376. *Substitution in Arylsulphon-1- and -2-naphthalides.*

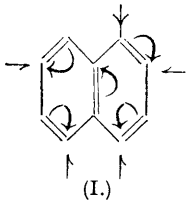
By Raphael Consden and Joseph Kenyon.

Although the recorded data are scanty, substitution in arylsulphon-1- and -2-naphthalides indicates that the sulphonamido-group has an activating power comparable with that of hydroxyl. Under mild conditions *p*-toluenesulphon-1-naphthalide gives the 2 : 4-dinitro-derivative, and the corresponding 2-naphthalide readily undergoes nitration in positions 1 and 6 (Morgan and Evens, J., 1919, **115**, 1127). Employing *m*-nitrobenzenesulphon-2-naphthalide, Bell (J., 1929, 2784) has shown that trinitration takes place in positions 1 : 6 : 8. The similarity in behaviour between a naphthol and a naphthalide is shown also by *p*-toluenesulphon-1 (and -2)-naphthalides undergoing coupling with diazotised amines as readily as do the corresponding naphthols (Witt, *Ber.*, 1894, **27**, 2370).

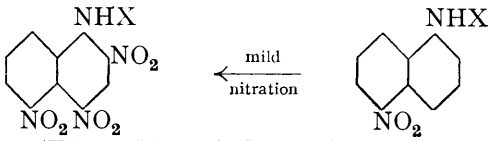
It appeared of interest to ascertain whether an arylsulphon-1-naphthalide would be nitrated in the same way as α-naphthol. In harmony with electronic considerations (I), the latter substance undergoes nitration in positions 2 : 4 : 5 and 2 : 4 : 7 (Ekstrand, *Ber.*, 1878, **11**, 162; Kehrmann and Haberkant, *ibid.*, 1898, **31**, 2420; Steiner, *ibid.*, 1900, **33**, 3285). By the nitration of 2 : 4-dinitro-α-naphthol with fuming nitric acid or a mixture of acetic and nitric acids 2 : 4 : 5- and 2 : 4 : 7-trinitro-α-naphthols were produced in the ratio of about 5 : 2; position 5 therefore appears to be more highly activated than position 7.

Nitration of m-*nitrobenzenesulphon-1-naphthalide* yields first the 2 : 4-*dinitro*-derivative;

further entry of a nitro-group occurs in position 5. Apparently no substitution takes place in position 7, but, since the 2 : 4 : 5-*trinitro*-derivative (II) is obtained under fairly mild conditions, there can be no doubt that position 5 is activated by the 1-arylsulphonamido-group. The trinitro-compound was oriented by its preparation from the 5-*nitro*-compound.



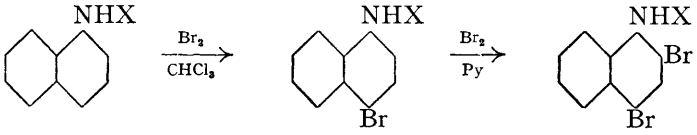
(I.)



(II.) (X = $NO_2 \cdot C_6H_4 \cdot SO_2$)

Attempts to prepare the 4-nitro-derivative by nitration of *p*-toluenesulphon-1-naphthalide in acetic acid solution or by means of dilute nitric acid yielded mainly 2 : 4-dinitro-1-*p*-toluenesulphon-naphthalide, a result in agreement with the findings of Hodgson and Walker (J., 1934, 180) : there was obtained, however, by the former procedure a small proportion of 2-*nitro*-1-p-*toluenesulphon-naphthalide*.

Bromination of *m*-nitrobenzenesulphon-1-naphthalide is in marked contrast to nitration. In chloroform solution, even with two molecular proportions of bromine, this substance gave only the 4-*bromo*-derivative (III). It has, however, been shown by Bell (J., 1931,



(III.) (IV.)

