Formation of *N*–heterocycles by the reaction of thiols with glyoxamides: Exploring a connective Pummerer–type cyclisation

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Supporting Information

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1-Methyl-3-ethylacetylsulfanyl-1,3-dihydroindol-2-one 14[1]

As for general procedure A. Glyoxamide **9** (108 mg, 0.67 mmol, 1 eq), on treatment with ethylthioglycolate (73 µl, 0.67 mmol, 1 eq), TFAA (847 µl, 5.99 mmol, 9 eq) and BF_3•OEt_2 (400 µl, 3.33 mmol, 5 eq), and after purification by column chromatography using 30% EtOAc in petroleum ether as eluant, gave **14** (120 mg, 0.45 mmol, 67% from hydroxyamide, 2 steps) as an orange oil. δ_H (500 MHz, $CDCl_3$) 1.18 (3H, t, J = 7.2 Hz, C*H*$_3$CH$_2$), 3.14 (3H, s, C*H*$_3$N), 3.19 (1H, d, J = 15.5 Hz, 1H of C*H*$_2$S), 3.73 (1H, d, J = 15.5 Hz, 1H of C*H*$_2$S), 4.08 (2H, q, J = 7.2 Hz, C*H*$_2$CH$_3$), 4.48 (1H, s, C*H*S), 6.76 (1H, d, J = 7.8 Hz, ArC*H*), 7.01 (1H, dt, J = 0.8, 7.6 Hz, ArC*H*), 7.25 (1H, t, J = 7.8 Hz, ArC*H*) and 7.32 (1H, d, 7.4 Hz, ArC*H*). δ_C (75 MHz, $CDCl_3$) 14.4 (*C*H$_3$CH$_2$), 27.0 (*C*H$_3$N), 31.8 (*C*H$_2$S), 43.9 (*C*HS), 61.8 (*C*H$_2$CH$_3$), 108.6 (Ar*C*H), 123.2 (Ar*C*H), 125.0 (Ar*C*), 125.5 (Ar*C*H), 129.6 (Ar*C*H), 144.4 (Ar*C*), 170.2 (*C*=O amide) and 175.3 (*C*=O ester). υ_{max}/(cm^{-1}) 2985, 1714 (C=O), 1465, 1358, 1271, 1131 and 924. *m/z* (CI^+ mode) 283 ($(M+NH_4)^+$, 18%) 266 ($(M+H)^+$, 100%), 238 (21%), 179 (38%), 166. (17%) and 148 (12%). *m/z* ($M+NH_4^+$) 283.1105, $C_{13}H_{19}O_3N_2S$ requires 283.1111.

5-Bromo-3-phenylsulfanyl-1-propyl-1,3-dihydroindol-2-one 15

As for general procedure A. Glyoxamide **10** (167 mg, 0.62 mmol, 1 eq) on treatment with thiophenol (64 µl, 0.62 mmol, 1 eq), TFAA (0.79 ml, 5.57 mmol, 9 eq) and BF_3•OEt_2 (432 µl, 3.09 mmol, 5 eq) and after purification by column chromatography using 10% EtOAc in petroleum ether as eluant gave **15** (187 mg, 0.51 mmol, 83% from glyoxamide) as a red oil. δ_H (300 MHz, $CDCl_3$) 0.79 (3H, t, J = 7.4 Hz, C*H*$_3$), 1.33-1.44 (2H, m, C*H*$_2$), 3.31-3.40 (1H, m, 1H of C*H*$_2$N), 3.50-

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3.60 (1H, m, 1H of C*H*$_2$N), 4.50 (1H, s, C*H*S), 6.52 (1H, d, J = 8.3 Hz, Ar*H*), 7.15-7.37 (6H, m, 6 × Ar*H*) and 7.52-7.54 (1H, m, Ar*H*). δ_C (75 MHz, $CDCl_3$) 11.5 (*C*H$_3$), 20.7 (*C*H$_2$), 42.1 (*C*H$_2$N), 49.2 (*C*HS), 110.0 (Ar*C*H), 115.2 (Ar*C*), 128.7 (Ar*C*H), 128.8 (Ar*C*H), 128.8 (Ar*C*H), 128.9 (Ar*C*H), 129.0 (Ar*C*H), 132.0 (Ar*C*), 132.9 (Ar*C*), 134.0 (Ar*C*H), 135.0 (Ar*C*H), 142.8 (Ar*C*) and 173.6 (*C*=O). υ_{max}/(cm^{-1}) 3055, 2949, 2860, 1681 (C=O), 1450, 1327, 1080, 879 and 725. *m/z* (CI+ mode), 379 $(M+NH_4)^+$ 50%), 362 ($(M+H)^+$, 100%), 284 (28%), 271 (34%), 254 (52%), 193 (22%) and 176 (40%). *m/z* (M) 362.0210, $C_{17}H_{17}ONBrS$ requires 362.0209.

5-Bromo-3-ethylacetylsulfanyl-1-propyl-1,3-dihydroindol-2-one 16

As for general procedure A. Glyoxamide **10** (164 mg, 0.61 mmol, 1 eq) on treatment with ethylthioglycolate (67 µl, 0.61 mmol, 1 eq), TFAA (0.77 ml, 5.47 mmol, 9 eq) and BF_3•OEt_2 (425 µl, 3.04 mmol, 5 eq) and after purification by column chromatography using 10% EtOAc in petroleum ether as eluant gave **16** (179 mg, 0.48 mmol, 79% from hydroxyamide, 2 steps) as an orange oil. δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, J = 7.6 Hz, C*H*$_3$), 1.21 (3H, t, J = 7.3 Hz, C*H*$_3$CH$_2$C=O), 1.68 (2H, m, C*H*$_2$), 3.18 (1H, d, J = 15.5 Hz, 1H of C*H*$_2$S), 3.58 (2H, m, C*H*$_2$,), 3.77 (1H, d, J = 15.5 Hz, 1H of C*H*$_2$S), 4.09 (2H, q, J = 7.3 Hz, C*H*$_2$CH$_3$), 4.48 (1H, s, C*H*S), 6.65 (1H, d, J = 8.5 Hz, Ar*H*), 7.35 (1H, dd, J = 1.9, 8.5 Hz, Ar*H*) and 7.45 (1H, s, Ar*H*). δ_C (75 MHz, $CDCl_3$) 11.6 (*C*H$_3$), 14.4 (*C*H$_3$CH$_2$), 20.9 (*C*H$_2$), 31.8 (*C*H$_2$S), 42.2 (*C*H$_2$N), 43.6 (*C*HS), 61.9 (CH$_2$*C*H$_3$), 110.3 (Ar*C*H), 115.4 (Ar*C*), 127.4 (Ar*C*), 128.8 (Ar*C*H), 132.4 (Ar*C*H), 142.9 (Ar*C*), 170.0 (*C*=O amide) and 174.7 (*C*=O ester). υ_{max}/(cm^{-1}) 3421, 3058, 2969, 2933, 2876, 1725, 1606, 1481, 1339, 1268, 1180, 1028, 811 and 736. *m/z* (ES+ mode) 578.1 (32%)

and 394.1 ($(M+Na)^+$, 100%). *m/z* (M+Na) 394.0069, $C_{15}H_{18}O_3NBrSNa$ requires 394.0083.

5-Fluoro-3-phenylsulfanyl-1-propyl-1,3-dihydroindol-2-one 17

As for general procedure A Glyoxamide **11** (167 mg, 0.80 mmol, 1 eq), on treatment with thiophenol (81 µl, 0.80 mmol, 1 eq), TFAA (1.01 ml, 7.18 mmol, 9 eq) and BF_3•OEt_2 (558 µl, 3.99 mmol, 5 eq), and purification by column chromatography using 10% EtOAc in petroleum ether as eluant, gave **17** (168 mg, 0.56 mmol, 70% from hydroxyamide, 2steps) as a orange oil. δ_H (300 MHz, $CDCl_3$) 0.71 (3H, t, J = 7.4 Hz, C*H*$_3$), 1.29-1.35 (3H, m, C*H*$_2$), 3.26-3.31 (1H, m, 1H of C*H*$_2$N), 3.45-3.51, (1H, m, 1H of C*H*$_2$N), 4.42 (1H, s, C*H*S), 6.74 (1H, dd, J = 4.1, 8.5 Hz, Ar*H*), 6.98 (1H, dt, J = 2.7, 8.7 Hz, Ar*H*) and 7.15 (1H, ddd, J = 0.9, 2.7, 7.5 Hz, Ar*H*). δ_C (75 MHz, $CDCl_3$) 11.5 (*C*H$_3$), 20.7 (*C*H$_2$), 42.1 (*C*H$_2$N), 49.5 (*C*HS), 109.0 (Ar*C*H, d, J = 8.1 Hz), 113.4 (ArC*H*, d, J = 25.3 Hz), 115.5 (Ar*C*H, d, J = 23.6 Hz), 128.3 (Ar*C*, d, J = 8.6 Hz), 128.9 (2 × Ar*C*H), 129.2 (Ar*C*H), 130.3 (Ar*C*), 134.9 (2 × Ar*C*H), 139.7 (Ar*C*, d, J = 2.1 Hz), 159.2 (Ar*C*F, d, J = 240.7 Hz) and 173.9 (*C*=O amide). υ_{max}/(cm^{-1}) 3057, 2947, 2854, 1699 (C=O), 1465, 1342, 1188, 1124, 811 and 746. *m/z* (EI^+ mode) 301 (M^+ 12%), 192 (100%), 164 (11%), 109 (16%) and 65 (7%). *m/z* (M+H) 302.1012, $C_{17}H_{17}ONFS$ requires 302.1009.

3-(4-Bromo-benzylsulfanyl)-5-fluoro-1-propyl-1,3-dihydro-indol-2-one 18

As for general procedure A Glyoxamide **11** (236 mg, 1.13 mmol, 1 eq), on treatment with 4-bromo benzyl mercaptan (230 mg, 1.13 mmol, 1 eq), TFAA (1.43 ml, 10.2 mmol, 9 eq) and BF_3•OEt_2 (695 µl, 5.65 mmol, 5 eq), and

purification by column chromatography using 12.5% EtOAc in petroleum ether as eluant, gave **18** (322 mg, 0.81 mmol, 72% from hydroxyamide, 2 steps) as a dark orange oil. δ_H (500 MHz, $CDCl_3$) 0.89 (3H, t, J = 7.6 Hz, C*H*$_3$), 1.59 (2H, sextet, J = 7.6 Hz, C*H*$_2$), 3.47-3.56 (2H, m, C*H*$_2$N), 3.60 (1H, d, J = 13.2 Hz, 1H of C*H*$_2$Ph), 4.03 (1H, s, C*H*S), 4.06 (1H, d, J = 13.2 Hz, 1H of C*H*$_2$Ph), 6.63 (1H, dd, J = 4.1, 8.5 Hz, Ar*H*), 6.88-6.94 (2H, m, 2 × Ar*H*), 7.15 (2H, d, J = 8.5 Hz, 2 × Ar*H*) and 7.33 (2H, d, J = 8.5 Hz, 2 × Ar*H*). δ_C (75 MHz, $CDCl_3$) 11.6 (*C*H$_3$), 21.0 (*C*H$_2$), 33.8 (*C*H$_2$S), 42.2 (*C*H$_2$N), 43.5 (*C*HS), 109.2 (Ar*C*H, d, J = 8.3 Hz), 113.3 (Ar*C*H, d, J = 24.9 Hz), 115.5 (Ar*C*H, d, J = 23.5 Hz), 121.6 (Ar*C*), 127.2 (Ar*C*, d, J = 8.3 Hz), 131.2 (2 × Ar*C*H), 131.9 (2 × Ar*C*H), 136.4 (Ar*C*), 139.7 (Ar*C*), 159.3 (Ar*C*F, d, J = 239.8 Hz) and 175.3 (*C*=O). $\upsilon_{max}/(cm^{-1})$ 3048, 2965, 2931, 2874, 1711 (C=O), 1488, 1383, 1267, 1199, 1070, 872. *m/z* (ES+ mode) 454 (29%), 417 ($(M+Na)^+$ 100%), 396 (61%), 393 (45%), 160 (37%). *m/z* (M + H) 394.0260. $C_{18}H_{18}ONBrFS$ requires 394.0271.

