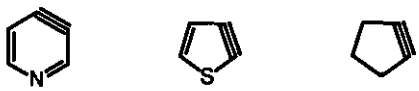
APPROACHES TO THE GENERATION OF 2,3-INDOLYNE

Samuel C. Conway and Gordon W. Gribble*

Department of Chemistry, Dartmouth College, Hanover, New Hampshire 03755, USA

Abstract–Several unsuccessful attempts to generate and trap 1-phenylsulfonyl-2,3-indolyne (**4**) from 2-lithio-3-bromo-1-phenylsulfonylindole (**9**) and 2-lithio-3-iodo-1-phenylsulfonylindole (**12**), generated by different methods, are described. The remarkable stability of **9** and **12** towards elimination parallels previous observations involving the stability of 2-lithio-3-bromobenzo[*b*]furan and other *ortho*-metalated halogenated five-membered ring heterocycles.

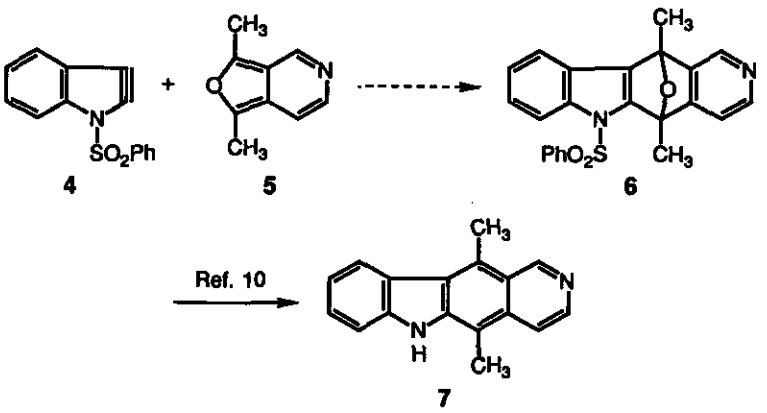
The generation and subsequent reactions of benzyne (dehydrobenzene) and other arynes represent a valuable and versatile methodology in organic synthesis.[1,2] In particular, arynes have been employed with remarkable success in Diels-Alder and 1,3-dipolar cycloadditions,[2a,k,l] and, more recently, these species have been found to be extraordinarily useful in regioselective nucleophilic addition reactions.[2b-h] Unfortunately, with the notable exception of 3,4-pyridyne (**1**),[3,4] heterocyclic arynes, "hetarynes," have not enjoyed the same success as benzynes, and have proven to be surprisingly difficult to generate.[4] Of the many possible five-membered ring hetarynes, only 2,3-thiophyne (**2**) and 2,3-benzo[*b*]thiophyne have seemingly been generated.[4a,b,5] In addition, convincing evidence for the intermediacy of cyclopentyne (**3**) has been uncovered.[6]



1 **2** **3**

Our dual interest in generating novel arynes[7] and in developing new synthetic routes to the ellipticine (6*H*-pyrido[4,3-*b*]carbazole) family of antitumor alkaloids[8] led us to consider the strategy shown in Scheme I, involving a Diels-Alder reaction between 2,3-indolyne (**4**) and the known furo[3,4-*c*]pyridine (**5**) ring system.[9] In fact, in prior research, we synthesized **6** from the cycloaddition of 3,4-pyridyne (**1**) with 1,3-dimethyl-1-phenylsulfonyl-4*H*-furo[3,4-*b*]indole.[10]

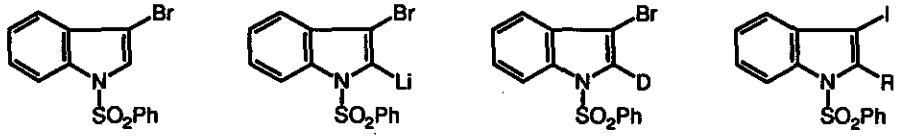
Scheme I



We now wish to disclose our attempts to generate 1-phenylsulfonyl-2,3-indolyne (**4**).

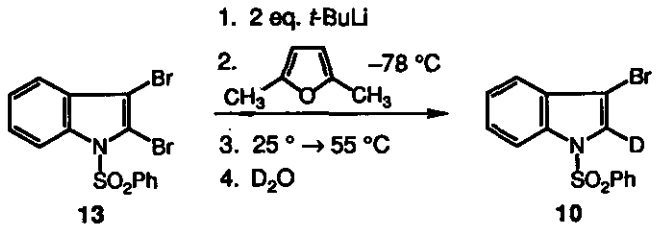
Results and Discussion

Although Müller was unsuccessful in generating 2,3-indolyne from 1-methyl-2-lithio-3-chloroindole and other potential indolyne precursors,[11] we felt that a better leaving group than chloride should be investigated in this reaction, since elimination of LiBr and LiI are at least 20 and 100 times faster, respectively, than LiCl in the generation of benzyne.[12] Furthermore, the propensity for 3-lithioindoles to undergo ring fragmentation[13] or rearrangement[14] induced us to explore initially only 2-lithioindole intermediates. Bromination of 1-phenylsulfonylindole according to the published procedure[15] affords 3-bromo-1-phenylsulfonylindole (**8**) in nearly quantitative yield. Lithiation at the C-2 position was achieved by treatment of **8** with lithium diisopropylamide (LDA) in THF, and the resulting anion (**9**) was heated at reflux for 2 days in the presence of anthracene as a Diels-Alder diene trap. Quenching the cooled solution with D_2O gave **10**, with complete deuteration at the C-2 position (^1H and ^{13}C nmr), isolated in 50% yield. No evidence for the formation of a Diels-Alder cycloadduct involving **4** and anthracene was observed when **9** was heated in the presence of anthracene.