2340) that the reactivity of a sulphonamido-substituent is enhanced by salt formation in pyridine, owing to the production of a negative nitrogen pole : $\cdot NH \cdot SO_2R \longrightarrow \cdot \bar{N} \cdot SO_2R, \overset{+}{H}NC_5H_5$. When bromination by this method was tried, compound (III) gave an almost theoretical yield of the 2 : 4-*dibromo*-derivative (IV). Bromination of the unsubstituted naphthalide in pyridine solution with one molecular proportion of bromine gave a mixture of (IV) and unchanged material, so bromination of an arylsulphon-1-naphthalide in pyridine solution is parallel to nitration in acetic acid solution.

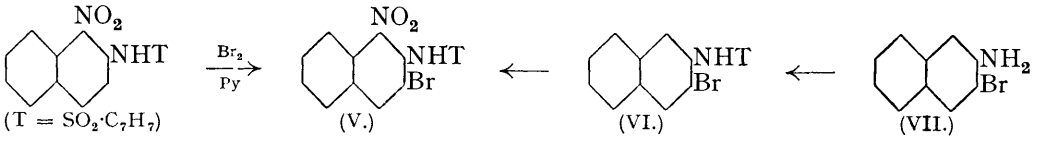
The failure of arylsulphon-1-naphthalides to undergo bromination in the 2-position by ordinary means is further exemplified by 4-nitro-1-*p*-toluenesulphon-naphthalide being unacted upon by bromine in chloroform solution, but yielding the 2-*bromo*-derivative in pyridine solution.

Bromination of 1-naphthalides is therefore in marked contrast to their nitration. Whereas three nitro-groups can be introduced with ease, only dibromination can occur, and special conditions are necessary for the entry of a bromine atom in the 2-position. This difference between bromination and nitration has an interesting analogy in the reactions of a 2-arylsulphonamidodiphenyl (Bell, *loc. cit.*) : 2-*m*-nitrobenzenesulphonamidodiphenyl undergoes facile trinitration in acetic acid solution; 2-*p*-toluenesulphonamidodiphenyl, in chloroform solution, undergoes monobromination only to give the 5-bromo-derivative, and this in pyridine solution undergoes further bromination in the 3-position.

Bromination of an arylsulphon-2-naphthalide in chloroform solution appears to proceed normally (Bell, J., 1932, 2732), to give first the 1-bromo- and then the 1 : 6-dibromo-derivative; bromination in chloroform solution therefore seems to be parallel to nitration in acetic acid solution. In pyridine solution, bromination occurs in the 1- and the 3-position (Bell, *loc. cit.*); this type of reaction has now been extended to 1-nitro-2-*p*-toluenesulphon-naphthalide, the analogous 3-*bromo*-1-*nitro*-2-*toluenesulphon-naphthalide* (V) being obtained.

The orientation of (V) indicated by the scheme below necessitated the preparation of 3-*bromo*-2-*naphthylamine* (VII); this was obtained by the reduction of 1 : 3-dibromo-2-

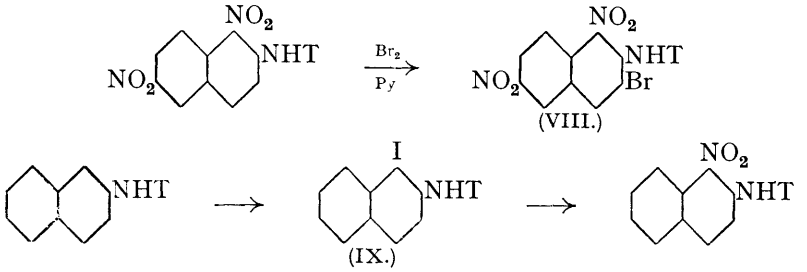
naphthylamine (Bell, *loc. cit.*) with tin and hydrochloric acid (cf. Franzen and Staüble, *J. pr. Chem.*, 1920, **101**, 58, on the reduction of brominated β-naphthols and β-naphthylamines).



