

REACTIONS OF 2,2'-METHYLENE-BIS (CYCLOHEXANONE) WITH HYDROGEN PEROXIDE AND PEROXY ACIDS

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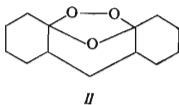
The oxidation of *meso*-form of 2,2'-methylene-bis(cyclohexanone) or its racemate, respectively by peroxy-compounds differs from the oxidation of cyclohexanone, the difference being in the dependence upon the reaction medium and the kind of isomer used. Whereas the oxidation of the *meso*-form by organic peroxy acids in non-aqueous media gives 6,6'-methylene-bis(6-hexanolide), the racemate yields, under identical reaction conditions, exclusively 7-(2-oxocyclohexyl)heptane-6-olide; when the oxidation was carried out in aqueous solution two isomeric forms of tricyclo-[7, 4, 0, 0^{2,7}]-1-tridecene ozonide have been isolated. The yield of both forms, that have not yet been described, depends on the isomerism of the initial 2,2'-methylene-bis(cyclohexanone).

The increasing importance of 6-hexanolide polymers is reflected in the interest about the synthetic routes leading to this monomer; the majority of preparative processes employs the oxidation of cyclohexanone either by Caro's acid¹⁻³ or by hydrogen peroxide in alkaline solution⁴. Lately, according to the patent literature survey, organic peroxy acids are also successfully used for the oxidation. These are prepared either from 85% hydrogen peroxide and formic⁵ or acetic⁶ acid; water free peroxy acids are then prepared again *via* the reaction of concentrated hydrogen peroxide with acid anhydrides such as acetic anhydride⁷, maleic anhydride⁸ and others. The most satisfactory results were obtained when cyclohexanone was oxidized by 25% solution of water free peracetic acid (prepared by the reaction of acetaldehyde with oxygen) in organic solvents⁹⁻¹². The oxidation of 2-alkylcyclohexanones by peracetic acid in solution yielded a series of compounds that are assumed to be 6-alkyl-6-hexanolides; some alkylene-bis(6-hexanolides) such as 6,6'-methylene-bis(6-hexanolide)¹³ have been prepared in a similar way.

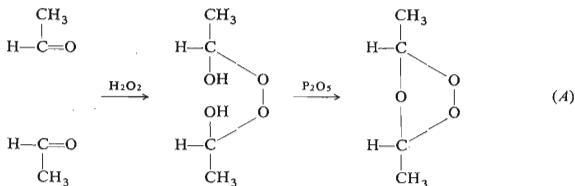
This work deals with the oxidation of 2,2'-methylene-bis(cyclohexanone). Cyclohexanone or its homologues when treated with peroxy compounds yields 6-hexanolide or its derivatives. On the other hand the activity of peroxidic compounds upon 2,2'-methylene-bis(cyclohexanone) (*I*) is not so straightforward and the products composition is dependent both on the type of a peroxy compound and on a reaction medium. When attempting to oxidize the diketone *I* by 30% hydrogen peroxide in alkaline solution at 40°C we isolated only the initial diketone (75%), whereas the oxidation of this ketone by Caro's acid resulted in the formation of very unstable explosive products of a peroxidic character whose structure has not yet been established. We have found that, contrary to the oxidation of cyclohexanone leading to 6-hexanolide formation, 6,6'-methylene-bis(6-hexanolide) is formed from *I* by

oxidation by peroxy acids in a completely water free system. The previously described preparation of 6,6'-methylene-bis(6-hexanolide) *via* oxidation of 2,2'-methylene-bis(cyclohexanone) by peracetic acid¹³ seems very dangerous, taking into account the reaction temperature which is maintained in order to remove acetic acid and its anhydride from the reaction system by distillation. We managed to arrange more gentle conditions for the isolation of the product when we employed permaleic acid; the maleic acid formed during the reaction is easily removed by filtration.

Rather surprising results were obtained from the runs where the diketone *I* was oxidized by water solutions of peroxy acids. The oxidation by performic acid (prepared from 85% formic acid and 85% hydrogen peroxide) resulted in a so far undescribed compound of a general formula $C_{13}H_{20}O_3$. The same compound was isolated after the reaction of 30% hydrogen peroxide with *I* in the presence of vanadium pentoxide or pervanadium compounds. Originally it was expected that dioxodicarboxylic acid will be formed (analogically as in the case of 3,7-dimethyl-6-oxooctanoic acid obtained by oxidation of methone¹⁴). The formula $C_{13}H_{20}O_3$ can be assigned to the ozonide of tricyclo[7,4,0,0^{2,7}]-1-tridecene:

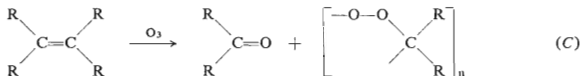
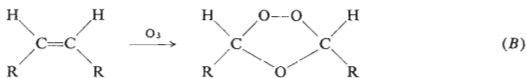


According to the literature data¹⁵⁻¹⁶, the ozonides are formed from two molecules of aldehydes and ketones, respectively, only in those cases where the oxidation of the carbonyl compounds is immediately followed by dehydration caused by the presence of dehydration agents such as phosphorus pentoxide. Thus an easy cyclization leading to the formation of a five membered ring is made feasible:

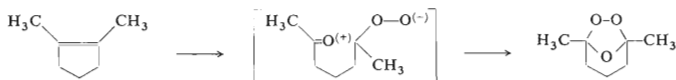


The ozonide structure of the product has, in this case, been proven by the ozonolysis of 2-butene. The structures of the resulting ozonide was identical with that obtained in reaction (A). The identity of both products has also helped to support the Staudinger's formulation of ozonides as peroxidic acetals. Though the reaction of ozone with unsaturated compounds is nowadays commonly used as a method of organic analysis, the products of this reaction are very rarely precisely defined

ozonides. Well defined and pure ozonides have only been prepared in the case of aldozonides whereas instead of corresponding ketozonides equimolar quantities a ketone and polymeric peroxidic derivatives¹⁷ have been isolated:

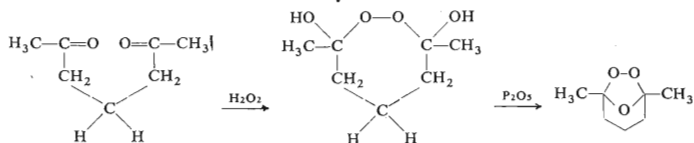


Criegee and coworkers¹⁷ have systematically studied the reaction of ozone with unsaturated compounds and they came to the conclusion that ketozonides can only be formed from hydrocarbons containing the double bond in a five-membered ring; the formation of ketozonides is, in this case, easier because of the intramolecular interaction of a keto group with the intermediately formed ion. The existence of this intermediate has been proven by the authors¹⁸:

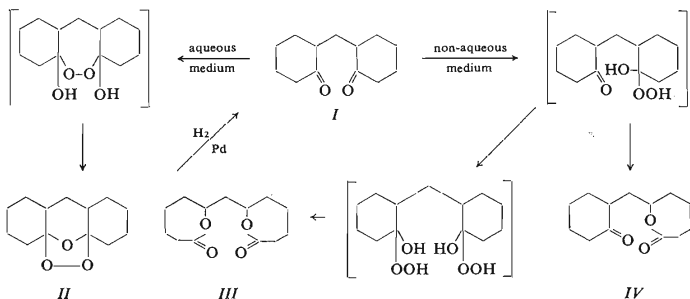


The steric factors for this intramolecular reaction are much less favourable in the case of cyclohexene derivatives so that the ozonides derived from these olefins are formed only in traces.

The formation of the ozonide *II* by oxidation of diketone *I* by peroxy compounds in aqueous solution can be explained, besides the above mentioned facts, also by the known data about the influence of substituents. Whereas the ozonolysis of 1,2-dimethyl-1-cyclopentene gives the corresponding ozonide in 90% yield, the 1-methyl derivatives yielded only 50% of the ozonide and in the case of cyclopentene only 7% of ozonide is formed¹⁹. Criegee and coworkers¹⁹ have prepared 1,2-dimethyl-1-cyclopentene ozonide in 50% yield by the reaction of 2,6-dioxoheptane with ether solution of hydrogen peroxide followed by dehydration in the presence of phosphorus pentoxide. The reaction is analogous with that employed for the preparation of 2-butene ozonide.



As it was found that α,α' -dihydroxydialkyl peroxides are generally formed in aqueous solutions of peroxides, whereas non-aqueous media are required for geminal hydroperoxides preparation²⁰, it is possible to explain the formation of substance *II*, as well as of 6,6'-methylene-bis(6-hexanolide) *III*, during the oxidation of diketone *I*, by the existence of transient peroxy compounds in dependence on the environment (see Scheme 1).



