

is in accord with our previous studies of the influence of polar substituents on the stereoselectivity of ozonide formation.⁹ Selected desilylation provided the corresponding alcohols, **5x** and **5n**, which were readily separable by chromatography on silica gel (31 and 1% yields, respectively, from **3**). Further derivatization of the alcohols, without disruption of the ozonide, proved to be relatively simple. Thus, the major epimeric (*exo*) alcohol **5x** was converted to the crystalline *p*-nitrobenzoate; X-ray diffraction fully confirmed the assigned structure and stereochemistry.⁸

To initiate rearrangement, a better leaving group was required.¹⁰ Thus, **5x** was converted to the sensitive trifluoromethanesulfonate ester (**2x**) under standard conditions.¹¹ Much to our delight, this triflate rearranged spontaneously during chromatography on silica gel. The product, eluted from the column along with unconsumed **2x**, was the enol ether **6**, resulting from ring expansion of the ozonide. The reaction could be run more conveniently by simply stirring the triflate **2x** in a slurry of dichloromethane and silica gel, resulting in a 65% yield of **6**. Unfortunately, this procedure was not totally satisfactory: the efficiency of the reaction proved to be particularly sensitive to the source of silica gel, even to the point where some brands of silica failed to promote the rearrangement at all. A search for better reaction conditions was well-rewarded by the finding that **2x** was smoothly converted to **6** simply by stirring at room temperature in CH₃CN buffered with NaHCO₃. In this way, the rearranged peroxide was obtained in up to 90% yield. The structure of **6** follows from spectroscopic data¹² and is supported by its conversion with ozone to the lactone endoperoxide **7**, a compound previously reported by Adam.¹³ The enol ether **6** is, not surprisingly, sensitive to acids and bases, but is not especially difficult to handle. Purification can be accomplished by chromatography and bulb-to-bulb distillation (40 °C/12 mm). Samples of **6** can be kept for months at -10 °C.

The ease of ionization/rearrangement of **2x** is striking and suggests that triflate loss is assisted by neighboring-group participation of the antiperiplanar peroxide group. Consistent with this interpretation, the epimeric *endo*-triflate **2n**, prepared from the minor alcohol ozonide **5n**, does not rearrange under these conditions. Indeed, when the diastereomeric mixture of alcohols is processed through the sulfonation/rearrangement sequence, the unchanged *endo*-triflate **2n** can be recovered efficiently after essentially complete conversion of the *exo* isomer to **6**.

These results establish the cationic ring expansion of ozonides as a viable route to 1,2,4-trioxanes. Further work, to explore the scope and limitations of this process, is in progress and will be reported in due course.

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Supplementary Material Available: ¹H and ¹³C NMR and IR spectral data for **2–5** and X-ray data including coordinates, bond

distances, bond angles, and torsion angles for the *p*-nitrobenzoate of **5x** (7 pages); observed and calculated structure factors for the *p*-nitrobenzoate of **5x** (7 pages). Ordering information is given on any current masthead page.

Isomerism in the Mo₂(μ-O₂CCF₃)₄/bpy Reaction System: Thermal and Photochemical Conversion of the Ion-Pair Complex [Mo₂(μ-O₂CCF₃)₂(bpy)₂](O₂CCF₃)₂ to the Unbridged Neutral Isomer Mo₂(η¹-O₂CCF₃)₄(bpy)₂

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The development of carboxylate chemistry is a central theme in transition-metal chemistry.³ Research in this area ranges from biological modeling applications⁴ to catalysis⁵ and materials chemistry.^{6–8} Our involvement in M₂(O₂CR)₄ chemistry stems from a desire to understand the factors that influence the binding of neutral N-donor chelates to systems with four relatively rigid bridging groups. Novel perturbations of the tetrabridged structures were found for products of bipyridine reactions with Cu₂(O₂CC-H₃)₄ and Rh₂(O₂CCH₃)₄.^{9,10} In the latter case, the 1:1 adduct, Rh₂(O₂CCH₃)₄(bpy), was found to exhibit an unsymmetrical structure containing a chelating acetate ligand.¹⁰ This paper describes the synthesis of two isomers obtained from reactions of a quadruply bonded dimolybdenum tetracarboxylate compound with bpy, along with the remarkable photochemical and thermal conversion of the bridged form to an unsupported structure.

