

Reactions of Some Sulphur-containing Indoles with Arensulphonyl Azides.

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The reaction of arenesulphonyl azides with 2-alkylthioindoles yields 3,3'-azoindoles; however 1-methyl-2-methylthioindole reacts with *p*-chlorobenzenesulphonyl azide to form 2-*p*-chlorophenylsulphonylamino-1-methyl-3-methylthioindole. Indoline-2-thione and its *N*-methyl derivative react with arenesulphonyl azides to form thiadiazoloindoles and $\Delta^{3,3'}$ -bi-indoline-2,2'-dithiones.

SIMPLE 2-mono- and 1,2-di-alkylindoles react with arenesulphonyl azides affording a mixture of 3,3'-azoindoles and 3-arylsulphonylaminoindoles (I).¹ We now report the reactions of some 2-alkylthioindoles.

2-Methylthioindole (II; R¹ = H, R² = Me)² reacted with tosyl azide and with *p*-chlorobenzenesulphonyl (Cbs) azide forming 2,2'-bismethylthio-3,3'-azoindole (III; R¹ = H, R² = Me) in *ca.* 50% yield; no other product was isolated. The ethylthio-derivative (II; R¹ = H, R² = Et)³ yielded the azoindole (III; R¹ = H, R² = Et) and the *N*-methyl compound (II; R¹ = R² = Me)² afforded a small quantity of (III; R¹ = R² = Me).

The u.v. spectra of these azo-compounds were similar to those reported¹ for simple azoindoles and their n.m.r. spectra contained characteristic signals at low field from C(4)H.¹ Simple 2,2'-dialkyl 3,3'-azoindoles fragment in the mass spectrometer by hydrogen-transfer followed by N-N cleavage,¹ the base peaks being (*M*/2 + 1). These sulphur-containing compounds fragment differently, as illustrated by the breakdown of (III; R¹ = R² = Me).

¹ A. S. Bailey and J. J. Merer, *J. Chem. Soc. (C)*, 1966, 1345.

² T. Hino, K. Tsuneoka, M. Nakagawa, and S. Akaboshi, *Chem. and Pharm. Bull. (Japan)*, 1969, **17**, 554.

³ M. Nakagawa and T. Hino, *Tetrahedron*, 1970, **26**, 4491.

The molecular ion (m/e 380) is the base peak and other significant peaks are at m/e 322 and 290. It is unlikely that these ions are formed by loss of the N and Me groups forming part of the indole rings and we suggest that the methyl groups joined to sulphur and the nitrogen atoms forming the azo-bond are lost, yielding ions of types (IV) and (V). (The constitutions of these ions were confirmed by high resolution measurements.) The mass spectrum of 2,2'-bismethylthioazobenzene (VI)⁴ contains peaks at m/e 274 (M , 6%), 259 (100%), 244 ($M - 2\text{Me}$, 5%), 216 ($M - \text{N}_2 - 2\text{Me}$, 3%), 184 ($M - \text{N}_2 - \text{Me} - \text{MeS}$, 6%), and 108 ($\text{C}_6\text{H}_4\text{S}$, 13%).

The major product of the reaction between 1-methyl-2-methylthioindole (II; $\text{R}^1 = \text{R}^2 = \text{Me}$) and Cbs azide was a colourless solid, $\text{C}_{16}\text{H}_{15}\text{ClN}_2\text{O}_2\text{S}_2$. Two structures were considered for this compound: (I; $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{SMe}$, $\text{R}^3 = \text{Cl}$), by analogy with the reaction of 1,2-dimethylindole with tosyl azide, and (VII), the result of migration of the sulphur atom from C(2) to C(3). The n.m.r. spectrum of the material in $(\text{CD}_3)_2\text{SO}$ would fit either structure, but the n.m.r. spectrum of a colourless solution in CDCl_3 showed that the compound is a tautomeric mixture of structures (VII) and (VIII) in the ratio 2.4:1 (*cf.* the behaviour of 1,3-dialkyl-2-aryl-sulphonylaminoindoles).⁵ We have never observed any tautomerism of the type (I) \rightleftharpoons (IX).⁶ The n.m.r. spectrum of our product does not support structure (IX) (in particular the position of the NMe signal), and a compound of type (IX) would be orange-coloured and fluoresce in solution.⁷ The isolation of compound (VII) provides further evidence that attack of azides on indoles under neutral conditions⁸ gives an intermediate of type (X). Migration of SEt from C(2) to C(3) has been observed^{3,9} during the oxidation of 2-ethylthio-3-methylindole.