SCHEME 1

Whereas the formation of 2-butene ozonide and 1,2-dimethyl-1-cyclopentene ozonide, resp. requires the presence of phosphorus pentoxide, the dehydration described here proceeds spontaneously. This is probably due to the extraordinary easy formation of the tetrasubstituted six-membered tetrahydropyran cycle. It is in agreement with the above mentioned findings of Criegee concerned with the influence of substituents upon the stability of the ozonide (similar effects have been reported by a number of authors, *e.g.* in the case ϵ -caprolactam²¹). The presence of two cyclohexane cycles obviously enhances the probability of closure of the tetrahydropyran cycle even more than the above mentioned substitution by the methyl group. This follows from the spontaneous dehydration.

Besides the elemental analysis the ozonide structure of *II* has been supported by infrared and mass spectroscopy and furthermore by the hydrogenation of *II* in the liquid phase in the presence of palladium. The hydrogen consumption was theoretical²² and the reaction yielded quantitatively 2,2'-methylene-bis(cyclohexanone).

The ozonide *II* is, unlike the so far described ozonides, an extraordinary stable compound; its catalytical reduction proceeds very slowly, acidolysis does not take place even in boiling solution of acetic acid whereas the acidolysis of other ozonides leads, according the literature data¹⁶, to the formation of corresponding ketones and acids.

The formation of ozonide *II* as well as of the compound *III* (insufficiently characterized in an American patent¹³) is in agreement with the present knowledge about the isomery of 2,2'-methylene-bis(cyclohexanone). This compound has two isomers; the former (*Ia*) melts, according to the literature data²³, at 58–61°C, the latter (*Ib*) is a liquid at room temperature. It was originally assumed that this phenomenon is caused by atropoisomerism²⁴ but later on this isomerism was explained by the presence of two asymmetrical carbon atoms and the isomers were assigned the racemic and *meso*-forms²⁵. Palsky²⁶ has determined the structure of the isomer *Ia* as the racemic mixture, whereas the isomer *Ib* was observed to occur in the *meso*-form. These conclusions were drawn on the basis of interpretation of NMR spectra of isomeric glycols obtained by reduction of the isomers *Ia* and *Ib*. The formation of two isomeric forms of ozonide *II* observed during the oxidation of diketone *I* in aqueous media is in agreement with the existence of two stereoisomers of the diketone *I*. The ozonide isomers are following: a racemic isomer and a *meso*-form; the change of isomerism can be excluded on the basis of reaction yields and the uniformity of the reaction products. On the other hand, the oxidation of both isomeric forms of diketone *I* in nonaqueous media yields quite different products: 7-(2-oxocyclohexyl)-heptane-6-olide (*IV*) is formed from *Ia* instead of the expected *rac*-6,6'-methylene-bis(6-hexanolide) *IIIa*, whereas *meso*-6,6'-methylene-bis(6-hexanolide) was isolated as the only product of the oxidation of *Ib*.

The formation of *IIIa* from *Ia* is improbable as it follows both from the steric configuration of the diketone *I* isomers and from the character of transient products formed during the oxidation. The oxidation of racemate ends in the stage of formation of oxolactone *IV*. Similarly difficult steric conditions exist *e.g.* in the case of 2,2'-bis(cyclohexanone) where one of the stereoisomers of this diketone gives only corresponding oxolacton and oxolactam resp. instead of the expected bislactone resp. bislactame. Diastereoisomerism has not yet been described neither in ozonides nor in bislactones.

EXPERIMENTAL

Melting points have not been corrected. The infrared spectra were taken on a Zeiss UR-10 instrument using chloroform as a solvent.

Oxidation of 2,2'-Methylene-bis(cyclohexanone) (*I*) in Aqueous Solution

a) *Oxidation by performic acid.* 12.1 g (0.30 mol) of 85% hydrogen peroxide was added dropwise to 102 g (1.88 mol) of 85% formic acid, and, after two hours' stirring at room temperature, 26 g (0.125 mol) of the racemic diketone (*Ia*) (prepared according the reference²³) was added stepwise during the interval of another thirty minutes. Finally 20 ml of tetrachloromethane was added. The reaction mixture was then stirred for another hour at room temperature, the tetrachloromethane layer was separated and the water layer was extracted by shaking it with 4 × 100 ml of tetrachloromethane. The joined extracts were shaken with 5% ferric sulphate solution, then washed with water and dried over anhydrous sodium sulphate. After distilling off the tetra-

chloromethane, 20.8 g (74.3% theory) of *rac*-tricyclo[7, 4, 0, 0^{2,7}]-1-tridecene ozonide has been isolated in form of a white crystalline compound m.p. 58–60°C. After three-fold crystallization from isopropyl alcohol the melting point of the isomer *Ia* was 69–71°C. The infrared spectrum of the purified product, in comparison with that of the raw product, did not contain the absorption band corresponding to the carbonyl group. For C₁₃H₂₀O₃ (224.3) calculated: 69.61% C, 8.99% H; found: 70.11% C, 9.05% H.

