The Action of Bentonitic Earth on Natural Product Epoxides (1)

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The ring opening of the epoxide group in the epoxiguaianolides by commercially available bentonitic earth produces specifically the *trans* diol in good yield under mild conditions.

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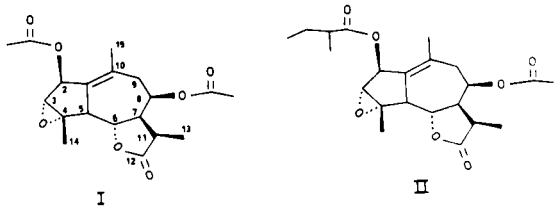
Several naturally occurring sesquiterpene lactones possessing epoxide substituents at specific sites in the carboxylic framework have been reported in recent years (2). The specific ring opening reactions of the epoxide groups in these lactones are particularly difficult and give low yields because nucleophilic reagents often affect the other functional groups present in the molecule. In most cases, the regioselectivity and stereospecificity of the reactions generating the diols from the epoxides, are controlled by the other functional groups commonly present in the molecule (3).

We wish to communicate the advantage of using bentonitic earth (Tonsil Optimum Extra) (4) for the formation of glycols from natural products containing an oxirane ring.

Using benzene as a solvent, Tonsil opens the 3,4-epoxisesquiterpene lactones I and II (5) (Figure 1) regioselectively and stereospecifically yielding the *vicinal trans* diols, III and IV (Figure 2).

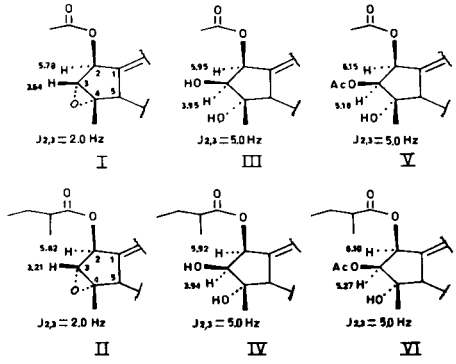


I II

FIGURE 1

The reagent attacks the less substituted carbon atom as is observed when the ring opening reaction is performed under normal S_{N_2} conditions (6). The other functional groups attached to these molecules are not affected by the Tonsil under our reaction conditions.

The stereochemical assignments of the generated diols are based on chemical shifts and coupling constants of protons affected by the reaction group transformation (7). Thus the observed $J_{2,3} = 5.0$ Hz in derivatives III to VI is consistent with values reported for *cis* analogous protons of related polyhydroxylated sesquiterpene lactones (8). The relative orientation of the new group at C-3 can be deduced as β from the above coupling constant. The *trans* relationship between the adjacent α hydroxyl group at C-4 in III and IV is supported by the very small shift observed for the C-14 methyl protons compared with the same methyl group signals in the original epoxides I and II. Also chemical shift values reported for protons of β methyl at C-4 bearing a hydroxyl group on the same carbon (9) are very similar to those shown in Figure 2.



I III V

II IV VI

FIGURE 2

EXPERIMENTAL

Epoxiguaianolides I and II were isolated from *Stevia serrata Robinson* following the method previously described (4).

Glycol III.

To a suspension of 5 g of Tonsil Optimum Extra in 20 ml of anhydrous benzene was added 125 mg of I and the mixture stirred for 70 hours at room temperature. The reaction was filtered and the solid washed with acetone. Evaporation of the organic fractions afforded a gum which was purified by preparative silica tlc (ethyl acetate/hexane, 3:4); 90 mg, 72% of pure glycol III was obtained after acetone/hexane crystallization mp 199-200°; $[\alpha]_D$ -77.27° (0.10, methanol); ir (chloroform): 3450, 1140 and 1085 cm^{-1} (OH), 1770 (C=O lactone), 1735 (C=O acetate); nmr (deuteriochloroform): δ ppm downfield from TMS, (multiplicity of signal designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet), 2.75 (2H, s, OH two exchangeable hydroxyl protons); 5.95 (1H, m, C-2), 5.27 (1H, d, C-8), 4.70 (1H, t, C-6), 3.95 (1H, d, C-3), 2.1 (3H, s, C-2 acetate), 2.03 (3H, s, C-8 acetate), 1.65 (3H, m, Me-15), 1.57 (3H, s, Me-14), 1.18 (3H, d, Me-13); ms: m/z M^+ 382, base peak 262 (M^+ -AcOH-AcOH); uv (ethanol): λ max 212 nm (ϵ 4976).

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Anal. Calcd. for $C_{19}H_{26}O_8$: C, 59.68; H, 6.80; O, 33.50. Found: C, 59.36; H, 6.89; O, 33.43.

Acetylation of III.

A solution of III (118 mg) in pyridine (0.5 ml) was treated with acetic anhydride (5 ml) for 18 hours at 25° followed by normal work-up, to give V, 128 mg, 98% yield, mp 235-238°; $[\alpha]_D$ -118.86° (0.12 methanol); ir (chloroform): 3460 and 1140 cm^{-1} (OH) 1775 (C=O lactone), 1740 (C=O acetate); nmr (deuteriochloroform): 2.71 (1H, s, OH exchangeable hydroxyl proton), 6.15 (1H, m, C-2), 5.31 (1H, d, C-8), 4.76 (1H, t, C-6), 5.18 (1H, d, C-3), 2.08 (3H, s, C-2 acetate), 2.06 (3H, s, C-3 acetate), 2.0 (3H, s, C-8 acetate), 1.65 (3H, m, Me-15), 1.52 (3H, s, Me-14); 1.18 (3H, d, Me-13); ms: m/z M^+ 424; base peak m/z 244 (M^+ -Ac OH-Ac OH-AcOH); uv (ethanol): λ max 210 nm (ε 6228).

