DIMETHYLDIOXIRANE EPOXIDATION OF ENOL PHOSPHATES

Waldemar Adam*, Lazaros Hadjiarapoglou and Jasna Klicic

Institute of Organic Chemistry, University of Würzburg, Am Hubland,D-8700 Würzburg, F.R.G.

Summary: The novel epoxides 2 of a variety of enol phosphates 1 were readily prepared by epoxidation with dimethyldioxirane at subambient temperatures; at room temperature these labile epoxides 2 rearranged into the corresponding α-dialkoxyphosphinyloxy-substituted carbonyl products 3.

Epoxides are useful intermediates in organic synthesis [1], which are usually available by direct oxyfunctionalization of the corresponding olefins. For example electron-donating substituents increase the electron density of the C=C bond and consequently various enol systems [2] are easily oxidized by electrophilic oxygen transfer agents such as peroxy acids. Since the resulting epoxides readily undergo acid-catalyzed rearrangement to give the corresponding carbonyl products, such peroxy acid epoxidations have only limited success.

Although enol phosphates are of considerable biochemical interest [3], epoxides of enol phosphates are essentially unknown compounds [4]. Phosphoenolpyruvate (PEP), the most common enol phosphate, is a very important biological intermediate [5], representing the last phosphorylated three-carbon-atom species in glycolysis, is an intermediate in fermentation, and also plays a role in the fixation of carbon dioxide. Methyl 3-[(dimethoxyphosphinyl)oxy]crotonate ($R=CH_3$), or more commonly known as Phosdrin, is frequently employed as insecticide.
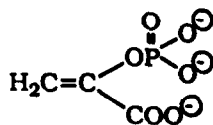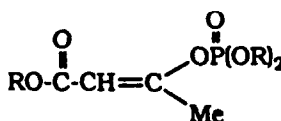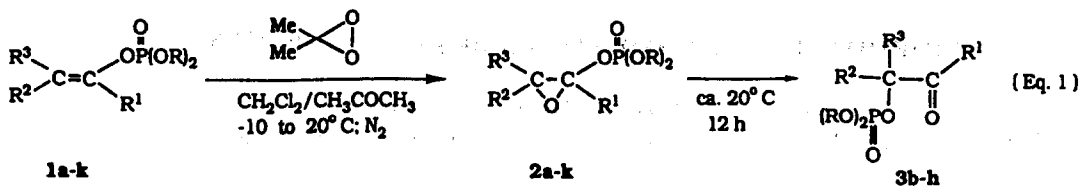

(PEP)   (Phosdrin)

In view of the fact that isolated dimethyldioxirane [6], as acetone solution [7], has proved itself as convenient oxidant for the preparation of hydrolytically sensitive epoxides of enolic substrates such as enol ethers [8], enol silyl ethers [9], enol esters and lactones [10], β-oxo enol ethers [11], and 2,3-dimethylbenzo[b]furans (to be published), we decided to apply this powerful and selective oxygen transfer agent for the epoxidation of enol phosphates.

Presently we report the preparation of the labile epoxides 2a-k from the enol phosphates 1a-k (Eq. 1) in excellent yields (cf. Table 1). On standing at room temperature (ca. 20 °C), the epoxy enol phosphates 2 rearranged into the corresponding α-dialkoxyphosphinyloxy-substituted carbonyl compounds 3.

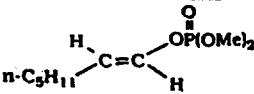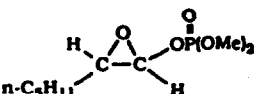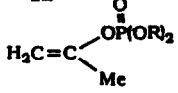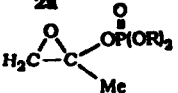$$R^3\!\!-\!\!\underset{R^2}{\overset{}{C}}\!\!=\!\!\underset{R^1}{\overset{OP(OR)_2}{\overset{\|}{\overset{O}{C}}}} \quad \xrightarrow[\substack{CH_2Cl_2/CH_3COCH_3 \\ -10 \text{ to } 20^\circ C;\ N_2}]{\substack{Me\diagdown\ \diagup O \\ Me\diagup\diagdown O}} \quad R^3\!\!-\!\!\underset{R^2}{\overset{}{C}}\!\!-\!\!\underset{R^1}{\overset{OP(OR)_2}{\overset{\|}{\overset{O}{C}}}} \quad \xrightarrow[12\,h]{ca.\ 20^\circ C} \quad \underset{(RO)_2PO}{\overset{R^3}{R^2\!-\!C}}\!\!-\!\!\underset{O}{\overset{R^1}{\overset{}{C}}} \quad (Eq.\ 1)$$

