776. *Macrocyclic Compounds. Part IV.*[1] *A Rapid Semi-quantitative Method of Routine Ozonolysis of Cyclic Olefins.*

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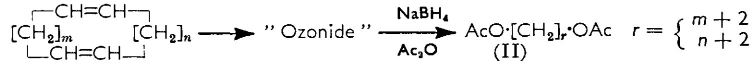
An olefin is ozonolyzed in propan-1-ol and treated directly with sodium borohydride to give a mixture of diols with almost no side-products. The mixture is acetylated and analysed in a temperature-programmed gas chromatograph. Inclusion of an internal standard allows semiquantitative determinations. The method is particularly well suited for cyclic olefins as these give rise only to diols; simple volatile alcohols ($<C_5$) from acylic olefins escape detection.

In connection with studies of the base-catalyzed isomerization of macrocyclic acetylenes to polyenes,[2] as well as of the isomerization of macrocyclic dienes (I) to other positional isomers,[3] it became necessary to use ozonolysis to establish the structures of the products.

Two main methods have been in use for the identification of the ozonolysis products of unsaturated compounds:[4] oxidative decomposition (although seriously limited by secondary reactions [5]) to acids, which are subsequently isolated by crystallization, chromatography,[6] etc., or to ketones; and reductive decomposition to aldehydes, or ketones, which are transformed into derivatives (*e.g.*, 2,4-dinitrophenylhydrazones) and separated by similar techniques.[7] We have found these methods of isolation to be slow and difficult, and have therefore tried to replace them by gas-chromatographic methods. Gas chromatography has already been used to study directly the primary gaseous ozonization products of simple olefins,[8] but in the present case only the examination of stable decomposition products was of interest. The acids obtained by oxidative decomposition were therefore directly esterified with diazomethane [9] and analysed by gas chromatography. Although the esterification and separation posed no problem, a great variety of products was obtained (Fig. a) from a test substance (cyclotetradeca-1,8-diene) which in principle should give only one compound (dimethyl pimelate). This confirms the occurrence of rearrangements [5] during the oxidative decomposition.

To avoid such secondary reactions, the ozonolysis products were reduced directly to diols. Lithium aluminium hydride and sodium borohydride are known [10,11] to reduce ozonides to alcohols in excellent yields. For reasons of solubility sodium borohydride was employed, with propan-1-ol as solvent both for the ozonolysis and for the reduction. In this way the "ozonides" (or rather the hydroperoxides and aldehydes formed therefrom with propanol [4]) were reduced *in situ* to give rather cleanly the expected diols (see Figure and Table). The products were analysed by temperature-programmed gas chromatography after conversion into the acetates by treatment with acetic anhydride; the diols themselves often gave a tailing of the peaks in the chromatogram with resulting poor resolution. For the simple cyclic dienes (I) [12] the reactions can be formulated as follows:



$$\left[\begin{array}{c}\text{CH=CH}\\ [\text{CH}_2]_m \qquad [\text{CH}_2]_n\\ \text{CH=CH}\end{array}\right] \longrightarrow \text{" Ozonide "} \xrightarrow[\text{Ac}_2\text{O}]{\text{NaBH}_4} \text{AcO}\cdot[\text{CH}_2]_r\cdot\text{OAc} \qquad r = \begin{cases} m+2 \\ n+2 \end{cases}$$

(I) (II)

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[1] Part III, Dale, *J.*, 1963, 93.

[2] Part II, Hubert and Dale, *J.*, 1963, 86.

[3] Part V, Dale and Hubert, following paper.

[4] Bailey, *Chem. Rev.*, 1958, **58**, 925.

[5] Benton, Kiess, and Harwood, *J. Amer. Oil Chemists' Soc.*, 1959, **36**, 457.

[6] Howe, *J. Chromatography*, 1960, **3**, 389; Hartley and Lawson, *ibid.*, 1960, **4**, 410; Occolowitz, *ibid.*, 1961, **5**, 373.

[7] Roberts and Green, *Ind. Eng. Chem.*, *Analyt. Ed.*, 1946, **18**, 335.

[8] Vrbaški and Cvetanović, *Canad. J. Chem.*, 1960, **38**, 1063.