The *naphthalide* (VI) on nitration in acetic acid solution yielded (V). 3-*Bromo*-1-*nitro*-2-*naphthylamine* on deamination gave 3-bromo-1-nitronaphthalene (Veselý and Chudozilow, *Chem. Listy*, 1925, **19**, 260; Hodgson and Elliott, J., 1934, 1705), which was identical with that obtained by the deamination of 2-bromo-4-nitro-1-naphthylamine.

1 : 6-Dinitro-2-*p*-toluenesulphon-naphthalide also underwent bromination in pyridine solution; the constitution of the product could not be proved owing to the failure of (V) to undergo further nitration, yet there can be little doubt that it is the 3-*bromo*-derivative (VIII), by analogy with the bromination product of the 1-nitro-naphthalide.

The above results show that bromination of 2-naphthalides is not in marked contrast to nitration as is the case with 1-naphthalides. Three substituting groups can be made to enter the nucleus, and in this respect 2-naphthalides bear an interesting analogy to 4-arylsulphonamidodiphenyls (Bell, J., 1928, 2118; 1930, 1076). Nitration takes place in positions 3 : 4′ : 5 and bromination by ordinary means in positions 3 : 4′ and then (in pyridine) in position 5; in both the naphthalene and the diphenyl series, bromination in pyridine appears to be homonuclear.



The enhanced reactivity of the sulphonamido-group in pyridine solution is further illustrated by the formation of iodo-derivatives. For example, *p*-toluenesulphon-2-naphthalide in pyridine solution gives the 1-*iodo*-derivative (IX) with iodine, iodine chloride, or iodine trichloride. This compound readily reacts with nitrous acid to give the 1-nitro-naphthalide, a reaction which serves to determine its constitution.

p-Toluenesulphon-*p*′-toluidide, 2-*p*-toluenesulphonamidodiphenyl, and 4-*p*-toluenesulphonamidodiphenyl also gave *iodo*-derivatives by each of these methods.

Experimental.

m-*Nitrobenzenesulphon*-1-*naphthalide*, obtained from the interaction of α-naphthylamine and *m*-nitrobenzenesulphonyl chloride in pyridine, formed plates, m. p. 162—164°, from acetic acid (Found : N, 8·6. $C_{16}H_{12}O_4N_2S$ requires N, 8·5%).

Nitration. (a) The naphthalide (30 g.) was suspended in acetic acid (240 c.c.) and warmed gently on the steam-bath with the addition of concentrated nitric acid (18 c.c.) in acetic acid (18 c.c.). Nitration occurred with dissolution of the naphthalide. After cooling, the yellow crystalline precipitate of 2 : 4-*dinitro*-1-m-*nitrobenzenesulphon-naphthalide* was collected and recrystallised from acetic acid, forming needles (24 g.), m. p. 185—188° (Found : N, 13·4. $C_{16}H_{10}O_8N_4S$ requires N, 13·4%). Hydrolysis with concentrated sulphuric acid furnished 2 : 4-dinitro-1-naphthylamine, m. p. 235°.

(b) The dinitro-naphthalide (5 g.) was added slowly to ice-cold fuming nitric acid (15 c.c.). After ¼ hour, the solution was diluted with acetic acid (20 c.c.) and filtered from 2 : 4 : 5-*trinitro*-1-m-*nitrobenzenesulphon-naphthalide*, m. p. 215° (decomp.) after recrystallisation from

acetic acid (Found : N, 14·8. $C_{16}H_9O_{10}N_5S$ requires N, 15·1%). Apart from a further quantity of this substance, no other product was obtained by dilution of the mother-liquor.

(c) The dinitro-naphthalide (5 g.) was gently heated on the water-bath with a mixture of acetic acid (10 c.c.) and fuming nitric acid (10 c.c.). Nitration occurred with dissolution of the naphthalide and, on cooling, the 2 : 4 : 5-trinitro-derivative separated, identical with that obtained in (b).

