J. Org. Chem. **1989**, *54*, 1379–1383

Zinc Chloride Catalyzed Rearrangements of 1,2-Dialkynyl-1,2-dihydroxy-3,6-dimethoxy-3,5-cyclohexadienes to Bicyclo[2.2.2]octadienones and Bicyclo[3.2.1]octadienones

Mario Fernandez, Shoumo Chang, Joseph Ziller, Robert J. Doedens, and Harold W. Moore*

Department of Chemistry, University of California, Irvine, Irvine, California 92717

Received July 25, 1988

Reported here are unusual rearrangements of 1 and 3 to the bicyclooctadienones 2 and 4. This was accomplished when a carbon tetrachloride solution of respectively 1 and 3 was refluxed for 2 h in the presence of zinc chloride. The structure and stereochemistry of 2 were deduced by NMR proton–carbon correlations, NOE studies, and ultimately a complete X-ray crystal structure determination. Under the same conditions the rearrangement of 3 takes a different course, and the [3.2.1] system 4 is formed. The structures of 4 were unambiguously determined by X-ray diffraction on one member of this series.

We recently reported the unusual rearrangement of the cyclohexadiene 1, 1,2-bis(phenylethynyl)-1,2-dihydroxy-3,6-dimethoxy-3,5-cyclohexadiene, to the bicyclooctadienone 2, 1,4-dimethoxy-5-phenyl-3-(phenylethynyl)-3-hydroxybicyclo[2.2.2]octadien-2-one, upon treatment with zinc chloride in carbon tetrachloride.[1,2] Described here are the details of this reaction as well as an interesting variation of the rearrangement, i.e., 3, the monotrimethylsilyl derivatives of 1 were observed to rearrange to the bicyclo[3.2.1]octadienones 4 when subjected to the same reaction conditions.

Scheme I

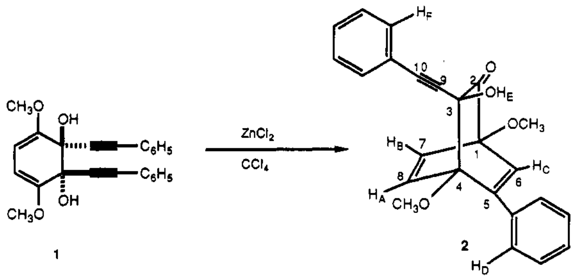

Table I. Positional Parameters of Non-Hydrogen Atoms of Bicyclo[2.2.2]octadienone

atom	*x*	*y*	*z*	*U* (eq)[a]
C(1)	0.803 85 (19)	0.093 52 (10)	0.857 76 (17)	45 (1)
C(2)	0.868 12 (18)	0.097 36 (9)	0.775 33 (16)	42 (1)
C(3)	0.873 45 (18)	0.021 82 (9)	0.710 93 (17)	43 (1)
C(4)	0.920 33 (22)	−0.037 33 (10)	0.817 61 (20)	53 (2)
C(5)	0.853 12 (23)	−0.039 74 (11)	0.896 17 (20)	56 (2)
C(6)	0.744 54 (20)	0.018 99 (10)	0.871 08 (18)	48 (1)
C(7)	0.648 88 (19)	−0.000 70 (9)	0.729 60 (17)	43 (1)
C(8)	0.721 63 (17)	0.002 29 (9)	0.630 29 (16)	40 (1)
C(9)	0.704 10 (18)	−0.069 09 (9)	0.560 71 (16)	43 (1)
C(10)	0.672 47 (18)	−0.122 02 (9)	0.490 39 (17)	45 (1)
C(11)	0.627 19 (19)	−0.183 60 (9)	0.400 55 (16)	43 (1)
C(12)	0.488 96 (20)	−0.201 77 (10)	0.347 48 (19)	50 (2)
C(13)	0.442 54 (24)	−0.258 59 (11)	0.256 94 (20)	58 (2)
C(14)	0.532 51 (25)	−0.297 76 (11)	0.217 82 (20)	60 (2)
C(15)	0.669 49 (26)	−0.280 63 (12)	0.270 91 (23)	67 (2)
C(16)	0.718 04 (24)	−0.224 02 (12)	0.362 32 (22)	59 (2)
C(17)	0.913 62 (18)	0.169 14 (9)	0.740 81 (18)	44 (1)
C(18)	0.978 34 (21)	0.220 48 (11)	0.840 23 (22)	55 (2)
C(19)	1.003 42 (26)	0.292 07 (12)	0.809 55 (25)	68 (2)
C(20)	0.965 27 (27)	0.313 84 (12)	0.681 44 (26)	71 (2)
C(21)	0.905 29 (27)	0.263 30 (12)	0.582 38 (25)	69 (2)
C(22)	0.880 34 (23)	0.190 96 (12)	0.611 64 (21)	57 (2)
C(23)	1.088 96 (24)	0.031 13 (18)	0.686 94 (33)	74 (2)
C(24)	0.585 75 (45)	0.072 30 (17)	0.954 74 (45)	96 (4)
O(1)	0.943 97 (13)	0.021 66 (7)	0.625 81 (13)	55 (1)
O(2)	0.661 14 (13)	0.061 00 (6)	0.541 22 (12)	46 (1)
O(3)	0.529 60 (13)	−0.015 79 (7)	0.698 68 (12)	53 (1)
O(4)	0.681 57 (16)	0.013 97 (8)	0.962 19 (13)	67 (1)

[a] *U* (eq) is one-third of the trace of the orthogonalized *U* matrix. The *U* (eq) values have been multiplied by 10e^3.

