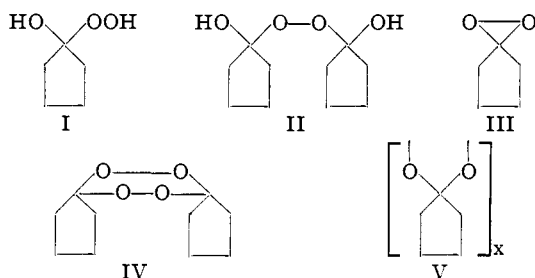


[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 197]

Studies in Organic Peroxides. VI. Cyclane Peroxides¹

BY NICHOLAS A. MILAS, S. ARTHUR HARRIS² AND PAUL C. PANAGIOTAKOS

When cyclic ketones are allowed to react with anhydrous hydrogen peroxide three types of peroxides may form: 1-hydroxycyclanyl hydroperoxide-1 (I), 1,1'-dihydroxydicyclanyl peroxide-1,1' (II) and cyclanylidene peroxides (III, IV, and V). Using cyclopentyl as the cyclopoly-methylene radical these may be illustrated as follows



In certain cases, especially with cyclopentanone and straight chain ketones like acetone, type I reverts spontaneously to type III, IV or V, whereas in other cases this reaction needs a suitable dehydrating agent.

Inasmuch as very little work has been reported in this field³ and we became interested in exploring it, the present communication describes some of our results in the synthesis of a number of cyclane peroxides. Hydrogen peroxide in aqueous solutions with a suitable catalyst or persulfuric acid have been found convenient reagents for the oxidation of cyclic ketones to the corresponding dicarboxylic acids.^{3,4} However, when hydrogen peroxide is used in non-aqueous solvents such as ether or *t*-butyl alcohol, very little or no oxidation occurs but instead peroxides of the type I, II, IV and V are formed.

Experimental Part

1-Hydroxycyclopentyl Hydroperoxide-1 (I).—The cyclopentanone (Eastman Kodak Company) used was purified by fractionation and the fraction boiling at 129–130° collected. A solution of 5 g. of the ketone in 100 cc. of 0.6 molal hydrogen peroxide in anhydrous ether was allowed to stand at room temperature for a few days.

(1) For other papers in this series see *THIS JOURNAL*, **55**, 349, 352 (1933); **56**, 1219, 1221 (1934); **60**, 2434 (1938).

(2) Fellow of the Massachusetts Pharmaceutical Corporation.

(3) Cf. Baeyer and Villiger, *Ber.*, **33**, 863 (1900); Stoll and Scherrer, *Helv. Chim. Acta*, **13**, 142 (1930).

(4) Ruzicka and Stoll, *ibid.*, **11**, 1159 (1928).

The ether was then removed at room temperature under reduced pressure and the viscous residue subjected to a vacuum of about 1 mm. for several hours to remove any unconverted ketone and free hydrogen peroxide. The viscous residue, 6.2 g., was analyzed for active oxygen using an acetone solution of sodium iodide acidified with acetic acid and titrating the liberated iodine against standard sodium thiosulfate.

Anal. Calcd. for $C_5H_{10}O_3$: active (O), 13.6. Found: active (O), 13.9, 14.4.

This experiment was repeated a number of times with both ether and *t*-butyl alcohol as solvents with identical results. It may be mentioned here that the peroxide is highly explosive and on one occasion when the equivalent of 10 g. of cyclopentanone was used with the corresponding amount of hydrogen peroxide in ether, a violent explosion occurred causing a considerable amount of damage, as the ether was being removed under vacuum at the temperature of the water-bath.

1,1'-Dihydroxydicyclopentyl Peroxide-1,1' (II).—A solution of 5 g. of cyclopentanone in 50 cc. of 0.6 molal hydrogen peroxide in anhydrous ether was allowed to stand at room temperature for a few days, then the ether was removed under reduced pressure and the viscous residue subjected to a vacuum of about 1 mm. for a few hours to remove all volatile products. The residue, 5.5 g., was analyzed for active oxygen.

Anal. Calcd. for $C_{10}H_{18}O_4$: active (O), 7.92. Found: active (O), 8.12, 7.84.

