The Reactions of Arenesulphonyl Azides with Indole and with 1-Methylindole

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Heating indole with arenesulphonyl azides yields 2-arylsulphonyliminoindolines; similar treatment of 1-methylindole affords mainly the 2-arylsulphonylimino-1-methylindolines with, as minor products, the 3-arylsulphonylaminoindoles. In the presence of pyridine, 2-arylsulphonylimino-3-diazoindolines are formed.

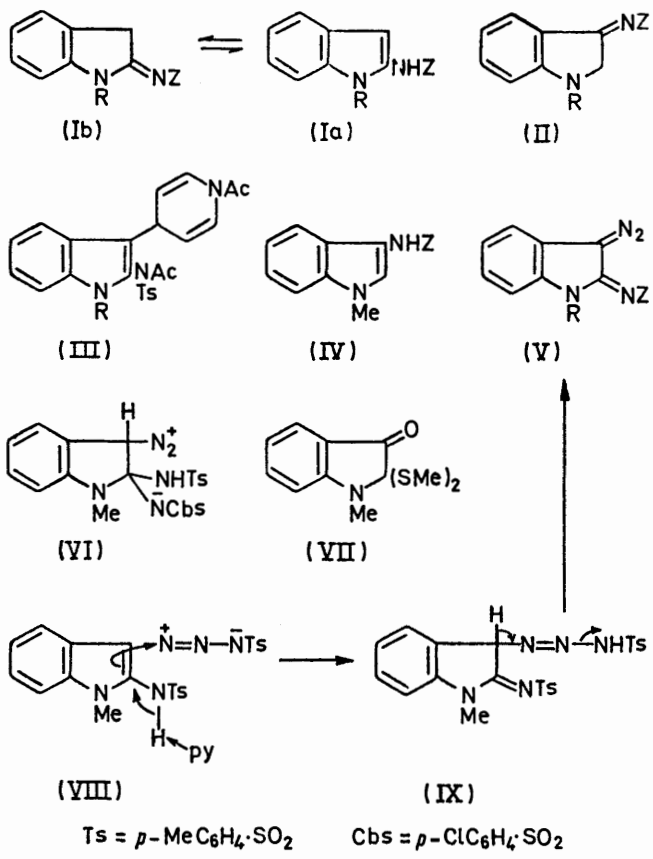
WE have reported briefly[1,2] on the reaction of arenesulphonyl azides with indole and also with 1-methylindole; we now give the details of this work.

Indole reacts smoothly with tosyl azide and with *p*-acetylaminobenzenesulphonyl azide, forming compounds to which we assign structures (I; R = H, Z = Ts) and (I; R = H, Z = *p*-AcNH·C_6H_4·SO_2). In dimethyl sulphoxide solution there is present an equilibrium mixture of the two forms (Ia) and (Ib). For compound (I; R = H, Z = Ts) the value of the equilibrium constant, $K = [(Ia)]/[(Ib)]$, is 1·08; this was measured by comparing the intensity of the n.m.r. signal at τ 4·23 [C(3)H of (Ia)] with that at 5·87 [C(3)H_2 of (Ib)]. For compound (I; R = H, Z = *p*-AcNH·C_6H_4·SO_2), $K = 1{\cdot}12$. It was impossible to examine the n.m.r. spectra of solutions in [^{2}H]chloroform. If these compounds had the alternative structures (II) they would be orange in colour and show a strong fluorescence.[3,4]

Warming 1-methylindole with tosyl azide at 55° gave 1-methyl-2-*p*-tolylsulphonylaminoindoline (I; R = Me, Z = Ts). With *p*-chlorobenzenesulphonyl azide (CbsN$_3$), 1-methylindole reacted smoothly at room temperature forming compound (I; R = Me, Z = Cbs); at 50° the

[1] A. S. Bailey, M. C. Churn, and J. J. Wedgwood, *Tetrahedron Letters*, 1968, 5953.
[2] A. S. Bailey, W. A. Warr, G. B. Allison, and C. K. Prout, *J. Chem. Soc.* (*C*), 1970, 956.
[3] A. S. Bailey, R. Scattergood, and W. A. Warr, *J. Chem. Soc.* (*C*), 1971, 2479.
[4] A. S. Bailey, A. J. Buckley, and W. A. Warr, *J.C.S. Perkin I*, 1972, 1626.

