5.15 (2 H, s, C**H_2**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.6 (**C**), 134.5 (**C**), 132.8 (**C**), 129.1 (**C**), 129.0 (**C**H), 128.8 (**C**H), 128.1 (**C**H), 128.0 (**C**H), 126.9 (**C**), 126.8 (**C**H), 125.6 (**C**H), 125.2 (**C**H), 124.2 (**C**), 122.5 (**C**H), 121.8 (**C**H), 117.6 (**C**H), 70.0 (**C**H_2) ppm. **LRMS** (ESI^+): 231 ($[M-H]^{+\bullet}$, 100%), 202 ($[M-CH_2O]^{+\bullet}$, 95%). These data are largely consistent with those extracted from an isomeric mixture.[11]



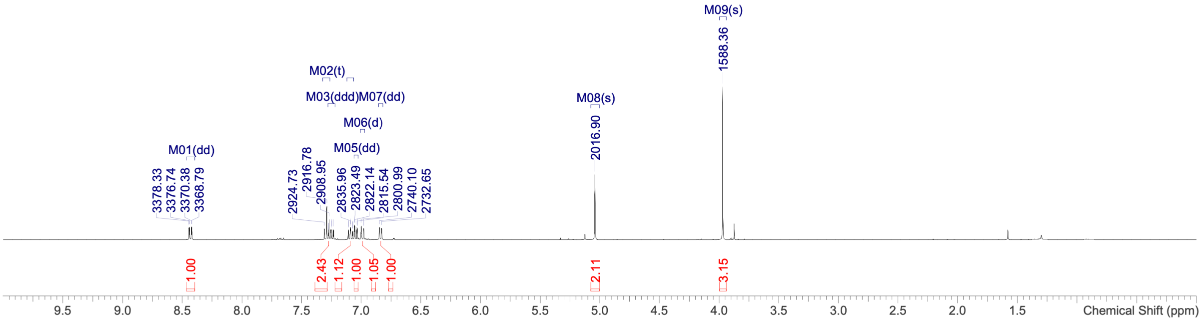


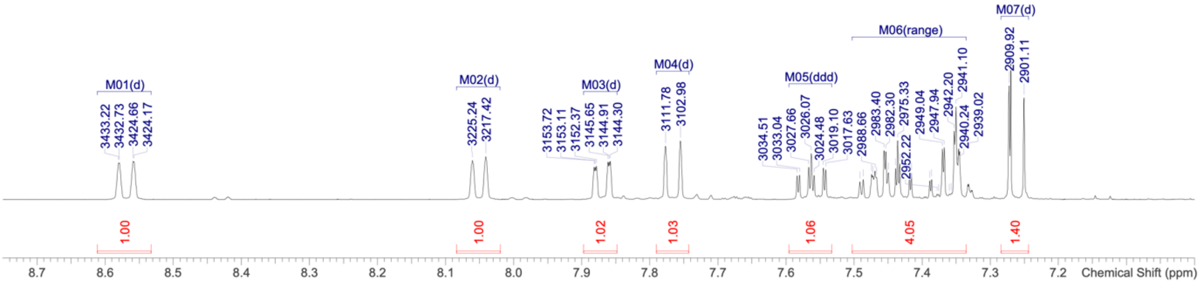


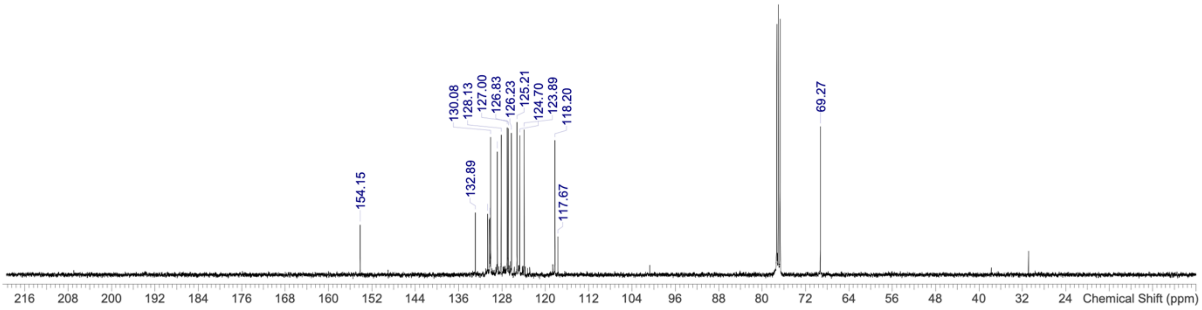
<u>5*H*-Bibenzo[*c*,*f*]chromene</u>, **20**.



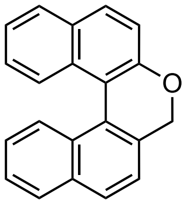
Using the flow photochemical set-up, a solution of iodonaphthyl ether **19** (574 mg, 1.59 mmol) in MeCN (80 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (25 mL) and sat. $Na_2S_2O_3$ (25 mL) were added. The aqueous phase was separated and extracted with DCM (2 × 25 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (2.5% acetone in petrol) to afford the title compound **20** (178 mg, 0.765 mmol, 48%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 3059 (w), 2973 (w), 2844 (w), 1619 (w), 1595 (m), 1513 (m), 1384 (m), 1238 (m), 1207 (m), 1018 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.57 (1 H, br d, *J* = 8.6 Hz, Ar**H**), 8.05 (1 H, d, *J* = 7.8 Hz, Ar**H**), 7.87 (1 H, d with fine splitting, *J* = 8.3 Hz, Ar**H**), 7.77 (1 H, d, *J* = 8.8 Hz, Ar**H**), 7.56 (1 H, ddd, *J* = 8.4, 6.9, 1.5 Hz, Ar**H**), 7.50 – 7.34 (4 H, m, 4 × Ar**H**), 7.26 (1 H, d, *J* = 8.8 Hz, Ar**H**), 5.07 (2 H, s, C**H₂**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.2 (**C**), 132.9 (**C**), 130.6 (**C**), 130.3 (**C**), 130.2 (**C**), 130.1 (**C**H), 128.8 (**C**H), 128.1 (**C**H), 127.0 (**C**H), 126.8 (**C**H), 126.2 (**C**H), 125.2 (**C**H), 124.7 (**C**H), 123.9 (**C**H), 118.2 (**C**H), 117.7 (**C**), 69.3 (**C**H₂) ppm. **LRMS** (EI$^+$): 231 ([M-H]$^{+\bullet}$, 90%), 202 (100%). These data are consistent with literature values.[12]



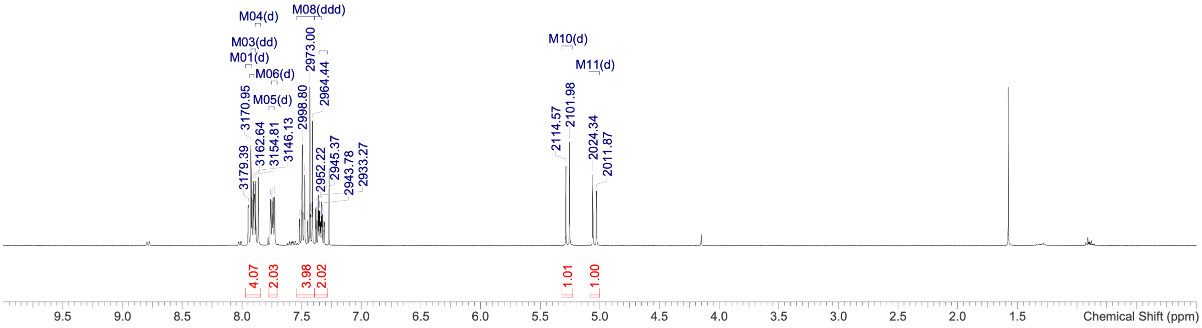


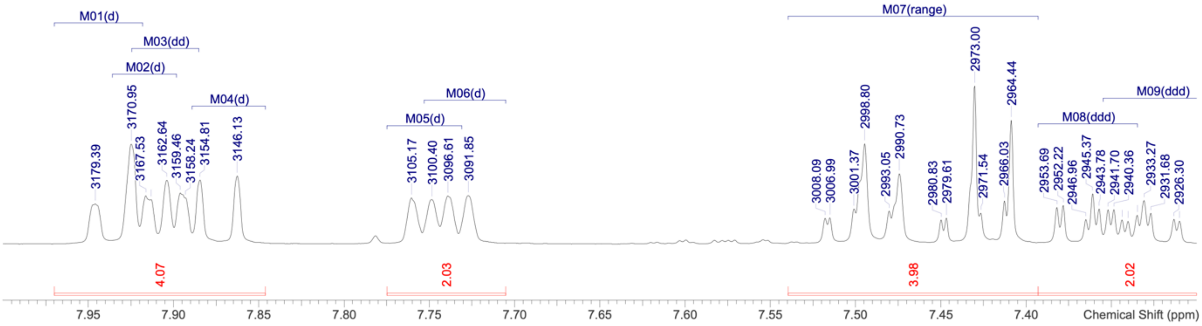


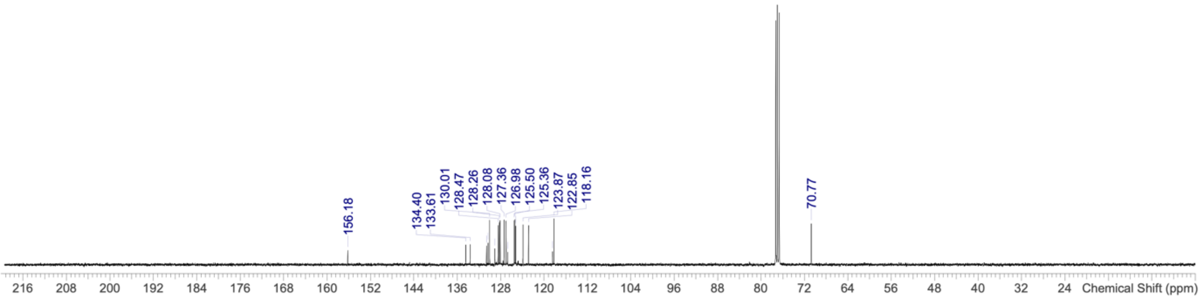
4*H*-Benzo[*f*]naphtho[2,1-*c*]chromene, **25**.



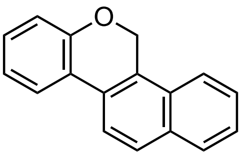
Using the flow photochemical set-up, a solution of iodonaphthyl ether **21** (750 mg, 1.83 mmol) in MeCN (91 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (20 mL) were added. The aqueous phase was separated and extracted with DCM (4 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (2.5% acetone in petrol) to afford the title compound **25** (139 mg, 0.494 mmol, 27%) as a pale pink solid. **MP**: 169 – 171 °C, **IR** ν_{max} (film, cm^{-1}): 3052 (br), 1617 (w), 1592 (w), 1508 (m), 1465 (w), 1334 (w), 1238 (s), 1214 (w), 1050 (m), 1006 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.94 (1 H, br d, *J* = 8.4 Hz, Ar**H**), 7.92–7.86 (3 H, m, 3 × Ar**H**), 7.75 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.74 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.50 (1 H, obscured, Ar**H**), 7.49 (1 H, d, *J* = 8.7 Hz, Ar**H**), 7.43 (1 H, obscured, Ar**H**), 7.42 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.36 (1 H, ddd, *J* = 8.3, 6.7, 1.4 Hz, Ar**H**), 7.33 (1 H, ddd, *J* = 8.4, 6.8, 1.4 Hz, Ar**H**), 5.27 (1 H, d, *J* = 12.8 Hz, C**H**H), 5.04 (1 H, d, *J* = 12.5 Hz, CH**H**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.2 (**C**), 134.4 (**C**), 133.6 (**C**), 130.6 (**C**), 130.3 (**C**), 130.0 (**C**H), 129.0 (**C**), 128.5 (**C**H), 128.3 (**C**H), 128.1 (**C**H), 127.4 (**C**H), 127.0 (**C**H), 126.7 (**C**), 125.5 (**C**H), 125.4 (**C**H), 125.2 (**C**H), 123.9 (**C**H), 122.9 (**C**H), 118.4 (**C**), 118.2 (**C**H), 70.8 (**C**H_2) ppm. **LRMS** (ESI+): 283 ($[M+H]^+$, 100%). **HRMS** (ESI+): Found 283.1113, $[M+H]^+$ $C_{21}H_{15}O$ requires 283.1117. These data are consistent with literature values.[7]





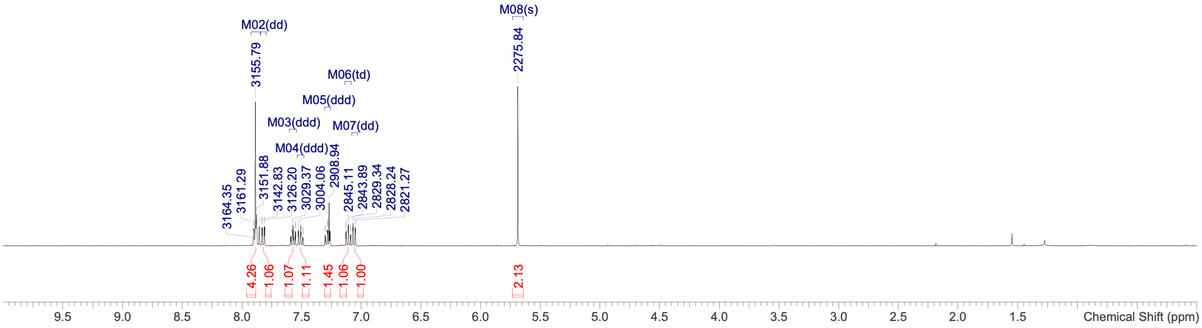


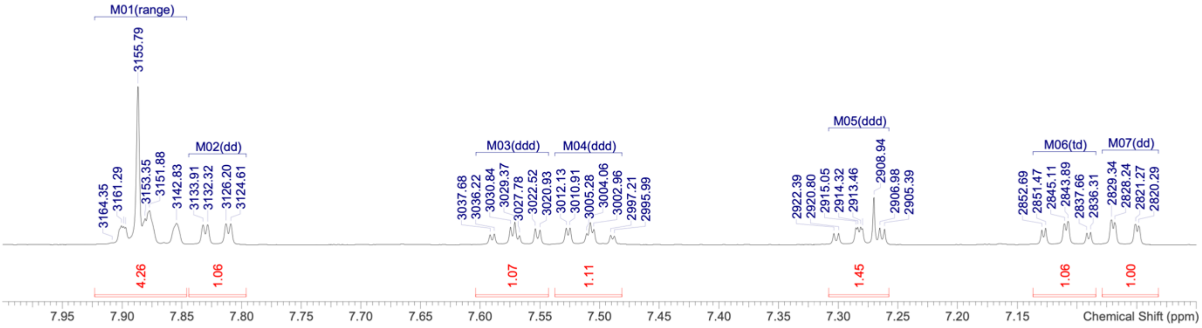
5*H*-Naphtho[1,2-*c*]chromene, **26**.

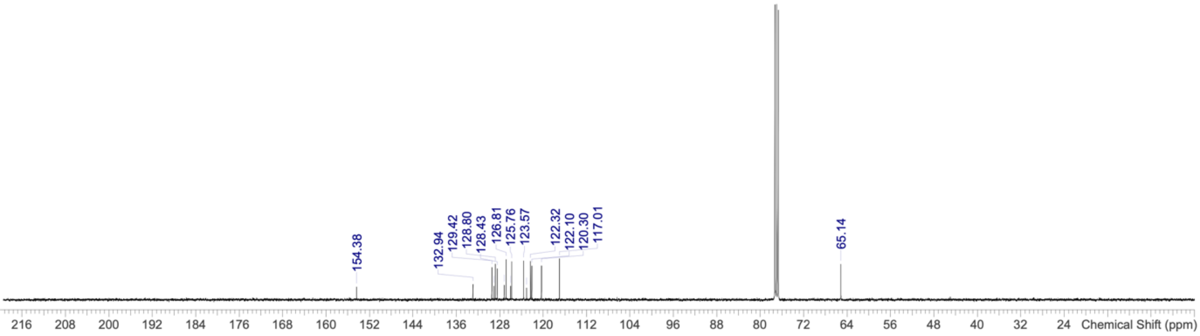


Using the flow photochemical set-up, a solution of aryl iodide **22** (500 mg, 1.39 mmol) in MeCN (70 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (4 × 20 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (15% acetone in petrol) to afford the title compound **26** (251 mg, 1.08 mmol, 78%) as a white solid. **IR** ν_{max} (film, cm^{-1}): 1603 (w), 1488 (w), 1472 (m), 1219 (m), 1189 (m), 1125 (w), 1054 (m), 1006 (w). **^{1}H NMR** (400 MHz, $CDCl_3$): δ

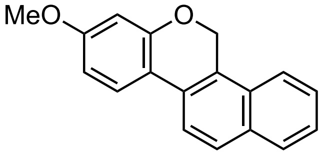
7.92 – 7.85 (4 H, m, 4 × ArH), 7.82 (1 H, dd, *J* = 7.7, 1.6 Hz, ArH), 7.57 (1 H, ddd, *J* = 8.4, 6.9, 1.5 Hz, ArH), 7.51 (1 H, ddd, *J* = 8.1, 6.9, 1.2 Hz, ArH), 7.28 (1 H, ddd, *J* = 8.1, 7.4, 1.6 Hz, ArH), 7.11 (1 H, app. td, *J* = 7.6, 1.3 Hz, ArH), 7.06 (1 H, dd, *J* = 8.0, 1.0 Hz, ArH), 5.69 (2 H, s, CH_2) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.4 (**C**), 132.9 (**C**), 129.4 (**C**H), 129.1 (**C**), 128.8 (**C**H), 128.4 (**C**H), 127.2 (**C**), 126.8 (**C**H), 126.0 (**C**), 125.8 (**C**H), 123.6 (**C**H), 123.0 (**C**), 122.3 (**C**H), 122.1 (**C**H), 120.3 (**C**H), 117.0 (**C**H), 65.1 (**C**H_2) ppm. **LRMS** (ESI+): 232 ([M]$^{+\bullet}$, 75%), 231 (100%), 207 (90%), 202 (63%).[13]



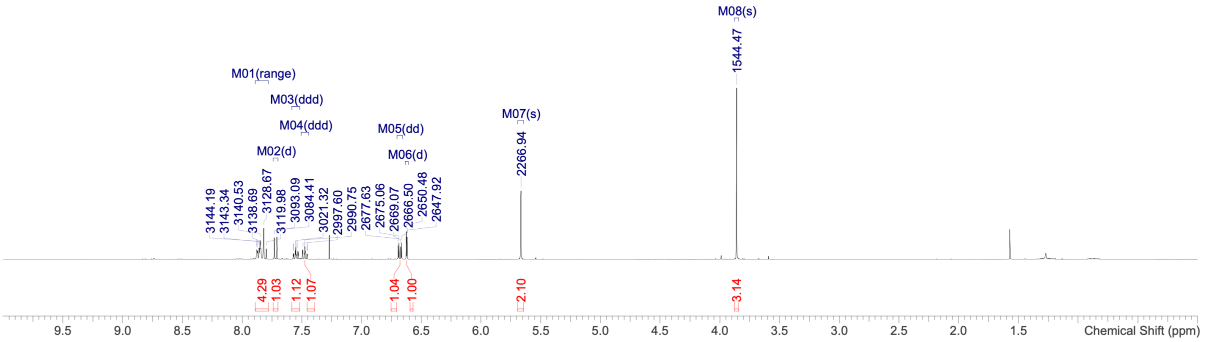


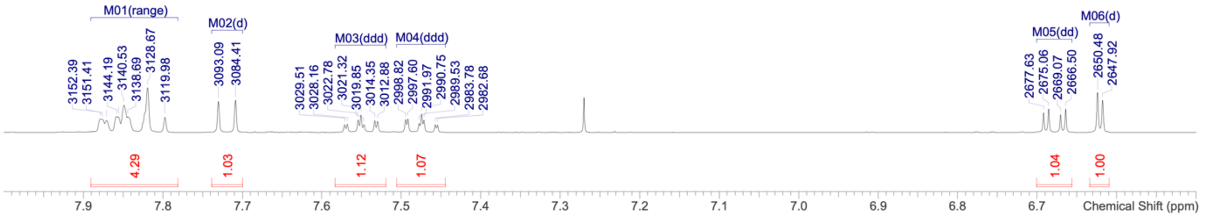


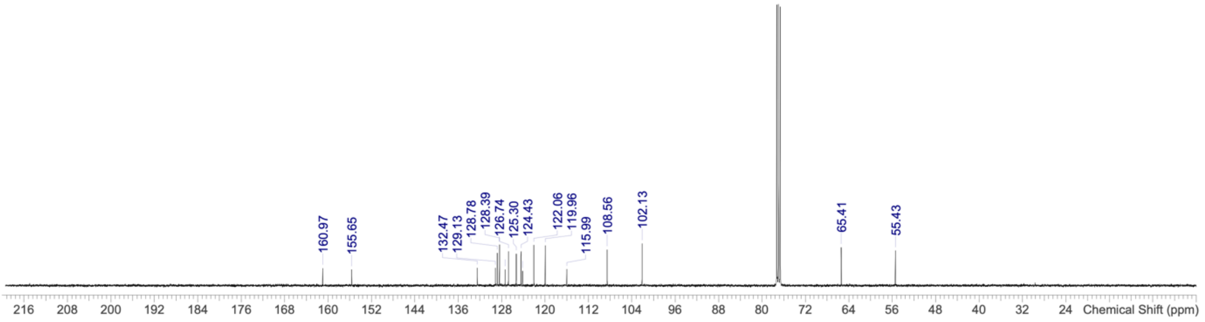
8-Methoxy-5*H*-naphtho[1,2-*c*]chromene, **27**.



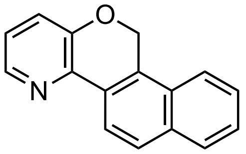
Using the flow photochemical set-up, a solution of iodoaryl ether **23** (390 mg, 1.00 mmol) in MeCN (50 mL, 0.02 M) was irradiated for a residence time of 1 h then concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **27** (130 mg, 0.50 mmol, 50%) as a white solid. **MP**: 132 – 135 °C, **IR** ν_{max} (film, cm^{-1}): 2956 (w), 1607 (m), 1501 (m), 1458 (m), 1313 (m),1270 (s), 1191 (w), 1164 (w), 1032 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 – 7.89 (4 H, m, 4 × ArH), 7.72 (1 H, d, *J* = 8.7 Hz, ArH), 7.55 (1 H, ddd, *J* = 8.3, 6.9, 1.4 Hz, ArH), 7.47 (1 H, ddd, *J* = 8.1, 6.9, 1.2 Hz, ArH), 6.68 (1 H, dd, *J* = 8.6, 2.6 Hz, ArH), 6.62 (1 H, d, *J* = 2.6 Hz, ArH), 5.67 (2 H, s, CH_2), 3.86 (3 H, s, OCH_3) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.0 (**C**), 155.7 (**C**), 132.5 (**C**), 129.1 (**C**), 128.8 (**C**H), 128.4 (**C**H), 127.4 (**C**), 126.7 (**C**H), 125.3 (**C**H), 124.4 (**C**H), 124.2 (**C**), 122.1 (**C**H), 120.0 (**C**H), 116.0 (**C**), 108.6 (**C**H), 102.1 (**C**H), 65.4 (**C**H_2), 55.4 (**C**H_3) ppm. **LRMS** (ESI+): 263 ([M+H]$^+$, 100%). **HRMS** (APPI): Found 262.0985, [M+H]$^+$ $C_{18}H_{14}O$ requires 262.0988.[13]



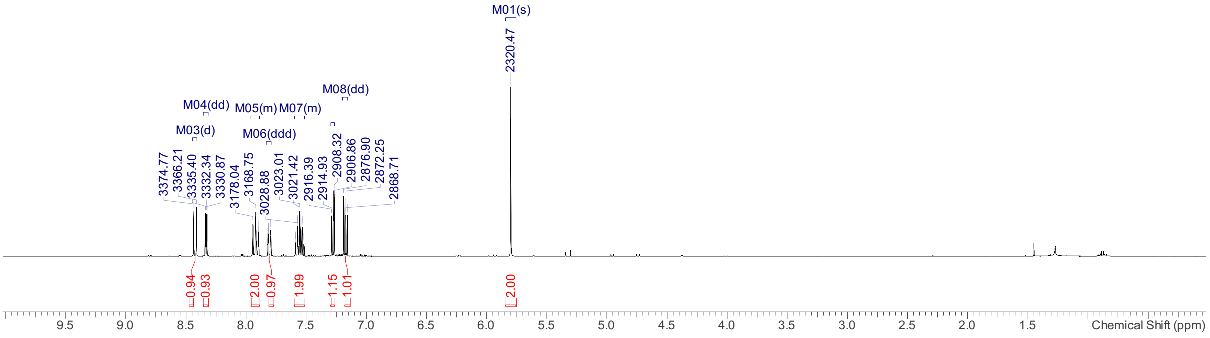


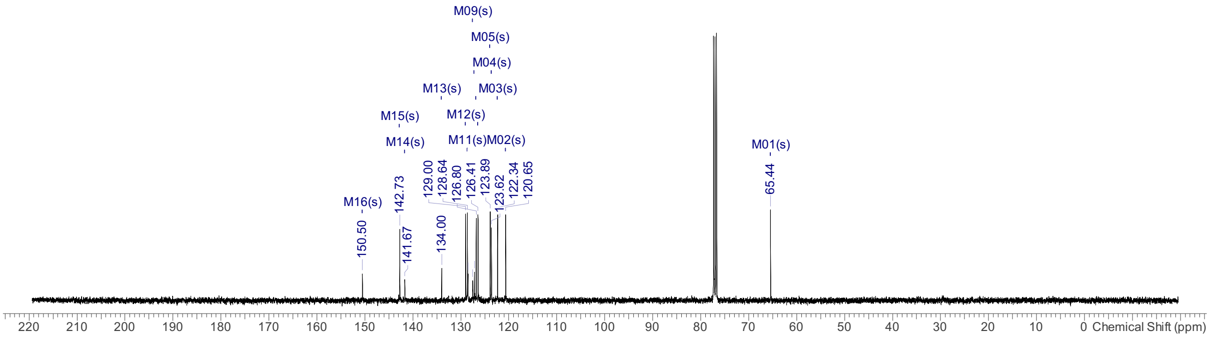


11*H*-Benzo[7,8]isochromeno[4,3-*b*]pyridine, **28**.

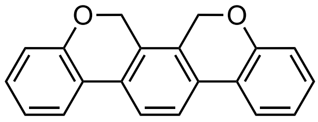


Using the flow photochemical set-up, a solution of 2-iodopyrid-3-yl ether **24** (400 mg, 1.11 mmol) in MeCN (55 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (20 – 40% EtOAc/petrol) to afford the title compound **28** (117 mg, 0.50 mmol, 45%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 3060 (br), 1465 (s), 1423 (s), 1276 (s), 1205 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.42 (1H, d, *J* = 8.6 Hz, Ar**H**), 8.33 (1H, dd, *J* = 4.5, 1.5 Hz, Ar**H**), 7.94 – 7.89 (2H, m, 2 × Ar**H**), 7.81 (1H, ddd, *J* = 8.0, 2.1, 0.9 Hz, Ar**H**), 7.59 – 7.52 (2H, m, 2 × Ar**H**), 7.28 (1H, dd, *J* = 8.0, 1.5 Hz, Ar**H**), 7.17 (1H, dd, *J* = 8.2, 4.7 Hz, Ar**H**), 5.80 (2H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.5 (**C**), 142.7 (**C**H), 141.7 (**C**), 134.0 (**C**), 129.0 (**C**H), 128.6 (**C**H), 128.5 (**C**), 127.5 (**C**), 127.2 (**C**), 126.8 (**C**H), 126.4 (**C**H), 123.9 (**C**H), 123.6 (**C**H), 122.3 (**C**H), 120.7 (**C**H), 65.4 (**C**H$_2$) ppm. **LRMS** (ESI$^+$): 234 [M+H]$^+$. **HRMS** (ESI$^+$): Found 234.0919, $C_{16}H_{12}NO$ [M+H]$^+$ requires 234.0913.

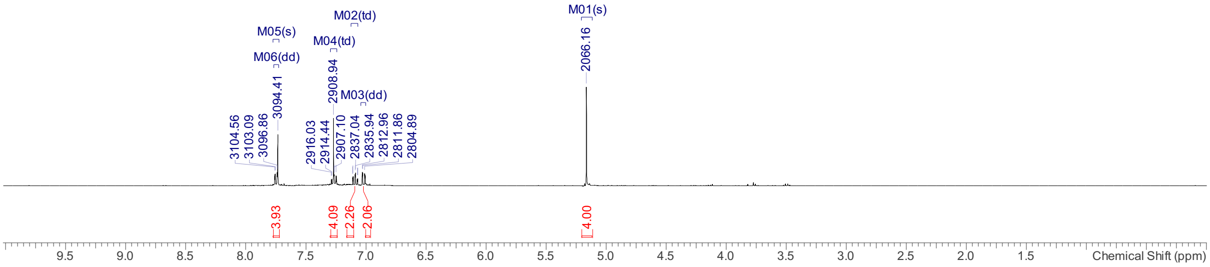


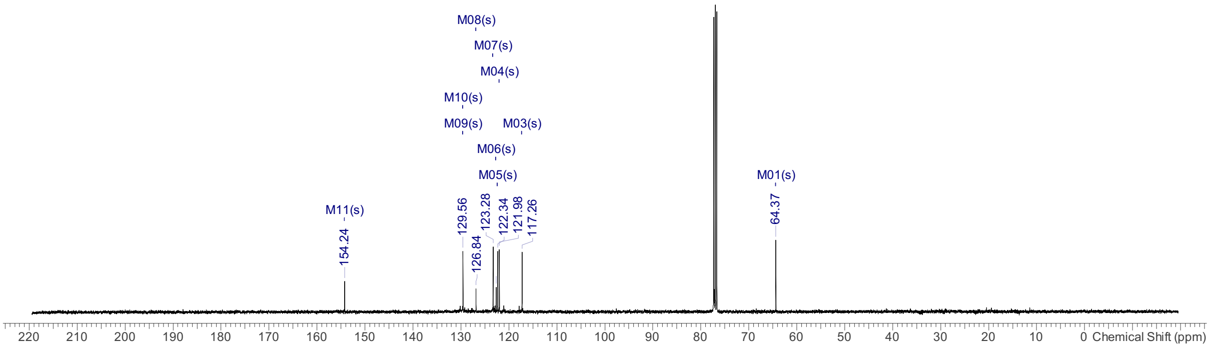


6,7-Dihydrobenzo[2,1-*c*:3,4-*c′*]dichromene, **31**.

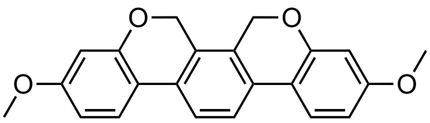


Using the flow photochemical set-up, a solution of diiodide **29** (300 mg, 0.55 mmol) in MeCN (55 mL, 0.01 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 20% Et_2O/petrol) to afford the title compound **31** (108 mg, 0.38 mmol, 69%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 2923 (br), 1605 (m), 1468 (s), 1216 (s), 1041 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75 (2H, dd, *J* = 7.7, 1.5 Hz, 2 × Ar**H**), 7.73 (2H, s, 2 × Ar**H**), 7.27 (2H, td, *J* = 7.7, 1.6 Hz, 2 × Ar**H**), 7.09 (2H, td, *J* = 7.6, 1.2 Hz, 2 × Ar**H**), 7.02 (2H, dd, *J* = 8.1, 1.2 Hz, 2 × Ar**H**), 5.16 (4H, s, 2 × C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.2 (2 × **C**), 129.58 (2 × **C**), 129.56 (2 × **C**H), 126.8 (2 × **C**), 123.3 (2 × **C**H), 122.7 (2 × **C**), 122.3 (2 × **C**H), 122.0 (2 × **C**H), 117.3 (2 × **C**H), 64.4 (2 × **C**H$_2$) ppm. **LRMS** (EI): 286 (100%, M^+), 255 (21%), 142 (20%). **HRMS** (EI): Found 286.0988, $C_{20}H_{14}O_2$, M^+ requires 286.098.



