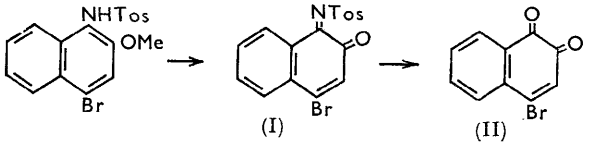
156. *Sulphonamides as a Source of Quinones.*

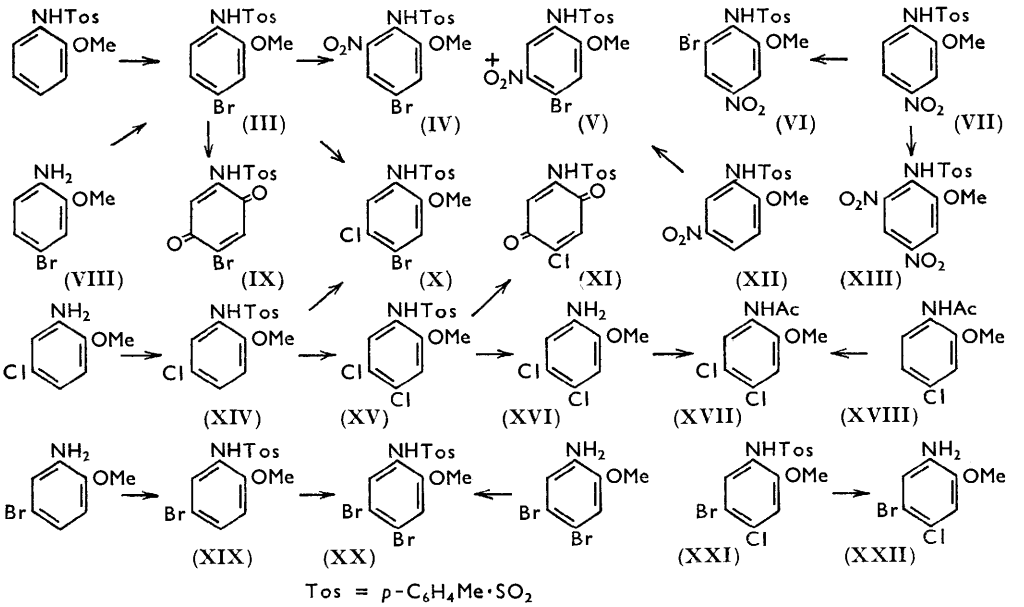
By F. Bell.

Although a naphthaquinone toluene-*p*-sulphonimide was hydrolysed by nitric acid to the 1,2-quinone, this reagent nitrated various *N*-toluene-*p*-sulphonylanisidines. Some of the sulphonylanisidines were converted into quinones by chromic acid but the sulphonamido-group remained intact during these reactions.

2-Methoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamines are readily oxidised to 1,2-naphthaquinone 1-toluene-*p*-sulphonimides,[1] *e.g.*, (I), and it appeared possible that the latter might by hydrolysis be made to yield *o*-quinones. It was found that the toluene-*p*-sulphonimido-group could be most conveniently removed by use of nitric acid and in this way 4-chloro- and 4-bromo-1,2-naphthaquinone (II) were readily obtained.



An attempt was next made to extend this reaction to similarly substituted *N*-toluene-*p*-sulphonyl-*o*-anisidines, which were prepared according to the accompanying flow sheet. First it was found that 4-nitro-2-methoxy-*N*-toluene-*p*-sulphonylaniline (VII) with nitric acid underwent, not oxidation, but further nitration the second nitro-



group entering position 6 (XIII). This may be contrasted with the nitration of the corresponding acetyl derivative to the 4,5-dinitro-derivative and underlines the much more powerful directing action of the toluene-*p*-sulphonamido-group than of the acetamido-group. The quantitative comparisons made by Orton and Bradfield [2] and Bradfield and Jones,[3] which suggest that the two groups have almost the same directing power, are true only for the rather unusual conditions of substitution which they used.

[1] Bell, *J.*, 1959, 524.
[2] Orton and Bradfield, *J.*, 1927, 986.
[3] Bradfield and Jones, *J.*, 1928, 3073.

Monobromination of 2-methoxy-*N*-toluene-*p*-sulphonylaniline was best accomplished by use of *N*-bromosuccinimide in pyridine. This 4-bromo-derivative (III) with nitric acid gave a mixture of nitro-derivatives (IV and V), and so chromic acid in acetic acid was employed for oxidation. There was obtained then in small yield a compound regarded as (IX).

