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Full Paper

A Novel Organic Electron Donor Derived from *N*-Methylisatin*

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We report the reactivity of an electron donor derived from *N*-methylisatin on reduction by sodium amalgam. Transfer of a clear supernatant solution to iodoarenes affords the products of two-electron reduction. Reductions of sulfones, activated arenesulfonamides, and Weinreb amides are also reported.

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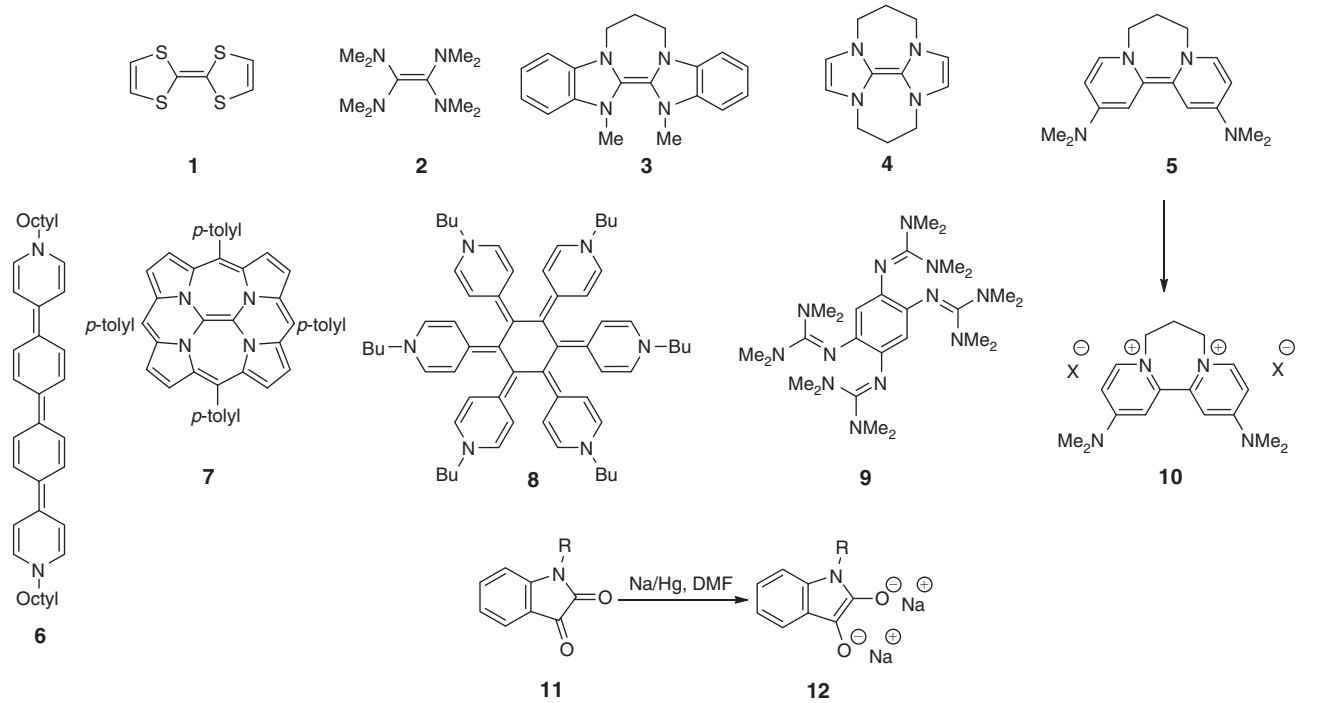
Reduction of organic substrates through electron transfer is currently a hot topic in synthetic chemistry. New reagents have been derived from ground-state metal complexes,[1] photoexcited metal complexes,[2] ground-state organic compounds,[3] and photoexcited organic compounds.[4]

Our interest in this area arose when we explored the reactivity of the sulfur-containing electron donor tetrathiafulvalene (TTF) **1**[5] (Scheme 1). This compound is strong enough to reduce arenediazonium salts but is considerably weaker than the nitrogen-containing donors **2**–**9**, some of which are structurally similar to TTF. For the donors **3**–**8**,[6–13] the aromatic nature of their oxidation products adds to the driving force for their reactivity. Thus, loss of two electrons from donor **5** affords the aromatic disalt **10**. In contrast, donor **9** starts as an aromatic



Scheme 1.

*This paper is dedicated to the memory of Professor Athel Beckwith.

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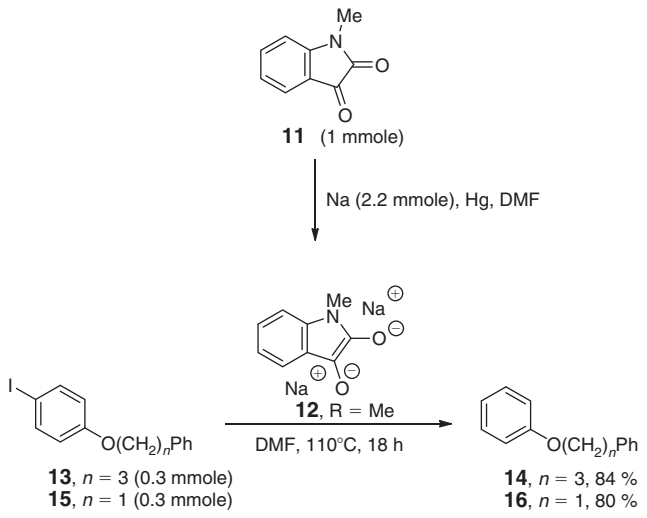
system, but loss of two electrons sacrifices the aromaticity as it converts into a quinonoid dication structure.

Our research has recently focussed on the reagents **2**–**5**, all of which, like TTF **1**, have a very electron-rich alkene substituted by two or more heteroatoms. We now wondered about the effect of anionic heteroatom substituents on electron-rich alkenes, and our attention focussed on isatins. Reduction of 1-methylisatin should afford the disalt **12**, where the five-membered ring appears to be intensely electron-rich (Scheme 2). Prospective donor **12** features an aromatic system, namely an indole; loss of two electrons would lead back to *N*-methylisatin **11**, which is not aromatic, and so this should moderate the electron-donating properties.