Similarly, 2-lithio-3-iodo-1-phenylsulfonylindole (**12**) was generated from **11** as described earlier[13a] and heated at 50-60 °C in the presence of different diene traps (furan, 2,5-dimethylfuran, anthracene, tetracyclone) for several

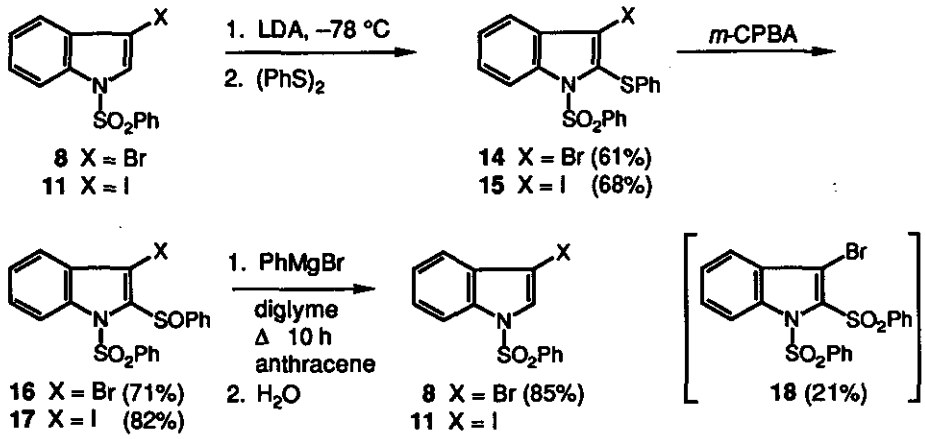
days with no evidence of the elimination of LiI and subsequent trapping of indolyne (4). In order to generate the 2-lithio-3-bromo species (9) in the absence of the nucleophilic diisopropylamine, we synthesized dibromoindole (13) in 73% yield by quenching 9 with CNBr. As shown below, treatment of 13 with *tert*-butyllithium (2 equiv.[16]) at –78 °C, followed by the addition of 2,5-dimethylfuran, heating at 50-55 °C for 45 min, and quenching with D_2O gave 10 in 83% yield. There was again no evidence for loss of LiBr from intermediate (9) leading to indolyne (4).



13 10

Repeating this experiment in the presence of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) and heating at 120 °C afforded only 3-bromo-1-phenylsulfonylindole (8). A third route to the 2-lithio-3-haloindoles (9) and (12) was fashioned after the new benzyne and pyridyne generation method of Furukawa,[17] which involves Grignard reagent-induced elimination of diphenyl sulfoxide and halide from an appropriate *o*-halodiphenyl sulfoxide. The requisite 3-halo-2-phenylsulfinyl-1-phenylsulfonylindoles (16 and 17) were synthesized as shown in Scheme II.

Scheme II



8 X = Br
11 X = I

14 X = Br (61%)
15 X = I (68%)

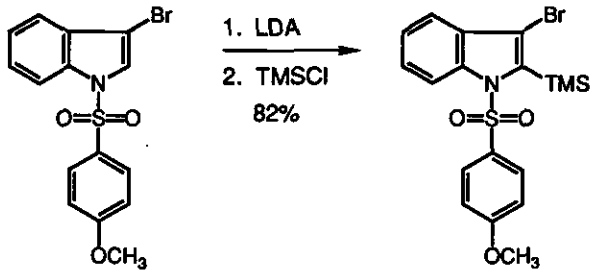
16 X = Br (71%)
17 X = I (82%)

8 X = Br (85%)
11 X = I

18 (21%)

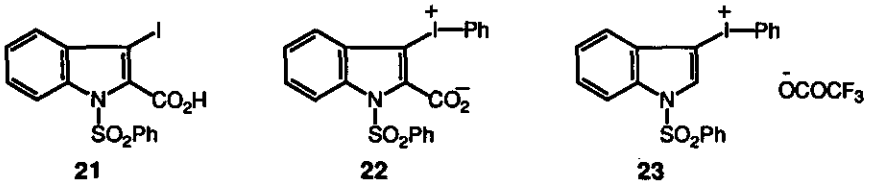
The 2-lithio species (**9**) and (**12**) were quenched with diphenyl disulfide to afford the thiophenyl compounds (**14**) and (**15**) in good yields. Oxidation of **14** with *m*-chloroperbenzoic acid (*m*-CPBA)[18] proceeded rapidly to afford the desired sulfoxide (**16**) in 71% yield, along with 21% of sulfone (**18**). In contrast to the oxidation of the bromo sulfide (**14**), the *m*-CPBA oxidation of iodo sulfide (**15**) to sulfoxide (**17**) was very slow, requiring 2 days and excess oxidant for completion. Interestingly, sodium periodate,[19] potassium hydrogen persulfate,[20] or sulfuryl chloride[21] did not oxidize **15** to **17**. Unfortunately, treatment of **16** and **17** with phenylmagnesium bromide in diglyme in the presence of a diene trap, such as anthracene, followed by prolonged heating, furnished only haloindoles (**8**) and (**11**) in high yields. The benzyne-generation technique of Cunico[22] was also explored. Thus, as shown in Scheme III, 2-trimethylsilyl-3-bromo-1-(4-methoxyphenylsulfonyl)indole (**20**)[23] was prepared. However, attempts to induce 2,3-indolyne formation by the treatment of **20** with *n*-Bu_4NF in the presence of 2,5-dimethylfuran at room temperature and then heating at reflux gave black tar and no identifiable products.

