hexane. This solution was chromatographed on 5 g of silica gel eluting with benzene–hexane–formic acid (50:50:1). The first band (11 mg) was dihydrouliginosin B, identified by chromatographic and spectroscopic comparison with authentic material. The second band (10.5 mg) was obtained as an amorphous powder when a methanol solution was taken to dryness *in vacuo*. Recrystallization from hexane–ethyl acetate gave material which melted at 156.0–158.5°.

Anal. Calcd for $C_{28}H_{36}O_8$: C, 67.18; H, 7.25. Found: C, 67.12; H, 7.23.

Nmr spectrum: 1.20, 1.22 (overlapping doublets, $J = 6.7$ cps); 1.50 (singlet); 1.54 (singlet); 1.86 (triplet, $J = 6.2$ cps); 2.62 (triplet, $J = 6.5$ cps); 3.48 (singlet, 2 H); 4.10 (septuplet, $J = 6.9$ cps, 2 H); 9.30 (singlet); 11.02 (singlet); 14.05 (singlet); 18.80 (singlet).

λ_{max} (ϵ) (cyclohexane): 231 (24,600) and 283 mμ (19,500).

ν_{max} (carbon tetrachloride): 3198 (broad), 2723 (w, broad), 2660 (w, broad), 2973 (s), 2930 (s), 2868 (w), 1640 (s), 1603 (vs), 1483 (m), 1422 (s), 1379 (m), 1348 (m), 1282 (m), 1259 (m), 1237 (m), 1190 (m), 1155 (m), 1137 (m), and 1113 (m) cm^{-1}.

Bromouliginosin B. Uliginosin B (48.7 mg, 0.0978 mmol) was dissolved in 1 ml of carbon tetrachloride. The solution was cooled to 0° and 0.96 ml of a 0.102 *M* solution of bromine in carbon tetrachloride (0.098 mmol of bromine) was added. The solvent was immediately removed *in vacuo* to give a pale yellow, noncrystalline residue. A solution of this material in 2 ml of pyridine was heated at 100° for 1 hr. The pyridine was neutralized with excess 10% sulfuric acid, and the product was extracted from this mixture with dichloromethane. Removal of the solvent gave 59.3 mg of a dark orange gum which was chromatographed on silica gel. Benzene rapidly eluted 38.7 mg of a pale yellow material. After several recrystallizations from acetonitrile, this material melted at 155.0–158.0° and had a density (by density gradient) of 1.377 g/cm^2.

Anal. Calcd for $C_{28}H_{33}BrO_8$: C, 58.23; H, 5.76; Br, 13.84. Found: C, 58.57; H, 5.91; Br, 13.84.

λ_{max} (ϵ): 234 (27,000) and 290 mμ (34,000).

ν_{max}: 3170 (broad), 2979 (s), 2933 (m), 2868 (w), 2637 (w), 1642 (vs), 1605 (vs), 1479 (m), 1433 (w), 1387 (s), 1367 (m), 1275 (s), 1193 (s), 1126 (s), 1039 (w), and 928 (w) cm^{-1}.

Nmr spectrum: 1.20 (doublet, $J = 6.5$ cps, 12 H), 1.35 (weak), 1.51 (slightly broad singlet, 6 H), 1.62 (sharp singlet, 6 H), 3.50 (broad singlet, 2 H), 4.0 (complex multiplet, 2 H), 7.04 (singlet, 1 H), 9.89 (singlet, 1 H), 11.47 (singlet, 1 H), 16.39 (singlet, 1 H), 18.90 (singlet, 1 H).

Acknowledgment. We thank Drs. L. Shadoff, J. P. Heeschen, T. W. Shannon, and W. J. Potts for determining and discussing spectra of uliginosins A and B and their derivatives. Drs. R. M. Brooker and H. L. Taylor kindly supplied us with uliginosins A and B.

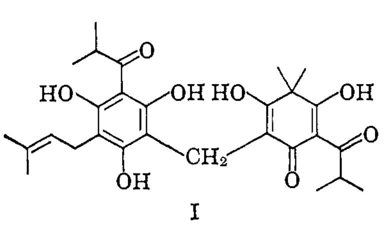
The Structure Determination of Antibiotic Compounds from *Hypericum uliginosum*. II.[1] The Molecular and Crystal Structure of Bromouliginosin B

William L. Parker, J. J. Flynn, and F. P. Boer

Contribution from the Dow Chemical Company, Eastern Research Laboratory, Wayland, Massachusetts 01778. Received February 26, 1968

Abstract: The crystal and molecular structure of bromouliginosin B, $C_{28}H_{33}BrO_8$, a derivative of an antibiotic from *Hypericum uliginosum*, has been determined by a single-crystal, three-dimensional X-ray diffraction study. The compound crystallizes in the centrosymmetric space group $P\bar{1}$, and there are two molecules in each triclinic unit cell of dimensions $a = 10.44$, $b = 10.79$, $c = 13.37$ Å; $\alpha = 103° 37'$, $\beta = 99° 11'$, and $\gamma = 102° 44'$. The intensity data were obtained on a Picker automatic diffractometer and the structure was solved by the heavy atom method. Least-squares refinement including anisotropic thermal motion converged to a discrepancy index $R = 10.6\%$. The structure consists of filicinic acid and phloroglucinol moieties linked by a methylene bridge and held in a rigid conformation by two hydrogen bonds. Two other hydrogen bonds with unusually short oxygen–oxygen distances occur in the molecule, and these correlate with very low nmr chemical shifts for the chelated protons.

Uliginosins A (I) and B (IIa) are antibiotics isolated from *Hypericum uliginosum*, a woody herb found in Mexico and Central America. The detailed structure is reported here as determined for a suitable heavy atom derivative by single-crystal X-ray diffraction methods. This investigation was undertaken concurrently with the chemical studies[1] for several reasons. First, we wished to support the logic leading to postulated structures for uliginosins A and B based on the available spectroscopic and chemical evidence. An X-ray study appeared to be less time consuming and more rewarding than confirmation of the structure by traditional degradative methods. Synthesis also appeared to be a less attractive route to proof of structure because of published work on the synthesis of fern constituents that are closely related chemically to these compounds.[2,3] A second reason for undertaking the



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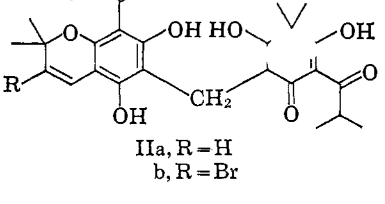

IIa, R = H
b, R = Br

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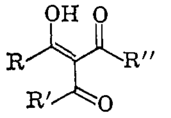
[1] Paper I: W. L. Parker and F. Johnson, *J. Am. Chem. Soc.*, **90**, 4716 (1968).

