

Ozonolysis of long-chain cyclic acetals: formation of monoesters

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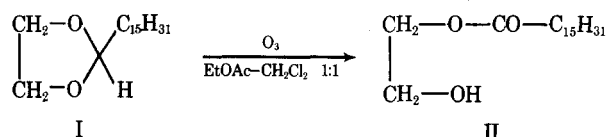
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Summary A procedure is described for the quantitative conversion of saturated long-chain cyclic acetals of diols to the corresponding *O*-acyl diols. Acetal ozonolysis proceeds in ethyl acetate–methylene chloride solution at -16 to -18°C without over-oxidation.

Supplementary key words diol cyclic acetals · diol monoesters · ester synthesis · oxidative acetal cleavage

In the present communication we describe a convenient and rapid procedure for the quantitative conversion of long-chain cyclic acetals to fatty acid esters. The conversion is accomplished by ozonolysis. Acetal ozonolysis proceeds in a more specific and predictable manner than the ozonolytic cleavage of ether bonds (1–3) and can be controlled through careful choice of solvents, temperature, and reaction time.

We found that with ethyl acetate–methylene chloride 1:1 as reaction medium, at -16 to -18°C , saturated long-chain cyclic acetals of diols differing in a number of structural parameters are completely cleaved and specifically oxidized to diol monoesters within 40 min. Overoxidation and other side reactions do not occur.



2-Pentadecyl-1,3-dioxolane I was quantitatively converted to the corresponding glycol monoester II, as judged by adsorption thin-layer chromatography; developing solvent, hexane–diethyl ether 60:40 (v/v). The reaction product was identified as glycol monohexadecanoate by its R_F value (0.3), melting point (51.5 – 52.5°C ; lit., Ref. 4, 52 – 53°C), mixture melting point (51.5 – 52.5°C), infrared spectrum, and by the retention time of its trimethylsilyl derivative in gas–liquid chromatography (R_T 19.9 min). The data were in agreement with those of a standard synthesized by an alternate route (4, 5). Ozonolysis of the long-chain cyclic acetals of other symmetrical diols, such as 1,3-propanediol, 1,4-butanediol, and 2,3-butanediol, similarly produced the respective diol monoesters only, which were identified by comparison of their chromatographic (5, 6) and spectroscopic (7, 8) properties with those of authentic standards.

Ozonolysis of long-chain cyclic acetals of asymmetrical diols usually produces two types of isomeric diol monoesters.

The proportion of isomers formed is dependent upon the size and geometry of the acetal ring and upon the degree and type of branching next to the acetal linkages. For example, *cis*- and *trans*-2-pentadecyl-4-methyl-1,3-dioxolanes, as they were obtained from 1,2-propanediol and hexadecanal by *p*-toluenesulfonic acid-catalyzed condensation (9), afforded upon ozonolysis 68% of the 2-*O*-hexadecanoyl-1,2-propanediol and 32% of the 1-isomer, whereas from cyclic acetals of 1,3-butanediol, 58% of the primary and 42% of the secondary esters were formed. The composition of the ozonolysis products was determined by gas–liquid chromatography of the trimethylsilyl diol monoesters, and the isomeric structures were established by gas–liquid chromatography–mass spectrometry. The mass spectra of the trimethylsilyl derivatives of the primary monoesters of 1,2-propanediol (R_T 17.6 min) and 1,3-butanediol (R_T 25.2 min) showed the characteristic ion $[\text{CH}_3\text{CH-O-Si}(\text{CH}_3)_3]^+$ at m/e 117, whereas the monoester isomers bearing the acyl function at the secondary hydroxy group of 1,2-propanediol (R_T 16.6 min) and 1,3-butanediol (R_T 22.8 min) were reliably identified by occurrence of a prominent ion $[\text{CH}_2\text{-O-Si}(\text{CH}_3)_3]^+$ at m/e 103.

Preliminary studies have shown that the products of acetal ozonolysis are most reasonably explained by an initial electrophilic attack of ozone on the acetal carbon, in analogy to the accepted mode of ether ozonolysis (1, 2). Thus, a mechanism of acetal cleavage can be postulated that involves ozone insertion at C-2 of the acetal ring and formation of an intermediary hydrotrioxide. Stabilization of the intermediate through hydrogen bonding, preferentially to the least hindered or more nucleophilic acetal oxygen, would permit a concerted cyclic electron shift, elimination of molecular oxygen, and formation of diol monoester. Thus, the site of hydrogen bonding in the hydrotrioxide would determine the type of monoester isomer formed.

Procedure. Long-chain cyclic acetals of diols (1–10 mg) dissolved in 2 ml of ethyl acetate–methylene chloride 1:1 (v/v)¹ were kept at -16 to -18°C (salt/ice bath) in a small test tube and treated with a stream of ozone (microozonizer, Supelco, Inc., Bellefonte, Pa.) for 40 min at an oxygen flow rate of 18–20 ml/min. The solvent was removed at room temperature by a stream of dry nitrogen, and the residue was dried in vacuo.

For the preparation of trimethylsilyl derivatives, the products of ozonolysis were dissolved in 0.25 ml of pyridine (refluxed and redistilled over KOH) and treated at room temperature with 0.10 ml of hexamethyldisilazane and 0.05 ml of trimethylchlorosilane (Applied Science

¹ Ethyl acetate (Fisher Scientific, Fair Lawn, N.J.), pesticide grade, was redistilled. Methylene chloride (Matheson Coleman & Bell, Norwood, Ohio), reagent grade, was treated with ozone at room temperature for 15 min, washed with concentrated sulfuric acid, and redistilled over phosphorus pentoxide.

Laboratories, State College, Pa.). After 30 min and occasional agitation, 0.75 ml of hexane was added, and the mixture was centrifuged. The trimethylsilyl derivatives of diol monoesters in the supernate were directly subjected to gas-liquid chromatography using a Hewlett-Packard 5750 instrument with flame ionization detector. The glass column, 300 × 0.2 cm ID, packed with 10% SP-1000 on Gas-Chrom P, 80-100 mesh (Supelco) was operated at 210°C using helium (20 ml/min) as carrier gas. Mass spectra were recorded on a Hitachi Perkin-Elmer single-focusing instrument, RMU-6D, at 70 eV ionization potential.

The procedure of ozonolytic acetal cleavage has been found equally useful for the preparation of 2-acyl derivatives of long-chain 1,2-alkanediols (10); it also opens an attractive route for the synthesis of ester lipids, in particular radioactively labeled ones, in high yields without the difficulties that are commonly encountered in acylations on a small scale.² Furthermore, long-chain cyclic acetals are of interest as derivatives for the analysis of short-chain diols, which are produced through degradation of naturally occurring diol lipids (9) or through reductive ozonolysis of polyunsaturated aliphatic moieties (11), and for the analysis of the aldehydogenic moieties of plasmalogen-type lipids (12, 13). Ozonolysis offers a convenient method for the complementary identification of such diol cyclic acetal mixtures as trimethylsilyl diol monoesters.

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² Baumann, W. J., and T. H. Madson. Unpublished results.

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