Similarly oxidation of 4,5-dichloro-2-methoxy-*N*-toluene-*p*-sulphonylaniline (XV) by chromic acid gave a complex mixture from which was isolated a quinone regarded as (XI). Oxidation of 4,5-dibromo- (XX) and 4-bromo-5-chloro-2-methoxy-*N*-toluene-*p*-sulphonylaniline (X) led to no definite products.

Madesani [4] states that bromination of *o*-methoxyacetanilide yields the 5-derivative. In our hands his method led principally to the 4-derivative (cf. the tritylation of this compound [5]), although, in agreement with Madesani, we find the dibromination to lead to the 4,5-dibromo-derivative.

Experimental

4-Chloro-1,2-naphthaquinone.—Nitric acid (1 c.c.) in acetic acid (2 c.c.) was added to a warm solution of 4-chloro-1,2-naphthaquinone 1-toluene-*p*-sulphonimide [1] (1 g.) in acetic acid (10 c.c.). The resultant yellow solution was diluted to yield an orange-yellow precipitate, which after recrystallisation from acetic acid formed needles, m. p. 134—136°, alone or mixed with 4-chloro-1,2-naphthaquinone prepared by the method of Fieser and Dunn.[6] The latter was kindly supplied by Mr. H. G. Heller, A. H.-W. C., who has shown the description of this compound by Hodgson and Elliott [7] to be in error.[8]

*4-Bromo-1,2-naphthaquinone 1-Toluene-*p*-sulphonimide* (I).—Fuming nitric acid (2 c.c.) in acetic acid (4 c.c.) was added to a warm suspension of 4-bromo-2-methoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine (2 g.) in acetic acid (20 c.c.). The immediate red precipitate (1·6 g.; m. p. *ca.* 206°) gave the *imide* as red prisms, m. p. 212—214°, on recrystallisation from acetic acid (Found: C, 52·3; H, 3·4. $C_{17}H_{12}O_3NSBr$ requires C, 52·3; H, 3·1%). This compound was readily converted by nitric acid in acetic acid into 4-bromo-1,2-naphthaquinone, m. p. *ca.* 150°, the identity of which was confirmed by preparation of the quinoxaline derivative, needles, m. p. 186° (from acetic acid), and by conversion into 2-hydroxy-1,4-naphthaquinone anil, m. p. 266°, and 2-hydroxy-1,2-naphthaquinone, m. p. 186—188° (Fries and Schimmelschmidt [9] give m. p. 154°, 186°, 265°, and 189° respectively). 4-Bromo-2-ethoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine may be used in this preparation.

*Nitration of 2-Methoxy-*N*-toluene-*p*-sulphonylaniline.*—(*a*) Fuming nitric acid (1·25 c.c.) in acetic acid (2·75 c.c.) was added to the compound (2·5 g.) in warm acetic acid (20 c.c.). The slightly impure 4-nitro-derivative, m. p. 170—174° (2·1 g.), soon crystallised (lit.,[10] m. p. 175°). This nitro-compound was unchanged when heated with an excess of sulphuryl chloride or with an excess of chlorine in acetic acid. (*b*) Fuming nitric acid (2 c.c.) in acetic acid (2 c.c.) was added to the nitro-compound (2 g.) in warm acetic acid (20 c.c.), and after ½ hr. the mixture was diluted. The precipitate was repeatedly recrystallised from acetic acid to give rosettes of pale yellow prisms, m. p. 190—194°, of the *4,6-dinitro-derivative* (XIII) (Found: C, 46·3; H, 3·7. $C_{14}H_{13}O_7N_3S$ requires C, 45·8; H, 3·5%), which was immediately hydrolysed by cold sulphuric acid to 2-methoxy-4,6-dinitroaniline, m. p. 178° (acetyl derivative, m. p. 204°).

*2-Bromo-6-methoxy-4-nitro-*N*-toluene-*p*-sulphonylaniline* (VI).—*N*-Bromosuccinimide (1 mol.) was added to 2-methoxy-4-nitro-*N*-toluene-*p*-sulphonylaniline in pyridine. After ½ hr. the *product* was precipitated by addition of hydrochloric acid; it was recrystallised from acetic acid, eluted from alumina by ethyl acetate, and again recrystallised from acetic acid, forming pale yellow needles, m. p. 156° (Found: C, 42·1; H, 3·3. $C_{14}H_{13}O_5N_2SBr$ requires C, 41·9; H, 3·2%).