X-ray analysis was the opportunity that it provided to correlate a substantial body of interesting spectroscopic data with detailed features of molecular structure which are unavailable from degradative or synthetic studies.

In particular, we were interested in the detailed structure of the portions of the molecule around the two chelated protons in uliginosin compounds which give rise to extremely low-field absorption in their nmr spectra. The lowest absorption in uliginosin B (18.79 ppm downfield from tetramethylsilane) is characteristic of an enolized β-triketone structure,[4] III, which occurs in a variety of natural products.[5]



III

To the best of our knowledge, this type of structure has not previously been examined by X-ray diffraction methods. The other very low field absorption (16.42 ppm) in uliginosin B has been assigned[1] to an *o*-hydroxyphenone structure. Because the observed chemical shift is nearly 2.5 ppm lower than the value expected for a proton in this environment,[6] the interatomic distances and angles in this part of the molecule are of special interest. These values will also reflect the importance of various resonance structures involving conjugated double bonds and hydrogen bonds. A suitable heavy atom derivative, bromouliginosin B (IIb), was prepared by treatment of uliginosin B with bromine followed by dehydrohalogenation in pyridine.[1]

Experimental Section

Prior to our detailed X-ray investigation of bromouliginosin B, a number of preliminary precession photographs of the parent material, uliginosin B, were obtained using Cu Kα radiation. The crystals grew as very thin platelets, with their short dimension corresponding to the *c* axis of the monoclinic cell (of dimensions a = 10.53, b = 9.03, c = 27.66 Å, and β = 96° 40′). The calculated density of 1.268 g cm^{-3} assuming a molecular weight of 498.60 and four molecules per unit cell agreed reasonably with the experimental value of 1.24 obtained by the density gradient technique. The extinction of 0k0 reflections for k odd, and h0l for $h + l$ odd established the centrosymmetric space group P2$_1$/n. Regrettably, this material was not a good candidate for a complete structure determination because of the presence of planes of weak reflections in the reciprocal lattice at intervals of $c^*/3$. The intensities of the reflections also dropped off quite rapidly with increased values of 2θ. The relative intensities of the reflections due to the superlattice varied considerably from crystal to crystal, but since all crystals examined gave relatively poor quality diffraction patterns we shifted our attention to the bromo derivative.

A number of pale yellow crystals of bromouliginosin B were carefully grown from acetonitrile. The most suitable of these, in the form of an irregular platelet approximately 0.15 × 0.20 × 0.06 mm in size, was carefully centered on a Picker automatic four-circle diffractometer. Lattice constants were obtained by a least-squares refinement of the setting angles of ten reflections with Cu Kα radiation (λ 1.5418 Å). The parameters of the reduced triclinic cell (space group P1 or P$\bar{1}$), a = 10.438 ± 0.012, b = 10.792 ± 0.014, c = 13.367 ± 0.017 Å, α = 103° 37′ ± 3′, β = 99° 11′ ± 3′, and γ = 102° 44′ ± 3′, give a calculated density for $C_{28}H_{33}BrO_8$ of 1.378 g cm^{-3} with two molecules per unit cell. The experimental density as measured by the density-gradient technique using potassium tartrate and potassium sodium tartrate solutions (calibrated with binary solutions of bromo- and chlorobenzene) was 1.377 ± 0.002 g cm^{-3}.

The intensity data were collected using the 2θ scan mode of the diffractometer with Ni-filtered Cu Kα radiation. The take-off angle of the tube was 3°, and a counter aperture, 4.0 × 4.0 mm was placed 30 cm from the crystal. Scan angles of 1.94 to 2.74° were found to be sufficient for all reflections over the range (0 to 108°) of 2θ examined. The scan speed was 2°/min. Two stationary-crystal–stationary-counter background counts of 15 sec were taken at each end of the scan.

Two different sets of intensity data were collected to guard against the effects of instrument malfunctions when the diffractometer was running unattended. A total of 2010 independent reflections were measured. The net intensity, $I = N_0 - KN_b$, for each reflection was assigned an error

$$\sigma(I) = [(0.05I)^2 + N_0 + K^2N_b]^{1/2}$$

where N_0 was the gross count, N_b the background count, and K the ratio of scan time to background time. These σ's were used to calculate the weights $w(F) = 4F^2/\sigma^2(F^2)$ for the least-squares refinement,[7] where the quantity $\Sigma w(|F_o| - |F_c|)^2$ was minimized. To avoid biasing the data set with a large number of low-intensity reflections of questionable reproducibility, data for which $\sigma(I)/I >$ 0.25 were regarded as absent reflections and omitted from the refinement. The intensities were then corrected for Lorentz and polarization effects and the two data sets were merged. Thirty-five reflections, suspected to be erroneous because of instrument malfunctions and not common to both data sets, were later rejected, leaving a final data set of 1584 reflections. No absorption corrections were made, but the linear absorption coefficient μ = 26.2 cm^{-1} suggests that transmission factors range between 0.6 and 0.9. The reliability factors, R_1 and R_2, used in least-squares refinement, are given by $\Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $(\Sigma w(|F_o| - |F_c|)^2/\Sigma wF_o^2)^{1/2}$, respectively. The crystallographic computer programs OR-FLS, ERFR-2, OR-FFE, and OR-TEP[8] were used for processing the data.

Structure Determination and Refinement

The structure of bromouliginosin B was determined by a relatively straightforward application of the heavy-atom method. A three-dimensional electron density map was calculated based on the phases of the bromine atom, which had previously been located from the normal-sharpened Patterson function. Of the 40 highest peaks in the map, 37 gave chemically reasonable coordinates for atoms of bromouliginosin B. Several cycles of refinement of the atomic coordinates and isotropic thermal parameters of these atoms reduced R_1 from an initial value of 0.45 to 0.19, but unusually high thermal parameters were obtained for C(20) and C(21). An electron density map calculated at this time also revealed considerable residual density in the region of these atoms. Therefore, a second electron density map was calculated based on 34 atoms, but omitting C(20), C(21), and C(35). The last of these atoms was under suspicion because of its rather long C–C bond distance. While C(35) appeared in the map at its previous position, a study of the electron density in the region of C(19) indicated that a rotationally disordered isopropyl group could be the source of our difficulty. Continued

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(2) W. Ried and R. Mitteldorf, *Chem. Ber.*, **89**, 2595 (1956).

