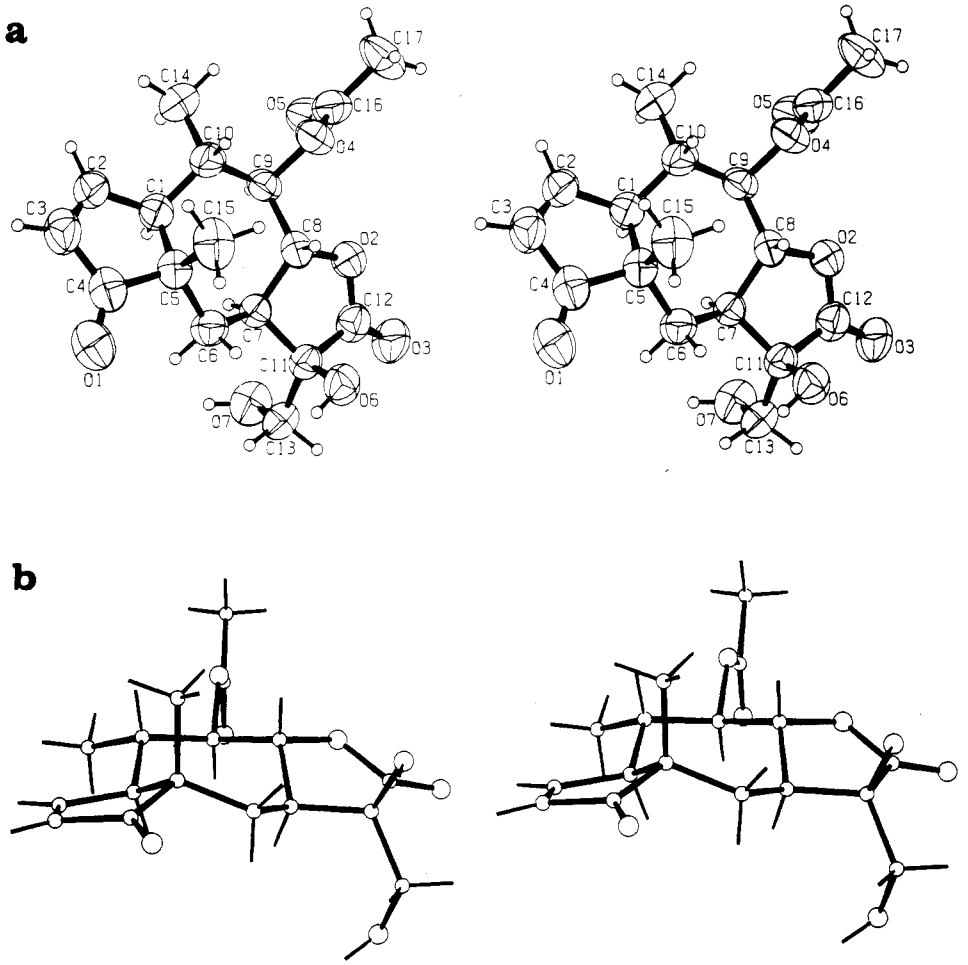

Figure 1. (a) Stereoscopic view of amblyodiol molecule with ellipsoids of thermal motion. (b) Side view of molecular framework.

toward C-8 rather than C-6. In the case of amblyodiol the C-11 stereochemistry can be rationalized by invoking enzymatic hydroxylation from the less hindered β side of an 11,13-unsaturated amblyodiol precursor in the manner in which bromination of pulchellin yields the dibromide4.[7]

Experimental Section

Single crystals of amblyodol were prepared by slow crystallization from ethyl acetate–hexane. The crystals were trigonal, space group $P3_2$ (for the configuration shown) or $P3_1$, with a = 9.682 (2) Å, c = 15.549 (6) Å, and d_{calcd} = 1.335 g cm^{-3} for Z = 3 ($C_{17}H_{22}O_7$, M_r = 338.36). The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). The size of the crystal used for data collection was approximately 0.25 × 0.25 × 0.5 mm. A total of 1551 accessible reflections were measured for $\theta < 70°$, of which 1397 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure[9] and was refined by full-matrix least-squares methods. In the final refinement anisotropic thermal parameters were used for the nonhydrogen atoms, and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices are R = 0.054 and R_w = 0.062 for the 1397 observed reflections. The final difference map has no peaks greater than 0.4 eÅ^{-3}.

Supplementary Material Available: Tables I–IV listing final atomic parameters, final anisotropic thermal parameters, bond lengths, and bond angles for compound 1 (4 pages). Ordering information is given on any current masthead page.

(9) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr. Sect. A* 1971, *A27*, 368.