5-Fluoro-3-(6-hydroxy-hexylsulfanyl)-1-propyl-1,3-dihydroindol-2-one 19

As for general procedure A. Glyoxamide **11** (233 mg, 1.11 mmol, 1 eq), on treatment with 6-mercapto-1-hexanol (151 µl, 1.11 mmol, 1 eq), TFAA (1.42 ml, 10.0 mmol, 9 eq) and BF_3•OEt_2 (685 µl, 5.56 mmol, 5 eq), and purification by column chromatography using 15% EtOAc in petroleum ether as eluant, gave **19** (257 mg, 0.79 mmol, 71% from hydroxyamide, 2 steps) as a dark orange oil. δ_H (500 MHz, $CDCl_3$) 0.88 (3H, t, J = 7.6 Hz, C*H*$_3$), 1.22-1.34 (5H, m, 2 × C*H*$_2$ and 1H of C*H*$_2$), 1.42-1.34 (2H, m, C*H*$_2$), 1.58-1.67 (3H, m, C*H*$_2$ and 1H of C*H*$_2$), 2.37-2.42 (1H, m, 1H of C*H*$_2$S), 2.55-2.61 (1H, m, 1H of C*H*$_2$S), 3.53-3.66 (3H, m, C*H*$_2$O and 1H of C*H*$_2$N), 4.22 (1H, s, C*H*S), 4.23-4.26 (1H, m, 1H of C*H*$_2$N),

6.06 (1H, broad s, O*H*), 6.69 (1H, dd, J = 4.1, 8.5 Hz, Ar*H*), 6.92 (1H, dt, J = 1.9, 8.5 Hz, Ar*H*) and 7.07 (1H, J = 1.3, 2.9, 7.6 Hz). δ_C (125 MHz, $CDCl_3$) 11.3 (*C*H_3), 20.5 (*C*H_2), 25.0 (*C*H_2), 27.9 (*C*H_2), 28.1 (*C*H_2), 28.4 (*C*H_2), 29.5 (*C*H_2), 41.6 (*C*H_2OH), 44.9 (*C*HS), 68.6 (*C*H_2N), 108.9 (Ar*C*H, d, J = 7.5 Hz), 113.2 (Ar*C*H, d, J = 30 Hz), 115.4 (Ar*C*H, d, J = 28.75 Hz), 127.8 (Ar*C*, d, J = 7.5 Hz), 139 (Ar*C*), 159.2 (Ar*C*F, d, J = 240 Hz) and 175.1 (C=O). $\upsilon_{max}/(cm^{-1})$ 3528, 3419, 2935, 2863, 1785, 1716, 1611, 1489, 1454, 1347, 1165, 951 and 875. *m/z* (ES+ mode) 348 ($(M+Na)^+$ 100%), 343 (22%) and 326 ($(M+H)^+$ 63%). *m/z* (M+H) 326.1584, $C_{17}H_{25}O_2NFS$ requires 326.1585.

Methyl 3-(5-fluoro-2-oxo-1-propylindolin-3-ylsulfanyl) propanoate 20

As for general procedure A. Glyoxamide **11** (197 mg, 0.93 mmol, 1 eq) on treatment with methyl-3-mercapto-propionate (101 µl, 0.93 mmol, 1 eq), TFAA (1.19 ml, 8.39 mmol, 9 eq) and BF_3•OEt_2 (574 µl, 4.66 mmol, 5 eq) and purification by column chromatography using 20% EtOAc in petroleum ether as eluant, gave **20** (197 mg, 0.62 mmol, 67% from hydroxyamide, 2 steps) as a light orange oil. δ_H (300 MHz, $CDCl_3$) 0.98 (3H, t, J = 7.4 Hz, C*H*$_3$), 1.53 (2H, sextet, J = 7.4 Hz, C*H*$_2$), 2.63 (2H, t, J = 7.1 Hz, SCH$_2$C*H*$_2$C=O), 2.77-2-86 (1H, m, 1H of C*H*$_2$S), 2.98-3.07 (1H, m, 1H of C*H*$_2$S), 3.58-3.69 (2H, m, C*H*$_2$N), 3.67 (3H, s, CO$_2$C*H*$_3$), 4.30 (1H, s, C*H*S), 6.74 (1H, dd, J = 4.1, 8.5 Hz, ArC*H*), 6.85 (1H, dt, J = 2.6, 8.5 Hz, ArC*H*) and 7.15 (1H, ddd, J = 0.9, 2.6, 7.8 Hz, ArC*H*). δ_C (75 MHz, $CDCl_3$) 11.6 (*C*H_3), 20.9 (*C*H_2), 25.2 (*C*H_2S), 34.5 (*C*H_2C=O), 42.1 (*C*H_2N), 45.0 (*C*HS), 52.1 (CO$_2$*C*H$_3$), 109.3 (Ar*C*H, d, J = 8.1 Hz), 113.5 (Ar*C*H, d, J = 25.0 Hz), 115.6 (Ar*C*H, d, J = 23.3 Hz), 127.6 (Ar*C*, d, J = 8.3 Hz), 139.6 (Ar*C*, d, J = 2.0 Hz), 159.4 (Ar*C*F, d, J = 243.6 Hz), 172.2 (*C*=O amide) and 175.1 (*C*=O

ester). $\upsilon_{max}/(cm^{-1})$ 2938, 1715 (C=O), 1613, 1448, 1345, 1165 and 981. *m/z* (CI^+ mode) 312 ((M^+ + H), 24%), 194 (100%), 136 (14%), 108 (15%), 72 (19%) and 60 (42%). *m/z* (M+H) 312.1066, $C_{15}H_{19}O_3NFS$ requires 312.1064.

5-Fluoro-3-ethylacetylsulfanyl-1-propyl-1,3-dihydroindol-2-one 21

As for general procedure A. Glyoxamide **11** (146 mg, 0.70 mmol, 1 eq) on treatment with ethylthioglycolate (53 µl, 0.49 mmol, 0.7 eq), TFAA (887 µl, 6.28 mmol, 9 eq) and BF_3•OEt_2 (488 µl, 3.49 mmol, 5 eq) and after purification by column chromatography using 10% EtOAc in petroleum ether as eluant, gave **21** (150 mg, 0.44 mmol, 63% from hydroxyamide, 2 steps) as a yellow oil. δ_H (300 MHz, $CDCl_3$) 0.95 (3H, t, J = 7.4 Hz, C*H*$_3$), 1.25 (3H, t, J = 7.2 Hz, C*H*$_3$CH$_2$), 1.68 (2H, m, C*H*$_2$), 3.23 (1H, d, J = 15.6 Hz, 1H of C*H*$_2$S), 3.64 (2H, t, J = 7.4 Hz, C*H*$_2$N), 3.84 (1H, d, J = 15.6 Hz, 1H of C*H*$_2$S), 4.17 (2H, q, J = 7.2 Hz, OC*H*$_2$CH$_3$), 4.53 (1H, s, C*H*S), 6.74 (1H, dd, J = 4.2, 8.4 Hz, ArC*H*), 6.98 (1H, dt, J = 2.4, 8.4 Hz, ArC*H*) and 7.15 (1H, ddd, J = 0.9, 2.7, 7.5 Hz, ArC*H*). δ_C (75 MHz, $CDCl_3$) 11.6 (*C*H$_3$), 14.3 (*C*H$_3$CH$_2$O), 20.9 (*C*H$_2$), 31.8 (*C*H$_2$S), 42.1 (*C*H$_2$N), 43.9 (*C*HS), 61.8 (O*C*H$_2$CH$_3$), 109.3 (Ar*C*H, d, J = 8.0 Hz), 113.6 (ArC*H*, d, J = 24.9 Hz), 115.8 (Ar*C*H, d, J = 23 Hz), 126.8 (Ar*C*, d, J = 8.2 Hz), 139.7 (Ar*C*, d, J = 2.1 Hz), 159.2 (Ar*C*F, d, J = 241 Hz), 170.0 (*C*=O amide) and 174.9 (*C*=O ester). $\upsilon_{max}/(cm^{-1})$ 2947, 1718 (C=O), 1486, 1276, 1130, 1026 and 813. *m/z* (EI^+ mode) 312 (M^+ 31%), 194 (100%), 136 (40%), 109 (21%) and 58 (13%). *m/z* (M+H) 312.1062, $C_{15}H_{19}O_3NFS$ requires 312.1064.

(2*R*)-2-Dibenzylamino-3-((3*R*/*S*)-5-fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-3-ylsulfanyl)propionic acid methyl ester 22a

As for general procedure A. Glyoxamide **11** (96 mg, 0.46 mmol, 1 eq) on treatment with 2(*R)*-methyl-2-(dibenzylamino)-3-mercaptopropanoate (144 mg, 0.46 mmol, 1 eq), TFAA (583 µl, 4.13 mmol, 9 eq) and BF_3•OEt_2 (282 µl, 2.29 mmol, 5 eq) and purification by column chromatography using 20% EtOAc in petroleum ether as eluant, gave **22a** as an inseparable 1:1.5 mixture of diastereoisomers (120 mg, 0.23 mmol, 52% from hydroxyamide, 2 steps) as an oil. $[\alpha]_D$ = –52.47 (c = 5.1, CH_2Cl_2). δ_H (500 MHz, $CDCl_3$) 0.74-0.79 (6H, m, 2 × C*H*$_3$), 1.33-1.40 (4H, m, 2 × C*H*$_2$), 2.65-2.68 (1H, m, 1H of C*H*$_2$CHS one isomer), 2.79-2.85 (3H, m, 1H of C*H*$_2$CHS one isomer and C*H*$_2$CHS one isomer), 3.18 (1H, t, J = 7.4 Hz, SC*H*CH$_2$ one isomer), 3.37 (1H, d, J = 13.7 Hz, 1H of C*H*$_2$Ph one isomer), 3.38-3.48 (4H, m, 1H of NC*H*$_2$ both isomers, SC*H*CH$_2$ one isomer, 1H of C*H*$_2$Ph one isomer), 3.51-3.57 (2H, m, 1H of NC*H*$_2$ both isomers), 3.63 (3H, s, C*H*$_3$OC=O one isomer), 3.65 (3H, s, C*H*$_3$OC=O one isomer), 3.69 (1H, d, J = 13.7 Hz, 1H of C*H*$_2$Ph one isomer), 3.75 (1H, d, J = 13.7 Hz, 1H of C*H*$_2$Ph one isomer), 4.58 (1H, s, C*H*S one isomer), 4.72 (1H, s, C*H*S one isomer), 6.76-6.95 (8H, m, 8 × ArC*H*) and 7.12-7.28 (18H, m, 18 × ArC*H*). δ_C (75 MHz, $CDCl_3$) 11.3 (2 × *C*H$_3$), 20.9 (2 × *C*H$_2$), 29.4 (*C*H$_2$CHS, one isomer), 29.6 (*C*H$_2$CHS, one isomer), 51.7 (2 × *C*H$_3$O), 52.0 (2 × *C*H$_2$N), 54.5 (*C*H$_2$Ph, one isomer), 54.7 (*C*H$_2$Ph one isomer), 60.7 (S*C*HCH$_2$, one isomer), 61.2 (S*C*HCH$_2$, one isomer), 72.9 (*C*HS, one isomer), 73.2 (*C*HS, one isomer), 116.5 (Ar*C*H, one isomer, d, J = 22.7), 116.7 (Ar*C*H, one isomer, d, J = 22.6), 127.5 (2 × Ar*C*H), 127.5 (2 × Ar*C*H), 128.5 (4 × Ar*C*H), 128.6 (4 × Ar*C*H), 129.1 (4 × Ar*C*H), 129.3 (4 × Ar*C*H), 130.8 (4 × Ar*C*H), 135.9 (2 × Ar*C*), 139.1 (2 × Ar*C*), 161.5 (2 × Ar*C*F, J = 240.9 Hz), 170.2 (C=O amide, one isomer), 170.3 (C=O amide, one isomer), 171.8 (C=O ester, one isomer) and 171.9 (C=O ester, one isomer). υ_{max}/(cm^{-1}) 3402, 3029, 2947, 1729

(C=O), 1652, 1481, 1216, 1073 and 962. *m/z* (ES+ mode) 505 ((M+H) 82%), 382 (30%) and 264 (100%). *m/z* (M–H) 505.1968, $C_{29}H_{30}FN_2O_3S$ requires 505.1956.