(3) A. Penttilä and J. Sundman, *Acta Chem. Scand.*, **18**, 344 (1964).

(4) S. Forsén, F. Merenyi, and M. Nilsson, *ibid.*, **18**, 1208 (1964).

(5) C. H. Hassall, *Progr. Org. Chem.*, **4**, 115 (1958).

(6) S. Forsén, N. Nilsson, and C. A. Wachtmeister, *Acta Chem. Scand.*, **16**, 583 (1962).

(7) Atomic scattering factors for carbon, oxygen, and bromine and real and imaginary dispersion corrections for the scattering of Cu Kα radiation by bromine were obtained from "International Tables for X-Ray Crystallography," Vol. 3, The Kynoch Press, Birmingham, England, 1962, Tables 3.3.1A and 3.3.2B.

(8) OR-FLS, by W. R. Busing, K. O. Martin, and H. A. Levy, is a FORTRAN program for structure factor calculations and full-matrix, least-squares refinement of positional and thermal parameters. ERFR-2, by W. G. Sly, D. P. Shoemaker, and J. H. van der Hende, is a two- and three-dimensional Fourier program. OR-FEE, by W. R. Busing, K. O. Martin, and H. A. Levy, is a FORTRAN crystallographic function and error program. OR-TEP is a FORTRAN thermal-ellipsoid plot program for crystal structure illustrations by C. K. Johnson, Oak Ridge National Laboratory Report ORNL 3794, Revised, Oak Ridge, Tenn., June 1965.

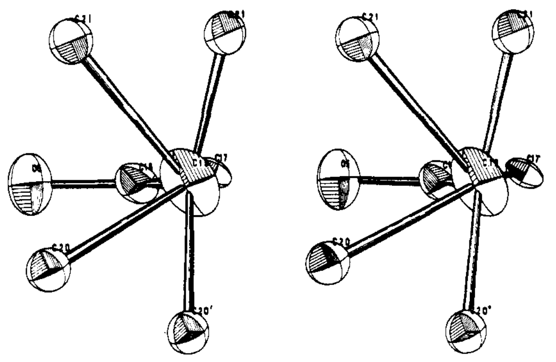

Figure 1. Rotationally disordered isopropyl group.

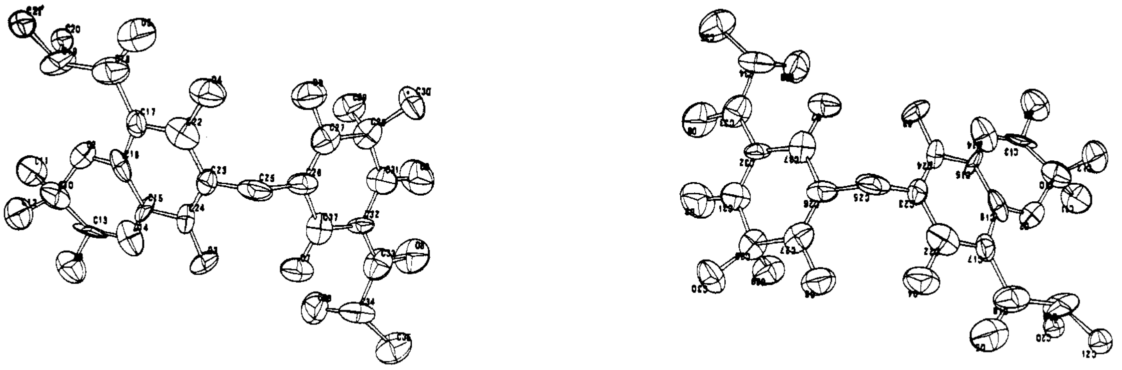

Figure 2. Bromouliginosin B showing ellipsoids of thermal motion.

refinement was successfully carried out assuming the presence of two rotamers, with relative weights 0.55 for C(20′) and C(21′) and 0.45 for C(20) and C(21) estimated from the peak heights in the electron density map. The fully refined disordered group is shown in Figure 1, in which the methyl groups are represented by spheres of radius 0.2 Å and the other atoms are represented by their anisotropic thermal ellipsoids. The dihedral angle between the two rotamers is 57 ± 4°. Evidence that this disordered model is essentially correct is given by the calculated angles C(20)–C(19)–C(21) = 111° and C(20′)–C(19)–C(21′) = 115°, which are quite reasonable. Two more cycles of isotropic refinement then reduced R_1 to 0.15 and R_2 to 0.19. In subsequent cycles of refinement, anisotropic thermal parameters were assumed for all 39 "atoms." Since the total number of parameters (352) exceeded the limits of our least-squares program (200), the refinement was carried out in blocks, defined by the two "halves" of the molecule on either side of the bridging methylene carbon, C(25). The resultant discrepancy indices were R_1 = 0.107 and R_2 = 0.138. In the final cycle of refinement, all 117 atomic coordinates were allowed to vary simultaneously, thus defining a full variance–covariance matrix for all positional parameters. The mean shift of atomic coordinates in the final cycle was 0.08σ, and the final values of R_1 and R_2 were 0.106 and 0.138, respectively.

A final electron density map, from which the 39 input atoms had been subtracted, yielded no residual peaks of height greater than 1.0 eÅ^{-3}. Several peaks may have corresponded to hydrogen atoms, but these were not sufficiently above the noise level to warrant refinement. Some of the regions of the map where hydrogen atoms might be expected on chemical grounds showed no significant density. The region of the map near the isopropyl group C(34)–C(35)–C(36) was examined carefully for the possible presence of a butyl group corresponding to a homologous impurity. While a number of peaks at the noise level were observed, efforts to rationalize them in terms of a chemically meaningful model were fruitless.

Observed and calculated structure factors have been published.[9] Table I lists the final atomic parameters and their standard deviations. The root mean square components of thermal displacement along the principal axes, as defined by the anisotropic thermal parameters, are compiled in Table II. The directions of thermal motion may be inferred from Figure 2 in which the three-dimensional structure of the molecule is shown using ellipsoids to represent the anisotropic thermal motion.

