Single-Crystal X-ray Analysis of 4,15-DAS (2). Crystal data for 4,15-diacetoxyscirpenol (2), $C_{19}H_{26}O_7$: clear colorless rod, 0.2 × 0.3 × 0.4 mm, monoclinic, space group $P2_1$, $a = 8.273$ (3) Å, $b = 10.536$ (3) Å, $c = 21.363$ (5) Å, $\beta = 99.5$ (1)°, $V = 1837$ (2) Å^3, and $\rho_{calc} = 1.325$ g/cm^3 for $Z = 4$. Diffraction data: Enraf-Nonius CAD4 automated κ-axis diffractometer, graphite-monochromated Mo radiation ($\lambda(K\alpha) = 0.71073$ Å), range $2.0 < 2\theta < 45.0°$, 2796 reflections (2487 unique, $R_i = 0.029$, 2065 observed, $I > 2.0\sigma(F)$); corrected for anomalous dispersion, Lorentz and polarization effects, but absorption ignored ($\mu = 0.945$ cm^{-1}). Solution: direct methods (SHELXS-86)[29] and difference Fourier syntheses. Refinement: anisotropic thermal coefficients for non-H atoms, hydroxyl H atoms located and refined, all other H atoms placed at calculated positions, all H atoms with fixed isotropic thermal parameters.[30] Final: no significant features in the final difference Fourier map (range $-0.30 < e/Å^3 < +0.32$); agreement factors, $R = 0.41$, $R_w = 0.050$, and $S = 1.019$.

Bioassay. The specific-pathogen-free (SPF) fertile chicken eggs, used for the chick embryo bioassay were purchased from Larson Lab-Vac Eggs, Inc., P.O. Box 474, Gowrie, IA 50543. The incubators used were the Imperial II produced by Lab-Line Instruments, Inc., and a Model 3212-10 produced by National Appliance Company. The temperature was maintained at 37 °C, and the relative humidity was kept at ~60%. Embryos were received within 24 h of laying, incubated for 5 days, and candled for viability. Typically a batch of 150 eggs would yield 120 acceptable eggs. Before dosing, the air cells were circled with a pencil and swabbed with 200-proof EtOH (Midwest Solvents Company of Illinois). An 18-gauge needle, sterilized in 200-proof EtOH, was used to puncture the shell above the encircled air cell. The toxins were dissolved in 200-proof EtOH, serial diluted, and 10 μL injected into the air cell with a microsyringe. The hole was then sealed Scotch tape. 10 μL of 200-proof EtOH was injected into the control eggs. In four days the eggs were candled and the number of dead embryos were determined for each dose level. The new trichothecenes 1 and 6 were bioassayed for toxicity using the chick embryo inoculations methods.[31,32] Preliminary results suggest that 6 is much less toxic than DAS (2), which has an LD^{50} value of 45 ng/egg.[31] However, 1 appears to be close to 2 in embryotoxicity.

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Supplementary Material Available: Table of general displacement parameter expressions (1 page). Ordering information is given on any current masthead page.

Configurations of the Isomeric 7-Oxiranylbicyclo[4.2.0]octan-7-ols

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The four racemic diastereoisomers of the title compound **1**, prepared by epoxidation of the exo and endo vinyl precursors **4** and **5**, were assigned tentative configurations in an earlier study.[1] The corresponding bromohydrins (**6b,c**) from the [1α,6α,7β,7(S*)]-(±)- and [1α,6α,7α,7(S*)]-(±)-isomers **1b** and **1c** were converted to cyclic carbonate derivatives **7** and **8**, the structures of which were established by X-ray analysis. This confirms the earlier assignments.

In an earlier report[1] we noted that the four racemic diastereoisomers of **1**, the title compound, each behaved in a different fashion when treated with catalytic boron trifluoride etherate under mild conditions. Three of the isomers underwent regio- and stereoselective rearrangements to ring-expanded hydroxymethyl-substituted ketones (**2a**, **2b**, and **3a**), and the fourth was recovered unchanged. Structural assignments for these hydroxymethyl ketone products were based on their β-elimination to characteristic enones and stereoselective conversion to corresponding cis or trans diols.

The isomeric epoxy cyclobutanols **1** were easily assigned as isomeric pairs, related to the exo and endo vinyl alcohols **4** and **5** from which they were prepared. Further identification within each pair proved impossible by spectroscopic methods, and we made tentative configurational assignments based on the stereoselectivity of the observed rearrangements.[2] These are shown in Scheme I; the configuration of the unreactive isomer **1b** being fixed by process of elimination.