We have observed^{6,8} diazo-transfer during the reaction of certain indoles with azides under basic conditions, and Buckley¹⁰ has found that oxindole and *N*-methyloxindole give isoindigo (XI; $\text{R} = \text{H}$, $\text{Y} = \text{O}$) and 1,1'-dimethylisoindigo (XI; $\text{R} = \text{Me}$, $\text{Y} = \text{O}$) with tosyl azide in pyridine. These compounds are probably formed *via* diazo-oxindoles (XII; $\text{Y} = \text{O}$).¹¹

Both tosyl azide and Cbs azide reacted vigorously with indoline-2-thione in pyridine solution forming a compound, $\text{C}_8\text{H}_5\text{N}_3\text{S}$, to which we ascribe structure (XIII; $\text{R} = \text{H}$) rather than the open-chain structure (XII; $\text{Y} = \text{O}$);

⁴ D. L. Chamberlain, D. Peters, and N. Kharasch, *J. Org. Chem.*, 1958, **23**, 381.

⁵ A. S. Bailey, A. J. Buckley, and W. A. Warr, *J.C.S. Perkin I*, 1972, 1626.

⁶ A. S. Bailey and A. J. Buckley, *J.C.S. Perkin I*, 1973, 1602.

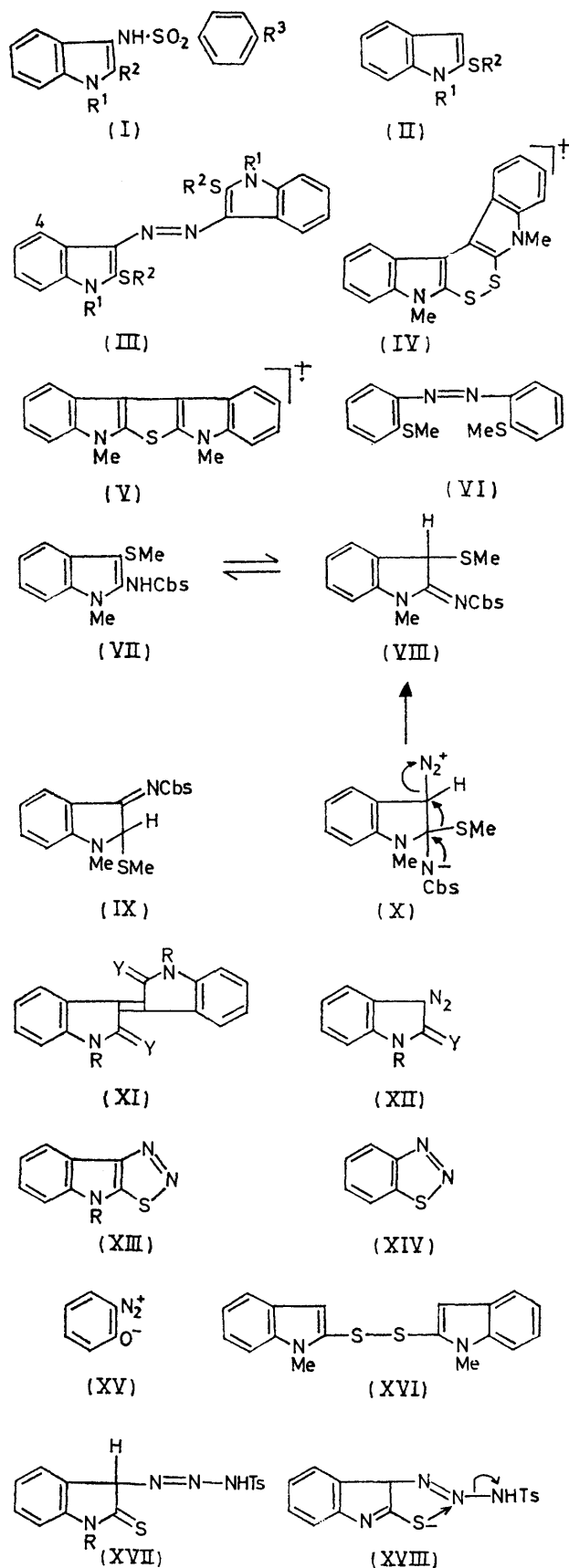
⁷ A. S. Bailey, R. Scattergood, and W. A. Warr, *J. Chem. Soc. (C)*, 1971, 2479; A. S. Bailey, P. A. Hill, and J. F. Seager, *J.C.S. Perkin I*, 1974, 967.

