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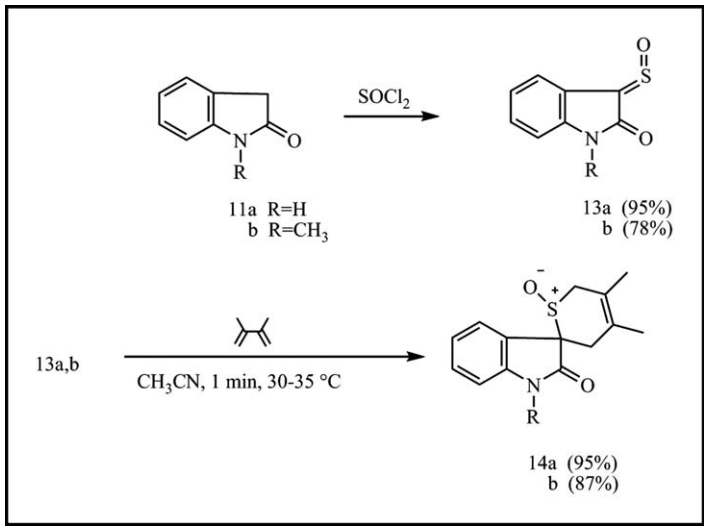

Oxindole was found to react readily with thionyl chloride to give (in an excellent yield) the isolable sulfine (**13a**), which on heating (refluxing acetonitrile) gave isoindigo (**15a**). The dark violet 3-sulfinato-oxindole (**13a**) readily reacted with 2,3-dimethylbutadiene to give a colorless cyclo-adduct (**14a**). The sulfine also reacted readily with various nucleophilic reagents, thus, thioloacetic acid gave 3-carboxymethylthiolo-oxindole (**23a**).

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INTRODUCTION

Sulfines, which can be considered as oxides of thiones, are nonlinear and have the general structure **1**, and as indicated in Figure 1, E and Z isomers are possible [1–6].

Several synthetic methods [1–6] for the production of sulfines are available and perhaps the simplest and most general route is given by Zwanenburg, which involves treatment of silylated molecules, such as silylated ketones with thionyl chloride [5–7]. In a few cases, keto derivatives have been reported to yield α-oxo-sulfines directly (*i.e.*, without activation). For example, Hull and Faull reacted the anion of ethyl 4-chloroacetoacetate with phenyl isothiocyanate in dimethoxyethane and obtained 52% of the thiophene derivative **2**. By changing the solvent to dioxane, the yield of **2** could be improved to 87%. The thiophene **2** reacted readily with thionyl chloride to yield the isolable α-oxosulfine **3** [8]. In terms of yields, acetonitrile was found to be a more suitable solvent than dimethoxyethane. The α-oxosulfine **3** could readily be intercepted by 2,3-dimethylbutadiene to give **4**, which could be fully characterized by ^{1}H and ^{13}C NMR spectroscopy. In Scheme 1, the sulfine **3** is drawn as the more stable E-isomer although the Z-isomer is more likely to be formed initially due to attack of $SOCl_2$ on the enol tautomer of **2**, which would yield an intermediate sulfinyl chloride stabilized by hydrogen bonding. This sulfinyl chloride is then biased to give primarily the Z-sulfine. However the E-isomer is thermodynamically more stable and will eventually be formed. The structure (determined by X-ray technique) of **4** showed that its sulfine precursor **3** leading to **4** had indeed exclusively been the E-isomer [6].

Interestingly, the related (to **2**) molecule **5**, when treated with $SOCl_2$, failed to yield an isolable sulfine. Instead, the coupled molecule **6** was isolated [8] indicating that the intermediate sulfine is unstable in this case. Interception with 2,3-dimethylbutadiene is however possible [6], which gave a separable mixture of diastereomers; thus, indicating that the kinetic product (the Z-isomer) only had been partially converted to the E-isomer. This type of cycloaddition with 2,3-dimethylbutadiene is a standard operation to trap and to characterize sulfines, as have been done with intermediate sulfines generated

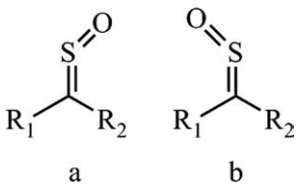


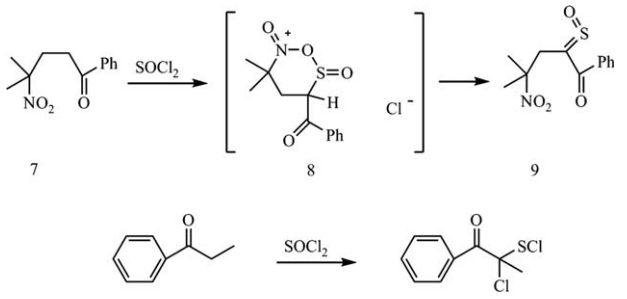
Figure 1. E and Z isomers of sulfines.

from doubly activated methylene compounds, such as dibenzoylmethane [2,7,9,10].