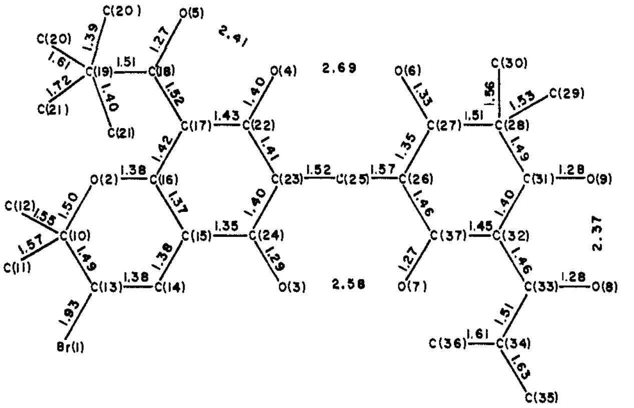

Figure 3. Interatomic distances (Å) in bromouliginosin B.

Discussion of the Structure of Bromouliginosin B

A compendium of important intramolecular bond distances, along with their standard deviations calculated from the least-squares, variance–covariance matrix, is presented in part A of Table III and in Figure 3. The filicinic acid and phloroglucinol parts of the

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[9] As Table I which has been deposited as Document No. 9866 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington, D. C. 20540. A copy may be secured by citing the document number and by remitting $1.25 for photprints, or $1.25 for 35-mm microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.

Table I. Final Structure Parameters[a,b]

Atom	x/a	y/b	z/c	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br(1)	−0.0178 (3)	0.5818 (3)	−0.2361 (2)	195	225	87	91	34	71
O(2)	0.1662 (12)	0.3757 (11)	−0.0620 (9)	149	92	82	50	31	16
O(3)	0.3124 (13)	0.8169 (11)	0.1448 (9)	235	63	95	81	42	27
O(4)	0.4349 (12)	0.4859 (12)	0.2876 (10)	157	158	104	75	37	73
O(5)	0.3625 (16)	0.2593 (14)	0.1797 (11)	286	162	130	96	33	53
O(6)	0.4038 (13)	0.6191 (12)	0.4751 (8)	183	121	110	70	46	53
O(7)	0.3603 (13)	0.9702 (12)	0.3342 (9)	231	119	100	65	46	65
O(8)	0.1813 (15)	1.1228 (14)	0.5753 (11)	253	171	151	129	123	36
O(9)	0.2040 (15)	0.9403 (15)	0.6394 (11)	251	247	112	103	105	68
C(10)	0.1378 (19)	0.4193 (20)	−0.1601 (13)	157	174	52	53	−7	54
C(11)	0.0229 (22)	0.2949 (20)	−0.2300 (14)	231	120	66	−47	−42	−59
C(12)	0.2681 (20)	0.4374 (20)	−0.2026 (16)	176	159	129	60	108	46
C(13)	0.0983 (20)	0.5443 (20)	−0.1264 (16)	210	177	133	121	100	147
C(14)	0.1574 (20)	0.6331 (23)	−0.0288 (15)	146	233	63	61	26	41
C(15)	0.2430 (15)	0.6031 (15)	0.0456 (11)	106	60	54	71	9	−4
C(16)	0.2412 (15)	0.4722 (19)	0.0278 (12)	57	197	38	61	27	36
C(17)	0.3034 (16)	0.4199 (16)	0.1048 (13)	119	86	50	7	43	8
C(18)	0.3120 (19)	0.2790 (19)	0.0942 (17)	138	107	129	15	40	60
C(19)	0.2738 (24)	0.1780 (17)	−0.0122 (16)	266	23	117	−13	27	15
C(20)	0.2446 (74)	0.0407 (51)	0.0196 (55)	404	103	301	123	201	89
C(20′)	0.1498 (50)	0.0892 (54)	−0.0235 (41)	233	248	195	15	91	41
C(21)	0.3725 (90)	0.1844 (74)	−0.0723 (60)	504	333	238	−4	251	90
C(21′)	0.4081 (84)	0.1093 (75)	−0.0125 (51)	646	413	240	401	112	46
C(22)	0.3702 (16)	0.5195 (20)	0.2021 (14)	68	187	95	62	38	69
C(23)	0.3778 (16)	0.6554 (16)	0.2184 (12)	114	86	50	50	32	12
C(24)	0.3104 (16)	0.6949 (17)	0.1373 (12)	100	97	37	38	15	−6
C(25)	0.4699 (17)	0.7510 (17)	0.3202 (14)	140	111	101	42	69	78
C(26)	0.3886 (16)	0.7939 (16)	0.4049 (13)	99	86	78	27	3	43
C(27)	0.3645 (16)	0.7290 (17)	0.4775 (14)	86	103	84	15	2	19
C(28)	0.2900 (15)	0.7688 (16)	0.5628 (13)	87	114	91	13	81	26
C(29)	0.1545 (18)	0.6654 (19)	0.5372 (15)	126	137	117	24	59	50
C(30)	0.3755 (20)	0.7759 (20)	0.6719 (13)	186	179	49	41	2	35
C(31)	0.2534 (18)	0.8949 (18)	0.5617 (14)	147	142	93	78	66	49
C(32)	0.2789 (15)	0.9656 (15)	0.4880 (12)	96	58	73	11	35	38
C(33)	0.2308 (18)	1.0841 (19)	0.4955 (14)	133	129	102	70	22	17
C(34)	0.2432 (18)	1.1661 (19)	0.4183 (16)	126	134	126	20	29	88
C(35)	0.2282 (21)	1.3131 (20)	0.4727 (17)	198	120	165	86	58	37
C(36)	0.1234 (23)	1.0927 (20)	0.3152 (15)	237	147	95	78	27	18
C(37)	0.3424 (15)	0.9119 (17)	0.4050 (13)	69	125	69	26	10	13

[a] Values in parentheses are the standard deviations multiplied by 10^4. [b] The anisotropic thermal parameters are defined by $T = \exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}kh + 2\beta_{13}hl + 2\beta_{23}kl)]$ and have been multiplied by 10^4. The values have two significant figures.