On reaction with magnesium bromide, each of the epoxy cyclobutanol isomers (**1a–d**) gave a unique crystalline bromohydrin (**6a–d**), which reverted to the parent epoxide on mild base treatment (Scheme II). Clearly, an X-ray structure analysis of one bromohydrin from each pair (**6a** or **6b** and **6c** or **6d**) would establish unquivocally the configurations of all the epoxide isomers; however, all our efforts to obtain crystals suitable for this purpose were unsuccessful. Finally, assuming that cyclic ester derivatives of the bromohydrins might give better results, we studied their reactions with oxalyl chloride and were gratified to obtain good yields of useable products (**7** and **8** from **6b** and **6c**, respectively). Although we expected cyclic oxalates from this reaction, the ^{13}C NMR spectra of **7** and **8** displayed single carbonyl signals at ca. δ 153 ppm, characteristic of cyclic carbonates.[3] X-ray diffraction analysis of these two isomers not only confirmed their cyclic carbonate structure but also established the relative configuration at C-9 (the side chain chiral center), as shown in Figure 1. Since this center remains fixed throughout all the conversions originating from **1** (and **6**), **1b** is thereby

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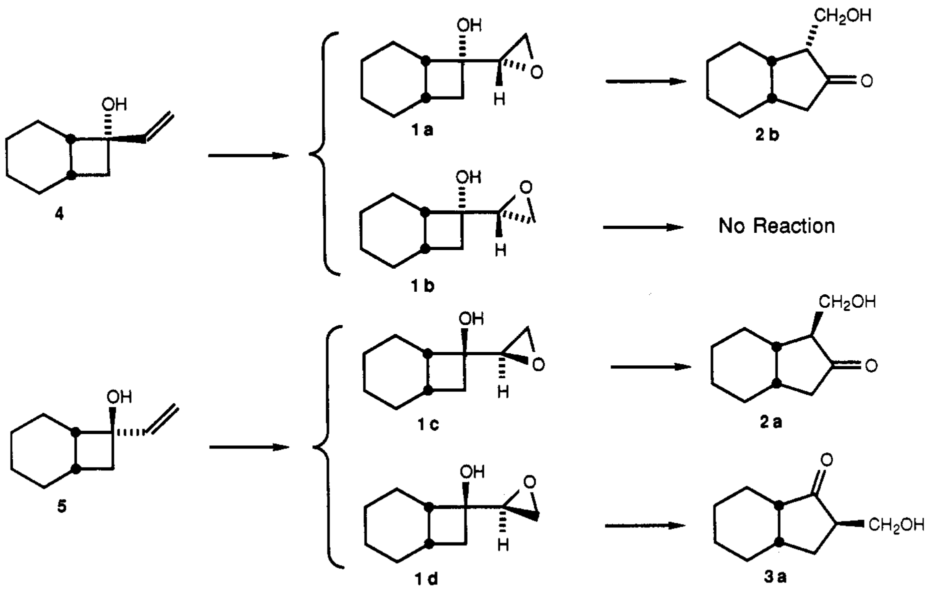
[1] Hwang, C.-S.; Reusch, W. *Heterocycles* **1987**, *25*, 589.

[2] If these rearrangements proceed via an antiperiplanar orientation of the oxirane CH–O bond and the migrating ring residue, both molecular model (Dreiding) inspection and molecular mechanics calculations point to the assignments given in Scheme I.

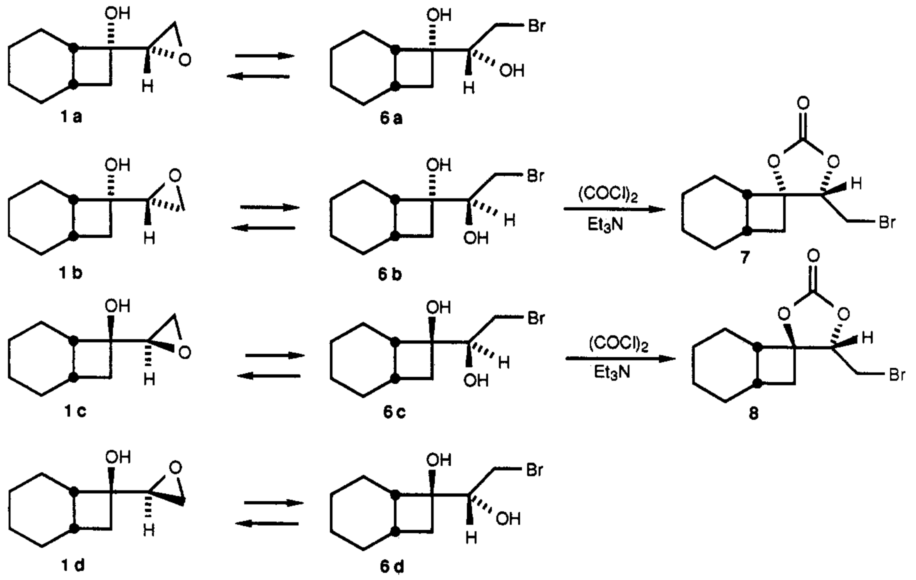
[3] Levy, G. C.; Lichter, R. L.; Nelson, G. L. *Carbon-13 Nuclear Magnetic Resonance Spectroscopy*, 2nd ed.; Wiley: New York, 1980; p 156.

