Oxidation of Alicyclic Compounds with Pernitrous Acid

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It has been reported by many workers[1-5] that the reaction of hydrogen peroxide with nitrous acid, nitrate, nitrite, etc. produces unstable peroxy compounds of nitrogen. Baeyer and Villiger[1] inferred the formation of an unstable pernitrous acid as an intermediate during the reaction between hydrogen peroxide and nitrous acid, and Rasig[2] showed the presence of pernitric acid (formulated as HNO_4) from the fact that a mixture of hydrogen peroxide and nitrous acid was a stronger oxidizing agent than either of its components. Kortum and Finckh[3] observed that the transient yellow color solution, prepared by mixing acidified hydrogen peroxide with sodium nitrite, had an ultraviolet absorption band with a maximum close to that of nitrate ions, but about fifteen times more intense and much broader. Halfpenny and Robinson[4] suggested the formation of pernitrous acid and further proposed the homolytic fission of pernitrous acid to give a hydroxy radical and nitrogen dioxide on the grounds of the polymerization of methylacrylate or reaction with simple aromatic compounds.

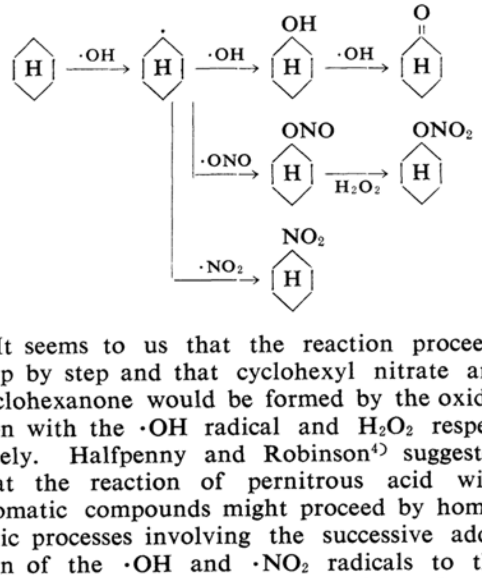
Laville et al.[5] supported the above considerations and postulated the nitration process of quinoline by the free radical mechnism. Recently, Johnson and Lockett[6] reported the mechnism of pernitrous acid formation from their observation of the effect of oxygen and hydrogen peroxide on the oxidzing action of nitrous acid. This investigation was carried out in order to obtain some information about the oxidation behavior of aliphatic compounds with the pernitrous acid produced as an active oxidizing species in the reaction system. Cyclohexane and cyclohexene were chosen as the starting materials.

Results and Discussion

When cyclohexane and cyclohexene were oxidized by hydrogen peroxide containing nitrous acid in a slightly acidic solution, several compounds were obtained as the reaction products. When cyclohexane was treated with pernitrous acid at 0~2°C, cyclohexanol was obtained as the main product, and cyclohexanone, cyclohexyl nitrate and nitrocyclohexane were also confirmed by gas chromatography, infrared spectra and/or the identification of derivatives. It was assumed that these products would be produced by the following course, in which the hydroxy radical resulting from the homolytic fission of pernitrous acid initially attacks cyclohexane and in which, after the abstraction of the hydrogen atom, the cyclohexyl radical formed reacts with the $\cdot OH$, $\cdot ONO$ and $\cdot NO_2$ radicals.

$$H_2O_2 + HNO_2 \rightarrow HOONO + H_2O$$

$$HOONO \rightarrow \cdot OH + \cdot ONO \leftrightarrow \cdot NO_2$$



It seems to us that the reaction proceeds step by step and that cyclohexyl nitrate and cyclohexanone would be formed by the oxidation with the $\cdot OH$ radical and H_2O_2 respectively. Halfpenny and Robinson[4] suggested that the reaction of pernitrous acid with aromatic compounds might proceed by homolytic processes involving the successive addition of the $\cdot OH$ and $\cdot NO_2$ radicals to the aromatic nucleus and that the abstraction of nuclear hydrogen by the hydroxy radical would not occur. However, the reaction of saturated hydrocarbons with these agents may proceed via the immediate hydrogen abstraction, followed by recombination with other radicals.