Formation of 2 was realized in 60% yield when a carbon tetrachloride solution of 1 was refluxed for 4 h in the presence of zinc chloride (Scheme I). The structure of 2 is based upon a detailed NMR analysis as well as upon an X-ray crystallographic study (Figure 1). Even though the structure was unambiguously established by the X-ray study, a brief description of the NMR data is in order since it too pointed directly to structure 2 and thus illustrates the power of modern high-field NMR analysis.[3] The 500-MHz ^{13}C NMR spectrum of 2 indicated the presence of quaternary centers, an alkyne and alkene linkages, aromatic carbons, and a carbonyl group. Moreover, vicinal and long-range proton carbon correlations revealed that the methoxy groups are attached to quaternary centers and that one of the aromatic rings is attached to the alkynyl group and the other is linked to the alkene moiety. These conclusions come from the following data. Low-energy irradiation of the methoxy group absorptions (3.18 and 3.75 ppm) showed them to respectively correlate with the quaternary carbon centers, C-4 (87.32 ppm) and C-1 (88.09 ppm). Irradiation of H$_F$ (7.43 ppm) showed it to correlate with C-10 (88.75 ppm) and H$_D$ (7.60 ppm) to correlate with C-5 (148.08 ppm). The alkenyl proton absorption H$_A$ (6.75 ppm) was observed to correlate with C-1 (88.09 ppm), C-5 (148.05 ppm), and C-3 (67.91 ppm), and H$_B$ (6.79 ppm) and H$_C$ (6.28 ppm) correlated with C-4 (87.32 ppm). In addition H$_A$, H$_B$, and H$_C$ all correlate with the carbonyl carbon, C-2 (194.67 ppm). A final piece of information corroborating structure 2 was the fact the H$_E$ (hydroxyl proton) correlates with C-4 (87.59 ppm), C-8 (194.86 ppm), and C-9 (87.59 ppm). The stereochemistry at C-3 was established by NOE experiments, which clearly showed the aromatic rings situated on opposite sides of the bicyclic framework. This structure assignment was, of course, conclusively confirmed by the X-ray study noted above.

Surprisingly, when 1 was silylated upon treatment with trimethylsilyl cyanide, and the resulting monotrimethyl-

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(1) Fernandez, M.; Pollart, D. J.; Moore, H. W. *Tetrahedron Lett.* **1988**, 2765.

(2) For discussions on the synthesis of the starting cyclohexadienes, see: Wriede, U.; Fernandez, M.; West, K. F.; Harcourt, D.; Moore, H. W. *J. Org. Chem.* **1987**, *52*, 4485. Moore, H. W.; West, K. F.; Wriede, U.; Chow, K.; Fernandez, M.; Nguyen, N. V. *J. Org. Chem.* **1987**, *52*, 2537.

(3) (a) Bax, A. D. *J. Magn. Reson.* **1984**, *57*, 314. (b) Marshall, J. L. *Carbon-Carbon and Carbon-Proton Couplings*; Verlag Chemie International: Weinheim, 1983; pp 11–51.

0022-3263/89/1954-1379$01.50/0

Table II. Positional Parameters of Non-Hydrogen Atoms of Bicyclo[3.2.1]octadienone

atom	*x*	*y*	*z*	*U* (eq)
C(1)	0.6283 (4)	0.1640 (3)	0.116 80 (10)	336 (14)
C(2()	0.7238 (4)	0.2103 (3)	0.073 57 (11)	370 (16)
C(3)	0.6087 (4)	0.2157 (3)	0.033 90 (10)	412 (16)
C(4)	0.4969 (4)	0.1003 (3)	0.032 04 (11)	405 (17)
C(5)	0.4922 (4)	−0.0030 (3)	0.063 80 (11)	360 (16)
C(6)	0.6065 (4)	0.0013 (3)	0.103 32 (10)	338 (15)
C(7)	0.1855 (5)	0.2823 (6)	0.131 55 (18)	830 (31)
C(8)	0.3729 (5)	0.1474 (5)	0.208 63 (14)	678 (25)
C(9)	0.4227 (6)	0.4572 (4)	0.184 19 (16)	696 (28)
C(10)	0.7392 (6)	0.4628 (4)	0.088 01 (17)	641 (27)
C(11)	0.3838 (4)	−0.1239 (3)	0.059 85 (10)	375 (16)
C(12)	0.4310 (4)	−0.2634 (4)	0.067 67 (12)	490 (19)
C(13)	0.3333 (5)	−0.3759 (4)	0.060 47 (15)	611 (25)
C(14)	0.1862 (5)	−0.3500 (5)	0.046 48 (14)	627 (26)
C(15)	0.1370 (4)	−0.2122 (5)	0.039 40 (14)	625 (23)
C(16)	0.2357 (4)	−0.0994 (4)	0.045 75 (13)	510 (21)
C(17)	0.6522 (5)	−0.1545 (4)	0.168 44 (14)	655 (25)
C(18)	0.7619 (4)	−0.0321 (4)	0.084 49 (13)	428 (19)
C(19)	0.8244 (4)	0.0825 (4)	0.067 64 (13)	480 (20)
C(20)	0.7169 (3)	0.1769 (3)	0.159 67 (11)	375 (16)
C(21)	0.7781 (4)	0.1864 (3)	0.195 77 (11)	401 (17)
C(22)	0.8442 (4)	0.1889 (3)	0.241 49 (11)	413 (17)
C(23)	0.7862 (5)	0.2777 (4)	0.274 81 (13)	570 (22)
C(24)	0.8450 (6)	0.2727 (5)	0.319 33 (14)	685 (26)
C(25)	0.9584 (5)	0.1801 (6)	0.329 78 (13)	720 (28)
C(26)	1.0171 (5)	0.0907 (6)	0.296 34 (16)	788 (30)
C(27)	0.9612 (4)	0.0959 (5)	0.252 53 (14)	622 (25)
O(1)	0.4924 (2)	0.2399 (2)	0.119 55 (7)	386 (11)
O(2)	0.8132 (3)	0.3326 (2)	0.077 44 (9)	486 (14)
O(3)	0.6141 (3)	0.3092 (3)	0.005 19 (8)	650 (17)
O(4)	0.5480 (3)	−0.0797 (2)	0.140 13 (7)	422 (12)
Si	0.3711 (1)	0.2791 (1)	0.161 17 (3)	426 (5)