Reaction of Mo₂(O₂CCF₃)₄ (0.20 g, 0.31 mmol) with 2,2'-bipyridine (0.097 g, 0.62 mmol) in CH₃CN (10 mL) at room temperature led to the rapid formation of red microcrystals. After reduction in volume, the solution yielded additional product, which was collected by filtration, washed with diethyl ether (3 × 5 mL), and dried in vacuo. The total yield of [Mo₂(O₂CCF₃)₂(bpy)₂][O₂CCF₃]₂ (**1**) was 0.252 g (85%).¹¹ Large X-ray quality crystals were grown by slow diffusion of a diethyl ether solution of bpy into a solution of Mo₂(O₂CCF₃)₄ in CH₃CN through a hexane interface layer.¹² An IR spectrum of the crystals revealed

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(11) Anal. Calcd for C₂₈H₁₆N₄F₁₂O₈Mo₂: C, 35.10; H, 1.67. Found: C, 34.89; H, 1.99.

(8) The equatorial methine proton (δ 3.58 ppm) of the *exo* isomer appears as a narrow multiplet ($w_{1/2} \sim 7.7$ Hz); the corresponding (axial) proton in the *endo* isomer appears as a doublet of doublets (δ 3.62 ppm, $J = 5.7, 10.2$ Hz). Spectral data for these compounds, as well as X-ray data for the *p*-nitrobenzoate of **5x**, is available as supplementary material.

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(12) 6-Methylene-2,3,5-trioxabicyclo[2.2.2]octane (**6**): ¹H NMR (CDCl₃, 300 MHz) δ 5.51 (dd, $J = 2.5, 4.9$ Hz, 1 H), 4.52 (m, 1 H), 4.37 (d, $J = 2.1$ Hz, 1 H), 4.12 (d, $J = 2.1$ Hz, 1 H), 2.47 (m, 1 H), 2.30 (m, 1 H), 2.17 (m, 1 H), 1.91 ppm (m, 1 H); ¹³C NMR (CDCl₃, 22.5 MHz, off-resonance decoupling multiplicities in parentheses) δ 155.5 (s), 96.5 (d), 85.5 (t), 74.0 (d), 25.0 (t), 23.7 ppm (t); IR (neat liquid film) ν 1669, 1090, 1053 cm⁻¹; MS m/e 128 (5), 57 (12), 55 (10), 44 (10), 43 (44), 42 (100). Anal. Calcd for C₆H₈O₃: C, 56.25; H, 6.29. Found: C, 55.85; H, 6.13.

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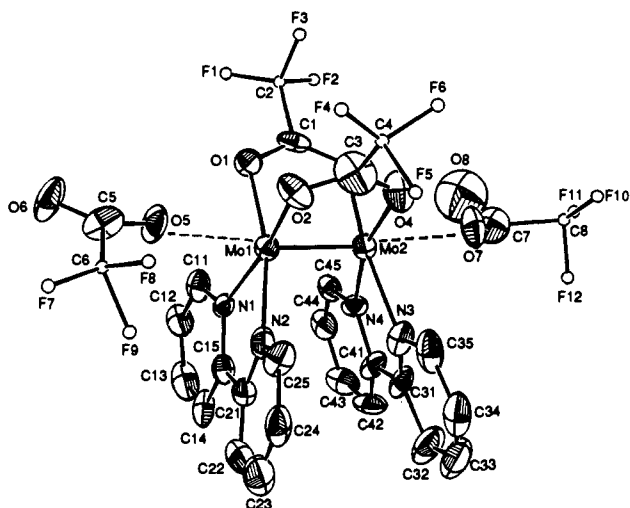


Figure 1. Selected bond distances (Å) and angles (deg) for **1**: Mo1–Mo2, 2.181 (2); Mo1–O1, 2.119 (8); Mo2–O7, 2.472 (9); Mo1–N1, 2.13 (1); C1–C2, 1.55 (2); C1–O1, 1.19 (1); C2–F1, 1.26 (2); N1–Mo1–N2, 76.0 (4); N1–Mo1–Mo2, 100.6 (2); O1–Mo1–Mo2, 90.8 (2); O1–Mo1–O2, 88.0 (3); N1–Mo1–O1, 96.2 (3); Mo1–Mo2–O7, 169.0 (3).