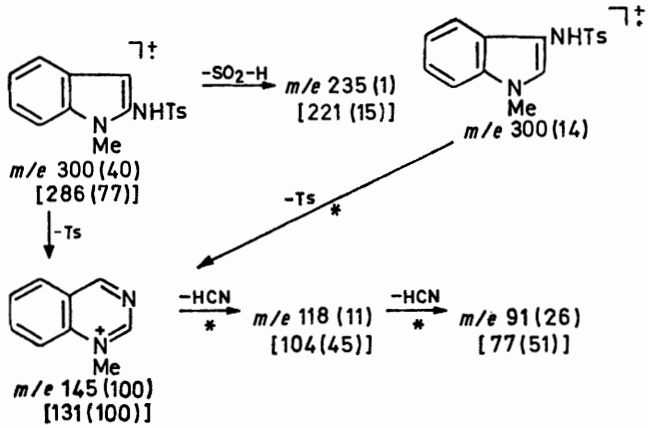
reaction was violent. In chloroform solution the two compounds were entirely in form (Ib) but the n.m.r. spectrum of a solution in dimethyl sulphoxide of compound (I; R = Me, Z = Ts) shows the presence of 15%



of form (Ia) and for (I; R = Me, Z = Cbs) the presence of 10% of form (Ia). Both compounds (I; R = H, Z = Ts) and (I; R = Me, Z = Ts) reacted with acetic anhydride in pyridine solution giving compounds (III; R = H) and (III; R = Me) in high yield. Similar reactions are known [5] with simple indoles.

A second compound, isomeric with (I; R = Me, Z = Ts), was isolated from the reaction between 1-methylindole and tosyl azide. The mass spectrum gave little structural information but the u.v. spectrum was similar to that of 1,2-dimethyl-3-*p*-tolylsulphonylaminoindole.[6] The position of the *N*-methyl signal in the n.m.r. spectrum of the compound indicated that it was an indole and not an iminoindoline; we consider it to be the 3-substituted compound (IV; Z = Ts). The spectral data indicated the absence of any significant quantity of the tautomeric structure (II; R = Me, Z = Ts). The n.m.r. spectrum ($CDCl_3$) contained the following signals: τ 7·67 (tosyl Me), 6·32 (3H, s, NMe), 3·47 (1H, NH, exchanged in D_2O), and 2·35 (2H, d, *J* 8 Hz, low-field half of tosyl signal); the other aromatic protons formed a complex multiplet (2·6—3·2) but one signal (τ 3·0) appeared to be a singlet and was tentatively assigned to C(2)H. In the presence of tris[perfluorobutyryl-(pivaloyl)methanato]europium(III) [Eu(fod)$_3$] (0·78 mol. equiv.) the signals appeared at the following values: τ 7·32 (tosyl Me), 6·00 (NMe), 2·24 (high-field half of tosyl signal), −0·74 (low-field half of tosyl signal), 1·88 [1H, s, C(2)H], and −2·02 (NH). Dr. R. E. Richards measured the n.m.r. spectrum of a solution in [$^2H_6$]dimethyl sulphoxide at 270 MHz and observed the following signals: τ 7·70 (tosyl Me), 6·33 (NMe), 3·17 and 2·99 [two triplets, 1H each, from C(5)H and C(6)H (definite allocation between these two not made)], 2·96 [1H, sharp s, C(2)H], 2·80 and 2·45 (tosyl group signals), and 2·75 [two superimposed doublets belonging to C(4)H and C(7)H]. An *X*-ray crystal structure determination for compound (IV) has[7] confirmed our assignment.