Dicyclopentylidene Peroxide (IV).—When 1-hydroxycyclopentyl hydroperoxide-1 is allowed to stand at room temperature for several days crystals (needles) begin to come out. These were separated and dried on a porous plate. Cooling the viscous residue to 0° for some time enhances crystallization. These crystals melt rather sharply at 73–75° and the melt begins to show evolution of gas at 105°. They explode violently when heated on a steel spatula.

Anal. Calcd. for $C_5H_{10}O_3 \cdot \frac{1}{2}H_2O_2$: active (O), 17.8. Found: active (O), 18.7, 18.6, 18.64.

This peroxide also has been prepared by allowing cyclopentanone (1 cc.) to react with 30% hydrogen peroxide, "Albone C," (1 cc.) for two days, then cooling the clear solution in an ice-salt mixture whereby a white crystalline solid separated out. This solid was dried on a porous plate and found to have a m. p. of 73–75° and an analysis of 18.6% active oxygen.

In view of these results, we have come to the conclusion that this peroxide is probably 1-hydroxycyclopentyl hydroperoxide-1 with half a mole of hydrogen peroxide of crystallization. Because of its explosiveness we were unable to run combustions for carbon and hydrogen. This also has been the case with all other peroxides obtained from cyclopentanone.

Whenever the peroxide, m. p. 73–75°, was recrystallized from ether or from a 50–50 mixture of ether and petroleum ether, a new crystalline (needles) peroxide was obtained, m. p. 160° with effervescence. This peroxide is soluble in a number of organic solvents including ether, alcohol, acetone, dioxane, etc. It liberates iodine instantly from a sodium iodide solution in acetone acidified with acetic acid.

Anal. Calcd. for $C_5H_8O_2$: active (O), 16.0. Found: active (O), 16.13, 15.6, 16.5.

Inasmuch as the m. p. of this peroxide is too high for a five carbon substance, it was suspected early that it might be a polymer of cyclopentylidene peroxide. A molecular weight was therefore taken in *t*-butyl alcohol and in camphor and found to be 206 and 202, respectively, as against 200 calculated for dicyclopentylidene peroxide.

Polycyclopentylidene Peroxide.—When 1,1'-dihydroxydicyclopentylidene peroxide-1,1' (II) is allowed to stand at room temperature for several days a solid peroxide separates out which melts at 166° with effervescence. A mixed m. p. with dicyclopentylidene peroxide showed no depression. However, unlike the latter peroxide this is completely insoluble in ether, alcohol, acetone and other common organic solvents, and, in view of this property, fails to liberate iodine from an acidified acetone-sodium iodide solution even after five days of standing at room temperature. Dioxane was the only suitable solvent, from which it was recrystallized several times with no change in m. p. An attempt to determine its molecular weight was unsuccessful. An analysis for active oxygen in an acidified solution of sodium iodide in dioxane gave highly unsatisfactory results. Finally, when it was refluxed in an acetone-acetic acid-sodium iodide solution for one hour, using appropriate blanks, it yielded only about three-fourths of its active oxygen.

Anal. Calcd. for $(C_5H_8O_2)_2$: active (O), 16.0. Found: active (O), 12.6.

Although this peroxide is very inert, under ordinary conditions, it explodes violently when heated on a steel spatula. A yield of over 50% was obtained as cyclopentylidene peroxide from the original reaction product.

This same polymer was also obtained in smaller quantities together with the dimer when the peroxide of m. p. 73–75° was treated with various solvents.

1-Hydroxycyclohexyl Hydroperoxide-1.—Five grams of cyclohexanone (b. p. 155–156°) was mixed with 85 cc. of 0.6 molal hydrogen peroxide solution in anhydrous ether and the mixture allowed to stand at room temperature for one day. The ether was then removed under reduced pressure and the viscous residue allowed to stand at room temperature, whereby it crystallized out after one day. The crystals were dried on a porous plate; yield, 3.8 g.; m. p. 76–78° which did not change appreciably after recrystallization from ether.

Anal. Calcd. for $C_6H_{12}O_3$: active (O), 12.13. Found: active (O), 12.94, 12.96.

This peroxide is rather stable and explodes only mildly when heated on a steel spatula.