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[1] A. Baeyer and V. Villiger, *Ber.*, **34**, 755 (1901).

[2] F. Rasig, *Z. angew. Chem.*, **17**, 1419 (1904); *Ber.*, **40**, 4585 (1907).

[3] G. Kortum and B. Finckh, *Z. physik. Chem.*, **B48**, 32 (1941).

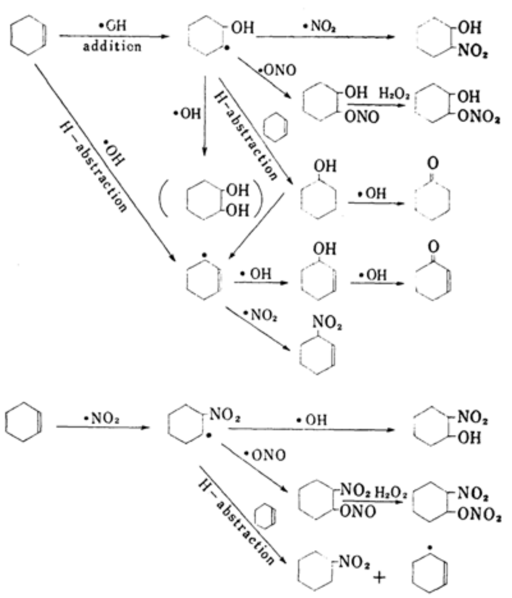
[4] E. Halfpenny and P. L. Robinson, *J. Chem. Soc.*, **1952**, 928, 939.

[5] J. R. Laville and W. A. Waters, *J. Chem. Soc.*, **1954**, 400.

[6] A. Johnson and A. P. Lockett, *Proc. Chem. Soc.*, **1961**, 218.

Cyclohexene was treated with pernitrous acid prepared from nitrous acid and an excess amount of hydrogen peroxide. From the water-insoluble part of the reaction products, cyclohexanol, cyclohexanone, cyclohexene-3-ol and cyclohexen-3-one were detected as oxygen-containing components; they were considered to be formed by the attack of the hydroxy radical on the double bond or the α-hydrogen atom of cyclohexene. The presence of nitrocyclohexane, 3-nitrocyclohexene and cyclohexyl nitrate as nitrogen-containing components may be assumed on the basis of the analysis of the infrared spectrum and the physical properties. *trans*-2-Nitrocyclohexyl nitrate was also isolated as a higher boiling product which might be formed by the hydrogen peroxide oxidation of the *trans*-2-nitrocyclohexyl nitrite produced by the reaction of the nitro radical with cyclohexene.[7] *trans*-2-Nitrocyclohexanol was obtained as a main product from the water-soluble part. The reduction of this part with lithium aluminum hydride gave *trans*-2-aminocyclohexanol and *trans*-cyclohexan-1, 2-diol, which was considered to be derived from *trans*-hydroxycyclohexyl nitrate. The presence of the nitrite was also detected by the infrared spectrum of the water-soluble part. In this experiment, no cis-isomers of these products were detected. The formation of *trans*-2-nitrocyclohexanol indicated that the simultaneous hydroxylation and nitration of the olefinic double bond with pernitrous acid might be possible. The yield of α-nitroalcohol was fairly low for the synthetic purpose because of the less selectivity of the reaction. The whole reaction might be interpreted by the free radical mechanism shown below. The hydroxy radical formed by the homolytic fission of pernitrous acid may attack an olefinic double bond or an α-hydrogen, and then the α-hydroxycyclohexyl radical or the cyclohexyl radical will be formed as the respective first intermediates, whereas the nitro radical may add to a double bond or may recombine with free radicals formed in this reaction system. These intermediate radicals may react with other radicals or may disproportionate to produce various products.