[a] *U* (eq) is one-third of the trace of the orthogonalized *U* matrix. The *U* (eq) values have been multiplied by $10E^4$.

Table III. Experimental Data for the X-ray Diffraction Study of Bicyclo[2.2.2]octadienone 3

formula	$C_{24}H_{20}O_4$
FW	372.4
crystal system	monoclinic
space group	$P2_1/n$
a, Å	10.5679 (17)
b, Å	17.9936 (29)
c, Å	11.0308 (16)
β	112.233 (12)
V, Å	1941.6 (5)
Z	4
D_{calcd}, g/cm^3	1.27
diffractometer	Nicolet P3
data collected	$+h,+k,\pm e$
scan type	coupled θ(crystal) − 2θ(counter)
scan width	$[2\theta(K\alpha_1) - 1.2] \rightarrow [2\theta(K\alpha_2) + 1.2]$
scan speed	4.0 deg min^{-1} (in 2θ)
$2\theta_{max}$, deg	50.0
unique reflections	3444
reflections with $F^2 > 0$	3123
no. of variables	333
R_F	5.7%
R_{wF}	5.5%
goodness of fit	1.42

silyloxy derivative **3a** subjected to the reaction conditions employed for the rearrangement of **1** to **2**, the reaction took an interesting new course. Here, the bicyclo[3.2.1]octadienone **4a** was obtained in 62% yield (Scheme II). The structure of this compound was again determined on the basis of its spectral properties and unambiguously established by a complete X-ray crystallographic study (Figure 2). The synthetic scope of this rearrangement was found to be reasonably general in that **1b–d** also give respectively **4b–d** when subjected to the reaction conditions. However, **1e** was found to be unreactive even after several hours under these conditions.

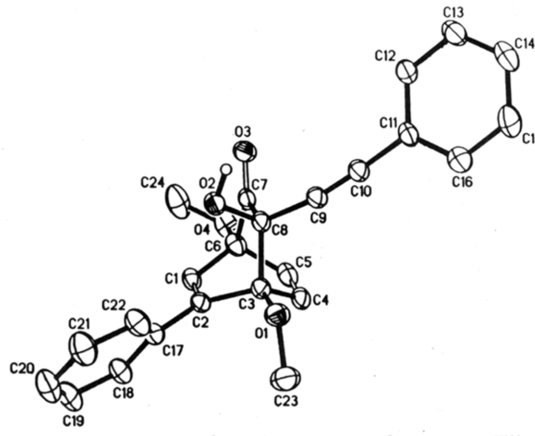
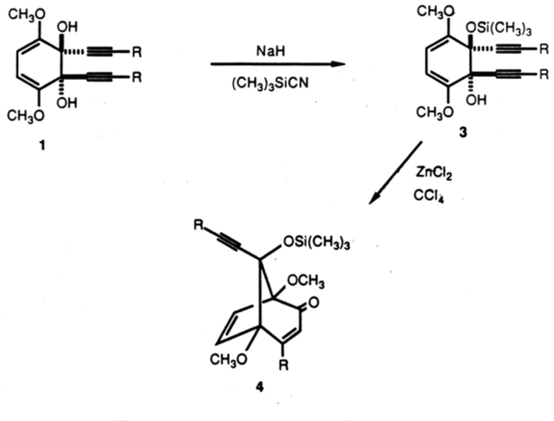


Figure 1. ORTEP view of bicyclo[2.2.2]octadienone **2**. Ellipsoids are drawn at the 30% level.

Table IV. Experimental Data for the X-ray Diffraction Study of Bicyclo[3.2.1]octadienone 4a

formula	$C_{27}H_{28}O_3Si$
FW	428.4
crystal system	orthorhombic
space group	$P2_12_12_1$
a, Å	8.824 (4)
b, Å	9.417 (4)
c, Å	29.073 (14)
V, Å^3	2415.9 (18)
Z	4
D_{calcd}, g/cm^3	1.18
diffractometer	Syntex $P2_1$
data collected	$+h,+k,+e$
scan type	coupled θ(crystal) − 2θ(counter)
scan width	$[2\theta(K\alpha_1) - 1.2] \rightarrow [2\theta(K\alpha_2) + 1.2]$
scan speed	4.0–16.0 deg min^{-1} (in 2θ)
$2\theta_{max}$, deg	55.0
unique reflections	3199
reflections with $F^2 > 3\sigma$ (F^2)	2219
no. of variables	289
R_F	4.0%
F_{wF}	5.1%
goodness of fit	1.49