Scheme III



19 **20**

Finally, an attempt was made to prepare the iodonium compound (**22**) from iodo acid (**21**) using the method of Beringer.[24] However, these reactions produced only tar. Likewise, we prepared the known iodonium salt (**23**),[25] but attempts to effect C-2 deprotonation with LDA and loss of iodobenzene led instead to the production of 3-iodoindole (**11**), perhaps *via* formation of benzyne rather than indolyne!



21 **22** **23**

Following the completion of this work, there appeared an X-ray crystallographic study of 2-lithio-3-bromobenzo-[*b*]furan which found that this species exists as a distorted *trans*-dimer and thus is not in a configuration conducive to elimination of LiBr.[26] A similar explanation may account for the pronounced stability of 2-lithio-3-haloindole intermediates such as **9** and **12**. It remains to be seen whether or not one of the several other methods for benzyne generation will serve to generate the elusive 2,3-indolyne.

EXPERIMENTAL

General. Melting points were determined with a Mel-Temp Laboratory Devices apparatus and are uncorrected. Ir spectra were recorded on a Perkin-Elmer Model 599 Infrared Spectrophotometer. Mass spectra were measured at 35 or 70 eV on a Finnigan 4023 mass spectrometer. Unless noted, ^{13}C and ^{1}H nmr spectra were recorded on a Varian XL-300 Fourier-transform NMR spectrometer (300 MHz), with tetramethylsilane as the internal reference; otherwise, spectra were measured on a Varian EM-360 spectrometer (60 MHz). Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA. Samples for elemental analysis were prepared by recrystallization to constant melting point, followed by drying in vacuo; two recrystallizations were usually sufficient. Flash chromatography was performed using 230-400 mesh silica gel 60 from EM Science. Thin layer chromatography (tlc) was performed on 0.2 mm silica gel 60 F_{254} plastic plates from E. Merck. Tetrahydrofuran was distilled from sodium/benzophenone, and diisopropylamine was distilled from calcium hydride. Reactions were performed in oven-dried glassware fitted with a magnetic stirrer, thermometer, and inlet for dry Ar gas. A dry ice/acetone bath was used to achieve -78 °C, and -100 °C was achieved with a dry ice/acetone/liquid nitrogen bath. Alkyllithium reagents were titrated with diphenylacetic acid prior to use.

Attempted generation of indolyne (4) from 3-bromo-1-phenylsulfonylindole (8). To a stirred solution of LDA (diisopropylamine, 0.43 ml, 3.1 mmol; *n*-BuLi, 2.0 ml of a 1.56 M solution in hexane, 3.1 mmol) in dry THF (40 ml) under Ar at -78 °C was added a solution of **8** (1.01 g, 3.00 mmol) and anthracene (0.71 g, 4.0 mmol) in dry THF (50 ml), dropwise via syringe, keeping the internal temperature below -60 °C. The yellow solution was slowly warmed to room temperature over 7 h, and then heated at reflux for 2 days. After being cooled back to room temperature, the reaction mixture was poured into 5% aqueous $NaHCO_3$ (40 ml) and extracted with CH_2Cl_2 (2 x 20 ml). The combined organic layers were washed successively with 5% aqueous $Na_2S_2O_3$ (30 ml), 10% aqueous $NaHCO_3$ (30 ml), H_2O (30 ml), brine (30 ml), and dried (Na_2SO_4). The solution was concentrated in vacuo to yield a thick brown oil. Tlc (Et_2O/hexane) showed both anthracene (Rf

0.58) and **8** (Rf 0.41). Flash chromatography (Et_2O/hexane) and isolation of the latter gave 0.51 g (50%) of **8**, which was identified by ir and nmr comparison with a known sample. A separate experiment that was quenched with D_2O gave **10**, with complete deuteration at the C-2 position (*vide infra*).