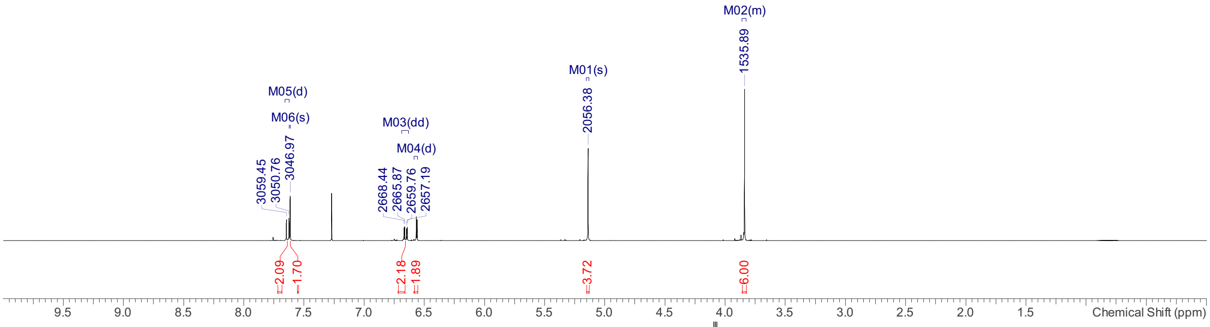


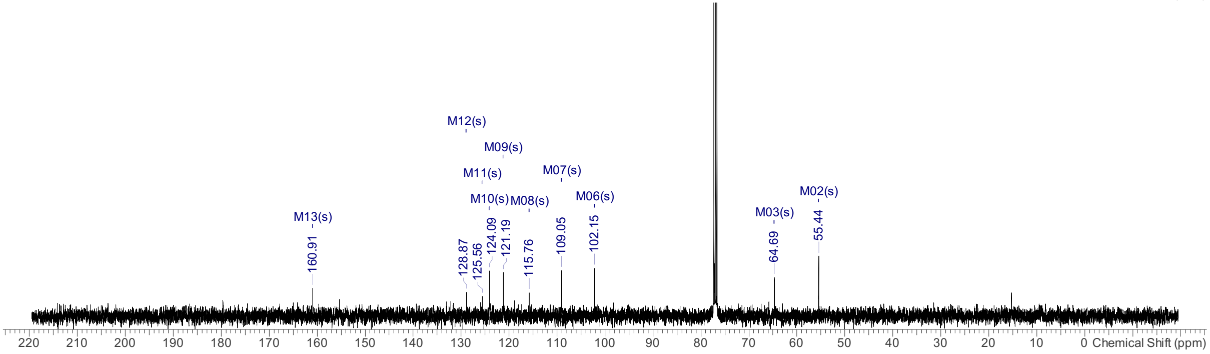
3,10-Dimethoxy-6,7-dihydrobenzo[2,1-*c*:3,4-*c′*]dichromene, **32**.



Using the flow photochemical set-up, a solution of diiodide **30** (450 mg, 0.75 mmol) in MeCN (75 mL, 0.01 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 20% Et_2O/petrol) to afford the title compound **32** (138 mg, 0.40 mmol, 53%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 2957 (br), 1619 (s), 1472 (s), 1274 (s), 1157 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.64 (2H, d, *J* = 8.7 Hz, 2 × Ar**H**), 7.61 (2H, s, 2 × Ar**H**), 6.65 (2H, dd, *J* = 8.7, 2.6 Hz, 2 × Ar**H**), 6.56 (2H, d, *J* = 2.7 Hz, 2 × Ar**H**), 5.14 (4H, s, 2 × C**H**$_2$), 3.84 (6H, s, 2 × C**H**$_3$) ppm. **^{13}C NMR** (100 MHz,

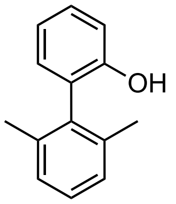
$CDCl_3$) δ 160.9 (2 × **C**), 128.9 (2 × **C**), 125.6 (2 × **C**), 124.1 (2 × **C**H), 121.2 (2 × **C**H), 115.8 (2 × **C**), 109.1 (2 × **C**H), 102.2 (2 × **C**H), 64.7 (2 × **C**H_2), 55.4 (2 × **C**H_3) ppm. **LRMS** (EI): 346 (100%, M^+), 207 (70%). **HRMS** (EI): Found 346.1200, $C_{22}H_{19}O_4$, M^+ requires 346.1200.

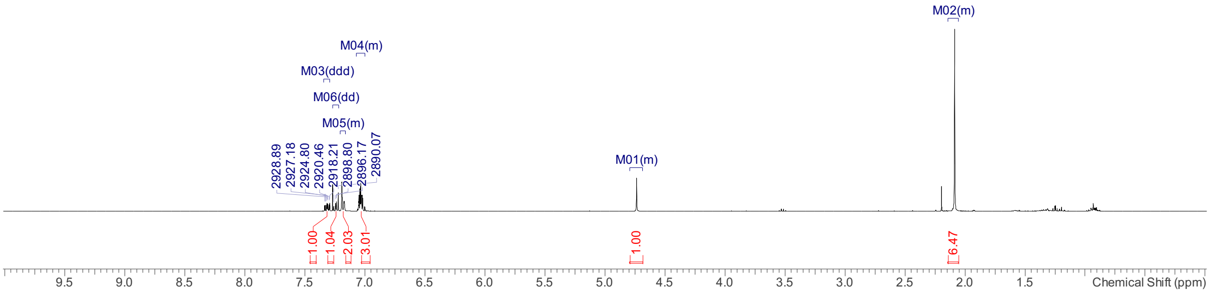


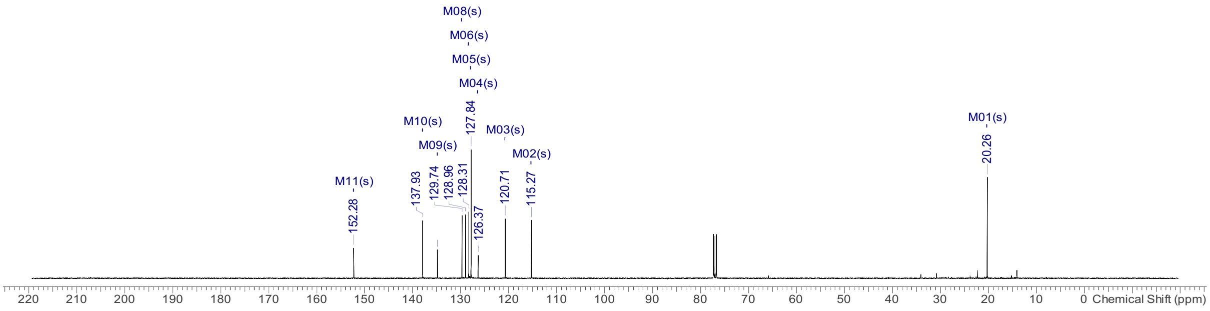


2',6'-Dimethyl-[1,1'-biphenyl]-2-ol, **33a**.

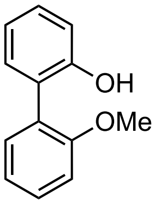
Using the flow photochemical set-up, a solution of benzyl *ortho*-iodoaryl ether **5n** (620 mg, 1.83 mmol) in MeCN (94 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (40 – 60% EtOAc/petrol) to afford the title compound **33a** (257 mg, 1.30 mmol, 77%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 3488 (br), 3038 (br), 1577 (m), 1488 (s), 1465 (s), 1223 (s), 1193 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.31 (1 H, ddd, *J* = 8.2, 6.6, 2.5 Hz, Ar**H**), 7.24 (1 H, dd, *J* = 8.7, 6.1 Hz, Ar**H**), 7.20 – 7.16 (2 H, m, 2 × Ar**H**), 7.06 – 7.00 (3 H, m, 3 × Ar**H**), 4.74 (1 H, s, O**H**), 2.09 (6 H, s, 3 × CH_3) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 152.3 (**C**), 137.9 (**C**), 134.8 (**C**), 129.7 (**C**H), 129.0 (**C**H), 128.3 (**C**H), 127.8 (2 × **C**H), 126.4 (**C**H), 120.7 (**C**), 115.3 (**C**H), 20.3 (2 × **C**H_3) ppm. **LRMS** (EI): 198.2 (81%, M^+), 183 (100%). **HRMS** (EI): Found 198.1039, $C_{14}H_{14}O$, M^+ requires 198.1039.[14]



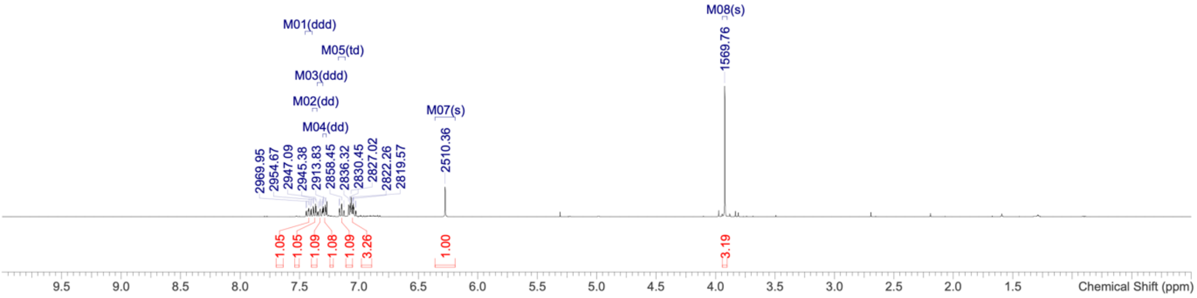


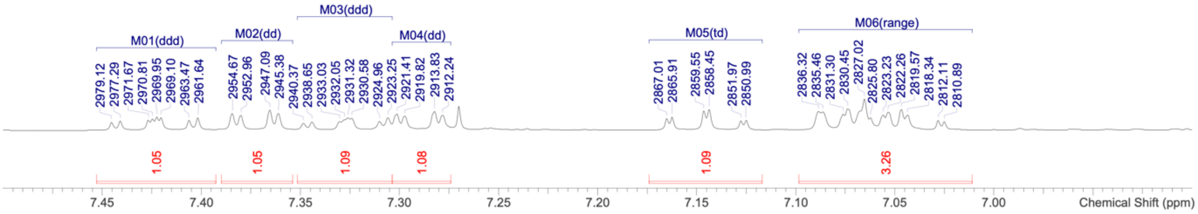


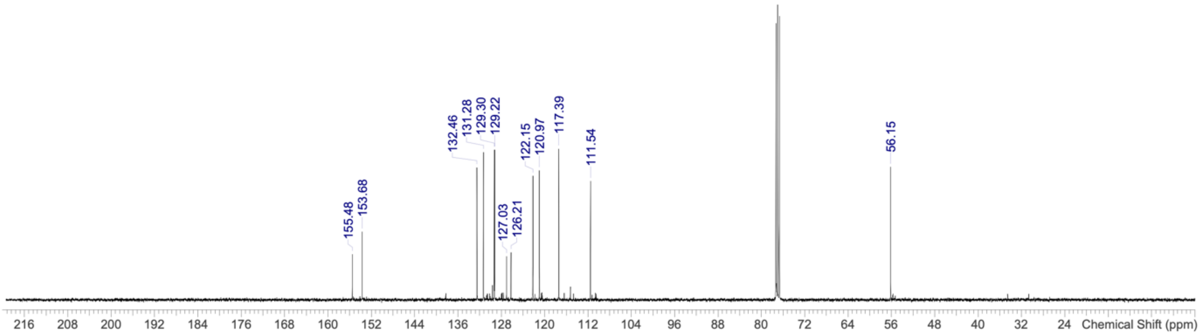
2'-Methoxy-[1,1'-biphenyl]-2-ol, **33c**.



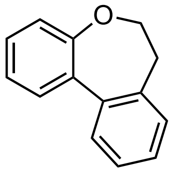
Using the flow photochemical set-up, a solution of benzyl *ortho*-iodoaryl ether **7p** (701 mg, 2.06 mmol) in MeCN (103 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (20 mL) and sat. $Na_2S_2O_3$ (20 mL) were added. The aqueous phase was separated and extracted with DCM (2 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% EtOAc in petrol) to afford the title compound **33c** (0.164 mg, 0.82 mmol, 40%) as a colourless oil. **IR** ν_{max} (film, cm^{-1}): 3390 (br), 1497 (m), 1480 (m), 1456 (m), 1272 (m), 1230 (s), 1178 (w), 1020 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.42 (1 H, ddd, *J* = 8.3, 7.5, 1.8 Hz, Ar**H**), 7.37 (1 H, dd, *J* = 7.6, 1.7 Hz, Ar**H**), 7.33 (1 H, ddd, *J* = 8.2, 7.3, 1.7 Hz, Ar**H**), 7.29 (1 H, dd, *J* = 7.6, 1.6 Hz, Ar**H**), 7.15 (1 H, app. td, *J*= 7.5, 1.0 Hz, Ar**H**), 7.01 – 7.10 (3 H, m, 3 × Ar**H**), 6.27 (1 H, s, O**H**), 3.92 (3 H, s, OC**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.5 (**C**), 153.7 (**C**), 132.5 (**C**H), 131.3 (**C**H), 129.3 (**C**H), 129.2 (**C**H), 127.0 (**C**), 126.2 (**C**), 122.2 (**C**H), 121.0 (**C**H), 117.4 (**C**H), 111.5 (**C**H), 56.2 (**C**H$_3$) ppm. **LRMS** (ESI+): 201 ([M+H]$^+$, 100%). These data are consistent with literature values.[15]





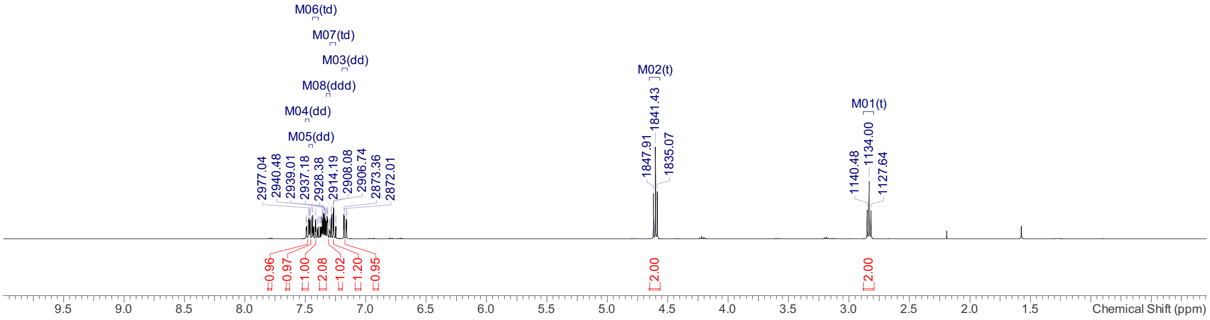


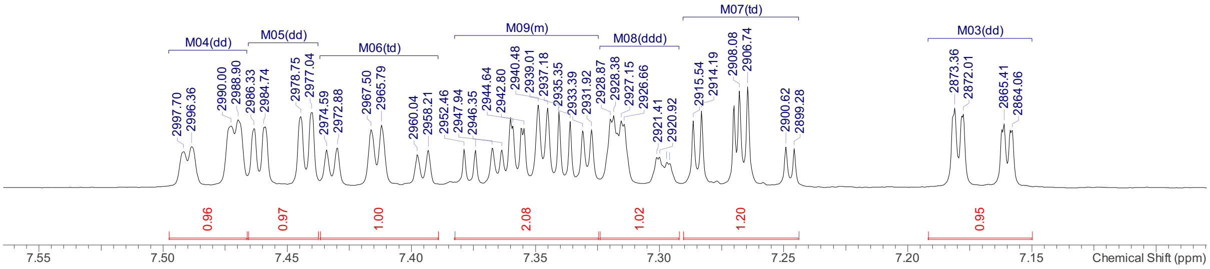
6,7-Dihydrodibenzo[*b*,*d*]oxepine, **39a**.

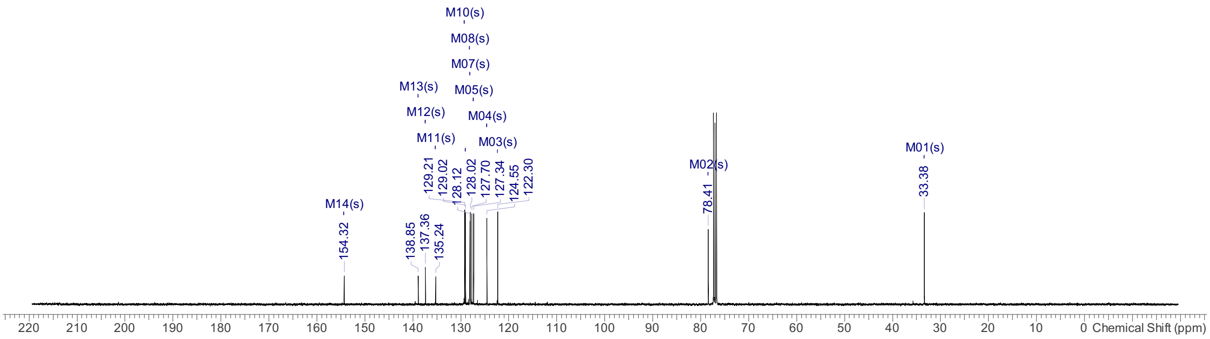


Using the flow photochemical set-up, a solution of homobenzyl *ortho*-iodophenyl ether **38a** (324 mg, 1.00 mmol) in MeCN (50 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 15% Et_2O/petrol) to afford the title compound **39a** (117 mg, 0.61 mmol, 61%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 3024 (br), 2871 (br), 1481 (s), 1437 (s), 1251 (m), 1221 (m), 1027 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (1 H, br dd, *J* = 7.5, 1.2 Hz, Ar**H**), 7.45 (1 H, dd, *J* = 7.6, 1.7 Hz, Ar**H**), 7.41 (1 H, app td, *J* = 7.3, 1.8 Hz, Ar**H**), 7.38 – 7.33 (2 H, m, 2 × Ar**H**), 7.31 (1 H, br dd, *J* = 7.1, 1.6 Hz, Ar**H**), 7.27 (1 H, dd, *J* = 7.5, 1.3 Hz, Ar**H**), 7.17 (1 H, dd, *J* = 8.0, 1.3 Hz, Ar**H**), 4.60 (2 H, t, *J* = 6.4 Hz, C**H**$_2$), 2.83 (2 H, t, *J* = 6.3 Hz, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.3 (**C**), 138.9 (**C**), 137.4 (**C**), 135.2 (**C**), 129.2 (**C**H), 129.0 (**C**H), 128.1 (**C**H), 128.0 (**C**H), 127.7 (**C**H), 127.3 (**C**H), 124.6 (**C**H), 122.3 (**C**H), 78.4 (**C**H$_2$), 33.4 (**C**H$_2$) ppm. **LRMS** (ESI$^+$): 197

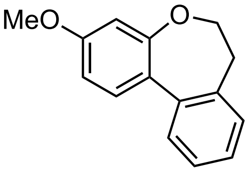
[M+H]$^+$. **HRMS** (ESI$^+$): Found 197.0962, $C_{14}H_{13}O$ [M+H]$^+$ requires 197.0961. These data are consistent with literature values.[16]



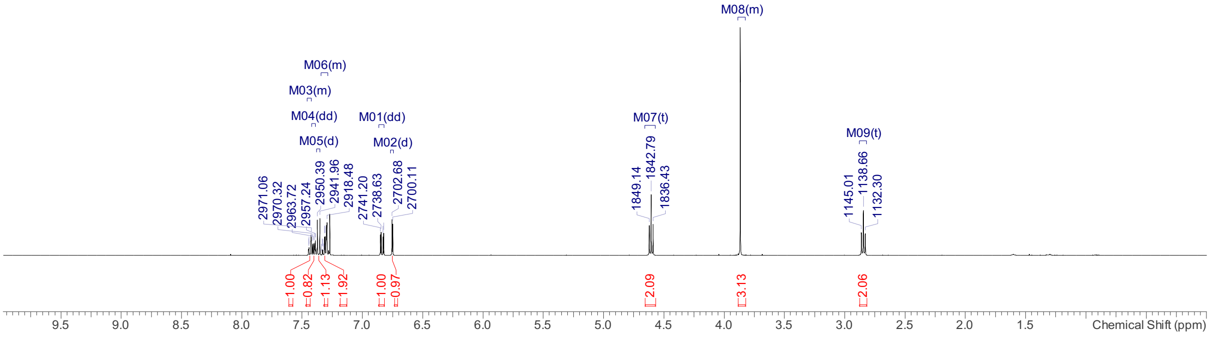


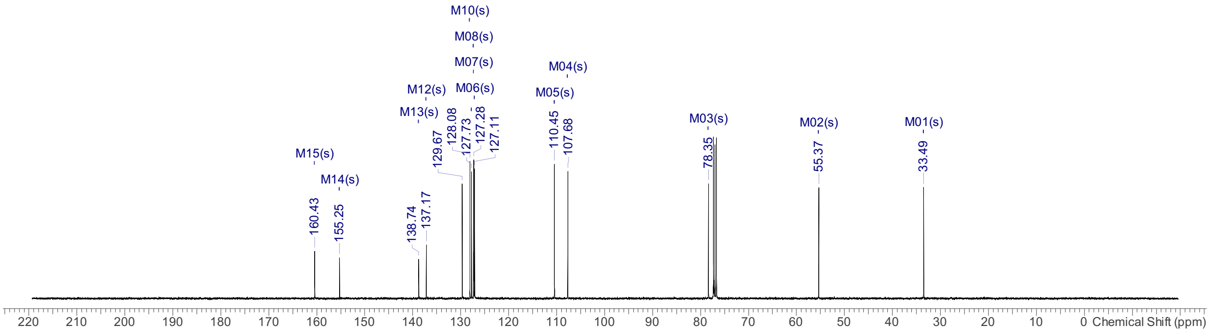


3-Methoxy-6,7-dihydrodibenzo[*b*,*d*]oxepine, **39b**.

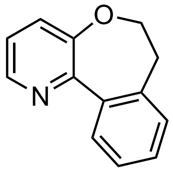


Using the flow photochemical set-up, a solution of homobenzyl *ortho*-iodoaryl ether **38b** (412 mg, 1.16 mmol) in MeCN (60 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (10 – 20% Et_2O/petrol) to afford the title compound **39b** (186 mg, 0.82 mmol, 71%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 3024 (br), 1608 (s), 1482 (s), 1281 (s), 1157 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43 (1 H, m, Ar**H**), 7.40 (1 H, dd, *J* = 6.5, 2.1 Hz, Ar**H**), 7.36 (1 H, d, *J* = 8.4 Hz, Ar**H**), 7.34 – 7.29 (2 H, m, 2 × Ar**H**), 6.84 (1 H, dd, *J* = 8.5, 2.6 Hz, Ar**H**), 6.75 (1 H, d, *J* = 2.6 Hz, Ar**H**), 4.61 (2 H, t, *J* = 6.4 Hz, C**H**$_2$), 3.87 (3 H, s, C**H**$_3$), 2.85 (2 H, t, *J* = 6.4 Hz, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.4 (**C**), 155.3 (**C**), 138.7 (**C**), 137.2 (**C**), 129.7 (**C**H), 128.0 (**C**H), 127.7 (**C**H), 127.32 (**C**), 127.28 (**C**H), 127.1 (**C**H), 110.5 (**C**H), 107.7 (**C**H), 78.4 (**C**H$_2$), 55.4 (**C**H$_3$), 33.5 (**C**H$_2$) ppm. **LRMS** (ESI$^+$): 227 [M+H]$^+$. **HRMS** (ESI$^+$): Found 227.1069, $C_{15}H_{15}O_2$ [M+H]$^+$ requires 227.1067.

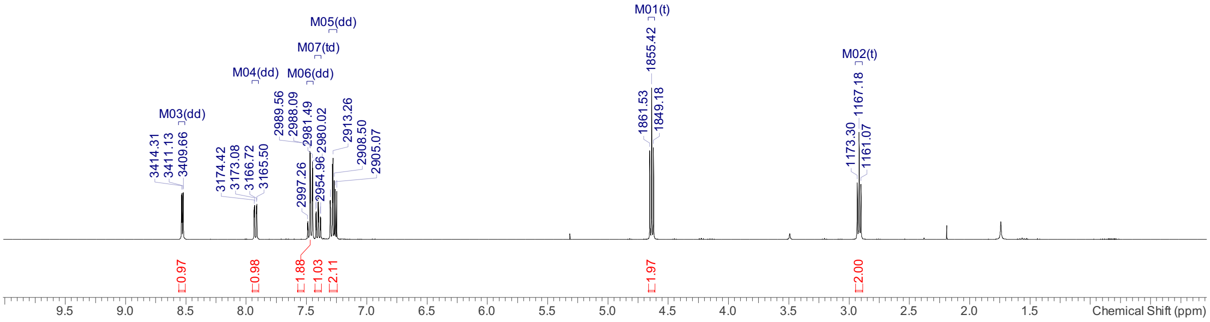


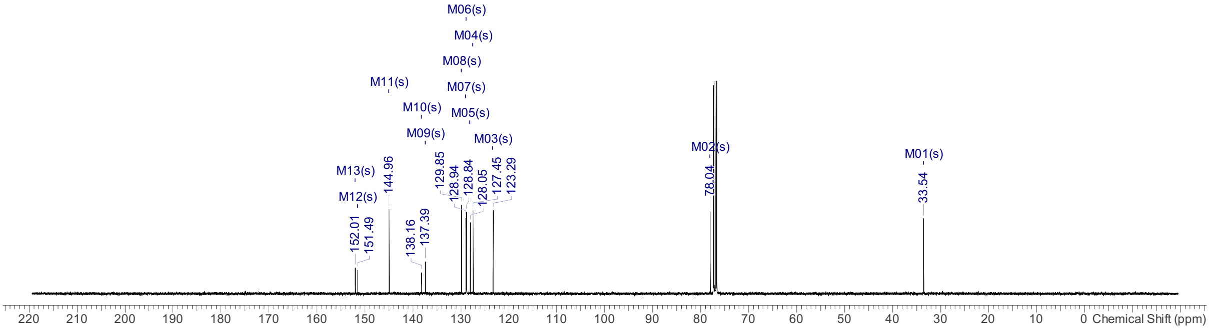


6,7-Dihydrobenzo[4,5]oxepino[3,2-*b*]pyridine, **39c**.

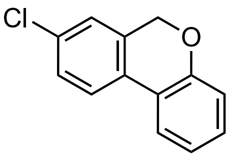


Using the flow photochemical set-up, a solution of homobenzyl 2-iodopyrid-3-yl ether **38c** (570 mg, 1.75 mmol) in MeCN (88 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (10 – 40% Et_2O/petrol) to afford the title compound **39c** (218 mg, 1.10 mmol, 63%) as a yellow oil. **IR** ν_{max} (film, cm^{-1}): 2924 (br), 1557 (s), 1442 (s), 1410 (s), 1286 (s), 1198 (m), 1041 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.53 (1H, dd, *J* = 4.7, 1.5 Hz, Ar**H**), 7.92 (1H, dd, *J* = 7.6, 1.3 Hz, Ar**H**), 7.49 – 7.45 (1H, m, Ar**H**), 7.46 (1H, dd, *J* = 8.1, 1.5 Hz, Ar**H**), 7.40 (1H, td, *J* = 7.5, 1.5 Hz, Ar**H**), 7.31 – 7.28 (1H, m, Ar**H**), 7.27 (1H, dd, *J* = 8.0, 4.6 Hz, Ar**H**), 4.64 (2H, t, *J* = 6.2 Hz, C**H**$_2$), 2.92 (2H, t, *J* = 6.1 Hz, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 152.0 (**C**), 151.5 (**C**), 150.0 (**C**H), 138.3 (**C**), 137.5 (**C**), 129.9 (**C**H), 128.9 (**C**H), 128.8 (**C**), 128.1 (**C**H), 127.4 (**C**H), 123.3 (**C**H), 78.0 (**C**H$_2$), 33.5 (**C**H$_2$) ppm. **LRMS** (ESI^+): 198 $[M+H]^+$. **HRMS** (ESI^+): Found 197.0843, $C_{13}H_{11}NO$ $[M+H]^+$ requires 197.0841.



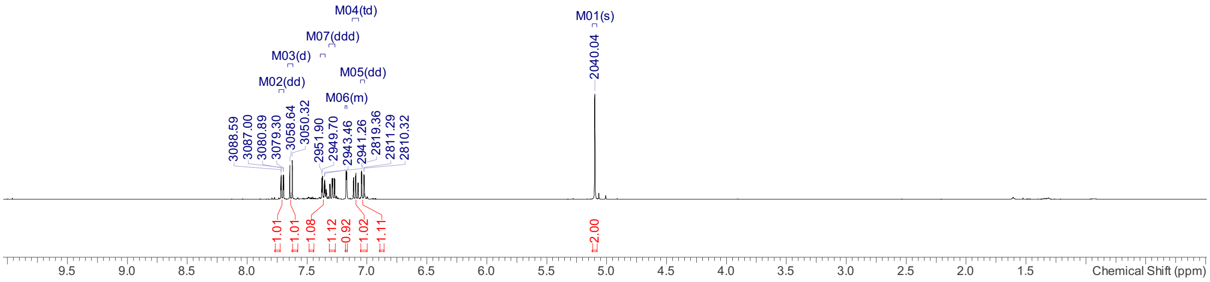


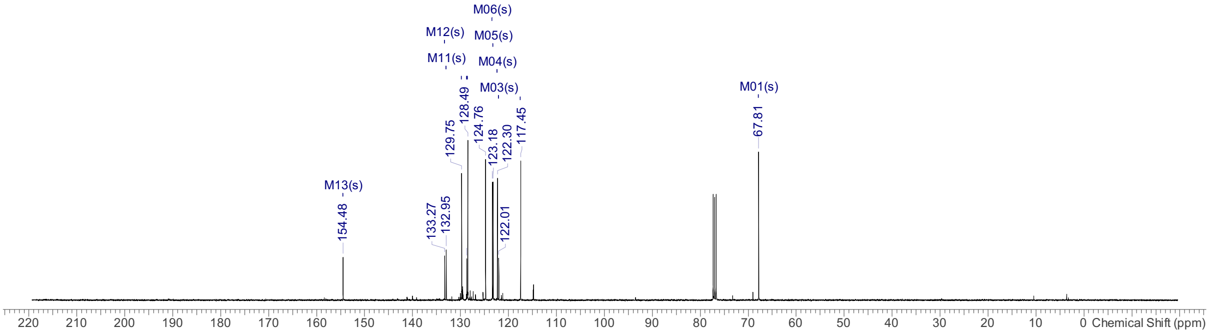
8-Chloro-6*H*-benzo[*c*]chromene, **42**.