⁸ A. S. Bailey, A. J. Buckley, W. A. Warr, and J. J. Wedgwood, *J.C.S. Perkin I*, 1972, 2411; A. S. Bailey, A. J. Buckley, and J. F. Seager, *ibid.*, 1973, 1809.

⁹ M. Nakagawa, H. Yamaguchi, and T. Hino, *Tetrahedron Letters*, 1970, 4035; T. Hino, H. Yamaguchi, and M. Nakagawa, *J.C.S. Chem. Comm.*, 1972, 473.

¹⁰ A. J. Buckley, D.Phil. Thesis, Oxford, 1972.

¹¹ E. J. Moriconi and J. J. Murray, *J. Org. Chem.*, 1964, **29**, 3577.



R = H, Y = S), since the material is colourless and there is no i.r. band at 2200 cm^{-1} ; benzothiadiazole (XIV) is colourless but the corresponding oxygen-containing compound (XV) is brightly coloured.¹² From the mother-liquors of this reaction a small quantity of the bi-indoline (XI; R = H, Y = S) was isolated. In contrast, the reaction of tosyl azide with 1-methylindoline-2-thione gave only a small quantity of the thiadiazoloindole (XIII; R = Me), the major product being the bi-indoline-2,2'-dithione (XI; R = Me, Y = S). The compound was insoluble in CDCl_3 and in Me_2SO , and an n.m.r. spectrum could not be obtained. Analytical and mass-spectroscopic data suggested the formula $\text{C}_{18}\text{H}_{14}\text{N}_2\text{S}_2$ and the u.v. extinction coefficients were greater than 10^5 . The compound is obviously not of the type (XVI) obtained² by the oxidation of *N*-methylindoline-2-thione with iodine. A sample of the bi-indoline (XI; R = Me, Y = S) was prepared by treating 1-methylindoline-2-thione with *p*-nitrosodimethylaniline, a reagent which converts *N*-methyloxindole into *N*-methylisindigo (XI; R = Me, Y = O).^{11,13} Since this reaction occurs¹⁴ by condensation of the nitroso-compound with $\text{C}(3)\text{H}_2$ it provides further support for the suggestion that the compound $\text{C}_{18}\text{H}_{14}\text{N}_2\text{S}_2$ contains two indoline units joined at C(3).

The differences between the reactions of indoline-2-thione and its *N*-methyl derivative may be due to the fact that the intermediate (XVII) in the diazo-transfer reaction contains an acidic proton¹⁵ when R = H and will exist in pyridine as the ionic form (XVIII) which can then lose toluene-*p*-sulphonamide to form (XIII). However when R = Me loss of toluene-*p*-sulphonamide would lead to (XII; R = Me, Y = S) which could either cyclise or lose nitrogen forming the 'dimer' (XI; R = Me, Y = S) as the major product [cf. the formation of (XI; R = Me, Y = O) from *N*-methyl-3-diazo-oxindole¹¹].

EXPERIMENTAL

General details and instruments used have been reported.⁷ U.v. spectra were determined for solutions in ethanol and n.m.r. spectra for solutions in CDCl_3 unless otherwise stated; i.r. spectra were recorded for Nujol mulls.