0022-3263/89/1954-4318$01.50/0

Scheme I



Scheme II



established as [1α,6α,7β,7(S^*)]-(±)-7-oxiranylbicyclo[4.2.0]octan-7-ol and **1c** is the [1α,6α,7α,7(S^*)]-(±)-isomer.[4]

The unusual conversion of a vicinal glycol to a cyclic carbonate by reaction with oxalyl chloride has precedent in the results from a study of reactions of dioxastannolanes with small diacid chlorides.[5] The reaction with oxalyl chloride proved anomalous and gave, along with the expected cyclic oxalate, the corresponding carbonate with loss of carbon monoxide. In the case of dioxastannolanes from highly substituted glycols the latter reaction was dominant.

Experimental Section

Reactions were conducted under a dry nitrogen or argon atmosphere, using dried and distilled solvents. Melting points were measured on a Thomas-Hoover capillary apparatus. Proton magnetic resonance spectra were taken in deuteriochloroform solution, using a Bruker WM 250 spectrometer, and are calibrated in parts per million (δ) from tetramethylsilane as an internal standard. Carbon-13 magnetic resonance spectra were taken at 69.8 MHz on the same spectrometer, using the same solvent and reference compound. Mass spectra were obtained using a Finnigan 4000 GC/MS spectrometer, operating at 70 eV El. X-ray data were measured on a Nicolet P3F diffractometer.

The preparation of and physical properties for compounds 1 through 6 were reported in an earlier paper.[1]

Cyclic Carbonate 7. Bromohydrin **6b** (308 mg, 1.24 mmol) was dissolved in methylene chloride (20 mL), cooled to 0 °C, and mixed in turn with triethylamine (0.5 mL) and oxalyl chloride (0.31 mL, 3.7 mmol). This mixture was stirred for 6 h at 0 °C and then quenched by addition to ice water (50 mL). Following extraction with methylene chloride (3 × 10 mL), the organic layers were washed with cold dilute hydrochloric acid and brine. The dried extract yielded a brown oil, which on flash chromatography[6] gave **7** (299 mg, 88%), as a colorless solid, mp 84–85 °C. Properties of **7**: ^{1}H NMR δ 1.1–1.8 (m, 8 H) 2.16 (m, 1 H), 2.43 (m, 3 H), 3.46 (dd, 1 H, J = 4.7 and 11.7 Hz), 3.61 (dd, 1 H, J = 4.4 and 11.7 Hz), 4.72 (dd, 1 H, J = 4.4 and 4.7 Hz) ppm; ^{13}C NMR δ 21.1, 21.7, 24.6, 25.6, 30.0, 31.7, 43.7 (overlapping signals), 81.8, 85.1, 153.0 ppm; IR 1810 cm^{-1}; mass spectrum, m/e (rel abundance) 195 (19), 193 (19), 151 (8), 139 (4), 82 (100), 67 (84).

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[4] *Chemical Abstracts Index Guide*, 1987, Appendix IV. According to this nomenclature system, **1a** and **1d** are respectively the [1α,6α,7β,7(R^*)]-(±)- and [1α,6α,7α,7(R^*)]-(±)-isomers.

[5] Davis, A. G.; Hua-De, P.; Hawari, J. A. *J. Organomet. Chem.* **1983**, *256*, 251.

