OZONOLYSIS OF NAPHTHOQUINONES—I

OZONOLYSIS OF 1:4-NAPHTHOQUINONE IN CHLOROFORM

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Abstract—During ozonisation of 1:4-naphthoquinone in chloroform at −5 to −8° about 70 per cent undergoes anomalous ozonolysis forming phenylglyoxal-*o*-carboxylic acid and probably carbon monoxide. The remaining 30 per cent forms a normal ozonide which rearranges to a mixed anhydride of formic acid and phenylglyoxal-*o*-carboxylic acid. Sodium iodide reduction of the normal ozonide produces *o*-phenylenediglycolaldehyde. An intramolecular benzoin condensation of this substance is discussed.

NAPHTHOQUINONES (especially the 1:4- or α-isomers) occur widely in nature and can be isolated from varied and unexpected sources. The yellow pigment lawson, (2-hydroxy-1:4-naphthoquinone) can be extracted from the leaves of *Lawsonia inermis*; phthiocol (2-hydroxy-3-methyl-1:4-naphthoquinone) has been isolated from *Mycobacterium tuberculosis*; echinochrome A (3-ethyl-2:5:6:7:8-pentahydroxy-1:4-naphthoquinone) occurs as a pigment in the eggs of *Arbacia punctulata* and other sea-urchins. Among other notable naturally occurring 1:4-naphthoquinones are vitamins K_1 and K_2.

Several naphthoquinones isolated are complex, and the elucidation of their structures present difficulties. In the determination of molecular constitution, ozonolysis occupies a prominent place, but only a few instances occur in the literature where naphthoquinones have been ozonised. Majima and Kuroda[1] ozonised shikonin (a dark red pigment from the roots of *Lithospermum erythrorhizon*) 2-(1-hydroxy-4-methyl-3-pentenyl)-5:8-dihydroxy-1:4-naphthoquinone(I), as well as its triacetyl
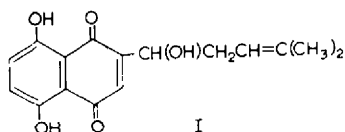
derivative. A pigment from the roots of *Alkanna tinctoria*, alkannin was ozonised by Dieterle, Salomon and Nosseck[2] who only identified oxalic acid. Later alkannin and its triacetyl derivative were ozonised by Brockmann[3] and its methyl ether by Raudnitz and Stein.[4] Brockmann also showed that alkannin and shikonin were optical isomers, alkannin being laevorotatory and shikonin dextrorotatory. In connection with the work on alkannin Raudnitz and Behrens[5] ozonised naphthazarin and two of its homologues.

Majima and Kuroda ozonised shikonin in a mixture of chloroform and water and isolated in this case only decomposition products of the side chain namely, acetone

[1] R. Majima and C. Kuroda, *Acta Phytochim., Tokyo* **1**, 43 (1922).
[2] H. Dieterle, A. Salomon and E. Nosseck, *Ber. Dtsch. Chem. Ges.* **64**, 2086 (1931).
[3] H. Brockmann, *Liebigs Ann.* **521**, 1 (1936).
[4] H. Raudnitz and W. Stein, *Ber. Dtsch. Chem. Ges.* **68**, 1479 (1935).
[5] H. Raudnitz and F. Behrens, *Ber. Dtsch. Chem. Ges* **68**, 1484 (1935).

peroxide and, on further oxidation with potassium permanganate, succinic acid. Triacetyl shikonin was ozonised in dry chloroform followed by hydrolysis of the ozonide with hot water. Again acetone peroxide was isolated and in addition 3:6-dihydroxyphthalic acid, which is of interest because it results from the cleavage of the double bond in the quinone ring. The degradation has, however, gone rather far as only two of the four extrabenzenoid carbon atoms of the ring are left.

