

CCLXXXVII.—*Nitrosation of Phenols. Part I.*
3-Chloro-4-nitrosophenol and its Conversion into
Two Isomeric Chloroquinonemonoximes.

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p-NITROSOPHENOL and its tautomeride, *p*-benzoquinonemonoxime, have hitherto never been definitely isolated as such, and in consequence have been regarded as existing either in dynamic equilibrium or entirely in the quinonoid form. The simple homologues and halogenated derivatives are regarded in like manner.

The authors claim to have obtained the individual tautomerides of 3-chloro-4-nitrosophenol, to have worked out the experimental conditions for the preparation of the real nitroso-compound, $\text{OH C}_6\text{H}_3\text{Cl}\cdot\text{NO}$, and to have accomplished its conversion by means of acids or alkalis of definite concentration into the quinoneoxime, $\text{O}:\text{C}_6\text{H}_3\text{Cl}:\text{NOH}$, which exhibits geometrical isomerism. The geometric isomerides are interconvertible, but such reversibility does not seem to apply to the nitroso- and quinonoid modifications.

The two general methods of preparing nitrosophenols, namely, the direct action of nitrous acid on phenols and the alkaline decomposition of the *p*-nitroso-derivatives of aromatic tertiary amines, will be shown to involve conditions which favour the stability of the quinonoid structure.

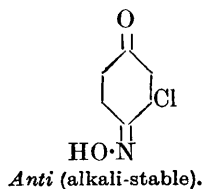
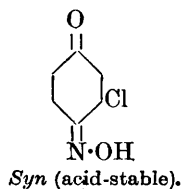
The direct action of nitrous acid on a phenol would appear to involve the minimum of complication, and the regulating influence of steric hindrance suggested to the authors a means of controlling any transformation likely to occur from the initial form of the product into its tautomeride. For such a purpose 3-chlorophenol appeared eminently suitable; moreover, its nitrosation was of interest in view of the very exhaustive investigations of Bridge and of Kehrman on the quinoneoxime derivatives from 2-chlorophenol.

The first method employed for the nitrosation of 3-chlorophenol was an adaptation of that described by Bridge (*Annalen*, 1893,

277, 85) for the preparation of *p*-nitrosophenol. The low melting point of the product indicated an equilibrium mixture of tautomers. Owing to steric hindrance, the rate of nitrosation was slow, so that during the reaction there were present together for an appreciable interval of time, 3-chlorophenol, 3-chloro-4-nitrosophenol, mineral acid, and nitrous acid. A discovery then considerably facilitated the quest for a more economical method. In the attempt to purify the final product by recrystallisation from hot dilute mineral acid, its melting point was raised by about 40°, owing to its conversion into a tautomeric form. Mineral acids, therefore, were detrimental to the preservation of the product in its initial form; steric hindrance, on the other hand, favoured its permanence. Baeyer and Caro (*Ber.*, 1874, 7, 807, 963) have shown that mineral acids promote the formation of condensation products of *p*-nitrosophenol and free phenol, and hot glacial acetic acid converts *p*-nitrosophenol into a complex capable of functioning as a substantive brown dyestuff (the Clayton Aniline Co., D.R.-P. 106036).

The exclusion of such acids so far as practicable from the nitrosating mixture should therefore favour the production only of the initial form of the reaction product. This deduction proved to be sound, for by the means described in the experimental section there was obtained in 60 per cent. yield from 3-chlorophenol a substance which the authors claim to be the first true nitrosophenol to be isolated.