3-Iodo-1-phenylsulfonylindole (11). The previously described "inverse addition" method was employed.[14] To a solution of indole (9.00 g, 76.8 mmol) in dry THF (100 ml) under Ar at -78 °C was added a solution of *n*-BuLi (50 ml of a 1.56 M solution in hexane, 78 mmol) over 45 min. The white suspension that resulted was warmed to 0 °C and added to a stirred solution of I_2 (20 g, 79 mmol) in dry THF (115 ml). The dark solution that resulted was treated with one drop of MeOH, and re-cooled to -78 °C. A solution of LDA (diisopropylamine, 11.1 ml, 78.6 mmol; *n*-BuLi, 50 ml of a 1.56 M solution in hexane, 78 mmol) in dry THF (100 ml) was slowly added, and the mixture was stirred at -78 °C for 30 min, after which $PhSO_2Cl$ (10.3 ml, 80.7 mmol) was added. After being warmed to room temperature overnight, the reaction mixture was cooled to -5 °C and poured into ice-cold 5% aqueous $NaHCO_3$ (750 ml) and extracted with Et_2O (3 x 300 ml). The combined organic layers were washed successively with a solution of $Na_2S_2O_3$ (9 g in 325 ml of H_2O, adjusted to pH 8 with $NaHCO_3$), H_2O (2 x 300 ml), brine (2 x 300 ml), and dried (Na_2SO_4). The solution was concentrated in vacuo to produce 34.3 g of purple oil. This was adsorbed onto 45 g of Florisil, and eluted with 1:1 Et_2O/hexane through a column of 235 g of Florisil to give brown crystals, which were recrystallized from Et_2O to yield 18.6 g (62%) of **11** as tan crystals: mp 127-129 °C (lit.,[14] mp 125-127 °C); ir (KBr) 3142, 1448, 1372, 1272, 1179, 1025, 933, 820, 759, 738, 730, 687 cm^{-1}; ms *m/z* 383, 242 (100); ^1H nmr ($CDCl_3$, 60 MHz) δ 8.1-7.7 (m, 3H), 7.64 (s, 1H), 7.5-7.2 (m, 6H).

2,3-Dibromo-1-phenylsulfonylindole (13). To a stirred solution of 3-bromo-1-phenylsulfonylindole (**8**) (1.54 g, 4.58 mmol) in dry THF (50 ml) under Ar at -78 °C was added a solution of LDA (2.1 ml of a 2.29 M solution in THF/heptane, 4.8 mmol) dropwise *via* syringe. The solution was stirred for 40 min at that temperature. A solution of CNBr (0.627 g, 5.91 mmol) in dry THF (9 ml) was then rapidly added, and the reaction mixture was permitted to warm to room temperature overnight. It was then poured into 5% aqueous $NaHCO_3$ (50 ml) and extracted with Et_2O (2 x 50 ml). The combined organic layers were washed successively with H_2O (2 x 75 ml), brine (75 ml), and dried ($MgSO_4$). The solution was concentrated in vacuo to yield orange crystals. Flash chromatography (CH_2Cl_2) and collection of the sole high-Rf product yielded 2.09 g of white powder, which was recrystallized from Et_2O to yield 1.38 g (73%) of **13** as white crystals, mp 141-143°C; ir (KBr) 1442, 1377, 1213, 1192, 1170, 1143, 1087, 737, 726, 692, 680, 589, 578 cm^{-1}; ms *m/z* 417, 415, 413,

274, 77 (100); ^{1}H nmr ($CDCl_3$) δ 8.35-8.25 (m, 1H), 7.9-7.85 (m, 2H), 7.6-7.3 (m, 6H); ^{13}C nmr ($CDCl_3$) δ 137.7, 136.5, 134.4, 129.3, 128.9, 127.1, 126.1, 124.6, 119.5, 115.3, 111.2, 106.7. Anal. Calcd for $C_{14}H_9NO_2Br_2S$: C, 40.51; H, 2.19; N, 3.37; Br, 38.50; S, 7.72. Found: C, 40.63; H, 2.18; N, 3.41; Br, 38.42; S, 7.81.

Attempted generation of indolyne from 13. Formation of 3-bromo-2-deutero-1-phenylsulfonylindole (10). To a stirred solution of **13** (0.653 g, 1.57 mmol) in dry THF (60 ml) under Ar at -78 °C was added a solution of *tert*-BuLi (2.20 ml of a 1.49 M solution in pentane, 3.28 mmol, 2.1 eq.) rapidly *via* syringe. After one minute, dry 2,5-dimethylfuran (2.0 ml, 18 mmol) was introduced, and the solution was warmed first to room temperature, and then to 50-55 °C for 45 min. It was then cooled back to room temperature and treated with D_2O. The reaction mixture was poured into H_2O (50 ml) and extracted with Et_2O (2 x 50 ml). The combined organic layers were washed successively with H_2O (2 x 75 ml), brine (75 ml), and dried ($MgSO_4$). The solution was concentrated in vacuo to yield yellow crystals which were purified by flash chromatography (CH_2Cl_2). The white crystals that resulted (0.439 g, 83%, mp 117-119 °C) were examined by nmr; the spectra were identical to those of 3-bromo-1-phenylsulfonylindole (**8**), except for the disappearance of the C-2 proton and collapse of the C-2 carbon into a multiplet, indicating deuterium incorporation at this position. The structure of the product was assigned as **10**. ^{1}H Nmr ($CDCl_3$) δ 8.05-7.95 (m, 1H), 7.9-7.8 (m, 2H), 7.45-7.2 (m, 6H); ^{13}C nmr ($CDCl_3$) δ 137.5, 134.0, 133.9, 129.6, 129.2, 126.6, 125.7, 124.7, 123.9, 119.9, 113.4, 99.5.

