Autoxidation of Esters. II. Cyclohexylenedimethylene Diacetate

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trans-1,4-Cyclohexylenedimethylene diacetate (CHDMDA) was reacted with oxygen in the temperature range 100–120°. The data obtained from this investigation indicate that CHDMDA is more reactive in autoxidation and gives a much more complicated mixture of oxidation products than the acyclic analog (isobutyl acetate). The oxidation of CHDMDA at 100° is strongly autocatalytic, and the rate is nearly independent of added *tert*-butyl peroxide initiator. Titratable hydroperoxide accounts for ~10% of the oxygen consumed during autoxidation, but carboxylic acid yield is relatively high. Products tentatively identified from the oxidation mixture are 4-oxocyclohexylmethyl acetate (**4**) and the cis–trans pair of 1-hydroxy-1,4-cyclohexylenedimethylene diacetate (**6**).

In a previous paper,[1] it was shown that a tertiary hydrogen β to the ester function on the alcohol moiety reacts with oxygen in much the same way a hydrocarbon hydrogen does. However, the hydroperoxide formed as a primary product of ester autoxidation seemed to be much more susceptible to decomposition than a simple, tertiary hydroperoxide. To determine the effect of placing the reacting tertiary hydrogens in a ring and to determine how a bifunctional substrate would react in autoxidation, the reaction of *trans*-1,4-cyclohexylenedimethylene diacetate (CHDMDA) with oxygen was studied.

Experimental Section

Materials.—*trans*-1,4-Dimethylcyclohexane (99% pure) was obtained from Chemical Samples Co. *tert*-Butyl peroxide (99% pure) was obtained from Wallace and Tiernan, Inc., Lucidol Div. (Both materials were used as obtained.) Peroxyacetic acid was obtained from FMC Corp.

***trans*- and *cis*-1,4-Cyclohexylenedimethylene Diacetate (CHDMDA).**—The Eastman *trans*-1,4-cyclohexanedimethanol (CHDM) used was recrystallized once from ethyl acetate to give 99.4% *trans*-CHDM as indicated by glpc. The recrystallized CHDM was acetylated with acetic anhydride, and the CHDMDA was recrystallized from a water–methanol solution for a net yield of 89%. After the product was thoroughly dried in a vacuum desiccator, a 70° melting point was obtained (lit.[2] mp 70°).

The Eastman practical grade CHDM used was distilled at 6.0 mm (95% reflux on ~100-plate column) to obtain the cis isomer. The head temperature of the column was 135° [lit.[3] bp, trans, 284° and, cis, 288° (760 mm)]. A pot residue from one of these distillations (90% cis as indicated by glpc) was exhaustively acetylated with acetyl chloride–pyridine reagent to give an oil, bp 107–108° (0.5 mm) [lit.[4] bp 156° (6.0 mm)].

Cyclohexylmethyl Acetate (CHMA).—The Eastman reagent grade cyclohexane–methanol used was acetylated with acetyl chloride–pyridine reagent to yield CHMA, bp 52–54° (2 mm) [lit.[5] bp 105° (56 mm)]. Glpc indicated that the product was free of alcohol but contained ~1% of unidentified impurity.

Possible CHDMDA Oxidation Products.—Two possible CHDMDA oxidation products were synthesized as glpc standards. 4-Oxocyclohexylmethyl acetate (**4**), bp 76–78° (0.08 mm), was obtained by ozonolysis in acetic acid followed by reduction with powdered zinc of 4-*exo*-methylenecyclohexylmethyl acetate (yield ~40%). The starting acetate, bp 72–73° (2.8 mm), was obtained by acetylating the corresponding alcohol (4-methylenecyclohexane–methanol)[2] with pyridine–acetic anhydride reagent (yield ~75%). (It was confirmed that no isomerization to the methylcyclohexene derivative had occurred.) The nmr spectrum of the product agrees with the proposed structure **4**: nmr ($CDCl_3$) δ 1.0–2.1 (m, 5, ring protons), 2.1–2.5 (m, 4, ring protons), 1.98 (s, 3, methyl protons), and 3.95 (d, 2, methylene protons).