2,2'-Bismethylthio-3,3'-azoindole (III; $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Me}$).—(a) 2-Methylthioindole (1 g) and tosyl azide (3.7 g) were heated at 60° for 24 h. Methanol (10 ml) was added and the solid (497 mg, 46%) was collected. (b) The indole (1.35 g) and Cbs azide (4.9 g) (60° ; 18 h) afforded 715 mg (49% yield). The azo-compound formed yellow-brown prisms, m.p. $226\text{--}227^\circ$ (from acetonitrile) (Found: C, 61.2; H, 4.5; N, 16.0; S, 17.5. $\text{C}_{18}\text{H}_{16}\text{N}_4\text{S}_2$ requires C, 61.4; H, 4.6; N, 15.9; S, 18.2%; λ_{max} 205, 246, 288, 400, 427sh, and 440 nm (ϵ 26,400, 16,900, 16,000, 16,000, 17,200, and 17,800); ν_{max} 3385 cm^{-1} ; τ [$(\text{CD}_3)_2\text{SO}$] 1.73 (2H, NH), 1.60 [2H, m, C(4)H], 2.5—2.9 (6H, m), and 7.23 (6H, s, SMe); m/e 352 (*M*, 100%), 337 (*M* - Me, 5%), m^* 322.6), 294 (*M* - N_2 -

2Me, 26%), 293 (22%), 262 (*M* - N_2 - Me - SMe, 63%), and 261 (25%). 2-Ethylthioindole and tosyl azide (60° 24 h) yielded 2,2'-bisethylthio-3,3'-azoindole (III; $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Et}$), orange prisms, m.p. $264\text{--}266^\circ$ (decomp.) (from 2-methoxyethanol) (yield 27%) (Found: C, 63.0; H, 5.4; N, 14.4; S, 17.0. $\text{C}_{20}\text{H}_{20}\text{N}_4\text{S}_2$ requires C, 63.2; H, 5.3; N, 14.7; S, 16.8%; λ_{max} 203, 239sh, 287, 402, and 432 nm (ϵ 35,200, 20,700, 19,800, 22,500, and 21,300); ν_{max} 3275br cm^{-1} ; τ [$(\text{CD}_3)_2\text{SO}$] 1.78 (2H), 1.52 (2H), 2.5—3.0 (6H, m), 6.77 (4H, q, *J* 7 Hz, S- $\text{CH}_2\text{-CH}_3$), and 8.67 (6H, t, *J* 7 Hz, $\text{CH}_2\text{-CH}_3$); m/e 380 (*M*, 100%), 351 (13%), 294 (50%), 293 (35%), 262 (90%), and 261 (37%). The methanolic residues yielded only the arenesulphonamide.