Of immediate interest is the work done by Raudnitz and Behrens on ozonisation of naphthazarin, methylnaphthazarin (2-methyl-5:8-dihydroxy-1:4-naphthoquinone) and a dimethylnaphthazarin with methyl groups in 2-position and 6- or 7-position. Naphthazarin yielded 3:6-dihydroxyphthalic acid where we again may observe a rather drastic degradation of the quinone ring. Methyl naphthazarin gave a substance which on the basis of its composition $C_{10}H_8O_6$ was assigned the structure(II) methyl
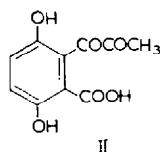
(3:6-dihydroxy-2-carboxy) glyoxal. Dimethylnaphthazarin gave a homologue of (II) with methyl in position 4 or 5. In none of the above-mentioned ozonolyses was the reaction between the quinone and ozone or reactions of the ozonide studied.

In the Criegee mechanism for ozonide formation,[6,7] the initial (but unspecified) adduct of ozone to the double bond breaks down to a carbonyl compound and a zwitterion. These two fragments will in some cases recombine to form a true ozonide, but in other cases the zwitterion may dimerise (or polymerise) leaving the carbonyl fragment as such:
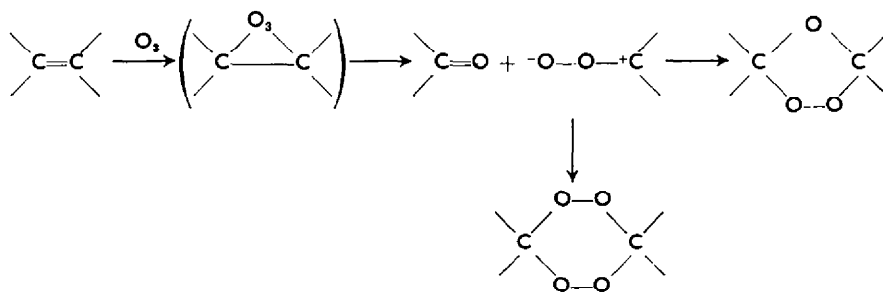
Other authors have discussed whether the addition of ozone to a double bond follows the rule of Markownikoff.[8,9] 1:4-Additions of ozone to such conjugated systems as furans and pyrroles have been investigated,[10] and attempts have been made to elucidate the mechanism of the initial attack of ozone on unsaturated systems and the nature of the primary addition compound.[11,12,13]

[6] R. Criegee, *Fortschr. Chem. Forsch.* 1, 528 (1949/1950)
[7] R. Criegee, A. Kerckow and H. Zinke, *Ber. Dtsch. Chem. Ges.* 88, 1878. (1955).
[8] P. S. Bailey, *Ber. Dtsch. Chem. Ges.* 88, 795 (1955).
[9] J. Meinwald, *Ber. Dtsch. Chem. Ges.* 88, 1889 (1955).
[10] P. S. Bailey and H. D. Colomb, *J. Amer. Chem. Soc.* 79, 4238 (1957).
[11] P. S. Bailey and S. S. Bath, *J. Amer. Chem. Soc.* 79, 3120 (1957).
[12] P. S. Bailey and J. B. Ashton, *J. Org. Chem.* 22, 98 (1957).
[13] P. S. Bailey, *Chem. & Ind.* 1148 (1957).

Ozone is classified as a "double bond reagent", by Badger,[14] and the mode of attack has been discussed by Brown[15] who assumes a one-stage process where ozone reacts with the bond of the lowest bond localisation energy. Wibaut and collaborators[16] have brought forth seemingly contrasting evidence for the electrophilicity of ozone. This would then imply a two-stage process with an initial attack on the carbon atom with the lowest atom localisation energy. These conflicting views seem now to have been reconciled by Bailey.[13]

In naphthoquinone(III) the reactivity towards ozone is dependent upon the localisation energy of the 2:3-double bond.

III   IV   V
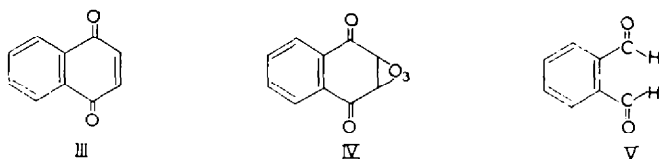
Assuming a complete localisation of the π-electrons in the idealised transition state IV and following the simple treatment of Kooyman and Ketelaar[17] an estimate could be obtained by subtracting the resonance energy of the "residual" molecule (here represented by phthalaldehyde V) from that of the "original" molecule(III). Unfortunately, the necessary thermochemical data are not available in the literature. The small resonance energy in p-benzoquinone is about 4 kcal/mole,[18] therefore the carbon–carbon double bonds in this molecule must be almost completely localised. Similarly, in the quinoid double bond of (III) a rather low localisation energy may be expected. This is in accordance with a qualitative observation made during ozonisation experiments with naphthoquinone. When ozone reacts with naphthoquinone in chloroform at -5 to $-8°$ a little ozone escapes indicating a slow reaction. This is not the case when ozonising a purely olefinic substance, but on the other hand, the volume of escaping ozone is not as large as when a purely aromatic substance is ozonised.