$$\mathrm{HOONO} \rightarrow \cdot\mathrm{OH} + \cdot\mathrm{ONO} \leftrightarrow \cdot\mathrm{NO_2}$$



When an excessive amount of sodium nitrite was used to prepare the pernitrous acid, 1-nitrocyclohexene and cyclohexane-φ-nitrosite were isolated in addition to the products described above. There products may be derived from the reaction of free nitrous acid.[8]

Cyclohexane-φ-nitrosite is produced in addition to the reaction product of pernitrous acid, so the excess amount of hydrogen peroxide must be used to avoid these side reactions.

Experimental

Materials.—The cyclohexane used was purified by treating it with fuming sulfuric acid and then by fractional distillation: b. p. 80.7°C, $n_D^{20}=1.4263$ (lit.[9] b. p. 80.7°C). Cyclohexene was prepared by the dehydration of cyclohexanol, and it was purified by fractional distillation before used: b. p. 82.5°C, $n_D^{20}=1.4449$ (lit.[10] b. p. 82.6°C).

These materials were confirmed to be pure by gas chromatography.

The Reaction of Cyclohexane with Pernitrous Acid.—Cyclohexane (1 mol.) was emulsified with a solution containing 100 ml. of 6% hydrogen peroxide, 5 ml. of 3 N hydrochloric acid and 80 ml. of water in 1 l. four-necked flask in a nitrogen atmosphere. A 5% sodium nitrite solution (150 ml.) and a 6% hydrogen peroxide solution (288 ml.) were simultaneously vigorously stirred drop by drop into the emulsion for about 1 hr. at 0∼2°C. The stirring was continued a further 4 hr. The organic layer from four runs experiments was separated and dried over anhydrous sodium sulfate. After the removal of the unreacted cyclohexane, the residual liquid was distilled under reduced pressure and 1 g. of an oily liquid (b. p. 39∼60°C/10 mmHg) was obtained; this was assumed to be

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[7] H. Baldock, N. Levy and C. W. Scaife, *J. Chem. Soc.*, **1949**, 2627.

[8] A. V. Topchiev and E. L. Fantalova, *Doklady Akad. Nauk S.S.S.R.* **88**, 83 (1953).

[9] A. Weiberger, "Technique of Organic Chemistry," Vol. VII, Interscience Publisher, Inc., New York (1955), p. 52.

[10] H. Gilman, "Organic Syntheses." Coll. Vol. I, 183 (1956).

a mixture of mono-functional cyclohexane derivatives. Four peaks were detected in this fraction by gas chromatography; two of them were identical with the those of cyclohexanol and cyclohexanone respectively; (column, silicon-550; 130°C). The fraction showed infrared absorption bands at 3320 cm^{-1} (OH); 1690 cm^{-1} (C=O); 1620, 1280, and 868 cm^{-1} (ONO_2) and 1545 and 1375 cm^{-1} (NO_2).[11] The reduction of this fraction with lithium aluminum hydride gave cyclohexylamine, which was identified as the hydrochloric acid salt (m. p. 203∼204°C (lit.[12] m. p. 203∼204°C)). This showed the presence of nitrocyclohexane in the above fraction. Cyclohexyl nitrate was assumed to be present on the basis of the infrared spectrum.