1a-k   **2a-k**   **3b-h**
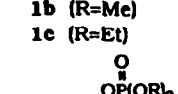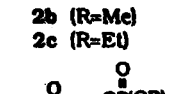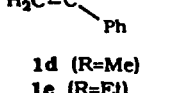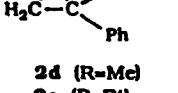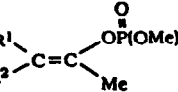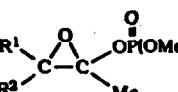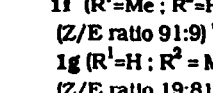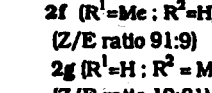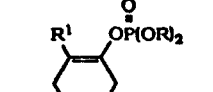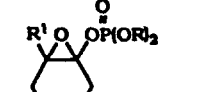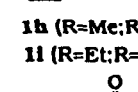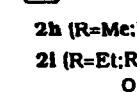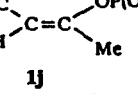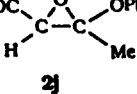
The convenient epoxidation procedure entailed adding rapidly a solution of dimethyldioxirane in acetone (ca. 0.072-0.085 M) [12], dried over molecular sieves 4Å at -20 °C, to a cooled (for specific conditions cf. Table 1), stirred solution of enol phosphate **1** (0.58-1.12 mmol) in abs. CH_2Cl_2 (10 ml) under a N_2 atmosphere. The stirring was continued until complete consumption (cf. Table 1) of the enol phosphate (disappearance of the characteristic stretching frequences at 1690-1630 cm^{-1} in the IR), the solvent and excess dimethyldioxirane removed under vacuum (0 °C; 15 torr) to yield the new epoxides **2** in high purity (IR, NMR) and excellent yields (≥ 95 %). The appearance of the epoxide proton signals at δ 2.32-5.02 and the ^{13}C NMR signal of the C-2 and C-3 epoxide carbon atoms at δ 79-88 and 52-61 confirmed the structure assignment of the epoxides **2**. As expected for this stereospecific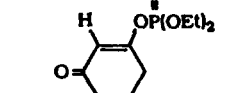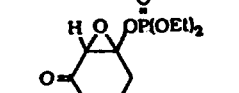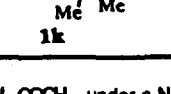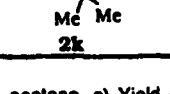 epoxidizing agent [6], the diastereomeric composition of the enol phosphates **1f** (Z/E ratio 91:9) and **1g** (Z/E ratio 19:81) was preserved in the corresponding epoxides **2f,g** (cf. Table 1).

When the same epoxidation procedure was applied to the enol phosphate **1j,k**, which possess β-electron-withdrawing substituents, the enol phosphates were isolated unchanged. Excess dimethyldioxirane, longer reaction times, and room temperature were necessary for complete conversion (98 %) of enol phosphate **1j,k** to the corresponding epoxides **2j,k**.

Most of the enol phosphate epoxides are labile substrates, e.g. the derivatives **2b-h** rearrange into the corresponding α-dialkoxyphosphinyloxy-substituted carbonyl compounds **3b-h** (Eq. 1) when allowed to stand in C_6D_6 solution at room temperature overnight. For this reason these isolated epoxides could not be purified for elemental analysis and were characterized on the basis of their spectral data. Relatively stable derivatives are the epoxides **2a,j,k**, which persist at room temperature for several days. In fact , epoxide **2a** was previously prepared [4a] from enol phosphate **1a** and constitutes hitherto the only authentic isolated example of this class of unusual epoxides. Thus, enol phosphate epoxides not bearing α-alkyl or α-aryl substituents, such as **2a**, or which possess β-carbonyl substituents, such as **2j,k**, are sufficiently stable at room temperature for handling. Presumably epoxide ring opening results in less stable cationic intermediates and consequently their rearrangement into **3** (Eq. 1) is less prone to occur.

In summary, dimethyldioxirane (as acetone solution) constitutes a convenient and an efficient oxygen transfer agent for the preparation of a variety labile epoxy enol phosphates (Eq. 1). These novel epoxides 2 should be of interest in organic synthesis .

Table 1 Dimethyldioxirane Epoxidation[a] of Enol Phosphates.