1-Methylisatin was formed as a red solid by reaction of isatin with sodium hydride in DMF and then addition of iodomethane.[14] When 1-methylisatin was reduced with sodium amalgam, a green, clear supernatant solution was formed. This was clearly separate from the residual amalgam and was transferred by cannula to the substrates and heated at 110°C for 18 h, with results as indicated below. To check the redox activity of the *N*-methylisatin, a cyclic voltammogram was recorded (see Supplementary Material) and this showed two quasi-reversible one-electron reductions at −0.9 and −1.9 V relative to Ag/AgCl. To determine the stoichiometry of the green reducing solution, an aliquot of this solution was titrated with excess iodine and back-titration with sodium thiosulfate showed that the green solution of the activated species transferred two electrons per molecule. Re-isolation of the material following oxidation with iodine afforded **11** in excellent yield, and hence we propose structure **12** for the green donor.



Scheme 2.

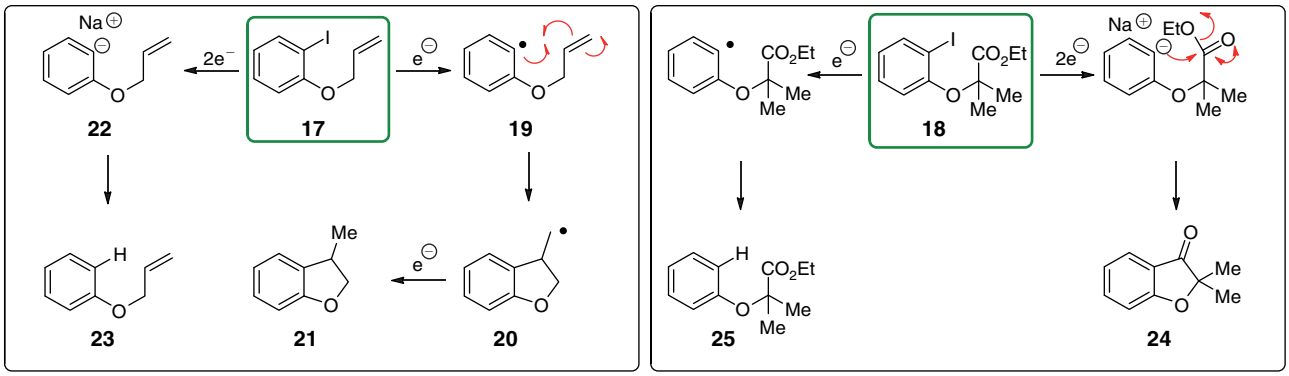
When added to iodoarene **13**, the reaction yielded the deiodinated arene **14** in a very good 84 % yield. To test that the reductive reactivity was due to the reduced 1-methylisatin, a blank reaction was conducted in its absence. Transferring the supernatant liquid above the sodium amalgam reassuringly gave no reduction of the iodoarene. To reinforce the easy reduction of iodoarene **13**, substrate **15** was reduced in like manner to afford the arene **16** (80 %).

To determine whether the reducing system had converted the iodoarenes into aryl radicals or aryl anions (strictly speaking, organosodium compounds), two probes were prepared. The allyl iodoaryl ether **17**,[15,16] on treatment with the reduced green solution formed with excess amalgam from methylisatin (3 equiv.), afforded only the de-iodinated product **23** (68 %), whereas the iodo ester **18**[8c,17] on reaction with the green solution afforded the indanone **24** (39 %) as well as the de-iodinated compound **25** (8 %) (Scheme 3). Cyclisation of aryl radicals onto allyl groups as for structure **19** was pioneered by Beckwith[15] and became a diagnostic reaction for aryl radicals; aryl anions do not cyclise in the presence of a reactive solvent like DMF. Similarly, cyclisation onto carboxylic esters is a hallmark of aryl anions, whereas aryl radicals do not cyclise onto esters.

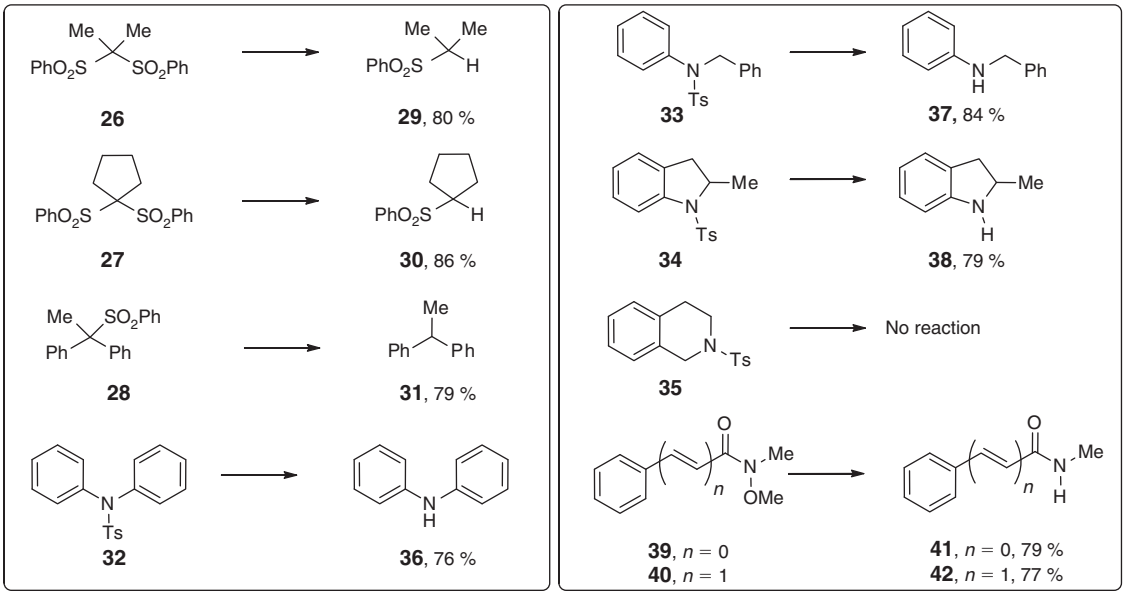
Therefore, the evidence from substrates **17** and **18** is in favour of aryl anions being formed here. This is consistent with the reduction potentials for aryl iodides being – 2 V versus saturated calomel electrode,[18] whereas the standard reduction potential E^0 of aryl radicals is ~0 V.[19]

Next, a set of sulfones **26**–**28** was prepared and reacted with the methylisatin-derived donor solution (Scheme 4). The *gem*-bissulfones **26** and **27** underwent desulfonation to their corresponding anions; on workup, these were protonated to **29** and **30** in 80 and 86 % yields respectively, whereas the activated monosulfone **28** afforded 1,1-diphenylethane **31** (79 %).