The Reaction of Cyclohexene with Pernitrous Acid.—A 5% sodium nitrite solution (150 ml.) and a 6% hydrogen peroxide solution (288 ml.) were added to an emulsion containing a 6% hydrogen peroxide solution (100 ml.), water (80 ml.) 3 N-hydrochloric acid (5 ml.) and cyclohexene (82 g.) in the manner described in the reaction of cyclohexane. The organic layer separated from ten runs was extracted with an aqueous sodium bicarbonate solution and was washed with water. After being dried over sodium sulfate, the organic layer was distilled to remove unreacted cyclohexene, and the residual oil was distilled under reduced pressure. From the fraction (1.2 g.) with a b. p. of 45∼57°C/3 mmHg, cyclohexanol, cyclohexanone, cyclohexyl nitrate and nitrocyclohexane were identified by gas chromatography, and 3-nitrocyclohexene was assumed to be present on the ground of its characteristic bands in the infrared spectrum: 1545 and 1368 cm^{-1} (NO_2) and 1665 cm^{-1} (C=C). The infrared analysis of this nitro-compound agreed with that of Brown.[13] The fraction (1.3 g.) (b. p. 58∼120°C/3 mmHg) was purified by chromatography using a silica gel column according to the procedure of Stevens;[14] it was judged to be *trans*-2-nitrocylohexyl nitrate from a comparison of its infrared spectrum with that of an authentic sample.[13] A mixture of the sodium carbonate solution and the washed water was acidified with N hydrochloric acid and mixed with the aqueous layer from ten runs. The resultant aqueous solution was extracted with chloroform, and the extract was dried over anhydrous sodium sulfate. The chloroform was evaporated, and 18.5 g. of the oily residue was distillated under reduced pressure; the following fractions were obtained:

Fraction 1: 7.8 g., b. p. 39∼64°/3 mmHg
Fraction 2: 7.7 g., b. p. 65∼104°C/3 mmHg
Residue: 2.9 g.

Fraction 1 was divided into three portions by preparative gas chromatography using a silicon-550 packed column. Each portion was distilled under reduced pressure. Cyclohexanol (3.4 g.) was isolated and identified as its α-naphthylurethane: (m. p. 128∼128.5°C (lit.[15] m. p. 128°C)); a mixed melting point with an authentic sample was not depressed.

Found: C, 57.79; H, 6.88. Calcd. for $C_{17}H_{19}NO_2$: C, 57.81; H, 7.11%.

The second portion (0.6 g. of liquid; b. p. 42∼43°C/3 mmHg) was identified as cyclohexen-3-ol by the infrared spectrum and its α-naphthylurethane derivative (m. p. 154∼155°C (lit.[16] m. p. 155°C)); a mixed melting point with an authentic sample showed no depression.

Found: C, 76.19; H, 6.15. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41%.

The third portion (1.4 g. of liquid; b. p. 54∼56°C/3 mmHg) was assumed to be cyclohexen-3-one on the basis of the bromine test and its infrared spectrum, which showed the strong characteristic band at 1680 cm^{-1} (conjugated carbonyl). Fraction 2 showed characteristic bands at 3320 cm^{-1} (OH); 1548 and 1375 cm^{-1} (NO_2); and 1625, 1275, 865, 760, and 690 cm^{-1} (ONO_2). Fraction 2 was reduced with lithium aluminum hydride. Fraction 2 (7.7 g.) was added drop by drop to a well-stirred solution of lithium aluminum hydride (9.0 g.) in ether (200 ml.). After the reaction mixture had been kept at 33°C for 5 hr., water (50 ml.) and a 20% aqueous solution of sodium potassium tartrate (150 ml.) were stirred in. The aqueous layer which separated was saturated with sodium chloride and then extracted with ether and ethanol. After these extracts had been mixed with the organic layer, the resultant mixture was dried over magnesium sulfate and the solvent was evaporated. The residual liquid was distilled under reduced pressure and 3 g. of a liquid (b. p. 70∼94°C/3 mmHg) was obtained. This fraction was cooled at 0°C, and the deposited crystalline solid was filtered. Recrystallization from a *n*-hexane-ligroin mixture gave *trans*-cyclohexan-1, 2-diol (0.7 g.), which was considered to be derived by the reduction of *trans*-hydroxycyclohexyl nitrite or *trans*-2-hydroxycyclohexyl nitrate (m. p. 103∼104°C (lit.[17] m. p. 103∼103.5°C)); a mixed melting point with an authentic sample showed no depression.