The ozonide of naphthoquinone does not separate during the reaction, but a viscous syrup is obtained after addition of petrol ether and this substance decomposes rapidly with the evolution of gas and acrid fumes in which carbon monoxide can be detected. The syrupy substance burns violently and liberates iodine from sodium iodide in glacial acetic acid, but due to its instability no attempt was made to determine the content of active oxygen. When kept under the solvent at about $+4°$ for some days it crystallises and carbon monoxide can be detected above the liquid. The crystalline substance does not contain active oxygen and is a monobasic acid, $C_9H_6O_4$. It reduces Tollens reagent but not Fehlings solution and gives a sparingly soluble derivative with o-phenylenediamine hydrochloride. This derivative, white needles, is a monobasic acid

[14] G. M. Badger, *Quart. Rev. Chem. Soc.* 5, 155 (1951).
[15] R. D. Brown, *Quart. Rev. Chem. Soc.* 6, 63 (1952).
[16] P. W. Haayman and J. P. Wibaut, *Rec. Trav. Chim.* 60, 842 (1941); J. P. Wibaut and E. C. Kooyman, *Ibid.* 65, 141 (1946); J. P. Wibaut and J. Van Dijk, *Ibid.* 65, 413 (1946); J. Van Dijk, *Ibid.* 67, 945 (1948); J. P. Wibaut, F. L. J. Sixma, L. W. F. Kampschmidt and H. Boer, *Ibid.* 69, 1355 (1950); H. Boer, F. L. J. Sixma and J. P. Wibaut, *Ibid.* 70, 509 (1951); F. L. J. Sixma, H. Boer and J. P. Wibaut, *Ibid.* 70, 1005 (1951); J. P. Wibaut and F. L. J. Sixma, *Ibid.* 71, 761 (1952); F. L. J. Sixma, *Ibid.* 71, 1124 (1952); L. W. F. Kampschmidt and J. P. Wibaut, *Ibid.* 73, 431 (1954); J. P. Wibaut and H. Boer, *Ibid.* 74, 241 (1955).
[17] E. C. Kooyman and J. A. A. Ketelaar, *Rec. Trav. Chim.* 65, 859 (1946).
[18] G. W. Wheland, *Resonance in Organic Chemistry* p. 99. New York (1955).

$C_{15}H_{10}O_2N_2$ related to quinoxaline. By cautious oxidation with nitric acid, $C_9H_6O_4$ was converted to phthalonic acid. This evidence strongly suggests that $C_9H_6O_4$ is phenylglyoxal-*o*-carboxylic acid (VI), or by analogy with phthalaldehydic acid and its
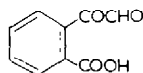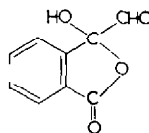

VI   VII

derivatives[19] may have a phthalide structure (VII). It is acidic and reacts with an ethereal solution of diazomethane with evolution of nitrogen. The infra-red spectrum of $C_9H_6O_4$ shows two bands at 1700 and 1722 cm^{-1} due to the aldehydic and ketonic carbonyl groups. A strong carboxyl frequency (deformation frequency) occurs at 1270 cm^{-1}. For comparison the spectra of phthalide carboxylic acid and phthalide were recorded and showed strong lactone bands at 1765 and 1740 cm^{-1} respectively. In this region the substance only shows a not very prominent shoulder. It may therefore be concluded that the acid $C_9H_6O_4$ occurs as (VI) but is perhaps in equilibrium with small amounts of (VII). This seems to be borne out by observations made during sublimation *in vacuo* at 130-140° (bath temperature). A gas is evolved and a white, macrocrystalline, substance sublimes, which was shown to be a mixture of phthalide
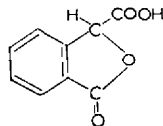