5-*Nitro*-1-m-*nitrobenzenesulphon-naphthalide*, obtained by the interaction in pyridine solution of *m*-nitrobenzenesulphonyl chloride and 5-nitro-α-naphthylamine (Morgan and Micklethwaite, J., 1906, **89**, 7), formed plates, m. p. 208—210°, from acetic acid or alcoholic pyridine (Found : N, 11·5. $C_{16}H_{11}O_6N_3S$ requires N, 11·3%).

Nitration. A mixture of this compound (2 g.) with acetic acid (15 c.c.) and nitric acid (2 c.c.) was warmed gently. The naphthalide dissolved and was thereafter precipitated as the 2 : 4 : 5-trinitro-derivative, m. p. 215° alone or mixed with that from (b) or (c) above. This substance on solution in hot pyridine and dilution with alcohol separated as the *pyridine* salt, m. p. 170—175° (Found : N, 15·2. $C_{16}H_9O_{10}N_5S,C_5H_5N$ requires N, 15·5%), which was reconverted into the naphthalide by admixture with hydrochloric acid or crystallisation from acetic acid.

Bromination of m-*Nitrobenzenesulphon*-1-*naphthalide.*—(a) To this compound (6 g.) in chloroform (25 c.c.), bromine (2 c.c.; 2 mols.) in chloroform (5 c.c.) was added. After the initial vigorous reaction, accompanied by evolution of hydrogen bromide, had abated, the solution was heated under reflux for 1 hour. The crystalline precipitate of 4-*bromo*-1-m-*nitrobenzenesulphon-naphthalide* was collected after cooling and recrystallised from acetic acid, forming colourless plates (7 g.), m. p. 174—176° (Found : Br, 19·3. $C_{16}H_{11}O_4N_2BrS$ requires Br, 19·7%). Its identity was established by hydrolysis with ice-cold concentrated sulphuric acid to give 4-bromo-α-naphthylamine, m. p. 102° (acetyl derivative, m. p. 193°).

(b) To a solution of the 4-bromo-naphthalide (2·5 g.) in pyridine, bromine (0·3 c.c.) was added drop by drop. After 12 hours, the semi-solid mass was triturated with hydrochloric acid, and the residue crystallised from a large bulk of acetic acid, from which it separated as short fine needles (2·6 g.), m. p. 232—233°. This was identical with the compound obtained from the interaction of 2 : 4-dibromo-α-naphthylamine (5 g.) and *m*-nitrobenzenesulphonyl chloride (3·7 g.) in pyridine and was therefore 2 : 4-*dibromo*-1-m-*nitrobenzenesulphon-naphthalide* (Found : N, 5·9. $C_{16}H_{10}O_4N_2Br_2S$ requires N, 5·8%).

Bromination of α-*Naphthylamine.*—The preparation of 2 : 4-dibromo-α-naphthylamine from the corresponding acetonaphthalide described by Meldola (J., 1883, **43**, 4; *Ber.*, 1878, **11**, 1904) is not a suitable method owing to the slowness with which 4-bromo-1-acetonaphthalide undergoes further bromination. A more convenient method has been found in the direct bromination of α-naphthylamine itself. α-Naphthylamine (28 g.), dissolved in acetic acid (100 c.c.), was added in the cold to a solution of bromine (22 c.c.) in acetic acid (200 c.c.). A pasty green mass was formed, and little hydrogen bromide evolved. The mixture was stirred on the water-bath with addition of a further quantity of acetic acid (100 c.c.). Hydrogen bromide was given off and the precipitate became white. The hydrobromide of 2 : 4-dibromo-α-naphthylamine was collected and washed with acetic acid, the yield being theoretical (75 g.). The salt (75 g.) was heated with alcohol (250 c.c.) under reflux, and a solution of sodium hydroxide (10 g.) in the minimum quantity of water added. Dissolution soon occurred, and after being filtered hot, 2 : 4-dibromo-α-naphthylamine, m. p. 116—118°, crystallised as brownish plates (acetyl derivative, m. p. 226°). Meldola (*loc. cit.*) gives m. p. 118—119° and 225° respectively.