1-Hydroxy-1,4-cyclohexylenedimethylene diacetate (**6**) was obtained as a crude mixture of isomers by epoxidizing 4-*exo*-methylenecyclohexylmethyl acetate with peroxyacetic acid in the presence of sodium acetate (1g). Peroxyacetic acid (6.7 g, ~45 mmol) was added to the acetate (7.24 g, ~43 mmol) in 50 ml of acetic acid containing 1 g of sodium acetate. After the heat of the initial reaction subsided, the mixture was heated on a steam bath for ~30 min, then cooled to 0°. The crystallized sodium acetate was filtered off, and the acetic acid was evaporated with a nitrogen stream at 100° to give a thick oil (6.3 g) which would not crystallize.

The infrared spectrum of the oil showed a strong hydroxyl absorption at 3500 cm^{-1} and a strong carbonyl absorption (from the acetate groups) at 1750 cm^{-1}. Glpc showed that the oil contained principally two components (partially resolved on an XE-60 silicone column) whose retention times were identical with those of two products from the oxidation of CHDMDA. An attempt by repetitive, preparative glpc to isolate the two components was unsuccessful; nmr spectra of the trapped effluent showed considerable vinyl proton signals which suggested dehydration of products on the column. The nmr spectrum of the crude oil was in agreement with the assigned structure of a cis–trans pair but was not conclusive because of the impurities present: nmr ($CDCl_3$) δ 0.8–2.1 (m, 15, ring and methyl protons), 3.8–4.1 (m, 3.7, methylene protons), and 3.0 (s, 1, hydroxyl proton). No vinyl hydrogens were indicated.

Oxidation Procedure.—The apparatus and its use were the same as in the preceding investigation.[1] The oxidation mixtures (substrate and initiator) were made up in the reaction bulb. The *trans*-CHDMDA was added as a melt. The bulb contents, after oxidation, were emptied as a melt and soldified into a cake, and the cake was pulverized for analysis. Corrections of pressure readings and calculations of rates were done as previously described.[1]

Product Analysis.—Iodometric titrations of oxidized CHDMDA were performed by the method of Mair and Graupner.[6] Benzene solutions of oxidized *trans*-CHDMDA were analyzed (without prior triphenylphosphine reduction since the hydroperoxide titers were so low) for products by glpc using temperature-programmed XE-60 silicone columns. Docosane was added to the solutions as internal standard. No response factors were determined; so the assumption that peak area is proportional to the weight of the material was used.

Results and Discussion

The rates of oxidation of *trans*-CHDMDA and related compounds, as well as the products of oxidation, are listed in Table I.

Rates.—Qualitatively, *trans*-CHDMDA is much more reactive to oxygen than is isobutyl acetate. At 100°, R_0 (initial and final rate of oxidation) for *trans*-CHDMDA is similar to R_0 for isobutyl acetate at 120°. However, the insensitivity of the CHDMDA oxidations

(1) D. E. Van Sickle, *J. Org. Chem.*, **37**, 1392 (1972).
(2) G. A. Haggis and L. N. Owen, *J. Chem. Soc.*, **404** (1953).
(3) Eastman Chemical Products, Inc., Technical Data Sheet No. X-105, p 2.
(4) J. Falbe, N. Huppes, and F. Korte, *Brennst. Chem.*, **47**, 207 (1966).
(5) A. MacLachlan, *J. Org. Chem.*, **29**, 1598 (1964).
(6) R. D. Mair and A. J. Graupner, *Anal. Chem.*, **36**, 194 (1964).