Found: C, 62.09; H, 10.40. Calcd. for $C_6H_{12}O_2$: C, 62.04; H, 10.41%.

The filtrate was dissolved in 50 ml. of benzene, and dry hydrogen chloride was passed through the solution. Recrystallization of the deposited solid gave 2 g. of *trans*-2-aminocyclohexanol hydrochloride (m. p. 175∼176°C (lit.[18] m. p. 176∼177°C)).

Found: C, 47.56; H, 9.29. Calcd. for $C_6H_{14}NOCl$: C, 47.52; H, 9.31%.

The Reaction of Cyclohexene with Hydrogen Peroxide and a Concentrated Sodium Nitrite Solution. — Cyclohexene (82.1 g.) was emulsified with a mixture of sulfuric acid (10 ml.) and water (80 ml.), and a sodium nitrite solution (69 g. in 250 ml. of water) and a 6% hydrogen peroxide solution (450 ml.) containing 17 ml. of water and 3 ml. of concentrated sulfuric acid were simultaneously added drop by drop to the emulsion at equal rate

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[11] J. F. Brown, *J. Am. Chem. Soc.*, **77**, 6341 (1955).

[12] O. Wallack, *Ann.*, **343**, 46 (1905).

[13] J. F. Brown, *J. Am. Chem. Soc.*, **77**, 6341 (1955).

[14] T. Stevens and W. D. Emmons, ibid., **79**, 6008 (1957).

[15] R. R. L. Shriner, R. C. Fason and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley & Sons, Inc., New York (1956).

[16] F. Clarke and L. N. Owen, *J. Chem. Soc.*, **1950**, 2103.

[17] A. Roebuck and H. Adkins, "Organic Syntheses," Coll. Vol. III, 217 (1948).

[18] G. E. McCasland, R. N. Clark and H. E. Caster, *J. Am. Chem. Soc.*, **71**, 637 (1949).

over a 2 hr. period while dry nitrogen was passed at $-5\sim-10$°C. The products, obtained from the two runs described above, were separated into three parts: a crystalline solid (1.6 g.) water-soluble products (10.0 g.) and water-insoluble products (5.5 g.). This solid was identified as cyclohexane-φ-nitrosite from its infrared spectrum which was in full accordance with that of Brown[19] (m. p. 153°C (decomp.)); it recrystallized from ethyl acetate; and a mixed melting point with an authentic sample showed no depression.

Found: C, 45.69; H, 6.52. Calcd. for $C_{12}H_{20}N_4O_6$: C, 45.56; H, 6.37%.

Distillation of the water-insoluble products gave 3-nitrocyclohexene (b. p. 54~56°C/1 mmHg Found: C, 56.82; H, 7.28. Calcd. for $C_6H_{10}NO_2$: C, 56.68; H, 7.14% and 1-nitrocyclohexene (b. p. 64~65°C/1 mmHg.

Found: C, 56.61; H, 7.29. Calcd. for $C_6H_{10}NO_2$: C, 56.68; H, 7.14%.

The infrared spectra of these nitro-compounds agreed with those of Brown.[11] Treatment of 1-nitrocyclohexene with semicarbazide acetate in methanol gave 2-nitrocyclohexylsemicarbazide after several days (m. p. 163~163.5°C (decomp.), from ethanol (lit.[20] m. p. 163°C)).

Found: C, 41.77; H, 6.97. Calcd. for $C_7H_{14}N_4O_3$: C, 41.62; H, 6.98%.

A small amount of *trans*-2-nitrocyclohexanol was obtained from the water-soluble products (b. p. 94 ~95°C/1 mmHg).

Found: C, 49.62; H, 7.91. Calcd. for $C_6H_{11}NO_3$: C, 49.64; H, 7.64%.

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[19] J. F. Brown, ibid., **77**, 6341 (1955).

[20] A. V. Topchiev and E. L. Fantalova, *Doklady Akad. Nauk S.S.S.R.*, **88**, 83 (1953).