The steric hindrance which favours the maintenance of the initial nitroso-structure also permits a regulated conversion into the quinoneoxime modification. This result, accomplished with the aid of hot acid or cold alkali, is in striking contrast to the extreme instability of unsubstituted nitrosophenols towards hot acids. Two stereoisomeric monoximes have been prepared which display the characteristic properties of geometric isomerides. The red modification of the quinoneoxime, produced by the action of hot dilute hydrochloric acid, is readily converted into an almost colourless form by alkalis, and *vice versa*. For the red oxime, the *syn*-configuration has been tentatively adopted as best accounting for its colour through the greater exertion of partial valencies or electronic interplay, whilst the *anti*-configuration has been assigned to the almost colourless, alkali-stable isomeride:



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This view is in consonance with the fact that hydrochloric acid is an effective agent for transforming *anti*-aldoximes into the hydrochlorides of the corresponding *syn*-compounds (Luxmoore, T., 1896, 69, 181). Hantzsch ("Grundriss der Stereochemie," 2nd edn., p. 130) classifies the oximes as acid- and alkali-stable, respectively, and notes the instability of the *anti*-compounds in presence of acids, especially hydrochloric acid. Our *anti*-compound is liberated in stable condition from its alkaline solutions by hydrochloric acid, a stability which is to be ascribed to the presence of the nuclear chlorine atom.

The occurrence of well-defined, isomeric nitrosophenols and quinoneoximes, and the knowledge of the conditions necessary for their isolation, render possible the interpretation of many of the difficulties encountered by previous workers on nitrosophenols. When nitroso- β -naphthol is treated with aniline in alcoholic solution, a yellow, crystalline compound, $C_{16}H_{12}ON_2$, is obtained, whereas in hot glacial acetic acid a more complex, dark red product, $C_{22}H_{16}ON_2$, results. It may be assumed that, in presence of basic aniline, nitroso- β -naphthol, reacting in the quinonoid form, condenses normally to give the compound $NPh:C_{10}H_6:NOH$, whilst, in the second reaction (we have found acetic acid to bring about conversion very slowly), the nitroso-form prevailing, an azo-compound such as $OPh \cdot C_{10}H_6 \cdot N:NPh$ is furnished by double condensation.

Bridge has shown (*Amer. Chem. J.*, 1892, 14, 276) that α -benzylhydroxylamine converts *p*-benzoquinone quantitatively into the quinoneoxime ether, $O:C_6H_4:N \cdot O \cdot CH_2Ph$, a substance identical with the compound he obtained from sodium or silver nitrosophenoxide and benzyl chloride. Bridge's conclusion, which is perfectly sound, is a natural consequence of the conditions employed inasmuch as the sodium and silver salts, having originated in an alkaline environment, would possess quinonoid formulæ at the outset. A more interesting result from our point of view was Bridge's preparation from silver nitrosophenoxide and acetyl chloride of *p*-benzoquinoneoxime acetate identical with the product from nitrosophenol and acetic anhydride. We have found that acetic anhydride converts 3-chloro-4-nitrosophenol into the corresponding oxime, and therefore Bridge's two products were identical owing to the conditions of reaction. It may be mentioned here that we have obtained *p*-nitrosophenol of much higher melting point than that officially recorded, which is evidence that the product as usually prepared is a mixture of tautomerides.

A long discussion between Bridge (*Annalen*, 1893, 277, 79) and Kehrman (numerous papers) settled the question of the existence

of stereoisomeric alkyl and acyl derivatives of 2-chlorobenzoquinone-4-oxime. Kehrman found that ortho-substitution in the quinones retards or inhibits the formation of oximes, but his conclusion that the retardation or inhibition is due less to the nature of the substituent than to its presence in the ortho-position to the quinone oxygen needs modification, for we have found that a halogen atom exerts a far greater influence than a methyl group, and have obtained indications of a specific effect for each halogen.

When hydroxylamine salts are used for oxime formation, the effect of the acid, generally hydrochloric acid, cannot be ignored, and failure of attempts to prepare dioximes by prolonged boiling with excess of the reagent is attributable to the acid producing a feebly reactive geometric isomeride.