TABLE I

OXIDATION OF *trans*-CHDMDA AND RELATED COMPOUNDS[a]

Run	Substrate, mmol	*tert*-Bu_2O_2, *M*	Initial R_0,[b] *M* $min^{-1} \times 10^4$	Final R_0,[c] *M* $min^{-1} \times 10^4$	Time, min	O_2 consumed, mmol	O_2H yield— Mmol[e]	O_2 consumed, %	Acid,[d] mmol	Products, mmol— 4[f]	6[f]	Other[f,g]
1[h]	CHDMDA 93.5	0.0218	5.9	17.3	125	3.1	0.35	11	1.8	0.20	0.32	0.34
2	CHDMDA 93.5	0.0129	0.6	1.5	520	1.0	0.21	21	0.65	0.09	0.22	0.20
3	CHDMDA 95.5	0.0214	1.2	~1.8	510	1.3	0.14	11	0.69	0.12	0.17	0.17
4	CHDMDA 98.7	0.0462	0.9	2.1	760	2.7	0.21	8	1.3	0.19	~0.40	0.36
5	CHDMDA 95.7	0.1610	1.1	3.7	1495	6.4	0.36	5.7	4.0	0.38	0.72	1.0
6	CHDMDA[i] 98.9	0.0228	0.32	0.32	1840	1.4	0.83	60	0.42			
7	CHMA 119	0.0225	0.55	0.71	1555	1.9	1.11	59	0.54			
8	$(CH_3)_2$-C_6H_{10} 133	0.0236	1.9	4.6	355	2.2	1.93	89	0.10			

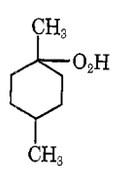
[a] Oxidations of neat materials; approximate concentrations at reaction temperature were 4–6 *M*; oxygen pressure ranged from 2 to 6 atm; 100° unless otherwise noted. [b,c] Initial and final rates of oxygen consumption, respectively, in mol $l.^{-1}$ min^{-1}. [d] By titration with aqueous NaOH. [e] By iodometric titration.[5] [f] Determined by glpc. [g] Mostly four products which elute after 6. [h] 120°. [i] Cis isomer.

to added *tert*-butyl peroxide precludes a quantitative comparison of the reactivities of CHDMDA and isobutyl acetate. Aside from run 2, in which the lowest *tert*-butyl peroxide concentration was used, the rate of oxidation was effectively zero order in initiator. Apparently, at 100°, *tert*-butyl peroxide provided only a small amount of the total radical generation.

At both 100 and 120°, the autocatalysis was strong with the final rate (after 1 to 5% conversion) being two or three times as fast as the initial rate. Evidently, and unlike that of the isobutyl acetate system, the decomposition of the primary product **1** proceeds through radical intermediates.

cis-CHDMDA oxidizes much slower than the trans isomer and without autocatalysis. No simple explanation is apparent. The CHMA (run 7) is about as reactive as the *trans*-CHDMDA on a per-tertiary-hydrogen basis.

Products.—Probably the most notable feature of the *trans*-CHDMDA oxidations is the very low hydroperoxide yield. The average value of the somewhat erratic yield is about 10%. As far as can be determined, the thermal instability of the expected *trans*-CHDMDA oxidation product **3** is unique to its structure. The oxidation of the hydrocarbon analog (1,4-dimethylcyclohexane) of CHDMDA is reported to give nearly quantitative yields of the hydroperoxide (at 95°), at least up to 10% conversions.[7] It has also been reported that 1,4-dimethylcyclohexane gives a "normal" oxidation product[8] (**1**) without participation