Reaction between 1-Methyl-2-methylthioindole and *p*-Chlorobenzenesulphonyl Azide.—A mixture of the indole (1.88 g) and the azide (4.5 g) was heated (45°) for 24 h. Methanol (30 ml) was added, the mixture was boiled and filtered hot, and the insoluble fraction (240 mg) was recrystallised from 2-methoxyethanol. 1,1'-Dimethyl-2,2'-bismethylthio-3,3'-azoindole (III; $\text{R}^1 = \text{R}^2 = \text{Me}$) formed orange-coloured plates, m.p. $230\text{--}232^\circ$ (Found: C, 62.9; H, 5.2; N, 14.6; S, 16.6. $\text{C}_{20}\text{H}_{20}\text{N}_4\text{S}_2$ requires C, 63.2; H, 5.3; N, 14.7; S, 16.8%; λ_{max} (CHCl_3) 242, 285, 300sh, 410, and 447 nm (ϵ 20,700, 18,800, 15,300, 23,500, and 22,200), τ 1.38 (2H, dd, *J* 7 and 2 Hz), 2.3—2.8 (6H, m), 6.07 (6H, s, NMe), and 7.37 (6H, s, SMe); m/e 380 (*M*, 100%), 365 (17%), m^* 350.6), 322 (31%), 321 (14%), 290 (87%), 275 (290 - Me, 51%), m^* 260.8, confirmed by high resolution measurements). The methanolic liquors were evaporated to ca. 10 ml and next day the solid (1.72 g) was collected. Recrystallisation from propan-1-ol gave a mixture of needles and prisms. Small quantities were separated by hand; the two forms had the same R_F values and gave the same iodine stain and fluorescence in u.v. light. The material was recrystallised from benzene-petroleum (b.p. $60\text{--}80^\circ$) (1.1 g) and then from acetic acid-methanol; 2-*p*-chlorophenylsulphonyl-amino-1-methyl-3-methylthioindole (VII) formed prisms, m.p. $155\text{--}157^\circ$ (Found: C, 52.4; H, 4.0; Cl, 9.8; N, 7.7; S, 17.4. $\text{C}_{18}\text{H}_{15}\text{ClN}_2\text{O}_2\text{S}_2$ requires C, 52.4; H, 4.1; Cl, 9.7; N, 7.6; S, 17.5%; λ_{max} 203, 226, and 288 nm (ϵ 27,500, 43,800, and 10,000); ν_{max} 1530, 1575, 1590, and 3225 cm^{-1} ; τ [$(\text{CD}_3)_2\text{SO}$] 0.6 (1H, NH, exchanged in D_2O), 2.20—2.95 (8H, m, ArH), 6.38 (3H, s, NMe of indole), and 8.10 (3H, s, SMe); τ (CDCl_3) 2.05 (d, *J* 8 Hz, low-field half of CbsN=C signal), 2.4—2.9 (m, ArH), 3.25 (NH, exchanged in D_2O), 4.52 [s, C(3)HSMe], 6.17 (s, NMe of indole), 6.70 (s, NMe of indoline), 8.10 (s, SMe of indole), and 8.46 (s, HC-S- CH_3); m/e 366 (*M*, 9%), 191 (*M* - Cbs, 100%), m^* 99.7), and 159 (8%).

[1,2,3]Thiadiazolo[5,4-*b*]indole (XIII; R = H).—Tosyl azide (3.2 g) was added to a solution of indoline-2-thione (2 g) in pyridine (20 ml); a vigorous exothermic reaction occurred and after 1 h the solvent was removed and methanol (10 ml) added. The solid (1.15 g) was recrystallised from ethanol (charcoal) and then from acetic acid; compound (XIII; R = H) formed needles, m.p. 180° (decomp.) (Found: C, 55.0; H, 3.0; N, 24.2; S, 18.0. $\text{C}_8\text{H}_5\text{N}_3\text{S}$ requires C, 54.9; H, 2.9; N, 24.0; S, 18.3%; λ_{max} 218, 256, 267, 274, and 310 nm (ϵ 39,800, 11,600, 10,900, 10,300, and 4900); ν_{max} 3100—3400 (NH) cm^{-1} ; τ [$(\text{CD}_3)_2\text{SO}$] 1.85 (1H, dd, *J* 8 and 1 Hz), 2.32 (1H, dd, *J* 8 and 1 Hz), 2.4—2.8 (2H,

¹² H. H. Hodgson and D. P. Dodgson, *J. Soc. Dyers and Colourists*, 1948, **64**, 65; *J. Chem. Soc.*, 1948, 870; H. H. Hodgson and E. Marsden, *J. Soc. Dyers and Colourists*, 1943, **59**, 271.

¹³ R. Stollé, R. Bergdoll, M. Luther, A. Auerhahn, and W. Wacker, *J. prakt. Chem.*, 1930, **128**, 1.

¹⁴ M. S. Kisteneva, *Zhur. obshchei. Khim.*, 1956, **26**, 1169, 2019 (*Chem. Abs.*, 1956, **50**, 16,747; 1957, **51**, 5044).

¹⁵ P. A. S. Smith, 'Open-chain Nitrogen Compounds,' vol. 1, Benjamin, New York, 1965, p. 160; Houben-Weyl, 'Methoden der Organischen Chemie,' 1955, vol. 9, p. 768.

m), and 4.8—5.8vbr (1H, NH, exchanged in D₂O); *m/e* 175 (*M*, 34%), 147 (*M* - N₂, 71%, *m** 123.5), 146 (53%), 120 (147 - HCN, 100%, *m** 98.0), and 103 (147 - CS, 32%). The methanolic mother liquors were evaporated and benzene (10 ml) added; toluene-*p*-sulphonamide (1.46 g) was collected. Chromatography (benzene-ethyl acetate) gave unchanged azide (530 mg), compound (XI; R = H, Y = S) (250 mg), compound (XIII; R = H) (620 mg, total yield 60%), and toluene-*p*-sulphonamide (690 mg). The reaction between the thione (1 g) and Cbs azide gave (XIII; R = H) (62%), *p*-chlorobenzenesulphonamide (64%), and (XI; R = H, Y = S) (220 mg).