absorptions arising from coordinated CF_3COO^- and bpy as well as ionic CF_3COO^- .¹³

An ORTEP plot of the compound is shown in Figure 1. Salient features are the presence of two equatorially bound bpy chelates on the same side of the molecule and two CF_3COO^- anions which occupy axial positions of the Mo_2 cation unit through weak ion-pair interactions (average Mo–O(ax) = 2.472 (8) Å).¹⁴ The effect of removing two bridging carboxylates and replacing them with nitrogen donor chelates is to weaken the bonding between the Mo atoms (Mo1–Mo2 = 2.181 (2) Å), as was found for the cations in $[\text{Mo}_2(\text{O}_2\text{CCH}_3)_2(\text{NCCCH}_3)_4](\text{BF}_4)_2$ (2.136 (1) Å).¹⁵ Axial interactions are also expected to be contributing to the M–M bond lengthening in these cases.¹⁶ For example, the Mo–Mo bond distance in $\text{Mo}_2(\text{O}_2\text{CCF}_3)_4$ is 2.090 (4) Å,¹⁷ whereas the corresponding distance in $\text{Mo}_2(\text{O}_2\text{CCF}_3)_4(\text{py})_2$ is 2.129 (1) Å.¹⁸

Variable-temperature ^1H NMR spectroscopic studies of **1** in d^6 -acetone and CD_3CN indicate solvent- and temperature-dependent behavior. At +50 °C in d^6 -acetone, the spectrum displays four sets of resonances due to magnetically equivalent environ-

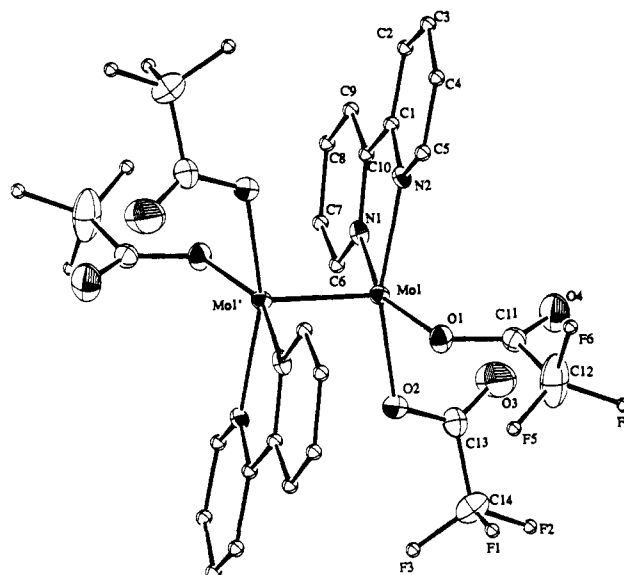


Figure 2. Selected bond distances (Å) and angles (deg) for **2**: Mo1–Mo1', 2.077 (1); Mo1–O1, 2.108 (4); Mo1–N1, 2.175 (5); C11–C12, 1.505 (9); C11–O4, 1.212 (7); C14–F1, 1.316 (9); Mo1–Mo1'–O1, 100.1 (1); Mo1–Mo1'–N1, 99.2 (1); N1–Mo1–N2, 72.7 (2); O1–Mo1–O2, 82.0 (2); N2–Mo1–O1, 97.3 (2); N1–Mo1–O1, 159.2 (2); Mo1–O1–C11, 114.1 (4).

ments for all $\text{C}_5\text{H}_4\text{N}$ rings on the two bpy ligands (δ , ppm: d, 8.70; d, 8.51; t, 7.98; t, 7.47). At 25 °C and below, the signals broaden and reappear as separate sets of resonances due to at least three different compounds. This behavior is consistent with the presence of several isomers in equilibrium.¹⁹ A ^{19}F NMR spectrum of **1** at 25 °C exhibits a broad resonance at $\delta = -74$ ppm and a sharper signal at -77.4 ppm. The signal becomes more complicated at low temperatures, with a series of resonances appearing between -72 and -78 ppm. Electrochemical studies performed in CH_3CN revealed an irreversible reduction at $E_{pc} = -1.1$ V vs Ag/AgCl.