*Bromination of 2-Methoxy-*N*-toluene-*p*-sulphonylaniline.*—*N*-Bromosuccinimide (1 mol.) was

[4] Madesani, *Gazzetta*, 1932, **62**, 56.
[5] Chuchani, *J.*, 1959, 1753.
[6] Fieser and Dunn, *J. Amer. Chem. Soc.*, 1937, **59**, 1019.
[7] Hodgson and Elliott, *J.*, 1935, 1850.
[8] Heller, Dissertation for the Associateship of the Heriot-Watt College, 1959.
[9] Fries and Schimmelschmidt, *Annalen*, 1930, **484**, 270.
[10] A.-G. Anilinfabrik., D.R.-P. 157,859; 163,516.

added to the compound in pyridine; after a short while, the whole was treated with dilute hydrochloric acid. The residual brown plastic mass was dissolved in boiling ethanol and allowed to crystallise. The first crop (1·2 g.) was essentially unchanged material; the second crop (1·9 g.), on two further recrystallisations from ethanol, gave the 4-bromo-derivative as plates, m. p. 114° (Found: C, 47·8; H, 4·2. Calc. for $C_{14}H_{14}O_3NSBr$: C, 47·2; H, 3·9%), alternatively obtained from 4-bromo-2-methoxyaniline, which was prepared by Madesani's method.[4] This base is described by Madesani as 6-bromo-2-methoxyaniline but the true structure is given by Kohn.[11] Chromic acid (1 g.) in water (2 c.c.) was added to a warm solution of this monobromo-compound (0·6 g.) in acetic acid (6 c.c.). After the brisk reaction the mixture was diluted and the precipitate purified by repeated recrystallisation from acetic acid, to give in small yield golden-yellow prisms, m. p. 206—208° (Found: C, 44·0; H, 3·1; OMe, 0. $C_{13}H_{10}O_4NSBr$ requires C, 43·8; H, 2·8%). This compound, which gives a damson colour with concentrated sulphuric acid, is probably 2-*bromo*-5-*toluene*-p-*sulphonamido*-1,4-*benzoquinone* (IX).

Nitration of 4-*Bromo*-2-*methoxy*-N-*toluene*-p-*sulphonylaniline*.—Fuming nitric acid (1 c.c.) in acetic acid (1·5 c.c.) was added to the compound (1 g.) in warm acetic acid (10 c.c.). The mixture was allowed to cool and the crop separated by fractional crystallisation into cream-coloured needles, m. p. 224—227°, of the 6-*nitro-derivative* (IV) (Found: C, 42·2; H, 3·2. $C_{14}H_{13}O_5N_2SBr$ requires C, 41·9; H, 3·2%), and pale yellow prisms, m. p. 200—203° of the 5-*nitro-derivative* (V) (Found: C, 42·0; H, 3·4%); the latter was alternatively prepared by interaction of 2-*methoxy*-5-*nitro*-N-*toluene*-p-*sulphonylaniline* (XII) (Found: C, 52·2; H, 4·5. $C_{14}H_{14}O_5N_2S$ requires C, 52·2; H, 4·3%) and *N*-bromosuccinimide in pyridine. The compound (XII), prepared from 2-methoxy-5-nitroaniline and toluene-*p*-sulphonyl chloride in pyridine, crystallised from acetic acid in prisms, m. p. 200—201°; it was unchanged by sulphuryl chloride, and the bromination was incomplete. The crude bromination product was dissolved in acetone and passed down a column of alumina; the first fraction consisted of unchanged material; this was followed by an intermediate fraction, m. p. *ca.* 185°, and then by the 4-bromo-derivative.

2-*Methoxy*-4,5-*dinitro*-N-*toluene*-p-*sulphonylaniline*.—Fuming nitric acid (1·5 c.c.), diluted with acetic acid (1·5 c.c.), was added to the 5-nitro-compound (XII) (1·5 g.) in hot acetic acid (25 c.c.), and the mixture kept just below the b. p. for 10 min. The crop obtained on cooling recrystallised from acetic acid to yield the *dinitro-compound* as prisms, m. p. 222—224° (Found: C, 46·0; H, 3·9. $C_{14}H_{13}O_7N_3S$ requires C, 45·8; H, 3·5%). Dissolution of this in cold concentrated sulphuric acid gave 2-methoxy-4,5-dinitroaniline, m. p. 188—189° (acetyl derivative, m. p. 163°).