VIII

and phthalide carboxylic acid (VIII). The latter may result from thermal rearrangement of (VII), and phthalide by decarboxylation of (VIII). The equilibrium between (VI) and (VII) must therefore be displaced towards (VII) at higher temperatures. The presence of (VI) and formic acid after ozonolysis of naphthoquinone was confirmed (see experimental section). An attempt to prepare (VI) by oxidation of acetophenone *o*-carboxylic acid with selenium dioxide was unsuccessful (compare Sato and Ohta[20]), the product of the oxidation was phthalide carboxylic acid.

Assuming the structure (IX) for the ozonide of naphthoquinone hydrolysis would give *o*-phenylenediglyoxal (X) and hydrogen peroxide, but (X) has not been isolated and traces only of hydrogen peroxide were detected during the treatment of the ozonide with water.
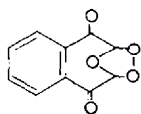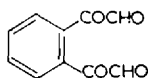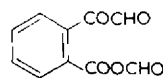
IX   X   XI

Ozonides can, like other peroxidic compounds, undergo rearrangements where one of the "peroxidic" oxygen atoms is interposed between two carbon atoms. In this

[19] D. D. Wheeler, D. C. Young and D. S. Erley, *J. Org. Chem.* 22, 547 (1957).
[20] T. Sato and M. Ohta, *Bull. Chem. Soc. Japan* 28, 480 (1955).

case such a rearrangement would lead to the structure(XI) which is a mixed anhydride of phenylglyoxal-*o*-carboxylic and formic acids. Treatment with water would give both acids while the substance itself under anhydrous conditions probably decomposes with evolution of carbon monoxide and formation of phenylglyoxal-*o*-carboxylic acid. Such decompositions of mixed anhydrides of formic acid with formation of carbon monoxide are well known. From the experimental data it may be assumed that (IX) is formed which rearranges into the mixed anhydride (XI) followed by decomposition to phenylglyoxal-*o*-carboxylic acid (VI) and carbon monoxide. When the ozonisation is complete, some of the ozonide has rearranged and decomposed. Addition of water will hydrolyse the anhydride thus accounting for formic acid. If the ozonisation mixture is left the remaining ozonide rearranges and evolves further amounts of carbon monoxide. After 5 hr when the mixture contained no more active oxygen, 6 per cent of formic acid was found, and this is probably due to traces of water formed during the ozonisation.

Another explanation may be so-called "anomalous" ozonolysis, which in the literature[21,22] is supposed to occur, if the double bond in question is conjugated with

XII
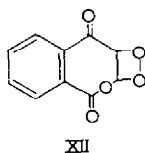
groups C=O, —CH$_2$OH, —S,— etc. In this case the peroxidic compound would perhaps have a structure as (XII) (or an ionic equivalent) which also could give phenylglyoxal-*o*-carboxylic acid, formic acid and carbon monoxide. Doubts are expressed in the literature, that structures of this type have more than transistory existence except at very low temperatures.

The ozonisation mixture on treatment with sodium iodide in glacial acetic acid, yielded a neutral product, C$_{10}$H$_{10}$O$_4$, which reduces Tollens reagent instantly and
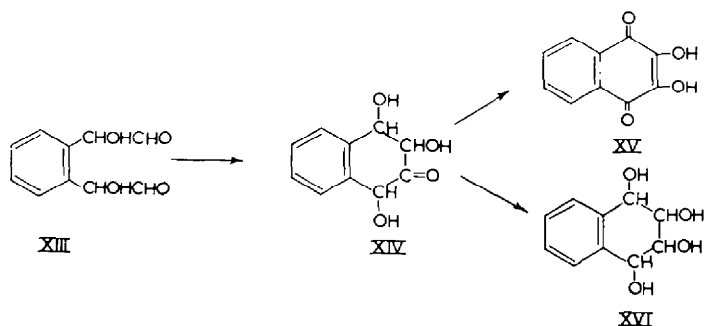
Fehlings solution in the cold. It was oxidised to phthalic acid by hydrogen peroxide and reacted with 2:4-dinitrophenylhydrazine to give a mixture of compounds from which only a monohydrazone could be isolated. Likewise only a monourethane was

[21] J. E. Löffler, *Chem. Rev.* 45, 385 (1949).
[22] R. Criegee, P. de Bruyn and G. Lohaus, *Liebigs Ann.* 583, 25 (1953).

isolated with phenyl*iso*cyanate. The most probable structure for $C_{10}H_{10}O_4$ is *o*-phenylenediglycolaldehyde (XIII).