The solvent dependence of the reaction was verified by the isolation of a second isomer from a less polar solvent. Crystals of $\text{Mo}_2(\eta^1\text{-O}_2\text{CCF}_3)_4(\text{bpy})_2 \cdot 2(\text{CH}_3)_2\text{CO}$ (**2**) were grown at -78 °C by layering a solution of $\text{Mo}_2(\text{O}_2\text{CCF}_3)_4$ (0.20 g, 0.31 mmol) dissolved in 3 mL of acetone with 2 equiv of bpy (0.095 g, 0.61 mmol) in 5 mL of hexane; yield: 0.250 g, 87%.¹² The infrared spectrum of **2** indicated the presence of coordinated bpy and trifluoroacetate but no bands attributable to ionic CF_3COO^- .²⁰ The X-ray structure of **2** revealed bpy ligands in an anti arrangement and, surprisingly, four monodentate trifluoroacetate groups (Figure 2). This result is unprecedented in quadruply bonded carboxylate chemistry, to our knowledge. Of importance to note in this unbridged molecule is the short Mo–Mo bond (2.077 (1) Å) as compared to the corresponding distance in isomer **1** or most other Mo_2^{4+} complexes containing bridging groups.¹⁶ In fact, molecule **2** possesses the shortest unsupported Mo–Mo quadruple bond reported to date.

$\text{Mo}_2(\eta^1\text{-O}_2\text{CCF}_3)_4(\text{bpy})_2$ was also synthesized by irradiating an CH_3CN solution of **1** at $\lambda \geq 499$ nm for 1 h, during which time the color noticeably changed from dark red to red-purple.

(12) Crystal data for **1**: $M = 956.32$, monoclinic, $P2_1/n$, $a = 17.26$ (1) Å, $b = 10.02$ (1) Å, $c = 20.06$ (2) Å, $\beta = 99.73$ (7)°, $V = 3422$ (6) Å³, $Z = 4$, D_{calc} = 1.856 g cm⁻³, $T = -80$ °C, $4^\circ \leq 2\theta \leq 45^\circ$ and 4411 unique reflections. The structure was collected on a Nicolet P3/F diffractometer with a Mo source and solved by SHELX86. Non-hydrogen atoms were located by difference Fourier syntheses and refined by using full-matrix least-squares programs in the SDP package. The final cycle converged with a shift/esd of 0.68 for 408 parameters and 2738 data with $F_o^2 > 3\sigma(F_o^2)$ to give R (R_w) = 8.7 (10.9). The highest peak in the final difference map was 1.6 e⁻/Å³ and is the ghost of a F atom. Crystal data for **2**: $M = 1072.32$, triclinic, $P\bar{1}$, $a = 8.851$ (2) Å, $b = 11.549$ (3) Å, $c = 11.841$ (3) Å, $\alpha = 65.75$ (2)°, $\beta = 69.40$ (2)°, $\gamma = 74.71$ (2)°, $V = 996.4$ (4) Å³, $Z = 1$, D_{calc} = 1.4062 g cm⁻³, $T = -78$ °C, $4^\circ \leq 2\theta \leq 116^\circ$ and 2960 unique reflections. Data were collected using Cu radiation on a P3/F diffractometer upgraded to a P3/V and solved by the solution and least-squares programs from the TEXSAN software package. A total of 2524 data with $F_o^2 > 3\sigma(F_o^2)$ were used to refine 280 variables to give residuals of R (R_w) = 4.5 (3.6). The quality-of-fit was 3.93 and the final shift/esd = 0.24.

(13) Selected infrared absorptions for a KBr pellet of **1** (cm⁻¹): OCOCF_3^- , 1690 s; $\mu\text{-CF}_3\text{COO}$ and bpy, 1600 br; bpy, 1495 w, 1470 w, 1445 m, 1230 sh, 1200 s; OCOCF_3^- , $\mu\text{-CF}_3\text{COO}$, and bpy, 860 w, 825 w, 800 w, 765 m, 730 m, 720 w.