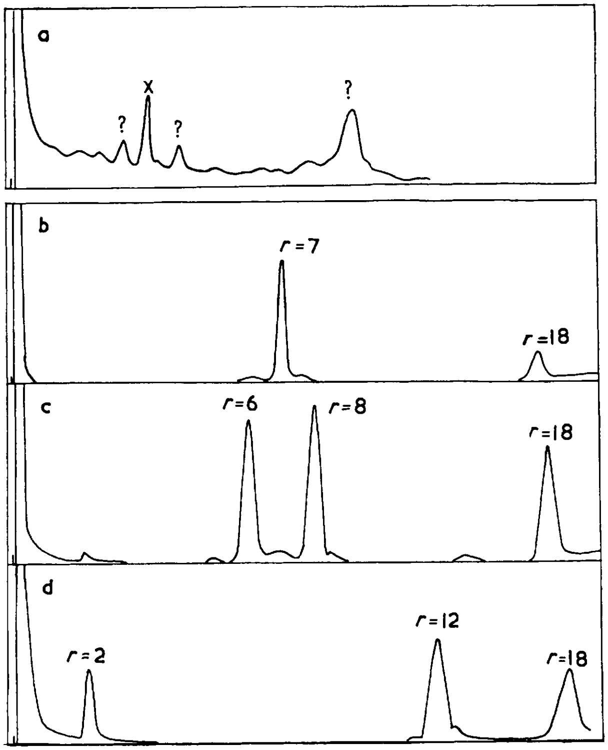
[9] Schlenk and Gellerman, *Analyt. Chem.*, 1960, **32**, 1412,

[10] Sousa and Bluhm, *J. Org. Chem.*, 1960, **25**, 108.

[11] Doering and Prinzbach, *Tetrahedron*, 1959, **6**, 24.

[12] Part I, Dale, Hubert, and King, *J.*, 1963, 73.

The method is especially suitable for cyclic olefins as all fragments are necessarily diols, and only the smallest of these, ethylene glycol, is to some extent lost with the solvents. Simple alcohols of low molecular weight, which may arise from open-chain olefins, escape detection. Thus, even n-pentyl acetate was mostly lost after the ozonolysis of dec-5-ene.



Gas chromatograms of ozonolysis products obtained (a) from cyclotetradeca-1,8-diene by oxidative decomposition and methylation; (b) from the same by borohydride reduction and acetylation; (c) from the 1,7-isomer as in (b); (d) from the 1,3-isomer as in (b). The last peak in (b), (c), and (d) represents the added standard.

The point X in (a) is $[CH_2]_5(CO_2Me)_2$. The values of r refer to the diacetates $AcO{\cdot}[CH_2]_r{\cdot}OAc$.

In such cases, a more elaborate procedure[11] has been used to separate alcohol fragments from the solvents.

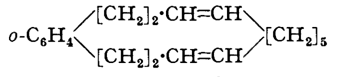
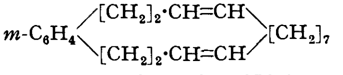
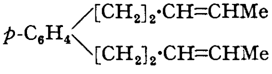
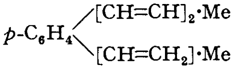
A quantitative determination of absolute yields is possible by mixing a weighed quantity of an internal standard with the weighed olefin, either before or after ozonolysis. Octadecamethylene diacetate was chosen most frequently as standard, because it is usually well separated in the chromatogram. Lower diols such as decane-1,10-diol and hexane-1,6-diol were used when they were not formed in the ozonolysis, in both cases systematic errors are kept small because of the structural similarity to the reduced ozonolysis products. The Table shows that the yields are very good, except when the ozonolysis is performed at the low temperature (—75°) at first thought to be necessary for a clean reaction; the ozonization then seems to be too slow. The molar ratios of pairs of ozonolysis products provide a more accurate measure (with an error usually much less than 5%) than do the individual yields. Abnormal results are observed when a product is too volatile (ethylene glycol) and in some cases of structural dissimilarity with the standards (aromatic diols).

EXPERIMENTAL

General Procedure.—The olefin (about 0·1 g.) is dissolved in propan-1-ol (25 ml.) or another alcohol, according to the solubility of the olefin, and ozone is bubbled through the solution at 20° for 30—40 min. The excess of ozone is removed by passing oxygen through the solution for 5 min., whereafter solid sodium borohydride (1·0 g.) is added at once. The mixture is stirred, heated on a steam-bath for 10 min., and acidified cautiously with 3N-hydrochloric acid until no more hydrogen is evolved and the salts are dissolved, and the whole concentrated almost to dryness in a rotating evaporator. Acetic anhydride (25 ml.) is then added, and after 15 minutes' heating on a steam-bath the excess of anhydride is evaporated. The semisolid residue is stirred with ether (50 ml.), the solids are filtered off, and the ether is evaporated. If low-molecular-weight products are expected, it is preferable to remove the acetic anhydride more completely, either by washing with aqueous sodium hydrogen carbonate, or by treatment with methanol and evaporation of the methyl acetate formed.

The oily residue is then analysed in a temperature-programmed gas chromatograph (F & M, Model 500, with a Gow-Mac hot-wire thermal conductivity detector). A 1/4″ × 2′ SE-30 Silicone Gum Rubber column (20% on 60—80 mesh firebrick) and a temperature increase of 11°/min. were used. The peaks are identified by means of authentic samples. When the

Gas-chromatographic determination of reduced ozonolysis products from olefins.