Sulfonamides **32**–**35** were prepared. Examples **32**–**34** were successfully deprotected with the green reagent as shown in Scheme 4 whereas **35** was left untouched. Rationalising the selectivity seen in the reactions in Scheme 4, we have previously shown that the reactivity of arenesulfonamides towards reduction depends on the leaving ability of the group attached to nitrogen.[8c] When that leaving group is an indolyl group and is



Scheme 3.



Scheme 4.

aniline-derived, then the nitrogen leaving group is resonance-stabilised and the reaction is assisted by this. However, if the nitrogen is part of a dialkylamino group such that no resonance stabilisation of the nitrogen is available, as would happen in substrate **35**, then the cleavage is much more difficult. This is also clearly represented in the examples shown here.

Finally, Weinreb amides **39** and **40** were prepared. These underwent reduction with cleavage of their N–O bonds to form amide products **41** (79 %) and **42** (77 %) respectively.[9c]

This shows that 1-methylisatin is reduced by excess sodium amalgam to an active electron donor that reductively cleaves iodoarenes, *gem*-bissulfones, activated arenesulfonamides, and Weinreb amides. In this respect, it mimics the chemistry of the strong electron donors **4** and **5**. This reductive reactivity may at first seem surprising, but the structural analogy of the dianion **12** with the electron-rich alkenes in the known strong electron donors **2**–**5** places the newly found reactivity in context.

Experimental

General

^{1}H NMR spectra were recorded at 400.13 or 500.13 MHz using a Bruker AV400, DPX400, or DRX500 spectrometer. ^{13}C NMR spectra were recorded at 100.6 or 125.7 MHz using a Bruker AV400, DPX400, or DRX500 spectrometer. Multiplicities of carbon resonances were obtained by recording J-modulated (JMOD) ^{13}C NMR spectra. Unless otherwise stated, NMR spectra were recorded using deuterochloroform ($CDCl_3$) as the solvent, and chemical shifts are reported in parts per million (ppm). Coupling constants, *J*, are reported in Hertz (Hz).

A Perkin–Elmer Spectrum One Fourier-transform (FT)-IR spectrometer was used to record infrared spectra. Melting points were recorded using a Gallenkamp 2C 7065 melting point apparatus.

UV-visible spectra were recorded with a VARIAN Cary 50 Probe UV-visible spectrophotometer.

Mass spectra were recorded using electron ionisation (EI), chemical ionisation (CI), or electrospray ionisation (ESI) techniques. High and low resolution mass spectra were recorded at the ESPRC National Mass Spectrometry Service Centre, Swansea, on a JLZX 102^{TM}, VGZAB-E^{TM}, or a VG^{TM} micromass instrument. Low-resolution mass spectra were recorded either on a ThermoFinnigan^{TM} PolarisQ ion trap spectrometer (EI and CI) or on a ThermoFinnigan LCQ DUO^{TM} mass spectrometer (for liquid chromatography (LC) mass spectrometry).

Column chromatography was performed using Prolabo 35–75-μm particle size silica gel 60 (200–400 mesh). Reactions were followed using TLC on Merck silica gel 60 F_{254} precoated aluminium plates. Visualisation was achieved under UVP Mineralight UVG-11 lamp or by developing plates with methanolic vanillin.

Chemical reagents used in all experiments were obtained from commercial suppliers. DCM, THF, diethyl ether, toluene, and hexane were dried using a Pure-Solv 400 solvent purification system.

Electrochemical measurements were carried out using an Autolab® PGSTAT302N potentiostat.

1-Methylisatin ***11***

Under inert atmosphere, sodium hydride (60 % in mineral oil, 3.26 g, 81.56 mmol, 1.2 equiv.) was washed with dry hexane three times and then dried under argon flow. A solution of isatin (10.0 g, 67.97 mmol, 1.0 equiv.) in dry DMF (100 mL) was slowly added to the sodium hydride at 0°C. The reaction mixture was stirred for 1 h at room temperature before being cooled down to 0°C. Iodomethane (5.08 mL, 81.56 mmol, 1.2 equiv.) in dry DMF (20 mL) was slowly added to the reaction mixture. The reaction mixture was stirred for 18 h. The solution was slowly quenched with water (30 mL) and further diluted with water (200 mL) and extracted with DCM (3 × 100 mL). The combined organic layers were washed with water (3 × 100 mL), brine (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was recrystallised from ethyl acetate to afford 1-methylisatin **11** (Chart 1) as a red solid (8.42 g, 75 %), mp 127–129°C (lit.[14] 132–134°C). *m*/*z* (EI$^+$) 161.0469; $C_9H_7NO_2$ (M^+) requires 161.0477. ν_{max} (neat)/cm^{-1} 3054, 2923, 1742, 1723, 1599, 1467, 1091. δ_H ($CDCl_3$, 400 MHz) 3.27

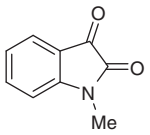


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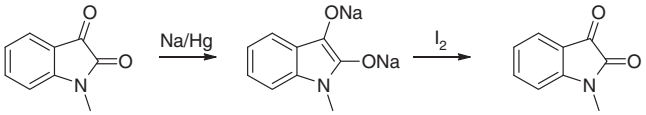
Chart 1.



11 **12** **11**

Scheme 5.

(3H, s, NCH_3), 6.91 (1H, d, *J* 7.7, ArH), 7.15 (1H, t, *J* 7.6, ArH), 7.61–7.65 (2H, m, ArH). δ_C ($CDCl_3$, 100 MHz) 26.3 (CH_3), 110.1 (CH), 117.3 (CH), 125.2 (CH), 138.5 (CH), 151.5 (C), 158.3 (C), 183.4 (C). *m/z* $(EI)^+$ 161 (M^+, 35 %), 104 (100), 78 (50).

*Generation of Donor **12** and Oxidation with Iodine: Regeneration of 1-Methylisatin **11** to Provide Evidence in Support of Structure **12***

Under an inert atmosphere, a sodium amalgam (1 %, 50 mg Na, 5.0 g Hg) was prepared and dry DMF (15 mL) was added, followed by 1-methylisatin (161 mg, 1.0 mmol, 1 equiv.). The reaction mixture was stirred at room temperature for 4 h. The green solution was then transferred by cannula to a solution of iodine (508 mg, 2 mmol, 2 equiv.) in dry DMF (15 mL). The reaction mixture was stirred at room temperature for 30 min, and then quenched with saturated sodium thiosulfate (100 mL) and extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with water (4 × 100 mL), brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford 1-methylisatin **11** (Scheme 5) as a red solid (147 mg, 91 %) with data matching those of the authentic material.