6-Methoxy-3-phenylsulfanyl-1-propyl-1,3-dihydroindol-2-one 23

As for general procedure A. Glyoxamide **12** (250 mg, 1.13 mmol, 1 eq) on treatment with thiophenol (464 µl, 4.52 mmol, 4 eq), TFAA (1.44 ml, 10.2 mmol, 9 eq) and BF_3•OEt_2 (695 µl, 5.65 mmol, 5 eq) and purification by column chromatography using 15% EtOAc in petroleum ether as eluant, gave **23** (158 mg, 0.50 mmol, 44% from hydroxyamide, 2 steps) as an oil (inseparable 5:1 mixture of regioisomers). δ_H (500 MHz, $CDCl_3$) 0.83 (3H, t, J = 7.4 Hz, C*H*$_3$ major), 0.88 (3H, t, J = 7.4 Hz, C*H*$_3$ minor), 1.37-1.55 (4H, m, C*H*$_2$ both isomers), 3.34-3.48 (2H, m, 1H of C*H*$_2$N both isomers), 3.54-3.66 (2H, m, 1H of C*H*$_2$N both isomers), 3.71 (3H, s, OC*H*$_3$ minor), 3.83 (3H, s, OC*H*$_3$ major), 4.54 (1H, s, C*H*S major), 4.81 (1H, s, C*H*S minor), 6.27 (1H, d, J = 2.2 Hz, Ar*H* major), 6.44-6.46 (1H, m, Ar*H* minor), 6.59 (1H, dd, J = 2.2, 8.3 Hz, Ar*H* major), 6.81-6.85 (1H, m, Ar*H* minor) and 7.13-7.42 (12H, m, 12 × Ar*H* both isomers). δ_C (75 MHz, $CDCl_3$) 11.4 (*C*H$_3$ minor), 11.6 (*C*H$_3$ of major), 20.8 (*C*H$_2$ of minor isomer), 21.1 (*C*H$_2$ major isomer), 42.1 (*C*H$_2$N both isomers), 49.1 (*C*HS major), 51.6 (*C*H$_3$O minor), 55.6 (*C*H$_3$O major), 58.2 (*C*HS minor), 96.7 (Ar*C*H major), 101.9 (Ar*C*H minor), 106.0 (Ar*C*H minor), 106.4 (Ar*C*H major), 113.9 (Ar*C*H minor), 114.2 (Ar*C*H minor), 118.4 (Ar*C* major), 120.5 (Ar*C* minor), 126.3 (Ar*C*H major), 128.7 (Ar*C*H major), 128.9 (2 × Ar*C*H major), 129.1 (Ar*C*H major), 130.4 (Ar*C*H minor), 130.6 (Ar*C*H minor), 131.3 (2 × Ar*C*H minor), 133.5 (Ar*C* minor), 133.8 (Ar*C* major), 134.6 (Ar*C*H major), 135.4 (Ar*C* minor), 145.1 (Ar*C* major), 161.0 (Ar*C*OMe major), 168.0 (Ar*C*OMe major) and 175.0 (*C*=O both isomers). $\upsilon_{max}/(cm^{-1})$ 3057, 2964,

2932, 1717 (C=O), 1622, 1501, 1467, 1371, 1268, 1131 and 982. *m/z* (ES+ mode) 336 (M+H, 100%). *m/z* (M+Na) 336.1030, $C_{18}H_{19}O_2NNaS$ requires 336.1029.

6-Methoxy-3-ethoxycarbonylmethylsulfanyl-1-propyl-1,3-dihydroindol-2-one 24

As for general procedure A Glyoxamide **12** (235 mg, 0.80 mmol, 1 eq) on treatment with ethylthioglycolate (467 µl, 4.26 mmol, 4 eq), TFAA (1.35 ml, 9.56 mmol, 9 eq) and BF_3•OEt_2 (654 µl, 5.31 mmol, 5 eq) and purification by column chromatography using 15% EtOAc in petroleum ether as eluant, gave **24** (136 mg, 0.42 mmol, 40% from hydroxyamide, 2 steps) as an oil (inseparable 5:1 mixture of regioisomers). δ_H (500 MHz, $CDCl_3$) 0.83 (6H, t, J = 7.5 Hz, C*H*$_3$ both isomers), 1.11-1.15 (6H, m, C*H*$_3$CH$_2$C=O both isomers), 1.53-1.59 (6H, m, C*H*$_2$ both isomers), 3.12 (1H, d, J = 15.6 Hz, 1H of C*H*$_2$S major), 3.25 (1H, d, J = 15.6 Hz, 1H of C*H*$_2$S minor), 3.47-3.51 (2H, m, C*H*$_2$N both isomers), 3.68 (3H, s, C*H*$_3$O major), 3.70 (1H, d, J = 15.6 Hz, 1H of C*H*$_2$S minor), 3.73 (1H, d, J = 15.6 Hz, 1H of C*H*$_2$S major), 3.76 (3H, s, C*H*$_3$O minor), 3.99-4.04 (3H, m, C=OC*H*$_2$C*H*$_3$ both isomers), 4.36 (1H, s, C*H*S major), 4.44 (1H, s, C*H*S minor), 6.27 (1H, d, J = 2.2 Hz, ArC*H* major), 6.35 (1H, d, J = 7.8 Hz, ArC*H* minor), 6.41 (1H, dd, J = 2.2, 8.2 Hz, ArC*H* major), 6.47 (1H, d, J = 8.5 Hz, ArC*H* minor) and 7.28 (1H, d, J = 8.2 Hz, ArC*H* major). δ_C (75 MHz, $CDCl_3$) 11.6 (*C*H$_3$ both isomers), 14.4 (*C*H$_3$CH$_2$C=O both isomers), 21.0 (*C*H$_2$ major), 21.1 (*C*H$_2$ minor), 31.7 (*C*H$_2$S major), 31.9 (*C*H$_2$S minor), 42.0 (*C*H$_2$N major), 42.2 (*C*H$_2$N minor), 42.5 (*C*HS minor) 43.4 (*C*HS major), 55.8 (*C*H$_3$O major), 56.0 (*C*H$_3$O minor), 61.6 (CH$_3$*C*H$_2$C=O minor), 61.7 (CH$_3$*C*H$_2$C=O major), 97.0 (Ar*C*H major), 102.2 (Ar*C*H minor), 106.2 (Ar*C*H minor), 106.4 (Ar*C*H major), 116.9 (Ar*C* minor),

126.3 (Ar*C*H major), 130.9 (Ar*C*H minor), 156.7 (Ar*C*OMe minor), 161.2 (Ar*C*OMe major), 170.2 (*C*=O amide, minor), 170.3 (*C*=O amide, major), 175.3 (*C*=O ester, minor) and 176.0 (*C*=O ester, major). $\upsilon_{max}/(cm^{-1})$ 2967, 2934, 2876, 1715 (C=O ester), 1622 (C=O amide), 1502, 1467, 1372, 1269, 1133, 1030, 984 and 896. *m/z* (CI^+ mode) 324 ($(M+H)^+$ 100%), 223 (18%) and 206 (44%). *m/z* (M+H) 324.1265, $C_{16}H_{22}O_4NS$ requires 324.1264.

1-((*S*)-1-Phenyl-1-ethyl)-3-ethylacetylsulfanyl-1,3-dihydro-indol-2-one 28

As for general procedure A. Glyoxamide **27** (53 mg, 0.21 mmol, 1 eq), on treatment with ethylthioglycolate (23 µl, 0.21 mmol, 1 eq), TFAA (177 µl, 1.26 mmol, 6 eq) and BF_3•OEt_2 (52 µl, 0.42 mmol, 2 eq), and after purification by column chromatography using 10% EtOAc in petroleum ether as eluant, gave **28** (47 mg, 0.13 mmol, 64% from hydroxyamide, 2 steps) as a clear oil (1:1 mixture of diastereoisomers). $[\alpha]_D$ = –117.80 (c = 2.18, CH_2Cl_2). δ_H (500 MHz, $CDCl_3$) 1.19 (3H, t J = 7.3 Hz, C*H*$_3$ one isomer), 1.20 (3H, t J = 7.3 Hz, C*H*$_3$ one isomer), 1.76 (3H, d, 7.3 Hz, C*H*$_3$ one isomer), 1.77 (3H, d, 7.3 Hz, C*H*$_3$ one isomer), 3.22 (1H, d, J = 15.5 Hz, 1H of C*H*$_2$S one isomer), 3.27 (1H, d, J = 15.5 Hz, 1H of C*H*$_2$S one isomer), 3.84 (1H, d, J = 15.5 Hz, 1H of C*H*$_2$S one isomer), 3.95 (1H, d, J = 15.5 Hz, 1H of C*H*$_2$S one isomer), 4.06-4.13 (4H, m, C*H*$_2$N both isomers), 4.56 (1H, s, C*H*S one isomer), 4.57 (1H, s, C*H*S one isomer), 5.77 (2H, sextet, J = 7.3 Hz, C*H* both isomers), 6.39-6.42 (2H, m, 2 × Ar*H* both isomers), 6.91 (2H, t, J = 7.6 Hz, 2 × Ar*H* both isomers), 6.98 (2H, t, J = 7.6 Hz, 2 × Ar*H* both isomers) and 7.18-7.32 (12H, m, 12 × Ar*H* both isomers). δ_C (75 MHz, $CDCl_3$) 14.4 (2 × *C*H_3), 16.3 (*C*H_2), 16.5 (*C*H_2), 31.8 (*C*H_2S), 32.0 (*C*H_2S), 43.7 (*C*HS), 43.9 (*C*HS), 49.4 (*C*HCH_3), 49.5 (*C*HCH_3), 61.8 (2 × *C*H_2N), 111.3 (2 × Ar*C*H), 122.7 (2 × Ar*C*H), 125.3 (Ar*C*H), 125.3 (Ar*C*H),

125.6 (Ar*C*H), 125.7 (Ar*C*H), 126.9 (4 × Ar*C*H), 127.8 (2 × Ar*C*H), 129.0 (2 × Ar*C*H), 129.0 (2 × Ar*C*H), 129.1 (2 × Ar*C*H), 139.2 (2 × Ar*C*), 139.2 (2 × Ar*C*), 142.3 (2 × Ar*C*), 170.3 (*C*=O amide), 170.3 (*C*=O amide), 175.4 (*C*=O ester) and 175.4 (*C*=O ester). $\upsilon_{max}/(cm^{-1})$ 3057, 2930, 2983, 1712, 1608, 1482, 1467, 1386, 1347, 1266, 1184, 1084, 1026, 736 and 699. *m/z* (ES+ mode) 378 $((M+Na)^+$ 100%) and 356 $((M+H)^+$ 52%). *m/z* (M+H) 356.1318, $C_{20}H_{22}O_3NS$ requires 356.1315.