Table II. Root-Mean-Square Amplitudes of Vibration (Å)[a]

Atom	Axis 1	Axis 2	Axis 3	Atom	Axis 1	Axis 2	Axis 3
Br(1)	0.241	0.298	0.368	C(20′)	0.297	0.362	0.441
O(2)	0.200	0.265	0.275	C(21)	0.236	0.426	0.605
O(3)	0.137	0.276	0.344	C(21′)	0.265	0.458	0.629
O(4)	0.210	0.271	0.322	C(22)	0.155	0.238	0.324
O(5)	0.260	0.327	0.385	C(23)	0.160	0.218	0.249
O(6)	0.218	0.280	0.317	C(24)	0.150	0.218	0.256
O(7)	0.194	0.293	0.340	C(25)	0.139	0.243	0.321
O(8)	0.179	0.328	0.407	C(26)	0.170	0.221	0.274
O(9)	0.222	0.335	0.388	C(27)	0.200	0.239	0.276
C(10)	0.152	0.299	0.306	C(28)	0.076	0.245	0.320
C(11)	0.183	0.280	0.401	C(29)	0.206	0.276	0.319
C(12)	0.186	0.284	0.371	C(30)	0.185	0.303	0.323
C(13)	0.073	0.257	0.407	C(31)	0.196	0.245	0.316
C(14)	0.221	0.265	0.348	C(32)	0.133	0.220	0.252
C(15)	0.069	0.206	0.277	C(33)	0.205	0.273	0.312
C(16)	0.121	0.176	0.320	C(34)	0.185	0.257	0.346
C(17)	0.163	0.203	0.282	C(35)	0.208	0.318	0.371
C(18)	0.198	0.277	0.326	C(36)	0.251	0.292	0.352
C(19)	0.103	0.314	0.387	C(37)	0.185	0.232	0.272
C(20)	0.189	0.347	0.541				

[a] Ordered on increasing magnitude.

molecule are linked together by the methylene carbon C(25) such that their planes form a dihedral angle[10] of about 59°. The molecules are held rigidly in this open-book conformation by the O(3)–O(7) and O(4)–O(6) hydrogen bonds. This general description of the molecular conformation accords well with the temperature dependence of the methyl resonances in the nmr spectrum of dihydrouliginosin B as discussed in the paper[1] on chemical characterization of these compounds.

Bond distances between tetrahedral carbons are all within three standard deviations of the accepted value[11] of 1.54 Å. However, some of these interatomic distances have deviations slightly larger than might be expected because these atoms are associated with disordered regions in the crystal. For example, in the rotationally disordered isopropyl group (Figure 1) each rotamer has a long and a short bond from the methyl groups to C(19). However, the average length of these four bonds is 1.53 Å. No attempt was made to represent C(19) by two partial atoms because these would be too close together to be resolved, but the approximation of using one atom for the center of both rotamers is probably responsible for the divergent bond lengths in this group. The bond lengths in the other isopropyl group [C(34)–C(35)–C(36)] are rather long. The homologous

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(10) Defined by the planes [C(16), C(22), C(24)] and [C(26), C(27), C(37)].

(11) Normal bond distances are taken from "Tables of Interatomic Distances and Configuration in Molecules and Ions," Supplement 1956–1959, Special Publication No. 18, The Chemical Society, London, England, 1965.

Table III. Intramolecular Distances and Angles

A. Bond Distances (Å)^a			
Br(1)–C(13)	1.93 (2)	C(19)–C(20)	1.61 (5)
O(2)–C(10)	1.50 (2)	C(19)–C(20′)	1.39 (5)
O(2)–C(16)	1.38 (2)	C(19)–C(21)	1.40 (6)
O(3)–C(24)	1.29 (2)	C(19)–C(21′)	1.72 (6)
O(4)–C(22)	1.40 (2)	C(22)–C(23)	1.41 (2)
O(5)–C(18)	1.27 (2)	C(23)–C(24)	1.40 (2)
O(6)–C(27)	1.33 (2)	C(23)–C(25)	1.52 (2)
O(7)–C(37)	1.27 (2)	C(25)–C(26)	1.57 (2)
O(8)–C(33)	1.28 (2)	C(26)–C(27)	1.35 (2)
O(9)–C(31)	1.28 (2)	C(26)–C(37)	1.46 (2)
C(10)–C(11)	1.57 (2)	C(27)–C(28)	1.51 (2)
C(10)–C(12)	1.55 (2)	C(28)–C(29)	1.53 (2)
C(10)–C(13)	1.49 (2)	C(28)–C(30)	1.56 (2)
C(13)–C(14)	1.38 (3)	C(28)–C(31)	1.49 (2)
C(14)–C(15)	1.38 (2)	C(31)–C(32)	1.40 (2)
C(15)–C(16)	1.37 (2)	C(32)–C(33)	1.46 (2)
C(15)–C(24)	1.35 (2)	C(32)–C(37)	1.45 (2)
C(16)–C(17)	1.42 (2)	C(33)–C(34)	1.51 (2)
C(17)–C(18)	1.52 (2)	C(34)–C(35)	1.63 (3)
C(17)–C(22)	1.43 (2)	C(34)–C(36)	1.61 (3)
C(18)–C(19)	1.51 (2)		
B. O····O Distances (Å)^a			
O(3)–O(7)	2.58 (2)	O(4)–O(6)	2.69 (2)
O(4)–O(5)	2.41 (2)	O(8)–O(9)	2.37 (2)
C. Bond Angles.^{b} Central Atom is Vertex			
Br(1)–C(13)–C(10)	115 (1)	C(17)–C(18)–C(19)	121 (2)
Br(1)–C(13)–C(14)	124 (1)	C(17)–C(22)–C(23)	124 (1)
O(2)–C(10)–C(11)	99 (1)	C(18)–C(17)–C(22)	119 (2)
O(2)–C(10)–C(12)	107 (1)	C(18)–C(19)–C(20)	102 (3)
O(2)–C(10)–C(13)	106 (1)	C(18)–C(19)–C(20′)	110 (3)
O(2)–C(16)–C(15)	123 (1)	C(18)–C(19)–C(21)	115 (4)
O(2)–C(16)–C(17)	113 (2)	C(18)–C(19)–C(21′)	103 (3)
O(3)–C(24)–C(15)	118 (1)	C(20)–C(19)–C(20′)	52 (3)
O(3)–C(24)–C(23)	123 (2)	C(20)–C(19)–C(21)	111 (4)
O(4)–C(22)–C(17)	121 (2)	C(20′)–C(19)–C(21′)	115 (4)
O(4)–C(22)–C(23)	116 (2)	C(21)–C(19)–C(21′)	49 (4)
O(5)–C(18)–C(17)	114 (2)	C(22)–C(23)–C(24)	118 (2)
O(5)–C(18)–C(19)	125 (2)	C(22)–C(23)–C(25)	117 (1)
O(6)–C(27)–C(26)	120 (2)	C(23)–C(25)–C(26)	112 (1)
O(6)–C(27)–C(28)	115 (1)	C(24)–C(23)–C(25)	124 (1)
O(7)–C(37)–C(26)	120 (1)	C(25)–C(26)–C(27)	123 (1)
O(7)–C(37)–C(32)	120 (2)	C(25)–C(26)–C(37)	117 (2)
O(8)–C(33)–C(32)	117 (2)	C(26)–C(27)–C(28)	125 (2)
O(8)–C(33)–C(34)	119 (2)	C(26)–C(37)–C(32)	120 (1)
O(9)–C(31)–C(28)	114 (1)	C(27)–C(26)–C(37)	120 (2)
O(9)–C(31)–C(32)	121 (2)	C(27)–C(28)–C(29)	108 (1)
C(10)–O(2)–C(16)	116 (1)	C(27)–C(28)–C(30)	109 (1)
C(10)–C(13)–C(14)	121 (2)	C(27)–C(28)–C(31)	112 (1)
C(11)–C(10)–C(12)	113 (2)	C(28)–C(31)–C(32)	125 (1)
C(11)–C(10)–C(13)	116 (2)	C(29)–C(28)–C(30)	111 (1)
C(12)–C(10)–C(13)	113 (2)	C(29)–C(28)–C(31)	104 (1)
C(13)–C(14)–C(15)	121 (2)	C(30)–C(28)–C(31)	113 (1)
C(14)–C(15)–C(16)	116 (2)	C(31)–C(32)–C(33)	118 (1)
C(14)–C(15)–C(24)	121 (2)	C(31)–C(32)–C(37)	118 (1)
C(15)–C(16)–C(17)	124 (2)	C(32)–C(33)–C(34)	124 (2)
C(15)–C(24)–C(23)	119 (2)	C(33)–C(32)–C(37)	124 (1)
C(16)–C(15)–C(24)	122 (1)	C(33)–C(34)–C(35)	109 (2)
C(16)–C(17)–C(18)	129 (2)	C(33)–C(34)–C(36)	108 (2)
C(16)–C(17)–C(22)	112 (2)	C(35)–C(34)–C(36)	110 (1)
D. O····O—C Angles^b			
O(3)–O(7)–C(37)	115 (1)	O(6)–O(4)–C(22)	114 (1)
O(4)–O(5)–C(18)	98 (1)	O(7)–O(3)–C(24)	116 (1)
O(4)–O(6)–C(27)	116 (1)	O(8)–O(9)–C(31)	91 (1)
O(5)–O(4)–C(22)	88 (1)	O(9)–O(8)–C(33)	93 (1)