*Determination of UV Spectrum of **12***

Under an inert atmosphere, a sodium amalgam (1 %, 50 mg Na, 5.0 g Hg) was prepared and dry DMF (15 mL) was added, followed by 1-methylisatin (161 mg, 1.0 mmol, 1 equiv.). The reaction mixture was stirred at room temperature for 4 h. A sample of the resulting green solution was diluted stepwise in dried benzene to a concentration of 1.25×10^{-6} M. The sample was sealed in a 1-cm^2 quartz cuvette and measurements taken. λ_{max} (DMF/benzene) 340 nm (ε 9.2×10^5), 598 nm (ε 1.1×10^5).

*Experiment to Determine the Number of Electrons Transferred from Donor **12***

A solution (10.10 mM) of methylisatin (57 mg, 0.354 mmol) in DMF (35 mL) was prepared, and treated with sodium amalgam to generate a green solution of donor **12**. An aliquot (10 mL) of this green solution was removed and reacted with an aliquot of iodine solution (10 mL, 16.62 mM in DMF) i.e. excess iodine. The unreacted iodine was then titrated with a solution of sodium thiosulfate pentahydrate (10.599 mM; 526 mg in 200 mL water).

The reaction was repeated three times. The results indicated donor **12** transferred two electrons to iodine.

Table 1. Titrations with sodium thiosulfate

Titration	Volume of $Na_2S_2O_3$ solution used [mL]
1	13.2
2	12.9
3	12.8
Average	12.97

mmoles of $Na_2S_2O_3$ used in titration = (10.599 × 0.01297) = 0.137.
∴ mmoles of unreacted I_2 quenched with $Na_2S_2O_3$ = (0.137/2) = 0.0687 mmol.

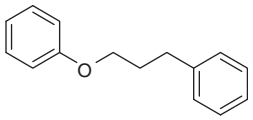


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Chart 2.

$Na_2S_2O_3$ titration against excess I_2 remaining after iodine quench of donor **12** solution is shown in Table 1.

Moles of I_2 (reacted with donor **12**) = total I_2 moles − moles of unreacted I_2 (quenched with $Na_2S_2O_3$) = 0.166 − 0.0687 = 0.0973 mmol. 0.101 mmol of donor **12** reacted with 0.0973 mmol of I_2.

Two electrons are required to reduce I_2 to $2I^-$; therefore, donor **12** is a two-electron donor.

*Standard Procedure for Reduction Applied to (3-Phenoxypropyl)benzene **14***

Under inert atmosphere, a sodium amalgam (1 %, 50 mg Na, 5.0 g Hg) was prepared and dry DMF (15 mL) was added, followed by 1-methylisatin (161 mg, 1.0 mmol, 3 equiv.). The reaction mixture was stirred at room temperature for 4 h. The green solution was then transferred by cannula to 1-iodo-4-(3-phenylpropoxy)benzene **13**[9j] (113 mg, 0.3 mmol, 1 equiv.). The reaction mixture was heated to 110°C for 18 h, then allowed to cool to room temperature. The mixture was diluted with water (40 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with water (3 × 20 mL), brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography, eluting with 0–10 % ethyl acetate/hexane, to afford 1-(3-phenoxypropyl)benzene **14** (Chart 2) as a colourless oil[9j] (60 mg, 84 %). *m/z* (ESI^+) 230.1538; $C_{15}H_{20}NO$ $(M + NH_4)^+$ requires 230.1539. ν_{max} (neat)/cm^{-1} 3061, 3025, 2879, 1600, 1497, 1245, 1038, 751. δ_H ($CDCl_3$, 400 MHz) 2.11–2.18 (2H, m, CH_2), 2.85 (2H, t, *J* 7.6, CH_2), 4.00 (2H, t, *J* 6.3, OCH_2), 6.92–6.99 (3H, m, ArH), 7.23–7.26 (3H, m, ArH), 7.28–7.34 (4H, m, ArH). δ_C ($CDCl_3$, 100 MHz) 30.9 (CH_2), 32.2 (CH_2), 66.7 (CH_2), 114.6 (CH), 120.6 (CH), 125.9 (CH), 128.5 (CH), 129.4 (CH), 141.6 (C), 159.0 (C). *m/z* (ESI^+) 212 ($[M]^+$, 20 %), 118 (10), 108 (13), 91 (22).

Blank reaction: a blank reaction was prepared using the procedure detailed above in the absence of 1-methylisatin. The liquid above the amalgam was transferred to the substrate by cannula. A ^1H NMR spectrum of the crude reaction mixture following workup identified 1-iodo-4-(3-phenylpropoxy) benzene **14** as the only component present. 1-(3-Phenoxypropyl) benzene was not observed.

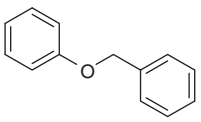

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Chart 3.

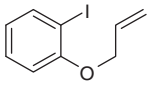

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Chart 4.

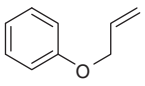

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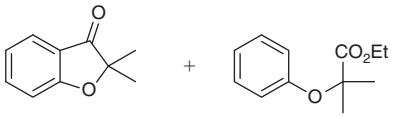
Chart 5.



24 **25**

Chart 6.

Benzyloxybenzene ***16***

The standard procedure for reduction was applied to 1-(benzyloxy)-4-iodobenzene **15**[9j] (103 mg, 0.3 mmol, 1 equiv.), which was reacted with 1-methylisatin **11** (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–10 % ethyl acetate/hexane to afford benzyloxybenzene **16** (Chart 3) as a colourless oil (49 mg, 80 %).[9j] *m/z* (CI^+) 185.0959; $C_{13}H_{13}O$ $(M+H)^+$ requires 185.0961. ν_{max} (neat)/cm^{-1} 3066, 3027, 2918, 1495, 1240, 727. δ_H ($CDCl_3$, 500 MHz) 5.11 (2H, s, OCH_2), 6.99–7.04 (3H, m, ArH), 7.28–7.33 (3H, m, ArH), 7.34–7.38 (2H, m, ArH), 7.41–7.50 (2H, m, ArH). δ_C ($CDCl_3$, 125 MHz) 69.4 (CH_2), 114.4 (CH), 120.5 (CH), 127.0 (CH), 127.4 (CH), 128.1 (CH), 129.0 (CH), 136.6 (C), 158.3 (C). *m/z* (CI) 275 (15 %), 185 ($[M+H]^+$, 100).