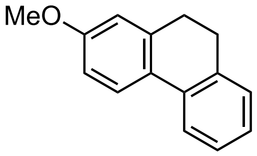
Using the flow photochemical set-up: A solution of benzyl phenyl ether **40** (461 mg, 1.34 mmol) in MeCN (67 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (2 – 10% Et_2O/petrol) to afford the title compound **42** (170 mg, 0.79 mmol, 59%) as a yellow solid. **MP**: 48 – 49 °C. **IR** ν_{max} (film, cm^{-1}): 3063 (br), 2847 (br), 1718 (m), 1606 (w), 1478 (s), 1242 (s), 1195 (w), 1026 (w). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71 (1H, dd, *J* = 7.7, 1.5 Hz, Ar**H**), 7.63 (1H, d, *J* = 8.3 Hz, Ar**H**), 7.36 (1H, dd, *J* = 8.2, 2.2 Hz, Ar**H**), 7.29 (1H, ddd, *J* =

8.2, 7.3, 1.6 Hz, Ar**H**), 7.17 (1H, m, Ar**H**), 7.09 (1H, app td, *J* = 7.6, 1.2 Hz, Ar**H**), 7.03 (1H, dd, *J* = 8.1, 0.9 Hz, Ar**H**), 5.10 (2H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 154.5 (**C**), 133.3 (**C**), 133.0 (**C**), 129.8 (**C**H), 128.7 (**C**), 128.5 (**C**H), 124.8 (**C**H), 123.4 (**C**H), 123.2 (**C**H), 122.3 (**C**H), 122.0 (**C**), 117.5 (**C**H), 67.8 (**C**H$_2$) ppm. **LRMS** (EI): 216 (100%, M$^+$), 181 (16%), 152 (23%). **HRMS** (EI): Found 216.0332, $C_{13}H_9ClO$, M$^+$ requires 216.0336. These data are consistent with literature values.[17]

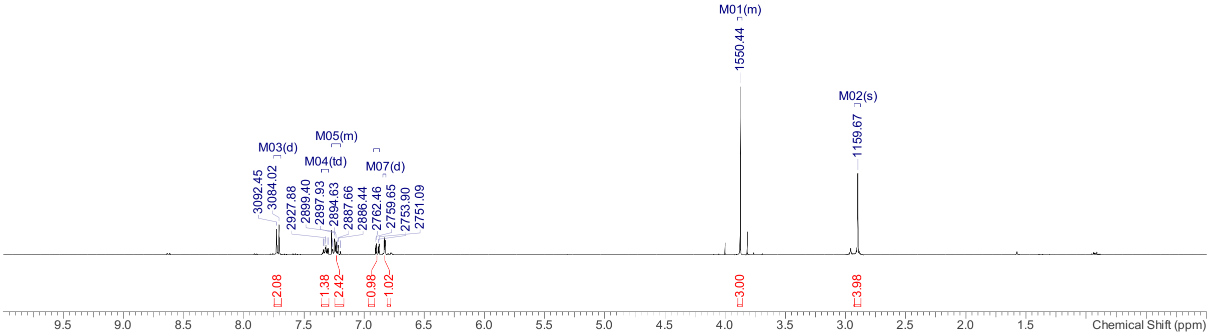


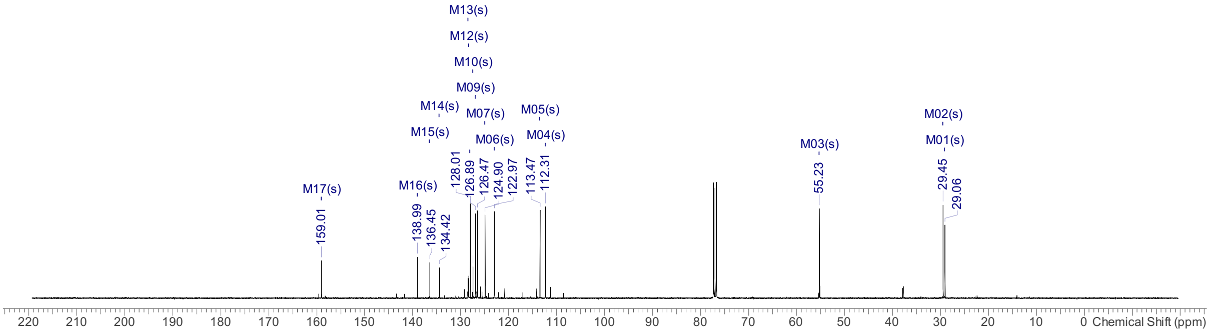


2-Methoxy-9,10-dihydrophenanthrene, **45**.



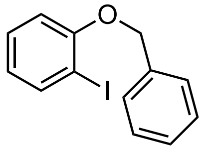
Using the flow photochemical set-up, a solution of aryl iodide **43** (351 mg, 1.03 mmol) in MeCN (50 mL, 0.02 M) was irradiated for a residence time of 1 h. The resulting solution was concentrated *in vacuo* then DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 30 mL), then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 15% Et_2O/petrol) to afford the title compound **45** (144 mg, 0.69 mmol, 67%) as an off-white solid. **MP**: 51 – 52 °C [Lit. 53 – 52 °C].[18] **IR** ν_{max} (film, cm^{-1}): 2934 (br), 1602 (s), 1483 (s), 1453 (s), 1260 (s), 1151 (m), 1043 (s). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 8.44 (1H, d, *J* = 8.4 Hz, Ar**H**), 8.44 (1H, d, *J* = 8.4 Hz, Ar**H**), 7.32 – 7.19 (3H, m, 3 × Ar**H**), 6.89 (1H, dd, *J* = 8.6, 2.8 Hz, Ar**H**), 6.83 (1H, d, *J* = 2.7 Hz, Ar**H**), 3.87 (3H, s, C**H**$_3$), 2.90 (4H, app. s, 2 × C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 159.0 (**C**), 139.0 (**C**), 136.5 (**C**), 134.4 (**C**), 128.0 (**C**H), 127.4 (**C**), 126.9 (**C**H), 126.5 (**C**H), 124.9 (**C**H), 123.0 (**C**H), 113.5 (**C**H), 112.3 (**C**H), 55.2 (**C**H$_3$), 29.5 (**C**H$_2$), 29.1 (**C**H$_2$) ppm. **LRMS** (EI): 210 (100%, M$^+$), 195 (40%), 165 (41%). **HRMS** (EI): Found 210.1039, $C_{15}H_{14}O$, M$^+$ requires 210.1039.[18]



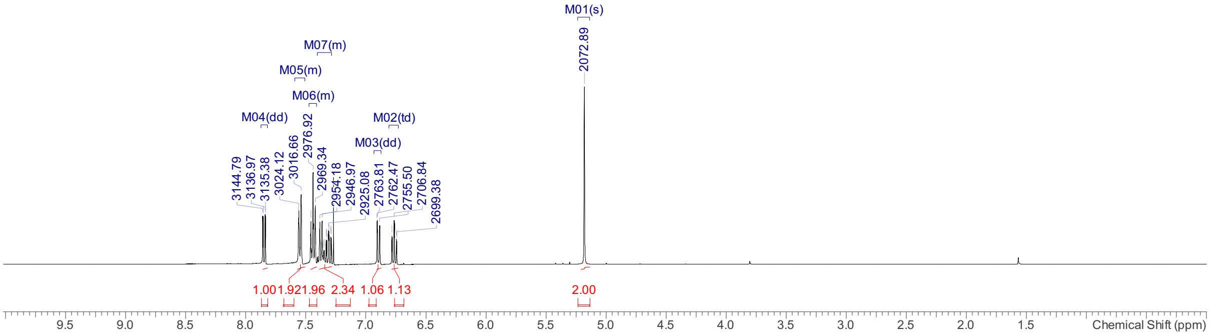


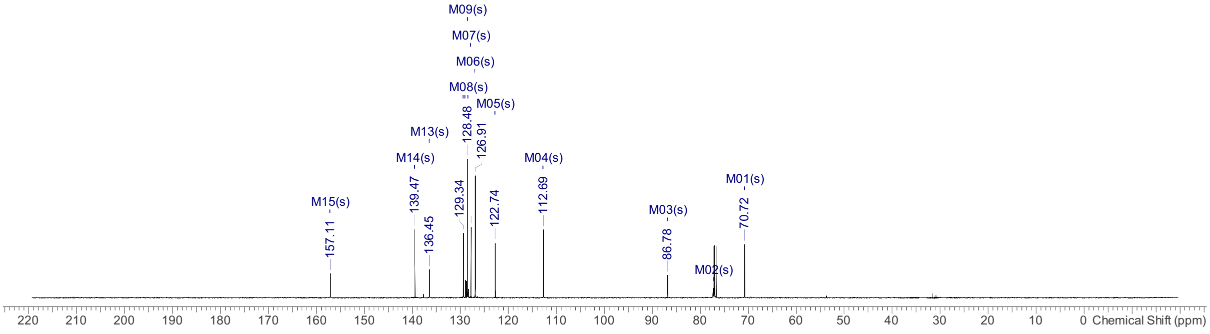
Preparation of Starting Materials

1-(Benzyloxy)-2-iodobenzene, **5a**.[2]

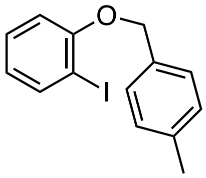


To a solution of 2-iodophenol (2.00 g, 9.1 mmol) in acetone (100 mL) was added benzyl bromide (1.19 mL, 10.0 mmol) and K_2CO_3 (1.89 g, 13.6 mmol). The reaction was heated at reflux for 18 h then cooled to RT, concentrated *in vacuo* and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL). The organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **5a** as an off-white solid (2.69 g, 8.68 mmol, 95 %). **IR** ν_{max} (film, cm^{-1}): 3060 (br), 1596 (s), 1493 (s), 1237 (s), 1217 (s), 1011 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.85 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.56 – 7.54 (2 H, m, 2 × Ar**H**), 7.46 – 7.42 (2 H, m, 2 × Ar**H**), 7.38 – 7.29 (2 H, m, 2 × Ar**H**), 6.90 (1 H, dd, *J* = 8.2, 1.3 Hz, Ar**H**), 6.76 (1 H, td, *J* = 7.6, 1.4 Hz, Ar**H**), 5.18 (2 H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.1 (**C**), 139.5 (**C**H), 136.5 (**C**), 129.3 (**C**H), 128.5 (2 × **C**H), 127.8 (**C**H), 126.9 (2 × **C**H), 122.7 (**C**H), 112.7 (**C**H), 86.8 (**C**), 68.4 (**C**H$_2$) ppm. **LRMS** (EI): 310 (55%, [M$^+$]), 217 (98%), 183 (54%), 89 (100%). **HRMS** (EI): Found 309.9851, $C_{13}H_{11}IO$ [M$^+$] requires 309.9849.

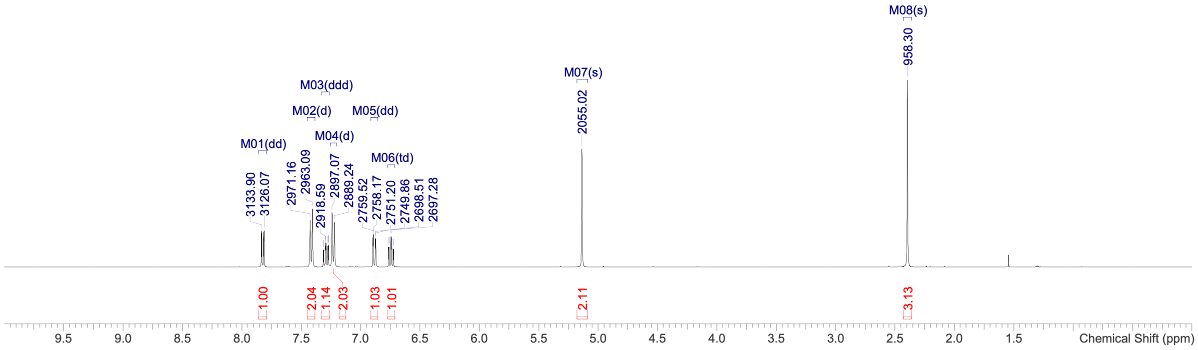


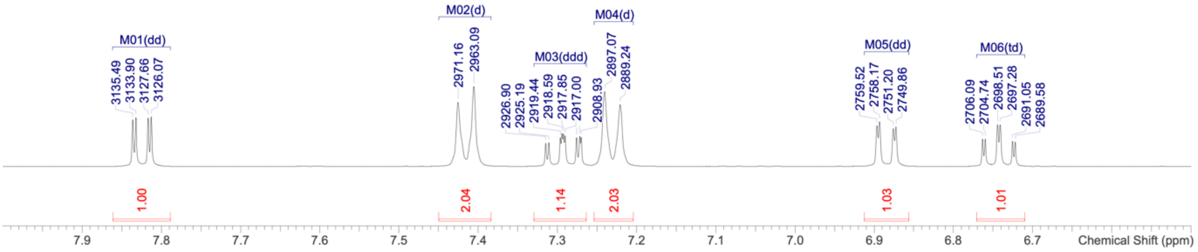


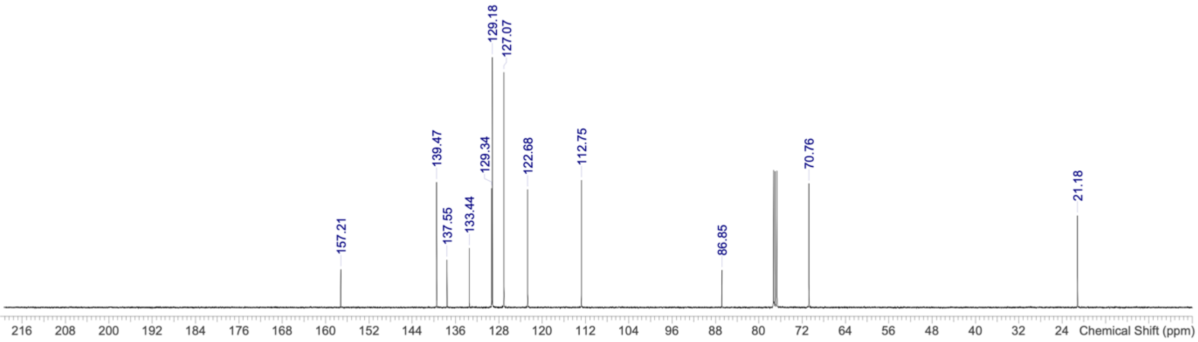
1-Iodo-2-((4-methylbenzyl)oxy)benzene, **5b**.[20]



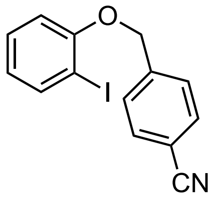
To a solution of 2-iodophenol (1.34 g, 6.10 mmol) in acetone (60 mL) was added 4-methylbenzyl bromide (1.12 g, 6.10 mmol) and K_2CO_3 (1.67 g, 12.1 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the organic phases were combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% EtOAc in petrol) to afford the title compound **5b** (1.75 g, 5.40 mmol, 89%) as a colourless oil. **IR** ν_{max} (film, cm^{-1}): 2919 (w), 1582 (m), 1518 (w), 1471 (s), 1376 (w), 1275 (s), 1245 (s), 1050 (m), 1017 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.42 (2 H, d, *J* = 8.1 Hz, 2 × Ar**H**), 7.29 (1 H, ddd, *J* = 8.3, 7.4, 1.6 Hz, Ar**H**), 7.23 (2 H, d, *J* = 7.8 Hz, 2 × Ar**H**), 6.88 (1 H, dd, *J* = 8.3, 1.3 Hz, Ar**H**), 6.74 (1 H, app. td, *J* = 7.6, 1.4 Hz, Ar**H**), 5.14 (2 H, s, C**H₂**), 2.39 (3 H, s, C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 157.2 (**C**), 139.5 (**C**H), 137.6 (**C**), 133.4 (**C**), 129.3 (**C**H), 129.2 (2 × **C**H), 127.1 (2 × **C**H), 122.7 (**C**H), 112.8 (**C**H), 86.9 (**C**), 70.8 (**C**H$_2$), 21.2 (**C**H$_3$). **LRMS** (EI) 324 ([M]$^+$, 35%), 220 (45%), 195 (75%), 105 (100%).



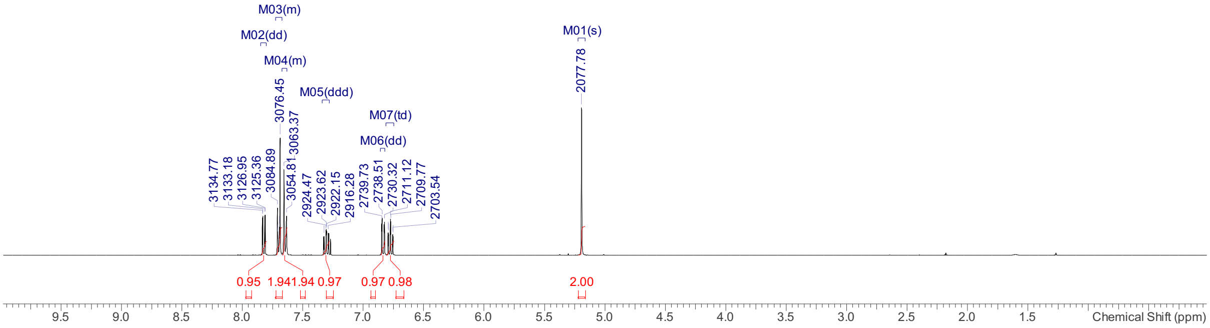


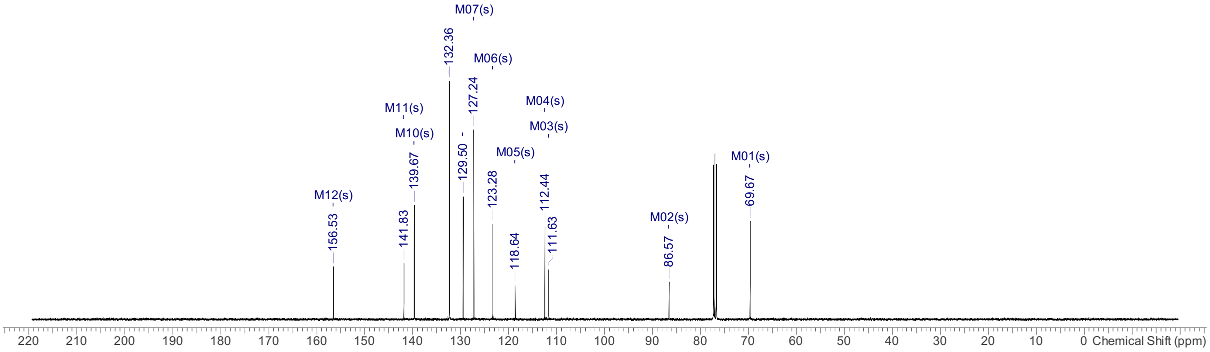


4-((2-Iodophenoxy)methyl)benzonitrile, **5c**.

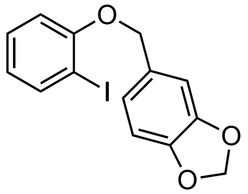


To a solution of 2-iodophenol (1.95 g, 8.86 mmol) in acetone (100 mL) was added 4-cyanobenzyl bromide (1.74 g, 8.88 mmol) and K$_2$CO$_3$ (2.46 g, 17.8 mmol). The reaction was heated at reflux for 18 h then cooled to RT, concentrated *in vacuo* and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL). The organic phases were combined, dried over MgSO$_4$ and concentrated *in vacuo* to afford the title compound **5c** as an off-white solid (2.71 g, 8.09 mmol, 91 %). **IR** ν_{max} (film, cm^{-1}): 3060 (br), 2227 (s), 1474 (s), 1437 (s), 1246 (s), 1017 (s). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 7.82 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.71 – 7.69 (2 H, m, 2 × Ar**H**), 7.66 – 7.63 (2 H, m, 2 × Ar**H**), 7.31 (1 H, ddd, *J* = 8.3, 7.5, 1.6 Hz, Ar**H**), 6.84 (1 H, dd, *J* = 8.2, 1.2 Hz, Ar**H**), 6.77 (1 H, td, *J* = 7.6, 1.3 Hz, Ar**H**), 5.19 (2 H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 156.5 (**C**), 141.8 (**C**), 139.7 (**C**H), 132.4 (2 × **C**H), 129.5 (**C**H), 127.2 (2 × **C**H), 123.3 (**C**H), 118.6 (**C**), 112.4 (**C**H), 111.6 (**C**), 86.6 (**C**), 69.7 (**C**H$_2$) ppm. **LRMS** (EI): 335 (33%, [M$^+$]), 207 (100%), 116 (76%). **HRMS** (EI): Found 334.9799, C$_{14}$H$_{10}$INO [M$^+$] requires 334.9802.

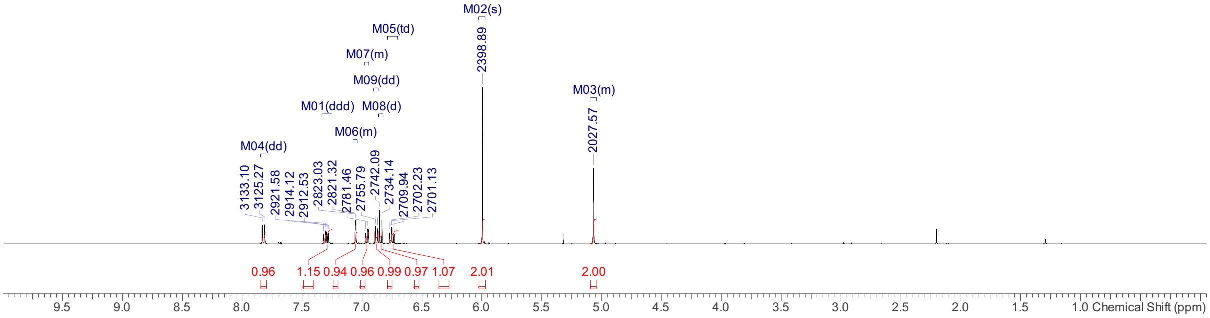


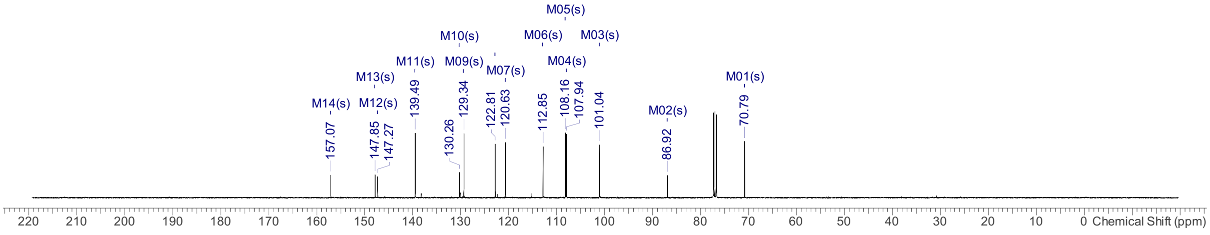


5-((2-Iodophenoxy)methyl)benzo[*d*][1,3]dioxole, **5d**.[20]

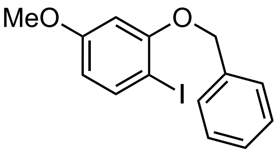


To a solution of 2-iodophenol (1.016 g, 4.62 mmol) in acetone (100 mL) was added 5-(bromomethyl)-1,3-benzodioxole (987 mg, 4.59 mmol) and K_2CO_3 (1.27 g, 9.19 mmol). The reaction was heated at reflux for 18 h then cooled to RT, concentrated *in vacuo* and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL). The organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **5d** as an off-white oil (1.42 g, 4.01 mmol, 87 %). **IR** ν_{max} (film, cm^{-1}): 3057 (br), 1581 (s), 1438 (s), 1243 (s), 1037 (s), 1016 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.30 (1 H, ddd, *J* = 8.2, 7.5, 1.6 Hz, Ar**H**), 7.05 (1 H, m, Ar**H**), 6.96 (1 H, m, Ar**H**), 6.88 (1 H, dd, *J* = 8.3, 1.3 Hz, Ar**H**), 6.84 (1 H, d, *J* = 8.0 Hz, Ar**H**), 6.75 (1 H, td, *J* = 7.6, 1.3 Hz, Ar**H**), 6.00 (2 H, s, C**H**$_2$), 5.07 (2 H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.1 (**C**), 147.9 (**C**), 147.3 (**C**), 139.5 (**C**H), 130.3 (**C**), 129.3 (**C**H), 122.8 (**C**H), 120.6 (**C**H), 112.9 (**C**H), 108.2 (**C**H), 107.9 (**C**H), 101.0 (**C**H$_2$), 86.9 (**C**), 70.8 (**C**H$_2$) ppm. **LRMS** (EI): 354 (37%, [M$^+$]), 135 (100%). **HRMS** (EI): Found 353.9745, $C_{14}H_{11}IO_3$ [M$^+$] requires 353.9747.



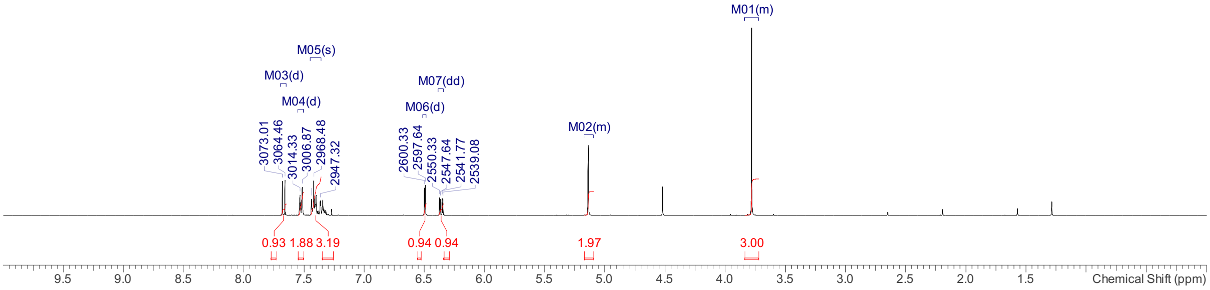


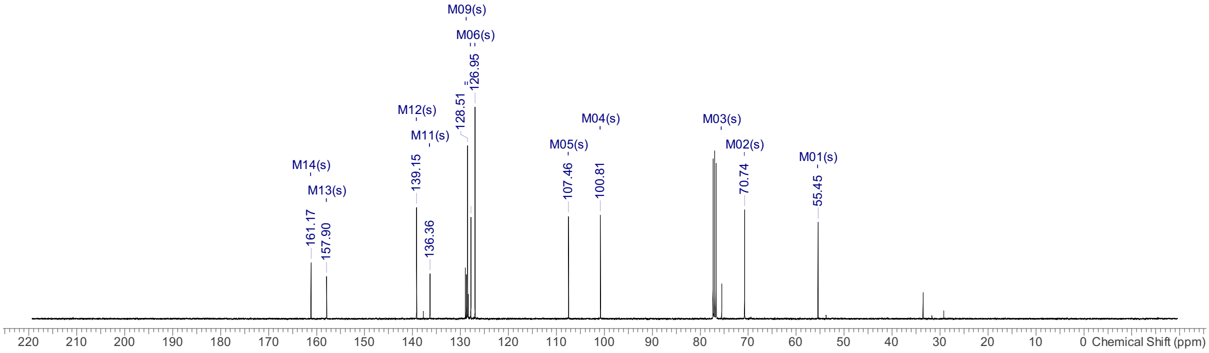
2-(Benzyloxy)-1-iodo-4-methoxybenzene, **5e**.[21]



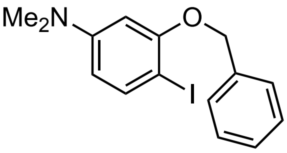
To a solution of 5-methoxy-2-iodophenol (1.70 g, 6.80 mmol) in acetone (100 mL) was added benzyl bromide (0.81 mL, 6.80 mmol) and K_2CO_3 (1.88 g, 13.6 mmol). The reaction was heated at reflux for 18 h then cooled to RT, concentrated *in vacuo* and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL). The organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **5e** as an off-white solid (2.10 g, 6.18 mmol, 91 %). **MP**: 92 – 93 °C. **IR** ν_{max} (film, cm^{-1}): 2935 (br), 1576 (s), 1300 (s), 1163 (s), 1012 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.67 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.53 – 7.51 (2 H, m, 2

× Ar**H**), 7.44 – 7.32 (3 H, m, 3 × Ar**H**), 6.50 (1 H, d, *J* = 2.7 Hz, Ar**H**), 6.36 (1 H, dd, *J* = 8.6, 2.7 Hz, Ar**H**), 5.14 (2 H, s, C**H**$_2$), 3.78 (3 H, s, C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 161.2 (**C**), 157.9 (**C**H), 139.2 (**C**H), 136.4 (**C**), 128.5 (2 × **C**H), 127.8 (**C**H), 127.0 (2 × **C**H), 107.5 (**C**H), 100.8 (**C**H), 75.5 (**C**), 70.7 (**C**H$_2$), 55.5 (**C**H$_3$) ppm. **LRMS** (EI): 340 (68%, [M$^+$]), 213 (93%), 91 (100%). **HRMS** (EI): Found 339.9953, $C_{14}H_{13}IO_2$ [M$^+$] requires 339.9955.

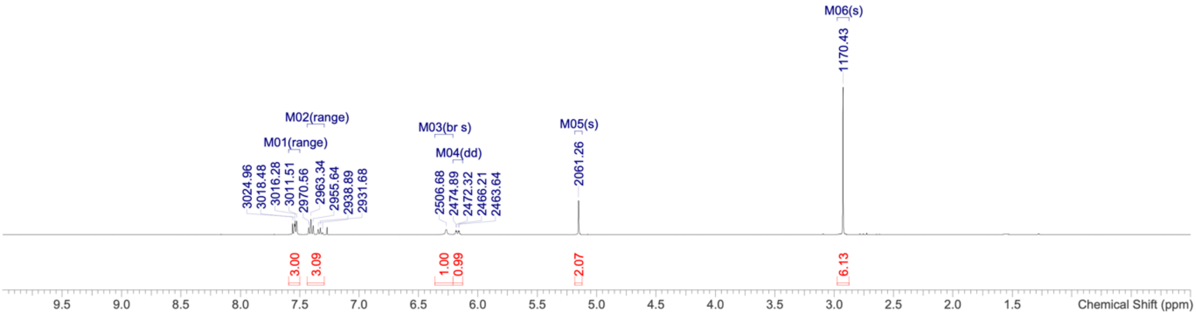


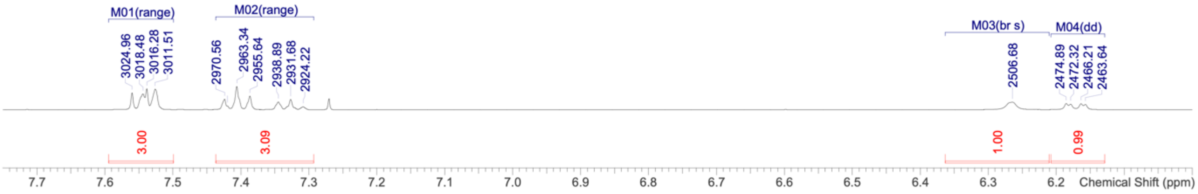


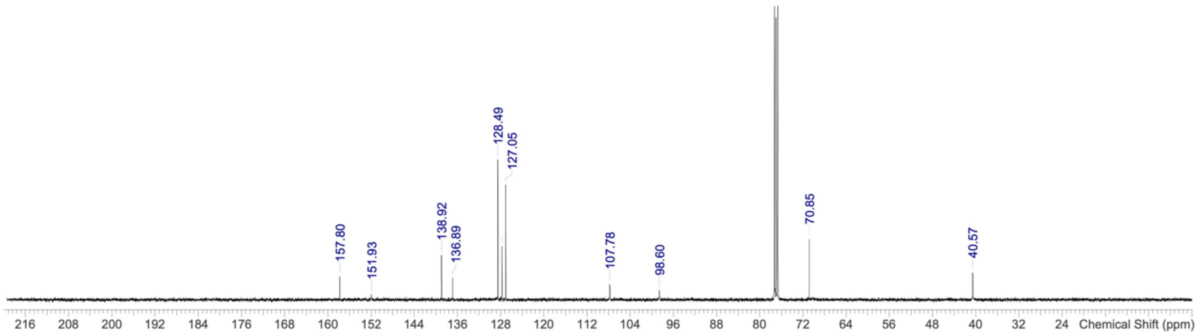
3-(Benzyloxy)-4-iodo-*N*,*N*-dimethylaniline, **5f**.