1-(6-Hydroxy-hexylsulfanyl)-3,4-methylenedioxy-3-propyl-1,3,4,5-tetrahydro-benzo[*d*]azepin-2-one 31

As for general procedure B. Glyoxamide **29** (50 mg, 0.20 mmol, 1 eq) on treatment with 6-mercapto-1-hexanol (27 µl, 0.20 mmol, 1 eq), TFAA (254 µl, 1.80 mmol, 9 eq) and BF_3•OEt_2 (123 µl, 1.00 mmol, 5 eq) and after purification with 20% EtOAc in petroleum ether as eluant, gave **31** (51 mg, 0.14 mmol, 68% from hydroxyamide, 2 steps) as a clear oil. δ_H (500 MHz, $CDCl_3$) 0.86 (3H, t, J = 7.4 Hz, CH_3), 1.32-1.41 (4H, m, 2 × CH_2), 1.58-1.70 (6H, m, CH_2CH$_3$ and 2 × CH_2), 2.57-2.62 (1H, m, 1H of CH_2), 2.72-2.78 (1H, m, 1H of CH_2), 2.88-3.00 (3H, m, CH_2 and 1H of CH_2), 3.13-3.22 (3H, m, CH_2 and 1H of CH_2), (1H, m, 1H of NCH_2CH$_2$ArC), 4.28 (2H, t, J = 7.0 Hz, CH_2N), 4.59 (1H, s, C*H*S), 4.66-4.71 (1H, m, 1H of NCH_2CH$_2$ArC), 5.84 (1H, d, J = 1.47 Hz, 1H of OCH_2O), 5.85 (1H, d, J = 1.47 Hz, 1H of OCH_2O), 6.44 (1H, s, ArC*H*) and 6.58 (1H, s, ArC*H*). δ_C (125 MHz, $CDCl_3$) 11.6 (*C*H$_3$), 21.5 (*C*H$_2$), 25.5 (*C*H$_2$), 28.7 (*C*H$_2$), 29.4 (*C*H$_2$), 32.8 (*C*H$_2$), 33.7 (*C*H$_2$), 34.0 (*C*H$_2$), 45.5 (*C*H$_2$), 50.4 (*C*H$_2$), 56.2 (*C*HS), 63.0 (*C*H$_2$N), 101.5 (O*C*H$_2$O), 110.1 (Ar*C*H), 111.8 (Ar*C*H), 125.8 (Ar*C*), 131.1 (Ar*C*H), 146.7 (Ar*C*O), 147.7 (Ar*C*O) and 170.3 (*C*=O). $\nu_{max}/(cm^{-1})$ 3426, 2928, 1638, 1504, 1485, 1424, 1384, 1307, 1266, 1225, 1124 and 1038. *m/z* (ES+ mode)

402 (M+Na, 62%) and 380 (M+H, 100%). *m/z* (M+H) 380.1896, $C_{20}H_{30}O_4NS$ requires 380.1890.

Pummerer–type cyclisation with sub–stoichiometric amounts of $Sc(OTf)_3$ – 21 and 5-fluoro-3-hydroxyl-1-propyl-1,3-dihydroindol-2-one 32

To a stirred solution of glyoxamide **11** (112 mg, 0.54 mmol, 1 eq) was added ethylthioglycolate (59 µl, 0.54 mmol, 1 eq) at room temperature. After 18 h, TFAA (453 µl, 3.21 mmol, 6 eq) was added. After a further 1 h, $Sc(OTf)_3$ (132 mg, 0.27 mmol, 0.5 eq) was added. After 1 h, the reaction was quenched with aqueous $NaHCO_3$ (15 ml), the organic layer was washed with aqueous $NaHCO_3$ (2 × 15 ml), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an orange oil. Purification by column chromatography using 15% EtOAc in petroleum ether as eluant, gave **32** (19 mg, 0.09 mmol, 17%) as an oil and **21** (122 mg, 0.39 mmol, 72% from hydroxyamide, 2 steps) as an oil. For **32**: δ_H (500 MHz, $CDCl_3$) 0.89 (3H, t, J = 7.4 Hz, C*H*$_3$), 1.62 (2H, sextet, J = 7.4 Hz, C*H*$_2$), 3.49-3.62 (2H, m, C*H*$_2$N), 4.90-5.10 (1H, broad s, O*H*), 5.05 (1H, s, C*H*OH), 6.69 (1H, dd, J = 4.0, 8.7 Hz, ArC*H*), 6.94 (1H, dt, J = 2.65, 8.9 Hz, ArC*H*) and 7.15 (1H, dd, J = 2.5, 7.6 Hz, ArC*H*). δ_C (125 MHz, $CDCl_3$) 11.3 (*C*H$_3$), 20.6 (*C*H$_2$), 41.9 (*C*H$_2$N), 69.8 (*C*HOH), 109.4 (Ar*C*H, d, J = 8.8 Hz), 113.5 (ArC*H*, d, J = 23.8 Hz), 115.8 (Ar*C*H, d, J = 22.5 Hz), 129.0 (Ar*C*, d, J = 8.8 Hz), 139. (Ar*C*, d, J = 1.25 Hz), 159.5 (Ar*C*F, d, J = 240 Hz) and 177.4 (*C*=O ester). υ_{max}/(cm^{-1}) 3417, 2927, 1725 (C=O), 1489, 1463, 1339, 1264, 1196 and 937. *m/z* (EI$^+$ mode) 209 (M$^+$, 35%), 151 (100%), 134 (30%), 122 (42%), 95 (60%), 83 (58%), 75 (73%) and 49 (80%). *m/z* (M-H) 208.0759, $C_{11}H_{11}O_2NF$ requires 208.0768.

Cross-over experiment – 14 and 19

To a stirred solution of glyoxamide **9** (43 mg, 0.26 mmol, 1 eq) in CH_2Cl_2 (3 ml) was added ethylthioglycolate (29 µl, 0.26 mmol, 1 eq) and the reaction mixture stirred at room temperature for 18 h. In a separate reaction flask, 6-mercapto-1-hexanol (38 µl, 0.26 mmol, 1 eq) was added to a solution of glyoxamide **11** (59 mg, 0.28 mmol, 1 eq) in CH_2Cl_2 (3 ml) at room temperature and the reaction also stirred for 18 h. The two reaction mixtures were then combined and the resulting solution stirred for 2.5 h. TFAA (475 µl, 3.36 mmol, 12 eq) was added followed by BF_3•OEt_2 (138 µl, 1.12 mmol, 4 eq) after a further 1 h. After 1 h the reaction was quenched with aqueous saturated $NaHCO_3$ (10 ml), the organic layers washed with aqueous saturated $NaHCO_3$ (2 × 10 ml), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by column chromatography using 20% EtOAc in petroleum ether as eluant gave **19** (73 mg, 0.22 mmol, 80%) and **14** (47 mg, 0.17 mmol, 68%).

3,5-*Bis*-phenylsulfanyl-1,7-dipropyl-5,7-dihydro-1*H*,3*H*-pyrrolo[3,2-*f*]indole-2,6-dione 43

As for general procedure C. *Bis*–glyoxamide **39** (140 mg, 0.45 mmol, 1 eq) on treatment with thiophenol (99 µl, 0.90 mmol, 2 eq), TFAA (1.15 ml, 8.12 mmol, 18 eq) and BF_3•OEt_2 (555 µl, 4.51 mmol, 10 eq), and after purification by column chromatography using 10% EtOAc in petroleum ether as eluant gave **43** (104 mg, 0.21 mmol, 47% from *bis*-hydroxyamide, 2 steps) as an oil (1:1.5 mixture of diastereoisomers). δ_H (500 MHz, $CDCl_3$) 0.71-0 .76 (6H, m, 2 × CH_3), 1.31-1.38 (4H, m, 2 × CH_2), 3.28- 3.33 (2H, m, NCH_2), 3.46-3.55 (2H, m, NCH_2), 4.44 (2H, s, 2 × C*H*S major), 4.48 (2H, s, 2 × C*H*S minor), 5.91 (1H, s, ArC*H* major), 5.93 (1H, s, ArC*H* minor), 7.09-7.13 (8H, m, 8 × ArC*H*), 7.16-7.21 (4H, m, 4 × ArC*H*),

7.29-7.32 (8H, m, 8 × ArC*H*), 7.38 (1H, s, ArC*H* major) and 7.40 (1H, s, ArC*H* minor). δ_C (75 MHz, $CDCl_3$) 11.6 (2 × *C*H_3), 20.9 (2 × *C*H_2), 42.1 (2 × *C*H_2N), 49.3 (2 × *C*HS major), 49.4 (2 × *C*HS minor), 90.7 (Ar*C*H), 119.8 (Ar*C*), 120.0 (Ar*C*), 122.8 (Ar*C*H), 129.0 (2 × Ar*C*H), 129.0 (2 × Ar*C*H), 129.1 (2 × Ar*C*H), 130.9 (Ar*C*), 131.2 (Ar*C*), 134.5 (2 × Ar*C*H), 134.8 (2 × Ar*C*H), 144.8 (Ar*C*), 145.1 (Ar*C*), 174.7 (*C*=O) and 174.9 (*C*=O). $\upsilon_{max}/(cm^{-1})$ 3058, 2931, 2662, 1705 (C=O), 1597, 1465, 1368, 1195, 1087 and 894. *m/z* (ES^+ mode) 811.3 (43%), 589.7 (22%), 511.2 ($(M+Na)^+$, 47%), 495.2 (30%), 417.4 (100%), 395.3 (27%) and 379.3 (16%). *m/z* (M+H) 489.1659, $C_{28}H_{29}O_2N_2S_2$ requires 489.1665.