1-(Allyloxy)-2-iodobenzene ***17***[16]

Sodium carbonate (0.7 g, 6.6 mmol, 3.0 equiv.) was added to a stirred solution of 2-iodophenol (0.49 g, 2.2 mmol, 1.0 equiv.) in dry DMF (20 mL). Allyl bromide (0.23 mL, 2.67 mmol, 1.2 equiv.) was then slowly added to the reaction mixture. The reaction mixture was heated to 80°C and stirred for 18 h. The reaction mixture was allowed to cool to room temperature and DMF removed under reduced pressure. The crude mixture was diluted with water (40 mL) and extracted with diethyl ether (3×20 mL). The combined organic layers were washed with water (3×20 mL), brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography, eluting with 0–10 % diethyl ether/light petroleum, to afford 1-(allyloxy)-2-iodobenzene **17** (Chart 4) as a yellow oil (497 mg, 86 %).[16] *m/z* (CI^+) 260.9764; $C_9H_{10}IO$ $(M+H)^+$ requires 260.9771. ν_{max} (neat)/cm^{-1} 3060, 2918, 2863, 1580, 1468, 1246. δ_H ($CDCl_3$, 500 MHz) 4.62 (2H, d, *J* 4.8, OCH_2), 5.34 (1H, dd, *J* 10.6, 1.5, CH=CH*H*), 5.56 (1H, dd, *J* 17.2, 1.5, CH=C*H*H), 6.05–6.14 (1H, m, C*H*=CH_2), 6.73 (1H, td, *J* 7.4, 1.4, ArH), 6.83 (1H, dd, *J* 7.4, 1.4, ArH), 7.32 (1H, td, *J* 7.4, 1.4, ArH), 7.81 (1H, dd, *J* 7.4, 1.4, ArH). δ_C ($CDCl_3$, 125 MHz) 69.2 (CH_2), 86.2 (C), 112.1 (CH_2), 117.1 (CH), 122.2 (CH), 128.9 (CH), 132.1 (CH), 139.1 (CH), 156.6 (C). *m/z* (CI^+) 260 ($[M+H]^+$, 100 %), 219 (20), 94 (15), 78 (25).

Allyloxybenzene ***23***

The standard procedure for reduction was applied to 1-(allyloxy)-2-iodobenzene **17** (87 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin **11** (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–15 % ethyl acetate/hexane to afford allyloxybenzene **23** (Chart 5) as a colourless oil (31 mg, 68 %). ν_{max} (neat)/cm^{-1} 3021, 2987, 2884, 1548, 795. δ_H ($CDCl_3$, 500 MHz) 4.56 (2H, dm, *J* 6.8, OCH_2), 5.31 (1H, dm, *J* 10.5, C*H*H=CH), 5.45 (1H, dm, *J* 17.2, CH*H*=*C*H), 6.05–6.15 (1H, m, C*H*=CH_2), 6.94–6.98 (3H, m, ArH), 7.30–7.34 (2H, m, ArH). δ_C ($CDCl_3$, 100 MHz) 68.2 (CH_2), 114.2 (CH_2), 117.1 (CH), 120.3 (CH), 128.9 (CH), 132.9 (CH), 158.1 (C). *m/z* (CI) 135 ($[M+H]^+$, 100 %), 122 (10), 108 (15), 94 (20), 78 (5).

2,2-Dimethylbenzofuran-3-one ***24*** *and Ethyl 2-Methyl-2-phenoxypropanoate* ***25***

The standard procedure for reduction was applied to ethyl 2-(2-iodophenoxy)-2-methylpropanoate **18**[8b] (111 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin **11** (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–10 % diethyl ether/pentane to afford 2,2-dimethylbenzofuran-3-one **24** (19 mg, 36 %) and 2-methyl-2-phenoxypropanoate **25** (Chart 6) (5.5 mg, 8 %) as colourless oils.

24 *m/z* (ESI^+) 163.0735; $C_{10}H_{10}O_2$ requires $(M+H)^+$ 163.0754. ν_{max} (neat)/cm^{-1} 2986, 2934, 1727, 1618, 1154, 760. δ_H ($CDCl_3$, 500 MHz) 1.48 (6H, s, $2 \times CH_3$), 7.08 (2H, m, ArH), 7.61–7.65 (1H, td, *J* 7.6, 1.4, ArH), 7.68 (1H, d, *J* 7.1, ArH). δ_C ($CDCl_3$, 125 MHz) 22.5 (CH_3), 87.3 (C), 113.1 (CH), 119.0 (C), 121.2 (CH), 124.4 (CH), 137.6 (CH), 170.4 (C), 203.9 (C).

25 *m/z* (ESI^+) 226.1440; $C_{12}H_{20}NO_3$ $(M+NH_4)^+$ requires 226.1438. ν_{max} (neat)/cm^{-1} 3064, 2989, 2940, 1733, 1580, 1495, 760. δ_H ($CDCl_3$, 500 MHz) 1.28 (3H, t, *J* 7.1, CH_3), 1.64 (6H, s, CH_3), 4.27 (2H, q, *J* 7.1, CH_2), 6.88–6.90 (3H, m, ArH), 6.99–7.03 (2H, m, ArH). δ_C ($CDCl_3$) 14.2 (CH_3), 25.5 (CH_3), 61.5 (CH_2), 79.1 (C), 119.2 (CH), 122.2 (CH), 129.9 (CH), 155.6 (C), 174.4 (CO). *m/z* (EI^+) 208 ($[M]^+$, 100 %), 135 (100), 94 (56), 66 (14).

Isopropylsulfonylbenzene ***29***

The standard procedure for reduction was applied to 1-(2-(phenylsulfonyl)propan-2-ylsulfonyl)benzene **26**[8c] (97 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin **11** (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–20 % ethyl acetate/hexane to afford isopropylsulfonylbenzene **29** (Chart 7) as a yellow oil (44 mg, 80 %). *m/z* (EI^+) 184.0554; $C_9H_{12}O_2S$ $(M)^+$ requires 184.0558. ν_{max} (neat)/cm^{-1} 3060, 2978, 2929, 1446,

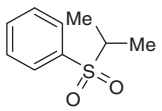


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Chart 7.

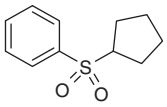

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Chart 8.

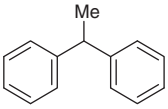

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Chart 9.

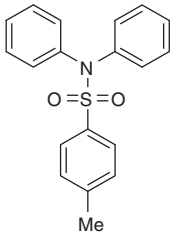

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Chart 10.

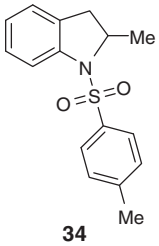

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Chart 11.