Chloro-compounds.—5-*Chloro*-2-*methoxy*-N-*toluene*-p-*sulphonylaniline*, obtained from the corresponding base and toluene-*p*-sulphonyl chloride in pyridine, crystallised from acetic acid in prisms, m. p. 140° (Found: C, 54·1; H, 4·4. $C_{14}H_{14}O_3NSCl$ requires C, 53·9; H, 4·5%). Excess of sulphuryl chloride was added to this compound (XIV) and, after the reaction had ceased, the excess was distilled off. The residual 4,5-*dichloro*-2-*methoxy*-N-*toluene*-p-*sulphonylaniline* (XV) formed needles, m. p. 163°, from acetic acid (Found: C, 48·6; H, 3·9. $C_{14}H_{13}O_3NSCl_2$ requires C, 48·6; H, 3·8%). This dichloro-derivative was obtained also by the action of excess of sulphuryl chloride on 2-methoxy-*N*-toluene-*p*-sulphonylaniline. With concentrated sulphuric acid it slowly gave 4,5-*dichloro*-2-*methoxyaniline* (XVI), which formed needles, m. p. 88°, from aqueous ethanol (Found: C, 44·6; H, 3·9. $C_7H_7ONCl_2$ requires C, 43·8; H, 3·6%). This base with cold acetic anhydride gave 4,5-*dichloro*-2-*methoxyacetanilide* (XVII), which crystallised from ethanol in prisms, m. p. 136—138° (Found: C, 46·2; H, 3·6. $C_9H_9O_2NCl_2$ requires C, 46·1; H, 3·8%); this was alternatively prepared by dropwise addition of sulphuryl chloride (2 mols.), diluted with chloroform, to a chloroform solution of 2-methoxyacetanilide.

Oxidation of 4,5-*Dichloro*-2-*methoxy*-N-*toluene*-p-*sulphonylaniline*.—Chromic acid (2 g.) in water (4 c.c.) was added to a warm solution of the compound (1 g.) in acetic acid (10 c.c.). The mixture was diluted and the precipitate crystallised from acetic acid, to yield yellow plates, m. p. 207—210°, sparingly soluble in benzene. This compound appears to be 2-*chloro*-5-*toluene*-p-*sulphonamido*-1,4-*benzoquinone* (XI) (Found: C, 50·1; H, 3·4; OMe, 0. $C_{13}H_{10}O_4NSCl$ requires C, 50·1; H, 3·2%). The mother-liquor contained material of lower m. p., which gave a deep-violet colour with concentrated sulphuric acid and had a perceptible

[11] Kohn, *J. Org. Chem.*, 1953, **18**, 530.

methoxyl content (4·8—6·6%). No definite product was isolated when 5-chloro-2-methoxy-*N*-toluene-*p*-sulphonylaniline was oxidised under the same conditions.

4-Bromo-5-chloro-2-methoxy-N-*toluene*-p-*sulphonylaniline*.—(*a*) *N*-Bromosuccinimide (1 mol.) was added to a solution of 5-chloro-2-methoxy-*N*-toluene-*p*-sulphonylaniline in pyridine. After a few minutes the product was precipitated by addition of hydrochloric acid and purified by recrystallisation from acetic acid. The *4-bromo-derivative* (X) formed prismatic needles, m. p. 157—159° (Found: C, 43·6; H, 3·5. $C_{14}H_{13}O_3NSClBr$ requires C, 43·0; H, 3·3%). (*b*) 4-Bromo-2-methoxy-*N*-toluene-*p*-sulphonylaniline was dissolved in an excess of sulphuryl chloride and the excess was then evaporated. The residual crystalline mass recrystallised from acetic acid, to yield a product, m. p. 157—159°, alone or mixed with that prepared as in (*a*). Oxidation of this bromochloro-compound with chromic acid in acetic acid gave only impure yellow material.