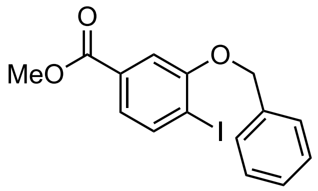
To a solution of 5-(dimethylamino)-2-iodophenol (717 mg, 2.73 mmol) in acetone (30 mL) was added benzyl bromide (470 mg, 2.75 mmol) and K_2CO_3 (813 mg, 5.45 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **5f** (751 mg, 2.13 mmol, 78%) as a pale green solid. **MP** 87 – 88 °C. **IR** ν_{max} (solid, cm^{-1}): 2889 (br), 1591 (s), 1557 (m), 1497 (s), 1356 (m), 1243 (s), 1162 (m), 1045 (w), 1028 (w). **^{1}H NMR** (400 MHz, CDCl$_3$): δ 7.50 – 7.59 (3 H, m, 3 × Ar**H**), 7.29 – 7.44 (3 H, m, 3 × Ar**H**), 6.27 (1 H, br s, Ar**H**), 6.17 (1 H, dd, *J* = 8.7, 2.6 Hz, Ar**H**), 5.15 (2 H, s, C**H$_2$**), 2.93 (6 H, s, 2 × C**H$_3$**) ppm. **^{13}C NMR** (100 MHz, CDCl$_3$) δ 157.8 (**C**), 151.9 (**C**), 138.9 (**C**H), 136.9 (**C**), 128.5 (2 × **C**H), 127.8 (**C**H), 127.1 (2 × **C**H), 107.8 (**C**H), 98.6 (**C**H), 70.9 (**C**H$_2$), 40.6 (2 × **C**H$_3$) ppm [one **C** not observed] ppm. **LRMS** (ESI): 354 (100%, [M+H]$^+$). **HRMS** (ESI+): Found 354.0352, [M+H]$^+$ $C_{15}H_{17}INO$ requires 354.0349.



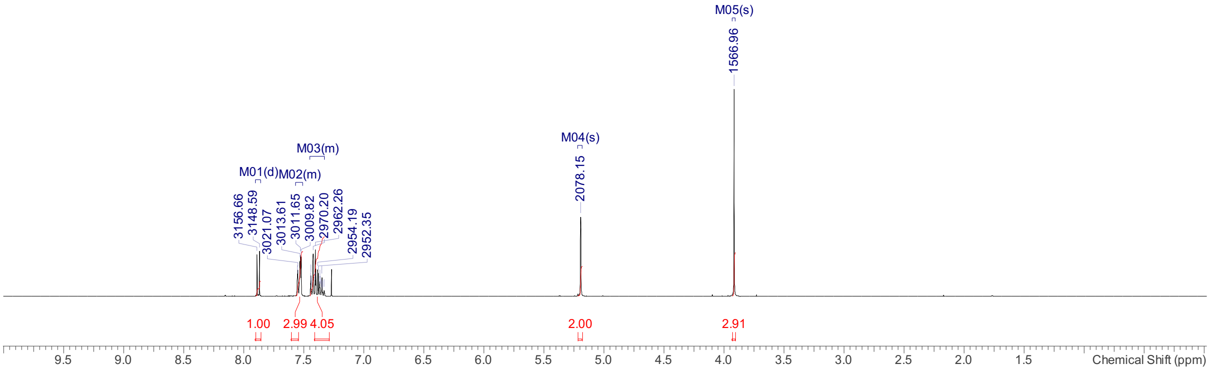


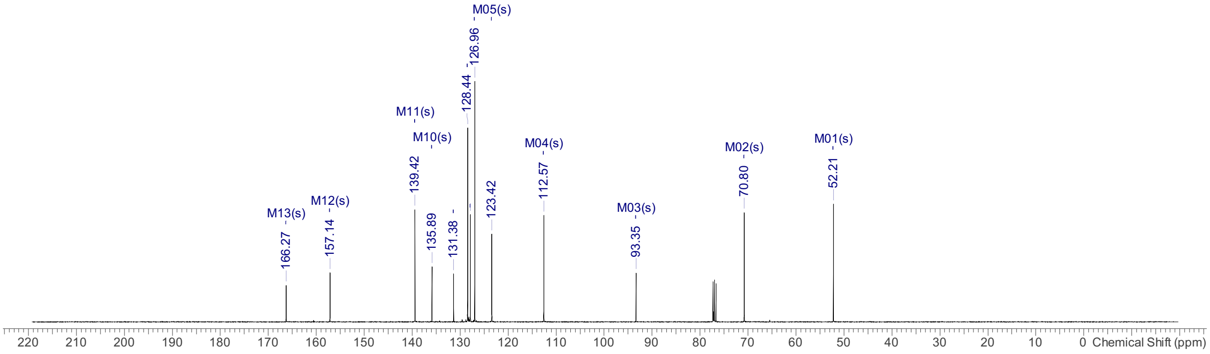


Methyl 3-(benzyloxy)-4-iodobenzoate, **5g**.[21]

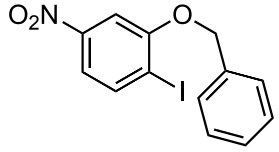


To a solution of methyl 3-hydroxy-4-iodobenzoate (1.51 mg, 5.45 mmol) in DMF (50 mL) was added benzyl bromide (0.65 mL, 5.45 mmol), NaI (20 mg) and K_2CO_3 (1.50 mg, 10.9 mmol). The reaction mixture was heated at 80 °C for 18 h then cooled to RT, diluted with water (50 mL) and extracted with EtOAc (3 × 100 mL). The organic phases were combined, washed with water (3 × 300 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **5g** as a yellow oil (1.48 g, 4.03 mmol, 74 %). **IR** ν_{max} (film, cm^{-1}): 3031 (br), 1712 (s), 1431 (m), 1405 (m), 1287 (s), 1235 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.88 (1H, d, *J* = 8.1 Hz, Ar**H**), 7.55 – 7.52 (3H, m, 3 × Ar**H**), 7.44 – 7.33 (4H, m, 4 × Ar**H**), 5.19 (2H, s, C**H**$_2$), 3.92 (3H, s, C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.3 (**C**), 157.1 (**C**), 139.4 (**C**H), 135.9 (**C**), 131.4 (**C**), 128.4 (2 × **C**H), 127.9 (**C**H), 127.0 (2 × **C**H), 123.4 (**C**H), 112.6 (**C**H), 93.4 (**C**), 70.8 (**C**H$_2$), 52.2 (**C**H$_3$) ppm. **LRMS** (EI): 368 (51%, M$^+$), 91 (100%). **HRMS** (EI): Found 367.9903, $C_{15}H_{13}IO_3$, M$^+$ requires 367.9904.

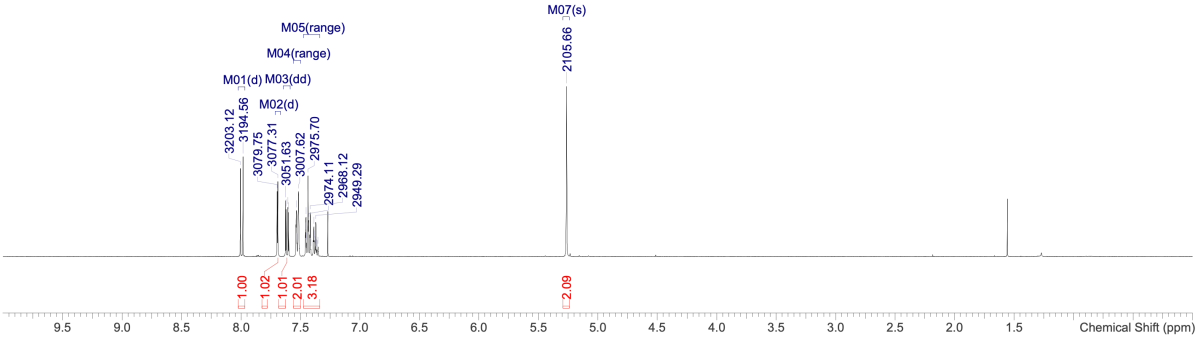


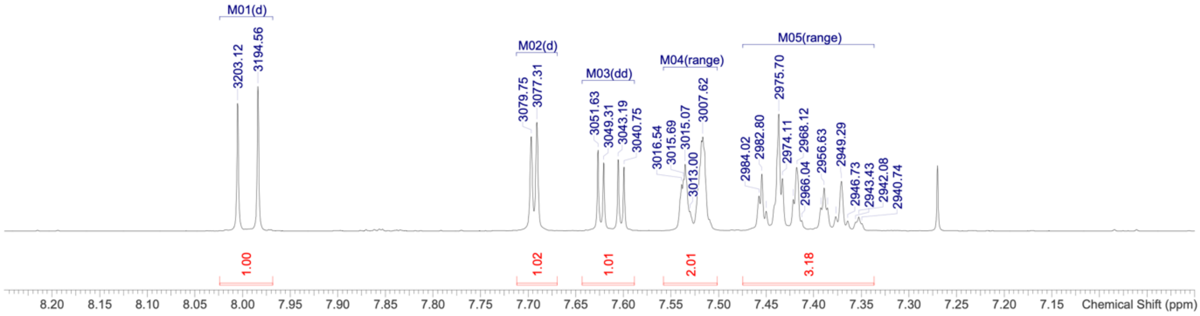


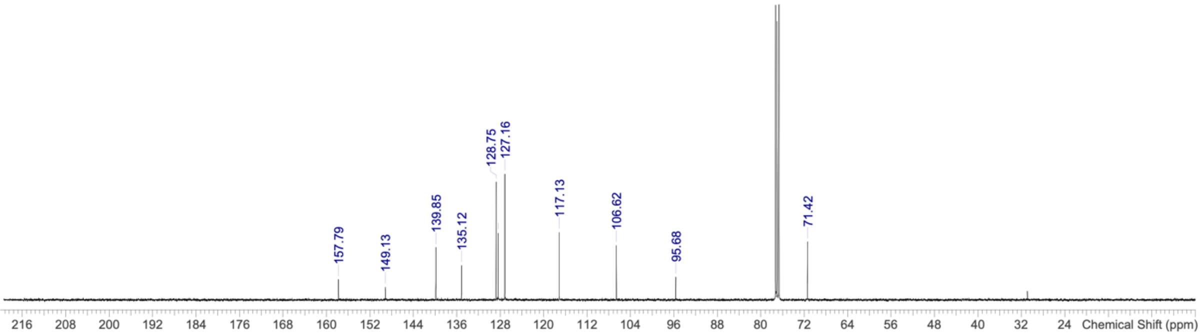
2-(Benzyloxy)-1-iodo-4-nitrobenzene, **5h**.

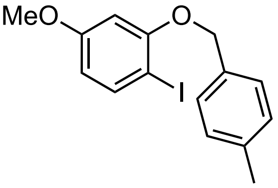


To a solution of 2-iodo-5-nitrophenol (555 mg, 2.10 mmol) in acetone (50 mL) was added benzyl bromide (358 mg, 2.10 mmol) and K_2CO_3 (580 mg, 4.20 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (30 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the organic phases were combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **5h** (693 mg, 1.95 mmol, 93%) as a pale yellow solid. **MP** 107 – 108 °C. **IR** ν_{max} (film, cm^{-1}): 1568 (w), 1516 (s), 1469 (m), 1409 (m), 1341 (s), 1303 (m), 1255 (m), 1021 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.69 (1 H, d, *J* = 2.5 Hz, Ar**H**), 7.61 (1 H, dd, *J* = 8.5, 2.4 Hz, Ar**H**), 7.50 – 7.56 (2 H, m, 2 × Ar**H**), 7.34 – 7.47 (3 H, m, 3 × Ar**H**), 5.26 (2 H, s, C**H**$_2$) ppm. ^{13}**C NMR** (100 MHz, CDCl$_3$) δ 157.8 (**C**), 149.1 (**C**), 139.9 (**C**H), 135.1 (**C**), 128.8 (2 × **C**H), 128.4 (**C**H), 127.2 (2 × **C**H), 117.1 (**C**H), 106.6 (**C**H), 95.7 (**C**), 71.4 (**C**H$_2$). **LRMS** (EI): 355 ([M]$^+$, 20%), 152 (30%), 91 ([M-C$_6$H$_3$INO$_3$]$^+$, 100%). **HRMS** (EI): Found 354.9696, [M]$^+$ C$_{13}$H$_{10}$INO$_3$ requires 354.9705.



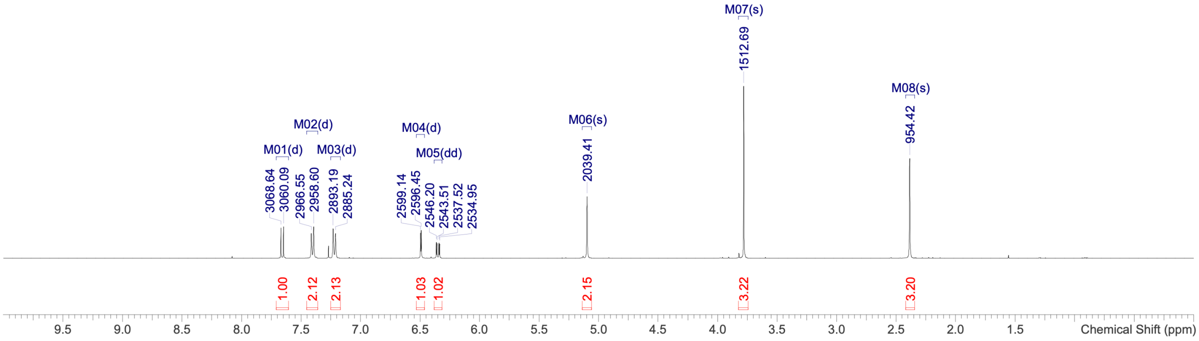


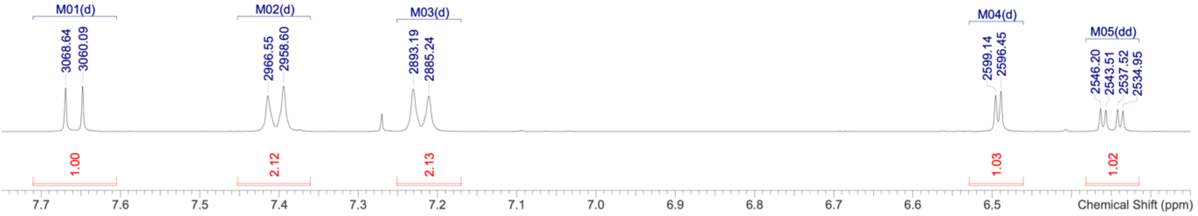


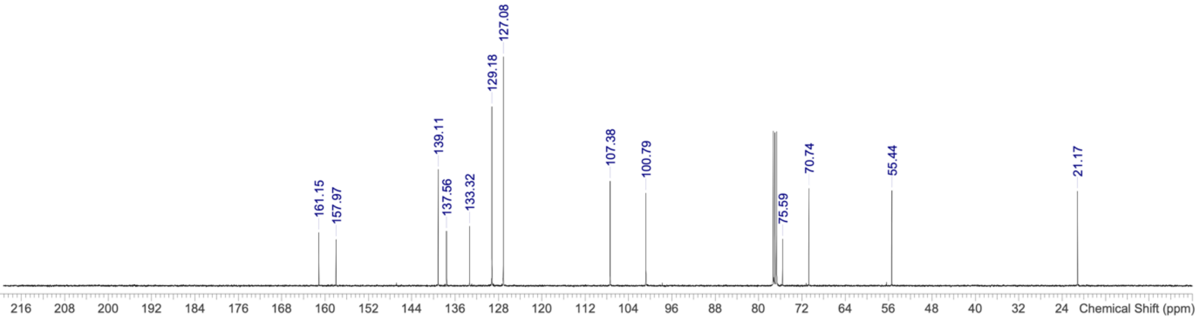


1-Iodo-4-methoxy-2-((4-methylbenzyl)oxy)benzene, **5i**.

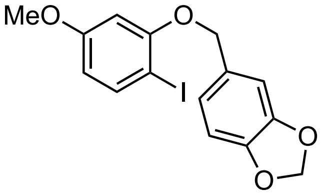
To a solution of 2-iodo-5-methoxyphenol (830 mg, 3.32 mmol) in acetone (60 mL) was added 4-methylbenzyl bromide (610 mg, 3.30 mmol) and K$_2$CO$_3$ (1.00 g, 7.24 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the combined organic phases were dried over MgSO$_4$, concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **5i** (0.88 g, 2.5 mmol, 76%) as a white solid. **MP** 64 – 65 °C. **IR** ν_{max} (film, cm^{-1}): 2981 (s), 2899 (m), 1576 (s), 1480 (m), 1460 (m), 1378 (m), 1300 (m), 1277 (m), 1253 (m), 1197 (m), 1163 (s), 1065 (m), 1012 (m). ^{1}**H NMR** (400 MHz, CDCl$_3$): δ 7.66 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.40 (2 H, d, *J* = 8.0 Hz, 2 × Ar**H**), 7.22 (2 H, d, *J* = 8.0 Hz, 2 × Ar**H**), 6.49 (1 H, d, *J* = 2.7 Hz, Ar**H**), 6.35 (1 H, dd, *J* = 8.6, 2.6 Hz, Ar**H**), 5.10 (2 H, s, C**H**$_2$), 3.78 (3 H, s, OC**H**$_3$), 2.39 (3 H, s, C**H**$_3$). ^{13}**C NMR** (100 MHz, CDCl$_3$) δ 161.2 (**C**), 158.0 (**C**), 139.1 (**C**H), 137.6 (**C**), 133.3 (**C**), 129.2 (2 × **C**H), 127.1 (2 × **C**H), 107.4 (**C**H), 100.8 (**C**H), 75.6 (**C**), 70.7 (**C**H$_2$), 55.4 (**C**H$_3$), 21.2 (**C**H$_3$) ppm. **LRMS** (ESI+): 355 ([M+H]$^+$, 75%), 354 (60%), 323 (100%), 228 (70%), 156 (60%). **HRMS** (ESI+): Found 377.0010, [M+Na]$^+$ C$_{15}$H$_{15}$INaO$_2$ requires 377.0009.



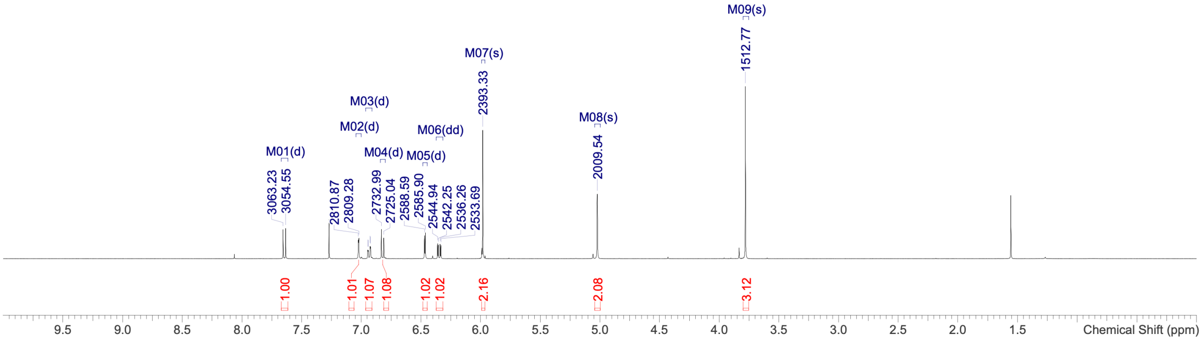


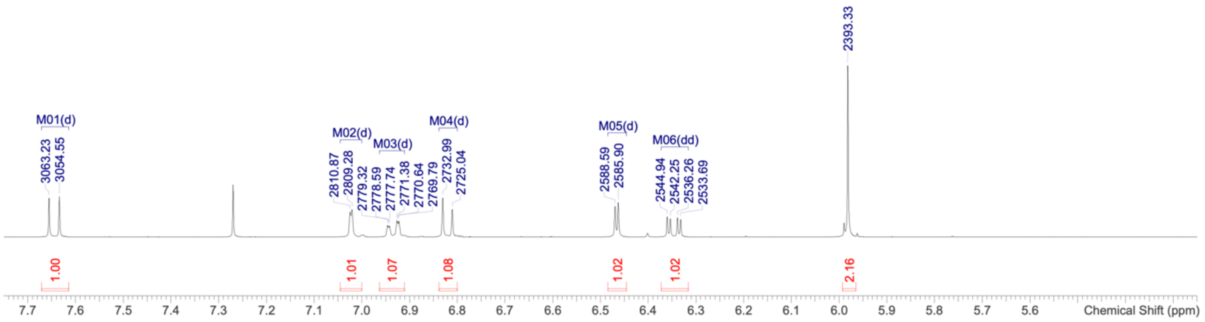


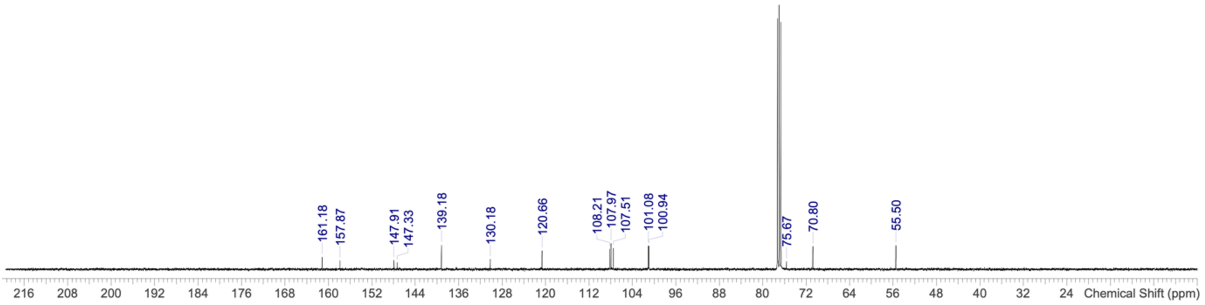
5-((2-Iodo-5-methoxyphenoxy)methyl)benzo[*d*][1,3]dioxole, **5j**.



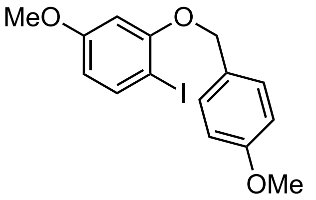
To a solution of 2-iodo-5-methoxyphenol (0.86 g, 3.4 mmol) in acetone (35 mL) was added 5-(bromomethyl)benzo[d][1,3]dioxole (0.74 g, 3.4 mmol) and K_2CO_3 (720 mg, 5.21 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (30 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **5j** (1.22 g, 3.2 mmol, 93%) as a white solid. **MP** 99 – 100 °C. **IR** ν_{max} (film, cm^{-1}): 2895 (br), 1577 (s), 1503 (s), 1491 (s), 1443 (s), 1302 (m), 1249 (s), 1201 (m), 1167 (s), 1038 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.64 (1 H, d, *J* = 8.7 Hz, Ar**H**), 7.02 (1 H, d, *J* = 1.6 Hz, Ar**H**), 6.93 (1 H, d with fine splitting, *J* = 8.0 Hz, Ar**H**), 6.82 (1 H, d, *J* = 8.0 Hz, Ar**H**), 6.47 (1 H, d, *J* = 2.7 Hz, Ar**H**), 6.35 (1 H, dd, *J* = 8.6, 2.6 Hz, Ar**H**), 5.98 (2 H, s, C**H**$_2$), 5.02 (2 H, s, C**H**$_2$), 3.78 (3 H, s, OC**H**$_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 (**C**), 157.9 (**C**), 147.9 (**C**), 147.3 (**C**), 139.2 (**C**H), 130.2 (**C**), 120.7 (**C**H), 108.2 (**C**H), 108.0 (**C**H), 107.5 (**C**H), 101.1 (**C**H$_2$), 100.9 (**C**H), 75.7 (**C**), 70.8 (**C**H$_2$), 55.5 (**C**H$_3$) ppm. **LRMS** (ESI+): 385 ([M+H]$^+$, 80%), 341 (80%), 167 (50%). **HRMS** (ESI+): Found 406.9753, [M+Na]$^+$ $C_{15}H_{13}INaO_4$ requires 406.9751.



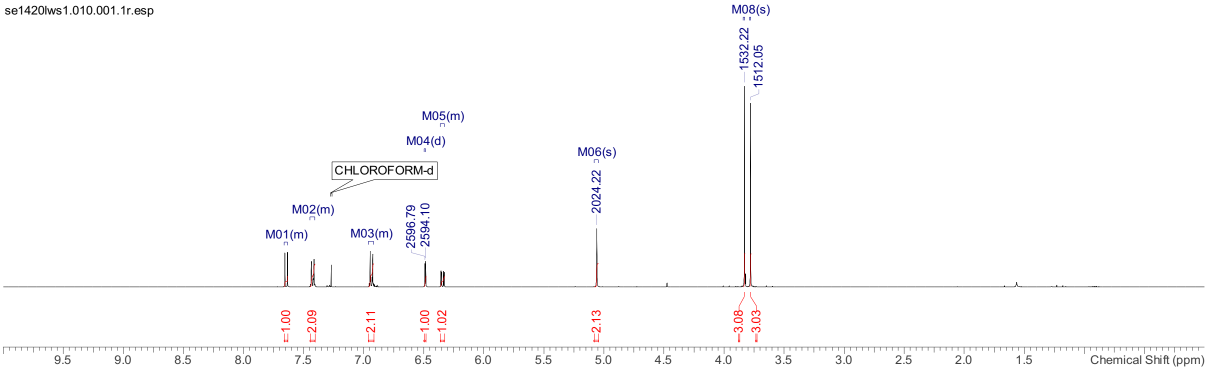


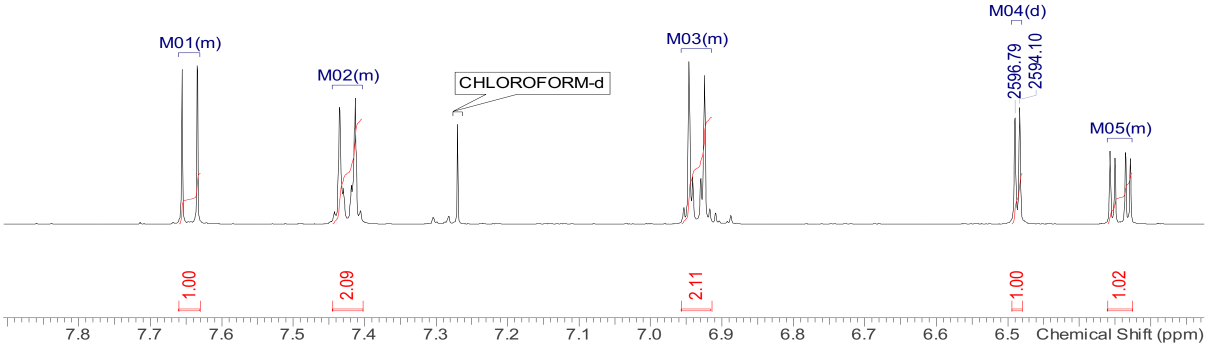


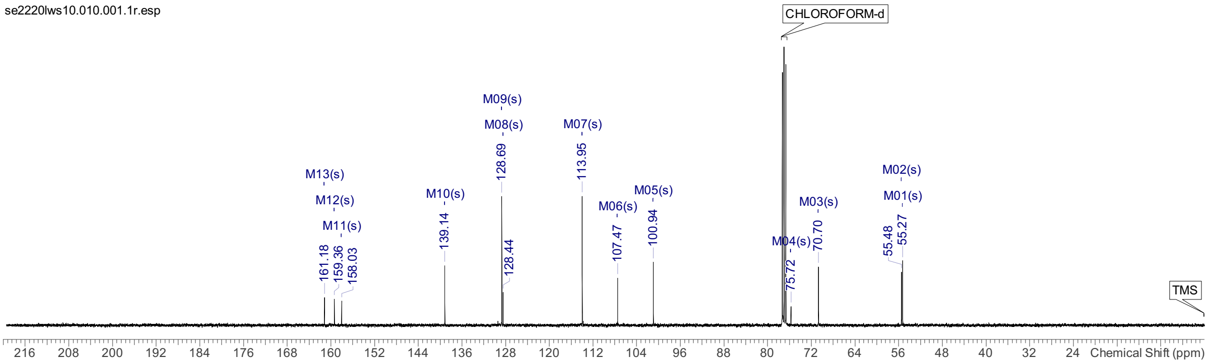
1-Iodo-4-methoxy-2-((4-methoxybenzyl)oxy)benzene, **5k**.



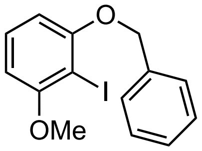
To a solution of 2-iodo-5-methoxyphenol (1.10 g, 4.40 mmol) in acetone (40 mL) was added 4-methoxybenzyl bromide (0.88 g, 4.35 mmol) and K_2CO_3 (1.21 g, 8.75 mmol). The reaction mixture was heated at reflux for 18 h then cooled to RT and partitioned between water (100 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% EtOAc in petrol) to afford the title compound **5k** (1.34 g, 3.62 mmol, 82%) as a colourless oil. **IR** ν_{max} (film, cm^{-1}): 1612 (w), 1576 (m), 1513 (m), 1462 (m), 1377 (w), 1300 (m), 1245 (s), 1197 (m), 1164 (s), 1055 (m), 1032 (m), 1012 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.64 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.42 (2 H, d, *J* = 9.9 Hz, 2 × Ar**H**), 6.94 (2 H, d, *J* = 9.8 Hz, 2 × Ar**H**), 6.49 (1 H, d, *J* = 2.7 Hz, Ar**H**), 6.34 (1 H, dd, *J* = 8.7, 2.7 Hz, Ar**H**), 5.06 (2 H, s, C**H**$_2$), 3.83 (3 H, s, OC**H**$_3$), 3.70 (3 H, s, OC**H**$_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 (**C**), 159.4 (**C**), 158.0 (**C**), 139.1 (**C**H), 128.7 (2 × **C**H), 128.4 (**C**), 114.0 (2 × **C**H), 107.5 (**C**H), 100.9 (**C**H), 75.7 (**C**), 70.7 (**C**H$_2$), 55.5 (**C**H$_3$), 55.3 (**C**H$_3$) ppm. **LRMS** (ESI+): 393 ([M+Na]$^+$, 90%), 365 (100%), 257 (70%). **HRMS** (ESI+): Found 392.9958, [M+Na]$^+$ $C_{15}H_{15}INaO_3$ requires 392.9958.



