The Synthesis, *X*-Ray Structural Analysis, and Anomeric Effect in *trans*-3,6-Dimethoxy-1,2,4,5-tetroxane

Chin-Yun Chiang, William Butler, and Robert L. Kuczkowski*

Department of Chemistry, University of Michigan, Ann Arbor, MI 48109, U.S.A.

The ozonolysis of 1,2-dimethoxyethylene produces *trans*-3,6-dimethoxy-1,2,4,5-tetroxane which has a chair conformation with diaxial methoxy substituents and carbon–oxygen bond distances characteristic of anomeric and *exo*-anomeric interactions between the methoxy groups and the ring.

The ozonolysis of methyl vinyl ether was recently reported to yield ozonides (1,2,4-trioxolanes) and novel 1,2-dioxolanes from reactions of the carbonyl oxide CH_2OO with, respectively, esters and the starting alkene.[1] We have now ozonized *cis*-1,2-dimethoxyethylene[2] in $CHCl_3$ and methyl formate solvents in a similar fashion[1] to examine if an analogous product can be isolated. It is apparent that neither ozonides nor dioxolanes are the main reaction products. Apart from polymeric residues and methyl formate which are produced in substantial amounts, two new products are observed in nearly equal quantities (total yields 5—23%). One of these was crystallized from a cold methyl formate solution and characterized as the *trans*-isomer of 3,6-dimethoxy-1,2,4,5-tetroxane.† The second compound is assigned to the *cis*-tetroxane isomer since its n.m.r. and chemical ionisation mass spectra (c.i.m.s.) are very similar to those of the *trans*-isomer. These compounds are the products expected from dimerization reactions of the carbonyl oxide HC(OMe)OO produced from cleavage of the alkene. A low stereoselectivity might be expected for the dimerization reaction since it is probably a stepwise $4\pi + 4\pi$ cycloaddition. The formation of a tetroxane in appreciable yields is more common from the ozonolysis of tetra-substituted alkenes,[3] but they are sometimes obtained from 1,2-disubstituted alkenes.[4]

The chair conformation of the *trans*-isomer is shown in Figure 1.‡ Unlike all other *trans*-disubstituted 1,2,4,5-tetroxanes[5] which have equatorial substituents, the methoxy groups are diaxial, characteristic of an anomeric interaction between the peroxide oxygen non-bonded electron pairs and the exocyclic C–O bonds.[6] In addition, the synclinal orientation of the O–Me group relative to the ring C–H bond places it in a position for an *exo*-anomeric interaction involving the methoxy oxygen non-bonded electrons and the ring C(3)–O(1) bond. The anomeric and *exo*-anomeric effects have the same electronic origin, *viz.* two-electron interactions between filled non-bonding and empty anti-bonding orbitals.[7]

In addition, the bond lengths C(3)–O(1) (1.413 Å), C(3)–O(2a) (1.399 Å), and C(3)–O(4) (1.369 Å) reveal a subtle interplay of the anomeric and *exo*-anomeric interactions. The severe shortening of C(3)–O(4) suggests a strong interaction of the non-bonded electrons on O(4) with the anti-bonding ring C–O orbitals. The lengthening of C(3)–O(1) compared to C(3)–O(2a) is consistent with the synclinal orientation of the methoxy group which places an sp^3-like lone