A hot alcoholic solution of (XIII) turned intensely violet on addition of potassium cyanide solution. On acidification *iso*naphthazarin (XV) separates. Assuming that (XIII) undergoes an intramolecular benzoin condensation to (XIV) *iso*naphthazarin formation must be accompanied by dehydrogenation. The yield of *iso*naphthazarin under varying conditions, was about one third of the theoretical amount. As a tentative hypothesis, three molecules of (XIV) could yield one *iso*naphthazarin of (XV) and two of hydroxytetralin (XVI) thus:

$$3C_{10}H_{10}O_4 = C_{10}H_6O_4 + 2C_{10}H_{12}O_4$$

The second condensation product has not been isolated.

Since the two C_2-side chains are intact in the reduction product $C_{10}H_{10}O_4$, they must be present in the ozonide which may be represented by (IX). The reduction of the ozonide to $C_{10}H_{10}O_4$ is in itself remarkable since two carbonyls have been reduced to secondary alcohol groups.

The reduction of the ozonide $C_{10}H_6O_5$ to $C_{10}H_{10}O_4$ requires six equivalents of iodide as compared with two equivalents in normal ozonide reductions. Based on the amount of liberated iodine it was found that about 30 per cent of the theoretical amount of ozonide was present immediately after the ozonisation. This is in good agreement with the values for formic acid and carbon monoxide. The amount of $C_{10}H_{10}O_4$ isolated was somewhat higher, about 36 per cent, probably due to contamination with some phenylglyoxal-*o*-carboxylic acid. Analysis for the latter substance, the reduction mixture was found to contain 70 per cent of the theoretical value. Reducing the ozonisation mixture with less than the required amount of sodium iodide necessary for reduction of 30 per cent of the ozonide still gave $C_{10}H_{10}O_4$ but in correspondingly lower yields, and the remainder of the reaction product was again exclusively phenylglyoxal-*o*-carboxylic acid.

Ozonolysis of 1:4-naphthoquinone may proceed via normal or abnormal ozonides but since the content of active oxygen in the reaction mixture decreases very slowly if kept at the same low temperature (-5 to $-8°$) the interaction between 1:4-naphthoquinone and ozone may be:

    (1) 70 per cent of the quinone undergoes anomalous ozonolysis producing free phenylglyoxal-*o*-carboxylic acid and carbon monoxide.

    (2) 30 per cent of the quinone converted to the normal ozonide (IX), which slowly rearranges to the mixed anhydride (XI) and decomposes further to (VI) and carbon monoxide.

The rearrangement of the normal ozonide is accompanied by evolution of heat and is not catalysed by *p*-toluenesulphonic acid or acetic acid. The presence of the mixed anhydride (XI) was determined by adding *n*-butyl alcohol to the ozonised solution and distillation of the mixture. An almost quantitative yield of *n*-butyl formate in an azeotropic mixture with *n*-butyl alcohol was obtained.

EXPERIMENTAL
(Melting points are uncorrected.)

Ozone was prepared using an apparatus consisting of ten Berthelot tubes (11000 V). Oxygen was carefully purified and the ozone–oxygen mixture was dried by passing

through a dry ice trap. Chloroform was used as solvent and was purified by distillation from phosphorus pentoxide. A gas washing bottle fitted with a sintered bottom to distribute the gas was used as a reaction vessel.