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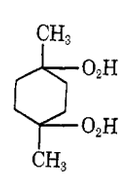
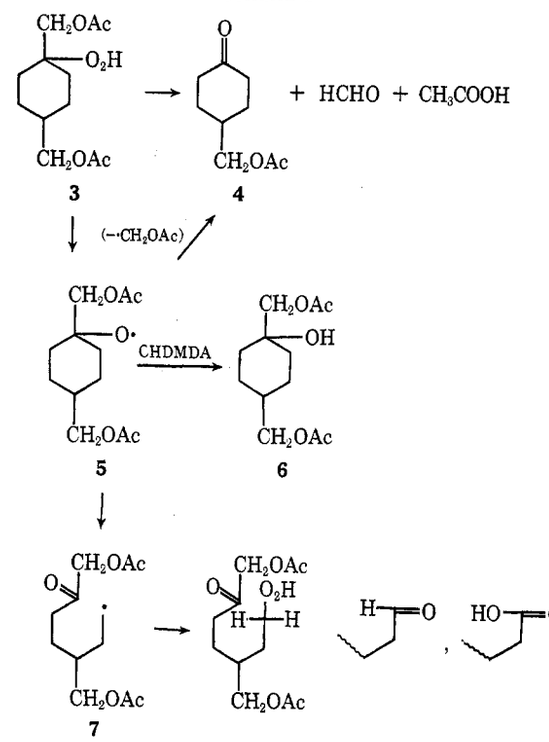


2

SCHEME I



of an intramolecular propagation step.[9] The dihydroperoxide **2** of 1,4-dimethylcyclohexane can be formed, however, with **1** being an intermediate.

In run 8, the initial oxidation rate of 1,4-dimethylcyclohexane was faster than the corresponding CHDMDA rate (run 3), and rate acceleration was fairly rapid. However, titratable hydroperoxide yield was high (although not so quantitative as previously reported[6]) and acid yield was low. Substitution of acetate groups on the methyl groups of the hydrocarbon obviously has a profound effect on the course of oxidation.

(7) V. Stannett, A. E. Woodward, and R. B. Mesrobian, *J. Phys. Chem.*, **61**, 360 (1957).

(8) R. Criegee and P. Ludwig, *Erdöel Kohle*, **15**, 523 (1962).

(9) F. F. Rust, *J. Amer. Chem. Soc.*, **79**, 4000 (1957).

The products of *trans*-CHDMDA oxidation which were identified support the premise of hydroperoxide **3** and its associated alkoxy radical **5** as major intermediates (Scheme I).

Whether **5** arises from thermolysis of **3** or from a nonterminating reaction of peroxy radicals during the oxidation cannot be determined with the limited data of this investigation. The rapid autocatalysis of the oxidation and the near zero order in added initiator suggest a facile cleavage of **3** to radicals. The unidentified products found by the glpc analysis are assumed to result from ring cleavage of radical **5** to radical **7** and so on or, possibly, from radical attack at the secondary ring hydrogens of the CHDMDA.

The amount of acid titrated in the oxidized *trans*-CHDMDA mixture increases almost proportionately to increasing conversion. However, the production of **4** falls far short of accounting for the acid formed (top line of Scheme I), even if it is assumed that the formaldehyde is quantitatively oxidized to formic acid.[1] Clearly, there are other sources of carboxylic acid in the oxidation mechanism.

The results of this and other investigations indicate that a multiplicity of products may be generated from the autoxidation of simple bifunctional esters. Much more work will be required to identify and authenticate all of the elementary steps of the oxidation mechanism of esters.

Registry No.—**4**, 33904-15-3; *trans*-1,4-cyclohexylenedimethylene diacetate, 10412-78-9; 4-*oxo*-methylenecyclohexylmethyl acetate, 33904-17-5.

Resin Acids. XXIII. Oxidation of Levopimaric Acid with Potassium Permanganate and Osmium Tetroxide[1,2]