Synthesis of 10,11-Anhydroerythromycin

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In the course of investigating synthetic modifications of the erythromycin aglycon fragment, we desired the 10,11-anhydro derivative **1**. Although there is a novel synthetic route[1] to **1**, it requires a masking–unmasking sequence of the 2′-hydroxyl as well as the 4″-hydroxyl functions which is time consuming; also, it substantially decreases the overall yield.

Our synthetic analysis was based upon the projection that it should be possible to *selectively* introduce an electron-stabilizing functionality at the 11,12-position. This moiety would then be subjected to base-catalyzed elimination. In principle, 11,12-cyclic carbonate **2** would fulfull our requirements. Thus, exposure of erythromycin (**3**) to ethylene carbonate in toluene does afford intermediate **2**,[2] and subsequent treatment of **2** with tetramethylguanidine in dimethoxyethane cleanly affords anhydro derivative **1** (Scheme I).

(1) J. Tadanier, J. Martin, R. Egan, A. Goldstein, R. Stanaszek, E. Hirner, and F. Fischer, *J. Org. Chem.*, **39**, 2495 (1974); J. Tadanier, J. Martin, A. Goldstein and E., Hirner, *ibid*, **43**, 2351 (1978).

(2) W. Slawinski, H. Bojarska-Dahlig, T. Glabski, I. Dziegielewska, M. Biedrzycki, and S. Naperty, *Recl. Trav. Chim. Pays-Bas*, **94**, 236 (1975); H. W. Murphy, V. C. Stephens, and J. Conine, *U.S.* Patent 3417077 (1968); H. Bojarska-Dahlig and W. Slawinski, *Rocz.* Chem., **46**, 221 (1972).

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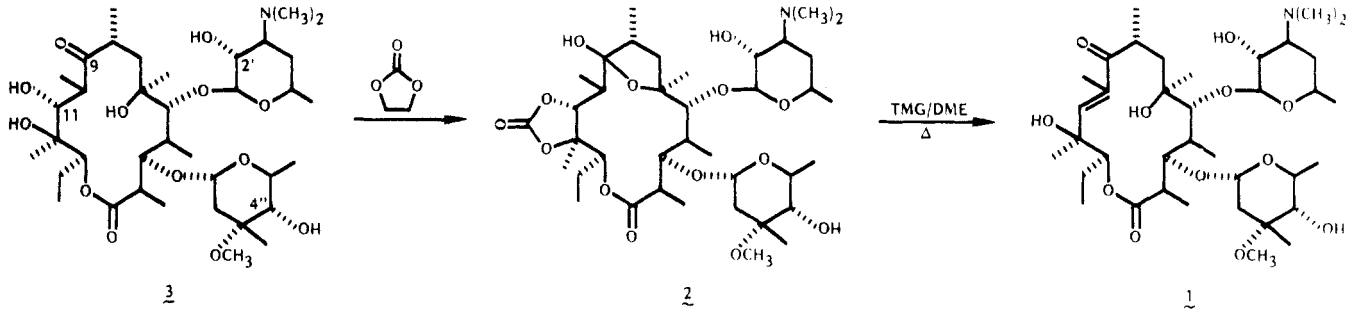
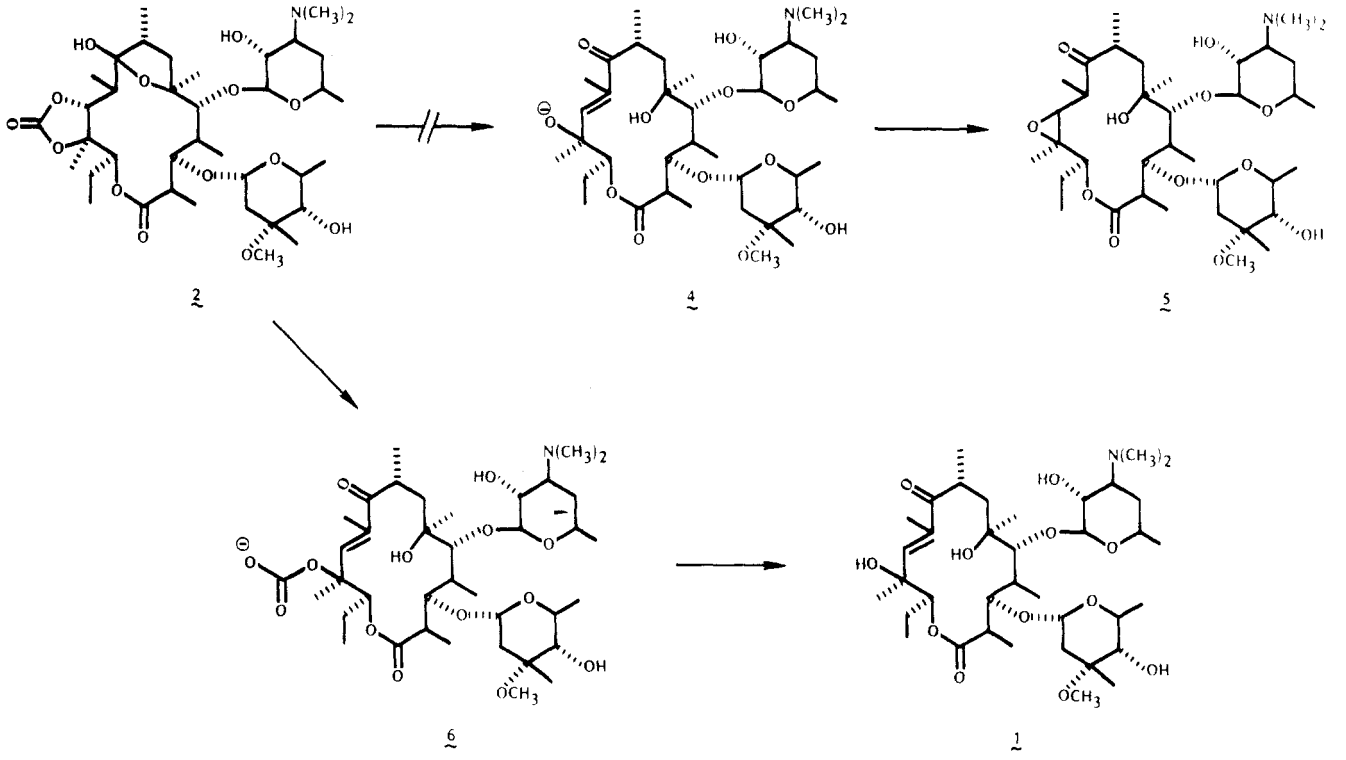
Scheme I