Scheme II



	R	% YIELD 3	% YIELD 4
a	$-C_6H_5$	56	62
b	$-C_4H_9$	65	68
c	$-CH_2OBzl$	70	83
d	$-CO_2C_2H_5$	80	47
e	-H	74	••

The mechanism of these unusual rearrangements can only be speculated upon at this time and one possibility is outlined in Scheme III. Here, it is proposed that zinc chloride coordinates with one of the alkyne bonds to give **5**. This then undergoes ring closure facilitated by the

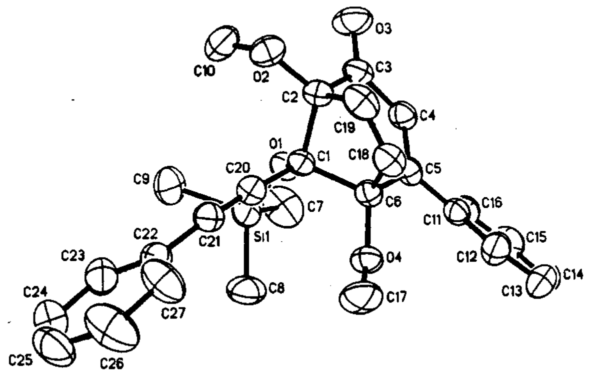
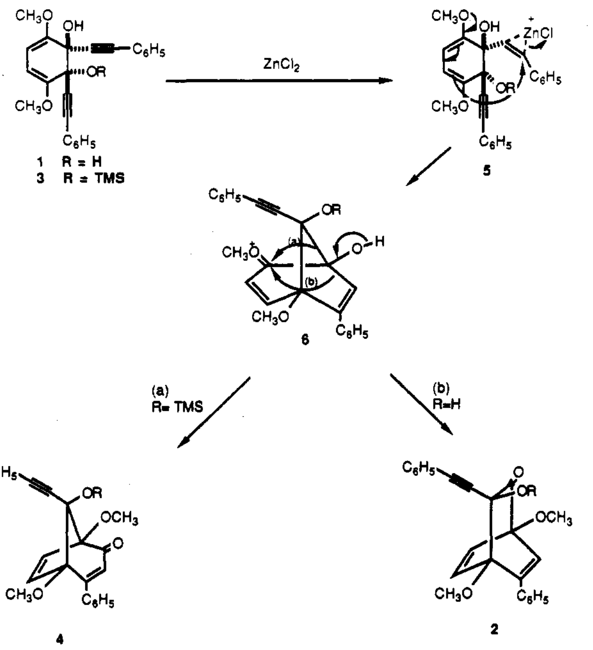


Figure 2. ORTEP view of bicyclo[3.2.1]octadienone 4a. Ellipsoids are drawn at the 50% level.

Scheme III



nonbonding electrons on one of the methoxy groups to give 6 (here drawn as if 1 had been protonated rather than coordinated to the Lewis acid). Carbocation 6 can then proceed to 2 via Wagner–Meerwein migration of bond b or to 4 by migration of bond a. The selectivity for these two possibilities remains a mystery.

In conclusion, an interesting set of rearrangements have been discovered. These provide synthetic routes for the assembles of bicyclo[2.2.2]- and -[3.2.1]octadienones in reasonable yields and in very few steps.[4,5] Since the starting cyclohexadienes are readily available, these results speak to a potentially useful rearrangement.

Experimental Section

Melting points were determined on a Büchi 510 capillary apparatus and are uncorrected. Microanalysis were performed by Robertson's Laboratories, Florham Park, NJ. Infrared spectra were run on a Perkin-Elmer 283 spectrophotometer in chloroform solution cells or KBr. In describing the infrared spectra, the following abbreviations were used: s, strong absorption; w, weak absorption; m, medium absorption. Infrared absorption are reported in cm^{-1} with polystyrene as the external standard. ^{1}H NMR and ^{13}C NMR spectra were obtained using a General Electric QE 300- and 500-MHz spectrometers. All NMR spectra were run in CDCl$_3$ and are reported relative to the internal standard tetramethylsilane (TMS) as values in parts per million. In describing the NMR data, the following abbreviation were used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad. Mass spectra were determined with a medium-resolution Finnigan 4000 GC/MS quadrupole spectrometer interfaced to a Nova 312 data system. High-resolution mass spectra were obtained from a 7070 EVG analytical organic mass spectrometer interfaced to a VG Analytical LTD 11/250 data system.

1,4-Dimethoxy-5-phenyl-3-(phenylethynyl)-3-hydroxybicyclo[2.2.2]octadien-2-one (2). A solution consisting of 0.50 g (1.34 mmol) of 1a and 0.050 g (0.36 mmol) of zinc chloride in 25 mL of dry carbon tetrachloride was refluxed for 4 h. The mixture was allowed to cool to room temperature, and the inorganic residues were removed by filtration through a bed of Celite. The solvent was evaporated, and the residue was passed through a flash column (silica gel, hexanes/ethyl acetate, 9:1) to give 0.30 g (60%) of 2 as a yellow oil, which upon addition of 5 mL of diisopropyl ether gave white crystals: mp 141–142 °C; ^{1}H NMR δ 7.35 (m, 10 H), 6.78 (q, 2 H, J = 1.17 Hz), 6.27 (d, 1 H, J = 1.12 Hz), 3.18 (s, 3 H), 3.75 (s, 3 H), 3.52 (s, 1 H), 3.27 (s, 3 H); ^{13}C NMR 194.86, 148.40, 136.04, 134.56, 132.18, 131.07, 128.98, 128.49, 128.46, 128.40, 128.36, 124.97, 122.05, 88.40, 87.59, 87.05, 86.03, 68.20, 54.62, 54.51; IR 3362 (br), 2218 (w), 1745 (s), 1600 (m), 1500 (s), 1450 (s), 1350 (s), 1170 (s), 760 (s); MS 372 (EI), 373 (CI). Anal. Calcd for $C_{24}H_{20}O_4$: C, 77.40; H, 5.4. Found: C, 77.42; H, 5.37.