Another stable α-oxosulfine is given by Black, who reported formation of the α-oxosulfine **9** from the nitroketone **7**. The nitro group is considered to play an important role as indicated in Scheme 2. The intermediate **8** could not be isolated but its presence was supported by an ABX pattern observed during an NMR study of the reaction [11]. The product, the stable α-oxo-sulfine **9**, featured diagnostic resonances at 188.9 and 189.3 ppm in the ^{13}C NMR spectrum.

The structure of **9** was confirmed by X-ray crystallography [11]. Simple aromatic ketones (like propiophenone) gave α-chlorosulfenyl chlorides and not α-oxosulfines (Scheme 2) [11].

Scheme 2



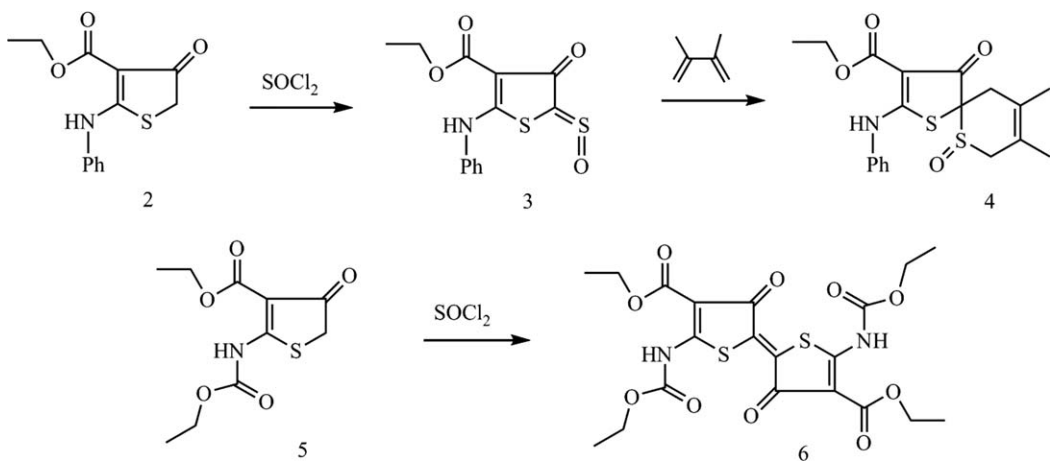
RESULTS AND DISCUSSION

It has now, somewhat surprisingly, been found that several sulfines in the indole series can readily and quickly (2–3 min) be prepared in excellent yields by the reaction of oxindole itself (**11a**) with thionyl chloride in acetonitrile at 30–35°C that gave the α-oxosulfine **13a** as a dark violet solid. *N*-Methyloxindole similarly gave **13b**. Many years ago, oxindole had been treated with thionyl chloride as reagent and solvent at reflux temperature. Under these conditions isoindigo (**15a**) was the sole product [12] and it seems that the sulfine **13a** has never been isolated before. The sulfine **13a** was isolated in 95% yield accompanied with a small amount of 3-chloro-oxindole (2%, isolated) and can be recrystallized from acetonitrile but prolonged heating in this medium will convert **13a** to isoindigo (Scheme 3).

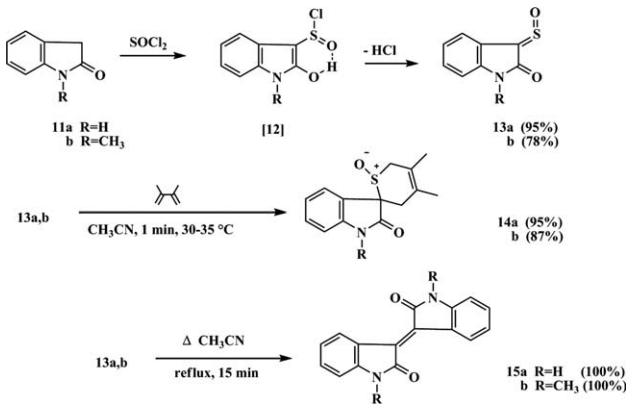
In analogy with the known sulfine **3**, the indolic sulfine **13a** and 2,3-dimethylbutadiene readily (within 2 min at 30–35°C in acetonitrile) gave the colorless adduct **14a** as a single diastereomer. The same is true for the *N*-methyl derivative **13b**, which gave **14b**. It is assumed that the sulfine **13a** is formed *via* an initial electrophilic attack in 3-position of oxindole leading to the nonisolable intermediate sulfinyl chloride **12**, which quickly will eliminate HCl leading to the α-oxosulfine **13a** (E-isomer). However, it is assumed that initially the kinetic product, the Z-isomer, is formed but that it will quickly be converted to the more stable E-isomer. This E-stereochemistry was deduced from the fact that only one isomer of the *S*-oxide **14a** was obtained. Interestingly, other sulfines generated in other ways, for example, *via* diazo compounds, usually will give diastereomeric mixtures with 2,3-dimethylbutadiene [13–16].