[6] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

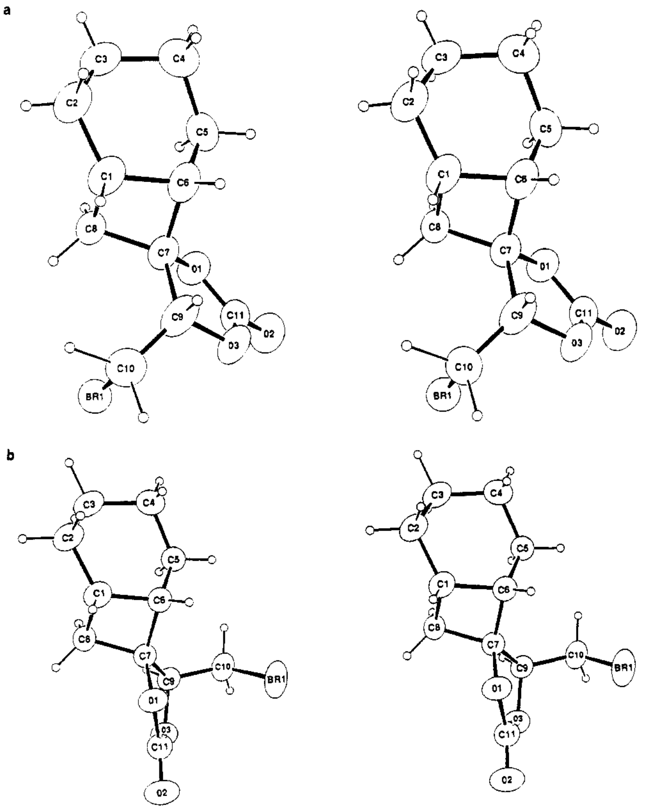

Figure 1. (a) ORTEP diagram of compound 7. (b) ORTEP diagram of compound 8.

Cyclic Carbonate 8. In a similar fashion bromohydrin **6c** (105 mg) was converted to **8**, mp 109–111 °C, in 52% yield. Properties of **8**: ^{1}H NMR δ 0.96–1.7 (m, 8 H), 1.98 (m, 1 H), 2.20 (m, 1 H), 2.29 (dd, 1 H, J = 11.6 and 11.8 Hz), 2.82 (m, 1 H), 3.49 (dd, 1 H, J = 4.2 and 12.1 Hz), 3.59 (dd, 1 H, J = 2.6 and 12.1 Hz), 4.62 (dd, 1 H, J = 2.6 and 4.2 Hz) ppm; ^{13}C NMR δ 20.8, 22.8, 23.9, 25.0, 28.7, 30.6, 37.1, 41.0, 80.6, 88.8, 153.6 ppm; IR 1810 cm^{-1}.

X-ray Crystallographic Study. Preliminary examination and data collection were performed with Mo Kα radiation (λ = 0.71073 Å) on a Nicolet P3F diffractometer. The data were collected at a temperature of 25 (1) °C using the $\theta - 2\theta$ scan technique. The scan rate was 2 deg/min (in 2θ). Data were collected to a maximum 2θ of 55 °C. The scan range (in degrees) was determined as a function of 2θ to correct for the separation of the Kα doublet,[7] the scan width was calculated as follows:

$$2\theta(\text{scan width}) = 2.00 + (2\theta(K_{\alpha_2}) - 2\theta(K_{\alpha_1}))$$

Lorentz and polarization corrections were applied to the data. The linear absorption coefficient is 35.7 cm^{-1} for Mo Kα radiation. A numerical absorption correction was made. Relative transmission coefficients ranged from 21.99 to 40.76 (av = 32.08) for **7**, and from 0.285 to 0.528 (av = 0.434) for **8**. A secondary extinction correction was applied.[8]

The structures were solved by the direct methods program SHELXS86.[9] All 15 non-H atoms were located from an E map. Hydrogen atoms were located, and their positions and isotropic thermal parameters were refined. The structures were refined by full-matrix least-squares methods where the function minimized was $\sum w(|F_o| - |F_c|)^2$ and the weight w is defined as 1.0 for all observed reflections.

Scattering factors were taken from Cromer and Waber.[10] Anomalous dispersion effects were included in F_c;[11] the values for $\Delta f'$ and $\Delta f''$ were those of Cromer.[12] Only the 1984 reflections having intensities greater than 3.0 times their standard deviation were used in the refinements. The final cycle refinements included 197 variable parameters and converged with unweighted and weighted agreement factors of: $R_1 = \sum|F_o - F_c|/\sum F_o = 0.060$ for **7** and 0.034 for **8**. $R_2 = \sqrt{(\sum w(F_o - F_c)^2/\sum wF_o^2)} = 0.055$ for **7** and 0.035 for **8**.

Acknowledgment. We thank the Walter Yates Scholarship Fund for an award to C.S.H. and Ernest Oliver for assistance in obtaining mass spectra.

Supplementary Material Available: X-ray data for **7** and **8**, experimental procedures, positional and thermal parameters, bond distances, bond angles, torsion angles, and a stereoview of the unit cell showing 20% probability ellipsoids (18 pages). Ordering information is given on any current masthead page.

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(7) *Data Collection Operation Manual*; Nicolet XRD Corp., 1981.

(8) Zachariasen, W. H. *Acta Crystallogr.* **1963**, *16*, 1139.

(9) Sheldrick, G. M. In *Crystallographic Computing 3*; Sheldrick, G. M., Kruger, C., Goddard, R., Eds.; Oxford University Press: London, 1985; pp 175–189 [ISBN 0 19 855 211 4].

(10) Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.2B.

(11) Ibers, J. A.; Hamilton, W. C. *Acta Crystallogr.* **1964**, *17*, 781.

(12) Cromer, D. T. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.3.1.