Pulsed Polarization Transfer via Long-Range ^{1}H–^{13}C Couplings on Compound 2. The long-range proton–carbon correlation via polarization transfer was done on a GN-500 spectrometer. The delay between the first two proton 90° pulses, which generate polarization transfer, was 100 ms to optimize the condition of correlating protons and carbons, which have coupling constants around 5 Hz. The delays between second proton 90° pulses and starting data acquisition were 100 35 or 20 ms, depending on the polarization transfer from CH, CH$_2$, or CH$_3$. The selective proton pulse was calibrated as 25 ms for 90°. This excluded the possibility of exciting carbon satellites more than 50 Hz away.

1,2-Bis(phenylethynyl)-3,6-dimethoxy-2-[(trimethylsilyl)oxy]-3,5-cyclohexadien-1-ol (3a). To 0.50 g (1.34 mmol) of 1a in 50 mL of dry THF, at 0 °C, was added 0.064 g (2.68 mmol) of sodium hydride followed by injection of 0.18 mL (2.68 mmol) of trimethylsilyl cyanide. The mixture was stirred at this temperature for 3 h. The solution was then filtered through a bed of Celite to remove the inorganic residues suspended in solution, and the filtrate was evaporated to give a yellow oil. The oil was dissolved in 2 mL of dichloromethane and passed through a flash column (silica gel, hexanes/ethyl acetate, 3:2); evaporation of the solvent gave 3a as a white solid that was recrystallized from diisopropyl ether to afford 0.29 g (56%) of white crystals: mp 122–123 °C; ^{1}H NMR δ 7.43 (m, 10 H), 5.03 (d, 1 H, J = 7.08 Hz), 4.94 (d, 1 H, J = 7.1 Hz), 3.71 (s, 3 H), 3.66 (s, 3 H), 3.64 (s, 1 H), 0.23 (s, 9 H); IR 3468 (s), 2220 (m), 1660 (s), 1495 (s), 1325 (s), 1350 (s), 1095 (s), 1040 (s). Anal. Calcd for $C_{27}H_{28}SiO_4$: C, 72.94; H, 6.34. Found: C, 72.85; H, 6.31.

1,2-Di-1-hexynyl-3,6-dimethoxy-1-[(trimethylsilyl)oxy]-3,5-cyclohexadien-2-ol (3b). A solution of 0.29 g (0.87 mmol) of 1b in 20 mL of dry THF at 0 °C was treated with 0.043 g (1.83 mmol) of sodium hydride followed by injection of 0.25 mL (1.83 mmol) of trimethylsilyl cyanide. The mixture was stirred at this temperature for 90 min, time after which TLC showed no more starting material. The solution was allowed to warm to room temperature, and the suspended inorganic materials were removed by filtration through a bed of Celite. Flash column chromatography (silica gel, hexanes/ethyl acetate, 4:1) afforded 0.23 g (65%) of 3b as a light yellow oil: ^{1}H NMR δ 4.92 (d, 1 H, J = 6.95 Hz), 4.84 (d, 1 H, J = 6.99 Hz), 3.65 (s, 3 H), 3.60 (s, 3 H), 2.80 (s, 1 H), 2.35 (m, 4 H), 1.49 (m, 8 H), 0.91 (m, 6 H), 0.21 (s, 9 H); IR 3550 (br), 2970 (s), 2950 (s), 2221 (br), 1470 (m), 1075 (s), 1050 (s); MS 405 (CI); exact mass calcd for $C_{23}H_{36}O_4Si$ 404.23767, found 404.23669.

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[4] For an excellent review on the synthesis of these bicyclic frameworks, see: *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley and Sons: New York, 1983; Vol. 5, pp 525–560.

[5] Among other biological properties, bicyclooctadienones have been shown to have antiinfluenza activity. See: Boigegrain, R.; Chenu, J.; Simiand, J. Eur. Pat. Appl. EP 1985, 130,882 (Cl,C07C61/13); *Chem. Abstr.* **1985**, *102*, 148783c. De la Cuesta, E.; Ballesteros, P.; Trigo, G. G. *J. Pharm. Sci.* **1984**, *73*, 1307.