$\Delta^{3,3'}$ -Bi-indoline-2,2'-dithione (XI; R = H, Y = S) formed yellow-brown prisms, m.p. 243—246° (decomp.) (from acetonitrile) (Found: C, 65.5; H, 3.9; N, 9.5; S, 21.0. C₁₆H₁₀N₂S₂ requires C, 65.3; H, 3.4; N, 9.5; S, 21.8%); λ_{\max} 224, 289, and 336sh nm (measured on saturated solution; ϵ_{\max} not determined); ν_{\max} 3350, 3370, and 3410 cm⁻¹; τ [(CD₃)₂SO] -1.94 and -1.40 (exchanged in D₂O) (NH and SH indicating tautomerism), 1.54 (m), and 2.4—3.2 (m) (the spectrum was weak and poorly resolved); *m/e* 294 (*M*, 79%), 293 (32%), 262 (*M* - S, 100%, *m** 233.5), 261 (67%), and 235 (262 - HCN, 21%, *m** 210.8).

Reaction of 1-Methylindoline-2-thione with Tosyl Azide.—The thione (2 g) was added in portions to a solution of the azide (2.42 g) in pyridine (20 ml). After 1 h the solvent was removed and methanol (10 ml) added. The solid which separated was recrystallised from pyridine-methanol (yield 1.0 g). The compound formed orange-coloured prisms, m.p.

209—210°. 1,1'-Dimethyl- $\Delta^{3,3'}$ -bi-indoline-2,2'-dithione (XI; R = Me, Y = S) separated from chloroform-methanol as a red-brown amorphous solid, m.p. 213—215° (Found: C, 67.9; H, 4.5; N, 8.9. C₁₈H₁₄N₂S₂ requires C, 67.1; H, 4.4; N, 8.7%); λ_{\max} (CHCl₃) 237, 291, 304, and 317 nm (ϵ 273,000, 127,000, 122,000, and 118,000) λ_{\min} 275 nm (ϵ 113,000); i.r. spectrum showed nothing informative above 1400 cm⁻¹; *m/e* 322 (*M*, 47%), 290 (*M* - S, 100%, *m** 261.2), 275 (290 - Me, 74%, *m** 260.6) and 260 (275 - Me, 28%, *m** 245.8). The methanolic mother liquors were evaporated and benzene added yielding toluene-*p*-sulphonamide (1.82 g). Chromatography then gave compound (XI; R = Me, Y = S) (750 mg) and 4-methyl[1,2,3]thiadiazolo[5,4-b]indole (XIII; R = Me), needles, m.p. 91—92° (from ethanol) (yield 105 mg) (Found: C, 57.3; H, 4.1; N, 22.2; S, 16.9. C₉H₇N₃S requires C, 57.1; H, 3.7; N, 22.2; S, 16.9%); λ_{\max} 222, 257, 272, 277sh, and 313 nm (ϵ 44,400, 13,800, 12,300, 11,800, and 6040); i.r. spectrum showed nothing informative; τ 1.89 (1H, m), 2.5—2.8 (3H, m), and 6.14 (s, NMe); *m/e* 189 (*M*, 89%), 161 (55%), 160 (43%), 146 (59%), 120 (37%), and 117 (100%).

To a solution of 1-methylindoline-2-thione (500 mg) in acetic acid (5 ml) was added *p*-nitrosodimethylaniline (250 mg). The solution was boiled for 15 min and the dark red solid (390 mg) collected; m.p. 210—213°, identical (t.l.c. and i.r. spectrum) with the compound obtained by treating the thione with tosyl azide.

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