(14) A complex with strong axial CF_3COO^- interactions is $\text{Pd}_2(\text{dppm})_2(\text{OCOCF}_3)_2$, for which Pd–O(axial) is 2.191 (12) Å. Krafft, T. E.; Hejna, C. I.; Smith, J. S. *Inorg. Chem.* **1990**, *29*, 2682.

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(20) Selected infrared absorptions for a Nujol mull of **2** between CsI plates (cm⁻¹): CF_3COO^- , 1700 s; CF_3COO^- and bpy, 1605 m; bpy, 1450 s, 1420 s; C–F, 1190 s, 1140 s; CF_3COO^- and bpy, 845 m, 840 m, 785 m, 770 s, 725 s, 720 s.

Large crystals of **2** slowly appeared over the period of several days after irradiation. The product was harvested in 50% yield and characterized by infrared spectroscopy as well as by a single-crystal X-ray study. This observation is consistent with excitation of the $\delta \rightarrow \delta^*$ transition for an unbridged solution isomer of **1** with subsequent rotation about the Mo-Mo bond to give **2**. For samples of **1** in CH_3CN , the $\delta \rightarrow \delta^*$ transition occurs as a broad feature at $\lambda = 520$ nm. Presumably the concentration of unbridged isomers of **1** can be increased by photochemical or thermal dissociation of Mo-O bridge bonds, and indeed, solutions of **1** in acetone or CH_3CN that have been subjected to light from an intense white light source or heated to reflux also yield large quantities of isomer **2**. Acetonitrile solutions of **1** stored in the dark give only trace quantities of **2** upon workup. These findings point to a subtle difference in energies between two isomeric forms of $\text{Mo}_2(\text{O}_2\text{CCF}_3)_4(\text{bpy})_2$ with preference for the neutral complex occurring in less polar solvents and under conditions that increase the likelihood of forming unbridged isomers. The high-temperature isomerization of **1** to **2** suggests that the unsupported structure is actually more thermodynamically stable than the cis-trifluoroacetate-bridged structure. Although this conclusion may appear to be counterintuitive, it is not unreasonable if one compares the bonding interactions in the two structures. Molecule **2** possesses a much shorter Mo-Mo bond and stronger Mo-O interactions than **1**. Additional work on this intriguing system is in progress.

Acknowledgment. We are grateful to the National Science Foundation for instrumentation grants (X-ray CHE-8908088 and NMR CHE-8800770) and grants to K.R.D. (CHE-8914915) and G.C. (CHE-8808019). We also thank Professor D. G. Nocera and Carolyn Hsu for use of the photochemical equipment and Steven C. Haefner for helpful discussions.

Supplementary Material Available: Tables and summaries of X-ray data, positional parameters, bond distances, bond angles, and thermal parameters for **1** and **2** (18 pages); tables of observed and calculated structure factors for **1** and **2** (45 pages). Ordering information is given on any current masthead page.

New Mechanistic and Stereochemical Insights on the Biosynthesis of Sterols from 2,3-Oxidosqualene

