284. *The Reactions of 2 : 6-Dichloro- and 2 : 4 : 6-Trihalogenonitrobenzenes with a Mercaptide Reagent.*

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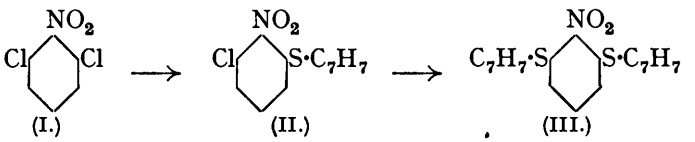
Complete replacement of halogen by *p*-tolylthio-groups results from the interaction of 2 : 6-dichloro-, 2 : 4 : 6-trichloro-, or 2 : 4 : 6-tribromo-nitrobenzene and salts of thio-*p*-cresol. Intermediate products have been isolated and identified, but the reactions present some unusual features, particularly in regard to the extent to which the two stages of the double replacement compete with each other at the 2 : 6-centres.

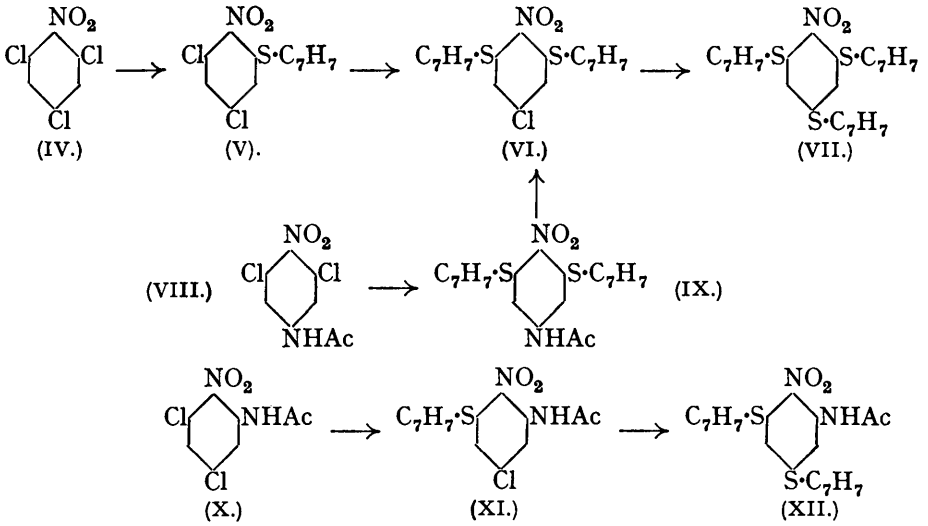
ALTHOUGH substitution of hydrogen at several nuclear centres in rapid succession is not uncommon among the anionoid reactions of benzene derivatives, yet replacement of potential anions at the cationoid centres of a nitrobenzene system is seldom so extensive. The cationoid driving force in the latter case seems to be more readily exhausted, so that, even where several replacements can be effected, the individual stages of the reaction do not generally compete with each other. It was therefore unexpected when, by the interaction of molecular proportions of alkaline thio-*p*-cresol and 2 : 6-dichloronitrobenzene (I), a considerable quantity of the latter compound was recovered and the product of the reaction under all the conditions employed consisted of a mixture of the *monothio-ether* (II) and the *dithio-ether* (III). The result is all the more surprising in that when 2 : 6-dichloronitrobenzene reacts with sodium methoxide, diethylamine (Holleman, de Mooy, and ter Weel, *Rec. Trav. chim.*, 1915, **35**, 1), piperidine (experimental), and ethanolamine (Kremer and Bendich, *J. Amer. Chem. Soc.*, 1939, **61**, 2658) only one chlorine atom is replaced.



(I.) (II.) (III.)

A similar contrast was found in the reactions of 2 : 4 : 6-trichloro- and 2 : 4 : 6-tribromonitrobenzene. Here again one chlorine atom is replaced in reaction with sodium alkyloxide (Bentley, *Amer. Chem. J.*, 1892, **14**, 363; Holleman and Haeften, *Rec. Trav. chim.*, 1921, **40**, 67) or piperidine (experimental), but with ammonia in large excess and at high temperatures the 2 : 6-diamines are formed (Beilstein and Kurbatow, *Annalen*, 1878, **192**, 233; Körner, *Gazzetta*, 1874, **4**, 422), conditions for obtaining monoamines not having been found (Holleman and Haeften, *loc. cit.*). In reaction with the mercaptide all three halogen atoms