3,5-*Bis*-ethoxycarbonylmethylsulfanyl-1,7-dipropyl-5,7-dihydro-1*H*,3*H*-pyrrolo[3,2-*f*]indole-2,6-dione 44

As for general procedure C. *Bis*–glyoxamide **39** (167 mg, 0.54 mmol, 1 eq) on treatment with ethylthioglycolate (118 µl, 1.08 mmol, 2 eq), TFAA (1.37 ml, 9.68 mmol, 18 eq), and BF_3•OEt_2 (662 µl, 5.38 mmol, 10 eq), and after purification by column chromatography using 30% EtOAc in petroleum ether as eluant gave **44** (138 mg, 0.27 mmol, 50% from *bis*–hydroxyamide, 2 steps) as an oil (1:1 mixture of diastereoisomers). δ_H (300 MHz, $CDCl_3$) 0.92 (6H, t, J = 7.2 Hz, 2 × C*H*$_3$), 1.22 (6H, t, J = 7.2 Hz, 2 × C*H*$_3$CH_2O), 1.68 (4H, sextet, J = 7.3 Hz, 2 × C*H*$_2$), 3.19-3.23 (2H, overlapping doublets, J = 15.6 Hz, 2 × 1H of C*H*$_2$S both isomers), 3.60-3.64 (4H, m, J = 7.4 Hz, 2 × C*H*$_2$N), 3.84 (2H, overlapping doublets, J = 15.6 Hz, 2 × 1H of C*H*$_2$S), 4.09-4.14 (4H, overlapping quartets, J = 7.2 Hz, 2 × OC*H*$_2$CH$_3$), 4.49 (2H, s, 2 × C*H*S), 6.24 (1H, s, ArC*H*) and 7.35 (1H, s, ArC*H*). δ_C (75 MHz, $CDCl_3$) 11.7 (2 × *C*H_3), 14.4 (2 × *C*H_3CH_2), 21.1 (2 × *C*H_2), 31.8 (2 × *C*H_2S), 42.1 (2 × *C*H_2N), 43.5 (2 × *C*HS), 61.9 (2 × *C*H_2CH$_3$), 91.3 (Ar*C*H), 118.4 (2 × Ar*C*),

122.8 (2 × Ar*C*), 145.3 (Ar*C*H), 170.2 (2 × *C*=O amide) and 175.9 (2 × *C*=O ester). $\upsilon_{max}/(cm^{-1})$ 2954, 1712 (C=O ester), 1604 (C=O amide), 1473, 1369, 1273, 1089 and 896. *m/z* (ES+ mode) 935 (32%), 772 (42%), 651 (62%), 531 (M+Na 71%), 427 (100%) and 261 (48%). *m/z* (M+Na) 531.1598, $C_{24}H_{32}O_6N_2NaS_2$ requires 531.1594.

3,5-*Bis*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-1,7-dipropyl-5,7-dihydro-1*H*, 3*H*, pyrrolo [3,2-*f*] indol-2,6-dione 45

As for general procedure C. *Bis*–glyoxamide **39** (519 mg, 1.71 mmol, 1 eq) on treatment with 1H, 1H, 2H, 2H-perfluorodecane-1-thiol (1.00 ml, 3.42 mmol, 2 eq), TFAA (4.31 ml, 30.5 mmol, 18 eq) and BF_3•Et_2O (2.37 ml, 16.9 mmol, 10 eq), and after purification by FSPE gave **45** (1.16 g, 0.95 mmol, 56% from *bis*–hydroxyamide, 2 steps) as a dark solid (1:1 mixture of diastereoisomers). mp 93.2 – 99.5 (recrystallised from petroleum ether/EtOAc). δ_H (500 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 7.4 Hz, 2 × CH_3), 1.62 (4H, m, 2 × CH_2), 2.08-2.36 (4H, m, 2 × CF_2CH_2), 2.70-2.74 (2H, m, 2 × 1H from CH_2S), 2.84-2.88 (2H, m, 2 × 1H from CH_2S), 3.54-3.64 (4H, m, 2 × NCH_2), 4.24 (2H, s, C*H*S), 6.26 (1H, s, 1 × Ar*H*) and 7.31 (1H, s, 1 × Ar*H*). δ_C (75 MHz, $CDCl_3$) 11.5 (2 × *C*H_3), 21.1 (2 × *C*H_2), 21.4 (2 × *C*H_2S), 32.1 (2 × CF_2CH_2, t, J = 21.7 Hz), 42.2 (2 × *C*H_2N), 44.6 (*C*HS), 44.7 (*C*HS), 91.3 (Ar*C*H), 118.8 (2 × Ar*C*), 122.5 (Ar*C*H), 145.2 (2 × Ar*C*) and 175.6 (2 × *C*=O). $\upsilon_{max}/(cm^{-1})$ 2971, 2359, 1715 (C=O), 1621, 1489, 1372 and 1205. *m/z* (AP+ mode) 1227 (28%) and 749 (100%).

1,7-Dibenzyl-3,5-*bis*(benzylsulfanyl)-5,7-dihydropyrrolo[3,2-f]indole-2,6(1H,3H)-dione 46

As for general procedure C. *Bis*–glyoxamide **40** (390 mg, 0.98 mmol, 1 eq) on treatment with benzyl thiol (229 µl, 1.95 mmol, 2 eq), TFAA (2.52 ml, 17.6 mmol, 18 eq) and BF_3•OEt_2 (1.36 ml, 9.75 mmol, 10 eq) and after purification by flash chromatography using 30% EtOAc in petroleum ether as eluant gave **46** (373mg, 0.61 mmol, 62% from *bis*–hydroxyamide, 2 steps) as a yellow solid (1:1 mixture of diastereoisomers). mp 70.5–71.6 °C (recrystallised from petroleum ether/EtOAc). δ_H (500 MHz, $CDCl_3$) 3.78 (1H, d, J = 13.3 Hz, 1H from SC*H*$_2$), 3.79 (1H, d, J = 13.3 Hz, 1H from SC*H*$_2$), 4.14-4.25 (4H, m, 2 × 1H from SC*H*$_2$ and 2 × SC*H*), 4.68-4.80 (4H, m, 2 × NC*H*$_2$), 6.02 (1H, s, Ar*H*), 6.02 (1H, s, Ar*H*) and 7.17-7.38 (22H, m, 22 × Ar*H*). δ_C (75 MHz, $CDCl_3$) 34.6 (2 × S*C*H$_2$), 43.0 (2 × S*C*H), 44.2 (2 × N*C*H$_2$), 92.8 (Ar*C*H), 118.9 (2 × Ar*C*), 122.2 (Ar*C*H), 127.5 (2 × Ar*C*H), 127.6 (2 × Ar*C*H), 128.7 (4 × Ar*C*H), 129.1 (4 × Ar*C*H), 129.4 (4 × Ar*C*H), 129.5 (4 × Ar*C*H), 135.5 (2 × Ar*C*), 137.4 (2 × Ar*C*), 144.1 (2 × Ar*C*) and 176.2 (2 × *C*=O). υ_{max}/(cm^{-1}) (CH_2Cl_2 evaporated film) 3060, 3029, 2929, 1712 (C=O), 1619, 1493 and 1160. *m/z* (CI^+ mode) 613 (M^+, 1%), 489 (30%), 367 (72%), 296 (30%), 264 (50%), 210 (44%), 193 (45%), 108 (100%), 91 (50%) and 79 (38%). *m/z* (M) 612.1973, $C_{38}H_{32}O_2N_2S_2$ requires 612.1978.

1,7-Dibenzyl-3,5-*bis*(phenylsulfanyl)-5,7-dihydropyrrolo[3,2-f]indole-2,6(1H,3H)-dione 47

As for general procedure C. *Bis*–glyoxamide **40** (332 mg, 0.83 mmol, 1 eq) on treatment with thiophenol (170 µl, 1.66 mmol, 2 eq), TFAA (2.14 ml, 14.9 mmol, 18 eq), and BF_3•OEt_2 (1.16 ml, 8.29 mmol, 10 eq), and after purification by column chromatography using 30% EtOAc in petroleum ether as eluant gave **47** (294 mg, 0.37 mmol, 45% from *bis*–hydroxyamide, 2 steps) as a brown solid (1:1

mixture of diastereoisomers). mp 71.9–72.9 °C (recrystallised from petroleum ether/EtOAc). δ_H (500 MHz, $CDCl_3$) 4.30 (2H, d, J = 15.7 Hz, 2 × 1H from NC*H*$_2$), 4.40-4.59 (2H, m, 2 × C*H*S), 4.74 (2H, d, J = 15.7 Hz, 2 × 1H from NC*H*$_2$), 5.64-5.65 (1H, m, Ar*H*), 6.69-7.33 (20H, m, Ar*H*) and 7.56 (1H, s, Ar*H*). δ_C (75 MHz, $CDCl_3$) 44.4 (2 × N*C*H$_2$), 49.5 (2 × *C*HS), 92.9 (Ar*C*H), 119.9 (2 × Ar*C*), 122.6 (Ar*C*H), 127.4 (2 × Ar*C*H), 127.8 (2 × Ar*C*H), 129.1 (4 × Ar*C*H), 129.3 (4 × Ar*C*H), 130.8 (2 × Ar*C*), 131.1 (2 × Ar*C*), 134.7 (4 × Ar*C*H), 135.0 (4 × Ar*C*H), 144.1 (2 × Ar*C*) and 174.7 (2 × *C*=O). $\upsilon_{max}/(cm^{-1})$ (CH_2Cl_2 evaporated film) 3060, 3033, 2921, 1717 (C=O), 1620, 1492 and 1161. *m/z* (ES+ mode) 644 (80%), 607 (M+Na, 100%), 582 (30%) and 549 (52%). *m/z* (M–H) 583.1520, $C_{36}H_{27}O_2N_2S_2$ requires 583.1519.

1,5-Dihexyl-3,7-*bis*-phenylsulfanyl-5,7-dihydro-1H,3H-pyrrolo[2,3-*f*]indole-2,6-dione 48

As for general procedure C. *Bis*–glyoxamide **41** (497 mg, 1.28 mmol, 1 eq) on treatment with thiophenol (260 µl, 2.65 mmol, 2 eq), TFAA (3.30 ml, 23.1 mmol, 18 eq), and BF_3•OEt_2 (1.79 ml, 12.8 mmol, 10 eq) and after purification by column chromatography using 20% EtOAc in petroleum ether as eluant gave **48** (396 mg, 0.69 mmol, 54% from *bis*–hydroxyamide, 2 steps) as an oil (>5:1 mixture of regioisomers). δ_H (500 MHz, $CDCl_3$) 0.82 (12H, t, J = 7.2 Hz, 4 × C*H*$_3$), 1.15-1.33 (32H, m, 4 × C*H*$_2$C*H*$_2$C*H*$_2$C*H*$_2$CH$_3$), 3.30-3.70 (8H, m, 4 × C*H*$_2$N), 4.45 (2H, s, 2 × C*H*S major), 4.46 (2H, s, 2 × C*H*S major), 4.47 (2H, s, 2 × C*H*S minor), 4.48 (2H, s, 2 × C*H*S minor), 6.62 (2H, s, 2 × ArC*H* major), 6.64 (2H, s, 2 × ArC*H* major), 6.64 (2H, s, 2 × ArC*H* minor), 6.68 (2H, s, 2 × ArC*H* minor) and 6.99-7.31 (20H, m, 20 × ArC*H*). δ_C (125 MHz, $CDCl_3$) 14.1 (*C*H$_3$), 22.5 (*C*H$_2$), 22.6 (*C*H$_2$), 26.5

(*C*H_2), 26.6 (*C*H_2), 27.2 (*C*H_2), 27.5 (*C*H_2), 29.7 (*C*H_2), 31.5 (*C*H_2), 40.4 (*C*H_2N), 49.5 (*C*HS), 106.1 (Ar*C*H), 106.2 (Ar*C*H), 106.3 (Ar*C*H), 106.4 (Ar*C*H), 127.1 (Ar*C*), 127.2 (Ar*C*), 127.3 (Ar*C*), 128.4 (Ar*C*H), 128.6 (Ar*C*H), 128.7 (Ar*C*H), 128.8 (Ar*C*H), 128.9 (Ar*C*H), 129.0 (Ar*C*H), 130.5 (Ar*C*), 134.0 (Ar*C*H), 134.1 (Ar*C*H), 134.5 (Ar*C*H), 134.8 (Ar*C*H), 138.9 (Ar*C*), 139.0 (Ar*C*), 139.2 (Ar*C*), 173.0 (*C*=O), 173.2 (*C*=O) and 173.4 (*C*=O). $\upsilon_{max}/(cm^{-1})$ 2929, 2857, 1711, 1473, 1344, 1169, 1126 and 866. *m/z* (ES+ mode) 595 (M+Na, 100%), 573 (M+H, 54%), 534 (100%) and 308 (42%). *m/z* (M+H) 573.2619, $C_{34}H_{41}O_2N_2S_2$ requires 573.2604.