In the presence of a base such as pyridine the reaction between 1-methylindole and arenesulphonyl azides takes a different course, compounds (V; R = Me, Z = Ts) and (V; R = Me, Z = Cbs) being obtained in high yield. These compounds must be formed *via* structure (I), since treating compound (I; R = Me, Z = Ts) with tosyl azide in the presence of pyridine gave (V; R = Me, Z = Ts), and under these conditions (I; R = H, Z = Ts) yielded (V; R = H, Z = Ts). Two possible routes may be considered for the transformation of



SCHEME 1 Principal fragments in the mass spectra of compounds (I) and (IV); figures in square brackets refer to compound (I; R = H, Z = Ts)

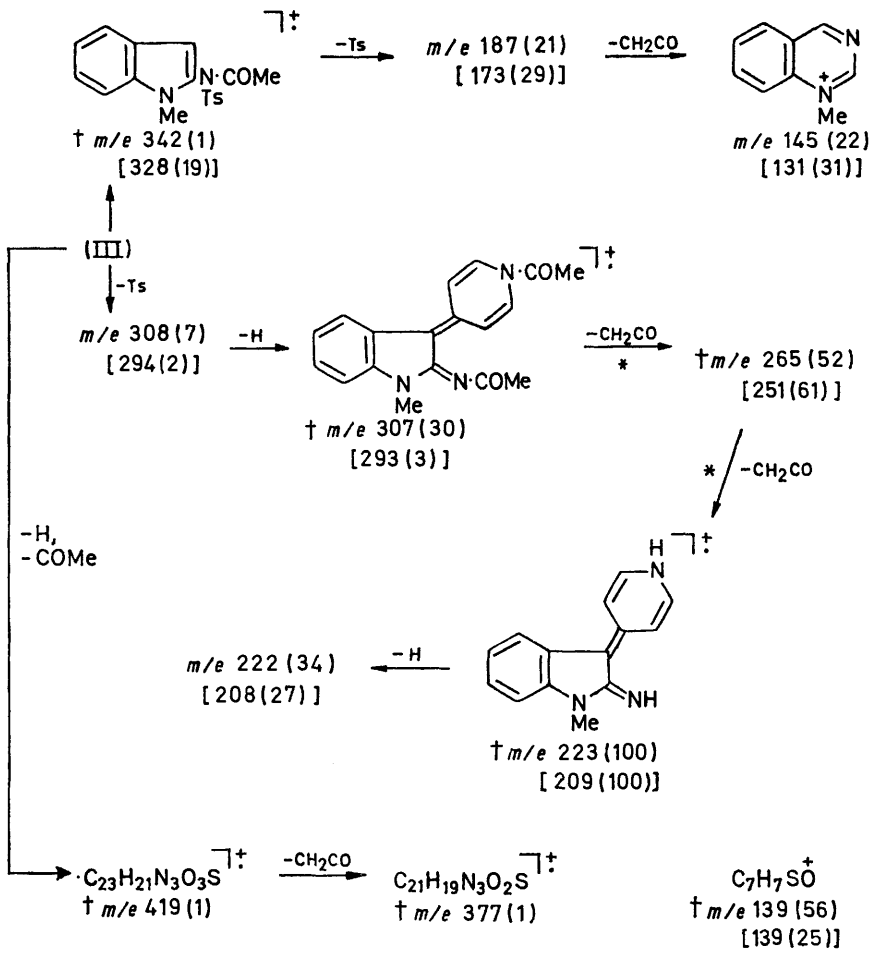
(I) ⟶ (V). In the first the azide adds to the indole (Ia), forming an adduct of type (VI); compound (VII) is known [8] and so structure (VI) is plausible. Compound (VI) then eliminates a molecule of arenesulphonamide, forming structure (V). If a compound of type (VI) is formed then *either* treating (I; R = Me, Z = Ts) with *p*-chlorobenzenesulphonyl azide *or* treating (I; R = Me, Z = Cbs) with tosyl azide ought to give the 'mixed' compound (VI) as a common intermediate, and so one ought to obtain the same diazo-compound (V;

[5] H. v. Dobeneck and W. Goltzsche, *Chem. Ber.*, 1962, **95**, 1484; H. Deubel, D. Walkenstein, H. Jokisch, T. Messerschmitt, S. Brodka, and H. v. Dobeneck, *ibid.*, 1971, **104**, 705; J. Bergman, *J. Heterocyclic Chem.*, 1970, **7**, 1071.