1,1'-Dihydroxydicyclohexyl Peroxide-1,1'.—A solution of 8.8 g. of cyclohexanone in 87 cc. of 0.55 molal hydrogen peroxide in anhydrous ether was allowed to stand for two days. The ether was then removed under reduced pres-

sure and the highly viscous residue was allowed to stand at 0° for twenty-four hours, whereby it was converted into a white crystalline mass which was recrystallized from ether; m. p. 68–70°. A yield of 4.1 g. of the pure product was obtained. This peroxide is insoluble in water and fails to liberate iodine from an acidified solution of potassium iodide. It was therefore analyzed by the acetone method used throughout this work.

Anal. Calcd. for $C_{12}H_{22}O_4$: active (O), 6.96. Found: active (O), 6.89.

When heated on a steel spatula this peroxide does not explode but burns with a smoky flame.

Hydroxymethylcyclohexyl Hydroperoxides and Peroxides.—Seven peroxides were obtained from the three methylcyclohexanones. For the hydroperoxides equimolecular proportions of the ketones (Eastman Kodak Company) and 0.6 molal hydrogen peroxide in anhydrous ether were mixed together and the mixtures allowed to stand at room temperature for some time. For the peroxides the molal ratio used of the ketone to peroxide was 2:1. After a number of days, in all cases the ether was removed under reduced pressure and the products obtained separated and analyzed. All peroxides thus obtained with the exception of those obtained from *o*-methylcyclohexanone were highly viscous liquids but failed to crystallize even when cooled to –20°. The viscosity of the peroxides from *o*-methylcyclohexanone was rather low and only increased slightly when cooled to –20°. Analytical and other data of these peroxides are given in Table I.

TABLE I
SUMMARY OF DATA FOR THE HYDROXYMETHYLCYCLO-
HEXYL HYDROPEROXIDES AND PEROXIDES

Peroxide	Formula	Yield, %	Active (O) Calcd.	Active (O) Found
1-Hydroxy-3-methylcyclohexyl hydroperoxide-1	$C_7H_{14}O_3$	89	10.95	10.25, 10.27
1-Hydroxy-2-methylcyclohexyl hydroperoxide-1	$C_7H_{14}O_3$	90	10.95	10.51
1-Hydroxy-4-methylcyclohexyl hydroperoxide-1	$C_7H_{14}O_3$	86	10.95	11.48, 11.30
1,1'-Dihydroxy-3,3'-dimethylcyclohexyl peroxide-1,1'	$C_{14}H_{26}O_4$	98	6.21	6.21
1,1'-Dihydroxy-2,2'-dimethylcyclohexyl peroxide-1,1'	$C_{14}H_{26}O_4$	89	6.21	6.13
1,1'-Dihydroxy-4,4'-dimethylcyclohexyl peroxide-1,1'	$C_{14}H_{26}O_4$	89	6.21	6.07

When 1-hydroxy-3-methylcyclohexyl hydroperoxide-1 was allowed to stand at room temperature for a number of days, crystals began to separate which, after several recrystallizations from anhydrous ether, melted rather sharply at 120–121°.

Anal. Calcd. for $C_7H_{12}O_2 \cdot \frac{1}{2}H_2O_2$: active (O), 16.5. Found: active (O), 16.0.

This peroxide is highly explosive when heated on a steel spatula and behaves in all respects like the cyclopentylidene peroxide with hydrogen peroxide of crystallization. However, after several crystallizations we were unable to obtain 3-methylcyclohexylidene peroxide free from hydrogen peroxide.

1-Hydroxycycloheptyl Hydroperoxide-1.—Five grams of cycloheptanone was mixed with 100 cc. of 0.55 molal hydrogen peroxide in anhydrous ether and the mixture

was allowed to stand at room temperature for several days. When the ether was removed under reduced pressure, the highly viscous residue (4.5 g.) partly crystallized out, and the crystals separated and dried on a porous plate; m. p. 92–94°.

Anal. Calcd. for $C_7H_{14}O_3$: active (O), 10.95. Found: active (O), 10.00.

The dihydroxycycloheptyl peroxide was not prepared.