Ozonisation of 1 :4-*naphthoquinone*. A solution of the quinone (5 g) in chloroform (150 ml) was ozonised for 1 hr. The solution lost its yellow colour and acquired a bluish tinge (dissolved ozone). Petrol ether (b.p. 30–40°, 300 ml) was added and the milky suspension chilled in a refrigerator for some hours until a syrup separated. A portion was allowed to decompose in a flask with a suspended strip of filter paper moistened with palladium chloride solution (0·05 mole PdCl₂, 0·2 mole Na₂SO₃ and 0·4 mole CH₃COONa). This blackened indicating the presence of CO.

Phenylglyoxal-o-*carboxylic acid* (VI). On leaving the syrup from the foregoing experiment under the chloroform–petrol ether at +4° for several days the greater part crystallised. In the space above the liquid moist palladium chloride paper rapidly became black. The crystalline substance did not decompose at room temperature and did not liberate iodine from sodium iodide in glacial acetic acid. It was recrystallised twice from glacial acetic acid–carbon tetrachloride (1:1) and from glacial acetic acid. m.p. 120–122° (Found: C, 60·7; H, 3·6; E, 177; $C_9H_6O_4$ requires C, 60·7; H, 3·4%; E, 178). To an aqueous solution of (VI) o-phenylenediamine in dilute hydrochloric acid was added when a mass of fine white needles was deposited which crystallised from ethanol, m.p. 277–277·5°. (Found: C, 71·9; H, 4·1; N, 11·2; E, 252. $C_{15}H_{10}O_2N_2$ requires C, 72·0; H, 4·0; N, 11·2 per cent; E, 250).

Oxidation of phenylglyoxal-o-*carboxylic acid to phthalonic acid*. The ozonisation mixture from naphthoquinone (5·0 g) was shaken mechanically with water until the chloroform layer gave a negative test with sodium iodide in glacial acetic acid. The aqueous solution was concentrated *in vacuo* to 45 ml. To 30 ml of this solution, concentrated nitric acid (15 ml) was added and the mixture heated on a steam-bath for 5 hr. A viscous yellow oil remained which crystallised on addition of ethanol and stirring (3·3 g), and on recrystallisation from water gave white crystals (0·6 g) m.p. 195° (decomp.) identified as phthalic acid. The mother liquor on concentration gave a yellow oil which slowly crystallised. It was dissolved in ether, filtered, and fractionally precipitated with petrol ether (b.p. 30–40°). The third crop (ether–petrol ether ratio 1:5) gave white crystals m.p. 142–143° (Found: C, 55·9, H, 3·3. Calc. for $C_9H_6O_5$: C, 55·7, H, 3·1 per cent).

Conversion of phenylglyoxal-o-*carboxylic acid* (VI) *into phthalidecarboxylic acid* (VIII) *and phthalide*. (VI) was sublimed *in vacuo* at 120° (bath temperature). The acid melted and began to froth, and at 132° white crystals appeared on the condenser and the pressure increased from 0·015 mm to 0·075 mm. At 138° the pressure reached 0·12 mm and began to fall as the frothing subsided. The white crystals on the condenser were treated with hot benzine (b.p. 70–80°) leaving a portion undissolved, which was twice recrystallised from ethyl acetate–benzine (1:10) and identified as phthalidecarboxylic acid, m.p. and mixed m.p. with an authentic specimen of (VIII) 155–157°. (Found: C, 60·5, H, 3·6. Calc. for $C_9H_6O_4$: C, 60·7; H, 3·4 per cent). The benzine extract on concentration yielded phthalide m.p. and mixed m.p. with an authentic specimen 69–72°.

Oxidation of acetophenone-o-*carboxylic acid with selenium dioxide*. To selenium dioxide (0·6 g) in boiling dioxan (10 ml) water was added dropwise until a clear solution was obtained to which acetophenone-o-carboxylic acid (1·05 g) was added

and the mixture refluxed for 15 hr. The black precipitate of selenium was removed by filtration, and the solution which only showed a weak reaction for selenium dioxide with aqueous sulphur dioxide, was concentrated to a yellowish brown syrup, which was dissolved in ethanol and filtered to remove traces of selenium. To the ethanolic filtrate o-phenylenediamine hydrochloride was added and the crystalline precipitate collected and crystallised from dilute acetic acid. The crystals sintered at 225° and melted at 232°, and mixed with an authentic specimen of the condensation product from phthalonic acid and o-phenylenediamine showed no depression. (Found: C, 67·9; H, 4·0; N, 10·4. Calc. for $C_{15}H_{10}O_3N_2$: C, 67·7; H, 3·8: N, 10·5 per cent). Titration of the derivative did not give good values. (Found: E, ca. 250. Calc. E, 266). The end-point (phenolphthalein) was not sharp, probably connected with the fact that the derivative is a hydroxyquinoxaline which can react as a dibasic acid with a second equivalence point at a high pH value.