1,5-Dihexyl-3,7-*bis*-ethoxycarbonylmethylsulfanyl-5,7-dihydro-1H,3H pyrrolo[2,3-*f*]indole-2,6-dione 49

As for general procedure C. *Bis*–glyoxamide **41** (471 mg, 1.21 mmol, 1 eq) on treatment with ethylthioglycolate (270 µl, 2.43 mmol, 2 eq), TFAA (3.13 ml, 21.8 mmol, 18 eq), and BF_3•OEt_2 (1.70 ml, 12.1 mmol, 10 eq) and after purification by column chromatography using 20% EtOAc in petroleum ether as eluant gave **49** (392mg, 0.66 mmol, 55% from *bis*–hydroxyamide, 2 steps) as a dark red solid (>5:1 mixture of regioisomers). mp 85.0–86.3 °C (recrystallised from petroleum ether/EtOAc). δ_H (500 MHz, $CDCl_3$) 0.88-0.93 (12H, m, 2 × $CH_2CH_2CH_3$ both isomers), 1.30 (12H, t, J = 7.1 Hz, 2 × OCH_2CH_3 both isomers), 1.29-1.40 (24H, m, 2 × $CH_2CH_2CH_2CH_3$ both isomers), 1.67-1.69 (8H, m, 2 × NCH_2CH_2 both isomers), 3.31 (2H, d, J = 15.7 Hz, 2 × 1H from CH_2S one isomer), 3.33 (2H, d, J = 15.7 Hz, 2 × 1H from CH_2S one isomer), 3.67-3.75 (8H, m, 2 × NCH_2 both isomers), 4.02 (2H, d, J = 15.7 Hz, 2 × 1H from CH_2S one isomer), 4.06 (2H, d, J = 15.7 Hz, 2 × 1H from CH_2S one isomer), 4.18-4.21 (8H, m, 2 × OCH_2CH_3 both

isomers), 4.59 (2H, s, 2 × C*H*S one isomer), 4.61 (2H, s, 2 × C*H*S one isomer) and 6.96 (4H, s, 2 × Ar*H* both isomers). δ_C (75 MHz, $CDCl_3$) 14.2 (*C*H_3), 14.4 (OCH_2CH_3), 22.8 (*C*H_2), 26.8 (*C*H_2), 27.6 (NCH_2CH_2), 31.6 (*C*H_2), 31.7 (*C*H_2S), 40.7 (N*C*H_2), 43.8 (*C*HS), 61.9 (OCH_2CH_3), 106.9 (Ar*C*H), 126.1 (Ar*C*), 139.4 (Ar*C*), 170.2 (*C*=O, amide) and 174.7 (*C*=O, ester). $\upsilon_{max}/(cm^{-1})$ (CH_2Cl_2 evaporated film) 2956, 2930, 2858, 2360, 1737 (C=O), 1687, 1477, 1261 and 1129. *m/z* (ES+ mode) 615.5 ($(M+Na)^+$, 100%), 593.2 ($(M+H)^+$, 12%), 543.6 (20%) and 536.4 (24%). *m/z* (M+Na) 615.2525, $C_{30}H_{44}O_6N_2NaS_2$ requires 615.2533.

1,5-Dihexyl-3,7-*bis*-(6-hydroxy-hexylsulfanyl)-5,7-dihydro-1H,3H-pyrrolo[2,3-*f*]indole-2,6-dione 50

As for general procedure C. *Bis*–glyoxamide **38** (225 mg, 0.58 mmol, 1 eq) on treatment with 6-mercapto-1-hexanol (158 µl, 1.16 mmol, 2 eq), TFAA (1.47 ml, 10.44 mmol, 18 eq), and BF_3•OEt_2 (713 µl, 5.80 mmol, 10 eq) and after purification by column chromatography using 20% EtOAc in petroleum ether as eluant gave **50** (219 mg, 0.35 mmol, 61% from *bis*–hydroxyamide, 2 steps) as a dark oil (3:1 mixture of regioisomers). δ_H (300 MHz, $CDCl_3$) 0.91 (12H, t, J = 7.0 Hz, 8 × C*H*$_3$), 1.28-1.46 (40H, m, 4 × C*H*$_2$C*H*$_2$C*H*$_2$CH$_3$ and 4 × C*H*$_2$C*H*$_2$), 1.55-1.80 (24H, m, 4 × C*H*$_2$CH$_2$N and 4 × C*H*$_2$C*H*$_2$), 2.56-2.89 (8H, m, 4 × C*H*$_2$S), 3.61-3.84 (8H, m, 4 × C*H*$_2$O), 4.31 (2H, s, 2 × C*H*S major), 4.32 (2H, s, 2 × C*H*S of minor), 4.34-4.38 (8H, m, 4 × C*H*$_2$N), 6.92 (2H, s, 2 × ArC*H* minor) and 6.93 (2H, s, 2 × ArC*H* major). δ_C (75 MHz, $CDCl_3$) 14.2 (*C*H_3), 22.8 (*C*H_2), 25.4 (*C*H_2), 26.8 (*C*H_2), 27.6 (*C*H_2), 28.2 (*C*H_2), 28.7 (*C*H_2), 29.1 (*C*H_2S), 29.2 (*C*H_2), 31.7 (*C*H_2), 40.7 (*C*H_2O), 45.1 (*C*HS), 45.3 (*C*HS), 62.3 (*C*H_2N), 106.5 (Ar*C*H),

127.0 (Ar*C*), 127.1 (Ar*C*), 139.2 (Ar*C*), 139.3 (Ar*C*), 175.0 (*C*=O) and 175.1 (*C*=O). υ_{max}/(cm^{-1}) 3449, 2929, 2856, 2361, 1717, 1474, 1341, 1168 and 1053. *m/z* (ES- mode) 619 (M-H 12%), 502 (37%), 416 (55%) and 284 (100%). *m/z* (M+H) 621.3767, $C_{34}H_{56}O_4N_2S_2$ requires 621.3754.

3,7-*Bis*(4-bromo-benzylsulfanyl)-1,5-dihexyl-5,7-dihydro-1H,3H-pyrrolo[2,3-*f*]indole-2,6-dione 51

As for general procedure C. *Bis*–glyoxamide **41** (225 mg, 0.58 mmol, 1 eq) on treatment with 4-bromobenzyl mercaptan (236 mg, 1.16 mmol, 2 eq), TFAA (1.47 ml, 10.44 mmol, 18 eq), and BF_3•OEt_2 (713 μl, 5.80 mmol, 10 eq) and after purification by column chromatography using 15% EtOAc in petroleum ether as eluant gave **51** (238 mg, 0.31 mmol, 54% from *bis*–hydroxyamide, 2 steps) as a red solid (>5:1 mixture of regioisomers and a 1:1 mixture of diastereoisomers). mp 181.1–188.6 °C (recrystallised from petroleum ether/EtOAc). δ_H (300 MHz, $CDCl_3$) 0.90-0.94 (12H, m, 4 × CH_3 both isomers), 1.26-1.45 (24H, m, 12 × CH_2 both isomers), 1.60-1.69 (8H, m, 4 × CH_2 both isomers), 3.55-3.70 (8H, m, 4 × CH_2N both isomers), 3.70 (2H, d, J = 13.5 Hz, 2 × 1H of CH_2S one isomer), 3.74 (2H, d, J = 13.5 Hz, 2 × 1H of CH_2S one isomer), 4.16 (2H, s, 2 × C*H*S one isomer), 4.18 (2H, s, 2 × C*H*S one isomer), 4.19 (2H, d, J = 13.5 Hz, 2 × 1H of CH_2S one isomer), 4.25 (2H, d, J = 13.5 Hz, 2 × 1H of CH_2S one isomer), 6.69 (2H, s, 2 × Ar*H* one isomer), 6.70 (2H, s, 2 × Ar*H* one isomer), 7.24 (4H, d, J = 8.5 Hz, 4 × Ar*H* one isomer), 7.27 (4H, d, J = 8.5 Hz, 4 × Ar*H* one isomer), 7.42 (4H, d, J = 8.5 Hz, 4 × Ar*H* one isomer) and 7.45 (4H, d, J = 8.5 Hz, 4 × Ar*H* one isomer). δ_C (75 MHz, $CDCl_3$) 14.3 (*C*H_3), 22.8 (*C*H_2), 26.8 (*C*H_2), 27.7 (*C*H_2), 31.7 (*C*H_2), 33.8 (*C*H_2S), 33.9 (*C*H_2S), 40.6 (*C*H_2N), 43.4 (*C*HS), 43.7 (*C*HS),

106.6 (Ar*C*H), 121.5 (Ar*C*), 126.2 (Ar*C*), 126.4 (Ar*C*), 131.2 (Ar*C*), 131.8 (Ar*C*), 131.9 (Ar*C*), 136.6 (Ar*C*), 136.7 (Ar*C*), 139.2 (Ar*C*), 174.7 (*C*=O) and 174.9 (*C*=O). $\upsilon_{max}/(cm^{-1})$ 2926, 2857, 1691 (C=O), 1474, 1350, 1172, 1071 and 1012. *m/z* (AP+ mode) 757 (M+H, 22%), 556 (100%) and 356 (24%). *m/z* (M+Na) 779.0960, $C_{36}H_{42}Br_2O_2N_2S_2Na$ requires 779.0947.

3,7-*Bis*(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylthio)-1,5-dihexyl-5,7-dihydropyrrolo[2,3-f]indole-2,6(1H,3H)-dione 52

As for general procedure C. *Bis*–glyoxamide **41** (154 mg, 0.39 mmol, 1 eq) on treatment with 1H, 1H, 2H, 2H-perfluorodecane-1-thiol (232 µl, 0.78 mmol, 2 eq), TFAA (992 µl, 7.02 mmol, 18 eq), and BF_3•OEt_2 (480 µl, 3.90 mmol, 10 eq) and after purification by flash chromatography using 15% EtOAc in petroleum ether as eluant gave **52** (291 mg, 0.22 mmol, 57%) as a 2:1 mixture of regioisomers. A pure sample of the major regiosiomer (1:1 mixture of diastereoisomers) was obtained as a light brown solid after further column chromatography (85 mg, 0.06 mmol, 17%). mp 135.8–140.8 °C (recrystallised from petroleum ether/EtOAc). δ_H (500 MHz, $CDCl_3$) 0.82 (12H, t, J = 7.1 Hz, 2 × CH_3), 1.17-1.33 (24H, m, 4 × CH_2CH_2CH_2CH_3), 1.56-1.64 (8H, m, CH_2CH_2N), 2.29-2.42 (8H, m, 2 × CF_2CH_2), 2.68-2.95 (8H, m, 4 × CH_2S), 3.54-3.74 (8H, m, 2 × CH_2N), 4.26 (2H, s, 2 × C*H*S one isomer), 4.27 (2H, s, 2 × C*H*S one isomer), 6.84 (2H, s, 2 × Ar*H* one isomer) and 6.85 (2H, s, 2 × Ar*H* one isomer). δ_C (75 MHz, $CDCl_3$) 13.8 (*C*H_3), 22.5 (*C*H_2), 26.5 (*C*H_2), 16.6 (*C*H_2), 27.3 (*C*H_2), 29.7 (*C*H_2), 31.9 (*C*H_2CF_2, t, J = 21.9 Hz), 40.6 (*C*H_2), 45.1 (*C*HS), 45.3 (*C*HS), 106.5 (Ar*C*H), 106.5 (Ar*C*H), 126.4 (Ar*C*), 139.2 (Ar*C*), 139.3 (Ar*C*) and 174.1 (*C*=O). $\upsilon_{max}/(cm^{-1})$ 3049, 2931, 2860, 1695 (C=O), 1472, 1346, 1203, 1147,

1087, 957 and 870. *m/z* (AP+ mode), 1311.8 (15%), 879.3 (62%), 833.3 (100%), 401.2 (52%) and 355.8 (20%).