1,2-Bis[3-(benzyloxy)-1-propynyl]-3,6-dimethoxy-1-[(trimethylsilyl)oxy]-3,5-cyclohexadien-2-ol (3c). A solution of 0.40 g (0.87 mmol) of **1c** in 50 mL of dry THF, at room temperature, was treated with 0.042 g (1.73 mmol) of sodium hydride and 0.23 mL (1.73 mmole) of trimethylsilyl cyanide. The mixture was stirred for 3 h, time after which the starting material was consumed. The inorganic solids suspended in solution were separated by filtration through a bed of Celite. The product was isolated by flash column chromatography (silica gel, hexanes/ethyl acetate, 4:1), which afforded 0.32 g (70%) of a colorless oil: ^{1}H NMR δ 7.4–7.2 (m, 10 H), 4.97 (d, 1 H, J = 6.92 Hz), 4.91 (d, 1 H, J = 7.07 Hz), 4.61 (s, 4 H), 4.22 (s, 2 H), 4.21 (s, 2 H), 3.68 (s, 3 H), 3.63 (s, 3 H), 2.98 (s, 1 H), 0.22 (s, 9 H); IR 3500 (br), 2215 (w), 1465 (m), 1090 (s), 1070 (s). MS 533 (CI); exact mass calcd for $C_{31}H_{36}O_6Si$ 532.227 49, found 532.227 26.

1,2-Bis(carbethoxyethynyl)-3,6-dimethoxy-1-[(trimethylsilyl)oxy]-3,5-cyclohexadien-2-ol (3d). A solution of 0.50 g (1.4 mmol) of **1d** in 40 mL of dry THF at 0 °C was reacted with 0.065 g (2.7 mmol) of sodium hydride and 0.37 mL (2.7 mmol) of trimethylsilyl cyanide. The mixture was stirred for 2 h and then allowed to warm to room temperature. After removal of the inorganic material, the solvent was evaporated, and the residue was passed through a flash column (silica gel, hexanes/ethyl acetate, 7:3) to afford 0.47 g (80%) of **3d** as light yellow oil: ^{1}H NMR δ 5.0 (d, 1 H, J = 7.03 Hz), 4.94 (d, 1 H, J = 7.03 Hz), 4.23 (m, 4 H), 3.70 (s, 3 H), 3.65 (s, 3 H), 2.05 (s, 1 H), 1.30 (m, 6 H), 0.26 (s, 9 H); IR 3490 (br), 2125 (m), 1730 (s), 1725 (s), 1260 (s), 1250 (s); MS 437 (CI); exact mass calcd for $C_{21}H_{28}O_8Si$ 436.1553, found 436.15518.

1,2-Diethynyl-3,6-dimethoxy-1-[(trimethylsilyl)oxy]-3,5-cyclohexadien-2-ol (3e). A mixture consisting of 0.10 g (0.45 mmol) of **1e**, 0.021 g (0.90 mmol) of sodium hydride, and 0.12 mL (0.90 mmol) of trimethylsilyl cyanide, in 10 mL dry THF, was stirred at room temperature for 2 h. The suspended solids in solution were separated by filtration through a bed of Celite, and the solvent was evaporated to give a dark yellow oil. This material was purified through a preparative plate (silica gel, hexanes/ethyl acetate, 3:2) to afford 0.098 g (74%) of **3e** as a colorless oil: ^{1}H NMR δ 4.99 (d, 1 H, J = 7.01 Hz), 4.92 (d, 1 H, J = 6.9 Hz), 3.70 (s, 3 H), 3.66 (s, 3 H), 3.04 (s, 1 H), 2.56 (s, 1 H), 2.47 (s, 1 H), 0.22 (s, 9 H); IR 3500 (br), 3320 (s), 3290 (s), 2260 (w), 2120 (w), 1660 (m); MS 293 (CI); exact mass calcd for $C_{15}H_{20}O_4Si$ 292.11247, found 292.11208.

1,5-Dimethoxy-4-phenyl-8-(phenylethynyl)-8-[(trimethylsilyl)oxy]bicyclo[3.2.1]octa-3,6-dien-2-one (4a). A solution of 0.200 g (0.45 mmol) of **3a** and 0.020 g (0.15 mmol) of zinc chloride in 20 mL of dry carbon tetrachloride was refluxed for 4 h. The solution was allowed to cool to room temperature, the inorganic residues were separated by filtration through a bed of Celite, and the filtrate was concentrated and passed through a flash column (silica gel, hexanes/ethyl acetate, 9:1). Evaporation of the solvent gave **4a** as a yellow solid that recrystallized from methanol to yield 0.125 g (62%) of light yellow rhombic crystals: mp 138–139 °C; ^{1}H NMR δ 7.41 (m, 10 H), 6.84 (d, 1 H, J = 6.39 Hz), 6.22 (d, 1 H, J = 6.43 Hz), 5.82 (s, 1 H), 3.80 (s, 3 H), 3.40 (s, 3 H), 0.24 (s, 9 H); ^{13}C NMR δ 194.53, 161.58, 141.09, 136.71, 131.73, 130.65, 129.41, 128.99, 128.64, 128.46, 127.74, 122.84, 122.55, 97.28, 88.00, 54.94, 54.65, 1.90; IR 2980 (s), 2965 (s), 2220 (w), 1685 (s), 1600 (m), 1450 (s), 1320 (s); MS 444 (EI, CI); Anal. Calcd for $C_{27}H_{28}O_4Si$: C, 72.94; H, 6.34. Found: C, 73.01; H, 6.48.