3-Bromo-1-phenylsulfonyl-2-phenylthioindole (14). To a stirred solution of LDA (diisopropylamine, 1.4 ml, 9.6 mmol; *n*-BuLi, 6.3 ml of a 1.56 M solution in hexane, 9.8 mmol) in dry THF (80 ml) under Ar at -78 °C was added a solution of 3-bromo-1-phenylsulfonylindole (**8**) (3.10 g, 9.22 mmol) in dry THF (50 ml), dropwise via syringe. The solution was stirred for 1 h at that temperature. A solution of $(PhS)_2$[27] (2.29 g, 10.5 mmol) in dry THF (30 ml) was then slowly added, keeping the internal temperature below -60 °C. After being warmed to room temperature overnight, the reaction mixture was poured into 5% aqueous $NaHCO_3$ (100 ml) and extracted with CH_2Cl_2 (2 x 50 ml). The combined organic layers were washed successively with 5% aqueous $Na_2S_2O_3$ (50 ml), 10% aqueous $NaHCO_3$ (50 ml), H_2O (50 ml), brine (50 ml), and dried (Na_2SO_4). The solution was concentrated in vacuo to yield a yellow oil, which was added to boiling 1:1 Et_2O/hexane and slowly cooled, forming 2.49 g (61%) of **14** as white crystals, mp 120.5-122.5 °C; ir (KBr) 1582, 1481, 1459, 1435, 1375, 1230, 1192, 1163, 1147, 1050, 1022, 750, 726, 697, 682, 589, 574, 563 cm^{-1}; ms *m/z* 445, 443, 223 (100); ^{1}H nmr ($CDCl_3$, 60 MHz) δ 8.5-8.1 (m, 1H), 7.9-7.6 (m, 2H), 7.6-6.7 (m, 11H); ^{13}C nmr (Me_2CO-d_6) δ

139.2, 138.4, 135.8, 135.4, 130.3, 129.9, 129.3, 128.6, 128.0, 127.9, 127.8, 127.3, 125.5, 121.2, 116.3, 115.2. Anal. Calcd for $C_{20}H_{14}NO_2BrS_2$: C, 54.06; H, 3.18; N, 3.15; Br, 17.98; S, 14.43. Found: C, 54.06; H, 3.21; N, 3.19; Br, 18.02; S, 14.49.

3-Bromo-2-phenylsulfinyl-1-phenylsulfonylindole (16) and 3-bromo-1,2-diphenylsulfonylindole (18). A mixture of *meta*-chloroperbenzoic acid (0.60 g, 80%, 2.8 mmol) and 3-bromo-1-phenylsulfonyl-2-phenylthioindole (**14**) (1.00 g, 2.25 mmol) were dissolved in CH_2Cl_2 (15 ml), placed under Ar, and the solution was stirred at room temperature for 14 h. Tlc revealed the formation of two distinct products, identified as the sulfoxide (**16**) and the corresponding sulfone (**18**), which were separated by flash chromatography (CH_2Cl_2) of the residue remaining after evaporation of the solvent.

Sulfoxide **16**: Rf (CH_2Cl_2) 0.36; yield, 0.73 g (71%): mp 184.5-186 °C (decomp.); ir (KBr) 1469, 1451, 1380, 1196, 1185, 1169, 1144, 1086, 1064, 1042, 1028, 777, 769, 760, 740, 715, 697, 619, 607, 587, 571 cm^{-1}; ms *m/z* 461, 459; ^1H nmr ($CDCl_3$, 60 MHz) δ 8.3-7.6 (m, 5H), 7.6-7.2 (m, 9H); ^{13}C nmr ($CDCl_3$) δ 142.7, 137.5, 136.2, 135.3, 134.6, 130.8, 129.5, 129.1, 128.9, 128.4, 127.1, 125.4, 124.7, 120.9, 114.6, 107.8. Anal. Calcd for $C_{20}H_{14}NO_3BrS_2$: C, 52.18; H, 3.07; N, 3.04; Br, 17.36; S, 13.93. Found: C, 52.01; H, 3.06; N, 3.04; Br, 17.43; S, 14.03.

Sulfone **18**: Rf (CH_2Cl_2) 0.57; yield, 0.22 g (21%): mp 217-219 °C; ir (KBr) 1495, 1451, 1388, 1335, 1193, 1176, 1163, 1143, 826, 763, 754, 735, 724, 695, 633, 603, 576 cm^{-1}; ms *m/z* 477, 475; ^1H nmr ($CDCl_3$,60 MHz) δ 8.3-7.9 (m, 3H), 7.9-7.6 (m, 2H), 7.6-7.2 (m, 9H); ^{13}C nmr ($CDCl_3$) δ 141.3, 138.0, 137.8, 134.3, 133.8, 133.7, 129.9, 129.0, 128.8, 128.5, 128.1, 127.3, 125.2, 122.5, 116.0, 114.2. Anal. Calcd for $C_{20}H_{14}NO_4BrS_2$: C, 50.43; H, 2.96; N, 2.94; Br, 16.77; S, 13.46. Found: C, 50.45; H, 2.94; N, 2.94; Br, 16.85; S, 13.41.