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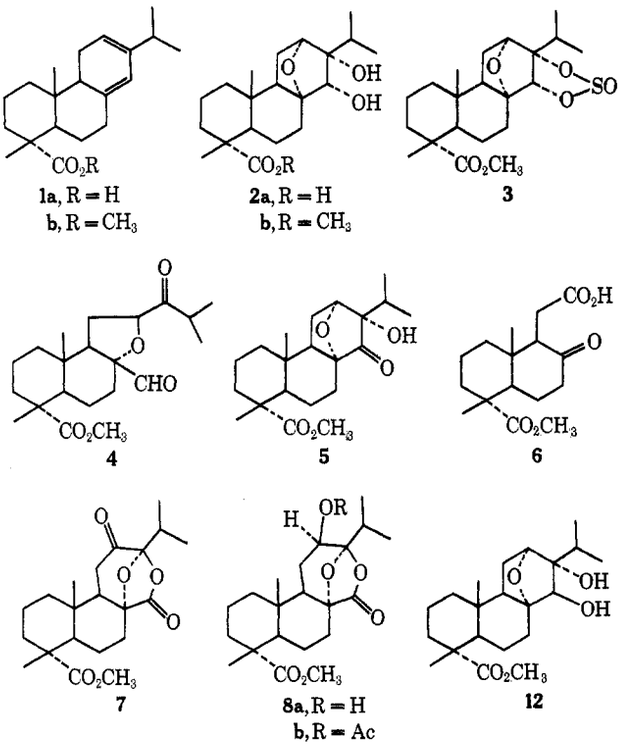
Structures have been deduced for the products resulting from the $KMnO_4$ and osmium tetroxide oxidation of levopimaric acid. The major product of $KMnO_4$ oxidation is 8α(12α)-oxido-13α,14α-dihydroxyabietan-18-oic acid (**2a**). The compounds produced by osmium tetroxide of methyl levopimarate are methyl 8α,14α-dihydroxyabiet-12-en-18-oate (**16**), methyl 12α,13α-dihydroxyabiet-8(14)-en-18-oate (**13**), and methyl 8α,12α,13α,14α-tetrahydroxyabietan-18-oate (**15**). The preparation of other enediols, epoxydiols, and tetraols derived from levopimaric acid is described.

Structure **2a** (exclusive of stereochemistry) was proposed after prolonged controversy[3] by Wienhaus and Marchand[4] for the major product resulting from the oxidation of levopimaric acid (**1a**) with aqueous permanganate. This formula has been generally accepted, but the evidence for the gross structure was not decisive and the stereochemistry assigned to it more recently on a provisional basis[5] remained unproved.[6] In the present communication we produce conclusive proof for formulation of this substance as **2a**. We also show that earlier structure assignments[8] for the diols obtained by osmylation of methyl levopimarate (**1b**) require correction.

Potassium Permanganate Oxidation.—The nmr spectrum of **2b**, obtained in 30% yield by oxidation of levopimaric acid followed by esterification, was in excellent agreement with the gross structure assigned to it by the German workers.[4] The presence of a secondary hydroxyl group on a carbon next to two tertiary centers and of an ether oxygen linking a tertiary and secondary carbon atom next to a methylene group was indicated by a doublet (J = 3 Hz) at 4.05 ppm, which collapsed to a singlet on addition of D_2O, and a multiplet at 3.30 ppm. The cis nature of the diol was easily established by the formation of a sulfite ester



(1) Previous paper: W. Herz and V. Baburao, *J. Org. Chem.*, **36**, 3899 (1971).

(2) Supported in part by grants from the National Science Foundation (GP-12582) and the Petroleum Research Fund, administered by the American Chemical Society (508-A1).

(3) For a review of work prior to 1953, see J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. III, 2nd ed, Cambridge University Press, New York, N. Y., 1952, p 438; Vol. V, 1957, pp 604–610.

(4) H. Wienhaus and B. Marchand, *Chem. Ber.*, **91**, 401 (1958).

(5) H. Kanno, W. H. Schuller, and R. V. Lawrence, *J. Org. Chem.*, **31**, 4138 (1966).

(6) Especially so since the structure of levopimaric acid dioxide, whose transformation products were compared with the transformation products of **2a**, has had to be revised.[7]

(7) W. Herz, R. C. Ligon, H. Kanno, W. H. Schuller, and R. V. Lawrence, *J. Org. Chem.*, **35**, 3338 (1970).

(8) B. Marchand, *Chem. Ber.*, **91**, 407 (1958).