the $^1$H or $^{13}$C NMR spectra of 3 over the temperature range $-80$ to $+140 \degree C$, reflecting the thermodynamic stability of the oxygens "in" conformer relative to the unobserved oxygens "out" conformer.

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Rearrangement of a Geometrically Restricted Triepoxide to the First Topologically Nonplanar Molecule: A Reaction Path Elucidated by Using Oxygen Isotope Effects on Carbon-13 Chemical Shifts

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The symmetrical triepoxide triisopropyl[tricyclo[3.3.3.0^3,9^5]undecane-2,2',6,2''-triisoxiran] (1) cleanly undergoes rearrangement to the triether 2,5,14-trioxahexacyclo[5.5.2.1.2^4,10.0^7.0^5.17]heptadecane (3), both thermally and with acid catalysis (Scheme I). To elucidate the reaction pathway for this novel rearrangement, we have developed and applied a new method of double-isotope labeling based on the perturbation of $^{13}$C NMR chemical shifts by isotopes of oxygen.

Triether 3 has been a target of our synthetic efforts because it is topologically unique. To our knowledge, it is the first organic molecule known which has a structure which cannot be represented as a planar graph. In addition, the rearrangement that produces 3 was especially interesting, because it proceeded via an unprecedented $2\pi + 2\pi + 2\sigma$ to $2\pi + 2\sigma + 2\sigma$ electrocyclic rearrangement2 (Scheme II, path a). Consideration of the conformations of 1, unsymmetrical triepoxide 2, and the all-carbon analogue of 1, triisopropyl[tricyclo[3.3.3.0^3,9^5]undecane-2,2',6,2''-triisoxiran]3,4 suggested that a conformation of 1 is possible which directs the lone pairs on each oxygen into the region of the antibonding orbitals of an adjacent C-O bond6 (Figure 1). These considerations, combined with the fact that the electrocyclic reaction represented in path a is orbital-symmetry allowed, made us optimistic that the rearrangement of 1 to 3 might be the first case of an electrocyclic reaction involving only $\sigma$ bonds. Although, an alternative route from 1 to 3 (path b) was also conceivable. Although unprecedented in its details, this route is more reminiscent of conventional epoxide chemistry.10

The bonds broken and created in path a are different from those broken and created in path b, making the two paths distinguishable. To make this distinction, we have exploited the known ability of isotopic substitution of $^{18}$O for $^{16}$O to produce perturbations in the NMR chemical shifts of atoms directly attached to oxygen.4 While the precise magnitude of this isotopic perturbation of chemical shift ($\Delta \delta$) depends on the nuclei involved and molecular structure, the $^{13}$C NMR spectrum of a compound partially labeled with $^{18}$O and $^{16}$O at a position adjacent to a single $^{13}$C-labeled atom will show two resonances, the downfield resonance arising from those $^{13}$C atoms bonded to $^{16}$O and the upfield resonance arising from those bonded to $^{18}$O.11 The relative intensity of the two resonances corresponds to the ratio of $^{16}$O and $^{18}$O labels in the adjacent position.12 In contrast, should the $^{13}$C chemical shift be unaffected by the labeling of the oxygen atoms, then the 13C NMR spectrum of a compound partially labeled with $^{18}$O and $^{16}$O at a position adjacent to a single $^{13}$C-labeled atom will show two resonances, the downfield resonance arising from those $^{13}$C atoms bonded to $^{16}$O and the upfield resonance arising from those bonded to $^{18}$O.13

Figure 1. Schematic representation of 1 observed from the "top" along the C3 axis.