1,5-Dihexyl-5,7-dihydro-1H,3H-pyrrolo[2,3-*f*]indole-2,6-dione 53 from 51

As for general procedure D. Compound **51** (49 mg, 0.06 mmol, 1 eq) on treatment with SmI_2 (2.80 ml of a 0.1 M solution in THF, 4.4 eq) and after purification by column chromatography using 30% EtOAc in petroleum ether as eluant gave **53** (17 mg, 0.06 mmol, 81%) as a grey solid. See data reported earlier.

***N*-(2-Benzenesulfonylethyl)phenyl amine 55**

Aniline (1.37 ml, 15.0 mmol, 1 eq), phenyl vinylsulfone (2.52 g, 15.0 mmol, 1 eq) and acetic acid (0.09 ml, 1.5 mmol, 0.1 eq) were placed in a microwave vessel with a magnetic stirrer and sealed. The reaction mixture was heated to 200 °C for 20 min and the cooled mixture was purified by column chromatography using 20 % EtOAc in petroleum ether as eluant to give **55** as a white solid (2.97 g, 11.4 mmol, 76 %). mp 76–78 °C (recrystallised from MeOH). δ_H (400 MHz, $CDCl_3$) 3.25 (2H, t, J = 6.3 Hz, NCH_2), 3.47 (2H, t, J = 6.3 Hz, CH_2SO_2), 6.43 (2H, d, J = 7.6 Hz, ArC*H*), 6.63 (1H, t, J = 7.3 Hz, ArC*H*), 7.04 (2H, dd, J = 8.5, 7.3 Hz, ArC*H*), 7.43-7.46 (2H, m, ArC*H*), 7.55 (1H, tt, J = 7.6, 1.6 Hz, ArC*H*), 7.78-7.81 (2H, m, ArC*H*). δ_C (125 MHz, $CDCl_3$) 37.9 (NCH_2), 54.8 (CH_2SO_2), 113.4 (2 × Ar*C*H), 118.7 (Ar*C*H), 128.0 (2 × Ar*C*H), 129.4 (2 × Ar*C*H), 129.5 (2 × Ar*C*H), 134.0 (Ar*C*H), 139.1 (Ar*C*N), 146.2 (Ar*C*SO_2). ν_{max}/cm^{-1} 2967, 2385, 2877, 1603, 1086 (S=O). *m/z* (ES^- mode) 261 (M, 15%), 260 (M^+, 85%), 155 (10%). *m/z* (MNa^+) 284.0715, $C_{14}H_{15}O_2NNaS$ requires 284.0716.

_N_-(2-Benzenesulfonylethyl)-2-hydroxy-_N_-phenylacetamide 57

To a solution of **55** (2.85 g, 11.0 mmol, 1 eq) and acetoxyacetic acid (1.55 g, 13.0 mmol, 1.2 eq) in CH_2Cl_2 (90 ml) were added *N*-(3-dimethylaminopropyl)-*N*-ethylcarbodiimide hydrochloride (2.51 g, 13.0 mmol, 1.2 eq) and 1-hydroxybenzotriazole hydrate (0.29 g, 2.2 mmol, 0.2 eq). The reaction was allowed to stir for 18 h at room temperature, quenched with 1 M HCl (50 ml) and extracted with CH_2Cl_2 (3 × 50 ml). The combined organic layers were then dried (Na_2SO_4) and concentrated *in vacuo*. The crude was taken on to the next step without further purification.

The crude acetoxyamide was dissolved in a suspension of K_2CO_3 (6.10 g, 44.0 mmol, 4 eq) in MeOH (80 ml) and H_2O (40 ml) and allowed to stir for 4 h. H_2O (40 ml) was added to the reaction mixture and the organic layer was extracted with EtOAc (3 × 50 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude mixture was purified by column chromatography using 60 % EtOAc in petroleum ether as eluant to give **57** as a clear oil (2.35 g, 7.37 mmol, 67 % over 2 steps). δ_H (400 MHz, $CDCl_3$) 3.10 (1H, br s, OH), 3.37-3.42 (2H, m, C*H*$_2$SO$_2$), 3.73 (2H, s, HOC*H*$_2$), 4.09-4.11 (2H, m, NC*H*$_2$), 7.12-7.15 (2H, m, ArC*H*), 7.39-7.46 (3H, m, ArC*H*), 7.56-7.59 (2H, m, ArC*H*), 7.68 (1H, tt, J = 7.6, 1.2 Hz, ArC*H*), 7.91 (2H, d, J = 7.3 Hz, ArC*H*). δ_C (100 MHz, $CDCl_3$) 43.8 (N*C*H$_2$), 53.1 (SO$_2$*C*H$_2$), 60.9 (HO*C*H$_2$), 128.1 (2 × Ar*C*H), 128.3 (2 × Ar*C*H), 129.6 (2 × Ar*C*H), 129.7 (Ar*C*H), 130.6 (Ar*C*H), 134.6 (2 × Ar*C*H), 138.8 (Ar*C*), 138.9 (Ar*C*) 172.6 (*C*=O). ν_{max}/cm^{-1} 3237 (OH), 2961, 2359, 2341, 1654, 1494, 1446, 1260, 1087 (S=O). (ES$^+$ mode) 320 (MH$^+$, 80%), 219 (10%). *m/z* (MH$^+$) 320.0946, $C_{16}H_{18}O_4NS$ requires 320.0951.

_N_-(2-Benzenesulfonylethyl)-_p_-tolylamine 56

p-Toluidine (0.20 g, 1.87 mmol, 1.2 eq.), phenylvinylsulfone (0.26 g, 1.55 mmol, 1 eq) and acetic acid (0.01 ml, 1.55 mmol, 0.1 eq) were placed in a microwave vessel with a magnetic stirrer and sealed. The reaction mixture was heated to 200 °C for 20 min and the cooled mixture was purified by column chromatography using 20 % EtOAc in petroleum ether as eluant to give **56** as a brown, waxy solid (0.29 g, 1.04 mmol, 67 %). mp 70-75 °C (recrystallised from MeOH). δ_H (400 MHz, $CDCl_3$) 2.13 (3H, s, Me), 3.28 (2H, t, J = 6.0 Hz, C*H*$_2$NH), 3.50 (2 H, t, J = 6.0 Hz, C*H*$_2$SO$_2$), 3.92 (1H, br s, NH), 6.37-6.40 (2 H, m, 2 × ArC*H*), 6.88-6.92 (2 H, m, 2 × ArC*H*), 7.49-7.52 (2 H, m, 2 × ArC*H*), 7.61 (1H, tt, J = 7.6, 1.3 Hz, ArC*H*), 7.83 (2 H, m, 2 × ArC*H*). δ_C (100 MHz, $CDCl_3$) 20.4 (Me), 38.1 (*C*H$_2$NH), 54.8 (*C*H$_2$SO$_2$), 113.4 (2 × Ar*C*H), 127.8 (Ar*C*Me), 128.0 (2 × Ar*C*H), 129.5 (2 × Ar*C*H), 129.9 (2 × Ar*C*H), 134.0 (Ar*C*H), 139.1 (Ar*C*NH), 144.2 (Ar*C*SO$_2$). ν_{max}/cm^{-1} 3390 (NH), 1084 (S=O). *m/z* (EI$^+$ mode) 275 (M, 30%), 133 (85%), 132 (55%), 120 (100%), 77 (30%). *m/z* (M) 275.0976, $C_{15}H_{17}O_2NS$ requires 275.0975.

_N_-(2-Benzenesulfonylethyl)-2-hydroxy-_N_-_p_-tolyl-acetamide 58

To a solution of **56** (1.79 g, 6.51 mmol, 1 eq) and acetoxyacetic acid (0.92 g, 7.82 mmol, 1.2 eq) in CH_2Cl_2 (50 ml) were added *N*-(3-dimethylaminopropyl)-*N*-ethylcarbodiimide hydrochloride (1.50 g, 7.82 mmol, 1.2 eq) and 1-hydroxybenzotriazole hydrate (0.18 g, 1.3 mmol, 0.2 eq). The reaction was allowed to stir for 18 h at room temperature, quenched with 1 M HCl (30 ml) and extracted with CH_2Cl_2 (3 × 50 ml). The combined organic layers were then dried (Na_2SO_4) and concentrated *in vacuo*. The crude was taken on to the next step without further purification.

The crude acetoxyamide was dissolved in a suspension of K_2CO_3 (3.60 g, 26.0

mmol, 4 eq) in MeOH (40 ml) and H_2O (20 ml) and allowed to stir for 4 h. H_2O (20 ml) was added to the reaction mixture and the organic layer was extracted with EtOAc (3 × 40 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude mixture was purified by column chromatography using 60 % EtOAc in petroleum ether as eluant to give **58** as a white, crystalline solid (1.55 g, 4.60 mmol, 71 % over 2 steps). mp 104-106 °C (recrystallised from MeOH). δ_H (400 MHz, $CDCl_3$) 2.34 (3H, s, Me), 3.12 (1H, t, J = 4.8 Hz, OH), 3.31-3.34 (2H, m, C*H*$_2$N), 3.68 (2H, d, J = 4.8 Hz, C*H*$_2$OH), 4.00-4.04 (2H, m, C*H*$_2$SO$_2$), 6.94-6.97 (2H, m, 2 × ArC*H*), 7.19 (2H, d, J = 7.8 Hz, 2 × ArC*H*), 7.53-7.57 (2H, m, 2 × ArC*H*), 7.64 (1H, tt, J = 7.6, 1.2 Hz, ArC*H*), 7.86-7.89 (2H, m, 2 × ArC*H*). δ_C (100 MHz, $CDCl_3$) 21.2 (Me), 43.6 (*C*H$_2$SO$_2$), 53.0 (*C*H$_2$N), 60.6 (*C*H$_2$OH), 127.7 (2 × Ar*C*H), 128.1 (2 × Ar*C*H), 129.5 (2 × Ar*C*H), 131.0 (2 × Ar*C*H), 134.1 (Ar*C*H), 135.8 (Ar*C*-Me), 138.7 (Ar*C*-N), 139.6 (Ar*C*-SO$_2$), 172.5 (C=O). ν_{max}/cm^{-1} 3447 (OH), 1643 (C=O), 1086 (S=O). *m/z* (CI$^+$ mode) 334 (M$^+$, 100%), 275 (50%), 192 (10%), 132 (55%), 119 (35%), 77 (30%). *m/z* (M) 333.1026, $C_{17}H_{19}O_4NS$ requires 333.1029.

1-(2-Benzenesulfonylethyl)-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-5-methyl-1,3-dihydroindol-2-one 60

To a solution of oxalyl chloride (0.43 ml, 4.93 mmol, 1.1 eq) in CH_2Cl_2 (15 ml) was added DMSO (0.64 ml, 8.97 mmol, 2 eq) at –78 °C. After 10 min, **58** (1.49 g, 4.48 mmol, 1 eq.) in CH_2Cl_2 (15 ml) was added. After a further 1 h, Et_3N (3.12 ml, 22.0 mmol, 5 eq) was added and the reaction allowed to warm to room temperature. After 3.5 h, $NaHCO_3$ (30 ml) was added to the reaction mixture and the organic layer was extracted with CH_2Cl_2 (3 × 30 ml), then the organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the crude glyoxamide,

which was used without further purification.

