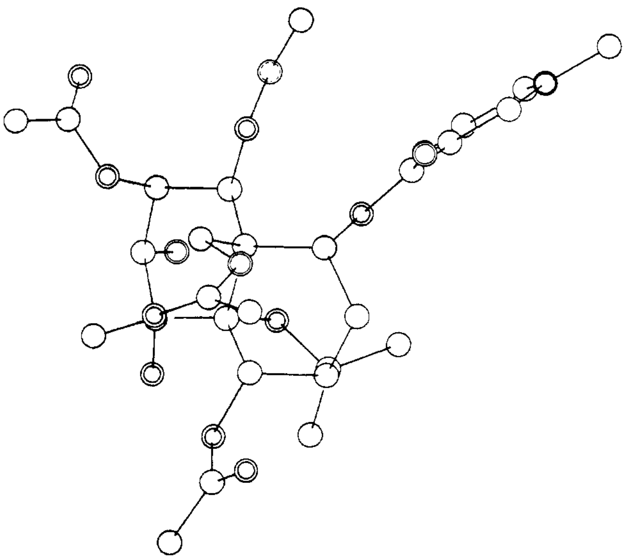


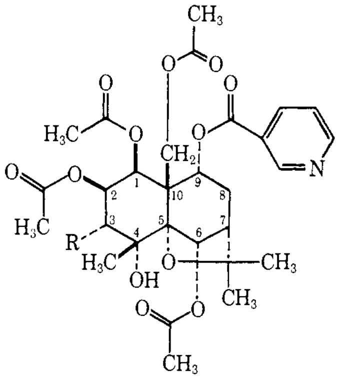
Figure 1. The maytoline methiodide cation as present in the crystal. Carbon atoms are denoted by single circles, oxygen atoms by double circles, and the nitrogen atom by the heavy circle.

characterized as containing a $C_{15}$ nucleus carrying four acetate and one nicotinate ester groups and a tertiary hydroxyl group. **1** also contained a secondary hydroxyl group. One oxygen atom in each compound remained unassigned.

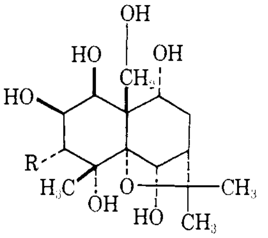
In order to determine the skeleton of the polyhydroxy nucleus and the locations of the acyl groups, the methiodide of **1** was prepared and examined by X-ray crystallography. Crystals of maytoline methiodide are monoclinic with space group $P2_1$, $a$ = 11.643 (3), $b$ = 14.621 (2), $c$ = 10.436 (2) Å, $\beta$ = 97.43 (1)°, and two molecules in the unit cell. The 1626 independent reflections significantly above background were measured by counter diffractometry with monochromatic Mo K$\alpha$ radiation ($\lambda$ 0.71069 Å). The structure was solved by the heavy-atom method and refined by use of the block-diagonal least-squares approximation to a final conventional $R$ index of 0.076. Anisotropic thermal parameters were used only for the iodine atom. No reliable decision on the absolute configuration of the molecule could be made by examination of Friedel pairs or by independent refinement of the two possible enantiomeric structures taking account of the anomalous dispersion of the iodine atom. A view of the structure of the cation as found in the crystal is shown in Figure 1.

From the nmr spectral evidence, maytine (**2**) presumably lacked an oxygen function at C-1 or C-3. Of the seven C-Me signals in the nmr spectra of **1** and **2**, those below $\tau$ 8.0 are readily assignable to three acetyl groups. The remaining four signals $\tau$ 8.3–8.5 can thus be assigned to the three C-Me groups and to a shielded acetyl group. Examination of models of **1** showed that only the C-1 acetyl group methyl should come under the diamagnetic influence of the nicotinoyl ring. (See also Figure 1 for the relative orientation in the crystal.) As this high-field acetyl group signal was present in both spectra, maytine can be assigned the structure **2**. In the spectra of tetrahydromaytine this fourth acetyl group signal appeared at lower field, $\tau$ 8.18.