(5) Balaban, A. T., Ed., "Chemical Applications of Graph Theory"; Academic Press: New York, 1976; p 84. Simmons, H. E., III; Maggio, J. E. Tetrahedron Lett. 1981, 287-290. For a molecule to have a topologically nonplanar graph, it is necessary (but not sufficient) that no planar representation of the molecule exists that has no bonds crossing. The catenanes (two interlocked rings) would be considered simply as two disconnected graphs in graph theory and are therefore planar. For a graph theoretical discussion of this, see: Busacker, R. G.; Saaty, T. L. Finite Graphs and Networks: An Introduction with Applications; McGraw-Hill: New York, 1965; p 7. Because double-bond isomerization (geometry) is not considered in graph theory, the more recent "betweenness" can be drawn without edge crossings and are also planar.

(6) A reaction similar to that reported here, although almost certainly not "electrocyclic" in nature, has been reported: Welte, C. der; Meijere, A. Angew. Chem., Int. Ed. Engl. 1976, 15, 868-867.  
(8) Deslongchamps, P. Heterocycles 1977, 7, 1271-1317.  
(11) In this work, the downfield and upfield resonances were assigned to the $^{16}$O- and $^{18}$O-labeled molecules, respectively, by comparing the intensities of the resonances with the amounts of M and M+2 ions appearing in the mass spectrum. All observed isotope effects on chemical shifts over one chemical bond are in this direction; upfield signals arise from the nuclei bound to the heavier isotope. A single example of a two-bond effect (0.004 ppm) has been reported by Veders.4
atom be directly bonded to an unlabeled oxygen, it will appear as a single NMR resonance.

Triepoxide 1 labeled with both $^{13}$C (90%) and $^{18}$O (45%) in one of the three epoxide groups was prepared by the route shown in Scheme III.\textsuperscript{12,13-15} The $^{13}$C NMR spectrum\textsuperscript{16} of $^{13}$C, [18O]-1 showed two resonances (46.77 and 46.74 ppm downfield of Me$_4$Si) having relative intensities of 55:45 (downfield:upfield). The isotopic perturbation of the $^{13}$C chemical shifts ($\Delta \delta$ 0.030)\textsuperscript{17} is the largest that has been reported to date for ether bonds. Replacement of the $^{13}$C-180 bond, producing triether 3, would produce triether $^{13}$C-180-1 showing two resonances with relative intensities of 55:45.

In fact, both thermal and acid-catalyzed rearrangement\textsuperscript{2} of [$^{13}$C,18O]-1 produced [$^{13}$C,18O]-3, displaying two $^{13}$C resonances ($\Delta \delta$ 0.023),\textsuperscript{17} with peak intensities in a ratio of 55:45. Thus, to within experimental error, none of 3 was formed from 1 via path a.\textsuperscript{18}

Although the approach we have outlined here should be useful for mechanistic studies, it was disappointing to find that reaction along path a was not observed in competition with that along path b. Despite many efforts to exclude traces of acid from both the substrate and the reaction vessel we cannot exclude the possibility that the rearrangement from 1 to 3 by path b is catalyzed by contaminants. Removing the influence of any contaminants, for example, by using a laser for multiphoton excitation,\textsuperscript{19} might permit us to observe the elusive $2a + 2a + 2a + 2a + 2a$ reaction. It is also possible that there exists no low-energy electrocyclic pathway, either because the conformation shown in Figure 1 is not energetically accessible or because additional geometric requirements exist for electrocyclic reactions that make and break only $\sigma$ bonds. One such requirement may be that the three atoms involved at any one reaction center must be collinear.\textsuperscript{20} Thus, the apparent difficulty in achieving such linearity in electrocyclic rearrangements involving only $\sigma$ bonds may account for their scarcity in organic chemistry. Interestingly, if we interpret the mode of rearrangement observed in terms of a rate-limiting heterolysis of the side C=O bond, molecular models suggest that there is an accessible conformation for the subsequent steps which, although not "concerted," permits each to proceed via a transition state having a linear arrangement of attacking oxygen, carbon, and leaving oxygen.

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\textsuperscript{(18)} Experimental uncertainty is a function of the signal/noise ratio of the spectra (about 40:1 in these experiments). The contribution of path a to the conversion from 1 to 3 is 0.3 ± 1.2%.