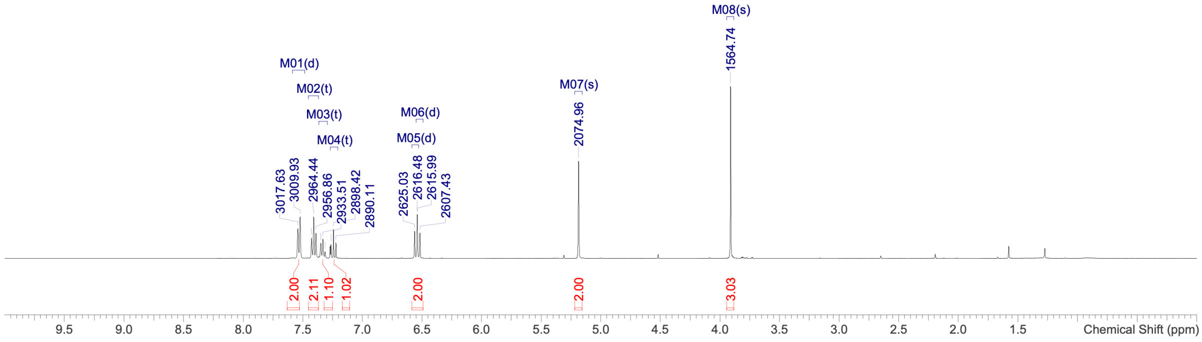


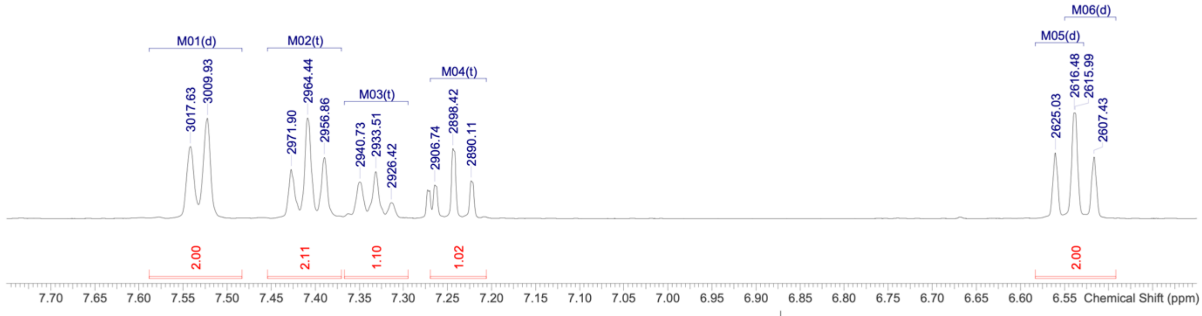


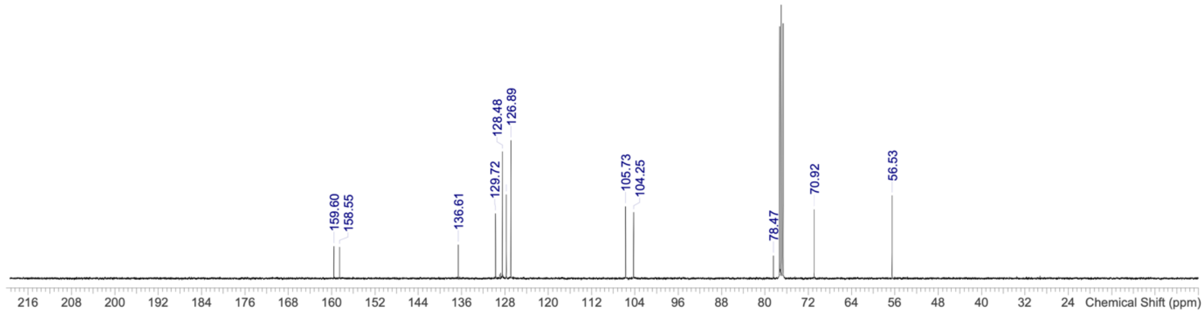
<u>1-(Benzyloxy)-2-iodo-3-methoxybenzene</u>, **5l**.



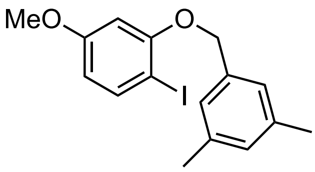
To a solution of 2-iodo-3-methoxyphenol (468 mg, 1.87 mmol) in acetone (20 mL) was added benzyl bromide (320 mg, 1.87 mmol) and K_2CO_3 (520 mg, 3.74 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the combined organic phases dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **5l** (640 mg, 1.88 mmol, quantitative) as a yellow oil that solidified on standing. **MP** 141 – 142 °C. **IR** ν_{max} (solid, cm^{-1}): 1586 (m), 1466 (m), 1432 (m), 1379 (w), 1292 (w), 1250 (s), 1094 (s), 1019 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.53 (2 H, app. d, *J* = 7.7 Hz, 2 × Ar**H**), 7.41 (2 H, app. t, *J* = 7.5 Hz, 2 × Ar**H**), 7.34 (1 H, t, *J* = 7.6 Hz, Ar**H**), 7.24 (1 H, t, *J* = 8.3 Hz, Ar**H**), 6.55 (1 H, d, *J* = 8.8 Hz, Ar**H**), 6.53 (1 H, d, *J* = 8.8 Hz, Ar**H**), 5.19 (2 H, s, C**H$_2$**), 3.91 (3 H, s, OC**H$_3$**). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.6 (**C**), 158.6 (**C**), 136.6 (**C**), 129.7 (**C**H), 128.5 (2 × **C**H), 127.8 (**C**H), 126.9 (2 × **C**H), 105.7 (**C**H), 104.3 (**C**H), 78.5 (**C**), 70.9 (**C**H$_2$), 56.5 (**C**H$_3$) ppm. **LRMS** (ESI+): 245 (50%), 214 ($[M+H-I]^+$, 100%), 213 ($[M-I]^+$, 65%), 180 (50%). **HRMS** (ESI+): Found 362.9860, $[M+Na]^+$ $C_{14}H_{13}INaO_2$ requires 362.9852.



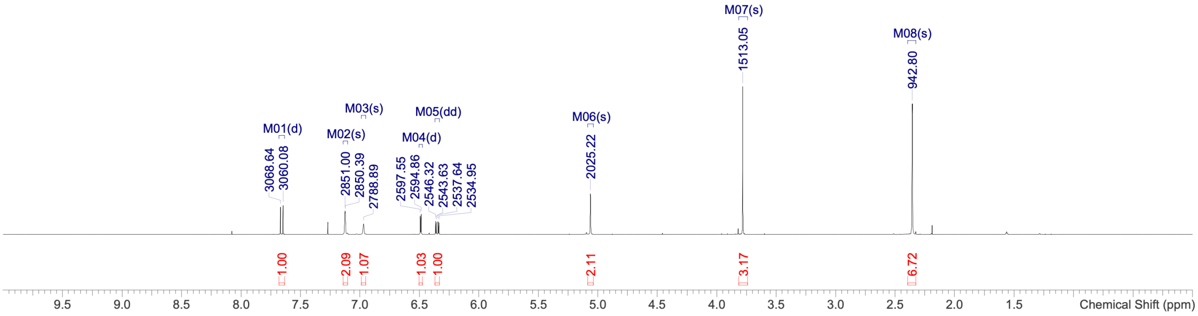


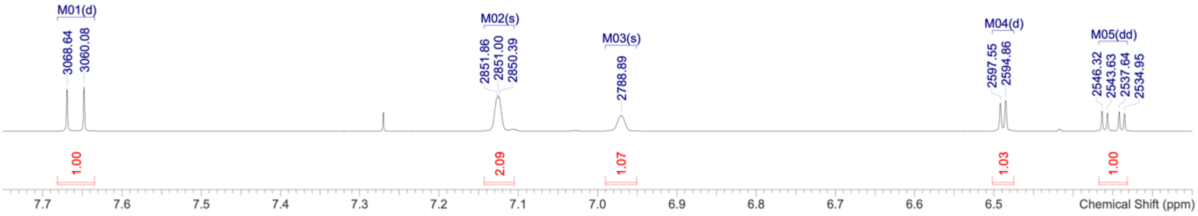


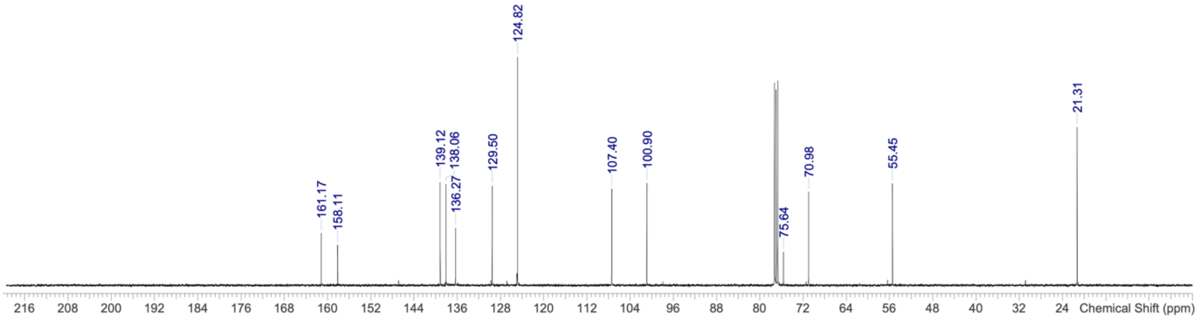
2-((3,5-Dimethylbenzyl)oxy)-1-iodo-4-methoxybenzene, **5m**.



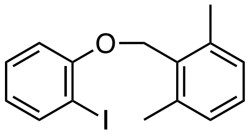
To a solution of 2-iodo-5-methoxyphenol (990 mg, 3.96 mmol) in acetone (40 mL) was added 3,5-dimethylbenzyl bromide (790 mg, 3.97 mmol) and K_2CO_3 (1.10 g, 7.96 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL) then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (10% acetone in petrol) to afford the title compound **5m** (1.45 g, 3.94 mmol, 99%) as a white solid. **MP** 65 – 66 °C. **IR** ν_{max} (solid, cm^{-1}): 2915 (br), 1576 (s), 1481 (m), 1439 (m), 1303 (m), 1277 (w), 1253 (m), 1200 (s), 1165 (s), 1056 (m), 1012 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.66 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.13 (2 H, s with fine splitting, 2 × Ar**H**), 6.97 (1 H, s with fine splitting, Ar**H**), 6.49 (1 H, d, *J* = 2.7 Hz, Ar**H**), 6.35 (1 H, dd, *J* = 8.7, 2.7 Hz, Ar**H**), 5.06 (2 H, s, C**H₂**), 3.78 (3 H, s, OC**H₃**), 2.36 (6 H, s with fine splitting, 2 × C**H**₃) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 (**C**), 158.1 (**C**), 139.1 (**C**H), 138.1 (2 × **C**), 136.3 (**C**), 129.5 (**C**H), 124.8 (2 × **C**H), 107.4 (**C**H), 100.9 (**C**H), 75.6 (**C**), 71.0 (**C**H₂), 55.5 (**C**H₃), 21.3 (2 × **C**H₃). **LRMS** (ESI+): 369 ([M+H]$^+$, 15%), 368 (80%), 360 (50%), 242 ([M-I]$^+$, 100%). **HRMS** (ESI+): Found 362.9860, [M+Na]$^+$ $C_{14}H_{13}INaO_2$ requires 362.9852.



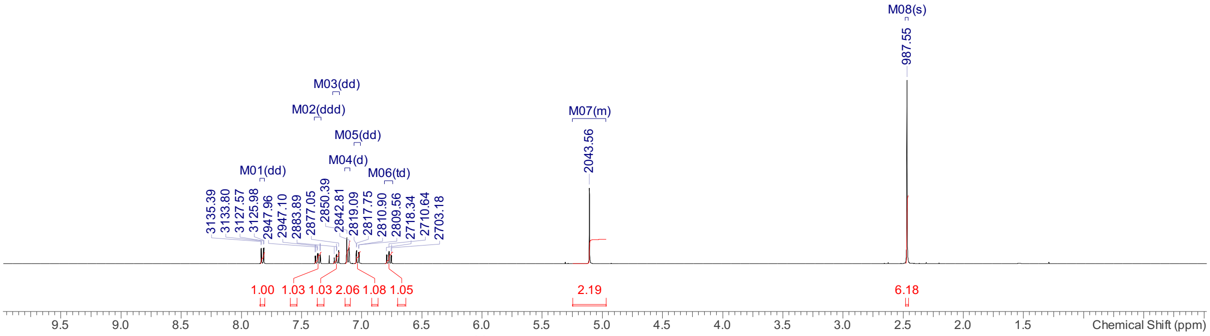


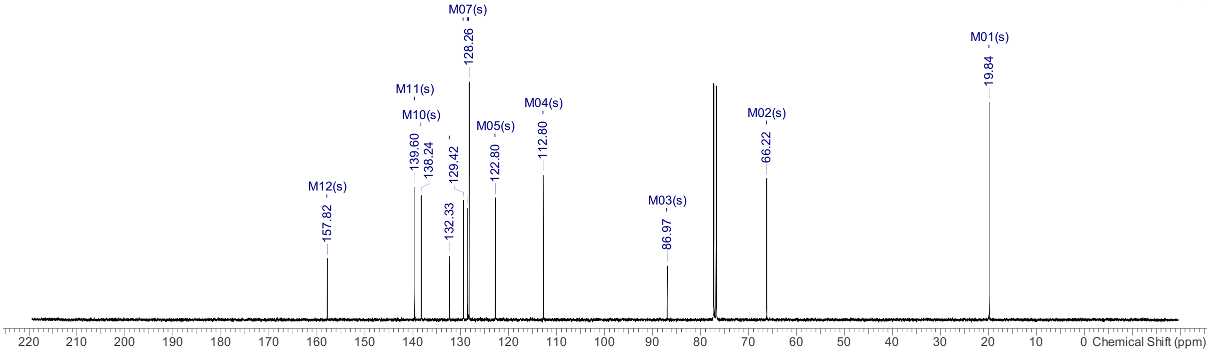


2-((2-Iodophenoxy)methyl)-1,3-dimethylbenzene, **5n**.

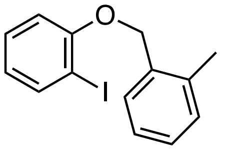


To a solution of 2-iodophenol (990 mg, 4.50 mmol) in acetone (50 mL) was added 2-(bromomethyl)-1,3-dimethylbenzene (900 mg, 4.50 mmol) and K_2CO_3 (1.24 g, 8.97 mmol). The reaction was heated at reflux for 18 h then cooled to RT, concentrated *in vacuo* and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **5n** as a yellow oil (1.05 g, 3.10 mmol, 69%). **IR** ν_{max} (film, cm^{-1}): 3063 (br), 1468 (s), 1231 (s), 1017 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.36 (1 H, ddd, *J* = 8.2, 7.3, 1.6 Hz, Ar**H**), 7.21 (1 H, dd, *J* = 8.2, 6.9 Hz, Ar**H**), 7.11 (2 H, d, *J* = 7.6 Hz, 2 × Ar**H**), 7.03 (1 H, dd, *J* = 8.2, 1.3 Hz, Ar**H**), 6.77 (1 H, td, *J* = 7.6, 1.3 Hz, Ar**H**), 5.11 (2 H, s, C**H₂**), 2.47 (6 H, s, 3 × C**H**₃) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.8 (**C**), 139.6 (**C**H), 138.2 (**C**H), 132.3 (**C**), 129.4 (**C**H), 128.6 (**C**H), 128.3 (2 × **C**H), 122.8 (**C**H), 112.8 (**C**H), 87.0 (**C**), 66.2 (**C**H₂), 19.8 (2 × **C**H₃) ppm. **LRMS** (EI): 338 (8%, [M$^+$]), 119 (100%), 91 (56%). **HRMS** (EI): Found 338.0160, $C_{15}H_{15}IO$ [M$^+$] requires 338.0162.

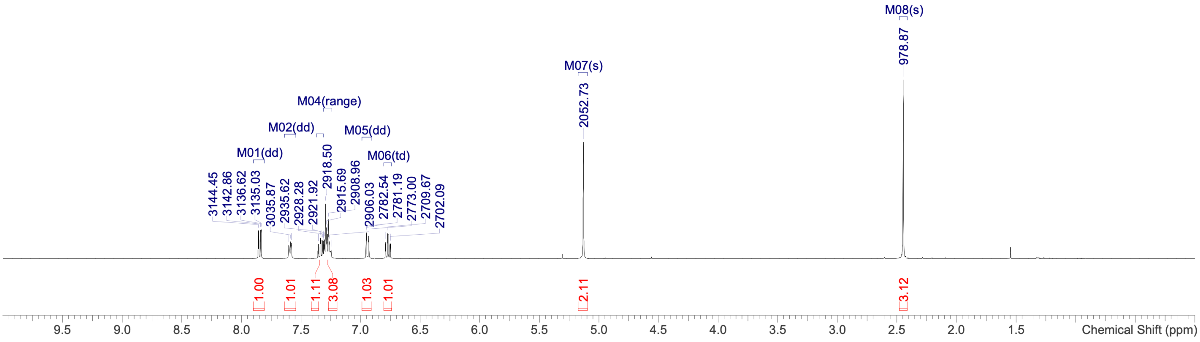


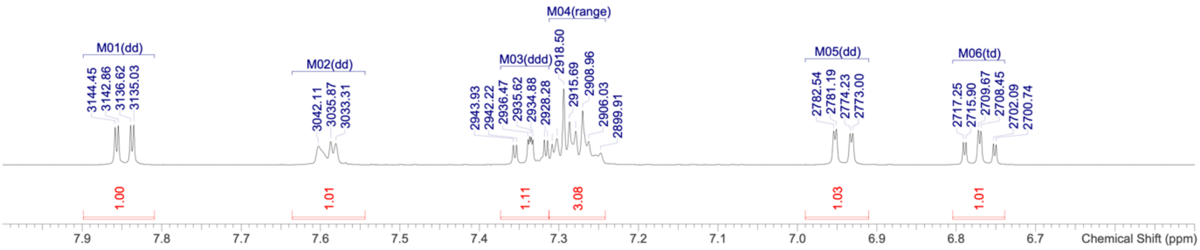


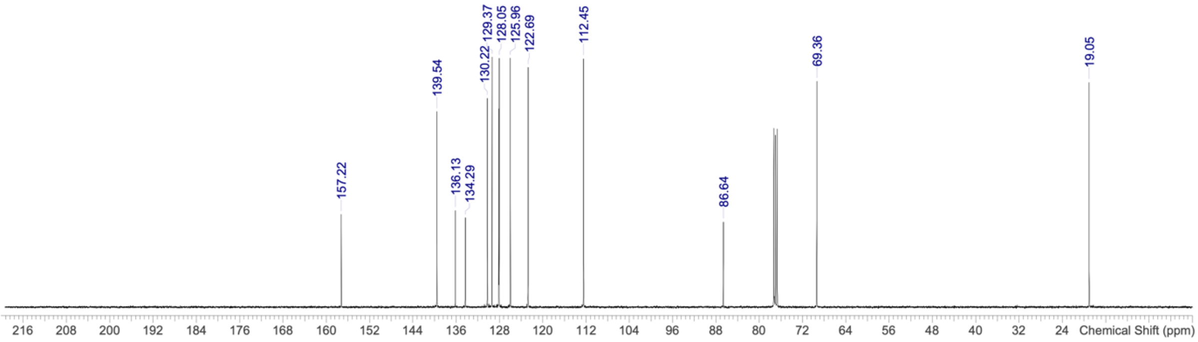
1-Iodo-2-((2-methylbenzyl)oxy)benzene, **5o**.[1, 23]



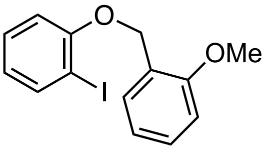
To a solution of 2-iodophenol (1.19 g, 5.40 mmol) in acetone (90 mL) was added 2-methylbenzyl bromide (0.72 mL, 5.40 mmol) and K_2CO_3 (1.54 g, 11.0 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% EtOAc in petrol) to afford the title compound **5o** (1.69 g, 3.6 mmol, 97%) as a pale yellow oil. **IR** ν_{max} (film, cm^{-1}): 1581 (m), 1466 (s), 1437 (m), 1374 (w), 1274 (s), 1240 (s), 1049 (m), 1016 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.85 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.59 (1 H, dd, *J* = 6.2, 2.7 Hz, Ar**H**), 7.34 (1 H, ddd, *J* = 8.3, 7.4, 1.7 Hz, Ar**H**), 7.24 – 7.31 (3 H, m, 3 × Ar**H**), 6.94 (1 H, dd, *J* = 8.3, 1.3 Hz, Ar**H**), 6.77 (1 H, td, *J* = 7.6, 1.3 Hz, Ar**H**), 5.13 (2 H, s, C**H$_2$**), 2.45 (3 H, s, C**H$_3$**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.2 (**C**), 139.5 (**C**H), 136.1 (**C**), 134.3 (**C**), 130.2 (**C**H), 129.4 (**C**H), 128.12 (**C**H), 128.05 (**C**H), 126.0 (**C**H), 122.7 (**C**H), 112.5 (**C**H), 86.6 (**C**), 69.4 (**C**H$_2$), 19.1 (**C**H$_3$) ppm. **LRMS** (EI): 324 ($[M]^+$,15%), 105 (100%). **HRMS** (APPI): Found 324.0005, $[M+H]^+$ $C_{14}H_{13}IO$ requires 324.0006.



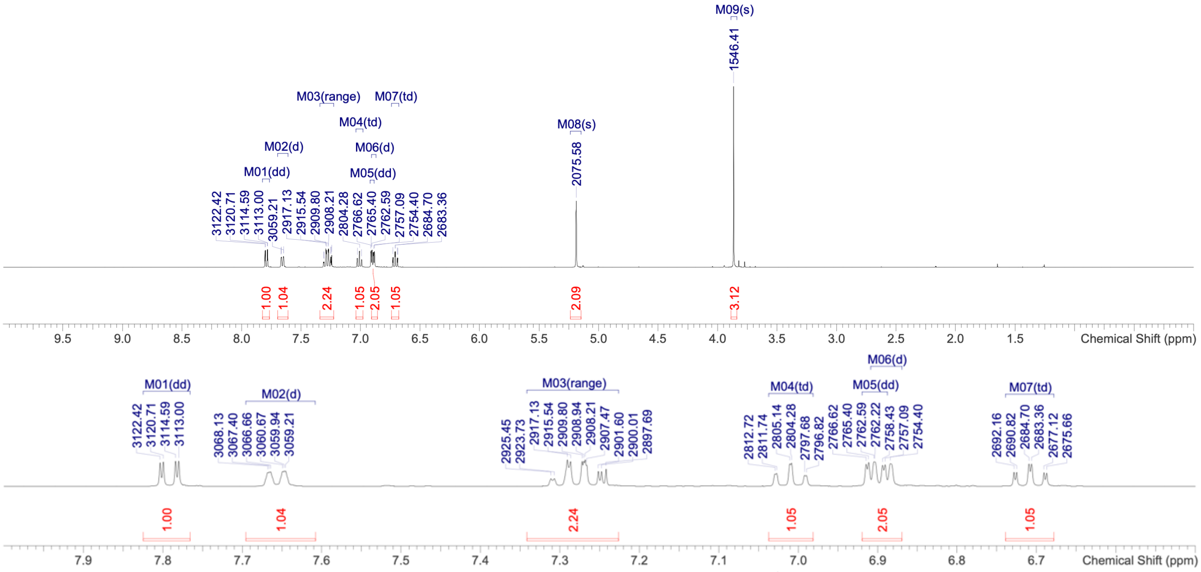


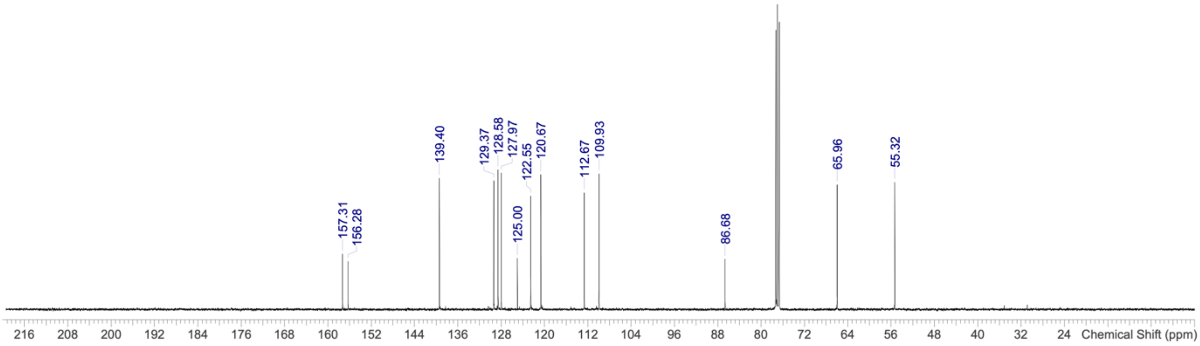


1-Iodo-2-((2-methoxybenzyl)oxy)benzene, **5p**.[24, 25]

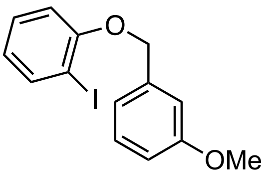


To a solution of 2-iodophenol (2.46 g, 11.1 mmol) in acetone (110 mL) was added 2-methoxybenzyl bromide (2.24 g, 11.1 mmol) and K_2CO_3 (3.24 g, 23.4 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (150 mL) and DCM (100 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **5p** (3.55 g, 10.4 mmol, 94%) as a pink solid. **IR** ν_{max} (film, cm^{-1}): 1582 (w) 1494 (m), 1463 (m), 1437 (m), 1242 (s), 1050 (m), 1030 (m), 1017 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (1 H, dd, *J* = 7.8, 1.7 Hz, Ar**H**), 7.66 (1 H, d with fine splitting, *J* = 7.5 Hz, ArH), 7.23 – 7.34 (2 H, m, 2 × ArH), 7.01 (1 H, app. td, *J* = 7.5, 0.9 Hz, ArH), 6.90 (1 H, dd, *J* = 8.3, 1.2 Hz, Ar**H**), 6.89 (1 H, app. d, *J* = 8.2 Hz, ArH), 6.71 (1 H, app. td, *J* = 7.6, 1.4 Hz, Ar**H**), 5.19 (2 H, s, C**H**$_2$), 3.86 (3 H, s, OC**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.3 (**C**), 156.3 (**C**), 139.4 (**C**H), 129.4 (**C**H), 128.6 (**C**H), 128.0 (**C**H), 125.0 (**C**), 122.6 (**C**H), 120.7 (**C**H), 112.7 (**C**H), 109.9 (**C**H), 86.7 (**C**), 66.0 (**C**H$_2$), 55.3 (**C**H$_3$) ppm. **LRMS** (EI): 340 ([M]$^+$, 28%), 219 ([M-$C_8H_{10}O$]$^+$, 40%), 121 ([M-C_6H_5IO]$^+$, 100%).



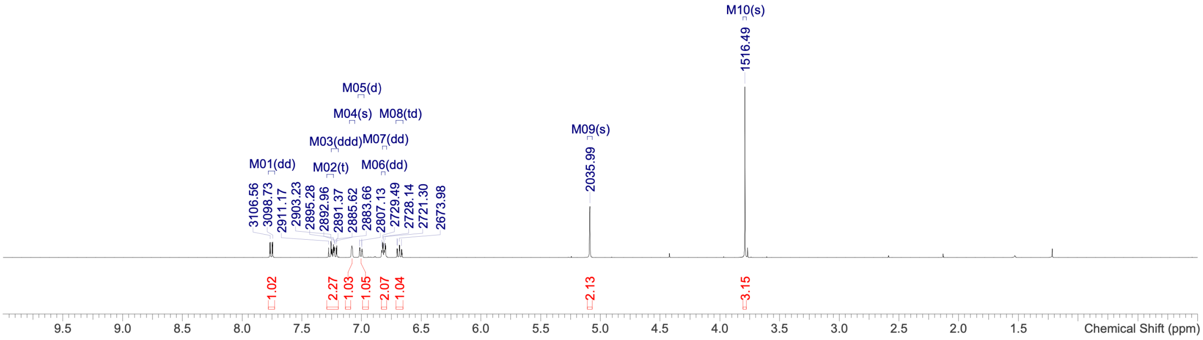


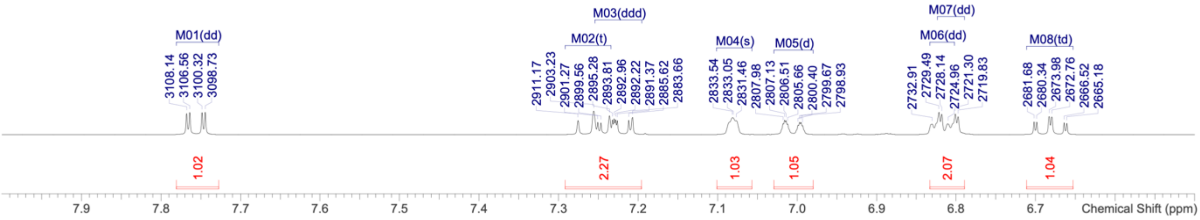
1-Iodo-2-((3-methoxybenzyl)oxy)benzene, **5q**.[25]

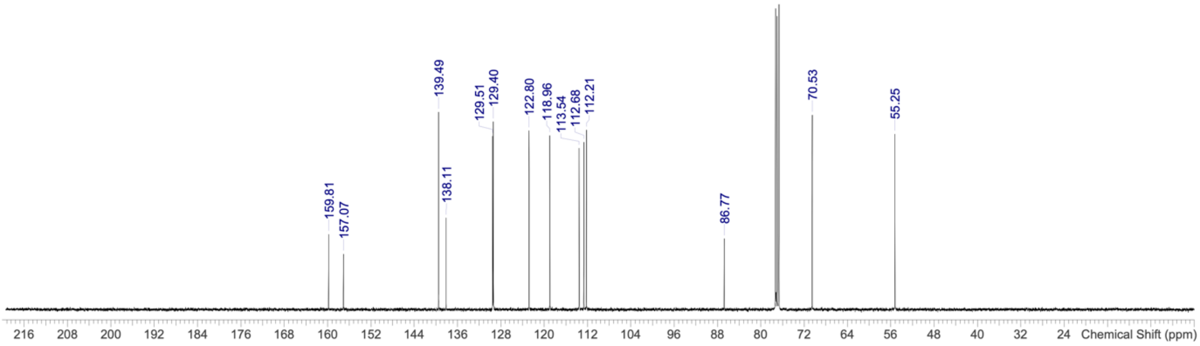


To a solution of 2-iodophenol (2.08 g, 9.45 mmol) in acetone (90 mL) was added 3-methoxybenzyl bromide (1.89 g, 9.60 mmol) and K_2CO_3 (2.60 g, 18.8 mmol). The reaction was heated at reflux for 18 h then cooled to RT, concentrated *in vacuo* and partitioned between water (100 mL) and DCM

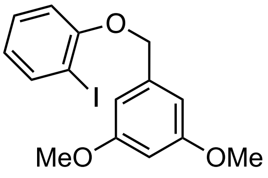
(100 mL). The aqueous phase was separated and extracted with DCM (4 × 20 mL) then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **5q** (3.04 g, 8.94 mmol, 94%) as a colourless oil. **IR** ν_{max} (film, cm^{-1}): 1584 (m), 1455 (m), 1436 (m), 1375 (w), 1263 (s), 1152 (m), 1048 (s), 1016 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (1H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.26 (1 H, t, *J* = 8.0 Hz, Ar**H**), 7.23 (1 H, ddd, *J* = 8.3, 7.5, 1.7 Hz, Ar**H**), 7.08 (1 H, s with fine splitting, Ar**H**), 7.01 (1 H, d with fine splitting, *J* = 7.5 Hz, Ar**H**), 6.82 (1 H, dd, *J* = 7.9, 2.4 Hz, Ar**H**), 6.81 (1 H, dd, *J* = 8.3, 1.4 Hz, Ar**H**), 6.68 (1 H, app. td, *J* = 7.6, 1.3 Hz, Ar**H**), 5.09 (2 H, s, C**H₂**), 3.79 (3 H, s, OC**H₃**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.8 (**C**), 157.1 (**C**), 139.5 (**C**H), 138.1 (**C**), 129.5 (**C**H), 129.4 (**C**H), 122.8 (**C**H), 119.0 (**C**H), 113.5 (**C**H), 112.7 (**C**H), 112.2 (**C**H), 86.8 (**C**), 70.5 (**C**H₂), 55.3 (**C**H₃) ppm. **LRMS** (ESI): 341 ([M+H]$^+$, 23%), 241 (100%).