1306, 1144. δ_H ($CDCl_3$, 400 MHz) 1.29 (6H, d, *J* 6.8, 2 × CH_3), 3.20 (1H, septet, *J* 6.8, C*H*(CH_3)$_2$), 7.57 (2H, t, *J* 7.4, ArH), 7.66 (1H, t, *J* 7.4, ArH), 7.88 (2H, d, *J* 7.4, ArH). δ_C ($CDCl_3$, 100 MHz) 15.2 (CH_3), 55.0 (CH), 128.5 (CH), 133.1 (CH), 136.5 (C). *m/z* (EI^+) 184 ($[M]^+$, 10 %), 142 (22), 78 (100), 51 (18).

Cyclopentylsulfonylbenzene ***30***

The standard procedure for reduction was applied to 1,1-diphenylsulfonylcyclopentane **27**[8c] (105 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin **11** (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–20 % ethyl acetate/hexane to afford cyclopentylsulfonylbenzene **30** (Chart 8) as an orange oil (54 mg, 86 %). *m/z* (ESI^+) 228.1055; $C_{11}H_{18}NO_2S$ $(M + NH_4)^+$ requires 228.1053. ν_{max} (neat)/cm^{-1} 3048, 2986, 1457, 1331, 1160, 975. δ_H ($CDCl_3$, 500 MHz) 1.60–1.65 (2H, m, CH_2), 1.77–1.91 (4H, m, CH_2CH_2), 2.07–2.10 (2H, m, CH_2), 3.50 (1H, quintet, *J* 7.9, CH), 7.57 (2H, tm, *J* 7.4, ArH), 7.65 (1H, tm, *J* 7.4, ArH), 7.92 (2H, dd, *J* 7.4, 1.3, ArH). δ_C ($CDCl_3$, 125 MHz) 25.8 (CH_2), 27.2 (CH_2), 64.2 (CH), 128.4 (CH), 129.1 (CH), 133.4 (CH), 139.1 (C). *m/z* (ESI^+) 443 (13 %), 352 (20), 228 ($[M + NH_4]^+$, 100).

1,1-Diphenylethane ***31***

The standard procedure for reduction was applied to (1-(phenylsulfonyl)ethane-1,1-diyl)dibenzene **28**[8c] (96 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin **11** (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with neat hexane to afford 1,1-diphenylethane **31** (Chart 9) as a colourless oil (43 mg, 79 %). *m/z* (EI^+) 182.1091; $C_{14}H_{14}$ $(M)^+$ requires 182.1096. ν_{max} (neat)/cm^{-1} 3061, 3026, 2968, 2927, 2873, 1597, 1493, 698. δ_H ($CDCl_3$, 400 MHz) 1.74 (3H, d, *J* 7.2, CH_3), 4.25 (1H, q, *J* 7.2, CH), 7.25–7.39 (10H, m, ArH). δ_C ($CDCl_3$, 100 MHz) 22.1 (CH_3), 45.1 (CH), 126.3 (CH), 127.8 (CH), 128.6 (CH), 146.6 (C). *m/z* (EI^+) 182 ($[M]^+$, 89 %), 167 (100), 152 (52), 77 (48), 51 (34).

*4-Methyl-*N,N*-diphenylbenzenesulfonamide* ***32***

To a solution of 1,2-diphenylamine (2.0 g, 11.81 mmol, 1.0 equiv.) in chloroform (30 mL) at 0°C, pyridine (1.93 mL, 23.63 mmol, 2.0 equiv.) was added. A solution of *p*-toluenesulfonyl chloride (2.49 g, 17.72 mmol, 1.5 equiv.) in chloroform (15 mL) was slowly added. The reaction mixture was stirred for 48 h. Water (30 mL) and diethyl ether (3 × 30 mL) were added and the combined organic layers were washed with 2 M HCl (5 mL), 5 % $NaHCO_3$ (5 mL), water (3 × 20 mL), brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was recrystallised from methanol to afford 4-methyl-*N*,*N*-diphenylbenzenesulfonamide **32** (Chart 10) as colourless crystals (3.20 g, 84 %), mp 142–143°C (lit.[20] 138–139°C). *m/z* (ESI^+) 324.1052; $C_{19}H_{18}NO_2S$ $(M + H)^+$ requires 324.1053. ν_{max} (neat)/cm^{-1} 3049, 2992, 2876, 1590, 1360, 1121. δ_H ($CDCl_3$, 400 MHz) 2.44 (3H, s, CH_3), 7.26–7.32 (12H, m, ArH), 7.59 (2H, d, *J* 6.6, ArH). δ_C ($CDCl_3$, 100 MHz) 21.6 (CH_3), 127.4 (CH), 127.8 (CH), 128.3 (CH), 129.2 (CH), 129.5 (CH), 137.6 (C), 141.6 (C), 143.6 (C). *m/z* (ESI^+) 664 ($[2M + NH_4]^+$) (35 %), 341 ($[M + NH_4]^+$) (75), 324 ($[M + H]^+$, 100), 169 (45).

2-Methyl-1-tosylindoline ***34***

Aqueous sodium hydroxide (50 %, 15.25 g, 190 mmol, 13 equiv.) was added to a solution of 2-methylindoline (2.0 g. 15.03 mmol, 1.0 equiv.) and tetrabutylammonium hydrogen sulfate (510 mg, 1.5 mmol, 0.1 equiv.) in DCM (150 mL). A solution of *p*-toluenesulfonyl chloride (3.80 g, 20 mmol, 1.3 equiv.) in DCM (15 mL) was added slowly to the reaction mixture. The mixture was stirred for 16 h at room temperature. The mixture was poured into water (200 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with water (3 × 50 mL), brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography, eluting with 0–10 % ethyl acetate/light petroleum to afford 2-methyl-1-tosylindoline **34** (Chart 11) as a red solid (3.36 g, 78 %),

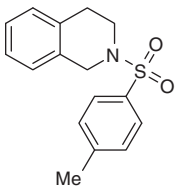

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Chart 12.

mp 59–61°C (lit.[21] 63–64°C). *m/z* (ESI$^+$) 288.1050; $C_{16}H_{18}NO_2S$ $(M+H)^+$ requires 288.1053. ν_{max} (neat)/cm^{-1} 2978, 2929, 1646, 1476, 1353, 1166. δ_H ($CDCl_3$, 400 MHz) 1.43 (3H, d, *J* 6.5, CH_3), 2.35 (3H, s, CH_3), 2.45 (1H, dd, *J* 16.0, 2.9, CH*H*), 2.89 (1H, dd, *J* 16.0, 9.4, CH), 4.35 (1H, m, NCH),7.00–7.06 (2H, m, ArH), 7.16 (2H, d, *J* 8.0, ArH), 7.20–7.21 (1H, m, ArH), 7.56 (2H, d, *J* 8.4, ArH), 7.65 (1H, d, *J* 8.0, ArH). δ_C ($CDCl_3$, 100 MHz) 21.5 (CH_3), 23.4 (CH_3), 36.2 (CH_2), 58.5 (CH), 117.1 (CH), 124.4 (CH), 125.2 (CH), 127.0 (CH), 127.7 (CH), 129.5 (CH), 131.6 (C), 135.4 (C), 141.1 (C), 143.7 (C). *m/z* (ESI$^+$), 592 (15 %), 305 (15), 288 ([M]$^+$, 100), 133 (6).