Olefin		Temp. of ozonolysis	Diol diacetates detected		Ratio ‡	Yield (%) §	
			a	*b*	*a*/*b*	*a*	*b*
Cyclic dienes (I):							
m	*n*						
4	4	−75°	II; *r* = 6	—	—	—	—
4	5	−75	II; *r* = 6	II; *r* = 7	0·99	—	—
		20			0·97	92 *	95 *
5	5	−75	II; *r* = 7	—	—	101	—
4	6	−75	II; *r* = 6	II; *r* = 8	0·97	90	93
2	8	−75	II; *r* = 4	II; *r* = 10	0·95	—	—
0	10	−75	II; *r* = 2	II; *r* = 12	0·83	86	104
5	6	−75	II; *r* = 7	II; *r* = 8	0·94	—	—
		20			0·97	85 *, 97 †	88,* 100 †
6	6	−75	II; *r* = 8	—	—	77	—
		20			—	89,* 93 †	—
7	7	−75	II; *r* = 9	—	—	50	—
		20			—	100,* 98 †	—
8	8	−75	II; *r* = 10	—	—	73	—
		20			—	99 †	—
9	9	20	II; *r* = 11	—	—	88,* 97 †	—
Other olefins:							
$\overline{[CH_2]_4\cdot[CH=CH]_4}$		20	II; *r* = 6	—	—	98*	—
 $o\text{-}C_6H_4\begin{cases}[CH_2]_2\cdot CH=CH\\ [CH_2]_2\cdot CH=CH\end{cases}[CH_2]_5$		−75	II; *r* = 7	$o\text{-}C_6H_4([CH_2]_3\cdot OAc)_2$	1·57	71	45
		20			1·13	76,* 78 †	67,* 69 †
 $m\text{-}C_6H_4\begin{cases}[CH_2]_2\cdot CH=CH\\ [CH_2]_2\cdot CH=CH\end{cases}[CH_2]_7$		−75	II; *r* = 9	$m\text{-}C_6H_4([CH_2]_3\cdot OAc)_2$	0·99	—	—
 $p\text{-}C_6H_4\begin{cases}[CH_2]_2\cdot CH=CHMe\\ [CH_2]_2\cdot CH=CHMe\end{cases}$		−75	—	$p\text{-}C_6H_4([CH_2]_3\cdot OAc)_2$	—	—	69
 $p\text{-}C_6H_4\begin{cases}[CH=CH]_2\cdot Me\\ [CH=CH_2]\cdot Me\end{cases}$		−75	—	$p\text{-}C_6H_4(CH_2\cdot OAc)_2$	—	—	91

* $HO[CH_2]_{10}\cdot OH$ as standard. † $HO\cdot[CH_2]_6\cdot OH$ as standard. ‡ Molar ratio from peak areas divided by corresponding mol. wt. § Yield (%) of diacetates by comparison with an internal standard ($AcO\cdot[CH_2]_{18}\cdot OAc$ except when otherwise noted).

ozonolysis is performed at −75° no improvement in yield is obtained; on the contrary, the reaction seems to be incomplete for the higher olefins (Table).

Absolute Determinations.—The above method is sufficient to establish the proportions of different products. When information is required about the absolute quantities formed from a weighed sample, a weighed quantity of an internal standard is added, preferably before ozonolysis. The standard may be octadecamethylene diacetate or, better, decane-1,10-diol or hexane-1,6-diol when these are not formed in the ozonolysis. (When pyrene was used as a standard, there was a systematic error of about 20%.) Peak areas of products and of the added standard, divided by the appropriate molecular weights, are then used to calculate the yields (Table).

Preparation of Olefins.—Most of the simple macrocyclic *cis,cis*-alkadienes (I) as well as the *cis*-cyclotetracosa-1,7,13,19-tetraene have been described earlier;[12] a few dienes are described in the following paper.[3] The first three compounds containing benzene nuclei of the Table were obtained by partial hydrogenation on a Lindlar catalyst of the corresponding diynes already described.[2] The first, cis,cis-*benzocyclopentadeca*-1,5,12-*triene* has m. p. 110° (Found: C, 89·85; H, 10·3. $C_{19}H_{26}$ requires C, 89·7; H, 10·3%). The next two compounds were liquids with imperfect analyses.

The synthesis of the last compound, *p*-dipenta-1′,3′-dienylbenzene, will be reported later.

The author is grateful to Dr. J. Dale for advice and for help in preparing the manuscript, to Professor H. B. Henbest for valuable suggestions, and to Mr. M. Hubert and Mr. H. De Greef for experimental assistance.

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[*Received, February 3rd,* 1963.]