Maytoline's characteristics resemble those of "Alkaloid A," $C_{29}H_{37}NO_{13}$, a weak base isolated in 1949 from the fruit of *Euonymus europaeus* L. (Celastraceae).[7] Alkaloid A was shown to contain four acetyl groups and an acylable hydroxyl group, but no further work was carried out. More complex Celastraceae alkaloids were isolated subsequently from *Euonymus europaeus* L.[8] and *Tripterygium wilfordii* Hook,[9] but were only partially characterized. These compounds apparently contained a common $C_{15}H_{26}O_{10}$ decahydroxy nucleus, containing two C-methyl groups, which may be closely related to maytol. The nicotinic acids isolated from these compounds all contained a $C_5$-carboxylic acid substituent at the 2 position. Hence maytoline and maytine appear to be the first completely characterized members of a novel alkaloid family.



**1**, R = OH
**2**, R = H



**3**, R = OH
**4**, R = H

(7) K. Doebel and T. Reichstein, *Helv. Chim. Acta*, 32, 592 (1949).
(8) M. Pailer and R. Libiseller, *Monatsh. Chem.*, 93, 403 (1962).
(9) M. Beroza, *J. Org. Chem.*, 28, 3562 (1963), and references therein.
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## Evidence for Epoxides as Intermediates in the Chromic Acid Oxidation of Olefins

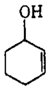
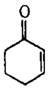
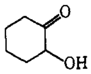
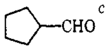
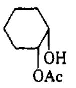
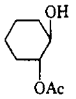
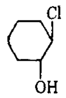
*Sir:*

We recently presented kinetic evidence suggesting epoxide formation as the rate-limiting step in the Cr(VI) oxidation of olefins in aqueous acetic acid.[1] In this communication we wish to report the first successful trapping and isolation of an epoxide formed in a chromic acid oxidation of a simple olefin.[2]

We found that the oxidation of cyclohexene in glacial acetic acid containing perchloric acid yields a mixture of *cis*- and *trans*-2-acetoxycyclohexanol, a small amount of cyclopentanecarboxaldehyde, 2-hydroxycyclohexanone, and the allylic oxidation products 2-cyclohexen-1-ol and 2-cyclohexen-1-one (Table I, experiment

(1) A. K. Awasthy and J. Roček, *J. Amer. Chem. Soc.*, 91, 991 (1969).
(2) Epoxides have previously been isolated in chromyl acetate[3,4] oxidations.
(3) M. A. Davis and W. J. Hickinbottom, *J. Chem. Soc.*, 2205 (1958), and preceding papers in the series.
(4) W. A. Mosher, F. W. Steffgen, and P. T. Lansbury, *J. Org. Chem.*, 26, 670 (1961).

Table I. Products of the Chromic Acid Oxidation of Cyclohexene and the Acetolysis of Cyclohexene Oxide[a]

| Expt | Reaction | LiCl, $M$ | % yield[b] | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | | |  |  |  |  [c] |  |  |  | |
| 1 | Oxidation | | 1.0 | 12.5 | 7.7 | 0.5 | 8.6 | 25.8 | | 56.1 |
| 2 | Acetolysis | | | | | 3.2 | 24.9 | 70.9 | | 99.0 |
| 3 | Acetolysis | 1.25 | | | | | | 2.8 | 97.2 | 100.0 |
| 4 | Oxidation | 1.25 | 3.6 | 25.1 | 6.9 | | 0.2 | 1.2 | 32.6 | 69.6 |
| 5 | Oxidation | 1.25[d] | 0.5 | 12.0 | 6.2 | 0.1 | 4.5 | 17.7 | 13.2 | 54.2 |

[a] In glacial acetic acid (0.10% water, w/w) 0.40 $M$ in perchloric acid. Initial concentrations in moles/liter: sodium dichromate dihydrate, 0.0264–0.0270; cyclohexene, 1.18; cyclohexene oxide, 0.128. Reaction time: 24 hr. The products were esterified with an excess of acetic anhydride in the presence of sodium acetate and analyzed in the fully acetylated forms by glpc on diethylene glycol succinate. (Analysis before esterification showed the presence of products listed in the table together with variable amounts of their corresponding acetates.) [b] Yields are based on the oxidant. [c] Determined as cyclopentylformaldehyde diacetate. [d] Final concentration; the oxidation was carried out as in experiment 1 and added to a solution of lithium chloride after 1.4 min.