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

[7] B. Denton and C. K. Prout, unpublished results.

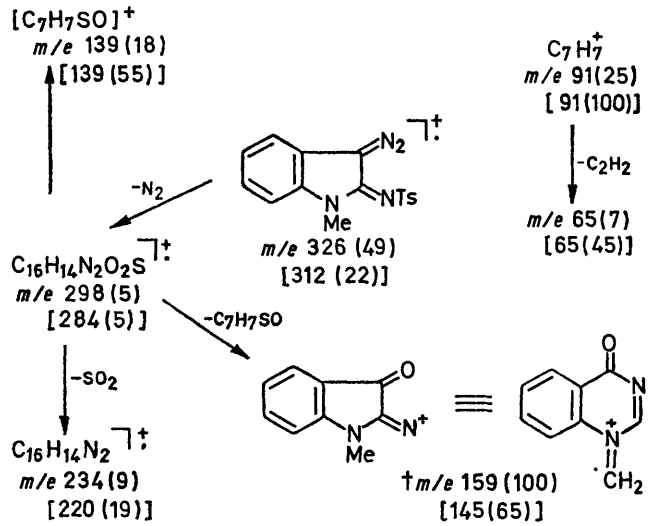
[8] J. T. Baker and C. C. Duke, *Tetrahedron Letters*, 1972, 307.



SCHEME 2 Mass spectral fragmentation of compound (III), the figures in square brackets refer to (III; R = H), and compositions confirmed by high resolution measurements are indicated by a dagger

R = Me, Z = Ts or Cbs) or a mixture of the two diazo-compounds. However when compound (I; R = Me, Z = Ts) was warmed with *p*-chlorobenzenesulphonyl azide in pyridine solution compound (V; R = Me, Z = Ts) was formed in high yield; similarly (I; R = Me, Z = Cbs) and tosyl azide gave (V; R = Me, Z = Cbs); *i.e.* no arylsulphonyl exchange occurred. For this reason we favour the alternative route involving direct attack of the indole on the azide [(VIII) ⟶ (IX) ⟶ (V)].[9]

The main fragmentations in the mass spectra of compounds (I) and (IV) are set out in Scheme 1. The molecular ion (*m/e* 300) in the spectrum of (IV; Z = Ts) was much less abundant than that of its isomer. In the mass spectra of compounds (III) the molecular ions were not detected. There are two fragmentation pathways, set out in Scheme 2. These spectra contained signals at *m/e* 139 which were fairly intense; this fragment, C_7H_7SO, has been observed in the spectra of sulphonamides, but the peak is generally of low intensity.[10] Scheme 3 shows the main fragmentations of



SCHEME 3 Principal mass spectral fragmentations of the diazo-compounds (V); figures in square brackets refer to (V; R = H)

[9] M. Regitz, *Angew. Chem. Internat. Edn.*, 1967, **6**, 733.
[10] S. Aftalion and G. Proctor, *Org. Mass Spectrometry*, 1969, **2**, 337; A. Bhati, R. A. W. Johnstone, and B. J. Millard, *J. Chem. Soc.* (*C*), 1966, 358; M. F. Grostic, R. J. Wnuk, and F. A. MacKellar, *J. Amer. Chem. Soc.*, 1966, **88**, 4664.

the diazo-compounds (V). Loss of nitrogen and of sulphur dioxide gave rise to small peaks, but very intense peaks (*m/e* 159, 145) are produced by transfer of oxygen to C-3 of the indole nucleus from the arylsulphonyl group. For compound (V; R = H, Z = Ts) the base peak appeared at *m/e* 91 (C_7H_7).