3-Iodo-1-phenylsulfonyl-2-phenylthioindole (15). To a stirred solution of LDA (diisopropylamine, 1.85 ml, 13.1 mmol; *n*-BuLi, 8.46 ml of a 1.56 M solution in hexane, 13.2 mmol) in dry THF (75 ml) under Ar at -78 °C was added a solution of 3-iodo-1-phenylsulfonylindole (**11**) (5.00 g, 13.0 mmol) in dry THF (50 ml), dropwise via syringe, keeping the internal temperature below -60 °C. The solution was stirred for 1 h at that temperature. A solution of $(PhS)_2$ (3.20 g, 14.7 mmol) in dry THF (30 ml) was then slowly added. After being warmed to room temperature overnight, the reaction mixture was poured into 5% aqueous $NaHCO_3$ (200 ml) and extracted with CH_2Cl_2 (2 x 100 ml). The combined organic layers were washed successively with 5% aqueous $Na_2S_2O_3$ (100 ml), 10% aqueous $NaHCO_3$ (100 ml), H_2O (100 ml), brine (100 ml), and dried (Na_2SO_4). The

solution was concentrated in vacuo to yield a yellow oil, which was added to 80 ml of boiling 3:3:1 Et_2O/EtOAc/hexane. The volume was reduced and the solution was slowly cooled, and 4.32 g (68%) of **15** was formed as pale yellow crystals: mp 136-137 °C; ir (KBr) 1579, 1473, 1433, 1372, 1189, 1028, 1019, 753, 741, 726, 682, 629, 601, 589, 575, 562 cm^{-1}; ms *m/z* 491, 349, 223 (100); ^1H nmr ($CDCl_3$, 60 MHz) δ 8.4-8.1 (m, 1H), 7.9-7.7 (m, 2H), 7.5-7.1 (m, 7H), 7.1-6.8 (m, 4H); ^{13}C nmr (Me_2CO-d_6) δ 139.2, 139.1, 136.2, 135.3, 132.5, 131.6, 130.3, 129.9, 128.5, 127.9, 127.7, 127.1, 125.5, 123.7, 116.3, 90.5. Anal. Calcd for $C_{20}H_{14}NO_2IS_2$: C, 48.89; H, 2.87; N, 2.85; I, 25.83; S, 13.05. Found: C, 48.90; H, 2.86; N, 2.83; I, 25.88; S, 13.10.

3-Iodo-1-phenylsulfonyl-2-phenylsulfinylindole (17). A mixture of *m*-CPBA (0.49 g of 80% solid, 2.3 mmol) and 3-iodo-1-phenylsulfonyl-2-phenylthioindole (**15**) (0.94 g, 1.9 mmol) were dissolved in CH_2Cl_2 (25 ml), placed under Ar, and the solution was stirred at room temperature for 48 h. The solvent was then concentrated in vacuo. Tlc analysis of the residue showed a major new component at Rf (CH_2Cl_2) 0.30, which was isolated by flash chromatography (CH_2Cl_2) to give 0.79 g (82%) of **17** as pale yellow crystals, mp 194-195 °C; ir (KBr) 1580, 1449, 1378, 1366, 1186, 1133, 1077, 1050, 1014, 809, 755, 743, 726, 697, 685, 609, 594, 577, 565 cm^{-1}; ms *m/z* 507, 380, 223 (100); ^1H nmr ($CDCl_3$, 60 MHz) δ 8.3-7.7 (m, 5H), 7.6-7.1 (m, 9H); ^{13}C nmr ($CDCl_3$) δ 142.9, 137.6, 137.1, 136.4, 134.6, 132.0, 130.8, 129.5, 129.0, 128.4, 127.2, 125.8, 124.8, 123.3, 114.6, 96.8. Anal. Calcd for $C_{20}H_{14}NO_3IS_2$: C, 47.35; H, 2.78; N, 2.76; I, 25.01; S, 12.64. Found: C, 47.26; H, 2.77; N, 2.73; I, 25.06; S, 12.69.

Attempted generation of indolyne (4) from 16. Diglyme (25 ml) was stirred with Drierite for 24 h, and distilled under Ar from $LiAlH_4$ directly into a dry flask containing **16** (0.474 g, 1.03 mmol) and anthracene (0.215 g, 1.21 mmol). The mixture was magnetically stirred at room temperature while a solution of PhMgBr (0.50 ml of a 3.0 M solution in Et_2O, 1.5 mmol) was added dropwise over 10 min. The mixture was stirred for 30 min, and was then heated to reflux for 10 h. After cooling, it was treated with MeI (0.25 ml, 4.0 mmol) and permitted to stand overnight. It was then poured into 5% aqueous $NaHCO_3$ (50 ml), and extracted with CH_2Cl_2 (3 x 50 ml). The combined extracts were washed with H_2O (3 x 50 ml), brine (50 ml), and dried (Na_2SO_4). Concentration in vacuo yielded an oil that was subjected to Kugelrohr distillation to remove residual solvent, and purified by flash chromatography (Et_2O/hexane) to afford 0.321 g (85%) of crystals identified as 3-bromo-1-phenylsulfonylindole (**8**).