*2-Tosyl-1,2,3,4-tetrahydroisoquinoline **35***

Triethylamine (1.07 mL, 7.67 mmol, 1.2 equiv.) was added to a solution of 1,2,3,4-tetrahydroquinoline (0.85 g, 6.39 mmol, 1.0 equiv.) in dry THF (10 mL) A solution of *p*-toluenesulfonyl chloride (1.46 g, 7.67 mmol, 1.2 equiv.) in THF (5 mL) was slowly added at 0°C. The reaction mixture was stirred for 18 h. The mixture was poured into water (50 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were washed with water (3 × 15 mL), brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography, eluting with 0–5 % ethyl acetate/light petroleum to afford 2-tosyl-1,2,3,4-tetrahydroisoquinoline **35** (Chart 12) as a white solid (1.50 g, 82 %), mp 141–143°C (lit.[22] 141–142°C). *m/z* (ESI$^+$) 288.1050; $C_{16}H_{18}NO_2S$ $(M+H)^+$ requires 288.1053. ν_{max} (neat)/cm^{-1} 2929, 2862, 2824, 1591, 1342, 1163. δ_H ($CDCl_3$, 400 MHz) 2.44 (3H, s, CH_3), 2.95 (2H, t, *J* 5.9, CH_2), 3.38 (2H, t, *J* 5.9, CH_2), 4.28 (2H, s, CH_2), 7.04–7.10 (2H, m, ArH), 7.16 (2H, d, *J* 6.4, ArH), 7.33 (2H, d, *J* 8.0, ArH), 7.75 (2H, d, *J* 6.4, ArH). δ_C ($CDCl_3$, 100 MHz) 21.5 (CH_3), 29.0 (CH_2), 43.8 (CH_2), 47.5 (CH_2), 126.3 (CH), 126.8 (CH), 127.8 (CH), 128.8 (CH), 129.6 (CH), 131.7 (C), 133.0 (C), 133.1 (C), 143.6 (C). *m/z* (ESI$^+$) 288 ([M]$^+$, 100 %), 310 (12), 279 (12), 186 (10).

*Diphenylamine **36***

The standard procedure for reduction was applied to 4-methyl-*N*,*N*-diphenylbenzenesulfonamide **32** (97 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–20 % ethyl acetate/hexane to afford diphenylamine **36** (Chart 13) as a white solid (39 mg, 76 %), mp 52–54°C (lit.[23] 50–53°C). *m/z* (ESI$^+$) 170.0966; $C_{12}H_{11}N$ $(M+H)^+$ requires 170.0964. ν_{max} (neat)/cm^{-1} 3385, 3038, 1591, 1495, 1314, 746. δ_H ($CDCl_3$, 400 MHz) 5.72 (1H, br s, NH), 6.97 (2H, t, *J* 6.4, ArH), 7.11 (4H, d, *J* 6.6, ArH), 7.32 (4H, t, *J* 6.5, ArH). δ_C ($CDCl_3$, 100 MHz) 117.4 (CH), 120.6 (CH), 128.9 (CH), 142.7 (C). *m/z* (ESI$^+$) 170 ([M + H]$^+$, 100 %), 114 (12).

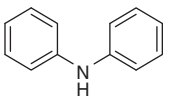

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Chart 13.

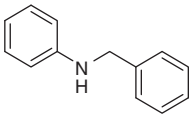

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Chart 14.

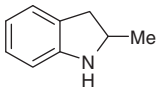

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Chart 15.

N-*Benzylaniline **37***

The standard procedure for reduction was applied to *N*-benzyl-4-methyl-*N*-phenylbenzenesulfonamide **33** (101 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin **11** (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–20 % ethyl acetate/hexane to afford *N*-benzylaniline **37** (Chart 14) as a white solid (46 mg, 84 %), mp 37–39°C (lit. 34–36°C).[24] *m/z* (ESI) 184.1119; $C_{11}H_{14}N$ $(MH)^+$ requires 184.1121. ν_{max} (neat)/cm^{-1} 3412, 3049, 3022, 1599, 1506, 689. δ_H ($CDCl_3$) 4.08 (1H, br s, NH), 4.41 (2H, s, NCH_2), 6.71–6.80 (2H, m, ArH), 6.81–6.83 (1H, m, ArH), 7.25–7.29 (2H, m, ArH), 7.29–7.47 (5H, m, ArH). δ_C ($CDCl_3$, 100 MHz) 47.9 (CH_2), 112.4 (CH), 117.1 (CH), 126.8 (CH), 127.1 (CH), 128.2 (CH), 128.8 (CH), 139.0 (C), 147.7 (C).

*2-Methylindoline **38***

The standard procedure for reduction was applied to 2-methyl-1-tosylindoline **34** (86 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–20 % ethyl acetate/hexane to afford 2-methylindoline **38** (Chart 15) as a colourless oil (31 mg, 79 %).[25] *m/z* (EI$^+$) 133.0884; $C_9H_{11}N$ $(M)^+$ requires 133.0891. ν_{max} (neat)/cm^{-1} 3368, 3027, 2956, 1607, 1481, 1248, 743. δ_H ($CDCl_3$, 400 MHz) 1.32, (3H, d, *J* 6.0, CH_3) 2.68 (1H, dd, *J* 15.4, 7.6, $ArCH_2$), 3.18 (1H, dd, *J* 15.4, 8.2, $ArCH_2$), 3.37–3.41 (1H, br, NH), 4.00–4.07 (1H, m, CH), 6.63 (1H, d, *J* 7.6, ArH), 6.71 (1H, t, *J* 7.4, ArH), 7.02 (1H, t, *J* 7.6, ArH), 7.11 (1H, d, *J* 7.3, ArH). δ_C ($CDCl_3$, 100 MHz) 21.8 (CH_3), 37.3 (CH_2), 54.7 (CH), 108.7 (CH), 118.1 (CH), 124.2 (CH), 126.7 (CH), 128.4 (C), 150.4 (C). *m/z* (ESI$^+$) 133 ([M]$^+$, 100 %), 94 (100), 78 (15).

