Pergamon

Tetrahedron Letters 39 (1998) 2899–2902

TETRAHEDRON
LETTERS

Cyclooctatetraene Tetraepoxides[1]

Robert W. Murray*, Megh Singh, and Nigam P. Rath

Department of Chemistry, University of Missouri-St. Louis,
St. Louis, MO, 63121, USA

Received 26 January 1998; revised 23 February 1998; accepted 25 February 1998

Abstract: Oxidation of cyclooctatetraene with excess dimethyldioxirane gives two previously unknown tetraepoxides. The structures of the tetraepoxides were established using X-ray crystallography. The reaction also gives a number of di- and triepoxides.

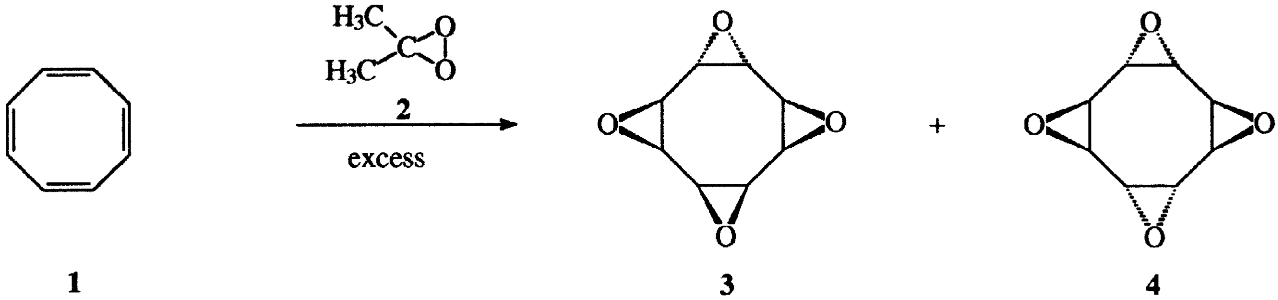
Cyclooctatetraene **1** was first described as a degradation product of the alkaloid pseudo-pelletierine in 1911 by Willstatter and Waser[2]. Early X-ray[3] and electron diffraction[4,5] studies showed that **1** exists in a non-planar tub form. NMR spectroscopy was used[6] to show that the molecule undergoes conformational isomerization at ordinary temperatures. Earlier treatment[7] of **1** with *m*-chloroperbenzoic acid led to the formation of three diepoxides. When trifluoroperacetic acid was used as oxidant the same three diepoxides were formed[7] as well as a triepoxide. We and others[8-15] have shown that dioxiranes are powerful O atom transfer reagents which can be used under very mild conditions and usually give high yields of epoxidation products. It seemed to us that dimethyldioxirane was likely to give a more complete oxidation of **1**.

We here report that treatment of **1** with excess dimethyldioxirane **2** gives the heretofore unknown tetraepoxides, *cis,cis,cis,trans*-cyclooctatetraene tetraepoxide **3** and *cis,trans,cis,trans* -cycloctatetraene tetraepoxide **4** in an 87:13 ratio (Scheme 1). In a sample reaction a solution of **1** (0.065 g, 0.624 mmol) was treated with 55 mL (3.85 mmol) of an 0.07 M acetone solution of **2** and the reaction was magnetically stirred at room temperature in the dark. The progress of the reaction was monitored by GLC and GC-MS. After 2 h the reaction mixture showed the presence of the monoepoxide of **1** as well as stereoisomeric diepoxides, stereoisomeric triepoxides and traces of stereoisomeric tetraepoxides. After 72 h the reaction mixture contained a triepoxide and two tetraepoxides. After 240 h of stirring the reaction mixture contained a trace of triepoxide with the tetraepoxides as the major products. At this time the solvent was removed and an additional quantity of **2** (25 mL) was added. Stirring was continued for an additional 164 h. The solvent was removed to give a colorless crystalline solid (0.1056 g, 100 %). ^{1}H NMR analysis of the solid indicated the

0040-4039/98/$19.00 © 1998 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)00493-6

presence of an analytically pure mixture of tetraepoxides 3 and 4 in an 87:13 ratio. The tetraepoxides were separated by repeated fractional crystallization. Tetraepoxide 3 was obtained as a colorless crystalline solid, mp > 320° C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.11 (d, J = 3.66 Hz, 2H), 3.28 (s, 2H), 3.35 (d, J = 3.66 Hz, 2H), 3.76 (s, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 52.64, 53.06, 53.13, 54.11; MS (EI, 70 eV): m/z (relative intensity) 150 (M^+-18, 0.05), 139 (1), 121 (3), 110 (5), 97 (9), 81 (71), 71 (100), 69 (16), 55 (28), 53 (32), Calcd for $C_8H_8O_4$ 168.15. Anal Calcd for $C_8H_8O_4$: C, 57.14; H, 4.80; Found: C, 56.79; H, 4.81. Tetraepoxide 4 was isolated as a colorless crystalline solid, mp 180-185° C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.17 (s, 8H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 52.71; MS (EI, 70 eV): m/z (relative intensity) 168 (M^+, 2), 139 (0.4), 110 (3), 97 (5), 81 (51), 71 (100), 68 (31), 55 (32), 53 (23), Calcd for $C_8H_8O_4$ 168.15. Anal Calcd for $C_8H_8O_4$: C, 57.14; H, 4.80; Found: C, 56.53; H, 4.72.