Bromination of 4-*Nitro*-1-p-*toluenesulphon-naphthalide.*—This substance was recovered unchanged after heating with a mixture of bromine and chloroform, but was brominated as follows : To 5 g. in pyridine, bromine (0·7 c.c.) was added drop by drop. After 12 hours the pyridine was removed by hydrochloric acid, and the gummy residue triturated with alcohol. Crystallisation from acetic acid furnished yellow rhombohedra, m. p. 193—195°, of 2-*bromo*-4-*nitro*-1-p-*toluenesulphon-naphthalide* (Found : N, 6·7. $C_{17}H_{13}O_4N_2BrS$ requires N, 6·65%). The constitution of this compound was confirmed by hydrolysis with ice-cold concentrated sulphuric acid to give 2-bromo-4-nitro-1-naphthylamine, m. p. 249° (Hodgson and Elliott, *loc. cit.*), alone or mixed with an authentic specimen.

Nitration of p-*Toluenesulphon*-1-*naphthalide.*—A mixture of the naphthalide (20 g.), acetic acid (100 c.c.), and concentrated nitric acid (7 c.c.) was shaken, the naphthalide rapidly dissolving with evolution of heat. After 20 minutes, yellow crystals of impure 2 : 4-dinitro-naphthalide appeared (cf. Hodgson and Walker, *loc. cit.*). The mother-liquors from the nitration mixture and recrystallisations were combined and diluted with water. The deposited gummy material

was dissolved in boiling alcohol, and the cold solution, after filtration from a further quantity of crystals, left for 12 hours; deep yellow plates (*ca.* 0·5 g.) of 2-*nitro*-1-p-*toluenesulphon-naphthalide*, m. p. 154°, were deposited (Found: N, 8·2. $C_{17}H_{14}O_4N_2S$ requires N, 8·2%). The constitution of this compound was confirmed by hydrolysis with sulphuric acid, 2-nitro-1-naphthylamine, m. p. 183° alone or mixed with an authentic specimen, being produced.

Nitration of 2 : 4-*Dinitro-α-naphthol* (Morgan and Evens, J., 1919, **115**, 1128).—(a) 5 G. were added to ice-cold fuming nitric acid (10 c.c.) and after 5 minutes the solution was diluted with acetic acid (10 c.c.) and left to crystallise. The almost pure 2 : 4 : 5-trinitro-α-naphthol (m. p. 183°) was collected and recrystallised from acetic acid, forming yellow prisms, m. p. 190° (2 g.). The nitric–acetic acid mother-liquor was poured into water; the gummy precipitate, after two crystallisations from acetic acid, yielded yellow needles, m. p. 145° (decomp.), of 2 : 4 : 7-trinitro-α-naphthol (0·8 g.).

(b) 2 : 4-Dinitro-α-naphthol (5 g.) was added in small quantities to a cold mixture of fuming nitric acid (10 c.c.) and acetic acid (10 c.c.). After standing at room temperature for 12 hours, the crystalline deposit of 2 : 4 : 5-trinitro-α-naphthol was collected and recrystallised (2 g., m. p. 190°) from acetic acid. The mother-liquor on dilution with water gave 2 : 4 : 7-trinitro-α-naphthol (0·9 g.).

1-*Bromo*-2-p-*toluenesulphon-naphthalide*.—To a mixture of the naphthalide (15 g.) and chloroform (50 c.c.) was added bromine (2·8 c.c.) in chloroform (10 c.c.). After the initial reaction, the solution was heated under reflux for 1½ hours. On cooling, white needles (3 g.) of 1-bromo-2-naphthylamine hydrobromide, m. p. 228° (decomp.), were deposited (converted by alkali into the free base, m. p. 63°). The filtered solution after evaporation to small bulk and dilution with ligroin deposited an oil, which solidified after trituration. This crystallised from alcohol in stout needles (15 g.), m. p. 100° alone or mixed with authentic 1-bromo-naphthalide (Bell, J., 1932, 2732).