1-(4-Methoxyphenylsulfonyl)indole. Freshly-powdered NaOH (10.00 g, 250 mmol) was added to a flask containing a magnetically-stirred solution of *n*-Bu_4NHSO_4 (0.70 g, 2.05 mmol) in CH_2Cl_2 (120 ml). The

resulting suspension was placed under Ar and cooled to 0 °C. Indole (9.36 g, 79.9 mmol) was added in one portion, followed by a solution of 4-methoxyphenylsulfonyl chloride (20.67 g, 100 mmol) in CH_2Cl_2 (40 ml), added at a sufficiently slow rate as to keep the internal temperature of the reaction mixture below 20 °C. The mixture was stirred for 2 h after being warmed to room temperature. Solid material was removed by filtration, and the filtrate was concentrated in vacuo. The resulting red oil was treated with boiling MeOH (100 ml) and slowly cooled to room temperature. The product was collected by decantation of the mother liquor, from which a second crop of crystals could be isolated after cooling to 0 °C. The total yield was 21.8 g (95%) of colorless crystals: mp 119-120 °C (lit.,[28] mp 112-114 °C); ^{1}H nmr ($CDCl_3$) δ 8.05-7.95 (m, 1H), 7.8-7.7 (m, 2H), 7.54 (d, *J*=3.7 Hz, 1H), 7.5-7.45 (m, 1H), 7.35-7.15 (m, 2H), 6.8-6.7 (m, 2H), 6.60 (dd, *J*=3.7, 0.8 Hz, 1H), 3.61 (s, 3H); ^{13}C nmr ($CDCl_3$) δ 163.5, 134.6, 130.6, 129.3, 128.8, 126.2, 124.3, 123.1, 121.3, 114.3, 108.8, 55.4.

3-Bromo-1-(4-methoxyphenylsulfonyl)indole (19). A solution of Br_2 (1.00 ml, 19.5 mmol) in dry CCl_4 (30 ml) was added dropwise to a stirred solution of 1-(4-methoxyphenylsulfonyl)indole (5.47 g, 19.0 mmol) in dry CCl_4 (60 ml) under Ar at 0 °C over 3 h. The resulting solution was stirred while being warmed to room temperature for 1 h, and poured into a separatory funnel containing 10% aqueous $NaHCO_3$ (100 ml). Dichloromethane (100 ml) was added to dissolve the precipitated product, the layers were well mixed, separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 75 ml). The combined organic layers were washed successively with 10% aqueous $NaHCO_3$ (100 ml), 10% aqueous $Na_2S_2O_3$ (100 ml), H_2O (2 x 100 ml), brine (200 ml), and dried (Na_2SO_4 plus some decolorizing carbon). After filtration, the solution was concentrated in vacuo to yield 7.01 g of off-white crystals. Recrystallization from Et_2O yielded 6.78 g (97%) of **19** as white crystals: mp 126-127 °C; ir (KBr) 1590, 1260, 1159, 1152, 1080, 1016, 754, 742, 698, 590, 578, 549 cm^{-1}; ms *m/z* 367, 365, 196, 194, 171, 107 (100); ^{1}H nmr ($CDCl_3$) δ 7.95-7.85 (m, 1H), 7.8-7.65 (m, 2H), 7.53 (s, 1H), 7.45-7.35 (m, 1H), 7.3-7.15 (m, 2H), 6.8-6.7 (m, 2H), 3.66 (s, 3H) ; ^{13}C nmr ($CDCl_3$) δ 163.9, 134.2, 129.7, 129.1, 129.1, 125.7, 124.7, 123.8, 112.0, 114.5, 113.5, 99.4, 55.6. Anal. Calcd for $C_{15}H_{12}NO_3BrS$: C, 49.19; H, 3.30; N, 3.82; Br, 21.82; S, 8.75. Found: C, 49.17; H, 3.29; N, 3.81; Br, 21.86; S, 8.69.

3-Bromo-2-trimethylsilyl-1-(4-methoxyphenylsulfonyl)indole (20). To a stirred solution of LDA (diisopropylamine, 0.30 ml, 2.1 mmol; *n*-BuLi, 1.50 ml of a 1.42 M solution in hexane, 2.13 mmol) in dry THF (60 ml) under Ar at -78 °C was added a solution of 3-bromo-1-(4-methoxyphenylsulfonyl)indole (**19**) (0.734 g, 2.00 mmol) in dry THF (8 ml), dropwise *via* syringe. The solution was stirred for 30 min at that temperature. Dry chlorotrimethylsilane (0.32 ml, 2.5 mmol) was then slowly added, keeping the internal temperature below -60