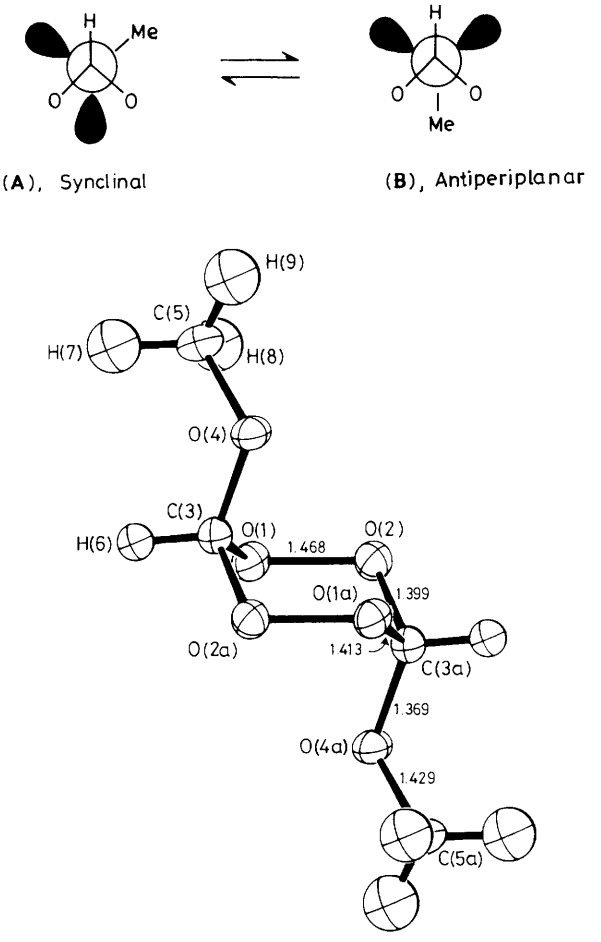

Figure 1. ORTEP drawing of structural parameters for *trans*-3,6-dimethoxy-1,2,4,5-tetroxane showing the 30% probability thermal ellipsoids. The bond distances are in Å and have a standard deviation 0.002 Å. Bond angles: O(2)O(1)C(3) 107.6(1), O(1)C(3)O(2a) 109.7(1), O(1)C(3)O(4) 113.6(1), O(2a)C(3)O(4) 109.7(1), C(3)O(4)C(5) 112.5(1)°. Torsional angles: C(3)O(1)O(2)C(3a) 61.9(2), O(2)O(1)C(3)C(2a) −63.4(2), O(2)O(1)C(3)O(4) 59.8(2), O(2)O(1)C(3)H(6) −176.8(2), O(1)C(3)O(4)C(5) 68.5(2), O(2a)C(3)O(4)C(5) −168.3(2), H(6)C(3)O(4)C(5) −48.1(2)°.

† *Selected spectroscopic data* for *trans*-isomer: ^{1}H n.m.r. δ ($CDCl_3$) 6.08 (s, 2H), 3.65 (s, 6H); ^{13}C n.m.r. δ ($CDCl_3$) 55.8 (qd, *J* 146.5, 4.2 Hz), 115.3 (dq, *J* 197.8, 4.5 Hz); c.i.m.s. *m/z* (intensity), 170.0666 (calc. 170.0664) (100%, $M + NH_4^+$), 187 (42%, $M + N_2H_7^+$).

cis-Isomer: ^{1}H n.m.r. δ ($CDCl_3$) 5.93 (s, 2H), 3.63 (s, 6H); ^{13}C n.m.r. δ ($CDCl_3$) 54.9 (qd, *J* 145.6, 3.5 Hz), 113.5 (dq, *J* 193.8, 4.8 Hz); c.i.m.s. 170 (100%, $M + NH_4^+$), 187 (53%, $M + N_2H_7^+$). *Caution*: No evidence of fast decomposition was observed during the work up and characterization of these potentially hazardous materials, but the normal precautions in handling peroxides should be observed. The *trans*-isomer melted sharply at 66 °C.

‡ *Crystal data for trans*-isomer: T = 227 K, monoclinic, space group $P2_1/n$, a = 10.207(4), b = 4.349(1), c = 7.215(2) Å, β = 95.48(3)°, U = 318.8(2) Å^3, Z = 2, D_c = 1.584. A total of 721 reflections were measured on a Syntax $P2_1$ diffractometer and 476 reflections with $I > 3\sigma(I)$ were used in subsequent structure solution and least-squares refinement. The molecule contains a crystallographically required inversion centre. The analysis gave a final R = 0.030 and R_w = 0.031 using anisotropic thermal parameters for all non-hydrogen atoms. Computer programs used included SHELX, ORTEP, and MULTAN 78. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