1). The solvolysis of cyclohexene oxide under the same conditions (in the absence of chromic acid) yields *cis*- and *trans*-2-acetoxycyclohexanol and cyclopentanecarboxaldehyde in a practically quantitative yield[5] and in about the same ratio (Table I, experiment 2).

Further evidence for the epoxide intermediacy in the chromic acid oxidation of olefins was obtained by a trapping experiment. Acetolysis of cyclohexene oxide in the presence of lithium chloride yielded *trans*-2-chlorocyclohexanol with a small amount of *trans*-2-acetoxycyclohexanol (Table I, experiment 3). When the oxidation of cyclohexene was carried out in the presence of lithium chloride, the formation of the 2-acetoxycyclohexanols and cyclopentanecarboxaldehyde was greatly reduced and a 32.6% yield of 2-chlorocyclohexanol was indeed obtained in their place (Table I, experiment 4). Combining this with the result of the previous experiment (experiment 3) one can estimate that a 33.6% yield of cyclohexene oxide was formed in the oxidation. This is in very good agreement with the sum of *cis*- and *trans*-2-acetoxycyclohexanol and cyclopentylformaldehyde from the oxidation (34.9%). Thus about 33% of the oxidation products are formed *via* cyclohexene oxide.

Because of the possibility that the presence of lithium chloride in the oxidation mixture might change the nature of the chromium species[6] involved in the oxidation, an experiment in which the oxidation and the reaction with chloride ion were separated was carried out. The olefin and chromic acid were allowed to react in the absence of lithium chloride (same conditions as in experiment 1)[8] and added, after 1.4 min, to a solution of lithium chloride in glacial acetic acid. The results (Table I, experiment 5) support the assumption that the epoxide is the reaction intermediate regardless of the presence or absence of chloride ions.[9]

Finally, we attempted a direct detection of cyclohexene oxide by glpc. The reaction mixture was added after 0.5 min to an aqueous solution of potassium hydroxide and immediately extracted with ether. Analysis of the extract showed 20.5% cyclohexene oxide along with 1.5% *cis*- and 6.0% *trans*-2-acetoxycyclohexanol (analyzed as the alcohols) and 14.0% 2-cyclohexen-1-one.

The trapping of cyclohexene oxide as *trans*-2-chlorocyclohexanol and its direct detection by glpc thus offer conclusive evidence that the epoxide is an important intermediate even in the oxidation of simple olefins. It is interesting to note that the yields of the products derived from epoxide formation are close to 33%. It cannot be excluded that larger amounts of the epoxide are formed but are in part destroyed by further rapid oxidation. However, 33% is rather suggestive of only one oxidation state of chromium (most likely chromium(VI) or chromium(V)) being responsible for epoxide formation.

The allylic oxidation products are clearly not formed *via* the epoxide and are most likely due to chromium(IV) oxidation. The reason for the increase in yield of these products in the presence of lithium chloride is not yet clear. The formation of comparable amounts of 2-hydroxycyclohexanone in the presence and absence of lithium chloride indicates that this compound is also formed by a route not involving an epoxide intermediate.

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(5) The formation of the cis isomer and the ring-contracted aldehyde suggests an A-1 mechanism for the epoxide cleavage. For a compound containing only secondary carbon atoms, this presents a rather surprising and unprecedented result, which however was found to be well reproducible. The similarity of the composition of the product obtained in the oxidation of cyclohexene and in the solvolysis of cyclohexene oxide presents a particularly strong argument in favor of an epoxide intermediate.

(6) Cohen and Westheimer observed a change in the uv spectrum of chromic acid in 86.5% acetic acid containing perchloric acid when sodium chloride was added and attributed it to the formation of the chlorochromate ion.[7]

(7) M. Cohen and F. H. Westheimer, *J. Amer. Chem. Soc.*, **74**, 4387 (1952).

(8) The oxidation was over in a matter of seconds as judged by the immediate change in color.

(9) The epoxide obviously undergoes very rapid solvolysis under the reaction conditions. Judging from the amount of *trans*-2-chlorocyclohexanol formed, it can be estimated that about 62% of the epoxide has already reacted 1.4 min or less after its formation.

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