were readily replaced, yielding 2 : 4 : 6-*tri*-p-*tolylthionitrobenzene* (VII). In each series also a mono- and a di-*p*-tolylthio-ether were isolated, forming together the product when 1 mol. of mercaptide was used; the dithio-ether was the chief product, accompanied by (VII), when 2 mols. were used. The orientation of these intermediates was established in the chloro-series by conversion of (V) into (VI) and by formation of the latter from 3 : 5-dichloro-4-nitroacetanilide (VIII) in the manner indicated. The monothio-ether intermediate between (VIII) and (IX) was not isolated, though it probably accompanied (IX) as part-product of the reaction between (VIII) and 1 mol. of mercaptide. On the other hand, the isomeric acetanilide (X) reacted in two distinct stages yielding a *monothio-ether* —assumed to be (XI)—and a *dithio-ether* (XII) according to the proportions used. From (XII) 2-*chloro*-4 : 6-*di*-p-*tolylthionitrobenzene*, isomeric with (VI) and not found in the products from (IV), was obtained by hydrolysis and subsequent application of the Sandmeyer reaction. Competition between the reaction stages appears, therefore, to be more pronounced when the halogen occupies the 2 : 6- rather than the 2 : 4-positions with respect to the nitro-group.



The reason for the exceptional behaviour of the mercaptide reagent is not clear. Piperidine also is a very reactive agent, so that mercaptide reactivity alone does not seem adequately to explain the results obtained. On the other hand, the effect to be attributed to the introduced thioaryl group requires further investigation, and discussion is postponed, but it is noteworthy that Fries and Ochwatt (*Ber.*, 1923, **56**, 1291) have reported a somewhat similar case of mercaptide reactivity in the reactions of chlorinated benzo- and naphthaquinones where, in contrast to the usual restricted or step-wise replacement of chlorine, thiol reagents effect complete replacement and intermediate compounds are isolable only with difficulty, if at all.

Experimental.

2-*Chloro*-6-*piperidinonitrobenzene*.—2 : 6-Dichloronitrobenzene was refluxed in an excess of piperidine for 30 mins. The oil obtained on pouring into water slowly solidified and was crystallised from alcohol, m. p. 63° (Found: N, 11·5. $C_{11}H_{13}O_2N_2Cl$ requires N, 11·6%).

2-*Chloro*-6-p-*tolylthionitrobenzene* (II).—Molecular proportions of 2 : 6-dichloronitrobenzene, thio-*p*-cresol, and sodium hydroxide were dissolved in aqueous alcohol and kept at room temperature for 3 weeks. The mixture of (III) (see below) and sodium chloride which separated was filtered off, and the filtrate was distilled in steam to remove unchanged dichloronitrobenzene. The non-volatile oil was extracted with benzene and, after evaporation of the solvent, yielded a solid (A) consisting of *p*-tolyl disulphide and the required *thio-ether*. The latter was obtained pure after several crystallisations from alcohol, and formed yellow prisms, m. p. 82—83° (Found: N, 5·1. $C_{13}H_{10}O_2NClS$ requires N, 5·0%). The corresponding *sulphone*, m. p. 151° (Found: N, 4·4. $C_{13}H_{10}O_4NClS$ requires N, 4·5%), was conveniently prepared by oxidising the crude

solid (A) with hydrogen peroxide in acetic acid at 100°, followed by crystallisation of the product from dilute acetic acid.

2 : 6-*Di*-p-*tolylthionitrobenzene* (III), yellow needles or plates, m. p. 168—169°, from acetic acid (Found : N, 3·8. $C_{20}H_{17}O_2NS_2$ requires N, 3·8%), was produced from the mercaptide and 2 : 6-dichloronitrobenzene even when the latter was employed in excess. It was best obtained when the reagents in the requisite proportion were refluxed in alcoholic solution, and it was oxidised in the usual manner to 2 : 6-*di*-p-*toluenesulphonylnitrobenzene*, m. p. 196° (Found : N, 3·4. $C_{20}H_{17}O_4NS_2$ requires N, 3·25%).

Mononitration of *s*-trichloro- or -tribromo-benzene requires careful control of the strength of nitrating agent employed and the literature references are not trustworthy. The following procedure gave good results : *s*-Trichlorobenzene (10 g.) was added to a mixture of fuming nitric acid (*d* 1·5; 32 c.c.) and concentrated nitric acid (*d* 1·42; 10—12 c.c.), and the whole heated at 100° for 40 mins. before being poured into water. After crystallisation from alcohol, 2 : 4 : 6-trichloronitrobenzene had m. p. 71° (lit., 69°). *s*-Tribromobenzene (17 g.) was nitrated similarly, but with only 15—20 mins.' heating.