5-Chloro-2-methoxy-4-nitro-N-*toluene*-p-*sulphonylaniline*.—Fuming nitric acid (2 c.c.) in acetic acid (3 c.c.) was added to a warm solution of 5-chloro-2-methoxy-*N*-toluene-*p*-sulphonylaniline (2 g.) in acetic acid (20 c.c.). On cooling, the solution deposited the *mononitro-derivative*, which formed prisms, m. p. 173°, from acetic acid (Found: C, 47·4; H, 3·6. $C_{14}H_{13}O_5N_2SCl$ requires C, 47·1; H, 3·6%), quickly hydrolysed by concentrated sulphuric acid to *5-chloro-2-methoxy-4-nitroaniline*, needles (from ethanol), m. p. 133° (Found: C, 42·0; H, 4·0. $C_7H_7O_3N_2Cl$ requires C, 41·5; H, 3·5%) [*acetyl derivative*, needles, m. p. 198°, from acetic acid (Found: C, 44·6; H, 3·5. $C_9H_9O_4N_2Cl$ requires C, 44·2; H, 3·7%)]. Slightly more vigorous nitration gave *5-chloro-2-methoxy-4,6-dinitro*-N-*toluene*-p-*sulphonylaniline*, which crystallised from ethyl acetate in almost colourless needles, m. p. 238—240° (Found: C, 41·8; H, 2·8. $C_{14}H_{12}O_7N_3SCl$ requires C, 41·8; H, 3·0%), hydrolysed by cold sulphuric acid to *5-chloro-2-methoxy-4,6-dinitroaniline*, which crystallised from ethanol in bright yellow needles, m. p. 172—174° (Found: C, 33·5; H, 2·8. $C_7H_6O_5N_3Cl$ requires C, 33·9; H, 2·4%).

4,5-Dibromo-2-methoxyacetanilide[4] (10 g.) was hydrolysed by concentrated hydrochloric (20 c.c.) in boiling ethanol (50 c.c.) (1 hr.). After cooling, the hydrochloride of the base was collected and decomposed by aqueous ammonia to yield 4,5-dibromo-2-methoxyaniline, m. p. 104°, which with toluene-*p*-sulphonyl chloride in pyridine gave *4,5-dibromo-2-methoxy*-N-*toluene*-p-*sulphonylaniline*, needles, m. p. 170—172° (from acetic acid) (Found: C, 39·2; H, 3·1. $C_{14}H_{13}O_4NSBr_2$ requires C, 38·6; H, 3·0%). No pure compound was isolated from the material obtained by oxidation of this sulphonanilide with chromic acid in acetic acid.

4-Bromo-2-nitroanisole was prepared from *o*-nitroanisole by Kohn and Karlin's method.[12] The crude product contained a small amount of 4,6-dibromo-2-nitrophenol. The recrystallised monobromo-compound was reduced by Kohn and Karlin's method but the base was removed in steam. Towards the end of the distillation there was obtained a small amount of *5-bromo-4-chloro-2-methoxyaniline*, which crystallised from ethanol in scales, m. p. 110° (Found: C, 35·8; H, 3·2. $C_7H_7ONBrCl$ requires C, 35·6; H, 3·0%), and gave an *acetyl derivative*, needles (from ethanol), m. p. 138° (Found: C, 38·8; H, 3·4. $C_9H_9O_2NBrCl$ requires C, 38·8; H, 3·2%). The main product on solution in cold acetic anhydride gave *5-bromo-2-methoxyacetanilide*, which crystallised from ethanol in plates, m. p. 124° (Found: C, 44·3; H, 4·1. $C_9H_{10}O_2NBr$ requires C, 44·3; H, 4·1%) (Madesani[4] claimed to have isolated this compound by the bromination of *o*-acetanisidine but gives m. p. 159—160°). With toluene-*p*-sulphonyl chloride the base gave *5-bromo-2-methoxy*-N-*toluene*-p-*sulphonylaniline*, prisms (from acetic acid), m. p. 134° (Found: C, 47·5; H, 3·9. $C_{14}H_{14}O_3NSBr$ requires C, 47·2; H, 3·9%). The sulphonamide with *N*-bromosuccinimide in pyridine gave its 4,5-dibromo-derivative, m. p. 170—172° (above), with sulphuryl chloride gave the *4-chloro-derivative*, prisms, m. p. 172—174° (from acetic acid) (Found: C, 43·1; H, 3·2. $C_{14}H_{13}O_3NSBrCl$ requires C, 43·0; H, 3·3%), and with fuming nitric acid in acetic acid gave the *4-nitro-derivative*, prisms, m. p. 180—182° (from acetic acid) (Found: C, 42·4; H, 3·3. $C_{14}H_{13}O_5N_2SBr$ requires C, 41·9; H, 3·2%).

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[12] Kohn and Karlin, *Monatsh.*, 1927, **48**, 617.
[13] Anderson and Duncan, *Chem. and Ind.*, 1959, 457.