The dark red and the yellow modification of nitroso-orcinol prepared by Henrich (*Ber.*, 1896, **29**, 989; 1899, **32**, 3419) from the corresponding sodium derivatives by hot and cold acid, respectively, now appear to furnish an example of geometrical isomerism analogous to that of 3-chlorobenzoquinone-4-oxime. Similar cases are found in the monoethyl ether (Kietz, *Monatsh.*, 1898, **19**, 536) and the methyl ether (Henrich and Rhodius, *Ber.*, 1902, **35**, 1475; *J. pr. Chem.*, 1904, [ii], **70**, 313, 332; 1905, [ii], **71**, 56) of nitrosoresorcinol. The latter authors describe what they believe to be the two modifications, $\text{OH}\cdot\text{C}_6\text{H}_3(\text{OMe})\cdot\text{NO}$ and $\text{O}\cdot\text{C}_6\text{H}_3(\text{OMe})\cdot\text{NOH}$. In view of their identical melting point and ready interconvertibility, we believe them to be stereoisomeric oximes; in which case the nitroso-form should exist as a third modification, a possibility contained in Henrich's data, in which he describes a soluble, brown compound of m. p. 138°. This work is at present under our consideration.

The isolation of pure, well-defined nitroso- and quinoneoxime isomerides affords an example of inhibited dynamic isomerism. By the ordinary methods of forming nitroso-compounds, 3-chlorophenol affords mixtures of the tautomeric isomerides, the state of equilibrium being determined by the character of the acidic medium. The change from nitroso- to oxime form is, however, very slow at the ordinary temperature in an acid environment owing to steric hindrance, but in its absence, as in ordinary phenol, it appears probable that the oxime form will predominate. Our examples afford direct evidence against Laar's speculative theory of tautomerism, according to which the phenomenon is regarded as being intramolecular.

EXPERIMENTAL.

3-Chloro-4-nitrosophenol.—After many trials with the object of improving the yield and obviating the formation of resinous

by-products, Bridge's method (*loc. cit.*) was modified as follows: Eight c.c. of concentrated sulphuric acid, diluted with 12 c.c. of water, were added during two to three hours to a vigorously stirred solution of 4 grams of 3-chlorophenol in 300 c.c. of water containing 2 grams of caustic soda and 10 grams of sodium nitrite, the temperature being maintained at about 0°. After many hours, a greenish-yellow, crystalline substance (3 grams; 60 per cent. of the theoretical yield), m. p. 129°, separated and the liquor contained nitrous acid; on one occasion, after the product was filtered off, the mother-liquor, which had been retained over the week-end, deposited large, star-shaped crystals, m. p. 129·6°, which were seen under the microscope to consist of aggregates of long needles.

The compound so formed is moderately soluble in cold alcohol or ether, giving greenish-yellow solutions (a characteristic of nitroso-compounds), but is almost insoluble in cold benzene. From alcohol diluted with water it crystallises in orange-yellow needles, m. p. 135°, from hot water in dark orange-yellow needles, m. p. 130°, and from hot benzene in greenish-yellow crystals melting at 135·8°. It dissolves in molten phenol or molten naphthalene, forming deep red solutions, gives a bluish-violet colour in Liebermann's reaction, and is non-volatile in steam. In the attempted steam-distillation a black residue, m. p. (if any) above 250°, was obtained and from the aqueous solution a red substance separated, its melting point, 130—165°, indicating partial conversion. No silver, mercury, or lead salt could be formed, and the nitroso-compound appeared to react as an alcohol rather than as a phenol (Found: Cl = 22·77; *M*, in freezing phenol, 152, 159. Calc. for $C_6H_4O_2NCl$, Cl = 22·52 per cent.; *M* = 157·5). From its low melting point, inability to form metallic salts, ease of conversion into the tautomeride, and general behaviour as an alcohol, the substance appears to be a true nitroso-compound.