pair on O(4) in an antiperiplanar orientation (**A**) to the C(3)–O(1) bond, enhancing the interaction with that bond.[7] An interesting question is why the methoxy substituent does not assume an antiperiplanar orientation to the ring hydrogen placing it over the tetroxane ring (**B**). Conformer (**B**) possesses two sp^3 lone pairs antiperiplanar to ring C–O bonds which should be more stable than (**A**), with only one antiperiplanar lone pair. The anti-conformer has been found in a microwave structure investigation of methoxyethylene ozonide (3-methoxy-1,2,4-trioxolane).[8] There is evidence based on a combination of dipole moment and n.m.r. data in an analogous 5-membered ring compound (2-methoxy-1,3-dioxolane) that the synclinal ⇌ anti equilibrium in solution also favours the anti-form.[9] Perhaps crystal packing interactions play a role in the conformational energetics about the C(ring)–O(Me) bond. They may also play a role in stabilizing the diaxial chair conformer (Figure 1) over the diequatorial chair form. In fact, the n.m.r. at −80 °C [in $(CD_3)_2CO$] resolves into two conformers in a 3 : 1 ratio. The more intense pair of signals is the downfield set (δ 6.44 and 3.75 *vs.* 6.30 and 3.56). Since methoxy group rotation about the C(ring)–O(Me)bond probably has a barrier of 1—3 kcal/mol[8] (1 cal = 4.184 J) while the chair–chair interconversion barrier is expected to be 10—15 kcal/mol,[10] it is the latter process which has been affected. The assignment of the more stable form from the chemical shifts is somewhat ambiguous since a downfield shift of the ring-H but an upfield shift of the methoxy-H is usually observed for the axial methoxy conformer in similar 1,3-dioxanes[11] and carbohydrates.[12] Since the anomeric effect usually stabilizes an axial methoxy group by 0.5—2.0 kcal/mol[6] over the equatorial position, it seems reasonable to assign tentatively the more intense signals to the diaxial conformer. Similarly, the observed diaxial form in the crystal is probably not surprising given the anomeric stabilization, although lattice forces may also play a role. The absence of any additional structural information on ring compounds containing two endocyclic oxygen atoms bonded to a carbon bearing an alkoxy substituent precludes making any further empirical correlations.

This work was supported by a grant CHE-8603834 from the National Science Foundation, Washington D.C. We are grateful to Dr. Primož Lorenčak and Brenda Wojciechowski for helpful discussions.

Received, 17th August 1987;§ Com. 1215

References

1 H. Keul, H.-S. Choi, and R. L. Kuczkowski, *J. Am. Chem. Soc.*, 1985, **50**, 3365.
2 J. T. Waldron and W. Snyder, *J. Org. Chem.*, 1973, **38**, 3059.
3 R. W. Murray, J. W.-P. Lin, and D. A. Grumke, *Adv. Chem. Ser.*, 1972, **112**, 9.
4 P. S. Bailey, 'Ozonation in Organic Chemistry,' Academic Press, New York, 1976, vol. 1, p. 32.
5 M. Schulz and K. Kirschke, in 'Organic Peroxides,' ed. D. Swern, Wiley–Interscience, New York, 1972, vol. 3, ch. 2.
6 A. J. Kirby, 'Anomeric Effect and Related Stereoelectronic Effects at Oxygen,' Springer–Verlag, Berlin, 1983.
7 P. Deslongchamps, 'Stereoelectronic Effects in Organic Chemistry,' Pergamon Press, London, 1983.
8 M. S. LaBarge, H. Keul, and R. L. Kuczkowski, *J. Am. Chem. Soc.*, in the press.
9 C. Altona and A. P. M. Van der Veek, *Tetrahedron*, 1968, **24**, 4377.
10 R. W. Murray, P. R. Story, and M. L. Kaplan, *J. Am. Chem. Soc.*, 1966, **88**, 526.
11 E. L. Eliel and F. W. Nader, *J. Am. Chem. Soc.*, 1970, **92**, 584.
12 A. S. Perlin, B. Casu, and H. J. Koch, *Can. J. Chem.*, 1970, **48**, 2596.

§ Received in revised form, 4th December 1987.