°C. After being warmed to room temperature overnight, the reaction mixture was poured into H_2O (50 ml) and extracted with Et_2O (2 x 50 ml). The combined organic extracts were washed with H_2O (50 ml), brine (75 ml), dried (Na_2SO_4), and concentrated in vacuo to yield a pink oil. Flash chromatography (1:1 CH_2Cl_2/hexane) and isolation of the major component yielded 0.723 g (82%) of **20** as a colorless oil which solidified upon standing under a stream of Ar. The analytical sample was recrystallized from petroleum ether (50-110 °C): mp 105-106.5 °C; ir (KBr) 1594, 1260, 1241, 1179, 1165, 1011, 839, 822, 753, 577, 554 cm^{-1}; ms *m/z* 439, 437, 424, 422, 269, 267, 107 (100); ^1H nmr ($CDCl_3$) δ 8.0-7.9 (m, 1H), 7.55-7.45 (m, 2H), 7.45-7.4 (m, 1H), 7.35-7.15 (m, 2H), 6.8-6.7 (m, 2H), 3.72 (s, 3H), 0.61 (s, 3H); ^{13}C nmr ($CDCl_3$) δ 163.4, 139.3, 138.6, 131.8, 129.0, 128.7, 126.3, 124.2, 120.2, 116.3, 115.3, 55.5, 2.5. Anal. Calcd for $C_{18}H_{20}NO_3BrSSi$: C, 49.31; H, 4.60; N, 3.19; Br, 18.23; S, 7.31. Found: C, 48.93; H, 4.54; N, 3.20; Br, 17.98; S, 7.19.

Attempted generation of indolyne from 20. 2,5-Dimethylfuran (10 ml) was distilled from powdered KOH directly into a dry flask containing **20** (0.172 g, 0.393 mmol). The resulting solution was heated to reflux under Ar, and a solution of *n*-Bu_4NF (1.0 ml of a 1.0 M solution in THF, 1.0 mmol) was added dropwise. After 4 h, analysis by tlc revealed complete loss of the starting material and a complex, inseparable mixture of products.

3-Iodo-1-phenylsulfonylindole-2-carboxylic acid (21). To a stirred solution of LDA (diisopropylamine, 1.85 ml, 13.1 mmol; *n*-BuLi, 8.46 ml of a 1.56 M solution in hexane, 13.2 mmol) in dry THF (100 ml) under Ar at -78 °C was added a solution of 3-iodo-1-phenylsulfonylindole (**11**) (5.00 g, 13.0 mmol) in dry THF (50 ml), dropwise via syringe, keeping the internal temperature below -60 °C. The solution was stirred for 1 h at that temperature, and then poured directly into a flask containing anhydrous Et_2O (200 ml) and solid CO_2 (12 g). A white precipitate formed within 3 min. The suspension was permitted to warm to 0 °C (15 min), and treated with 4M HCl to pH 2 (50 ml), keeping the temperature below 10 °C. The two-phase mixture that resulted was transferred to a separatory funnel; the layers were separated, and the aqueous portion extracted with Et_2O (2 x 50 ml). The combined organic layers were washed successively with H_2O (100 ml) and 1M NaOH (2 x 50 ml). The aqueous portion was acidified with cold 6M HCl to pH 2 and extracted with Et_2O (2 x 50 ml). The combined organic layers were washed successively with H_2O (60 ml), brine (60 ml), and dried (Na_2SO_4). The solution was concentrated in vacuo to yield 4.61 g (83%) of **21** as a white powder: mp 185-187 °C (decomp.). The analytical sample was prepared by recrystallization from CH_2Cl_2: mp 186-187 °C (decomp.); ir (KBr) 2750 (br), 1694, 1369, 1268, 1202, 1185, 1171, 1146, 1060, 750, 682, 598, 579 cm^{-1}; ms *m/z* 427, 383, 269 (100), 242; ^1H nmr (Me_2CO-d_6, 60 MHz) δ 8.68 (broad singlet, 1H), 8.1-7.8 (m, 3H), 7.6-7.2 (m, 6H); ^{13}C nmr (Me_2CO-

d_6) δ 162.9, 137.8, 136.1, 135.6, 135.5, 132.5, 130.3, 128.4, 128.2, 126.0, 123.8, 115.7, 73.4. Anal. Calcd for $C_{15}H_{10}NO_4IS$: C, 42.17; H, 2.36; N, 3.28; I, 29.71; S, 7.50. Found: C, 42.21; H, 2.37; N, 3.28; I, 29.64; S, 7.52.

Attempted synthesis of 3-phenyliodonium-1-phenylsulfonylindole-2-carboxylate (22). A mixture of conc H_2SO_4 (6 ml) and H_2O (2 ml) was added to $K_2S_2O_8$ (2.6 g, 9.6 mmol) in an Erlenmeyer flask at 0 °C. 3-Iodo-1-phenylsulfonylindole-2-carboxylic acid (**21**) (3.22 g, 7.54 mmol) was added in small portions, with good stirring. The mixture began to foam, and was stirred while warming to room temperature for 25 min. It was re-cooled to 0 °C, and benzene (2.5 ml) was added. The mixture was stirred at 0 °C until the benzene began to freeze, and then permitted to warm to room temperature and stirred for 25 min. Ice-cold H_2O (20 ml) was added dropwise, followed sequentially by cold CH_2Cl_2 (40 ml) and concd NH_4OH (26 ml), to pH 9. The layers were separated; the aqueous portion was extracted with CH_2Cl_2 (2 x 10 ml) and the combined organic portions filtered through Na_2SO_4 and concentrated to yield 2.26 g of brown solid. Comparison of ms and ir spectra showed the material to be unreacted **21**.

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