A solution of **13a** in DMSO-d_6 features a ^{13}C NMR spectrum similar to but distinctively different from that of isatin [17,18]. In isatin (**10**), the signals from carbon

Scheme 1



Scheme 3



atoms 2 and 3 appeared at 159.4 and 184.3 ppm [17], respectively, whereas the corresponding signals from the sulfine **13a** appeared at 160.0 and 168.9 ppm, respectively. In the proton NMR spectrum, the signal from the 4-H proton was shifted significantly more downfield in the spectrum of **13a** (8.08 ppm) as compared with 7.47 for isatin **10** and actually even more so in isoindigo **15a** (9.10 ppm). These data clearly indicate that the proton in position 4 is strongly influenced by the anisotropic deshielding of the cone of interaction from the SO group (for **13a**) and the C═O group in the neighboring ring (for **15a**).The general similarity of the spectra of **10** and **13a**, however, was taken as evidence that the species present in the solution is (**13a**) actually not an adduct, as a result of nucleophilic addition of DMSO to **13a**. A solution of **13a** in DMSO is, however, not permanently stable and after 7 days 90% of the sulfine will be converted to isoindigo **15a**. This type of conversion was faster for derivatives substituted with halogen atoms in the benzene ring.

The sulfines **13a** and **13b** can, under dry conditions, be stored for several months at room temperature without decomposition. In the presence of moisture, the sulfines will eliminate SO_2 and the starting materials, that is, the oxindoles **11a** and **11b**, will be formed slowly. This type of decomposition has been observed previously for other sulfine derivatives on several occasions [11,19]. When **13a** and **13b** are dissolved in chloroform and saturated with water, the cleavage process is quite quick (*e.g.*, total decomposition within 15 min at 40°C).

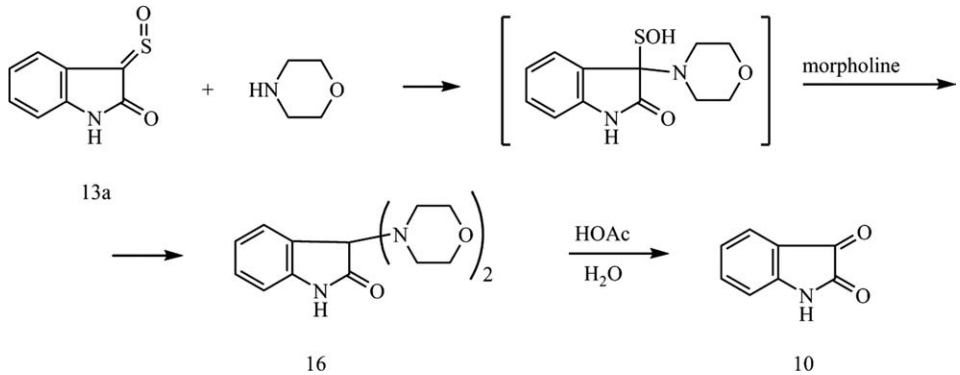
A number of substituted oxindoles, for example, [20–25] 6-chloro-oxindole, 6-bromo-oxindole, and 5-nitro-oxindole likewise could be converted to sulfines as well as adducts with 2,3-dimethyl-butadiene. All these derivatives of **13a** substituted in the benzene ring could readily be converted to ring-substituted derivatives of isoindigo.

As expected, the sulfine **13a** reacted readily with a number of nucleophilic reagents. Thus, morpholine gave the known [26] adduct **19** (previously prepared form isatin and morpholine) as shown in Scheme 4. Thus, addition of morpholine to a solution of the sulfine **13a** in acetonitrile at 35°C quickly faded the dark violet color and a solid precipitated within 2 min, which consists of **16** and morpholinium sulfite, which could be easily removed by extraction of the mixture with water. The nature of the side-product, morpholinium sulfite, was established in an independent experiment, wherein morpholine dissolved in water was reacted with sulfur dioxide. As indicated in Scheme 4, the sulfine **13a** could be converted to isatin **10**. However, simple treatment with water could not effect this transformation.