3-*Bromo*-2-*naphthylamine*.—A mixture of 1 : 3-dibromo-2-naphthylamine (Bell, *loc. cit.*) (5 g.), alcohol (40 c.c.), concentrated hydrochloric acid (40 c.c.), and granulated tin (5 g.) was heated under reflux for 2 hours. The filtered cold solution deposited 3-bromo-2-naphthylamine hydrochloride, which was decomposed with hot alcoholic sodium hydroxide to yield the free *base*; this formed lustrous plates (3 g.), m. p. 173°, from alcohol (Found: N, 6·2. $C_{10}H_8NBr$ requires N, 6·3%). By interaction with acetic anhydride, 3-bromo-2-naphthylamine furnished 3-*bromo*-2-*acetonaphthalide* in parallelepipeds, m. p. 177° (large depression when mixed with the base) (Found: N, 5·4. $C_{12}H_{10}ONBr$ requires N, 5·3%).

3-*Bromo*-2-p-*toluenesulphon-naphthalide*, obtained from the interaction of 3-bromo-2-naphthylamine and *p*-toluenesulphonyl chloride in pyridine, crystallised from alcohol in fine needles, m. p. 127—129° (Found: N, 3·8. $C_{17}H_{14}O_2NBrS$ requires N, 3·7%).

3-*Bromo*-1-*nitro*-2-p-*toluenesulphon-naphthalide*.—(a) This was prepared by the nitration of the 3-bromo-naphthalide (1 g.) in acetic acid (5 c.c.) and nitric acid (0·3 c.c.); it crystallised from alcoholic pyridine in pale yellow plates, m. p. 237—239° (decomp.).

(b) To 1-nitro-2-*p*-toluenesulphon-naphthalide (10 g.) (Morgan and Micklethwaite, J., 1912, **101**, 148) in pyridine solution, bromine (1·6 c.c.) was added drop by drop. After 12 hours the mass was triturated with dilute hydrochloric acid, and the solid product crystallised from alcoholic pyridine. This substance had m. p. 237—239° alone or mixed with that obtained in (a) and was therefore 3-*bromo*-1-*nitro*-2-p-*toluenesulphon-naphthalide* (Found: N, 6·6. $C_{17}H_{13}O_4N_2BrS$ requires N, 6·65%).

Reduction with either tin and hydrochloric acid or zinc and acetic acid furnished 3-*bromo*-2-p-*toluenesulphon*-1 : 2-*naphthylenediamine*, which crystallised from acetic acid in needles, m. p. 185° (Found: N, 7·0. $C_{17}H_{15}O_2N_2BrS$ requires N, 7·2%).

3-*Bromo*-1-*nitro*-2-*naphthylamine*, obtained by the careful addition of the 3-bromo-1-nitro-naphthalide to ice-cold concentrated sulphuric acid, formed orange needles, m. p. 105°, from alcohol (Found: N, 10·2. $C_{10}H_7O_2N_2Br$ requires N, 10·5%). This was converted by boiling with *N*-sodium hydroxide for 6 hours into 3-*bromo*-1-*nitro*-2-*naphthol*, which crystallised from alcohol in yellow plates, m. p. 131° (decomp.) (Found: N, 5·1. $C_{10}H_6O_3NBr$ requires N, 5·2%).

To a hot solution of the amine in acetic anhydride a drop of concentrated sulphuric acid was added. On cooling, 3-*bromo*-1-*nitro*-2-*acetonaphthalide* separated; it formed yellow needles from alcohol, m. p. 136° (Found: N, 9·0. $C_{12}H_9O_3N_2Br$ requires N, 9·1%).