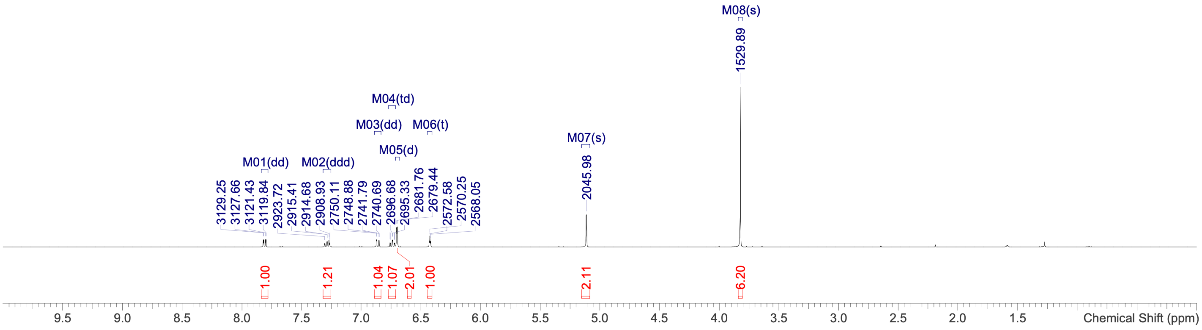


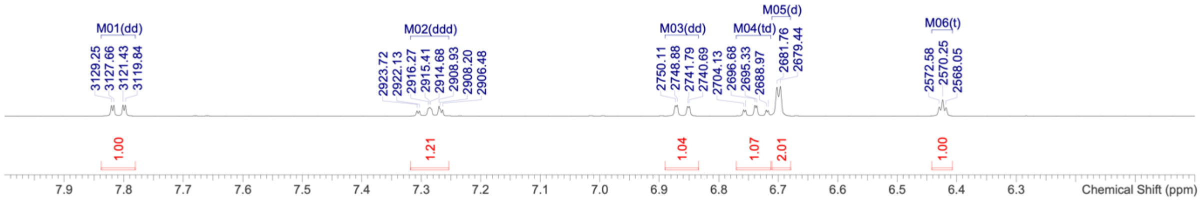


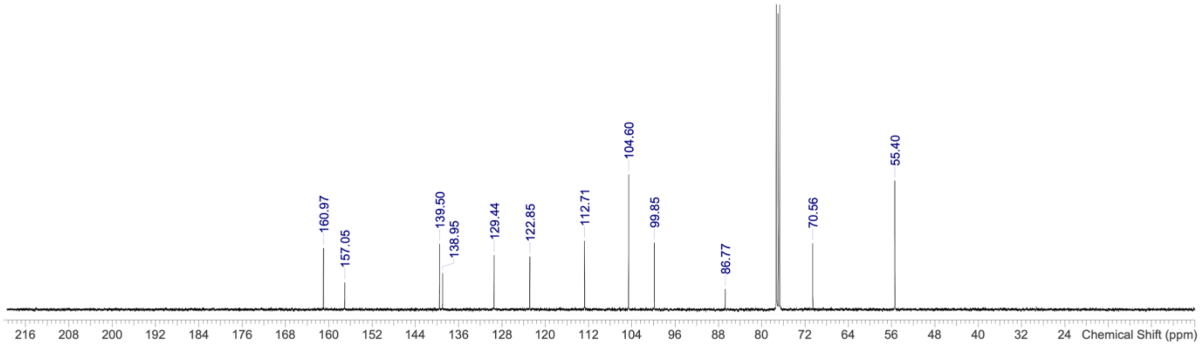
1-((2-Iodophenoxy)methyl)-3,5-dimethoxybenzene, **5r**.[1]



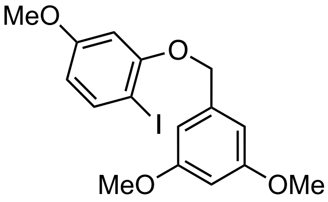
To a solution of 2-iodophenol (1.17 g, 5.32 mmol) in acetone (50 mL) was added 3,5-dimethoxybenzyl bromide (1.23 g, 5.32 mmol) and K_2CO_3 (1.50 g, 10.6 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (100 mL) and DCM (100 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **5r** (1.96 g, 5.29 mmol, 99%) as a white solid. **MP** 68 – 70 °C. **IR** ν_{max} (solid, cm^{-1}): 1593 (s), 1476 (s), 1451 (s), 1384 (m), 1335 (w), 1248 (s), 1172 (s), 1019 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.29 (1 H, ddd, *J* = 8.3, 7.5, 1.6 Hz, Ar**H**), 6.86 (1 H, dd, *J* = 8.3, 1.2 Hz, Ar**H**), 6.74 (1 H, app. td, *J* = 7.6, 1.3 Hz, Ar**H**), 6.70 (2 H, d, *J* = 2.3 Hz, 2 × Ar**H**), 6.42 (1 H, t, *J* = 2.3 Hz, Ar**H**), 5.11 (2 H, s, C**H₂**), 3.82 (6 H, s, 2 × OC**H₃**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.0 (2 × **C**), 157.1 (**C**), 139.5 (**C**H), 139.0 (**C**), 129.4 (**C**H), 122.9 (**C**H), 112.7 (**C**H), 104.6 (2 × **C**H), 99.9 (**C**H), 86.8 (**C**), 70.6 (**C**H₂), 55.4 (2 × **C**H₃) ppm. **LRMS** (ESI+): 371 ([M+H]$^+$, 100%). **HRMS** (ESI+): Found 371.0148, [M+H]$^+$ $C_{15}H_{16}IO_3$ requires 371.0139.



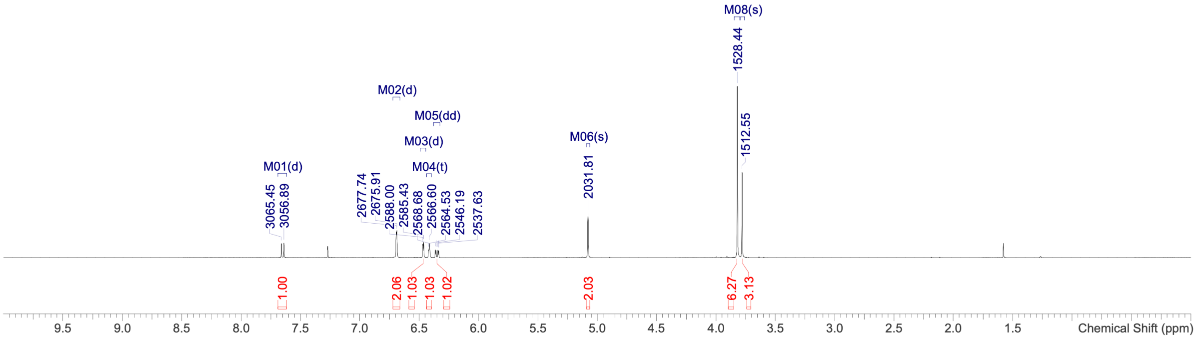


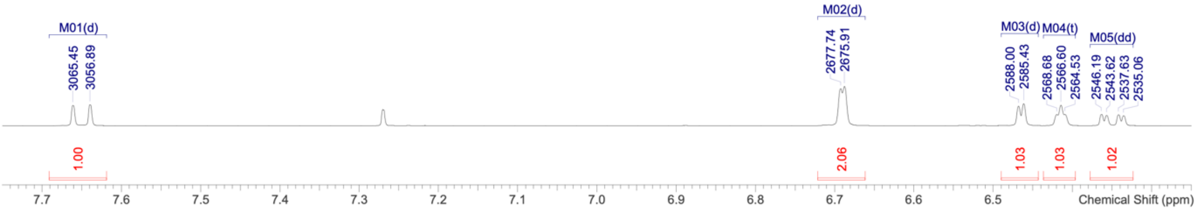


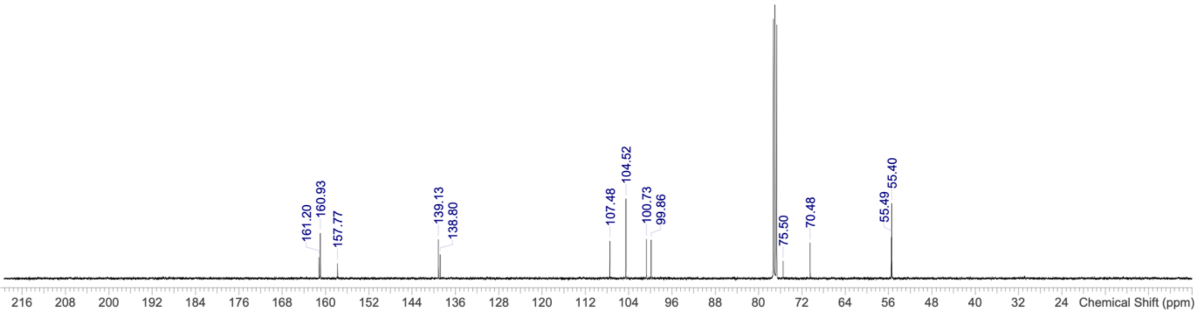
2-((3,5-Dimethoxybenzyl)oxy)-1-iodo-4-methoxybenzene, **5s**.



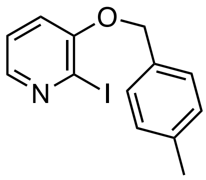
To a solution of 2-iodo-5-methoxyphenol (783 mg, 3.14 mmol) in acetone (30 mL) was added 3,5-dimethoxybenzyl bromide (730 mg, 3.14 mmol) and K_2CO_3 (870 mg, 6.30 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the organic phases were combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5 – 10% EtOAc in petrol) to afford the title compound **5s** (958 mg, 2.39 mmol, 76%) as a white solid. **MP** 73 – 74 °C. **IR** ν_{max} (solid, cm^{-1}): 2936 (w), 1589 (s), 1458 (m), 1375 (w), 1302 (m), 1203 (s), 1155 (s), 1055 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.65 (1 H, d, *J* = 8.6 Hz, Ar**H**), 6.69 (2 H, d, *J* = 1.8 Hz, 2 × Ar**H**), 6.46 (1 H, d, *J* = 2.6 Hz, Ar**H**), 6.41 (1 H, t, *J* = 2.1 Hz, Ar**H**), 6.35 (1 H, dd, *J* = 8.6, 2.6 Hz, Ar**H**), 5.08 (2 H, s, C**H**$_2$), 3.82 (6 H, s, 2 × OC**H**$_3$), 3.78 (3 H, s, OC**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 (**C**), 160.9 (2 × **C**), 157.8 (**C**), 139.1 (**C**H), 138.8 (**C**), 107.5 (**C**H), 104.5 (2 × **C**H), 100.7 (**C**H), 99.9 (**C**H), 75.5 (**C**), 70.5 (**C**H$_2$), 55.5 (**C**H$_3$), 55.4 (2 × **C**H$_3$) ppm. **LRMS** (ESI+): 401 ($[M+H]^+$, 16%), 274 (67%), 152 (60%), 151 ($[M–C_7H_6IO_2]^+$, 100%). **HRMS** (ESI+): Found 423.0072, $[M+Na]^+$ $C_{16}H_{17}INaO_4$ requires 423.0064.



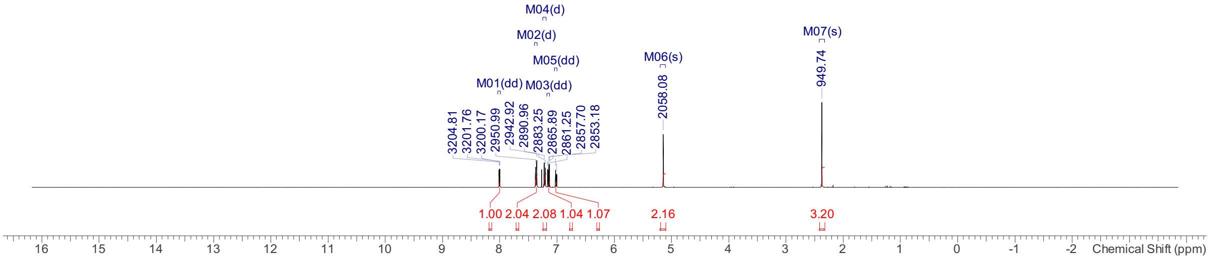


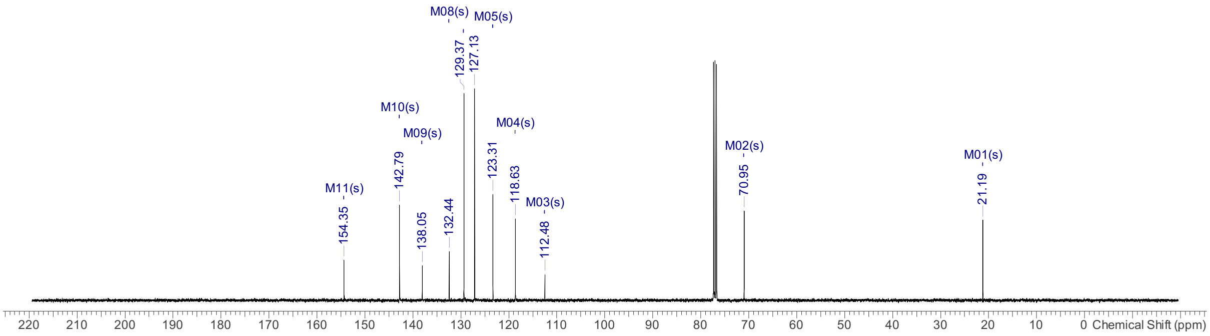


<u>2-Iodo-3-((4-methylbenzyl)oxy)pyridine</u>, **15b**.

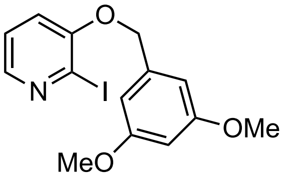


To a solution of 2-Iodo-3-hydroxypyridine (896 mg, 4.05 mmol) in DMF (50 mL) was added 4-methylbenzyl bromide (750 mg, 4.10 mmol), NaI (20 mg) and K_2CO_3 (1.12 g, 8.10 mmol). The reaction mixture was heated at 80 °C for 18 h then cooled to RT, diluted with water (50 mL) and extracted with EtOAc (3 × 100 mL). The organic phases were combined, washed with water (3 × 300 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **15b** as a yellow oil (1.073 g, 3.30 mmol, 80 %). **IR** ν_{max} (film, cm^{-1}): 3033 (br), 1557 (s), 1438 (s), 1404 (s), 1294 (s), 1198 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (1H, dd, *J* = 4.7, 1.6 Hz, Ar**H**), 7.36 (2H, d, *J* = 8.1 Hz, 2 × Ar**H**), 7.22 (2H, br d, *J* = 7.7 Hz, 2 × Ar**H**), 7.15 (1H, dd, *J* = 8.1, 4.6 Hz, Ar**H**), 7.02 (1H, dd, *J* = 8.1, 1.5 Hz, Ar**H**), 5.14 (2H, s, C**H**$_2$), 2.37 (3H, s, C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.4 (**C**), 142.8 (**C**H), 138.1 (**C**), 132.4 (**C**), 129.4 (2 × **C**H), 127.1 (2 × **C**H), 123.3 (**C**H), 118.6 (**C**H), 112.5 (**C**), 71.0 (**C**H$_2$), 21.2 (**C**H$_3$) ppm. **LRMS** (ESI$^+$): 326 [M+H]$^+$. **HRMS** (ESI$^+$): Found 326.0037, $C_{13}H_{13}IN_2O$ [M+H]$^+$ requires 326.0037.

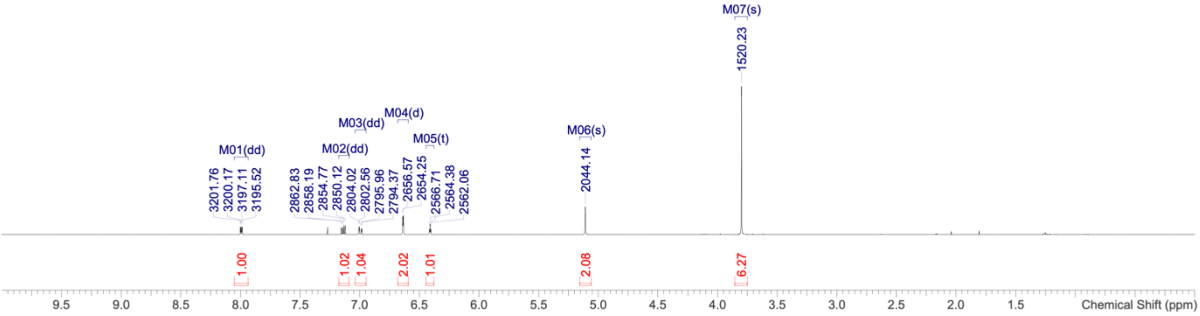


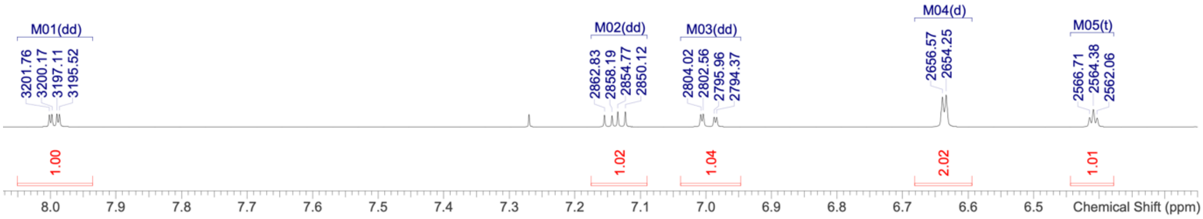


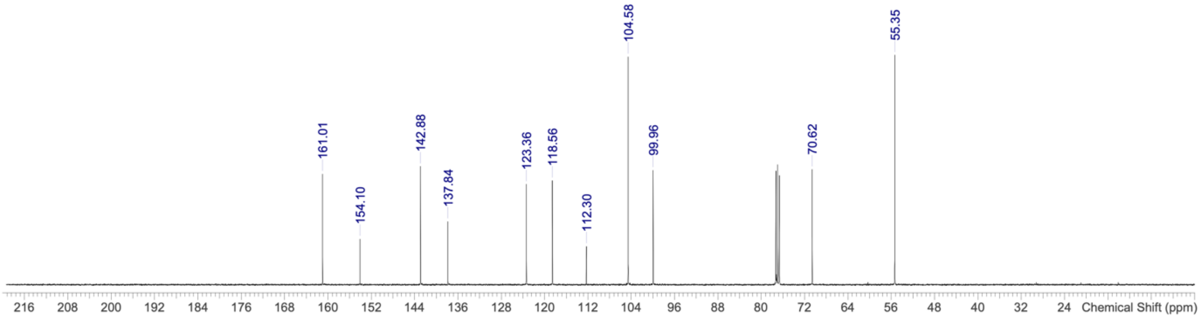
<u>3-((3,5-Dimethoxybenzyl)oxy)-2-iodopyridine</u>, **15c**.



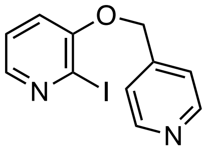
To a solution of 1-iodo-2-hydroxypyridine (1.56 g, 7.06 mmol) in acetone (70 mL) was added 3,5-dimethoxybenzyl bromide (1.63 g, 7.06 mmol) and K_2CO_3 (1.95 g, 14.0 mmol). The reaction mixture was heated at reflux for 16 h then cooled to RT and partitioned between water (100 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 30 mL) then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (30% EtOAc in petrol) to afford the title compound **15c** (2.25 g, 6.05 mmol, 87%) as a white solid. **MP** 66 – 68 °C. **IR** ν_{max} (film, cm^{-1}): 1598 (s), 1558 (m), 1456 (m), 1408 (m), 1373 (m), 1289 (m), 1203 (s), 1155 (s), 1067 (m), 1042 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (1 H, dd, *J* = 4.7, 1.6 Hz, Ar**H**), 7.14 (1 H, dd, *J* = 8.1, 4.7 Hz, Ar**H**), 7.00 (1 H, dd, *J* = 8.1, 1.5 Hz, Ar**H**), 6.64 (2 H, d, *J* = 2.3 Hz, 2 × Ar**H**), 6.41 (1 H, t, *J* = 2.3 Hz, Ar**H**), 5.11 (2 H, s, C**H$_2$**), 3.80 (6 H, s, 2 × OC**H$_3$**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.0 (**C**), 154.1 (**C**), 142.9 (**C**H), 137.8 (**C**), 123.4 (**C**H), 118.6 (**C**H), 112.3 (**C**), 104.6 (2 × **C**H), 100.0 (**C**H), 70.6 (**C**H$_2$), 55.4 (2 × **C**H$_3$) ppm. **LRMS** (ESI$^+$): 372 ([M+H]$^+$, 100%). **HRMS** (ESI$^+$): Found 372.0089, [M+H]$^+$ $C_{14}H_{15}INO_3$ requires 372.0091.



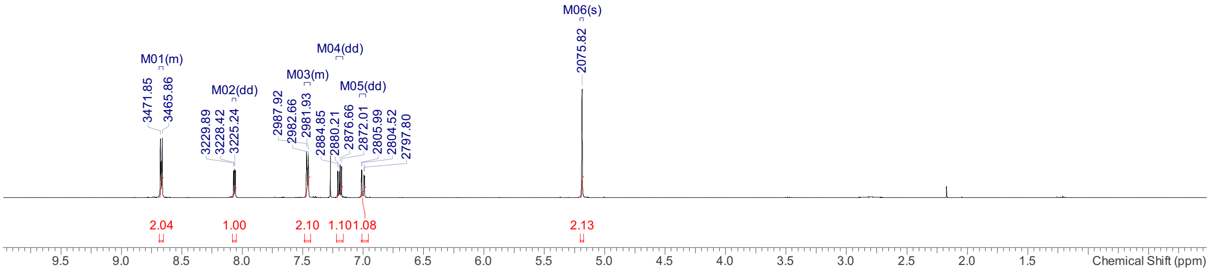


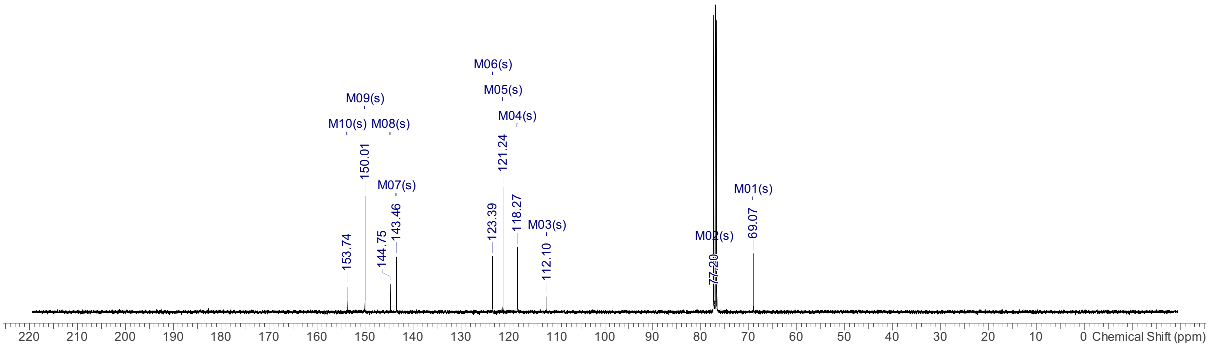


2-Iodo-3-(pyridin-4-ylmethoxy)pyridine, **15d**.

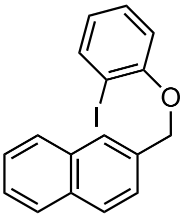


To a solution of 2-Iodo-3-hydroxypyridine (625 mg, 2.83 mmol) in DMF (50 mL) was added 4-(bromomethyl)pyridine hydrobromide (715 mg, 2.83 mmol), NaI (20 mg) and K_2CO_3 (1.17 g, 8.49 mmol). The reaction mixture was heated at 80 °C for 18 h then cooled to RT, diluted with water (50 mL) and extracted with EtOAc (3 × 100 mL). The organic phases were combined, washed with water (3 × 300 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **15d** as a yellow oil (627 mg, 2.01 mmol, 71 %). **IR** ν_{max} (film, cm^{-1}): 3033 (br), 1561 (m), 1458 (s), 1440 (s), 1408 (s), 1286 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.67 (1H, d, *J* = 6.0 Hz, Ar**H**), 8.67 (1H, d, *J* = 2.8 Hz, Ar**H**), 8.06 (1H, dd, *J* = 4.7, 1.5 Hz, Ar**H**), 7.47 – 7.45 (2H, m, 2 × Ar**H**), 7.19 (1H, dd, *J* = 8.2, 4.7 Hz, Ar**H**), 7.00 (1H, dq, *J* = 8.2, 1.5 Hz, Ar**H**), 5.19 (2H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.7 (**C**), 150.0 (2 × **C**H), 144.8 (**C**), 143.5 (**C**H), 123.4 (**C**H), 121.2 (2 × **C**H), 118.3 (**C**H), 112.1 (**C**), 69.1 (**C**H$_2$) ppm. **LRMS** (ESI$^+$): 313 [M+H]$^+$. **HRMS** (ESI$^+$): Found 312.9834, $C_{11}H_{10}IN_2O$ [M+H]$^+$ requires 312.9832.

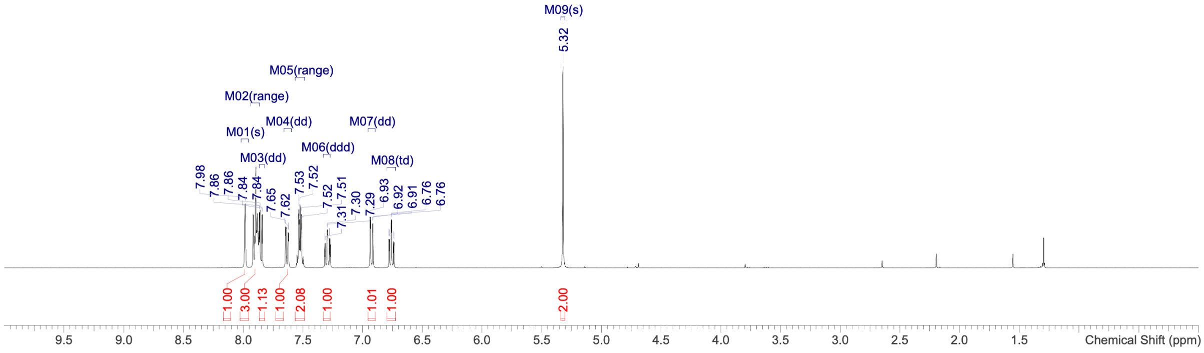


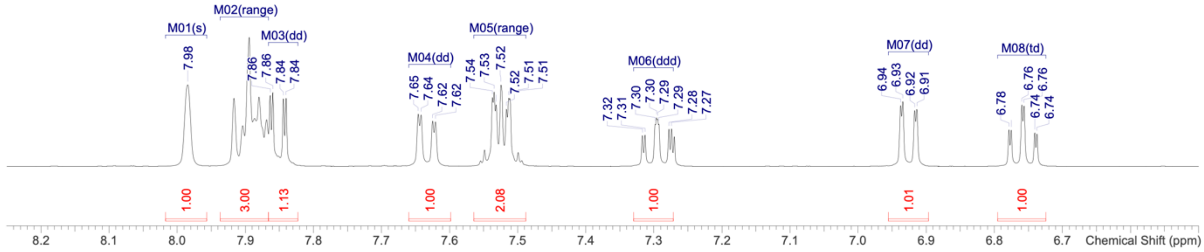


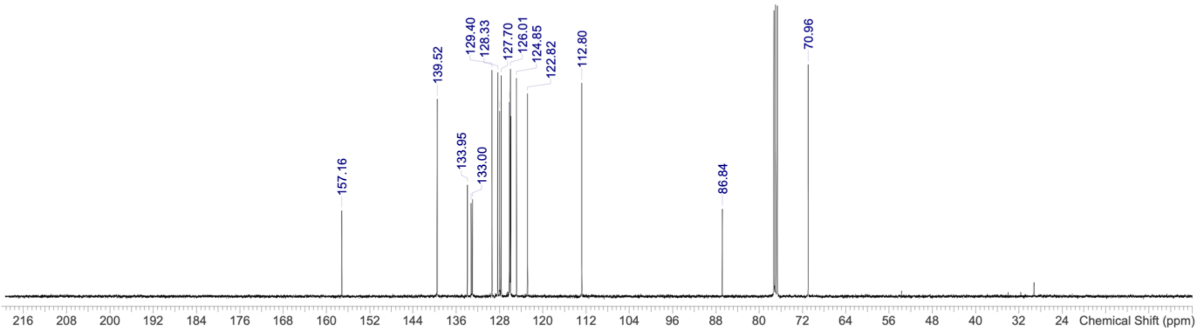
<u>2-((2-Iodophenoxy)methyl)naphthalene</u>, **17**.



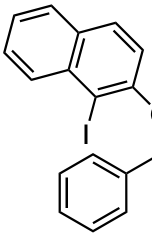
To a solution of 2-Iodo-3-hydroxypyridine (2.49 g, 11.3 mmol) in acetone (120 mL) was added 2-bromomethylnapthalene (2.50 g, 11.3 mmol) and K_2CO_3 (3.12 g, 22.6 mmol). The reaction mixture was heated at reflux for 18 h then cooled to RT and partitioned between water (100 mL) and DCM (100 mL). The aqueous phase was separated and extracted with DCM (4 × 20 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **17** (3.96 g, 11.0 mmol, 97%) as an off-white solid. **MP** 69 – 71 °C. **IR** ν_{max} (solid, cm^{-1}): 1579 (w), 1473 (m), 1458 (m), 1435 (m), 1276 (m), 1232 (m), 1048 (w), 1016 (m), 1000 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98 (1 H, s, Ar**H**), 7.87 – 7.94 (3 H, m, 3 × Ar**H**), 7.85 (1 H, dd, *J* = 7.8, 1.5 Hz, Ar**H**), 7.63 (1 H, dd, *J* = 8.4, 1.7 Hz, Ar**H**), 7.49 – 7.56 (2 H, m, 2 × Ar**H**), 7.30 (1 H, ddd, *J* = 8.3, 7.5, 1.6 Hz, Ar**H**), 6.93 (1 H, dd, *J* = 8.3, 1.3 Hz, Ar**H**), 6.76 (1 H, app. td, *J* = 7.6, 1.3 Hz, Ar**H**), 5.32 (2 H, s, C**H₂**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.2 (**C**), 139.5 (**C**H), 134.0 (**C**), 133.2 (**C**), 133.0 (**C**), 129.4 (**C**H), 128.3 (**C**H), 128.0 (**C**H), 127.7 (**C**H), 126.2 (**C**H), 126.0 (**C**H), 125.9 (**C**H), 124.9 (**C**H), 122.8 (**C**H), 112.8 (**C**H), 86.8 (**C**), 71.0 (**C**H_2) ppm. **LRMS** (EI): 360 ($[M]^+$, 40%), 141 (100%), 115 (65%). **HRMS** (EI): Found 360.0004, $[M]^+$ $C_{17}H_{13}IO$ requires 360.0006.