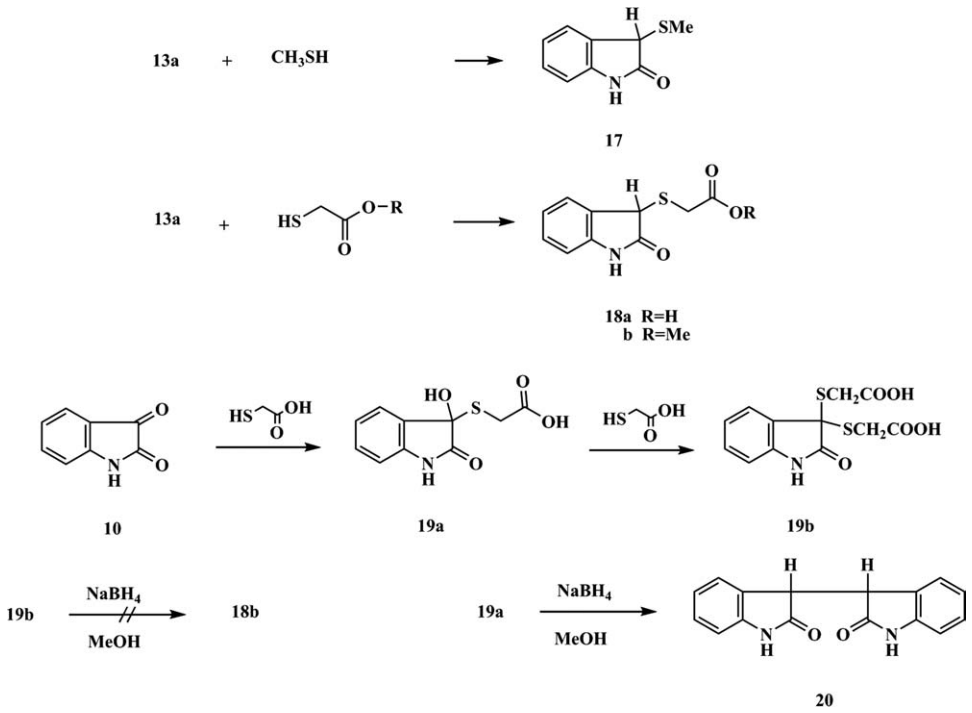
Thiols also reacted readily with the sulfine **13a**, thus, methanethiol gave the known [17] compound **17** and thiolacetic acid and methyl thiolacetate, respectively, the new molecules **18a** and **18b**, both in excellent yields. The NMR data of **18a** are in disagreement with those reported in the literature, wherein a mixture composed of isatin, pentafluoroaniline, and thiolacetic acid has been claimed to give **18a**. This unusual experiment should be repeated [27].

Although isatin and thiolacetic acid readily could be converted to the adduct **19a**, this molecule could not be converted to **18a** because the adduct **19a** is quite labile

Scheme 4



Scheme 5



under basic as well as acidic conditions. The product formed was a coupled reduction product of isatin, namely isatid **20**, a well-known molecule [28,29]. Treatment of the adduct **19a** with acetic anhydride at ambient temperature quickly cleaved the adduct yielding isatin **10**. The bis-adduct **19b**, however, is quite stable under these conditions (Scheme 5).

EXPERIMENTAL

Melting points were uncorrected and determined using a Büchi B-545 apparatus. NMR spectra were obtained in DMSO-d_6 on a Bruker 300-MHz spectrometer. IR (neat) was recorded with an Avatar 330 FTIR apparatus (Thermo Nicolet).

Ethyl 2-phenylamino-4-oxo-4,5-dihydrothiophene-3-carboxylate (2). Ethyl 4-chloro-acetoacetate (16.5 g, 0.1 mol) in dioxane (80 mL) was treated with sodium hydride (4.5 g, 60% in oil) at 30°C. When the evolution of hydrogen had ceased (~20 min), phenyl isothiocyanate (13.5 g, 0.1 mol) in dioxane (20 mL) was added at 25–30°C to the stirred mixture. The temperature was allowed to reach 40°C, and at this point, a thick slurry was formed. After 1 h at 35–40°C, the mixture was poured into water and the solid formed was collected, washed with water, and recrystallized from ethanol, 22.9 g (87%), mp. 146–148°C (lit. [8] 146–148°C). IR 3198, 2983, 2926, 1643, 1555, 1548, 1406, 1382, 1344, 1283, 1223, 1152, 1037, 997, 800, 784, 754 cm^{-1}; ^1H NMR δ: 1.25 (t, 3H, CH_3), 3.67 (s, 2H, CH_2), 4.22 (q, 2H, OCH_2), 7.36–7.51 (m, 5H, arom CH), 11.2 (br s, 1H, NH); ^{13}C NMR δ: 14.4 (q), 38.0 (t), 59.3 (t), 97.0 (s), 125.1 (d), 127.8 (d), 129.5 (d), 137.3 (s), 156.1 (s), 182.7 (s), 190.5 (s).

Ethyl 2-phenylamino-4-oxo-5-sulfinato-4,5-dihydrothiophene-3-carboxylate (3). The ester **2** (2.63 g, 10 mmol) in acetonitrile (35 mL) was treated with thionyl chloride (1.25 mL, 15 mmol) at 35°C. A precipitate of yellow needles was collected after 1 h, (2.90 g, 96%), mp. >260°C dec.; IR 3161, 2968, 1641, 1538, 1408, 1377, 1172, 1018, 941, 788 cm^{-1}; ^1H NMR δ: 1.44 (t, 3H, CH_3), 4.24 (q, 2H, OCH_2), 7.38–7.57 (m, 5H, arom CH), 11.4 (br. s, 1H, NH); ^{13}C NMR δ: 14.3 (q), 59.6 (t), 97.5 (s), 125.9 (d), 129.1 (d), 129.4 (d), 137.0 (s), 163.5 (s), 172.1 (s), 178.8 (s), 191.0 (s).