We have been informed by Dr. G. Wellman that he and Professor R. E. Harmon (Western Michigan University, Kalamazoo) have examined the reaction between 1-methylindole and tosyl azide; they have isolated and characterised both compounds (I; R = Me Z = Ts) and (IV; Z = Ts).

EXPERIMENTAL

General directions and instruments used have been reported.[3] The *N*-methylindole was purified by heating with sodium under nitrogen and was then distilled *in vacuo*.

2-p-*Tolylsulphonyliminoindoline* (I; R = H, Z = Ts).—Finely ground indole (3 g) was mixed with tosyl azide (4 g) and the mixture kept at 50° for 36 h. Methanol (30 ml) was added and the solid (4·4 g) collected. Two recrystallisations from n-propanol–acetic acid (7 : 3) gave colourless *needles* (I; R = H, Z = Ts), m.p. 208—209° (decomp.) (Found: C, 63·0; H, 5·2; N, 10·0. $C_{15}H_{14}N_2O_2S$ requires C, 63·0; H, 5·0; N, 9·8%); $\nu_{max.}$ (Nujol) 3100br (NH), 1610, and 1595 cm^{-1}; τ [$(CD_3)_2SO$] −1·56 (NH), −0·86 (NH), −0·55 (NH), 2—3·2 (8H, m, Ar), 4·23br [s, C(3)H of (Ia)], 5·87 [s, C(3)H_2 of (Ib)], and 7·61 (3H, s, tosyl Me].

The compound (0·8 g) was dissolved in a mixture of pyridine (5 ml) and acetic anhydride (5 ml). Next day the mixture was poured into methanol (5 ml) containing 2M-hydrochloric acid (5 ml). The solid was collected (1·08 g) and recrystallised from ethyl acetate. 1-*Acetyl*-1,4-*dihydro*-4-[2-(N-*acetyl*-p-*tolylsulphonylamino*)*indol*-3-*yl*]*pyridine* (III; R = H) formed white plates, m.p. 150—160° (decomp.) (Found: C, 64·2; H, 5·3; N, 9·5. $C_{24}H_{23}N_3O_4S$ requires C, 64·2; H, 5·2; N, 9·4%); $\nu_{max.}$ 1732, 1658 (CO), and 3240 (NH) cm^{-1}; τ [$(CD_3)_2SO$] −1·6 (NH), 1·8—3·3 [10H, m, Ar, C(2′)H, C(6′)H], 4·80—5·20 [2H, m, C(3′)H, C(5′)H], 5·70br [1H, C(4′)H], 7·54 (3H, s, TsN·CO·CH_3), 7·71 (3H, s, tosyl Me), and 8·10 (3H, s, pyridine N·CO·CH_3).

1-*Methyl*-2-p-*tolylsulphonyliminoindoline* (I; R = Me, Z = Ts).—A mixture of tosyl azide (8·0 g) and 1-methylindole (6·0 g) was heated (55°) for 24 h. Methanol was added and the solid collected (10·5 g). Recrystallisation from n-propanol–acetic acid followed by n-propanol gave *plates* (I; R = Me, Z = Ts), m.p. 200—201° (Found: C, 64·2, 64·1; H, 5·4, 5·4; N, 9·4, 9·3; S, 10·7. $C_{16}H_{16}N_2O_2S$ requires C, 64·0; H, 5·3; N, 9·3; S, 10·7%); $\nu_{max.}$ ($CHCl_3$) 1496, 1570br,s, and 1623w cm^{-1}; $\lambda_{max.}$ 220 and 281 nm (ε 26,600 and 23,000); τ ($CDCl_3$) 7·71 (tosyl Me), 6·65 (3H, s, NMe), 5·81 [2H, s, C(3)H_2], 2·5—3·1 (6H, m, Ar), and 2·08 (2H, d, *J* 8 Hz, low-field half of tosyl group); τ [$(CD_3)_2SO$] 6·68 (NMe, indoline form), 6·44 (NMe, indole form), 5·82 [C(3)H_2, indoline form], and 4·12 [C(3)H, indole form]; τ (CF_3·CO_2H) 7·45 (tosyl Me), 6·18 (3H, s, NMe), 5·42 (2H, s, CH_2), 2·25—2·60 (6H, m, Ar), and 1·95 (2H, d, *J* 9 Hz, low-field half of tosyl signal).