2 : 4-*Dibromo*-6-*piperidinonitrobenzene*, m. p. 167°, was obtained by refluxing *s*-tribromonitrobenzene in piperidine and pouring the product into water (Found : N, 7·7. $C_{11}H_{12}O_2N_2Br_2$ requires N, 7·7%). The corresponding dichloro-compound was obtained as an oil which could not be crystallised.

2 : 4 : 6-*Tri*-p-*tolylthionitrobenzene* (VII).—*s*-Trichloronitrobenzene (1 mol.), thio-*p*-cresol (3 mols.) and sodium hydroxide (3 mols.) were heated for 10 mins. in alcoholic solution. The semi-solid precipitate which formed was washed with water and extracted with a moderate quantity of hot acetic acid, leaving a sparingly soluble residue of di-*p*-tolylthio-ether (VI). The extract on cooling deposited the required *thio-ether* (VII), which, after further purification from the same solvent, was obtained in long yellow needles, m. p. 142° (Found : C, 66·4; H, 4·5. $C_{27}H_{23}O_2NS_3$ requires C, 66·1; H, 4·7%). Similar results were obtained with *s*-tribromonitrobenzene, and the addition of dioxan or longer heating assisted in carrying the reaction to completion. The corresponding *trisulphone* had m. p. 230° (from acetic acid) (Found : C, 55·2; H, 3·7. $C_{27}H_{23}O_8NS_3$ requires C, 55·3, H, 3·9%), and when heated with piperidine gave 1-*piperidino*-2 : 4 : 6-*tri*-p-*toluenesulphonylbenzene*, m. p. 188° (Found : C, 61·8; H, 5·5. $C_{32}H_{33}O_6NS_3$ requires C, 61·6; H, 5·3%), the nitro-group being replaced.

4-*Chloro*-2 : 6-*di*-p-*tolylthionitrobenzene* (VI).—A cold solution of *s*-trichloronitrobenzene (1 mol.) in alcohol–dioxan was treated with an aqueous alcoholic solution of the thiol and sodium hydroxide (2 mols.). The resulting clear solution slowly deposited the crude product, which was collected after 12 hours and crystallised from hot acetic acid, in which it was sparingly soluble. (The acetic acid mother-liquor retained some trithio-ether which had also been formed.) The *compound* had m. p. 206—207° with softening at 200° (Found : C, 59·9; H, 3·9. $C_{20}H_{16}O_2NClS_2$ requires C, 59·8; H, 4·0%); it was oxidised to 4-*chloro*-2 : 6-*di*-p-*toluenesulphonylnitrobenzene*, which formed colourless needles, m. p. 211° (Found : C, 51·7; H, 3·4. $C_{20}H_{16}O_6NClS_2$ requires C, 51·5; H, 3·4%). 4-*Piperidino*-2 : 6-*di*-p-*tolylthionitrobenzene*, yellow needles, m. p. 205°, was obtained by refluxing the dithio-ether (VI) in excess of piperidine for 3 hours (Found : N, 6·3. $C_{25}H_{26}O_2N_2S_2$ requires N, 6·2%).

2 : 4-*Dichloro*-6-p-*tolylthionitrobenzene* (V).—With molecular proportions of *s*-trichloronitrobenzene and mercaptide in alcohol, a precipitate of (VI) was again formed and, after 12 hours, it was filtered off and the filtrate distilled in steam. The non-volatile oily residue was dissolved in the minimum quantity of alcohol; it crystallised after several days. After further purification from alcohol it formed yellow needles, m. p. 97° (Found : C, 49·7; H, 2·9. $C_{13}H_9O_2NCl_2S$ requires C, 50·0; H, 2·9%), and yielded (VI), m. p. and mixed m. p. 205°, when further treated with the mercaptide (1 mol.) in alcohol. 2 : 4-*Dichloro*-6-p-*toluenesulphonylnitrobenzene* had m. p. 171° (Found : C, 45·5; H, 2·8. $C_{13}H_9O_4NCl_2S$ requires C, 45·1; H, 2·6%).

The following compounds were prepared from *s*-tribromonitrobenzene by corresponding methods : 4-*Bromo*-2 : 6-*di*-p-*tolylthionitrobenzene*, m. p. 210° (Found : C, 53·8; H, 3·8. $C_{20}H_{16}O_2NBrS_2$ requires C, 53·8; H, 3·6%); 4-*bromo*-2 : 6-*di*-p-*toluenesulphonylnitrobenzene*, m. p. 223° (Found : C, 47·3; H, 3·15. $C_{20}H_{16}O_6NBrS_2$ requires C, 47·1; H, 3·1%); 2 : 4-*dibromo*-6-p-*tolylthionitrobenzene*, m. p. 132° (Found : C, 39·1; H, 2·2. $C_{13}H_9O_2NBr_2S$ requires C, 38·7; H, 2·2%); and 2 : 4-*dibromo*-6-p-*toluenesulphonylnitrobenzene*, m. p. 182° (Found : C, 35·7; H, 2·2. $C_{13}H_9O_4NBr_2S$ requires C, 35·9; H, 2·1%).