The adduct (4). The yellow sulfine **3** (3.09 g, 10 mmol) was suspended in acetonitrile (85 mL) and 2,3-dimethylbutadiene in excess was introduced to the stirred mixture at 50–55°C. The solution obtained was concentrated and the colorless product was collected (3.25 g, 86%); mp. 200–202°C (lit. [6] 200–202°C); IR 3162, 3058, 2974, 1660, 1548, 1415, 1400, 1210, 1063, 1032, 800, 769, 696 cm^{-1}; ^1H NMR δ: 1.27 (t, 3H, CH_3), 1.59 (s, 6H, 2 CH_3), 2.75 (2H, CH_2), 3.45 (2H, CH_2), 4.26 (q, 2H, OCH_2), 7.40–7.55 (m, 5H, arom CH), 11.4 (s, 1H, NH); ^{13}C NMR δ: 14.3 (q), 19.0 (q), 19.2 (q), 39.7 (t), 52.3 (t), 59.7 (t), 79.0 (s), 97.2 (s), 119.1 (s), 125.4 (d), 126.7 (s), 128.3 (d), 129.7 (d), 137.2 (s), 164.2 (s), 180.4 (s), 188.1 (s).

2-Oxindole-3-thione *S*-oxide 13a. Thionyl chloride (15.0 mL) was added during 3 min to a stirred solution of oxindole (13.3 g, 0.1 mol) in acetonitrile (120 mL) at 25–30°C. The dark violet product started to separate within 1 min and the reaction is completed in 10 min. The sulfine **13a** was collected and dried in a desiccator (17.08 g, 95%); mp. ~120°C dec; IR: NH 3240 (br), 1702, 1666, 1607, 1456, 1326, 1201, 1126, 1089, 1070, 764 cm^{-1}; ^1H NMR δ: 6.83 (d), 7.00 (d), 7.40 (d), 8.07 (d, 4-H), 10.9 (s, NH); ^{13}C NMR δ: 110.5 (d), 122.1 (s), 122.6 (d), 126.1 (d), 134.3 (d), 140.7 (s), 166.0 (s), 169.0 (s); Anal. calcd. for $C_8H_5NO_2S$: C, 53.2; H, 2.88; N, 7.78 Found: C, 53.5; H, 3.15; N, 7.65.

***N*-Methyl-2-oxindole-3-thione *S*-oxide 13b.** The procedure given for the parent compound **13a** was used, except that methyl acetate was used as medium starting with *N*-methyl-oxindole. Before isolation of the product, part of the solvent was partially evaporated; (Yield 78%); mp 130–140°C (violent dec);^{1}H NMR δ: 3.12 (s, 3H, NCH_3), 7.05–7.11 (dd+d, 2H arom CH), 7.49 (dd, 1H, arom CH), 8.10 (d, 1H, 4-H); ^{13}C NMR δ: 125.8 (q), 109.5 (d), 120.9 (s), 121.7 (d), 125.8 (d), 134.2 (d), 141.8 (s), 164.5 (s), 168.2 (s); Anal. calcd. for $C_9H_7NO_2S$: C, 56.1; H, 3.70; N, 7.28. Found: C, 55.7, H, 3.80; N, 7.35.

The adduct 14a. The sulfine **13a** (179 mg, 1 mmol) was suspended in acetonitrile (5.0 mL), and 2,3-dimethyl-butadiene (123 mg, 1.5 mmol) was introduced at 30–35°C. The dark violet starting material went into solution and was soon replaced by the colorless adduct **14a**, which has a low solubility in acetonitrile, 247 mg, (95%); mp. 195–196°C; IR 3255, 2919, 2888, 1716 (s), 1617, 1469, 1324, 1186, 1030, 738, 678 cm^{-1}; ^{1}H NMR δ: 1,63 (s, 3H, CH_3), 1.79 (s, 3H, CH_3), 2.61 (2H, CH_2), 3.60 (2H, CH_2), 6.91 (d, 1H), 7.03 (dd, 1H), 7.20 (d, 1H), 7.33 (dd, 1H), 10.8 (s, 1H, NH) ^{13}C NMR δ: 19.2 (q), 19.6 (q), 35.4 (t), 50.1 (t), 66.1 (s), 109.8 (d), 118.2 (s), 122.1 (s), 125.3 (s), 125.3 (d), 125.8 (s), 129.7 (d), 143.1 (s), 174.5 (s). Anal. calcd. for $C_{14}H_{15}NO_2S$: C, 64.33; H, 5.78; N, 7.25; Found, C, 64.12; H, 5.90; N, 7.15.