1-*Acetyl*-1,4-*dihydro*-4-[2-(N-*acetyl*-p-*tolylsulphonylamino*)-1-*methylindol*-3-*yl*]*pyridine* (III; R = Me).—Acetic anhydride (4 ml) was added to a solution of compound (I; R = Me, Z = Ts) (0·2 g) in pyridine (2 ml). After 2 days methanol (5 ml) was added followed by 2M-hydrochloric acid. The solid was collected, washed with water, dried, and recrystallised from chloroform–methanol to give colourless *crystals* (0·16 g), m.p. 140—141° (Found: C, 64·2; H, 5·2; N, 9·6; S, 6·4. $C_{25}H_{25}N_3O_4S$ requires C, 64·8; H, 5·4; N, 9·1; S, 6·9%), $\nu_{max.}$ ($CHCl_3$) 1520br, 1562w, 1600, 1631, 1671, and 1721 cm^{-1}; τ ($CDCl_3$) 8·12 (3H, s, pyridine N·CO·CH_3), 7·70 (3H, s, tosyl Me), 7·53 (3H, s, SO_2·N·CO·CH_3), 6·36 (3H, s, indole NMe), 5·76br [1H, s, C(4′)H], 4·89—5·12 [2H, m, C(3′)H and C(5′)H], and 1·9—3·5 (10H, m, Ar, C(2′)H, and C(6′)H].

1-*Methyl*-3-(p-*tolylsulphonylamino*)*indole* (IV; Z = Ts).—Freshly prepared 1-methylindole (5 g) and tosyl azide (7·5 g) were heated (55°) for 24 h. Methanol (20 ml) was then added and the solid collected (9 g). Analysis of the mixture (n.m.r.) showed that the product contained 65% (I; R = Me, Z = Ts) and 35% (IV; Z = Ts). The solid was dissolved in boiling chloroform and the solution allowed to cool slowly; next day *compound* (IV; Z = Ts) (0·9 g) was collected (m.p. 182°); it formed white prisms, m.p. 184—185° (from benzene) (Found: C, 63·7; H, 5·1; N, 9·2; S, 10·5. $C_{16}H_{16}N_2O_2S$ requires C, 64·0; H, 5·3; N, 9·3; S, 10·7%); $\nu_{max.}$ (Nujol) 1595w, 1618w, and 3245m (NH) cm^{-1}; $\lambda_{max.}$ 222 and 284 nm (ε 42,100 and 6360); τ [$(CD_3)_2SO$] 7·70 (tosyl Me), 6·33 (3H, s, NMe), 2·6—3·3 (7H, m, Ar), 2·39 (2H, d, *J* 8 Hz, low-field half of tosyl signal), 0·37 (1H, NH, exchanged by D_2O).

2-(p-*Chlorophenylsulphonylimino*)-1-*methylindoline* (I; R = Me, Z = Cbs).—A mixture of 1-methylindole (2·5 g) and *p*-chlorobenzenesulphonyl azide (4·0 g) was kept at room temp. for 24 h (at 55° the mixture ignited). Methanol (10 ml) was then added and the solid was collected (4 g). The n.m.r. spectrum showed the solid was a mixture of 80% (I; R = Me, Z = Cbs) and 20% 3-(*p*-chlorophenylsulphonylamino)-1-methylindole (IV; Z = Cbs). Recrystallisation from n-propanol gave *compound* (I; R = Me, Z = Cbs) (3 g), m.p. 189—190° (Found: C, 56·1; H, 4·0; Cl, 11·0; N, 8·7; S, 10·1. $C_{15}H_{13}ClN_2O_2S$ requires C, 56·2; H, 4·1; Cl, 11·1; N, 8·7; S, 10·0%); $\nu_{max.}$ (Nujol) 1565br cm^{-1}; $\lambda_{max.}$ 223 and 281 nm (ε 23,000 and 19,300); τ ($CDCl_3$) 6·65 (3H, s, NMe), 5·78 [2H, s, C(3)H_2], 2·5—3·2 (6H, m, Ar), and 2·08 (2H, d, *J* 8 Hz, low-field half of Cbs signal); the spectrum in $(CD_3)_2SO$ showed the presence of 10% of the indole form and contained the following signals: τ 6·71 (s, indoline NMe), 6·44 (s, indole NMe), 5·81 [C(3)H_2 indoline], 4·15 [C(3)H, indole], 2·2—3·0 (m, Ar), 2·08 (d, *J* 8 Hz, low-field half of Cbs in indoline form), and −0·35br (s, NH, exchanged in D_2O). Prolonged shaking (24 h) led to exchange of protons at C-3 and disappearance of the signals at τ 4·15 and 5·81.