Anal. Calcd. for $C_{21}H_{28}O_9$: C, 59.43; H, 6.60; O, 33.96. Found: C, 59.47; H, 6.59; O, 33.84.

Glycol IV.

A 185 mg sample of II was stirred with 7 g of Tonsil in 20 ml anhydrous benzene for 110 hours. The reaction mixture was then filtered and the Tonsil washed with acetone. Evaporation of the organic portion yielded glycol IV which was crystallized from dichloromethane/hexane, 59% yield, 110 mg, mp 169.5-171°; $[\alpha]_D$ -56.96 (0.13 methanol); ir (chloroform): 3450, 1150 and 1090 cm^{-1}, (-OH and C-O), 1775 (C=O, lactone), 1730 (C=O, alkyl esters); nmr (deuteriochloroform): 3.16 ppm (2H, s, OH two exchangeable hydroxyl protons), 5.92 (1H, m, C-2), 5.32 (1H, d, C-8), 4.71 (1H, t, C-6), 3.94 (1H, d, C-3), 2.03 (3H, s, C-8 acetate), 1.65 (3H, m, Me-15), 1.56 (3H, s, Me-14), 1.18 (3H, d, Me-isovalerate ester), 1.18 (3H, d, Me-13), 0.9 (3H, t, Me-isovalerate ester); ms: m/z M^+ 424, base peak m/z 57 (C_4H_9 ion); uv (ethanol): λ max 213 nm (ε 4486).

Anal. Calcd. for $C_{22}H_{32}O_8$: C, 62.26; H,7.54; O, 30.18. Found: C, 62.18; H, 7.63; O, 29.92.

Acetylation of IV.

Treatment of a solution of glycol IV (120 mg) in pyridine (0.6 ml) with acetic anhydride (5 ml) for 18 hours at room temperature, followed by normal work-up afforded acetate VI which, after crystallization from chloroform/hexane, was obtained in 96% yield, 126 mg, mp 165-167°; $[\alpha]_D$ -85.55°; ir (chloroform): 3450 cm^{-1} (OH), 1148 (C-O), 1770 (C=O, lactone), 1735 (C=O, alkyl esters); nmr (deuteriochloroform): 2.56 ppm (1H, s, OH one exchangeable hydroxyl proton), 6.14 (1H, m, C-2), 5.3 (1H, d, C-8), 5.27 (1H, d, C-3), 4.73 (1H, t, C-6); 2.07 (3H, s, C-8 acetate); 2.06 (3H, s, C-3 acetate), 1.64 (3H, m, Me-15), 1.52 (3H, s, Me-14), 1.2 (3H, d, Me-13), 1.1 (3H, d, Me isovalerate ester), 0.91 (3H, t, Me isovalerate ester); ms: m/z M^+ 466, base peak m/z 43 (C_2H_3O); uv (ethanol) λ max 210 nm (ε 6563).

Anal. Calcd. for $C_{24}H_{34}O_9$: C, 61.80; H, 7.29; O, 30.90. Found: C, 61.67; H, 7.27; O, 30.85.

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REFERENCES AND NOTES

(1) Contribution No. 532 from Instituto de Quimica, U.N.A.M.

(2) L. A. Macaira, M. Garcia and J. A. Rabi, *J. Org. Chem.*, **42**, 4207 (1977); A. G. Gonzalez, J. Bermejo, J. L. Breton, G. M. Massanet, B. Dominguez and J. M. Amaro, *J. Chem. Soc., Perkin Trans. I*, 1663 (1976); B. Mompon and R. Toubiana, *Tetrahedron*, **33**, 2199 (1977); H. Furakawa, M. Itoigawa, N. Kumagai, K. Ito, A. T. McPhail and K. D. Onan, *Chem. Pharm. Bull.*, **26**, 1335 (1978); W. Herz, R. R. Murari and S. V. Govindan, *Photochemistry*, **18**, 1337 (1979).

(3) Recently, Posner, *et al.*, found that alumina catalyzes the opening of a variety of epoxides; G. H. Posner and D. Z. Rogers, *J. Am. Chem. Soc.*, **99**, 8208 (1977); G. H. Posner, *Angew. Chem., Int. Ed. Engl.*, **17**, 487 (1978) and refereneces therein.

(4) Tonsil is a bentonitic earth widely used in the industry, mainly as a filter aid and decoloring agent. The material employed consisted of: SiO_2 (72.5%), Al_2O_3 (13.0%), Fe_2O_3 (5.0%), MgO (1.5%), CaO (0.8%), moisture (8.5%) with *p*H 3.0.

(5) M. Salmón, E. Diaz and A. Ortega, *Rev. Latinoam. Quim.*, **8**, 172 (1977); M. Salmón, E. Diaz and A. Ortega, *J. Org. Chem.*, **38**, 1759 (1973).

(6) H. O. House, "Modern Synthetic Reactions", W. A. Benjamin Inc., New York 1965, Chapter 5.

(7) See reference (4) and experimental section for nmr assignment of signals.

(8) S. M. Kupchan, J. E. Kelsey, M. Maruyama, J. M. Cassady, J. C. Hemingway and J. R. Knox, *J. Org. Chem.*, **34**, 3876 (1969); H. Herz S. V. Govindan, M. W. Bierner and J. F. Blound, *ibid.*, **45**, 493 (1980).

(9) F. Shafizadeh and N. R. Bhadanene, *ibid.*, **37**, 3168 (1972); F. Hamada, T. Ohta and S. Nozoe, *Heterocycles*, **14**, 429 (1980).