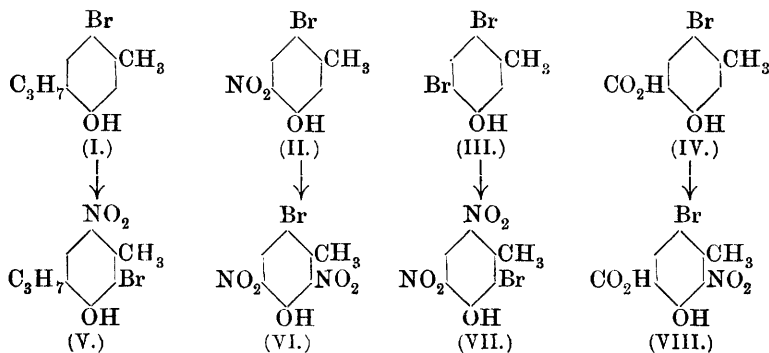


CLXXV.—*Experiments on the Migration of para-Halogen Atoms in Phenols.*

By IVAN RICHARD GIBBS and PHILIP WILFRED ROBERTSON.

It has been shown (Robertson, T., 1908, **93**, 793; Robertson and Briscoe, T., 1912, **101**, 1961) that certain para-halogen substituted phenols, for example, 6-bromothymol (I), behave peculiarly on nitration, in that the halogen atom is replaced by the nitro-group

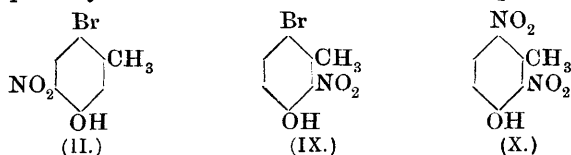
and migrates to the ortho-position (V). In the hope of discovering other cases of this somewhat remarkable transformation, and with the object of examining more closely its nature, we have investigated the same reaction in the case of certain other phenols (II, III, IV) of an analogous nature to 6-bromothymol. A synopsis of the results is indicated below:



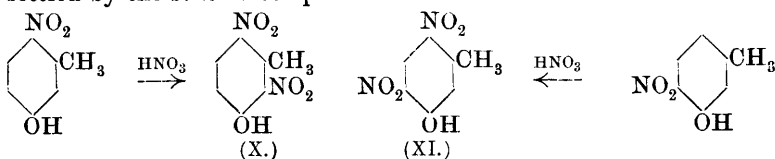
It is seen that 6-bromo-4-nitro-*m*-cresol (II) behaves normally on nitration, and the constitution of the product (VI) was fixed by the fact that a different substance (VII) resulted from the bromination of 4:6-dinitro-*m*-cresol, in which reaction there is no possibility of rearrangement.

In the nitration of 4:6-dibromo-*m*-cresol (III), migration of bromine occurs, and the second bromine atom is displaced with the formation of 2-bromo-4:6-dinitro-*m*-cresol (VII). In this reaction 2:4-dibromo-6-nitro-*m*-cresol is probably an intermediate product, for this substance is readily acted on by nitric acid with the formation of the dinitro-derivative (VII).

Under certain conditions, especially in cold dilute acetic acid, and in the absence of water, 6-bromo-3-hydroxy-*p*-toluic acid (IV) reacts normally with nitric acid. The carboxylic group, however, is eliminated or displaced with extraordinary ease in the *m*-cresol series, and in this reaction, in addition to the normal product (VIII), the following three substances (IX, II, X) were also found to be formed in different experiments. The conditions which determined the formation of one or other of these compounds were very subtle, seeming to depend on the rate of addition of the nitric acid, its quantity, the state of dilution, and the temperature:

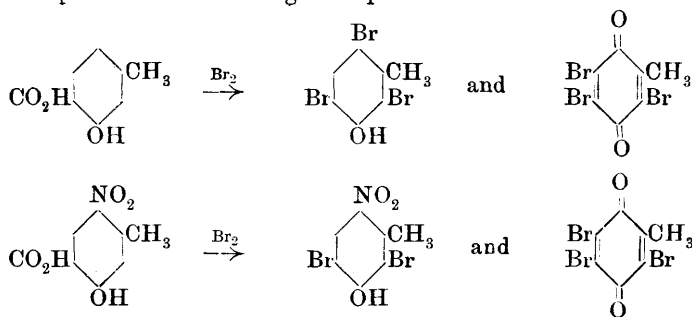


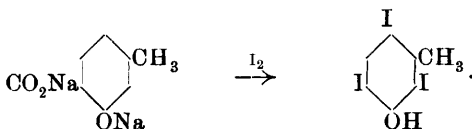
In none of the four compounds produced by the action of nitric acid on 6-bromo-3-hydroxy-*p*-toluic acid has there occurred a migration of the para-bromine atom to the ortho-position. The proof of the constitution of the bromonitro-3-hydroxy-*p*-toluic acid (VIII) was obtained from the consideration that a different isomeride was formed in the bromination of 6-nitro-3-hydroxy-*p*-toluic acid. The constitution of the dinitro-*m*-cresol (X) was settled by the scheme of operations indicated below:



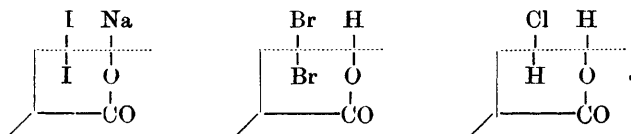
Three dinitro-*m*-cresols substituted in the ortho- or para-positions are theoretically possible; the 2:4-compound is already known (*Ber.*, 1890, **23**, 3479), and is different from either of the compounds X or XI, so that they must have the constitutions assigned to them. It is somewhat remarkable that in the nitration of 6-nitro-*m*-cresol the second nitro-group enters a position which would seem sterically unfavourable. Raiford observed (*J. Amer. Chem. Soc.*, 1914, **36**, 670) that on chlorination both the 4:6- and the 2:6-chloronitro-compounds are formed. By the most careful bromination, on the other hand, we have found that 2:4-dibromo-6-nitro-*m*-cresol was the only product.

Reference has been made above to the readiness with which the carboxyl group is eliminated or displaced from this type of compound on nitration. The same phenomenon was also frequently observed in the case of the action of the halogens, even in cold dilute acetic acid solution. Water accelerated this change, probably owing to increased ionisation; hydrogen chloride, on the other hand, had a retarding effect. If the temperature was allowed to rise, and especially in the presence of water, oxidation also tended to take place. The following examples are illustrations:

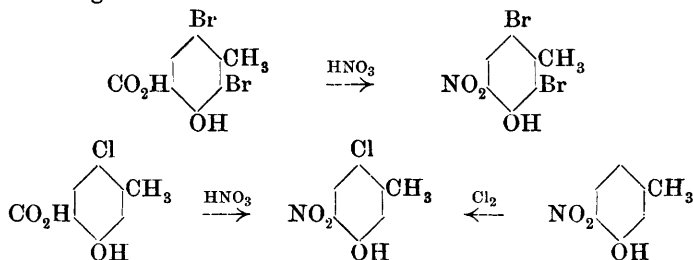




The fact that in the last case there was displacement only in the presence of alkali seems to indicate that these changes take place according to the following schemes:



The efficiency of hydrochloric acid in causing the elimination of a carboxylic group from an aromatic acid is probably due to a similar reaction (see above). This subject is at present being further investigated. The behaviour of nitric acid in replacing a carboxyl by the nitro-group may be explained by an analogous assumption. As further examples of this change may be cited the following:



The presence of the nitro-group in the 4-position in the chloro-nitro-*m*-cresol was proved by the fact that the same compound was formed on the chlorination of 4-nitro-*m*-cresol.

EXPERIMENTAL.

The compounds described below were purified by recrystallisation from aqueous acetic acid, and all cases of identity were established by the method of mixed melting points.

4:6-Dibromo-*m*-cresol (III).

Thirty grams of *m*-toluidine were boiled for four hours with slightly more than the theoretical quantity of acetic anhydride; water was added to decompose the unaltered anhydride, and the solution was made up to 500 c.c. with glacial acetic acid. Bromine

(2 mols.) dissolved in acetic acid was added slowly in the cold. On the addition of water the product separated as a white solid, which was found on recrystallisation to be pure 4:6-dibromoaceto-*m*-toluidide (compare *Ber.*, 1880, **13**, 971). On hydrolysis the corresponding toluidine was obtained, and was dissolved in much boiling dilute hydrochloric acid. On cooling slowly the hydrochloride was deposited in fine needles. The calculated quantity of sodium nitrite was slowly added with constant stirring in the cold; after two hours most of the solid had disappeared, and the solution was heated on the water-bath and finally distilled in a current of steam. The product obtained in this manner consisted partly of 4-bromotoluquinone, from which 4:6-dibromo-*m*-cresol was separated by treatment with aqueous alkali. On recrystallisation it was freed from traces of nitrophenols, and obtained in fine, white needles, melting at 55°:

0.1158 gave 0.1650 AgBr. Br=60.7.

$C_7H_6OBr_2$ requires Br=60.3 per cent.

This compound was readily nitrated in cold acetic acid solution, with the formation of 2-bromo-4:6-dinitro-*m*-cresol (VII).

2:6-Dinitro-*m*-cresol (X).

6-Nitro-*m*-cresol dissolved in excess of acetic acid was treated in the cold with the theoretical quantity of nitric acid in the same solvent. The sole product of the reaction was 2:6-dinitro-*m*-cresol, melting at 74°:

0.1066 gave 12.7 c.c. N_2 at 16° and 749 mm. N=14.4.

$C_7H_6O_5N_2$ requires N=14.2 per cent.

The same compound was one of the products of the nitration of 6-bromo-3-hydroxy-*p*-toluic acid. The constitution arrived at from the considerations in the theoretical part of the paper was confirmed by the fact that it yielded on bromination 4-bromo-2:6-dinitro-*m*-cresol, melting at 116° (compare *Annalen*, 1898, **303**, 29).

4:6-Dinitro-*m*-cresol (XI).