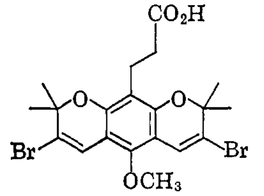
[a] Standard errors × 10^{-2} calculated from the variance–covariance matrix obtained in the final cycle of least squares are given in parentheses. [b] Standard errors in degrees are given in parentheses.

impurities present in the uliginosin compounds are probably due to valeroyl groups in place of the isobutyroyl groups,[12] and the disorder resulting from inclusion of this material in the crystal could affect these distances.

The average distance for bonds between trigonal and tetrahedral carbon atoms is 1.514 Å. All bonds of this type are very near this value except for the C(25)–C(26) bond which is rather long (1.57 Å) but still within acceptable limits. In the filicinic acid moiety, the short distance between C(26) and C(27) (1.35 Å) indicates that the double bond is localized in this position. The C(31)–C(32) distance (1.40 Å) shows partial double bond character due to delocalization of the double bond formally drawn between these atoms, while the C(26)–C(37), C(37)–C(32), and C(32)–C(33) distances (1.46, 1.45, and 1.46 Å, respectively) have values expected for single bonds between trigonal carbon atoms. These results agree qualitatively with bond orders calculated for the 3-acylfilicinic acid system.[13]

That the bond distances for the carbonyl groups [O(5)–C(18), O(7)–C(37), and O(8)–C(33)] are all intermediate between values expected for single and double carbon–oxygen bonds is attributed to hydrogen bonding and delocalization of the double bonds. Examination of structures of various hydrogen-bonded phenols[14] suggests that aromatic carbon–oxygen bonds are not significantly shortened by hydrogen bonding. The O(3)–C(24) distance of 1.29 Å is unusual in view of this generalization. (On the other hand, the O(4)–C(22) single bond distance of 1.40 appears normal.)

Two of the bond distances in the heterocyclic ring differ significantly from expected values. The O(2)–C(10) bond length (1.50 ± 0.02 Å) is significantly longer than the expected value of 1.43 Å for tetrahedral carbon–oxygen bonds. However, the corresponding bonds in dibromoeriostoic acid (IV), which are in a very similar environment, are reported to have lengths of 1.477 ± 0.010 and 1.462 ± 0.009 Å,[15] which agree well with the values that we have found. The bond between C(14) and C(15) (1.38 Å) is about 0.1 Å shorter than the value expected for a single bond between two trigonal carbon atoms. The adjacent bond between C(13) and C(14) is a little long for a double bond but it is within acceptable limits. Moreover, the double bond is twisted by 7.8 ± 2.9° [dihedral angle between planes C(10)–C(13)–C(14) and C(13)–C(14)–C(15)] and is therefore of interest in this respect.[16] The lengths of the C(13)–C(14), C(14)–C(15), and C(24)–O(3) bonds and the twist about the C(13)–C(14) bond may indicate a major resonance contribution by the zwitterion V.



IV

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(12) A. Penttilä and J. Sundman, *Acta Chem. Scand.*, **18**, 344 (1964); **17**, 191 (1963).

(13) S. Forsén, *Arkiv Kemi*, **20**, 25 (1962).

(14) "Table of Interatomic Distances and Configuration in Molecules and Ions," Special Publication No. 11, The Chemical Society, London, England, 1958, pp M213, M222, M240; ref 6, pp M129s, M130s, M152s, M155s, M169s.

(15) M. G. Paton, E. N. Maslen, and K. J. Watson, *Acta Cryst.*, **22**, 120 (1967).