Hydrolysis of the ozonide of 1:4-*naphthoquinone.* The latter (5 g) was ozonised and the chloroform solution immediately shaken with water (300 ml) until all active oxygen had disappeared. The aqueous layer was distilled and the distillate (250 ml, pH 2–3) was shown to contain formic acid and by titration with standard alkali was found 28 per cent of the theoretical value. If the ozonide solution was left for $5\frac{1}{2}$ hr at room temperature before treatment with water, (all active oxygen having disappeared) alkali titration indicated only 6 per cent of the theoretical value of formic acid.

To determine the amount of phenylglyoxal-o-carboxylic acid produced by the hydrolysis of the ozonide, 125 ml of the above-mentioned aqueous layer was treated with o-phenylenediamine (1 g) in dilute HCl solution. After 1 hr the derivative was filtered, washed with water and dried to constant weight (1·5 g), corresponding to 95 per cent of the theoretical value. For experimental control phenylglyoxal-o-carboxylic acid (0·1014 g) was dissolved in water and precipitated as described above, yielding 0·141 g of derivative, i.e. 99 per cent of the calculated amount.

Quantitative determination of carbon monoxide formed by decomposition of the ozonide. Dry air was passed through the ozonised solution of 1:4 naphthoquinone (2 g) and led through a dry ice trap to remove chloroform and other condensable impurities, and then through a tube filled with granulated iodine pentoxide maintained at 120°. Towards the end of the reaction it was necessary to warm the chloroform. The subsequent procedure is similar to that described by Bayer;[23] 29 per cent of the theoretical amount of carbon monoxide was formed which is high if the 6 per cent formic acid still present in the ozonide mixture after remaining several hours is taken into account.

Only traces of hydrogen peroxide were observed in the ozonised solution after vigorous shaking with ice water for some minutes and addition of potassium titanyl oxalate.

Reduction of 1:4-*naphthoquinone ozonide with sodium iodide.* The ozonised solution of 1:4-naphthoquinone (5 g) was treated with sodium iodide (20 g) in glacial acetic acid. The temperature rose to 30° and the liberated iodine was decolorised with aqueous sodium sulphite and the chloroform layer after washing with water to remove acetic acid was dried over sodium sulphate and evaporated to dryness in a stream of dry air, leaving a residue of brownish oil which crystallised from benzine (b.p.70–80°) and ethyl acetate (2:1) in white needles (0·4 g). The needles were sublimed *in vacuo*

[23] Bayer, "*Gasanalyse*", *Die Chemische Analyse XXXIX* p. 56. Stuttgart (1938).

(0·02 mm) and final crystallisation from ethyl acetate gave white needles m.p. 114–115°
(Found: C, 61·4; H, 5·2; $C_{10}H_{10}O_4$(XIII) requires C, 61·8; H, 5·2 per cent). The
iodine liberated during reduction of the ozonide was determined by titration with
sodium thiosulphate. Based on the oxidation of six equivalents of iodine, the yield of
(XIII) corresponded 29·4 per cent of the theoretical value, but the amount of (XIII)
isolated as above from the same volume of solution of the ozonide corresponded to
36 per cent.

Excess NaI in the reduction interfered with the isolation of (VI). Reduction with
the calculated amount of NaI and conversion of (VI) to the quinoxaline on treatment
with o-phenylenediamine indicated a yield of 70 per cent. Ozonisation at −60 to −70°
(solid CO_2 and acetone) did not increase the content of active oxygen. Reduction of
the ozonised solution of naphthoquinone (5 g) with NaI (4 g) in acetic acid (25 ml) and
titration with sodium thiosulphate showed that the NaI had been completely oxidised,
and the amount of $C_{10}H_{10}O_4$ (crude) was 1·1 g, 18 per cent of the theoretical value. In
addition aqueous extracts gave (VI) 85 per cent. To determine the decrease of active
oxygen after ozonisation of naphthoquinone (5 g), the solution was kept at −8° and
5 ml samples were withdrawn at intervals (starting from the disappearance of the
yellow colour of naphthoquinone) and run unto NaI in glacial acetic acid and titrated
with sodium thiosulphate.