1,5-Dimethoxy-4-butyl-8-(1-hexynyl)-8-[(trimethylsilyl)oxy]bicyclo[3.2.1]octa-3,6-dien-2-one (4b). A mixture of 0.050 g (0.124 mmol) of **3b** and 0.005 g (0.036 mmol) of zinc chloride in 10 mL of carbon tetrachloride, was refluxed for 2 h, time after which the color of the solution turned from light yellow to dark brown. The mixture was then allowed to warm to room temperature, and the suspended solids were separated by filtration through a bed of Celite. The solvent was evaporated, and the product was purified by a preparative plate (silica gel, hexanes/ethyl acetate, 9:1) to yield 0.034 g (68%) of **4b** as a colorless oil: ^{1}H NMR δ 6.57 (d, 1 H, J = 6.51 Hz), 5.95 (d, 1 H, J = 6.42 Hz), 5.49 (s, 1 H), 3.69 (s, 3 H), 3.62 (s, 3 H), 2.25 (t, 4 H, J = 7.15 Hz), 1.6-1.2 (m, 8 H), 0.91 (t, 6 H, J = 7.1 Hz), 0.22 (s, 9 H); ^{13}C NMR δ 194.95, 166.57, 138.62, 133.19, 119.98, 96.49, 95.33, 92.58, 88.71, 55.21, 54.53, 32.18, 30.44, 29.41, 22.67, 22.32, 18.19, 14.12, 13.77; IR 2990 (s), 2975 (s), 2225 (w), 1689 (s), 1470 (m), 1330 (m), 1135 (s); MS 405 (CI); exact mass calcd for $C_{23}H_{36}O_4Si$ 404.23767, found 404.2391.

1,5-Dimethoxy-4-benzyl-8-[3-(benzyloxy)-1-propynyl]-8-[(trimethylsilyl)oxy]bicyclo[3.2.1]octa-3,6-dien-2-one (4c). A mixture consisting of 0.10 g (0.188 mmol) of **3c** and 0.010 g (0.073 mmol) of zinc chloride in 20 mL carbon tetrachloride was refluxed for 2.5 h. The mixture was allowed to cool to room temperature, and the suspended inorganic solids were separated by filtration through a bed of Celite. The solvent was evaporated, and the residue was passed through a small flash column (silica gel, hexanes/ethyl acetate, 4:1) to yield 0.083 g (83%) of **4c** as a yellow oil: ^{1}H NMR δ 7.4–7.3 (m, 10 H), 6.68 (d, 1 H, J = 6.42 Hz), 6.02 (d, 1 H, J = 6.39 Hz), 5.86 (s, 1 H), 4.61 (s, 2 H), 4.55 (s, 2 H), 4.54 (s, 2 H), 4.24 (s, 2 H), 3.67 (s, 3 H), 3.66 (s, 3 H), 0.21 (s, 9 H); ^{13}C NMR δ 194.07, 160.99, 138.01, 137.45, 133.55, 128.64, 128.20, 128.12, 127.94, 127.63, 119.28, 95.22, 91.97, 84.49, 84.18, 72.99, 71.74, 71.53, 68.67, 68.01, 57.56, 55.37, 54.66, 1.82; IR 2960 (w), 2020 (w), 1695 (s), 1460 (m), 1152 (s), 1138 (s); MS 533 (CI); exact mass calcd for $C_{31}H_{36}O_6Si$ 532.22749, found 532.22880.

1,5-Dimethoxy-4-carbethoxy-8-(carbethoxyethynyl)-8-[(trimethylsilyl)oxy]bicyclo[3.2.1]octa-3,6-dien-2-one (4d). A solution of 0.17 g (0.39 mmol) of **3d** and 0.017 g (0.12 mmol) of zinc chloride in 25 mL of carbon tetrachloride was refluxed for 6 h. The solution was allowed to cool to room temperature, and the suspended solids were separated by filtration through a bed of Celite. The solvent was removed, and the residue was passed through a flash column (silica gel, hexanes/ethyl acetate, 4:1) to afford 0.080 g (45%) of **4d** as a light yellow oil: ^{1}H NMR δ 6.89 (d, 1 H, J = 6.52 Hz), 6.04 (d, 1 H, J = 6.58 Hz), 5.98 (s, 1 H), 4.25 (m, 4 H), 3.68 (s, 3 H), 3.65 (s, 3 H), 1.31 (m, 6 H), 0.20 (s, 9 H); ^{13}C NMR δ 193.64, 164.78, 162.86, 138.40, 137.08, 132.65, 124.74, 88.48, 87.05, 84.30, 83.98, 62.40, 61.74, 56.0, 54.86, 54.71, 14.27, 14.14, 1.45; IR 2250 (w), 1745 (s), 1725 (s), 1710 (s), 1270 (s), 1262 (s); MS 437 (CI); exact mass calcd for $C_{21}H_{28}O_8Si$: 436.15531, found 436.15501.

Collection of X-ray Data and Structure Solution. A colorless crystal of approximate dimensions 0.45 × 0.57 × 0.67 mm was mounted along its extended direction in a thin-walled glassy capillary. It was accurately aligned on the Nicolet P3 automated four-circle diffractometer at the University of California, Irvine. Subsequent setup operations (determination of accurate unit cell dimensions and orientation matrix) and collection of room-temperature (21 °C) intensity data were carried out using standard techniques similar to those of Churchill.[6] Final cell parameters are based on a least-squares analysis of 25 reflections in well-separated regions of reciprocal space, all having $27\sigma < 20 < 35\sigma$.

A careful survey of a preliminary data set revealed the systematic extinctions $h0l$ for $h + l = 2n + 1$ and $0k0$ for $k = 2n + 1$. The space group is thus uniquely defined as $P21/n$; a nonstandard setting of the centrosymmetric monoclinic space group $P21/c$ (C2h 5; No. 14).

All 3444 unique reflections were converted to unscaled $|F_o|$ values following corrections for Lorentz and polarization effects. A Wilson plot was used to place the data on an approximate absolute scale. Those 3123 reflections with $I > 0$ were considered observed.