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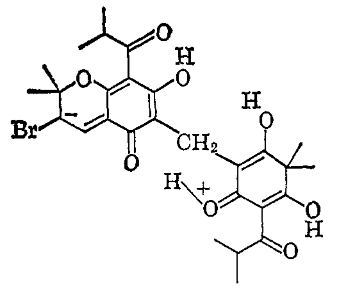

V

The rather short distance between C(11) and Br(1) (3.23 ± 0.02 Å) was also found in dibromoeriostoic acid (IV). Figure 4 shows this juxtaposition for bromouliginosin B in good perspective and also shows the conformation of the heterocyclic ring, which appears to be a deformed boat.

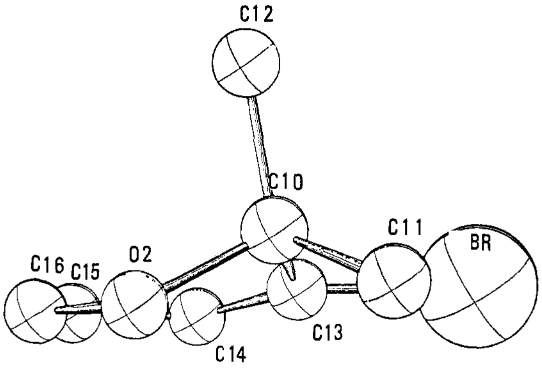

Figure 4. The heterocyclic ring in bromouliginosin B.

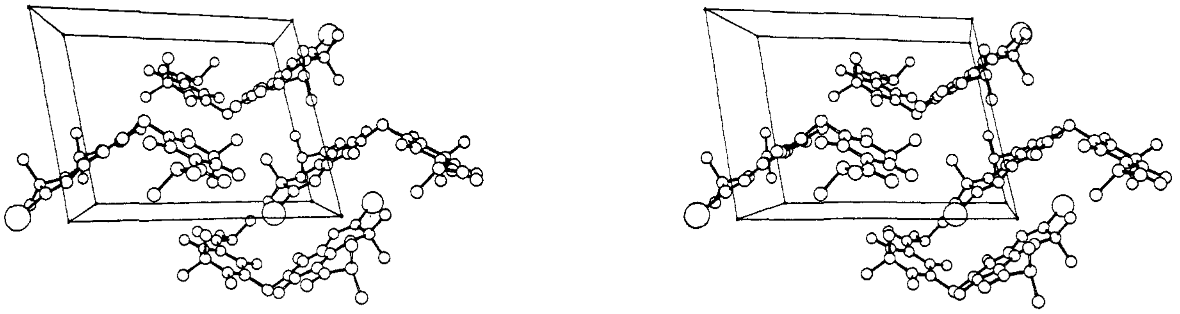

Figure 5. Molecular packing in bromouliginosin B. The triclinic unit cell is viewed down the y axis with the z axis horizontal.

A list of bond angles is given in part C of Table III. Most of the angles in the structure have values near the expected ones. The C(16)–C(17)–C(22) angle (112 ± 2°) is unusually small. The large C(16)–C(17)–C(18) angle (129 ± 2°) may result from bending of the acyl group at C(17) toward O(4) by hydrogen bonding. Steric interaction between the bromine atom and C(11) may be responsible for the large C(11)–C(10)–C(13) angle (116 ± 2°) and possibly also for the twist in the C(13)–C(14) double bond.

The aromatic ring is planar within the limits of error but the filicinic acid ring forms a shallow boat in which atoms C(31) and C(32) are respectively about 0.08 and 0.10 Å above a plane defined by C(27), C(26), and C(37). (The calculated distance of C(28) from this plane (0.004 Å) is negligible.) This boat conformation provides an interesting contrast to the essentially planar cyclohexadienone ring found in 2-bromo-α-santonin.[17]

Table IV. Intermolecular Contacts Less Than 3.8 Å

O(5)–C(30)′	3.26	O(8)–C(11)′	3.66
O(3)–C(20)′	3.38	C(25)–C(32)′	3.67
C(21′)–C(21′)′	3.40	O(6)–C(35)′	3.67
O(6)–C(35)′	3.40	C(26)–C(32)′	3.68
O(7)–C(30)′	3.46	O(3)–C(21′)′	3.68
C(25)–C(33)′	3.47	Br(1)–C(17)′	3.69
O(4)–C(12)′	3.47	C(12)–C(22)′	3.70
O(8)–C(25)′	3.52	O(6)–O(6)′	3.71
O(9)–C(36)′	3.52	O(5)–C(36)′	3.71
C(20′)–C(20′)′	3.53	Br(1)–C(22)′	3.73
O(3)–C(21)′	3.58	O(6)–C(34)′	3.74
C(21)–C(24)′	3.60	O(2)–C(14)′	3.76
C(37)–C(37)′	3.63	O(8)–C(12)′	3.77

As expected from the properties of bromouliginosin B and related compounds, all of the four hydroxylic protons are chelated. Part B of Table III lists the oxygen–oxygen distances in the chelate rings. The O(3)–O(7) and the O(4)–O(6) distances are in the range of most O–H–O distances, but the distance between O(4) and O(5) (2.41 Å) is unusually short. This value correlates well with the nmr spectrum in which a surprisingly low chemical shift (16.39 ppm downfield from tetramethylsilane) is found for this chelated proton. *o*-Hydroxyphenones usually absorb at higher field than this,[6] as discussed above and in more detail in ref 1. The proton at lowest field in the nmr spectrum (18.90 ppm) is chelated by O(8) and O(9). The extremely short distance between these oxygen atoms, 2.37 Å, is greater by only 0.03 Å than Pauling's calculated distance for a symmetrical O–H–O bond.[18]

The molecular packing for bromouliginosin B is shown in Figure 5. Planes of molecules parallel to [100] form wavy surfaces that stack like corrugated sheet metal. Adjacent planes are related by the inversion centers in the crystal. In Table IV, intermolecular contact distances below 3.8 Å are listed. The extremely short intermolecular C(21′)–C(21′)′ and C(20′)–C(20′)′ distances (3.40 and 3.53 Å, respectively) indicate that alternate rotamers at C(19) may be contiguous. For clarity, however, the rotamer containing the "half-atoms" C(20) and C(21) has been omitted from Figures 3 and 5. The C(25)–C(33′) distance (3.47 Å) is the smallest real carbon–carbon

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[17] J. D. M. Asher and G. A. Sim, *J. Chem. Soc.*, 6041 (1965).

[18] L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960, p 484.