Substrate	Equiv. of Dioxirane[b]	Temp. (°C)	Time (h)	Yield (%)[d]	Epoxide
1a (H, n-C_5H_{11}, $C=C$, H, $OP(OMe)_2$)	1.7	20	2	99	2a
1b (R=Me) ($H_2C=C$, $OP(OR)_2$, Me)	1.1	0	4.5	98	2b (R=Me)
1c (R=Et)	1.4	0	3.5	99	2c (R=Et)
1d (R=Me) ($H_2C=C$, $OP(OR)_2$, Ph)	1.3	-10	3.5	96	2d (R=Me)
1e (R=Et)	2.0	-10	2	99	2e (R=Et)
1f (R^1=Me ; R^2=H) (Z/E ratio 91:9)[d] (R^1, R^2, $C=C$, Me, $OP(OMe)_2$)	1.5	-10	2.5	ca. 100	2f (R^1=Me ; R^2=H) (Z/E ratio 91:9)
1g (R^1=H ; R^2=Me) (Z/E ratio 19:81)[d]	1.5	-10	2.5	ca. 100	2g (R^1=H ; R^2=Me) (Z/E ratio 19:81)
1h (R=Me;R^1=H) (R^1, $OP(OR)_2$ cyclohexene)	1.5	0	5	ca. 100	2h (R=Me;R^1=H)
1i (R=Et;R=Me)	1.6	-10	3	99	2i (R=Et;R=Me)
1j (EtOOC, H, $C=C$, $OP(OEt)_2$, Me)	3.6	20	48	98[e]	2j
1k (H, $OP(OEt)_2$, O=, Me, Me cyclohexenone)	6.0	20	91	98[f]	2k

a) In CH_2Cl_2/CH_3COCH_3 under a N_2 atmosphere. b) 0.07-0.09 $\underline{M}$ dimethyldioxirane in acetone. c) Yield of isolated pure product after evaporation of the solvent (0 °C; 15 torr), but rigorous purification was not possible in view of the labile nature of these epoxides. d) Diastereomeric composition of initial enol phosphate. e) A solution of enol phosphate 1 j (0.67 mmol) in abs. CH_2Cl_2 (10 ml) under N_2; the stirring was continued until complete consumption of the starting enol phosphate. f) A solution of dimethyldioxirane (3.45 mmol) was added in four portions (0 h; 7.5 h; 23 h; 43 h) to a stirred solution of enol phosphate 1 k (0.58 mmol) in abs. CH_2Cl_2 (10 ml) under N_2; the stirring was continued until complete consumption of the starting enol phosphate.

LITERATURE

[1]   a. H. O. House in W.A. Benjamin (Ed.): Modern Synthetic Reactions, 2nd Ed., Menlo Park, California 1972 , p. 300.
        b. J.G. Smith, Synthesis 1984, 629.

[2]   a. P. Fischer in S. Patai (Ed.): The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and their Sulphur Analogues, John Wiley and Sons, New York 1980, p. 779.
        b. G. M. Rubottom, M. A. Vasquez, D. R. Pelegrina, Tetrahedron Lett. (1974) 4319.
        c. L. A. Paquette, H. -S. Lin, J. C. Gallucci, Tetrahedron Lett. 28 (1987) 1363.

[3]   F. W. Lichtenthaler, Chem. Rev. 61 (1961) 607.

[4]   a. J. L. Kraus, G. Sturz, Bull. Soc. Chim. (1971) 4006.
        b. M. Murayama, S. Matsumura, T. Wada, Y. Ezure, Japan Kokai, 72, 39, 033; Chem. Abstr. 78 (1973) 71422 k .

[5]   D. E. Metzler in: Biochemistry. The Chemical Reactions of Living Cells, Academic Press , New York 1977, pp. 417-418.

[6]   a. W. Adam, R. Curci, J. O. Edwards, Acc. Chem. Res. 22 (1989) 205.
        b. R. Murray, Chem. Rev. 89 (1989) 1187.
        c. R. Curci in A.L. Baumstark (Ed.): Advances in Oxygenated Processes , Vol 2 , Chapter 1 , JAI Press, Greenwich CT 1990.

[7]   a. R. W. Murray, R. Jeyaraman, J. Org. Chem. 50 (1985) 2847.
        b. W. Adam, Y.-Y. Chan, D. Cremer, J. Gauss, D. Scheutzow, M. Schindler, J. Org. Chem. 52 (1987) 2800.
        c. P. E. Eaton, G. E. Wicks, J. Org. Chem. 53 (1988) 5353.

[8]   S. W. Baertschi, K. D. Raney, M. P. Stone, T. M. Harris, J. Am. Chem. Soc. 110 (1988) 7929.

[9]   a. W. Adam, L. Hadjiarapoglou, X. Wang, Tetrahedron Lett. 30 (1989) 6497.
        b. H. K. Chenault, S. J. Danishefsky, J. Org. Chem. 54 (1989) 4249.

[10]   W. Adam, L. Hadjiarapoglou, V. Jäger, B. Seidel, Tetrahedron Lett. 30 (1989) 4223.

[11]   W. Adam, L. Hadjiarapoglou, Chem. Ber. 123 (1990), in press.

[12]   The peroxide content was determined by oxidation of methyl phenyl sulfide to its sulfoxide, the latter quantitated by ^{1}H NMR.