3-*Diazo*-2-p-*tolylsulphonyliminoindoline* (V; R = H, Z = Ts).—A mixture of 2-*p*-tolylsulphonyliminoindoline (1 g), tosyl azide (2 g), and pyridine (1 ml) was heated for 24 h at 55°. To the purple melt, methanol (3 ml) was added. The mixture was boiled and then cooled, and the solid (0·53 g) was collected. The *compound* formed purple-coloured needles (from benzene), m.p. 186° (decomp.) (Found: C, 57·7; H, 4·0; N, 17·1; S, 10·5. $C_{15}H_{12}N_4O_2S$ requires C, 57·7; H, 3·9; N, 18·0; S, 10·3%); $\nu_{max.}$ (Nujol) 1580br, 1600, 2020 (CN_2), and 3280 (NH) cm^{-1}; $\lambda_{max.}$ 242, 275, 315, and 341 nm (ε 11,900, 29,800, 7220, and 6600); τ [$(CD_3)_2SO$] 7·64 (s, tosyl Me), 2·3—3·0 (6H, m, Ar), 2·14 (2H, d, *J* 8 Hz, low-field half of tosyl signal), and −1·55 (1H, s, NH exchanged in D_2O).

3-*Diazo*-1-*methyl*-2-p-*tolylsulphonyliminoindoline* (V; R = Me, Z = Ts).—(*a*) 1-Methylindole (10 g) and tosyl azide

(35 g) were mixed with pyridine (1 ml) and the mixture was heated (55°) for 24 h. Effervescence had then ceased and the resulting glass was boiled with methanol (20 ml); the mixture was cooled and the solid collected (20 g, 87%); m.p. 164—166° (decomp.). The *compound* formed pale orange-coloured needles (from ethyl acetate), m.p. 169—171° (decomp.) (Found: C, 59·3; H, 4·3; N, 16·5; S, 10·1. $C_{16}H_{14}N_4O_2S$ requires C, 58·9; H, 4·3; N, 17·2; S, 9·8%); $\nu_{max.}$ ($CHCl_3$) 1560m, 1600m, and 2130s cm^{-1}; $\lambda_{max.}$ (200—350 nm in EtOH, 350—650 nm in $CHCl_3$) 215, 246, 277, 314, and 442 nm (ε 28,300, 13,600, 28,400, 5860, and 90); τ ($CDCl_3$) 7·61 (tosyl Me), 6·58 (3H, s, NMe), 2·6—3·1 (6H, m, Ar), and 2·11 (2H, d, *J* 8 Hz, low-field half of tosyl signal).

(*b*) 1-Methyl-2-*p*-tolylsulphonyliminoindoline (1 g) and tosyl azide (2 g) were mixed with pyridine (1 ml) and the mixture was heated to 55° for 24 h. Methanol (3 ml) was added and the solid (0·8 g) collected and washed with methanol. The crude solid [m.p. 165—168° (decomp.)] showed one spot on t.l.c. and on recrystallisation from ethyl acetate gave compound (V; R = Me, Z = Ts), m.p. 169—171°, identical (i.r. and n.m.r.) with sample prepared in (*a*).