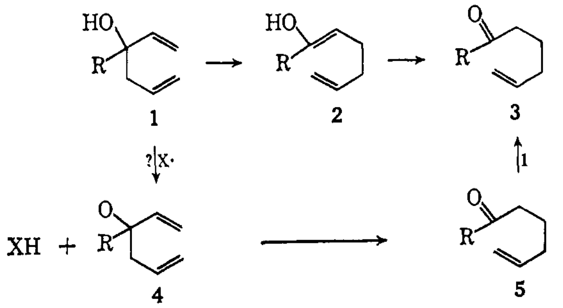
distance in the molecule. The unexpected conformation of the cyclohexadienone ring (shallow boat) may result from crystal packing forces transmitted at this contact point. No intermolecular hydrogen bonds exist in the crystal since the shortest intermolecular oxygen–oxygen distance [O(6)–O(6′)] is 3.71 Å.

Communications to the Editor

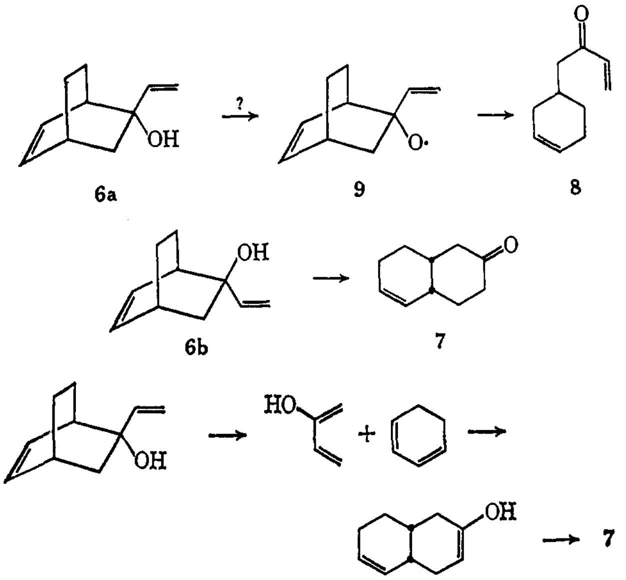
The Oxy-Cope Rearrangement. Evidence for an Intramolecular Mechanism and an Enolic Intermediate[1]

Sir:

The thermal rearrangements of 3-hydroxy-1,5-hexadienes (oxy-Cope rearrangements[2–4]) give unsaturated ketones as final products, hypothetically[2–4] by way of enolic intermediates **1** → **2** → **3**.



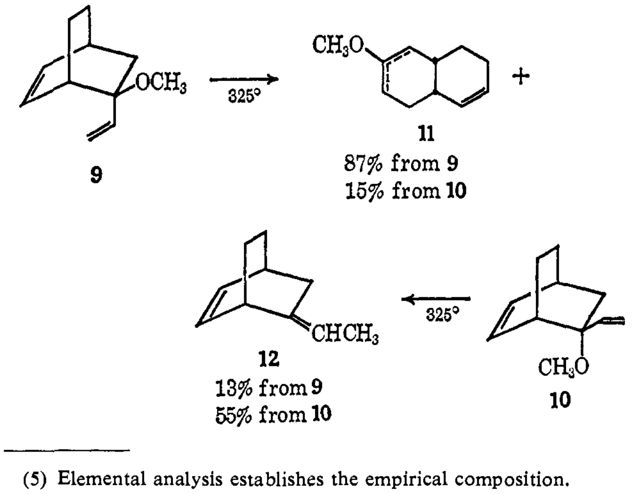
Alternatives to this scheme that have not been excluded rigorously include a mechanism in which hydrogen abstraction from the hydroxyl group, rearrangement (either concertedly or by β-eliminative fragmentation–recombination) of the resulting alkoxy radical (**4** → **5**), and abstraction from a second molecule of **1** would produce **3** and propagate a radical chain. This mechanism also would account for the hydrogen transfer products observed[2] when the two ends of the biallyl system are held remote from each other, as in 2-*exo*-vinyl-2-*endo*-hydroxybicyclo[2.2.2]oct-5-ene (**6a**). Although pyrolysis of the *endo* isomer **6b** gives largely the oxy-Cope rearrangement product **7**,[2] **6a** gives a substantial quantity of hydrogen-shifted monocyclic ketone **8**,[2] which might conceivably arise from β scission of a hypothetical 2-*exo*-vinyl-2-*endo*-alkoxy radical (**9**).



A second alternative mechanism for some of the observed[2] rearrangements is Diels–Alder retrogression–recombination. Although the hypothetical 2-hydroxy-1,3-butadiene intermediate might be expected to be unstable with respect to its tautomer, methyl vinyl ketone, the hydroxydiene is generated from pyrolysis in the vapor phase and therefore might very well survive long enough to be captured by cyclohexadiene before ketonization.

The present work in showing that 3-*methoxy*-1,5-hexadienes rearrange thermally to *enol ethers* provides strong presumptive evidence against the radical chain mechanism. Further experiments demonstrate the strict intramolecularity of the process and thereby eliminate the retro-Diels–Alder mechanism.

The epimeric ethers **9**[5] and **10**[5] are prepared from the corresponding alcohols[2] by successive treatment with potassium and methyl iodide. Identified in the mixture from gas-phase pyrolysis of either epimer are the



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[1] Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

[2] J. A. Berson and M. Jones, Jr., *J. Am. Chem. Soc.*, **86**, 5017, 5019 (1964).

[3] (a) A. Viola and L. Levasseur, *ibid.*, **87**, 1150 (1965); (b) A. Viola, E. J. Iorio, K. K. Chen, G. M. Glover, U. Nayak, and P. J. Kocienski, *ibid.*, **89**, 3462 (1967).

[4] (a) E. Urion, *Ann. Chim.*, **1**, 5 (1934); (b) M. J. Wiemann and S.-L. T. Thuan, *Compt. Rend.*, **246**, 2903 (1958); (c) J. Chuche and J. Wiemann, *ibid.*, **262**, 567 (1966); (d) E. Brown, P. Leriverend, and J. M. Conia, *Tetrahedron Letters*, 6115 (1966); (e) for a comparable rearrangement of a 3-hydroxy-1-en-5-yne, see J. W. Wilson and S. A. Sherrod, Abstracts of Papers, 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967, No. S146; *Chem. Commun.*, 143 (1968).

[5] Elemental analysis establishes the empirical composition.