The *meso*-form of the ozonide (*Iib*) was prepared in a similar way from the *meso*-form of the diketone (*Ib*). The residue after the removal of tetrachloromethane by distillation was only partially crystalline. The liquid part was thus separated and it was identified as the residual diketone *I*; the crystalline part (12.1 g, 43.2%) melted at 103–113°C. The pure isomer *Iib* was obtained by repeated crystallization from methanol in form of a white crystalline compound m.p. 119–120°C. For C₁₃H₂₀O₃ (224.3) calculated: 69.61% C, 8.99% H; found: 69.53% C, 9.05% H.

b) *Oxidation by hydrogen peroxide*. The diketone *Ia* (10.4 g; 0.05 mol) was dissolved in 20 ml of methanol containing 0.1 g of vanadium pentoxide and then 48 ml of 35% hydrogen peroxide was added dropwise over the interval of three hours. 6.4 g (61.5%) of white crystals (m.p. 65–68°C) separated after the mixture had been gently refluxed for two hours and left standing for twelve hours. The ozonide *Ia* (m.p. 69–71°C) was obtained by the crystallization from isopropyl alcohol.

When the diketone *Ib* was used instead of *Ia* then the course of reaction as well as the yields were similar.

The ozonide *Iib* (m.p. 119–120°C) was obtained after the crystallization from methanol. The melting point of the mixture of products obtained by mixing the isomers obtained through procedures *a* and *b* did not show any depression. Also the infrared spectra were identical.

Hydrogenation of *rac*-Tricyclo[7, 4, 0, 0^{2,7}]-1-tridecene Ozonide (*Ia*)

To the solution of 1.07 g of the ozonide in 25 ml of ethyl acetate 1 g of catalyst (palladium on the active charcoal) was added and the reaction mixture was saturated with hydrogen at 30°C. The hydrogen consumption (30 ml) remained constant after 150 minutes. Another 2 g of the catalyst were added; the overall consumption of hydrogen was then 108 ml. 0.88 g (88.5%) of a product were isolated. The infrared spectrum of this product was identical with that of 2,2'-methylene-bis(cyclohexanone).

Acidolysis of Ozonide *Ia*

The solution of 1.5 g of ozonide in 4 ml of glacial acetic acid was refluxed for 80 minutes. After dilution with water followed by the extraction with ether the original ozonide was recovered almost quantitatively.

Thermal Decomposition of Ozonide *Ia*

Several tenths of a gram of the ozonide (*Ia* and *Iib* resp.) were heated at 260°C in an evacuated glass ampoule for fifteen hours. A dark liquid product was identified by means of infrared spectroscopy as 2,2'-methylene-bis(cyclohexanone). There were also small amounts of side products present that contained carboxylic groups.

Oxidation of 2,2'-Methylene-bis(cyclohexanone) in Nonaqueous Media

To permaleic acid, prepared⁸ from 8 g (0.200 mol) 85% hydrogen peroxide and 26.2 g (0.267 mol) of maleic anhydride, 40 ml of methylene dichloride was added. To this solution 23.4 g (0.112 mol) of *meso*-diketone *Ib* dissolved in 50 ml of methylene dichloride was added dropwise maintaining the

temperature at 15–25°C by cooling. After filtering the maleic acid off, the filtrate was washed first with the solution of sodium carbonate, then with ferrous sulphate solution and then again with water; after drying and distilling the methylene dichloride off, 11.6 g (43.0%) of raw 6,6'-methylene-bis(6-hexanolide) (*IIIb*) was obtained. The repeated crystallization from methyl isobutyl ketone yielded pure *IIIb*, m.p. 135–136°C. The infrared spectrum of this compound has a significant absorption band at 1735 cm⁻¹ corresponding to the —CO—O— group. The spectrum is identical with that of a model 6-hexanolide. For C₁₃H₂₀O₄ (240.3) calculated: 64.98% C, 8.39% H; found: 64.91% C, 8.48% H.

The same procedure was employed during the oxidation of racemic diketone. The reaction yielded 18 g (66.7%) of 7-(2-oxocyclohexyl)heptane-6-olide (*IV*) in form of a viscous liquid that did not crystallize even after prolonged standing at 0°C. After repeated distillation the b.p. of 168–170°C/1.6 Torr was achieved. The infrared spectrum of this compound contains a broad absorption band in the region 1710–1735 cm⁻¹. For C₁₃H₂₀O₃ (224.3) calculated: 69.61% C, 8.99% H; found: 69.83% C, 9.25% H.

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