*Attempted Reduction of 2-Tosyl-1,2,3,4-tetrahydroisoquinoline **35***

The standard procedure for reduction was applied to 2-tosyl-1,2,3,4-tetrahydroisoquinoline **35** (86 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin **11** (161 mg, 1 mmol,

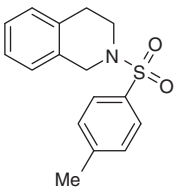

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Chart 16.

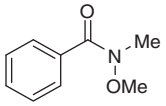

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Chart 17.

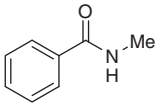

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Chart 18.

3 equiv.). The ^{1}H NMR of the crude reaction mixture showed only unreacted sulfonamide **35** (Chart 16).

N-*Methoxy*-N-*methylbenzamide* ***39***

Under an inert atmosphere, triethylamine (3.51 mL, 25 mmol, 2.5 equiv.) was added dropwise to a suspension of benzoyl chloride (1.4 mL, 10 mmol, 1.0 equiv.) and *N*,*O*-dimethylhydroxylamine hydrochloride (1.17 g, 12 mmol, 1.2 equiv.) in dry DCM (25 mL) at 0°C. The reaction mixture was stirred for 1 h at 0°C and for 16 h at room temperature. The mixture was further diluted with DCM (50 mL) and washed with 1 M HCl (50 mL), $NaHCO_3$ (3 × 50 mL), brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford *N*-methoxy-*N*-methylbenzamide **39** (Chart 17) as a yellow oil (1.36 g, 83 %).[26] *m/z* (ESI^+) 166.0861; $C_9H_{12}NO_2$ $(M+H)^+$ requires 166.0863. ν_{max} (neat)/cm^{-1} 3063, 2971, 2936, 1650, 1449, 1382, 710. δ_H ($CDCl_3$, 500 MHz) 3.36 (3H, s, CH_3), 3.56 (3H, s, CH_3), 7.28–7.48 (3H, m, ArCH), 7.67 (2H, dd, *J* 8.0, 1.4, ArH). δ_C ($CDCl_3$, 125 MHz) 33.3 (CH_3), 60.5 (CH_3), 127.5 (CH), 127.6 (CH), 130.1 (CH), 133.6 (C), 169.4 (C). *m/z* (ESI^+) 331 (10 %), 188 (6), 166 ($[M+H]^+$, 100).

N-*Methylbenzamide* ***41***

The standard procedure for reduction was applied to *N*-methoxy-*N*-methylbenzamide **39** (49 mg, 0.3 mmol, 1 equiv.). This was reacted with 1-methylisatin (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–30 % ethyl acetate/hexane to afford *N*-methylbenzamide **41** (Chart 18) as a colourless oil (32 mg, 79 %). ν_{max} (neat)/cm^{-1} 3325, 3057, 2969, 1650, 1550, 1310. δ_H ($CDCl_3$) 2.99 (3H, d, *J* 4.8, NCH_3), 6.6 (1H, br s, NH), 7.40 (2H, t, *J* 7.1, ArH), 7.49 (1H, t, *J* 7.1, ArH), 7.78 (2H, d, *J* 7.1, ArH). δ_C ($CDCl_3$) 26.3 (CH_3), 126.4 (CH), 128.0 (CH), 130.8 (CH), 134.1 (C), 169.4 (C).

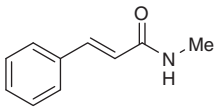

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Chart 19.

N-*Methylcinnamamide* ***42***

Similarly, *N*-methoxy-*N*-methylcinnamamide **40**[27] (58 mg, 0.3 mmol, 1 equiv.) was reacted with 1-methylisatin (161 mg, 1 mmol, 3 equiv.). The crude product was purified by silica gel chromatography, eluting with 0–30 % ethyl acetate/hexane to afford *N*-methylcinnamamide **42** (Chart 19) as a colourless oil (37 mg, 77 %). *m/z* (CI^+) 162.0912; $C_{10}H_{12}NO$ $(M+H)^+$ requires 162.0913. ν_{max} (neat)/cm^{-1} 3368, 3027, 2956, 1607, 1481, 1248, 743. δ_H ($CDCl_3$) 2.94 (3H, d, *J* 4.9, NCH_3), 6.52 (1H, d, *J* 15.6, C*H*=CH), 6.60 (1H, br s, NH), 7.31 (3H, dd, *J* 6.7, 2.9, ArH), 7.47 (2H, dd, *J* 6.7, 2.9, ArH), 7.63 (1H, d, *J* 15.6, CH=C*H*). δ_C ($CDCl_3$) 26.0 (CH_3), 120.3 (CH), 127.3 (CH), 128.3 (CH), 129.1 (CH), 134.3 (C), 140.1 (CH), 166.5 (C). *m/z* (CI^+) 162 ($[M]^+$, 100 %), 323 (15), 235 (15).

Cyclic Voltammogram of N-*Methylisatin (Blue Trace in Supplementary Material) with Standard Ferrocene (Red Trace in Supplementary Material)*

Cyclic voltammetry was carried out in a glove box under nitrogen using a glassy carbon working electrode, Ag/AgCl reference electrode and platinum counter-electrode. The glassy carbon working electrode, with a diameter of 7 mm (surface area of 38.48 mm^2), was cleaned before use using 1 micron alumina polish and distilled water on a Bueller polishing cloth and dried under compressed air. The counter-electrode consisted of a fine Pt wire, which was cleaned thoroughly before use by heating in a flame for 10 min and allowing to cool. Potentials are quoted with respect to the Ag/AgCl/sat. KCl reference electrode, in contact with 0.1 M tetrabutylammonium hexafluorophosphate in DMF. Samples and standards were made up in an electrolyte solution of 0.1 M tetrabutylammonium hexafluorophosphate in degassed anhydrous DMF. A ferrocene external standard (1.861 g, 10 mmol in 100 mL) was made up in a 0.1 M solution of the buffer and run before and after each measurement. The *N*-methylisatin was made up in a 0.1 M solution of the buffer (161.2 mg, 1 mmol in 10 mL).

Supplementary Material

The Supplementary Material contains cyclic voltammogram of *N*-methylisatin and ^{1}H NMR and ^{13}C-NMR spectra of compounds and can be found on the Journal's website.

Acknowledgements

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