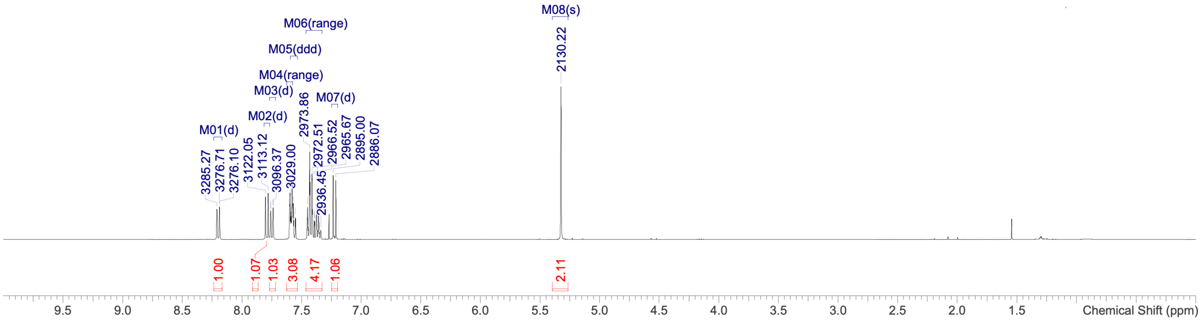


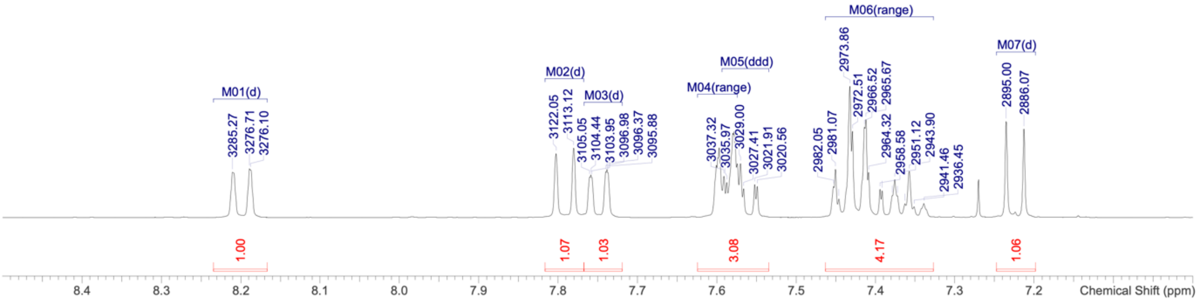


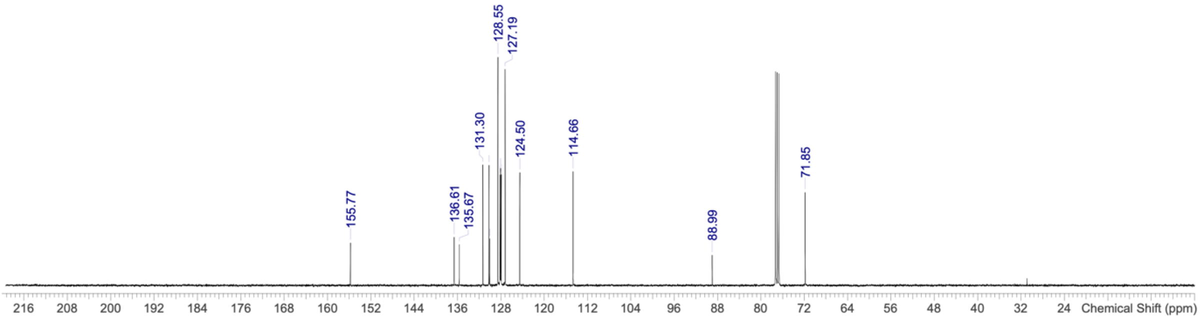
<u>2-(Benzyloxy)-1-iodonaphthalene</u>, **19**.[26-29]



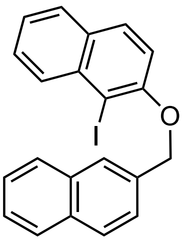
To a solution of 1-iodonaphthalen-2-ol (750 mg, 2.78 mmol) in acetone (50 mL) was added benzyl bromide (0.33 mL, 2.8 mmol) and K_2CO_3 (770 mg, 5.6 mmol). The reaction mixture was heated at reflux for 18 h then cooled to RT and partitioned between water (100 mL) and DCM (100 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* and purified by column chromatography (5% EtOAc in petrol) to afford the title compound **19** (943 mg, 2.62 mmol, 94%) as a white solid. **IR** ν_{max} (solid, cm^{-1}): 1620 (w), 1590 (w), 1497 (m), 1447 (w), 1328 (w), 1345 (w), 1260 (m), 1237 (m), 1147 (w), 1051 (m), 1020 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.20 (1 H, d with fine splitting, *J* = 8.6 Hz, Ar**H**), 7.79 (1 H, d, *J* = 8.9 Hz, Ar**H**), 7.75 (1 H, d with fine splitting, *J* = 8.1 Hz, Ar**H**), 7.57 – 7.62 (2 H, m, 2 × Ar**H**), 7.57 (1 H, ddd, *J* = 8.4, 6.9, 1.4 Hz, Ar**H**), 7.32 – 7.47 (4 H, m, 4 × Ar**H**), 7.22 (1 H, d, *J* = 8.9 Hz, Ar**H**), 5.32 (2 H, s, C**H$_2$**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.8 (**C**), 136.6 (**C**), 135.7 (**C**), 131.3 (**C**H), 130.2 (**C**H), 130.1 (**C**), 128.6 (2 × **C**H), 128.2 (**C**H), 128.1 (**C**H), 127.9 (**C**H), 127.2 (2 × **C**H), 124.5 (**C**H), 114.7 (**C**H), 89.0 (**C**), 71.9 (**C**H$_2$) ppm. **LRMS** (EI): 360 ([M]$^+$, 85%), 233 ([M - I]$^+$, 80%), 91 ([M - $C_{10}H_6IO$]$^+$, 100%).



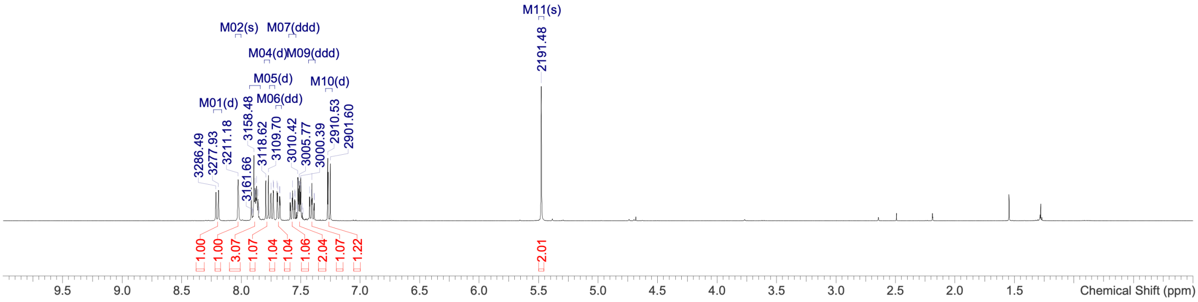


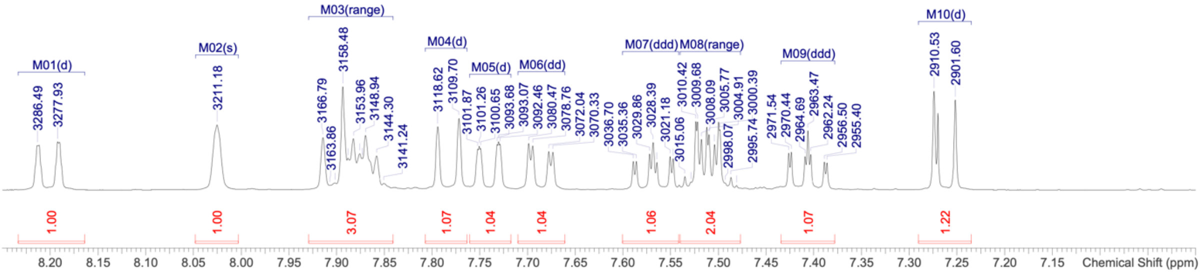


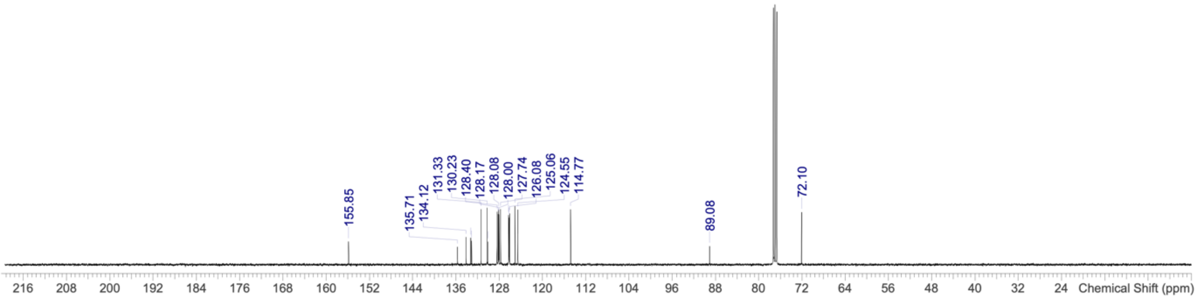
1-iodo-2-(naphthalen-2-ylmethoxy)naphthalene, **21**.[30]



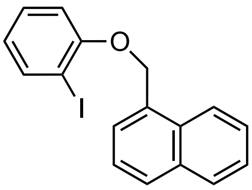
To a solution of 1-iodonaphthalen-2-ol (850 mg, 3.15 mmol) in acetone (30 mL) was added 2-bromomethylnaphthalene (700 mg, 3.17 mmol) and K_2CO_3 (870 mg, 6.30 mmol). The reaction mixture was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **21** (1.28 g, 3.1 mmol, 97%) as a yellow solid. **MP** 89 – 91 °C. **IR** ν_{max} (solid, cm^{-1}): 2981 (br), 1588 (w), 1498 (m), 1327 (m), 1267 (s), 1236 (s), 1063 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.20 (1 H, d with fine splitting, *J* = 8.6 Hz, Ar**H**), 8.03 (1 H, s, Ar**H**), 7.84 – 7.93 (3 H, m, 3 × Ar**H**), 7.78 (1 H, d, *J* = 8.9 Hz, Ar**H**), 7.74 (1 H, d with fine splitting, *J* = 8.2 Hz, Ar**H**), 7.69 (1 H, dd, *J* = 8.4, 1.7 Hz, Ar**H**), 7.57 (1 H, ddd, *J* = 8.5, 7.0, 1.3 Hz, Ar**H**), 7.48 – 7.54 (2 H, m, 2 × Ar**H**), 7.41 (1 H, ddd, *J* = 8.1, 6.9, 1.1 Hz, Ar**H**), 7.26 (1 H, d, *J* = 8.9 Hz, Ar**H**), 5.48 (2 H, s, C**H$_2$**) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.9 (**C**), 135.7 (**C**), 134.1 (**C**), 133.3 (**C**), 133.1 (**C**), 131.3 (**C**H), 130.2 (**C**H), 130.1 (**C**), 128.4 (**C**H), 128.2 (**C**H), 128.1 (**C**H), 128.0 (**C**H), 127.7 (**C**H), 126.24 (**C**H), 126.19 (**C**H), 126.1 (**C**H), 125.1 (**C**H), 124.6 (**C**H), 114.8 (**C**H), 89.1 (**C**), 72.1 (**C**H$_2$) ppm. **HRMS** (APPI): Found 410.0151, $[M]^+$ $C_{21}H_{15}IO$ requires 410.0162.





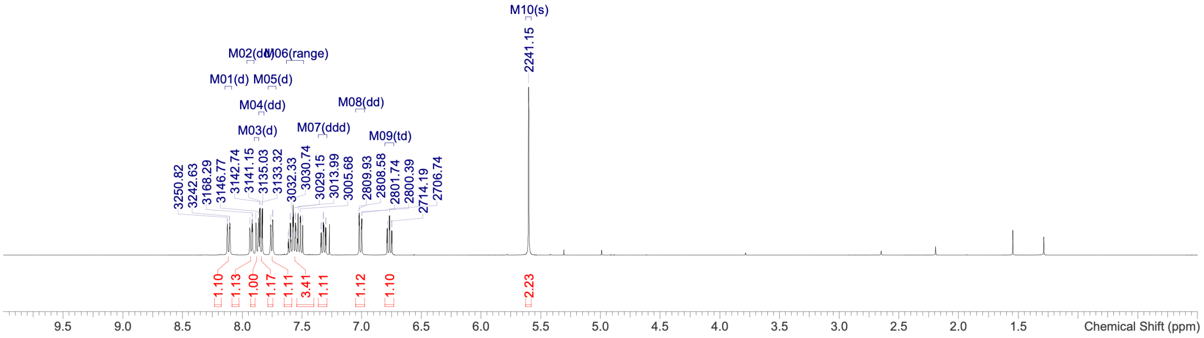


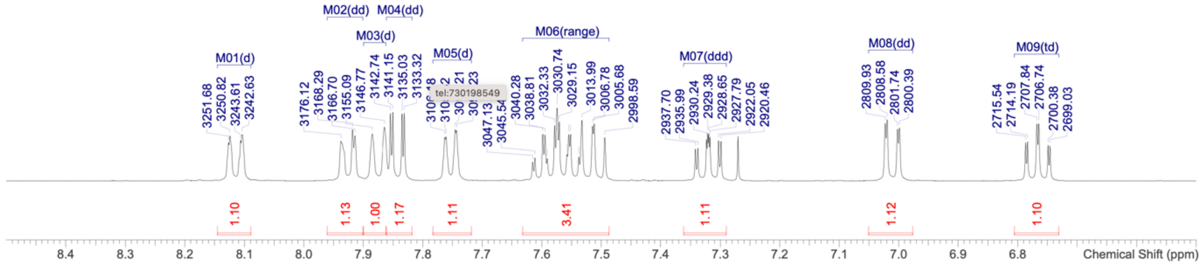
1-Iodo-2-(naphthalen-2-ylmethoxy)naphthalene, **22**.[19, 22b]

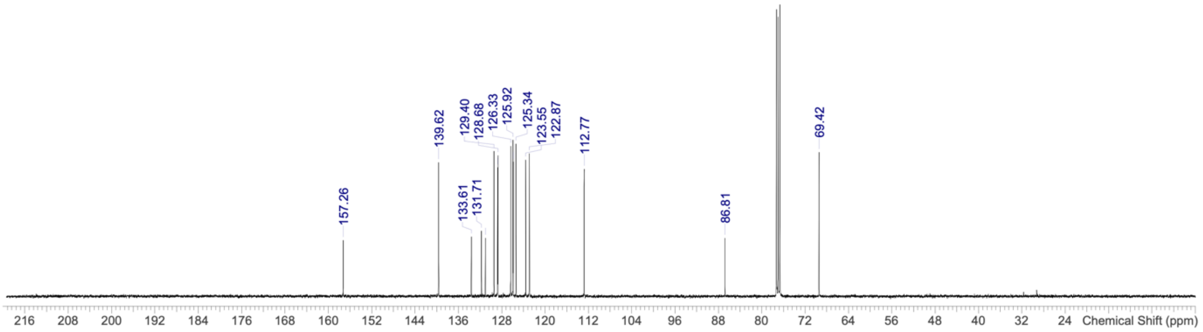


To a solution of 2-iodophenol (2.63 g, 12.0 mmol) in acetone (120 mL) was added 1-bromomethylnapthalene (2.63 g, 11.9 mmol) and K_2CO_3 (3.30 g, 23.9 mmol). The reaction was heated at reflux for 18 h, then cooled to RT and partitioned between H_2O (100 mL) and DCM (100 mL). The aqueous phase was separated and extracted with DCM (4 × 20 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **22** (4.19 g, 11.6 mmol, 98%) as an off-white solid. **IR** ν_{max} (solid, cm^{-1}): 1579 (w), 1566 (w), 1474 (m), 1458 (m), 1435 (m), 1276 (m), 1237 (s), 1048 (m), 1016 (s), 1000 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.12 (1 H, d with fine splitting, *J* = 8.3 Hz, Ar**H**), 7.93 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar**H**), 7.87 (1 H, d, *J* = 8.3 Hz, Ar**H**), 7.84 (1 H, dd, *J* = 7.8, 1.7 Hz, Ar**H**), 7.75 (1 H, d with fine splitting, *J* = 7.0 Hz, Ar**H**), 7.63 – 7.49 (3 H, m, 3 × Ar**H**), 7.32 (1 H, ddd, *J* = 8.3, 7.4, 1.7 Hz, Ar**H**), 7.01 (1 H, dd, *J* = 8.2, 1.3 Hz, Ar**H**), 6.77 (1 H, app. td, *J* = 7.6, 1.3 Hz, Ar**H**), 5.60 (2 H, s, CH$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.3 (**C**), 139.6 (**C**H), 133.6

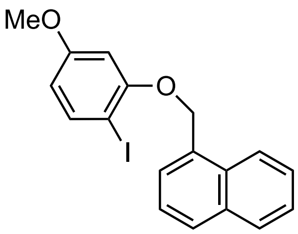
(**C**), 131.7 (**C**), 131.0 (**C**), 129.4 (**C**H), 128.8 (**C**H), 128.7 (**C**H), 126.3 (**C**H), 125.92 (**C**H), 125.87 (**C**H), 125.3 (**C**H), 123.6 (**C**H), 122.9 (**C**H), 112.8 (**C**H), 86.8 (**C**), 69.4 (**C**H_2) ppm. **LRMS** (EI): 360 ([M]$^+$, 12%), 141 (100%).



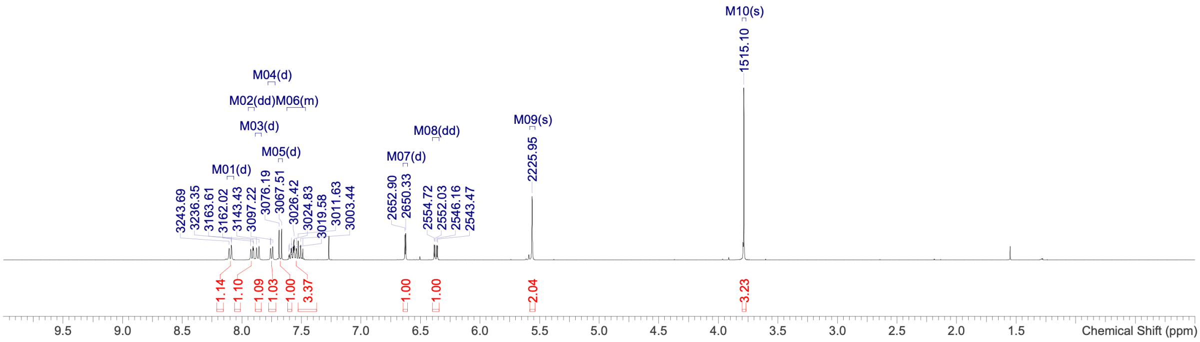


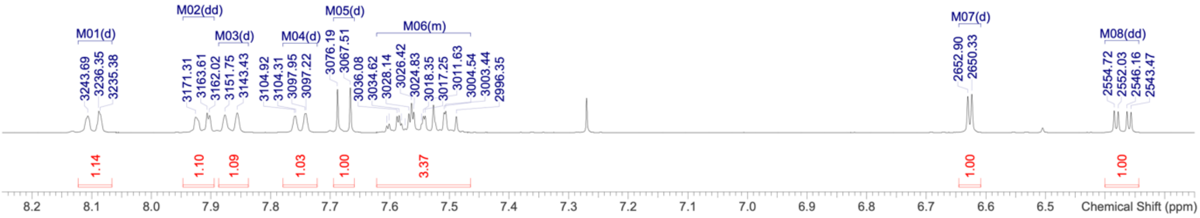


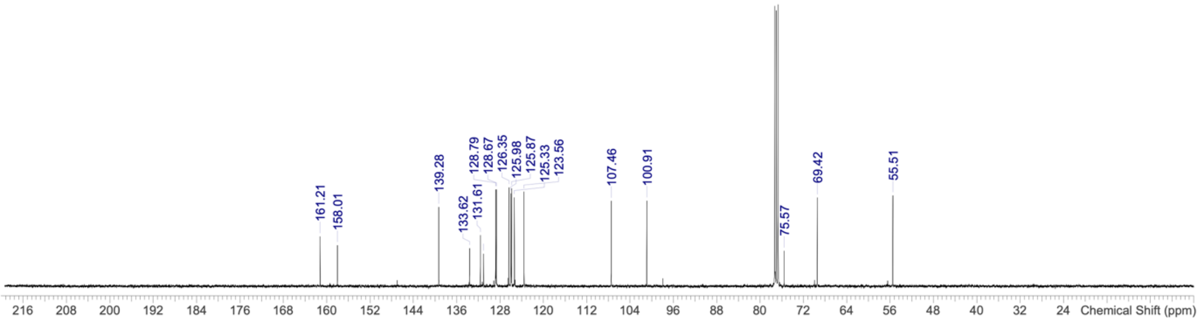
1-((2-iodo-5-methoxyphenoxy)methyl)naphthalene, **23**.



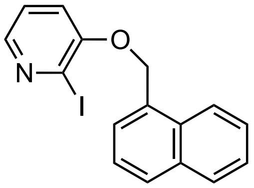
To a solution of 2-iodo-5-methoxyphenol (654 mg, 2.62 mmol) in acetone (30 mL) was added 1-bromomethylnaphthalene (580 mg, 2.62 mmol) and K_2CO_3 (720 mg, 5.21 mmol). The reaction was heated at reflux for 18 h then cooled to RT and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (2 × 20 mL) then the combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5% acetone in petrol) to afford the title compound **23** (969 mg, 2.48 mmol, 95%) as a white solid. **MP** 94 – 95 °C. **IR** ν_{max} (solid, cm^{-1}): 1576 (s), 1511 (m), 1463 (m), 1301 (s), 1279 (m), 1255 (m), 1199 (s), 1165 (s), 1055 (m), 1013 (m). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.10 (1 H, d with fine splitting, *J* = 8.3 Hz, Ar**H**), 7.91 (1 H, dd, *J* = 8.0, 1.6 Hz, Ar**H**), 7.87 (1 H, d, *J* = 8.3 Hz, Ar**H**), 7.75 (1 H, d with fine splitting, *J* = 7.0 Hz, Ar**H**), 7.68 (1 H, d, *J* = 8.7 Hz, Ar**H**), 7.47 – 7.61 (3 H, m, 3 × Ar**H**), 6.63 (1 H, d, *J* = 2.6 Hz, Ar**H**), 6.37 (1 H, dd, *J* = 8.6, 2.7 Ar**H**), 5.56 (2 H, s, C**H**$_2$), 3.79 (3 H, s, OC**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 (**C**), 158.0 (**C**), 139.3 (**C**H), 133.6 (**C**), 131.6 (**C**), 131.0 (**C**), 128.8 (**C**H), 128.7 (**C**H), 126.4 (**C**H), 126.0 (**C**H), 125.9 (**C**H), 125.3 (**C**H), 123.6 (**C**H), 107.5 (**C**H), 100.9 (**C**H), 75.6 (**C**), 69.4 (**C**H_2), 55.5 (**C**H_3) ppm. **LRMS** (ESI+): 391 ([M+H]$^+$, 10%), 280 (60%), 264 (100 %), 263 ([M-I]$^+$, 40%). **HRMS** (ESI+): Found 413.0010, [M+Na]$^+$ $C_{18}H_{15}INaO_2$ requires 413.0009.



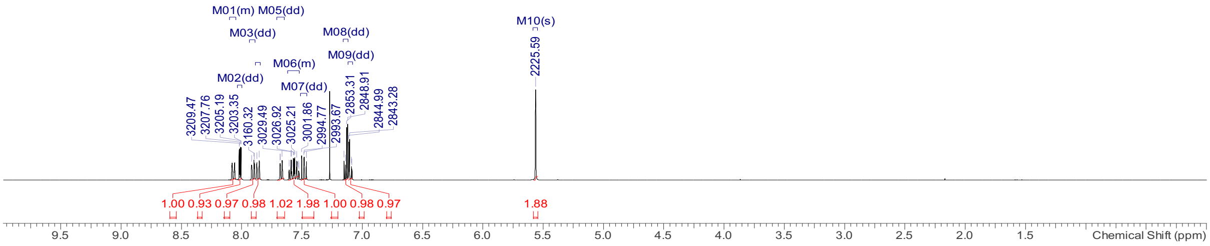


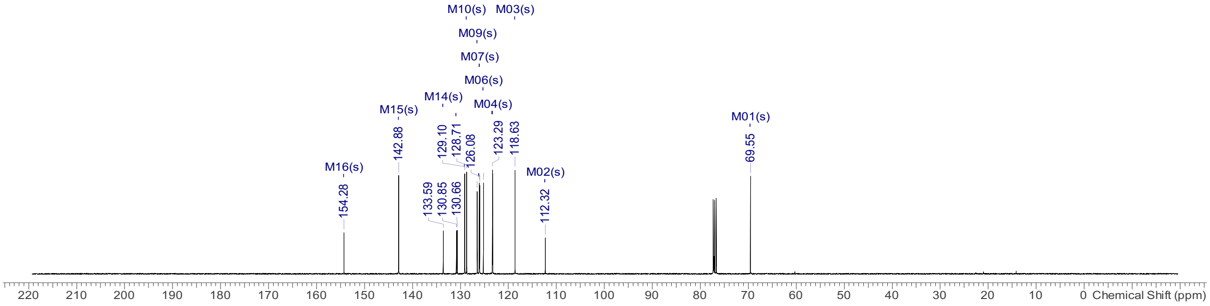


2-Iodo-3-(naphthalen-1-ylmethoxy)pyridine, **24**.[31]

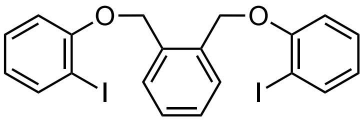


To a solution of 2-Iodo-3-hydroxypyridine (745 mg, 3.37 mmol) in DMF (50 mL) was added 1-(bromomethyl)naphthalene (747 mg, 3.37 mmol), NaI (20 mg) and K_2CO_3 (930 mg, 6.74 mmol). The reaction mixture was heated at 80 °C for 18 h then cooled to RT, diluted with water (50 mL) and extracted with EtOAc (3 × 100 mL). The organic phases were combined, washed with water (3 × 300 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **24** as a yellow oil (989 mg, 2.74 mmol, 81 %). **IR** ν_{max} (film, cm^{-1}): 3026 (br), 1555 (s), 1407 (s), 1289 (s), 1196 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07 (1H, m, Ar**H**), 8.01 (1H, dd, *J* = 4.3, 1.8 Hz, Ar**H**), 7.91 (1H, m, Ar**H**), 7.86 (1H, d, *J* = 8.3 Hz, Ar**H**), 7.67 (1H, m, Ar**H**), 7.61 – 7.52 (2H, m, 2 × Ar**H**), 7.48 (1H, dd, *J* = 8.2, 7.1 Hz, Ar**H**), 7.14 (1H, dd, *J* = 8.1, 4.4 Hz, Ar**H**), 7.10 (1H, dd, *J* = 8.2, 1.7 Hz, Ar**H**), 5.56 (2H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.3 (**C**), 142.9 (**C**H), 133.6 (**C**), 130.9 (**C**), 130.7 (**C**), 129.1 (**C**H), 128.7 (**C**H), 126.5 (**C**H), 126.1 (**C**H), 126.0 (**C**H), 125.2 (**C**H), 123.4 (**C**H), 123.3 (**C**H), 118.6 (**C**H), 112.3 (**C**), 69.6 (**C**H$_2$) ppm. **LRMS** (ESI$^+$): 362 [M+H]$^+$. **HRMS** (ESI$^+$): Found 362.0043, $C_{16}H_{13}INO$ [M+H]$^+$ requires 362.0036.

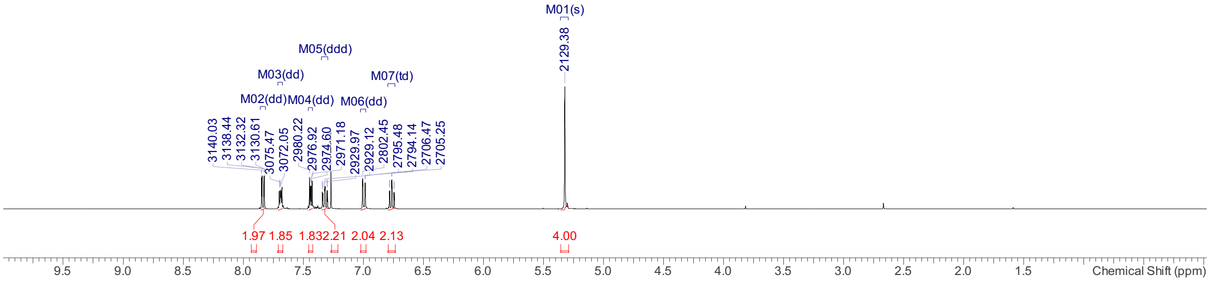


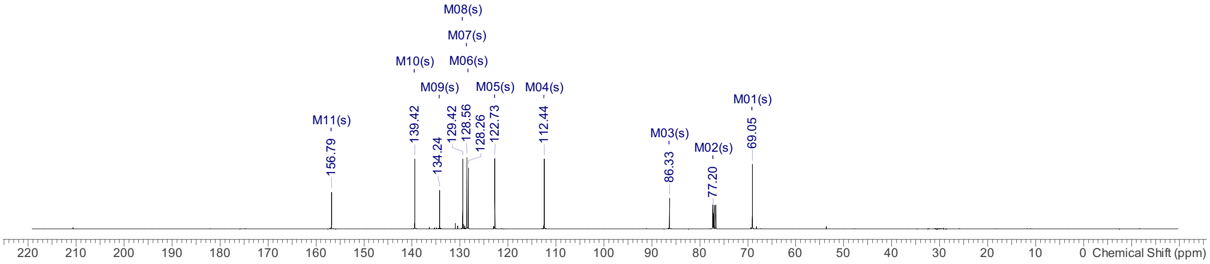


1,2-*Bis*((2-iodophenoxy)methyl)benzene, **29**.[32]

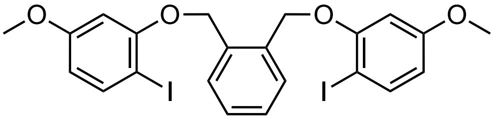


To a solution of 2-iodophenol (2.29 g, 10.4 mmol) in acetone (100 mL) was added 1,2-*bis*(bromomethyl)benzene (1.52 mg, 5.76 mmol) and K_2CO_3 (2.08 g, 15.1 mmol). The reaction was heated at reflux for 18 h then cooled to RT, concentrated *in vacuo* and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **29** as an off-white solid (2.33 g, 4.30 mmol, 74 %). **IR** ν_{max} (film, cm^{-1}): 3060 (br), 1561 (s), 1468 (s), 1438 (s), 1274 (s), 1240 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 (2H, dd, *J* = 7.8, 1.7 Hz, 2 × Ar**H**), 7.69 (2H, dd, *J* = 5.5, 3.4 Hz, 2 × Ar**H**), 7.44 (2H, dd, *J* = 5.6, 3.3 Hz, 2 × Ar**H**), 7.32 (2H, ddd, *J* = 8.3, 7.5, 1.6 Hz, 2 × Ar**H**), 7.00 (2H, dd, *J* = 8.3, 1.3 Hz, 2 × Ar**H**), 6.76 (2H, td, *J* = 7.6, 1.3 Hz, 2 × Ar**H**), 5.32 (4H, s, 2 × C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.8 (2 × **C**), 139.4 (2 × **C**H), 134.2 (2 × **C**), 129.4 (2 × **C**), 128.6 (2 × **C**H), 128.3 (2 × **C**H), 122.7 (2 × **C**H), 122.4 (2 × **C**H), 86.3 (2 × **C**), 69.1 (2 × **C**H$_2$) ppm. **HRMS** (ESI$^+$): Found 564.9137, $C_{20}H_{16}I_2NaO_2$, $[M+Na]^+$ requires 564.9132.