The adduct 14b. The same procedure as for **14a** was used. Yield (94%), mp. 191–192°C; IR; 3060 (w), 1704 (s), 1609, 1468, 1372, 1344, 1052 (s), 755 (s) cm^{-1}; ^{1}H NMR δ: 1.69 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 2.62 (2H, CH_2), 3.17 (s, 3H, NCH_3), 3.62 (2H, CH_2), 7.10–7.46 (m, 4H, arom CH); ^{13}C NMR δ: 19.2 (q), 19.6 (q), 26.6 (q), 35.3 (t), 50.2 (t), 65.5 (s), 108.9 (d), 118.2 (s), 122.7 (d), 124.6 (s), 125.0 (d), 125.7 (s), 129.8 (d), 144.5 (s), 172.9 (s). Anal. calcd. for $C_{15}H_{17}NO_2S$: C, 65.80; H, 6.23; N, 5.11 Found: C, 65.91; H, 6.32; N, 5.15.

6-Bromo-2-oxindole-3-thione *S*-oxide. The procedure given for **13a** was used, starting with 6-bromo-oxindole [24]. Yield 98%, mp. 140°C dec. ^{1}H NMR δ 7.10 (dd, 1H, 5-H), 7.18 (d, 1H, 7-H), 7.94 (d, 1H, 4-H). ^{13}C NMR δ: 113.3 (d), 123.5 (s), 125.3 (d), 127.1 (d), 127.2 (s), 141.8 (s), 165.7 (s), 167.8 (s). Anal. calcd. for $C_8H_4BrNO_2S$: C, 37.61; H, 1.57; N, 5.46 Found: C, 37.40; H, 1.66; N, 5.30.

Adduct between 6-bromo-2-oxindole-3-thione *S*-oxide and 2,3-dimethylbutadiene. The procedure described for **14a** was used. Yield 98%, mp. 220°C dec. IR 3110, 3080, 1720, 1609, 1447, 1038, 821 cm^{-1}; ^{1}H NMR δ 1.68 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 2.62 (2H, CH_2), 3.61 (2H, CH_2), 7.06 (d, 1H, 7-H, J = 1.83 ppm), 7.11 (d, 1H, 4-H, J = 8.25), 7.22 (dd, 1H, 5-H), 11.0 (s, 1H, NH). ^{13}C NMR δ; 19.7 (q), 20.1 (q), 35.7 (t), 50.8 (t), 66.7 (s), 113.2 (d), 118.8 (s), 123.1 (s), 125.0 (s), 125.2 (d), 126.4 (s), 127.6 (d), 145.3 (s), 175.1 (s). Anal. calcd. for $C_{11}H_{14}BrNO_2S$: C, 49.39; H, 4.13; N, 4.09 Found: C, 49.19; H, 4.29; N, 3.97.

6-Chloro-2-oxindole-3-thione *S*-oxide. The procedure above was used. Yield 92%, IR 3102, 1712, 1606, 1330, 1104, 1067, 808, 719 cm^{-1}; ^{13}C NMR δ 109.1 (d), 120.8 (d), 124.7 (s), 125.7 (s), 131.7 (d), 145.1 (s), 165.9 (s), 167.8 (s).

Adduct between 5-bromo-2-oxindole-3-thione *S*-oxide and 2,3-dimethylbutadiene. Yield: 87%, mp. 220°C dec. IR 3176, 3145, 2902, 1715, 1618, 1468, 1300, 1227, 1039, 823 cm^{-1}; ^{1}H NMR δ 1.70 (s, 3H, CH_3), 1.78 (s, 3H, CH_3), 2.57 (2H, CH_2), 3.62 (2H, CH_2), 6.88 (d, 1H, 7-H), 7.26 (d, 1H, 4-H), 7.53 (dd, 1H, 6-H), 11.0 (s, 1H, NH). ^{13}C NMR δ 19.2 (q), 19.6 (q), 34.7 (t), 50.0 (t), 65.9 (s), 111.7 (s), 113.6 (d), 117.8 (s), 125.7 (d), 127.7 (s), 127.9 (s), 132.4 (d), 142.3 (s), 174.1 (s).

Adduct between 6-chloro-2-oxindole-3-thione *S*-oxide and 2,3-dimethylbutadiene. Yield: 92%, mp. 190°C dec. IR 3193, 1720, 1614, 1481, 1449, 1322, 1238, 1040, 926, 806 cm^{-1}; ^{1}H NMR δ 1.68 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 2.56 (2H, CH_2), 3.62 (2H, CH_2), 6.93 (d, 1H, 7-H), 7.09 (dd, 1H, 5-H), 7.17 (d, 1H, 4-H), 11.0 (br s, 1H, NH). ^{13}C NMR δ; 19.2 (q), 19.6 (q), 35.1 (t), 50.2 (t), 66.0 (s), 109.9 (d), 113.6 (s), 121.7 (d), 124.0 (s), 125.8 (s), 126.7 (d), 134.1 (s), 144.6 (s), 174.6 (s). Anal. calcd. for $C_{14}H_{14}ClNO_2S$. C, 56.90; H, 4.75; N, 4.69. Found: C, 56.71; H, 4.90; N, 4.58.