To the crude glyoxamide in CH_2Cl_2 (72 ml) was added 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-thiol (0.93 ml, 3.14 mmol, 0.7 eq) and the reaction stirred for 18 h at room temperature. Trifluoroacetic anhydride (5.70 ml, 40.3 mmol, 9 eq) was added, stirred for 1 h, then $BF_3.OEt_2$ (2.76 ml, 22.4 mmol, 5 eq) was added and the reaction mixture was left for 3 h. The reaction mixture was quenched with $NaHCO_3$ (70 ml), extracted with CH_2Cl_2 (3 × 50 ml), the organic layers dried (Na_2SO_4) and concentrated *in vacuo*. The crude mixture was purified using FSPE to give **60** as a white solid (1.48 g, 1.87 mmol, 60 % over 2 steps). mp 104-107 °C (from MeOH). δ_H (400 MHz, $CDCl_3$) 2.28 (5H, m, Ar-Me and C*H*$_2$C$_8$F$_{17}$), 2.68-2.75 (1H, m, SC*H*H), 2.84-2.91 (1H, m, SCH*H*), 3.32-3.39 (1H, m, NC*H*H), 3.43-3.50 (1H, m, NCH*H*), 4.01-4.04 (3H, m, C*H*$_2$SO$_2$ and C*H*C=O), 6.73 (1H, d, J = 8.4 Hz, ArC*H*), 7.06-7.10 (2H, m, 2 × ArC*H*), 7.46-7.50 (2H, m, 2 × ArC*H*), 7.60 (1H, tt, J = 7.6, 1.0 Hz, ArC*H*), 7.81-7.84 (2H, m, 2 × ArC*H*). δ_C (100 MHz, $CDCl_3$) 21.0 (Me), 21.2 (S*C*H$_2$), 31.8 (*C*H$_2$C$_8$F$_{17}$), 34.4 (*C*H$_2$SO$_2$), 44.6 (*C*HC=O), 52.4 (*C*H$_2$N), 108.4 (Ar*C*H), 124.9 (Ar*C*), 126.2 (Ar*C*H), 127.9 (2 × Ar*C*H), 129.5 (2 × Ar*C*H), 130.0 (Ar*C*H), 133.4 (Ar*C*), 134.1 (Ar*C*H), 138.7 (Ar*C*), 139.6 (Ar*C*), 175.0 (C=O). ν_{max}/cm^{-1} 1716 (C=O), 1083 (S=O), 1234 (C-F). *m*/*z* (ES- mode) 792 (M- 100 %), 281 (40 %).

1-(2-Benzenesulfonylethyl)-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-5-methyl-3-(2-nitrobenzyl)-1,3-dihydroindol-2-one 62

To a solution of **60** (1.42 g, 1.80 mmol, 1 eq) in DMF (28 ml) was added K_2CO_3

(1.24 g, 9.00 mmol, 5 eq) and 2-nitrobenzyl bromide (1.16 g, 5.39 mmol, 3 eq) at room temperature and the reaction mixture was allowed to stir for 18 h. H_2O (30 ml) was added and the mixture extracted with Et_2O (3 × 30 ml). The organic layer was washed with H_2O (5 × 20 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude mixture was purified using FSPE to give **62** as a clear, viscous oil (1.37 g, 1.47 mmol, 82 %). δ_H (400 MHz, $CDCl_3$) 2.04-2.17 (2H, m, C*H*$_2$C$_8$F$_{17}$), 2.26 (3H, s, Me), 2.53-2.65 (2H, m, C*H*$_2$SO$_2$), 2.87-2.94 (1H, m, SC*H*H), 3.04-3.11 (1H, m, SCH*H*), 3.59 (1H, d, J = 13.6 Hz, C*H*HAr), 3.73-3.80 (1H, m, C*H*HN), 3.88-3.95 (1H, m, CH*H*N), 4.03 (1H, d, J = 13.6 Hz, CH*H*Ar), 6.51 (1H, d, J = 8.1 Hz, ArC*H*), 6.92 (1H, d, J = 1.3 Hz, ArC*H*), 7.00 (1H, d, J = 8.1 Hz, ArC*H*), 7.21 (2H, dt, J = 6.3, 2.2 Hz, 2 × ArC*H*), 7.32 (1H, dt, J = 75, 1.5 Hz, ArC*H*), 7.54-7.62 (3H, m, 3 × ArC*H*), 7.66 (1H, tt, J = 7.5, 1.3 Hz, ArC*H*), 7.85-7.88 (2H, m, 2 × ArC*H*). δ_C (100 MHz, $CDCl_3$) 20.0 (*C*H$_2$SO$_2$), 21.0 (Me), 31.3 (*C*H$_2$C$_8$F$_{17}$), 33.8 (*C*H$_2$N), 37.5 (*C*H$_2$Ar), 52.3 (S*C*H$_2$), 55.2 (*C*), 108.1 (Ar*C*H), 124.8 (Ar*C*H), 125.7 (Ar*C*H), 127.2 (Ar*C*), 128.0 (2 × Ar*C*H), 128.4 (Ar*C*H), 129.3 (Ar*C*), 129.6 (2 × Ar*C*H), 130.2 (Ar*C*H), 132.2 (Ar*C*H), 133.5 (Ar*C*H), 134.1 (Ar*C*H), 134.3 (Ar*C*), 138.1 (Ar*C*), 138.5 (Ar*C*), 150.0 (Ar*C*), 175.5 (C=O). ν_{max}/cm^{-1} 1710s (C=O), 1528 (NO_2), 1351 (NO_2), 1086 (S=O). *m*/*z* (ES+ mode) 951 (MNa+, 100 %).

11-(2-Benzenesulfonylethyl)-3-methyl-11H-10,11-diaza-benzo[b]fluorene 64

To a solution of SmI_2 in THF (60.3 ml, 0.1 M, 6.03 mmol, 9 eq) was added a thoroughly degassed solution of **62** (0.622 g, 6.70 mmol, 1 eq) in THF (6 ml) and MeOH (3 ml). The solution was allowed to stir for 4 h and then exposed to air. Saturated aqueous $Na_2S_2O_3$ (50 ml) was added, the organic layer extracted with Et_2O (3 × 30 ml), the combined organic layers dried (Na_2SO_4) and concentrated *in*

vacuo. The crude aniline was purified by column chromatography using 50 % EtOAc in petroleum ether as eluant. The product was then directly dissolved in a MeOH:AcOH (1:1) mix (10 ml) and heated to 100 °C for 18 h. K_2CO_3 was added to the mixture until basic pH was reached, the organic layer was extracted with EtOAc (3 × 10 ml), the combined organic layers dried (Na_2SO_4) and concentrated *in vacuo*. The crude mixture was purified by column chromatography using 20 % EtOAc in petroleum ether as eluant to give **64** as a light green solid (0.16 g, 0.40 mmol, 60 %). mp 153-154 °C (recrystallised from hexane). δ_H (400 MHz, $CDCl_3$) 2.58 (3H, s, Me), 3.96 (2H, t, J = 7.1 Hz, C*H*$_2$SO$_2$), 4.88 (2H, t, J = 7.1 Hz, C*H*$_2$N), 7.27-7.35 (3H, m, 3 × ArC*H*), 7.40-7.49 (3H, m, 3 × ArC*H*), 7.70-7.76 (3H, m, 3 × ArC*H*), 7.88 (1H, dt, J = 1.7, 0.8 Hz, ArC*H*), 7.97 (1 H, dd, J = 8.1, 1.5 Hz, ArC*H*), 8.03 (1H, dd, J = 8.6, 0.5 Hz, ArC*H*), 8.56 (1 H, s, ArC*H*). δ_C (100 MHz, $CDCl_3$) 21.3 (Me), 35.9 (*C*H$_2$N), 53.1 (*C*H$_2$SO$_2$), 108.7 (Ar*C*H), 109.9 (Ar*C*), 118.1 (Ar*C*), 120.7 (Ar*C*), 121.7 (Ar*C*H), 123.2 (Ar*C*H), 124.3 (Ar*C*), 127.2 (Ar*C*H), 127.5 (Ar*C*H), 127.6 (2 × Ar*C*H), 128.5 (Ar*C*H), 128.9 (2 × Ar*C*H), 129.4 (Ar*C*H), 130.0 (Ar*C*), 133.5 (Ar*C*H), 138.8 (Ar*C*), 139.5 (Ar*C*H), 146.5 (Ar*C*), 152.0 (Ar*C*). ν_{max}/cm^{-1} 1612 (C=C), 1446 (C=C), 1086 (S=O). *m/z* (ES$^+$ mode) 401 (MH$^+$, 100 %).

3-Methylneocryptolepine 66

Compound **64** (0.02 g, 0.05 mmol, 1 eq) was suspended in THF (0.5 ml) and potassium *tert*-butoxide (0.017 g, 0.15 mmol, 3 eq) was added at –78 °C. The reaction mixture was allowed to stir for 2 h. 2,2,2-Trifluoroethanol (0.015 ml, 0.2 mmol, 4 eq) was then added and the reaction was allowed to stir for 5 min, before methyl iodide (0.031 ml, 0.5 mmol, 10 eq) was added. The reaction was then heated under reflux for

18 h. The crude mixture was concentrated *in vacuo*, dissolved in CH_2Cl_2 (3 ml) and $NaHCO_3$ (3 ml) was added and the organic layer extracted with CH_2Cl_2 (3 × 3 ml). The organic layer was dried (Na_2SO_4), concentrated *in vacuo* and purified by column chromatography using EtOAc as eluant to give **66** as a dark orange/red solid (0.0086 g, 0.035 mmol, 70 %). mp 147-148 °C (recrystallised from hexane). δ_H (400 MHz, $CDCl_3$) 2.46 (3H, s, Me), 4.29 (3H, s, N-Me), 7.29-7.32 (1H, m, ArC*H*), 7.35-7.39 (1H, m, ArC*H*), 7.58 (1H, d, J = 8.0, ArC*H*), 7.68-7.70 (2H, m, 2 × ArC*H*), 7.78 (1H, dt, J = 18, 0.7 Hz, ArC*H*), 7.91 (1H, d, J = 7.8, ArC*H*), 8.42 (1H, s, ArC*H*). δ_C (100 MHz, $CDCl_3$) 21.5 (Me), 33.1 (N-Me), 114.1 (Ar*C*H), 117.3 (Ar*C*H), 120.8 (Ar*C*), 121.3 (Ar*C*H), 121.8 (Ar*C*H), 124.0 (Ar*C*), 127.9 (Ar*C*H), 128.3 (Ar*C*) 129.3 (Ar*C*), 130.0 (Ar*C*H), 130.3 (Ar*C*H), 130.5 (Ar*C*H), 137.0 (Ar*C*), 153.2 (Ar*C*), 156.0 (Ar*C*). ν_{max}/cm^{-1} 2920, 1646, 1496, 1200, 748. *m/z* (CI+ mode) 247 (MH+, 30 %), 246 (M, 20 %), 186 (30 %), 124 (50 %), 110 (70 %), 93 (100 %), 77 (60 %), 57 (60 %). *m/z* 246.1153, $C_{17}H_{14}N_2$ requires 246.1152.