4-*Nitro*-3 : 5-*di*-(p-*tolylthio*)*acetanilide* (IX).—An alcoholic solution of 3 : 5-dichloro-4-nitroacetanilide (1·1 g.), thio-*p*-cresol (1·1 g.), and sodium hydroxide (0·35 g.) was refluxed

for 20 mins. The resulting solid was filtered off, washed with water, and crystallised from boiling acetic acid, forming yellow needles, m. p. 261° (Found: C, 62·2; H, 4·5. $C_{22}H_{20}O_3N_2S_2$ requires C, 62·3; H, 4·7%). It was comparatively insoluble in the usual solvents, gave an intense blue coloration with concentrated sulphuric acid, but was hydrolysed smoothly when its suspension in dilute sulphuric–acetic acid was refluxed. 4-*Nitro*-3 : 5-*di*-(p-*tolylthio*)*aniline* had m. p. 270° (from acetic acid) (Found: C, 62·5; H, 4·8. $C_{20}H_{18}O_2N_2S_2$ requires C, 62·8; H, 4·7%) and was converted by the Hodgson–Walker procedure (J., 1933, 1620) into (VI), m. p. and mixed m. p. 205°.

5-*Chloro*-2-*nitro*-3-(p-*tolylthio*)*acetanilide* (XI).—An alcoholic solution of thio-*p*-cresol, sodium hydroxide, and 3 : 5-dichloro-2-nitroacetanilide (mol. proportions) was kept at room temperature for 24 hours. After some precipitated dithio-ether (XII) had been separated, the filtrate was diluted with water, and the resulting solid was crystallised several times from alcohol–acetic acid, yielding soft, pale yellow needles, m. p. 166—167° (Found: N, 8·5. $C_{15}H_{13}O_3N_2ClS$ requires N, 8·3%). It gave 5-*chloro*-2-*nitro*-3-(p-*tolylthio*)*aniline*, m. p. 110—111°, on hydrolysis (Found: C, 53·3; H, 3·5. $C_{13}H_{11}O_2N_2ClS$ requires C, 53·0; H, 3·7%).

2-*Nitro*-3 : 5-*di*-(p-*tolylthio*)*acetanilide* (XII).—An aqueous-alcoholic solution of thio-*p*-cresol (5 g.) and sodium hydroxide (1·6 g.) was added gradually to a hot solution of 3 : 5-dichloro-2-nitroacetanilide (5 g.) in alcohol. The precipitated solid, after being washed with water, crystallised from alcohol in yellow plates, m. p. 188° (Found: C, 62·5; H, 4·5. $C_{22}H_{20}O_3N_2S_2$ requires C, 62·3; H, 4·7%). On hydrolysis it yielded 2-*nitro*-3 : 5-*di*-(p-*tolylthio*)*aniline*, orange needles or plates, m. p. 117° (Found: C, 62·7; H, 4·7. $C_{20}H_{18}O_2N_2S_2$ requires C, 62·8; H, 4·7%).

2-*Chloro*-4 : 6-*di*-(p-*tolylthio*)*nitrobenzene* was obtained from the above aniline by Hodgson and Walker's procedure (*loc. cit.*). It formed plates, m. p. 104°, from acetic acid (Found: C, 59·75; H, 4·2. $C_{20}H_{16}O_2NClS_2$ requires C, 59·8; H, 4·0%) and yielded (i) the corresponding *bis-sulphone*, m. p. 174° (Found: C, 51·5; H, 3·3. $C_{20}H_{16}O_6NClS_2$ requires C, 51·5; H, 3·4%), on oxidation; (ii) 2-*piperidino*-4 : 6-*di*-(p-*tolylthio*)*nitrobenzene*, orange needles, m. p. 135° (Found: N, 6·2. $C_{25}H_{26}O_2N_2S_2$ requires N, 6·2%), when heated (2 hours) with piperidine; and (iii) the trithio-ether (VII) when treated with thio-*p*-cresol and sodium hydroxide in alcohol.

Piperidine Salt of Thio-p-*cresol*.—The *salt* was precipitated when its components were mixed in dioxan and was crystallised from alcohol. It was quite stable, was soluble in hydroxylated solvents, and gave the same replacement reactions as the sodium salt (Found: N, 6·5. $C_{12}H_{19}NS$ requires N, 6·7%).

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