3 2 1

Scheme II



2 4 5 6 1

It is interesting to note that none of epoxide **5**, that could result from intramolecular Michael[3] addition of the 12-alkoxy Michael donor **4** into the 10,11-enone, is observed under the reaction condition (Scheme II). Presumably, carbonate anion **6** is hydrolyzed upon aqueous workup; thus, intermediate **4**, which contains a Michael donor superior to intermediate **6**, is never present.

In summary, therefore, we have been able to convert erythromycin (**3**) into 10,11-anhydroerythromycin (**1**) via a simple, two-step process in excellent yield, without recourse to masking any of the peripheral functionality.

Experimental Section

General Methods. NMR spectra were obtained on a Varian XL-100 spectrometer. Cyclic carbonate **2** was prepared via literature methods.[2]

Preparation of 10,11-Anhydroerythromycin (1). To a dimethoxyethane solution (6 ml) of cyclic carbonate **2** (1.0 g, 1.2 mmol) was added in one portion tetramethylguanidine (1.0 g, 8.7 mmol). The mixture was stirred at reflux for 4 h, after which time TLC [silica, $CHCl_3/MeOH/NH_3$ (9:1:.1)] indicated no remaining starting material and one more polar UV-visible component. The mixture was allowed to cool to room temperature, and the contents were poured into a stirred mixture of methylene chloride and water. The pH was stabilized at 9.5 and the organic layer was separated, dried over anhydrous sodium sulfate, and concentrated at reduced pressure. The resulting colorless foam was slurried in hot water, and ethanol was added until the mixture became turbid. When the mixture was stirred for 2 h at room temperature, a colorless, crystalline material precipitated which was isolated by filtration. This material corresponded in all respects (^1H NMR, IR, and mass spectra) to the literature[1] value reported for 10,11-anhydroerythromycin (**1**). The yield was 83%. We report the ^{13}CNMR spectrum here for the first time: ^{13}C NMR ($CDCl_3$) 209.4, 175.3, 138.9, 138.6, 102.2, 94.1, 84.3, 83.5, 77.1, 76.6, 73.9, 73.6, 72.4, 70.3, 69.2, 66.0, 65.1, 49.1, 43.6, 42.9, 42.6, 40.3, 39.6, 34.2, 28.5, 23.5, 22.5, 21.7, 21.4, 20.9, 20.3, 17.5, 13.6, 11.6, 10.5, 9.3 ppm.

(3) A referee has pointed out that, although there is no prior evidence to support Michael addition mediated epoxide formation, the genesis of **5** could be rationalized in terms of a nucleophilic displacement via a C-12 alkoxide on an activated C-11 species as described in ref 1. The implication is that this is S_N2 in nature; however, we feel this is unlikely on the grounds that the diol is really a "cis" diol. If epoxide formation results via nucleophilic substitution, we view it more likely an S_N1-type process. In any event, we do not observe epoxide formation.

Registry No. **1**, 40554-80-1; **2**, 58781-37-6; tetramethylguanidine, 80-70-6.