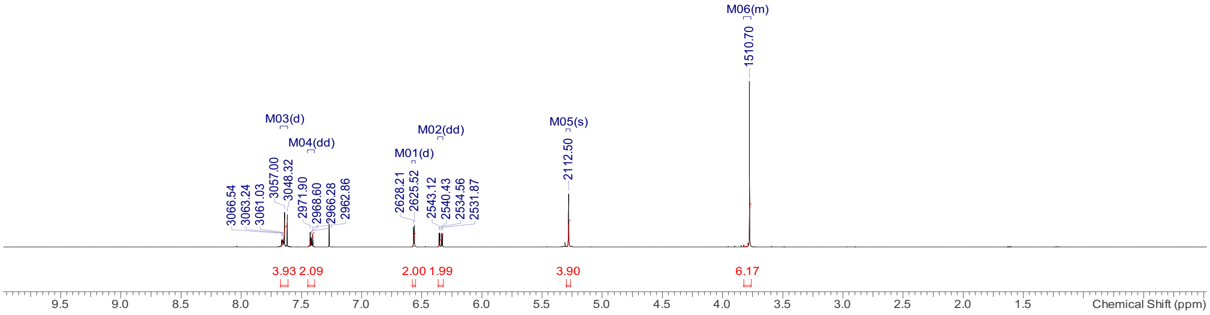


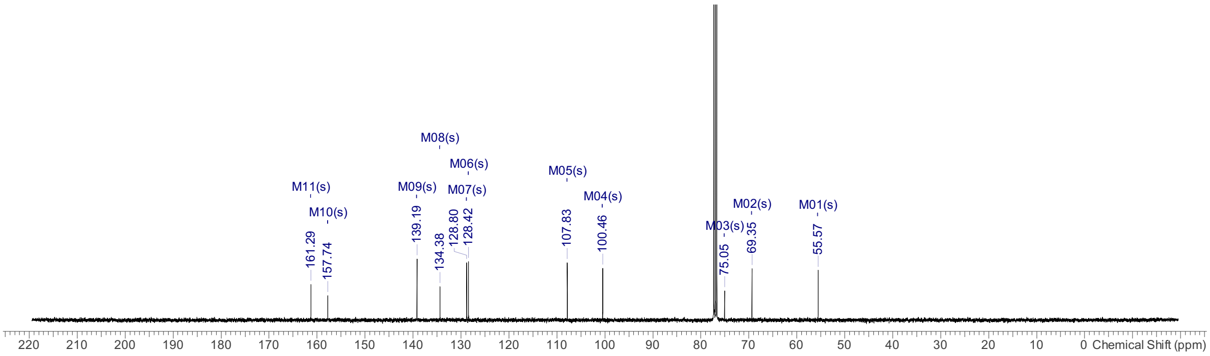


1,2-*Bis*((2-iodo-5-methoxyphenoxy)methyl)benzene, **30**.

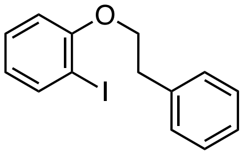


To a solution of 4-methoxy-2-iodophenol (1.06 g, 4.24 mmol) in acetone (100 mL) was added 1,2-*bis*(bromomethyl)benzene (562 mg, 2.13 mmol) and K_2CO_3 (1.18 g, 8.54 mmol). The reaction was heated at reflux for 18 h then cooled to RT, concentrated *in vacuo* and partitioned between water (50 mL) and DCM (50 mL). The aqueous phase was separated and extracted with DCM (3 × 20 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **30** as an off-white solid (1.023 g, 1.70 mmol, 80 %). **IR** ν_{max} (film, cm^{-1}): 2935 (br), 1577 (s), 1482 (s), 1201 (s), 1166 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.65 (2H, dd, *J* = 5.5, 3.3 Hz, 2 × Ar**H**), 7.63 (2H, d, *J* = 8.7 Hz, 2 × Ar**H**), 7.42 (2H, dd, *J* = 5.6, 3.3 Hz, 2 × Ar**H**), 6.57 (2H, d, *J* = 2.7 Hz, 2 × Ar**H**), 6.34 (2H, dd, *J* = 8.6, 2.7 Hz, 2 × Ar**H**), 5.28 (4H, s, 2 × C**H**$_2$), 3.78 (6H, s, 2 × C**H**$_3$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.3 (2 × **C**), 157.7 (2 × **C**), 139.2 (2 × **C**H), 134.4 (2 × **C**), 128.8 (2 × **C**H), 128.4 (2 × **C**H), 107.8 (2 × **C**H), 100.5 (2 × **C**H), 75.1 (2 × **C**), 69.4 (2 × **C**H$_2$), 55.6 (2 × **C**H$_3$) ppm. **HRMS** (ESI$^+$): Found 624.9349, $C_{22}H_{20}I_2NaO_2$, $[M+Na]^+$ requires 642.9343.

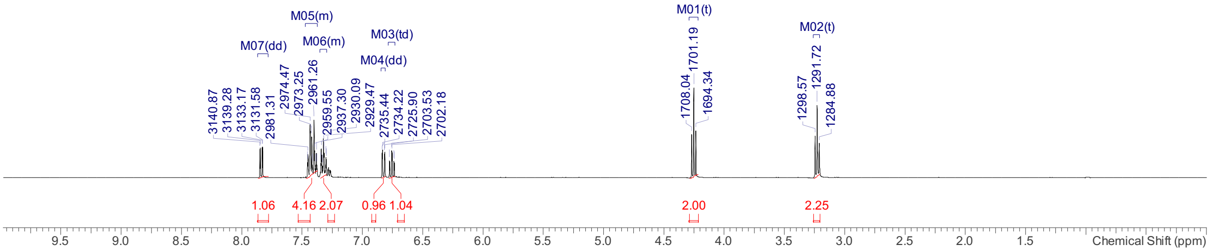


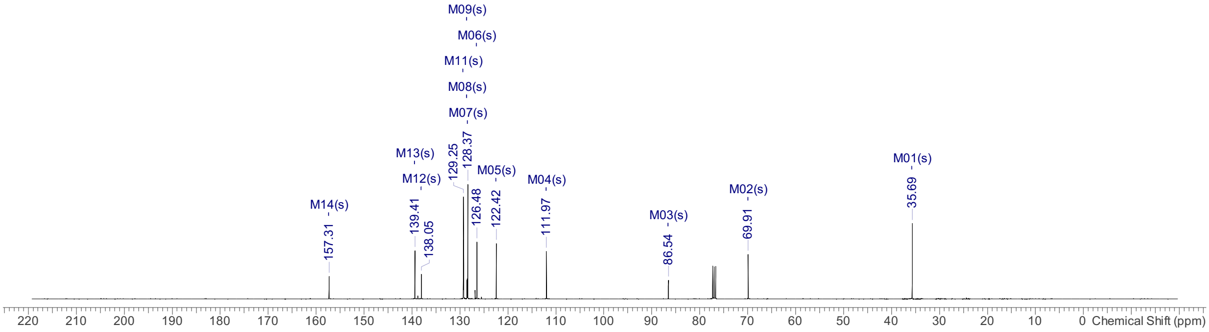


1-Iodo-2-phenethoxybenzene, **38a**.[33]

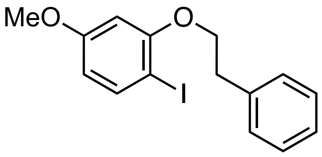


To a solution of 2-iodophenol (1.51 mg, 6.86 mmol) in DMF (50 mL) was added (2-bromoethyl)benzene (0.95 mL, 6.86 mmol) and K_2CO_3 (1.90 g, 13.8 mmol). The reaction mixture was heated at 80 °C for 18 h then cooled to RT, diluted with water (50 mL) and extracted with EtOAc (3 × 100 mL). The organic phases were combined, washed with water (3 × 300 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **38a** as a colourless oil (1.63 g, 5.03 mmol, 73 %). **IR** ν_{max} (film, cm^{-1}): 3026 (br), 1581 (s), 1462 (s), 1243 (s), 1016 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 (1 H, dd, *J* = 7.7, 1.6 Hz, Ar**H**), 7.46 – 7.30 (6 H, m, 6 × Ar**H**), 6.82 (1 H, dd, *J* = 8.3, 1.3 Hz, Ar**H**), 6.82 (1 H, td, *J* = 7.5, 1.3 Hz, Ar**H**), 4.25 (2 H, t, *J* = 6.9 Hz, C**H**$_2$), 3.23 (2 H, t, *J* = 6.9 Hz, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.3 (**C**), 139.4 (**C**H), 138.5 (**C**), 129.30 (**C**), 129.25 (2 × CH), 128.4 (2 × **C**H), 126.5 (**C**H), 122.4 (**C**H), 112.0 (**C**H), 86.5 (**C**), 69.9 (**C**H$_2$), 36.7 (**C**H$_2$) ppm. **LRMS** (EI): 324 (42%, [M$^+$]), 105 (100%). **HRMS** (EI): Found 324.0009, $C_{14}H_{13}IO$ [M$^+$] requires 324.0006.



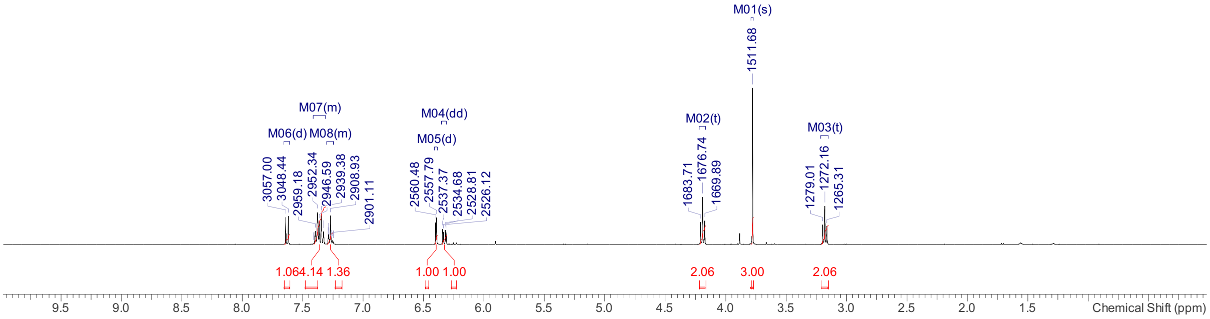


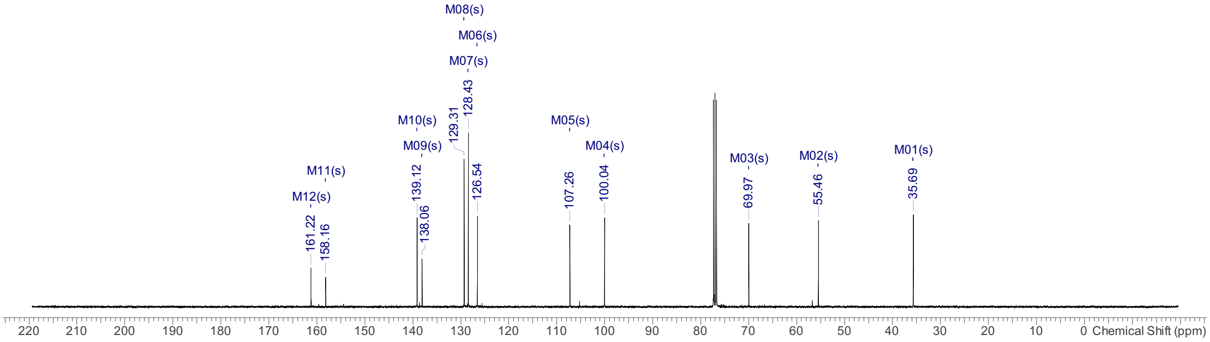
1-Iodo-4-methoxy-2-phenethoxybenzene, **38b**.



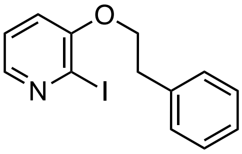
To a solution of 2-iodo-5-methoxyphenol (872 mg, 3.49 mmol) in DMF (50 mL) was added (2-bromoethyl)benzene (0.48 mL, 3.50 mmol) and K_2CO_3 (966 mg, 6.99 mmol). The reaction mixture was heated at 80 °C for 18 h then cooled to RT, diluted with water (50 mL) and extracted with EtOAc (3 × 100 mL). The organic phases were combined, washed with water (3 × 300 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **38b** as a colourless oil (1.03 g, 2.91 mmol, 83 %). **IR** ν_{max} (film, cm^{-1}): 2934 (br), 1577 (s), 1303 (s), 1202 (s), 1167 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.63 (1 H, d, *J* = 8.6 Hz, Ar**H**), 7.41 – 7.33 (4 H, m, 4 × Ar**H**), 7.27 (1 H, m, Ar**H**), 6.40 (1 H, d, *J* = 2.7 Hz, Ar**H**), 6.33 (1 H, dd, *J* = 8.6, 2.7 Hz, Ar**H**), 4.19 (2 H, t, *J* = 6.9 Hz, C**H**$_2$), 3.78 (3 H, s, C**H**$_3$), 3.18 (2 H, t, *J* = 6.9 Hz, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 (**C**), 158.2 (**C**), 139.1 (**C**H), 138.1

(**C**), 129.3 (2 × **C**H), 128.4 (2 × **C**H), 126.5 (**C**H), 107.3 (**C**H), 100.0 (**C**H), 70.0 (**C**H_2), 55.5 (**C**H_3), 35.7 (**C**H_2) ppm. **LRMS** (ESI$^+$): 355. **HRMS** (EI): Found 354.0111, $C_{15}H_{15}IO_2$ [M$^+$] requires 354.0111.

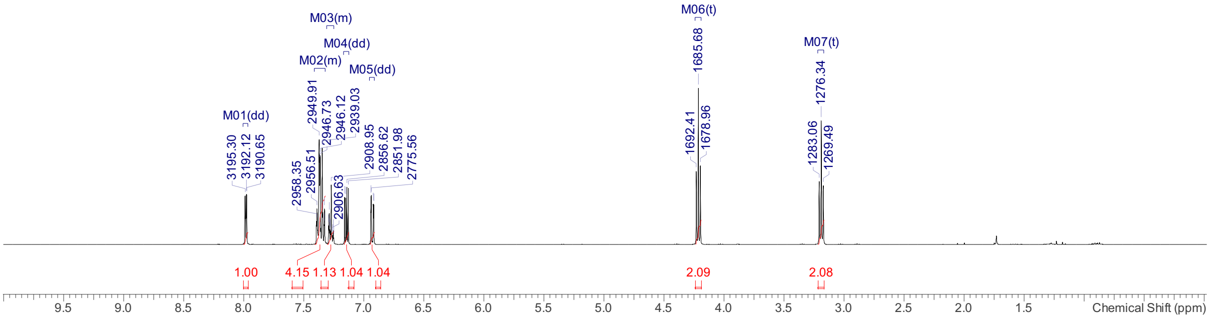


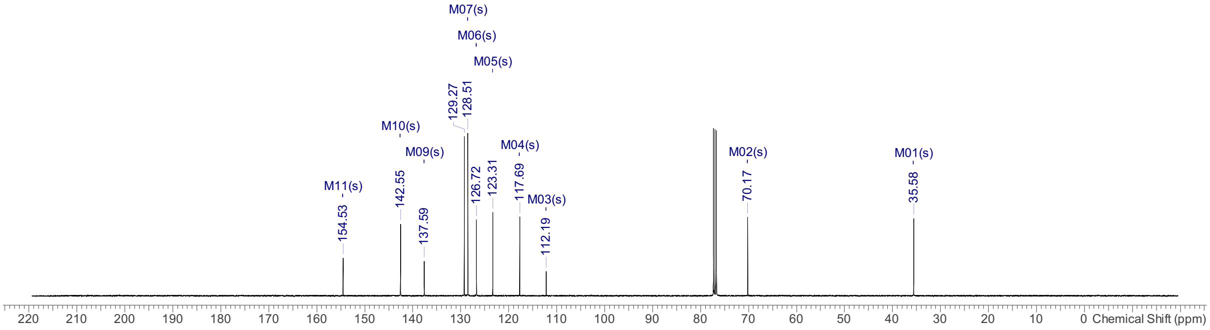


<u>2-Iodo-3-phenethoxypyridine</u>, **38c**.

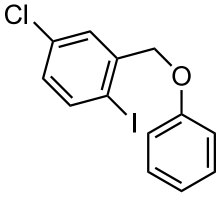


To a solution of 2-iodopyridin-3-ol (631 mg, 2.86 mmol) in DMF (50 mL) was added (2-bromoethyl)benzene (0.40 mL, 2.90 mmol) and K_2CO_3 (830 mg, 6.01 mmol). The reaction mixture was heated at 80 °C for 18 h then cooled to RT, diluted with water (50 mL) and extracted with EtOAc (3 × 100 mL). The organic phases were combined, washed with water (3 × 300 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **38c** as a yellow oil (815 mg, 2.51 mmol, 88 %). **IR** ν_{max} (film, cm^{-1}): 3022 (br), 1557 (s), 1408 (s), 1381 (s), 1283 (s), 1039 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98 (1H, dd, *J* = 4.7, 1.5 Hz, Ar**H**), 7.39 – 7.33 (4H, m, 4 × Ar**H**), 7.28 (1H, m, Ar**H**), 7.14 (1H, dd, *J* = 8.1, 4.6 Hz, Ar**H**), 6.93 (1H, dd, *J* = 8.1, 1.5 Hz, Ar**H**), 4.21 (2H, t, *J* = 6.7 Hz, C**H**$_2$), 3.19 (2H, t, *J* = 6.8 Hz, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.5 (**C**), 142.6 (**C**H), 137.6 (**C**), 129.3 (2 × **C**H), 128.5 (2 × **C**H), 126.7 (**C**H), 123.3 (**C**H), 117.7 (**C**H), 112.2 (**C**), 70.2 (**C**H_2), 35.6 (**C**H_2) ppm. **LRMS** (ESI$^+$): 326 [M+H]$^+$. **HRMS** (ESI$^+$): Found 326.0043, $C_{13}H_{13}INO_2$ [M+H]$^+$ requires 326.0036.

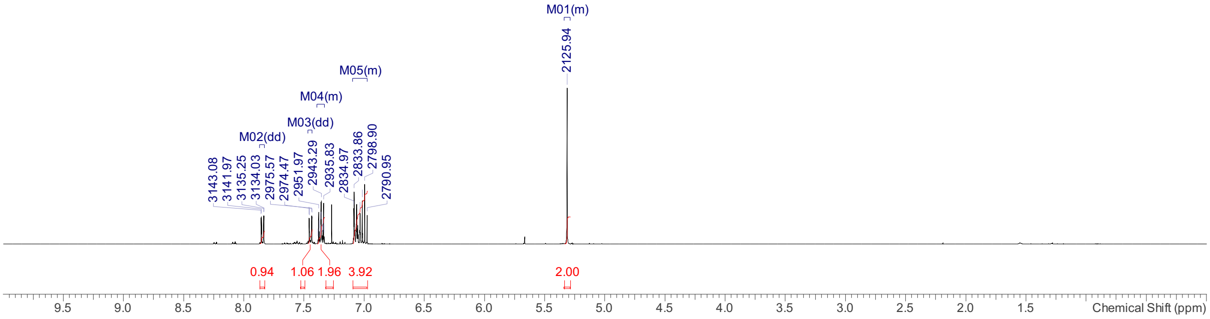


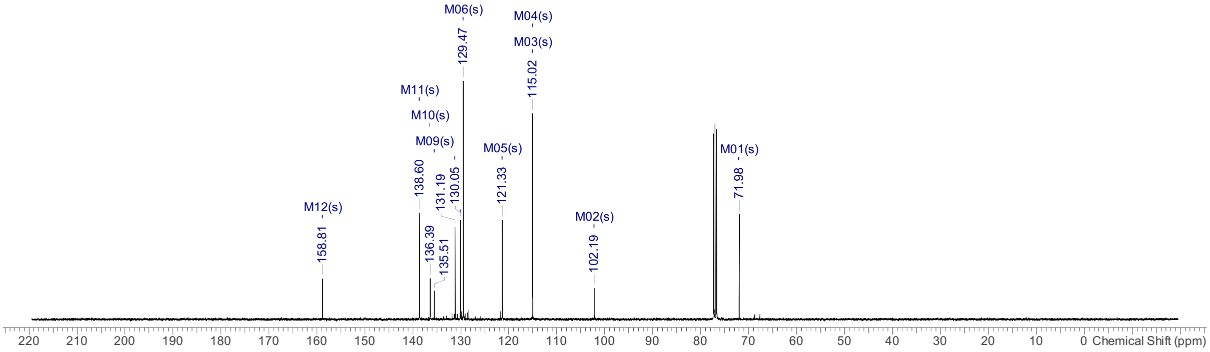


4-Chloro-1-iodo-2-(phenoxymethyl)benzene, **40**.[34]



To a solution of 4-chloro-1-iodo-2-methylbenzene (1.30 mL, 9.27 mmol) in chlorobenzene (30 mL) was added NBS (1.65 g, 9.27 mmol) and benzoyl peroxide (225 mg, 0.93 mmol). The reaction mixture was heated at 70 °C for 3 h then cooled to RT and concentrated *in vacuo.* DCM (30 mL) and sat. $Na_2S_2O_3$ (30 mL) were added, the aqueous phase was separated and extracted with DCM (3 × 30 mL), then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo* to afford a brown oil. DMF (50 mL), 2-iodophenol (2.05 g, 9.30 mmol) and K_2CO_3 (2.57 g, 18.6 mmol) were added, the reaction mixture was heated at 80 °C for 18 h then partitioned between water (50 mL) and EtOAc (100 mL). The aqueous phase was extracted with EtOAc (3 × 100 mL) then the combined organic phases were washed with water (5 × 300 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **42** as an off white solid (1.76 g, 5.11 mmol, 55 %). **MP**: 78 – 79 °C. **IR** ν_{max} (film, cm^{-1}): 3060 (br), 1598 (s), 1493 (s), 1233 (s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 (1H, dd, *J* = 7.9, 1.2 Hz, Ar**H**), 7.45 (1H, dd, *J* = 8.1, 1.1 Hz, Ar**H**), 7.38 – 7.32 (2H, m , 2 × Ar**H**), 7.09 – 6.98 (4H, m , 4 × Ar**H**), 5.31 (2H, s, C**H**$_2$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.8 (**C**), 138.6 (**C**H), 136.4 (**C**), 135.5 (**C**), 131.2 (**C**H), 130.1 (**C**H), 129.5 (2 × **C**H), 121.3 (**C**H), 115.0 (2 × **C**H), 102.20 (**C**), 72.0 (**C**H$_2$) ppm. **LRMS** (EI): 344 (48%, [M$^+$]), 251 (100%), 217 (43%). **HRMS** (EI): Found 343.9457, $C_{13}H_{11}IClO$ [M$^+$] requires 343.9459.





References

1. D. C. Harrowven, M. I. T. Nunn, N. A. Newman and D. R. Fenwick, *Tetrahedron Lett.*, 2001, **42**, 961.
2. M. E. Budén, M. D. Heredia, M. Puiatti and R. A. Rossi, *Org. Biomol. Chem.*, 2022, **20**, 228.
3. D. Hook, W. Dohle, P. R. Hirst, M. Pickworth, M. B. Berry and K. I. Booker-Milburn, *J. Org. Chem.*, 2005, **70**, 7558; D. C. Harrowven, M. Mohamed, T. P. Gonçalves, R. J. Whitby, D. Bolien and H. F. Sneddon, *Angew. Chem. Int. Ed.*, 2012, **51**, 4405; L. D. Elliott, J. P. Knowles, P. J. Koovits, K. G. Maskill, M. J. Robertson-Ralph, G. Lejeune, L. J. Edwards, R. I. Robinson, I. R. Clemens, B. Cox, D. D. Pascoe, G. Koch, M. Eberle, M. B. Berry and K. I. Booker-Milburn, *Chem. Eur. J.*, 2014, **20**, 15226; D. E. Collin, E. H. Jackman, N. Jouandon, W. Sun, D. C. Harrowven and B. Linclau, *Synthesis*, 2021, **53**, 1307; M. A. Manning, W. Sun, M. E. Light and D. C. Harrowven, *Chem. Commun.*, 2021, **57**, 4556; W. Sun, W. A. T. Raimbach, L. D. Elliott, K. I. Booker-Milburn and D. C. Harrowven, *Chem. Commun.*, 2022, **58**, 383; W. Sun, S. Kayal, W. A. T. Raimbach, X.-Z. Sun, M. E. Light, M. W. D. Hanson-Heine, M. W. George and D. C. Harrowven, *Chem. Commun.*, 2022, **58**, 1546.
4. C. Nottingham, V. Barber and G. C. Lloyd-Jones, *Org. Synth.*, 2019, **96**, 150.
5. A. Ahmed, S. Dhara and J. K. Ray, *Tetrahedron Lett.* 2013, **54**, 1673; R. Singha, A. Ahmed, Y. Nuree, M. Ghosha and J. K. Ray, *RSC Adv.*, 2015, **5**, 50174.

6. Y. He, X. Zhang, L. Cui, J. Wang and X. Fan, *Green Chem.*, 2012, **14**, 3429; T. Nishikata, H. Tsutsumi, L. Gao, K. Kojima, K. Chikama and H. Nagashima, *Adv. Synth. Catal.*, 2014, **356**, 951.
7. L.–C. Campeau, M. Parisien, A. Jean and K. Fagnou, *J. Am. Chem. Soc.*, 2006, **128**, 581.
8. A. M. Rosa, A. M. Lobo, P. S. Branco and S. Prabhakar, *Tetrahedron*, 1997, **53**, 285.
9. J.-Y. He , Q.-F. Bai, C. Jin and G. Feng, *Synlett*, 2018, **29**, 2311.
10. J. Wang, J. Zhao and H. Gong, *Chem. Commun.*, 2017, **53**, 10180.
11. S. K. Rastogi, D. C. Medellina and A. Kornienko, *Org. Biomol. Chem.*, 2014, **12**, 410.
12. M. D. Heredia, M. Puiatti, R. A. Rossia and M. E. Budén, *Org. Biomol. Chem.*, 2022, **20**, 228.
13. S. Koh, A. Pounder, E. Brown and W. Tam, *Org. Lett.*, 2020, **22**, 3433.
14. P. Poonpatana, G. dos Passos Gomes, T. Hurrle, K. Chardon, S. Bräse, K.-S. Masters and I. Alabugin, *Chem. – Eur. J.*, 2017, **23**, 9091.
15. W. Zhang, W. Yang and W. Zhao, *J. Org. Chem.*, 2020, **85**, 8702.
16. Z. Shen, L. Zhou, C. Wu, Q. Zhou and H.-G. Qianghui, *Org. Biomol. Chem.*, 2022, **20**, 8869.
17. Z. Shen, Z. Ni, S. Mo, J. Wang and Y. Zhu, *Chem. – Eur. J.*, 2012, **18**, 4859.
18. R. Jana, I. Chatterjee, S. Samanta and J. K. Ray, *Org. Lett.*, 2008, **10**, 4795.
19. R. Sanz, D. Miguel, A. Martínez and A. Pérez, *J. Org. Chem.* 2006, **71**, 4024.
20. Y.-M. Wang, C. N. Kuzniewski, V. Rauniyar, C. Hoong and F. D. Toste, *J. Am. Chem. Soc.*, 2011, **133**, 12972.
21. R. Dirr, C. Anthaume and L. Désaubry, *Tetrahedron Lett.*, 2008, **49**, 4588; M. Tsukayama, *Heterocycles*, 1997, **45**, 1131.
22. A. R. Flynn, K. A. Mcdaniel, M. E. Hughes, D. B. Vogt and N. T. Jui, *J. Am. Chem. Soc.*, 2020, **142**, 9163; Y. An, B.-S. Zhang, Z. Zhang, C. Liu, X.-Y. Gou, Y.-N. Ding and Y.-M. Liang, *Chem. Commun.*, 2020, **56**, 5933; J. Fan, Q.-J. Yao, Y.-H. Liu, G. Liao, S, Zhang and B.-F. Shi, *Org. Lett.*, 2019, **21**, 3352.
23. H. Jiang, Z. Wu and Y. Zhang, *Chem. Sci.*, 2021, **12**, 8531.
24. R. Sanz, D. Miguel, A. Martinez and A. Perez, *J. Org. Chem.*, 2006, **71**, 4024.
25. H. Iwasaki, T. Eguchi, N. Tsutsui, H. Ohno and T. Tanaka, *J. Org. Chem.*, 2008, **73**, 7145.
26. Y. Satkar, L. F. Yera-Ledesma, N. Mali, D. Patil, L. A. Segura-Quezada, P. I. Ramírez-Morales, C. R. Solorio-Alvarado and P. Navarro-Santos, *J. Org. Chem.*, 2019, **84**, 4149.
27. N. Sakiyama, K. Noguchi and K. Tanaka, *Angew. Chem. Int. Ed.*, 2012, **51**, 5976.
28. M. Hapke, K. Kral, C. Fischer, A. Spannenberg, A. Gutnov, D. Redkin and B. Heller, *J. Org. Chem.*, 2010, **75**, 3993.
29. Y. Tan, Z. Zhao, Z. Chen, S. Huang, S. Jia, L. Peng, D. Xu, W. Qin and H. Yan, *Org. Lett.*, 2020, **22**, 4461.
30. M. Alcarazo, C. Golz, M. Simon and J. Zhang, *Angew. Chem. Int. Ed.*, 2020, **59**, 5647.
31. Z. Chi, Y. Gao, L. Yang, C. Zhou, M. Zhang, P. Cheng and G. Li, *Chin. Chem. Lett.*, 2022, **33**, 225.
32. G. Brizius, K. Billingsley, M. D. Smith and U. H. F. Bunz, *Org. Lett.*, 2003, **5**, 3951.
33. U. F. Röhrig, S. R. Majjigapu, P. Vogel, A. Reynaud, F. Pojer, N. Dilek, P. Reichenbach, K. Ascenção, M. Irving, G. Coukos, O. Michielin and V. Zoete, *J. Enzyme Inhib. Med. Chem.*, 2022, **37**, 1773.
34. Y.-W. Li, H.-X. Zheng, B. Yang, X.-H. Shan, J.-P. Qu and Y.-B. Kang, *Org. Lett.*, 2020, **22**, 4553.