The structures were solved by direct methods using the program MITHRIL.[7] All crystallographic calculations were performed with our locally modified version of the UCLA Crystallographic Computing Package[8] at the University of California, Irvine. The structures were refined by using full-matrix least-square methods. The weighting scheme using $p = 0.05$ has been previously described.[9] All hydrogen atoms were located from a series of difference-Fourier syntheses. The model converged with RF = 5.7%, RWF = 5.5%, and GOF = 1.42 for 333 variables refined against those 3123 data with $I > 0$. A final difference-Fourier synthesis was featureless.

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The analytical scattering factors of Cromer and Waber[10a] for neutral atoms were used throughout the analysis; both real (D f') and imaginary (i D f'') components of anomalous dispersion were included.[10b]

Acknowledgment. We wish to thank the National Institutes of Health (Grant CA-11890) for financial support of this work. Funds for the purchase of the Nicolet R3n/V diffractometer system were made available from the National Science Foundation under Grant CHE-8514495.

Registry No. 1a, 118895-55-9; **1b**, 118895-56-0; **1c**, 118895-57-1; **1d**, 118895-58-2; **1e**, 118895-59-3; **2**, 118895-60-6; **3a**, 118895-61-7; **3b**, 118920-50-6; **3c**, 118895-62-8; **3d**, 118895-63-9; **3e**, 118895-64-0; **4a**, 118895-65-1; **4b**, 118895-66-2; **4c**, 118895-67-3; **4d**, 118895-68-4; $ZnCl_2$, 7646-85-7; $(CH_3)_3SiCN$, 7677-24-9.

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Corner Attack on *exo*- and *endo*-Tricyclo[3.2.1.0^{2,4}]octane by Deuteron and Mercuric Ions

James M. Coxon,* Peter J. Steel,* and Barry I. Whittington

Department of Chemistry, University of Canterbury, Christchurch, New Zealand

Merle A. Battiste

University of Florida, Gainesville, Florida 32611

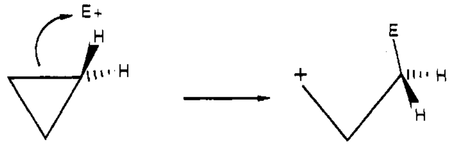
Received August 9, 1988

Reaction of *endo*-tricyclo[3.2.1.0^{2,4}]octane (1) with deuteron in methanol-d_1 gave a mixture (62:38) of methoxy ethers **3b** and **4b** from cleavage of the most substituted cyclopropane bond. The reaction proceeds by attack of deuterium at the corner of the cyclopropane. Trapping of the intermediate cation **5b** is competitive with rearrangement to the nonclassical cation **6b**. Reaction of *exo*-tricyclo[3.2.1.0^{2,4}]octane (**2**) under similar conditions gave methoxy ether **11b**, which results from rupture of an external cyclopropyl bond, and methoxy ether **12b** formed from rupture of the internal cyclopropyl bond with inversion at the site of both electrophilic and nucleophilic attack. Reaction of hydrocarbon 1 with mercuric acetate in methanol gave 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]octane (**3c**) from attack of the mercuric ion at the corner of the cyclopropane and nucleophilic attack by methanol with inversion without skeletal rearrangement. Similar reaction of the exo hydrocarbon **2** gave product **12c** from internal bond rupture without molecular rearrangement and with inversion of configuration at the site of electrophilic and nucleophilic attack. In addition an almost equal quantity of **11c**, a product of rupture of the external cyclopropyl bond, was formed. The stereochemistry of mercuric ion and deuteron attack at C2 at the corner of the cyclopropane ring of 1 and **2** is rationalized by consideration of the symmetry and energy of the molecular orbitals involved.

Acid- or electrophile-promoted ring cleavage of cyclopropanes has been the subject of considerable speculation.[1] The regiochemistry of reaction is often rationalized by a modified version of Markovnikov's rule, which states[2] that the ring opens between the carbons bearing the largest and smallest number of alkyl substituents. Thus, for cyclopropanes substituted at only one carbon the product(s) can be rationalized by ring opening leading to the more substituted carbocation. However, with substituents on two carbons, products are generally observed to result from both Markovnikov-type addition and from cleavage of the most substituted cyclopropyl bond.[1] The two possible reaction trajectories for electrophilic attack on cyclopropane are shown in Scheme I. For substrates suitably labeled to allow the relative configurations at C1 and C2 in the product to be established, these two processes can be differentiated. For example, DePuy[3] found that *cis*-1,2,3-trimethylcyclopropane reacted with deuteron to give 68% retention of configuration at the site of deuteron attack and 32% inversion, as measured from the ratio of *erythro* and *threo* products. Wiberg[1b] has referred to retention (b, Scheme I) as cleavage of the C–C bond syn to the entering proton and to inversion (a, Scheme I) as cleavage of the C–C bond anti to the entering proton. Subsequent attack by the nucleophile in this system occurred with inversion.

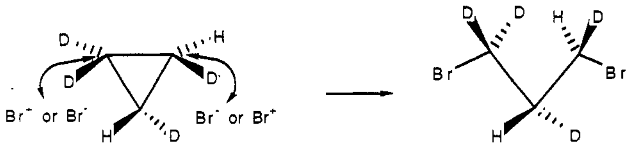
Scheme I

(a) Corner attack by electrophile (with inversion of configuration)



(b) Edge attack by electrophile (with retention of configuration)

Scheme II



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