The dissolution of 3-chloro-4-nitrosophenol in phenol should be effected at a temperature only slightly exceeding the melting point of the solvent, on account of its acidic nature. To establish whether the phenol had exerted any conversion influence or not, it was extracted from the cryoscopic mixture by cold water; a yellow solid, m. p. 130°, remained and therefore the phenol had acted merely as a solvent.

It has been proved experimentally that the nitroso-group is in the para-position to the hydroxyl group, but as the work has involved the preparation of several new compounds, the authors reserve this proof for a later publication.

Conversion of 3-Chloro-4-nitrosophenol into Stereoisomeric 3-Chloro-benzoquinone-4-oximes.—When a solution of 3-chloro-4-nitroso-

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phenol in boiling dilute hydrochloric acid (1 part of acid to 2 of water) is cooled, dendritic crystals are deposited which vary in colour from reddish-orange to scarlet in different preparations and melt at about 170° . Crystallised from hot benzene, in which they are sparingly soluble, these yield clusters of orange or brownish-red plates, m. p. 172° (decomp.); occasionally, broad parallelograms are obtained. The melting points vary slightly according to the duration of the treatment with hydrochloric acid; the products having the lower melting points are doubtless mixtures of the geometrical isomerides produced by the acid. Prolonged boiling with moderately concentrated hydrochloric acid produces a red, crystalline substance, m. p. $210\text{--}215^{\circ}$ (compare Bridge, *loc. cit.*).

The red oxime forms a deep orange-yellow solution in alcohol, an orange solution in ether, and a deep red solution in phenol, and responds to Liebermann's nitroso-reaction, the colour being permanganate blue. No silver salt has as yet been obtained (Found: Cl = 22.03; M , in phenol, = 157.3. Calc. for $C_6H_4O_2NCl$, Cl = 22.52 per cent.; M = 157.5). The orange-red crystals recovered from phenolic solution melted at 170° .

Conversion of the Red into the Pale Yellow Isomeride.—When the above red compound was dissolved in dilute sodium hydroxide solution, no frothing (see later) occurred, and the cold solution on acidification deposited a very pale yellow precipitate which, under the microscope, was seen to consist of very characteristic, long, slender needles. The substance was practically pure, melting at $176\text{--}178^{\circ}$, and at 178° after recrystallisation from benzene (Found: Cl = 22.91 per cent.; M , in phenol, = 161.3, 155.7). The higher the melting point the paler is the colour of the product, indicating the removal of the original coloured isomeride. The substance forms pale yellow solutions in alcohol and ether, from which it crystallises readily, and an orange-yellow solution in phenol. It is sparingly soluble in cold or hot benzene, and on prolonged heating with benzene an insoluble resinous substance gradually forms. It responds to Liebermann's nitroso-reaction, giving a pure blue colour, and reacts with alcoholic silver nitrate to form a silver salt.

Interconversion of the Geometrical Isomerides.—The pale yellow compound of m. p. 178° is sparingly soluble in boiling dilute hydrochloric acid; the solution on cooling deposits the red form in dendritic masses, m. p. $170\text{--}172^{\circ}$, which are reconverted into the pale yellow form by treatment with alkali as above. A mixture of equal quantities of the two modifications melted at 170.6° .

Action of Alkalis on 3-Chloro-4-nitrosophenol.—In order to find

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out whether the pale yellow isomeride could be obtained directly from 3-chloro-4-nitrosophenol, a series of experiments with alkalis was undertaken.

The nitroso-compound dissolved in dilute solutions of caustic soda (2—10 per cent.) with much frothing (in contrast to the dissolution of the red oxime, which occurs without frothing), forming a deep red solution. Frothing commenced after an interval of a few seconds, and if the solutions were acidified prior to its appearance, brown precipitates having melting points varying from 166° to 146° were obtained, the more dilute solutions furnishing the substances of higher m. p.'s. Conversion had therefore taken place, but prolonged exposure to the alkali caused further changes and black precipitates of indefinite nature were produced.