(*c*) The reaction described in (*b*) was repeated with *p*-chlorobenzenesulphonyl azide (2 g) in place of tosyl azide. The crude solid product (0·7 g) (m.p. 166—169°) gave one spot on t.l.c. and was identical with the compound obtained in (*a*) (i.r. and n.m.r.) (Found: C, 58·8; H, 4·3; Cl, 0; N, 16·8; S, 9·9%).

2-p-*Chlorophenylsulphonylimino*-3-*diazo*-1-*methylindoline* (V; R = Me, Z = Cbs).—(*a*) A mixture of 1-methylindole (2·5 g), *p*-chlorobenzenesulphonyl azide (9·2 g), and pyridine (1 ml) was kept at room temperature overnight and then heated to 55° for 24 h. Methanol (10 ml) was added and the solid collected [m.p. 173—175° (decomp.); 6·0 g, 90%). It formed pale orange coloured *needles* (from ethyl acetate), m.p. 176—179° (decomp.) (Found: C, 52·2; H, 3·2; Cl, 10·2; N, 15·6; S, 9·3. $C_{15}H_{11}ClN_4O_2S$ requires C, 51·9; H, 3·2; Cl, 10·3; N, 16·2; S, 9·2%); $\nu_{max.}$ (Nujol) 1540br, 1573w, and 2115s cm^{-1}; $\lambda_{max.}$ 213, 277, 293sh, 330sh, and 405sh nm (ε 31,400, 26,500, 8100, 3000, and 90); τ [$(CD_3)_2SO$] 6·57 (3H, s, NMe), 2·3—2·9 (6H, m, Ar), and 2·13 (2H, d, *J* 8 Hz, low-field portion of $ArSO_2$ signal).

(*b*) 2-*p*-Chlorophenylsulphonylimino-1-methylindoline (0·33 g), tosyl azide (0·5 g), and pyridine (0·5 ml) were mixed and heated to 55° for 36 h. Methanol (5 ml) was added and the solid (0·20 g) collected. The solid showed one spot on t.l.c., had m.p. 172—173° (decomp.) (Found: C, 52·2; H, 3·2; Cl, 10·2; N, 15·6; S, 9·3%), and was identical with the product obtained in (*a*) (i.r., n.m.r., and mass spectra).

(*c*) The foregoing reaction was repeated with the indoline (0·5 g), *p*-chlorobenzenesulphonyl azide (0·5 g), and pyridine (1 ml) and gave compound (V; R = Me, Z = Cbs) (0·5 g) (Found: C, 52·1; H, 3·4; Cl, 9·9%).

2-p-*Acetylaminophenylsulphonyliminoindoline* (I; R = H, Z = *p*-AcNH·C_6H_4·SO_2).—Indole (0·5 g) was heated (50°; 36 h) with *p*-acetylaminobenzenesulphonyl azide (1 g), and methanol was added. The solid (1 g) was collected and recrystallised from methanol–chloroform (2 : 1) giving white *needles*, m.p. 230—232° (decomp.) (Found: C, 57·7; H, 4·8; N, 13·2; S, 9·8. $C_{16}H_{15}N_3O_3S$ requires C, 58·3; H, 4·6; N, 12·8; S, 9·7%); $\nu_{max.}$ (Nujol) 1595, 1610, 1678 (CO), 3100, and 3300 (NH) cm^{-1}; τ [$(CD_3)_2SO$] 7·90 (3H, s, CO·CH_3), 5·84 [s, C(3)H_2 of (Ib)], 4·20br [s, C(3)H of (Ia)], 2·0—3·2 (8H, m, Ar), −0·34 (1H, s, N*H*·COMe), −0·51 (NH), −0·90 (NH), and −1·59 (NH).

We thank Dr. and Mrs. R. E. Richards for measuring and interpreting the n.m.r. spectra, and Mr. A. E. Williams (I.C.I. Ltd., Organics Division) for measuring the mass spectrum of compound (III; R = Me) at high resolution.

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