Reduction of 3-bromo-1-nitro-2-naphthylamine with tin and hydrochloric acid proceeded no further than 3-*bromo*-1 : 2-*naphthylenediamine*, which formed needles, m. p. 85° (decomp.), from aqueous alcohol (Found: N, 11·5. $C_{10}H_9N_2Br$ requires N, 11·8%). The 1-nitro-group,

unlike the 1-bromine atom in 1 : 3-dibromo-2-naphthylamine, was not removed. The diamine gave, with benzil in hot alcoholic solution, the *quinoxaline* derivative, which formed yellow plates, m. p. 195—199°, from acetic acid (Found : N, 6·8. $C_{24}H_{15}N_2Br$ requires N, 6·8%); it gave an intense violet coloration with concentrated sulphuric acid.

Bromination of 1 : 6-*Dinitro*-2-p-*toluenesulphon-naphthalide*.—This compound (4 g.) gave with bromine (0·33 c.c.) in pyridine 3-*bromo*-1 : 6-*dinitro*-2-p-*toluenesulphon-naphthalide*, which formed pale yellow rhombs, m. p. 228—231° (decomp.), from acetic acid (Found : N, 9·1. $C_{17}H_{12}O_6N_3BrS$ requires N, 9·0%). Hydrolysis with concentrated sulphuric acid furnished 3-*bromo*-1 : 6-*dinitro*-2-*naphthylamine*, which formed golden needles, m. p. 238—241°, from alcohol (Found : N, 13·9. $C_{10}H_6O_4N_3Br$ requires N, 13·5%). A hot solution of this amine in acetic anhydride, on the addition of a drop of concentrated sulphuric acid, deposited 3-*bromo*-1 : 6-*dinitro*-2-*acetonaphthalide* which formed white needles, m. p. 273—277° (decomp.), from acetic acid (Found : N, 12·0. $C_{12}H_8O_5N_3Br$ requires N, 11·9%).

Iodination of Sulphonanilides.—To *p*-toluenesulphon-2-naphthalide (5 g.) in pyridine, iodine, iodine chloride, or iodine trichloride (1 mol.) was added. After 12 hours, treatment with hydrochloric acid produced an oil. The excess of iodine was removed with sulphur dioxide, and the oily residue rendered solid by trituration with alcohol. Crystallisation from alcohol furnished stout prisms (average yield, 2·5 g.), m. p. 126—127°, of 1-*iodo*-2-p-*toluenesulphon-naphthalide* (Found : N, 3·3. $C_{17}H_{14}O_2NIS$ requires N, 3·3%). The constitution of this compound was confirmed by warming 1 g. in acetic acid on the water-bath with addition of sodium nitrite (0·2 g.) for 3 hours. The deep brown solution, on cooling, deposited 1-nitro-2-*p*-toluenesulphon-2-naphthalide, m. p. 160° alone or mixed with an authentic specimen.

Attempts to convert the iodo-naphthalide into the amine by hydrolysis with concentrated sulphuric acid or alcoholic hydrochloric acid were unsuccessful, the product decomposing rapidly after basification and liberating iodine. This confirms Meldola's observation (J., 1885, **47**, 520) on the instability of 1-iodo-2-naphthylamine.

The following iodo-derivatives also were obtained by the above methods : 3-*Iodo*-2-p-*toluenesulphonamidodiphenyl*, prisms, m. p. 114—115°, from alcohol (Found : N, 3·1. $C_{19}H_{16}O_2NIS$ requires N, 3·1%). 3-*Iodo*-4-p-*toluenesulphonamidodiphenyl*, m. p. 109—115° (Found : N, 3·1. $C_{19}H_{16}O_2NIS$ requires N, 3·1%). 2-*Iodo*-p-*toluenesulphon*-p-*toluidide*, m. p. 127—132° (Found : N, 3·4. $C_{14}H_{14}O_2NIS$ requires N, 3·6%).

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