In 2 per cent. sodium carbonate solution the nitroso-compound dissolved forming a red solution, from which it was reprecipitated unchanged by dilute hydrochloric acid. In 10 per cent. solution, however, the yellow precipitate obtained on acidification melted at 153—154°, indicating partial conversion, whilst dissolution in a cold saturated solution (about 16.5% Na_2CO_3 at 15°) followed immediately by acidification in the cold gave a pale yellow substance of m. p. 173—174°, showing that complete transformation had occurred. If the alkaline solution was kept for two hours before being acidified, a dull red substance of indefinite m. p. (140—160°) was then obtained, prolonged exposure having again caused complex changes.

Results could not be obtained with 2 per cent. sodium bicarbonate solution, the nitroso-compound being too insoluble, but it dissolved in the saturated solution (about 8 per cent. at 15°), giving a red solution which on acidification yielded a reddish-yellow product of m. p. 172°. Complete transformation into the quinoneoxime had therefore occurred, but only partial conversion into the pale yellow tautomeride; the acidic character of the sodium bicarbonate may have not only produced a mixture of the geometrical isomerides but also prevented complications.

Ammonia and pyridine also bring about conversion. The direct conversion of 3-chloro-4-nitrosophenol into the pale yellow quinone-oxime by alkalis is therefore free from complication only under special conditions, in contrast to the quantitative character of the transformation of the red isomeride.

Conversion during the Direct Nitrosation of 3-Chlorophenol.—When nitrosation was carried out so that mineral acid or even acetic acid was in excess, products were obtained melting at 160° and upwards, the best yields being obtained when the dilution was sufficient to retain most of the product in solution. It is

this result that led to the realisation of the correct conditions for the formation of the true nitroso-compound.

Comparative Reactions of the Three Isomerides. Solubility in Dilute Alcohol (3 parts of Alcohol to 1 part of Water).—The nitroso-compound is the most soluble, giving a greenish-yellow solution. The red oxime is much more soluble than its pale yellow isomeride; both solutions have an orange tinge.

Coloration with Ferric Chloride.—When ferric chloride was added to the above solutions, the nitroso-compound developed a deep olive-brown, and the two oximes a much lighter orange-brown colour.

An alcoholic solution of the nitroso-compound and excess of ferric chloride was kept until crystallisation occurred, when crystals of m. p. about 172° were obtained, showing the converting influence of ferric chloride.

Liebermann's Nitroso-reaction.—To 0.05 gram of each isomeride, 0.1 gram of phenol and 1 c.c. of concentrated sulphuric acid were added.

	Nitroso-compound.	Red oxime.	Yellow oxime.
First colour to appear	Green	Deep green	Deep green
Changing to	Prussian blue	Slowly to blue	Rapidly to blue
Colour after addition to 30 c.c. of 10% NaOH	Very intense blue	Greenish-blue	Greenish-blue
Colour of 10 c.c. of above solution diluted to 50 c.c. with water	Weak lilac blue	Deep pure blue	Deep pure blue
Colour of original alkaline solution after two days	Violet	Permanganate blue	Permanganate blue, not quite so deep as with the red oxime

Summary.

(1) 3-Chloro-4-nitrosophenol, the first true nitrosophenol to be isolated, has been prepared by a modification of the general nitrosation method.

(2) This 3-chloro-4-nitrosophenol is changed into quinoneoxime tautomerides by the regulated action of acids or alkalis. The difference of the melting points of the nitroso- and oxime forms is $40-50^{\circ}$.

(3) Acids produce a red tautomeride, which appears to be the *syn*-form, whilst alkalis convert this into the *anti*-modification, which is almost colourless in the solid state, but forms deep red solutions in aqueous alkalis.

(4) The *syn*- and *anti*-forms are interconvertible, but so far neither modification has been reconverted into the nitroso-compound.

(5) The moderate stability of 3-chloro-4-nitrosophenol which has

enabled it to be isolated is ascribed to the steric effect of the chlorine atom.

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