This was obtained by the cautious nitration in the manner described above of 4-nitro-*m*-cresol, and formed dull, yellow crystals, melting at 60°:

0.2421 gave 29.3 c.c. N_2 at 15° and 751 mm. N=14.5.

$C_7H_6O_5N_2$ requires N=14.2 per cent.

On bromination it formed 2-bromo-4:6-dinitro-*m*-cresol (VII).

6-Bromo-2-nitro-m-cresol (IX).

When the nitration of 6-bromo-3-hydroxy-*p*-toluic acid was carried out in aqueous acetic acid, and especially if the temperature was allowed to rise, a small quantity of a compound melting at 105° was isolated:

0.1785 gave 9.3 c.c. N₂ at 22° and 765 mm. N=6.1.

C₇H₆O₃NBr requires N=6.0 per cent.

The distinct yellow colour of this substance was an indication of the presence of the nitro-group in the ortho-position with respect to the hydroxyl group.

6-Bromo-4-nitro-m-cresol (II).

This compound was obtained by adding the calculated quantity of bromine in acetic acid solution to 4-nitro-*m*-cresol in the same solvent. It formed yellowish-green needles, moderately soluble in water, melting at 127°:

0.1623 gave 0.1331 AgBr. Br=34.9.

C₇H₆O₃NBr requires Br=34.5 per cent.

It was also one of the products of the nitration of 6-bromo-3-hydroxy-*p*-toluic acid in aqueous acetic acid solution. On nitration it yielded 6-bromo-2:4-dinitro-*m*-cresol (VI), in which reaction there has been no migration of the para-halogen atom.

6-Chloro-4-nitro-m-cresol.

This was prepared by passing the theoretical quantity of chlorine into an acetic acid solution of 4-nitro-*m*-cresol.

It was also obtained by the action of nitric acid on 6-chloro-*m*-cresol in glacial acetic acid solution, and on 6-chloro-3-hydroxy-4-toluic acid in aqueous acetic acid solution. It crystallised in long, yellowish-green needles, melting at 89°:

0.1838 gave 11.5 c.c. N₂ at 22° and 773 mm. N=7.4

C₇H₆O₃NCl requires N=7.5 per cent.

Attempts were made to nitrate this substance; it was in all cases, however, recovered unchanged.

2-Bromo-4:6-dinitro-m-cresol (VII).

This compound was obtained in the following reactions:

(1) By the bromination of 4:6-dinitro-*m*-cresol.

(2) By the nitration of 4:6-dibromo-*m*-cresol, in which reaction there has occurred bromine migration and bromine displacement.

(3) By the nitration of 2:4-dibromo-6-nitro-*m*-cresol, which change indicates that this substance is an intermediate product in (2).

(4) By the nitration of 2:6-dibromo-*m*-cresol.*

(5) By the action of excess of nitric acid on 2:4:6-tribromo-*m*-cresol.

When prepared by any of these methods the compound melted at 104°:

0.1470 gave 12.4 c.c. N₂ at 19° and 755 mm. N=9.9.

C₇H₅O₅N₂Br requires N=10.0 per cent.

6-Bromo-2:4-dinitro-m-cresol (VI).

6-Bromo-4-nitro-*m*-cresol yielded this substance on nitration. It formed yellow crystals melting at 78°:

0.1650 gave 13.9 c.c. N₂ at 20° and 762 mm. N=9.9.

C₇H₅O₅N₂Br requires N=10.0 per cent.

2-Bromo-6-nitro-3-hydroxy-p-toluic Acid.

On cautious bromination in the cold, 6-nitro-3-hydroxy-*p*-toluic acid formed the above compound; as is frequently observed in the case of *p*-nitrophenols, the substance was almost pure white. It melted at 203°:

0.2210 gave 9.4 c.c. N₂ at 17° and 768 mm. N=5.1.

C₈H₆O₅NBr requires N=5.1 per cent.

In the presence of water, however, carbon dioxide was evolved even in the cold, and the chief product of the bromination was 2:4-dibromo-6-nitro-*m*-cresol. If the solution was warmed, the reaction proceeded still further, and considerable quantities of tribromotoluquinone were also formed.

6-Bromo-2-nitro-3-hydroxy-p-toluic Acid (VIII).

This was one of the products of the nitration of 6-bromo-3-hydroxy-*p*-toluic acid if the reaction was allowed to take place in cold acetic acid solution and in the absence of water. It formed yellow crystals melting at 178°:

0.2115 gave 0.1454 AgBr. Br=29.2.

C₈H₆O₅NBr requires Br=29.0 per cent.

With regard to the preparation of the 6-bromo-3-hydroxy-*p*-toluic acid employed in this reaction, it should be noted that the bromination must be performed in cold acetic acid solution and in

* This substance was obtained as an oil by the distillation in a vacuum of the calcium salt of 2:6-dibromo-3-hydroxy-*p*-toluic acid.

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the absence of water to avoid the formation of tribromo-*m*-cresol and tribromotoluquinone. Even under these conditions the product was contaminated with considerable quantities of the dibromo-acid. This difficulty was to some extent overcome by employing the methyl ester for the bromination.

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