6,6′-Dichloroisoindigo. The 6-chloro-S-oxide (2.0 g) obtained above was heated at reflux in acetonitrile (50 mL) for 1 h and the dark blue precipitate of 6,6′-dichloroisoindigo was collected and washed with ethanol. Yield: 96% mp. > 300°C. The spectroscopic data were in agreement with those in the literature [30,31].

5-Nitro-2-oxindole-3-thione *S*-oxide. The procedure above was used. Yield: 75%, mp. (violent dec.) 140°C. ^{1}H NMR δ; 7.03 (d, 7-H, J_1 = 8.75), 8.27 (dd, 6-H, J_1 = 8.75, J_2 = 2.31), 8.72 (d, 4-H, J_2 = 2.31), 11.6 (s, NH). ^{13}C NMR δ; 110.7 (d), 120.4 (d), 121.4 (s), 129.6 (d), 142, 2 (s), 145.7 (s), 166.0 (s), 167.0 (s). No acceptable elemental analysis data could be obtained for this molecule, but its adduct could be analyzed.

Adduct between 5-nitro-2-oxindole-3-thione *S*-oxide and 2,3-dimethylbutadiene. The procedure above was used. Yield: 84%, mp. 150°C dec. ^{1}H NMR δ: 1.67 (s, 3H, CH_3), 1.73 (s, 3H, CH_3), 2.50 (2H, CH_2), 3.65 (2H, CH_2), 7.09 (d, 1H, 7-H), 7.93 (d, 1H, 4-H), 8.30 (dd, 1H, 6-H, J_1 = 8.75, J_2 = 2.31), 11.5 (s, 1H, NH). ^{13}C NMR δ; 19.2 (q), 19.5 (q), 34.4 (t), 50.3 (t), 65.9 (s), 109.9 (d), 118.1 (s), 120.5 (d), 125.9 (s), 126.1 (s), 126.8 (d), 142.4 (s), 149.3(s), 175.0 (s). Anal. calcd. for $C_{14}H_{14}N_2O_4S$: C, 31.30; H, 4.59; N, 4.56. Found: C, 31.19; H, 4.63; N, 4.45.

Isoindigo 15a. The sulfine **13a** (1.79 g, 10 mmol) in acetonitrile (35 mL) was refluxed until no more precipitate of the product **15a** was formed (∼15 min). Yield: (100%); mp. >300°C; ^{1}H NMR δ; 6.83 (d), 6.91 (dd), 7.40 (dd), 9.06 (d), 10.9 (s, NH); ^{13}C NMR δ; 109.5 (d), 121.1 (d), 121.7 (s), 129.4 (d), 132.4 (d), 133.4 (s), 144.2 (s), 169.1 (s). UV in agreement with data in ref. 30. The ^{1}H NMR data were in agreement with those in the literature [32,33]. However, the signal just above 9.0 ppm was incorrectly reported as a singlet.

***N*,*N*′-Dimethylisoindigo 15b.** The same procedure as for **15a** was used, Yield 100%, mp. 270–271°C (lit. [33] 270°C; 267–269°C [34]); IR 3130 (w), 2980 (w), 1681 (s), 1605, 1469, 1374, 1338, 1089, 1076, 944, 866, 773, 740 cm^{-1}; ^{1}H NMR δ: 3.20 (s, 6H, $2NCH_3$), 7.0–7.5 (m, 6H, arom CH), 9.12 (2d, 2H, 4-H); ^{13}C NMR δ: 26.1 (q), 108.5 (d), 120.6 (s), 121.8 (d), 129.1 (d), 132.7 (d), 132.8 (s), 145.1 (s), 168.0 (s).

3,3′-Bis(morpholino)oxindole 16. Morpholine (261 mg, 3 mmol) was added to the sulfine **13a** (358 mg, 2 mmol) in acetonitrile (6 mL). A white solid appeared within 2 min, which was collected and washed with water after 30 min at 25°C, 395 mg (64%), mp. 177–179°C (lit. [26] 177–179°C). The spectral data were in agreement with those in the literature [26].

***S*-Methyl-3-thiolo-oxindole 17.** A stream of methanthiol was introduced into a stirred suspension of the sulfine **13a**, 1.79 g, 10 mmol) in acetonitrile (80 mL) at 35°C. When the dark violet starting material had been consumed (~1 h) the solution was evaporated and the crude product recrystallized form ethanol, 1.41 g (72%) mp. 125–127°C (lit. [18] 125.5–127°C). The NMR data were in agreement with those reported in the literature [21]. The signal from the 3-C carbon atom resonated at 45.5 ppm.