In the earlier oxidation of 1 using peracids [6] a diepoxide was formed which showed conformational isomerization as disclosed by heating a sample and measuring the NMR spectrum to coalescence. An isomeric diepoxide showed no evidence of such isomerization [6]. Low temperature ^{1}H and ^{13}C NMR spectra of 3 and 4 were measured over the range 300 to 166 K with no indication of conformational isomerization. *A priori* the reaction could give 4 diepoxides, three triepoxides, and four tetraepoxides. Full details on the reaction procedure, the actual products obtained, and structural assignments in the di- and triepoxides will be given in the full paper.



Scheme 1

The structures of tetraepoxides 3 and 4 were determined by X-ray diffraction. The structure of 3 (Figure 1) clearly shows the *cis,cis,cis,trans* arrangement of the epoxide O atoms. The structure suggests that this material could act as an ionophore. We are currently carrying out complexation studies of 3 with cations. The X-ray structure of 4 (Figure 2) confirms the *cis,trans,cis,trans* stereochemistry in this tetraepoxide.

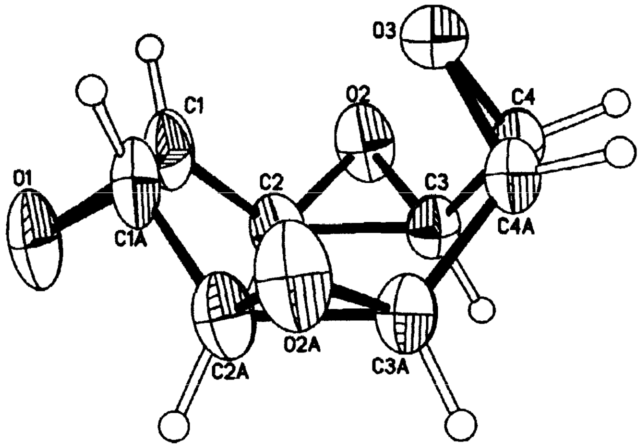


Figure 1. X-ray Crystal Structure of **3**.

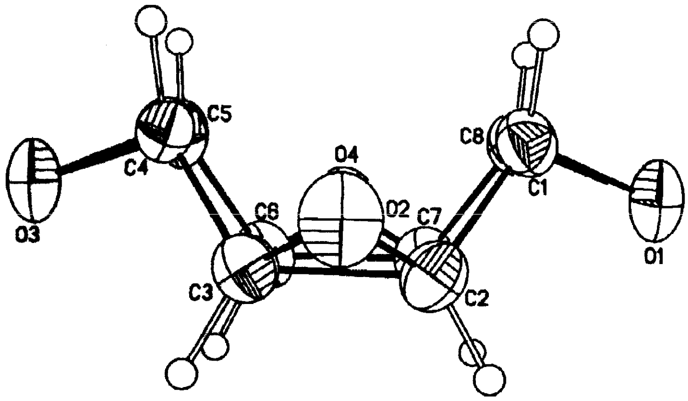


Figure 2. X-ray Crystal Structure of **4**.

Acknowledgments: We are grateful to the National Institute of Environmental Health Sciences, NIH, for support of this work (Grant number ES01984). Its contents are solely the responsibility of the authors and do not represent the official views if the NIEHS, NIH. The Varian XL-300 NMR was purchased with support from the National Science Foundation.

REFERENCES AND NOTES

1. Chemistry of Dioxiranes Part 38, Part 37: Murray, R.W., Singh, M., Rath, N.P., Polycyclic Arom. Compounds, submitted.
2. Willstatter, R.; Waser, E. *Ber.* **1911**, *44*, 3422-3445.
3. Bordner, J.; Parker, R.G.; Stanford, R.H. *Acta Cryst.* **1972**, *B28*, 1069-1075.
4. Karle, I. L. *J. Chem. Phys.* **1952**, *20*, 65-70.
5. Bastiansen, O.; Hedberg, L.; Hedberg, K. *J. Chem. Phys.* **1957**, *27*, 1311-1317.
6. Anet, F.A.L.; Bourn, A.J.R.; Lin, Y.S. *J. Am. Chem. Soc.* **1964**, *86*, 3576-3577.
7. Anastassiou, A.G.; Reichmanis, E. *J. Org. Chem.* **1973**, *38*, 2421-2422.
8. Murray, R.W. *Chem. Rev.* **1989**, *89*, 1187-1201.
9. Curci, R. In *Advances in Oxygenated Processes*; Baumstark, A.L., Ed.; JAI Press, Greenwich, CT. 1990; Vol.2, Chapter 1, pp 1-59.

10. Adam, W.; Hadjiarapoglou, L.P.Curci, R.; Mello, R. In *Organic Peroxides*; Ando, W., Ed.; J.Wiley and Sons; New York. 1992, Chapter 4, pp 195-219.
11. Adam, W.; Curci, R.; Edwards, J.O. *Acc. Chem. Res.* **1989**, *22*, 205-211.
12. Adam, W.; Hadjiarapoglou, L.P. *Top. Curr. Chem.* **1993**, *49*, 2227-2248.
13. Curci, R.; Dinoi, A.; Rubono, M.F. *Pure and Appl. Chem.* **1995**, *67*, 811-822.
14. Murray, R.W.; Singh, M. In *Comprehensive Heterocyclic Chemistry II*, Katritzky, A.R.; Rees, C.W.; Scriven, E.F.V., Eds., Pergamon Press, Oxford, 1996, Chapter 1.14, 429-456.
15. Clennan, E.L. *Trends Org. Chem.* **1995**, *5*, 231-252.