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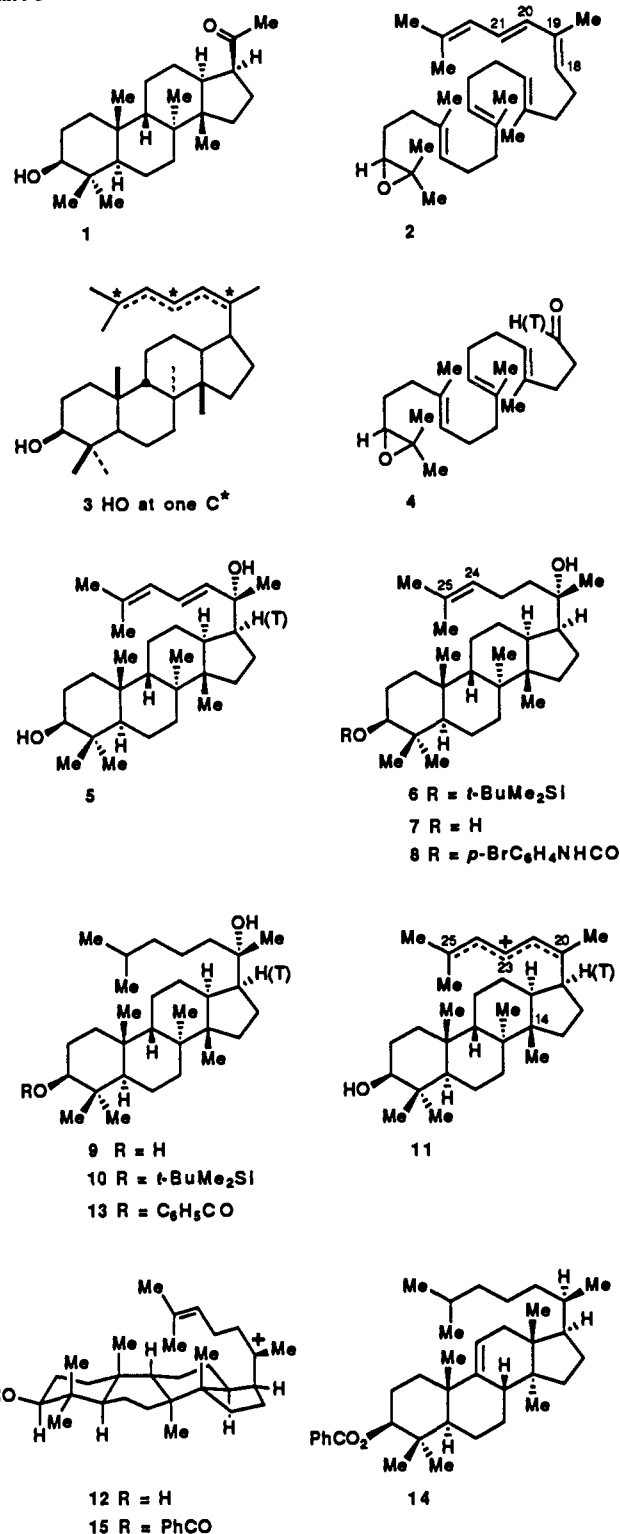
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The enzymic cyclization of 2,3-oxidosqualene to lanosterol is of great interest from both chemical and biochemical perspectives. The recent demonstration that the 20-oxa analogue of 2,3-oxidosqualene is converted by the cyclase from yeast to the 17β -acetyl sterol **1**¹ has provided new information on the stereochemical course of the cyclization and has suggested a more detailed analysis of the previously reported bioconversion of (20*E*)-20,21-dehydro-2,3-oxidosqualene (**2**) to a protosterol of gross structure **3**² (Chart I). We report herein on the complete structure of **3** and its bearing on the detailed mechanism of action of the cyclase.

Tritiated (\pm)-**2** was synthesized from epoxy aldehyde **4**¹ by Wittig coupling² (7:3 mixture of 18*E* and 18*Z* isomers, separable by HPLC). Biosynthetic experiments were carried out using sterol-free microsomal enzyme of *Saccharomyces cerevisiae* (yeast) which had been purified by successive chromatography on DEAE and hydroxylapatite columns.³ The structures of **2** (more polar

Chart I



isomer) and the less polar 18*Z* isomer were clear from ¹H NMR NOEDIFF measurements at 500 MHz. Whereas the 18*Z* isomer of **2** was not transformed into sterol by the cyclase, **2** was converted in ca. 30% yield (HPLC analysis) to a protostanediol, which was demonstrated to be **5** by 500-MHz ¹H NMR analysis and comparison with synthetic compounds as described below.⁴ Incubation of **2** with a cyclase-containing homogenate of porcine liver² at 23

(3) Corey, E. J.; Matsuda, S. P. *J. Am. Chem. Soc.*, preceding paper in this issue.

(4) Preparative-scale enzymic experiments were performed using sterol-free enzyme from yeast at 23 °C for 24 h. After chromatographic purification, pure **5** was isolated in 17% yield.

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