***S*-Carboxymethyl-3-thiolo-oxindole 18a.** The sulfine **13a** (358 mg, 2 mmol) was added to a solution of thioloacetic acid (202 mg, 2.3 mmol) in acetonitrile (8 mL). As there seemed to be no reaction at ambient temperature the reaction mixture was heated at reflux for 20 min. During this period, the solution became colorless. After concentration and treatment with ether, the product was obtained as colorless crystals, 360 mg, (81%) mp. 160–162°C. IR 3280, 1700, 1621, 1469, 1177, 1120, 872, 740 cm^{-1}; ^1H NMR δ: 3.48 (q, 2H, CH_2, $J = 15.2$ ppm), 4.81 (s, 1H, 3-CH), 6.85–7.34 (m, 4H, arom CH), 10.6 (s, 1H, NH), 12.8 (br. s, 1H, OH). ^{13}C NMR δ: 40.7 (t), 50.6 (d), 109.6 (d), 121.8 (d), 124.9 (d), 126.4 (s), 129.5 (d), 143.0 (s), 170.0 (s), 175.2 (s). Anal. calcd. for $C_{10}H_9NO_3S$: C, 53.80; H, 4.07; N, 6.27; Found: C, 53.63; H, 4.20; N, 6.05.

Methyl *S*-carboxymethyl-3-thiolo-oxindole 18b. Methyl thioloacetate (233 mg, 2.3 mmol) was added to the sulfine **13a** (351 mg, 2.0 mmol) in acetonitrile (6.0 mL) at 45°C. The color faded quickly. After 10 min the solution was evaporated and the oil obtained was treated with methyl acetate/diisopropyl ether (1:4), which gave crystals of the product, 371 mg (79%), mp. 109–110°C; IR: 3146, 1730, 1704, 1673, 1617, 1470, 1281, 1266, 1005, 743, 676 cm^{-1}; ^1H NMR 3.53 (q, 2H, CH_2), 3.63 (s, 3H, OCH_3), 4.84 (s, 1H, 3-CH), 6.83–7.33 (m, 4H, arom CH), 10.6 (s, 1H, NH); ^{13}C NMR 40.1 (t), 50.6 (q), 52.2 (d), 109.7 (d), 121.8 (d), 125.2 (d), 126.3 (s), 129.4 (d), 143.0 (s), 169.1 (s), 175.1 (s). Anal. calcd. for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90 Found: C, 55.73; H, 4.78, N, 5.90.

The monocarboxylic acid 19a. Isatin (14.7 g, 0.1 mmol) and thioloacetic acid (9.2 g, 0.1 mol) was heated in dioxan (30 mL) for 0.5 h. After concentration, the residue was treated with methanol/water 1:2, which gave the title compound, 20.1 g (84%), mp. 191–193°C. IR 3288, 3100–2550, 1728, 1693, 1613, 1469, 1422, 1267, 1131, 916, 822, 749 cm^{-1}; ^1H NMR δ: 3.75 (2H, q), 6.88 (d, 1H), 7.02 (dd, 1H), 7.13 (dd, 1H), 7.39 (d, 1H), 10.4 (s, 1H); ^{13}C NMR δ: 29.7 (t), 77.9 (s), 109.9 (d), 121.9 (d), 124.0 (d), 129.1 (s), 130.1 (d), 139.8 (s), 171.1 (s), 174.6 (s). Anal. calcd. for $C_{10}H_8NO_4S$: C, 50.20; H, 3.79; N, 5.84; Found: C, 49.81; H, 3.85; N, 5.72.

The dicarboxylic acid 19b. Isatin (14.7 g, 0.1 mmol) and thioloacetic acid (20.2 g, 0.22 mmol) in dioxane (50 mL) was heated to reflux for 3 h. After concentration, the residue was treated with methanol/water 1:1, which quickly yielded crystals of the product 26.8 (86%); mp. 202–204 °C. IR 3288, 3170–2300, 1731, 1697, 1615, 1469, 1175, 1057, 904, 750 cm^{-1}; ^1H NMR δ: 3.96 (s, 4H), 6.90 (d, 1H), 7.03 (dd, 1H), 7.29 (dd, 1H), 7.33 (d, 1H), 10.9 (s, 1H, NH), 12.7 (s, 2H, OH); ^{13}C NMR δ: 32.4 (t), 55.1 (s), 110.3 (d), 122.4 (d), 124.3 (d), 127.8 (s), 130.1 (d), 140.3 (s), 170.0 (s), 173.6 (s). Anal. calcd. for $C_{12}H_{11}NO_5S_2$: C, 45.99; H, 3.54; N, 4.47 Found: C, 45.85; H, 3.66; N,4.32.

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