Time (hr):	0	1	2	3	4	15
Titration value (ml):	23·3	21·6	21·0	20·3	19·8	16·1

The rate of decrease of active oxygen was not altered significantly by addition of
acetic acid or p-toluenesulphonic acid. At the ordinary temperature the ozonised
solution lost active oxygen in 2 hr.

To a solution of XIII (0·43 g) in hot water (50 ml) hydrogen peroxide (6 ml, 35 per
cent) was added, and on evaporation to dryness gave yellowish white crystals (0·3 1g, 84
per cent) which were identified as phthalic acid.

2:4-Dinitrophenylhydrazine (1 g) in dilute HCl (110 ml) and XIII (0·23 g) in ethanol
(10 ml) gave a red crystalline hydrazone m.p. 164° (decomp). (Found: C, 51·1;
H, 3·7; N, 14·6. $C_{16}H_{14}O_7N_4$ requires C, 51·3; H, 3·8; N, 15·0 per cent),
corresponding to (XIV). With phenylisocyanate (2 ml) and triethylamine (2 drops),
XIII (0·21 g) in hot benzine (b.p. 90–100°, 10 ml) on refluxing for 30 min deposited
white needles, m.p. 144–145° (Found: C, 64·7; H, 5·2; N, 4·4. $C_{17}H_{15}O_5N$ requires
C, 65·2; H, 4·8; N, 4·5 per cent), corresponding to addition of XIII (1 mole) and
phenylisocyanate (1 mol).

Intramolecular benzoin condensation of (XIII). To a solution of (XIII) (381 mg) in
hot ethanol (5 ml) an aqueous solution of KCN (5 ml, 1 N) was added. The mixture
assumed a deep violet colour and after heating (2 min) was acidified with 2 N HCl.
After dilution with water (50 ml) and cooling the dark red product was sublimed *in
vacuo* and crystallised from benzene, m.p. 276°, and identified as isonaphthazarin (XV)
(Found: C, 62·9; H, 3·3 Calc. for $C_{10}H_6O_4$ C, 63·2; H, 3·2 per cent) With acetic
anhydride a *diacetyl derivative* was obtained, crystallising from aqueous acetone
(charcoal), m.p. 110° (Found: C, 61·4; H, 3·8. Calc. for $C_{14}H_{10}O_6$ C, 61·3; H, 3·7
per cent). The identities of isonaphthazarin and its diacetyl derivative were established

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by comparison of their X-ray powder diagrams with those of authentic samples. Some examples of the yield of condensations and the conditions are given below.

$C_{10}H_{10}O_4$(mg)	Ethanol	KCN	Boiling	Yield (mg)	
645	15 ml	10 ml, 1 N	1 min	235	
2000	20 ml	0·5 g, 10 ml H_2O	1 min	650	(hydrogen
282	3 ml	0·1 g, 100 ml H_2O	5 min	100	atm).

Existence of the mixed anhydride (XI). To the ozonised solution of naphthoquinone (10 g) in chloroform (250 ml) pure *n*-butyl alcohol was added in 30 min and the temperature rose to 35°. Distillation of the mixture through a Widmer column gave a fraction (3·23 g, b.p. 102–106°), and the hydrolysis indicated 2·07 g (32 per cent) *n*-butyl formate. Refractionation gave the azeotrope (b.p. 105–106°) with an ester content of 76 per cent. The binary azeotrope of *n*-butyl formate and *n*-butyl alcohol is reported[24] to have b.p. 105·8° and an ester content of 76·4 per cent. The identity of the azeotrope was established by comparison of its infra-red spectrum with that of an authentic sample.

[24] Hannotte, *Bull. Soc. Chim. Belg.* **35**, 90 (1926).