1-Hydroxycycloöctyl Hydroperoxide-1.—A solution of 4.4 g. of cycloöctanone in 120 cc. of 0.55 molal hydrogen peroxide in anhydrous ether was allowed to stand at room temperature for several days. To remove the excess hydrogen peroxide the mixture was then shaken several times with a saturated ammonium sulfate solution until the aqueous layer gave a negative test for hydrogen peroxide. The ether layer was then dried with anhydrous magnesium sulfate, filtered and the ether removed under reduced pressure. A highly viscous semi-solid product, 4.4 g., was obtained which became curdy on standing for several weeks at room temperature, but failed to crystallize even when cooled to -78° .

Anal. Calcd. for $C_8H_{16}O_3$: active (O), 10.00. Found: active (O), 9.65.

1,1'-Dihydroxycycloöctyl Peroxide-1,1'.—This peroxide was prepared in the same manner as the mono-

cycloöctyl except that the proportions of reagents used were different. A solution of 2.6 g. (0.0206 mole) of cycloöctanone in 22 cc. of 0.55 molal hydrogen peroxide in anhydrous ether was allowed to stand at room temperature for several days. It was then shaken several times with a saturated solution of ammonium sulfate until the latter showed no test for hydrogen peroxide. Finally, the ethereal solution was dried with anhydrous magnesium sulfate, filtered and the ether removed under reduced pressure. A yield of 2.2 g. of highly viscous product was obtained which failed to crystallize.

Anal. Calcd. for $C_{16}H_{30}O_4$: active (O), 5.59. Found: active (O), 5.53.

We are indebted to Dr. R. B. Woodward of Harvard University for supplying the C_7 and C_8 ketones.

Summary

Seventeen cyclane peroxides have been prepared by the interaction of hydrogen peroxide in anhydrous ether with a number of cyclic ketones.

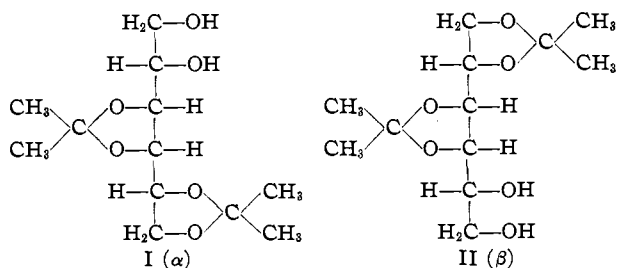
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[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Structures of the Diacetone Dulcitol¹

BY RAYMOND M. HANN, W. DAYTON MACLAY AND C. S. HUDSON

Recently Pizzarello and Freudenberg² have proposed structures for the two diacetone dulcitol³ that were originally described by Fischer,³ assigning to the α -diacetone dulcitol the structure of 3,4:5,6-diacetone dulcitol (I) and to the β -isomer that of 1,2:3,4-diacetone dulcitol (II).



Pizzarello and Freudenberg point out that the proposed structures are enantiomorphous and they emphasize that the ready separation of the α - and β -diacetone dulcitol³ by fractional crystallization is thus in conflict with general experience. It also

may be added that the substances exhibit very different melting points, solubilities and crystalline forms (as shown by optical crystallographic measurements), all of which facts seem to exclude the idea of enantiomorphism. Neither of them is optically active. The basis of assignment of the enantiomorphous structures was (1) that lead tetraacetate oxidation in benzene solution of both diacetone dulcitol³ yielded formaldehyde, indicating the presence of contiguous hydroxyl groups, one of which must be primary, in the molecules and (2) that α -diacetone dulcitol could be transformed by alkaline permanganate oxidation to a derivative of D-galactonic acid (potassium diacetone D-galactonate) and (3) that β -diacetone dulcitol under similar oxidative procedure yielded the enantiomorphous derivative of L-galactonic acid (potassium diacetone L-galactonate). A review of the earlier researches of Fischer³ and of Fischer and Bergmann⁴ upon the diacetone dulcitol³ revealed that these substances undergo several interesting

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Pizzarello and Freudenberg, *THIS JOURNAL*, **61**, 611 (1939).

(3) Fischer, *Ber.*, **48**, 269 (1915).

(4) Fischer and Bergmann, *ibid.*, **49**, 289 (1916).