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THE STRUCTURE OF BARTEMIDIOLIDE, A CLERODANE-TYPE DITERPENE FROM *BACCHARIS ARTEMISIOIDES*

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Key Word Index—*Baccharis artemisioides*; Compositae; diterpene; clerodane; bartemidiolide; X-ray analysis.

Abstract—The structure and stereochemistry of a clerodane-type diterpene from *Baccharis artemisioides* which we have named bartemidiolide, 15,16-3α,4α-diepoxy-*trans*-cleroda-13(16),14-diene-20,12*S*-19,2|β|-diolide, have been determined by X-ray crystallographic analysis and spectroscopic data.

INTRODUCTION

A number of species of the large American genus *Baccharis* are known to be poisonous and are still used in folk medicine [1]. We have previously reported the isolation of hawtriwaic acid and of two new clerodanes, namely bacrispine and 1-deoxybacrispine, from *B. crispa*, a species known to possess medicinal properties [2, 3]. The labdane batudioic acid and the clerodane tucumanoic acid were isolated from *B. tucumanensis* [4, 5]. Furthermore, from *B. articulata* the clerodane barticulidiol has been isolated [6]. We wish to report now the isolation from *B. artemisioides* H. and A. of a new clerodane type compound named bartemidiolide (**1**), the structure of which was determined by using X-ray single crystal analysis.

RESULTS AND DISCUSSION

Bartemidiolide (**1**), $C_{20}H_{22}O_6$ (M^+358), is a furanoditerpene with two lactone rings. Appropriate crystals of **1** for X-ray analysis were obtained from methylene chloride solution by slow evaporation; space group $P2_12_12_1$ orthorombic, $a = 6.981$ (0.001), $b = 10.571$ (0.001); $c = 23.793$ (0.001) Å, and $Z = 4$. The structure was solved by direct methods and refined using 2040 unique reflections with $F_0 > 3\sigma$ (F_c). The non-hydrogen atoms were treated with anisotropic temperature factors. All hydrogens were found from a difference Fourier map and refined with isotropic temperature factors. Full matrix least-squares refinement converged to $R = 0.03$. The final difference Fourier map revealed only randomly distributed electron density.

A computer generated stereoscopic view of the X-ray model is presented in Fig. 1. A characteristic feature of this compound is the δ lactone ring coming across ring A from C-2 to C-5. Ring A itself assumes a clear boat shape H-10 being α-axial. Ring B has a chair conformation with C-10 below the plane and C-7 above it. The plane of the γ-lactone ring is perpendicular to that of ring B, whereas the furan ring is flat and perpendicular to the ring of the γ-lactone.

With this structure in hand, the ^{1}H NMR spectrum was completely resolved. The secondary Me-17 group gives rise to a doublet, $J = 6.7$, at δ 1.10 and the tertiary Me-18 a singlet at δ 1.34. By irradiating the former signal, the axial αH-8 was influenced, thereby disclosing its location as being a wide multiplet centred at δ 1.6. Decoupling H-8 disclosed the signal of H-7 at δ 1.98, which was related to an α-axial stereochemistry due to its wider *W*1/2 shape. This wider shape is explained by the occurrence of two axial–axial couplings of H-6 with H-7 and H-7 with H-8, and of the two geminal H-7 protons coupling. The positions of these values were assigned using 2D techniques. The epoxidic H-3 was assigned the signal of δ 3.46, doublet of $J = 4.5$, which is coupled with H-2 the signal of which appears at δ 4.87 as a triplet of doublets $J = 4.5$, 4.5, 1.5. The two H-1 signals were shown by 2D measurements to be at δ 1.51 and 2.18 (*ddd*). The geminal coupling constant for H-1, $J = 11.5$, was disclosed when the signal of H-10 (at δ 2.3) was irradiated producing a double doublet for H-1, $J = 11.5$, 4.5. From the decoupling measurements one can derive that the signal of H-1 at δ 1.51 is coupled to H-2 with $J = 4.5$, whereas the second H-1 at δ 2.18 is coupled to the same proton with $J = 1.5$.

The furan ring protons have their signals at δ 6.36 for H-14, double doublet of $J = 2$ and 1, the former being due to coupling with the vicinal H-15, the latter with H-16. This proton has its signal at δ 7.44 as a narrow doublet of $J = 1$. Furthermore, H-15 appears as a doublet of $J = 2.0$ at δ 7.33.

The γ-lactone ring has three protons to be accounted for. H-12 has its signal at δ 5.38 *dd* of $J = 8.0$, 8.0 appearing as a triplet. The two H-11s which appear within a complex signal pattern were identified using decoupling experiments together with a simple 2D proton–proton technique. βH-11 is at δ 2.4 *dd* of $J = 14.0$ and 8.0. αH-11 is at δ 2.25 with similar *J* values.

The ^{13}C NMR assignments for the bartemidiolide structure are given in Table 1, they are based on the chemical shifts and the multiplicities observed in the offset decoupled spectra and supported by the data compiled and given in ref [7].

EXPERIMENTAL

Mps: uncorr; analytical TLC: silica gel F_{254}; ^{1}H and ^{13}C NMR: 270 MHz and 22.63 MHz respectively in the Fourier

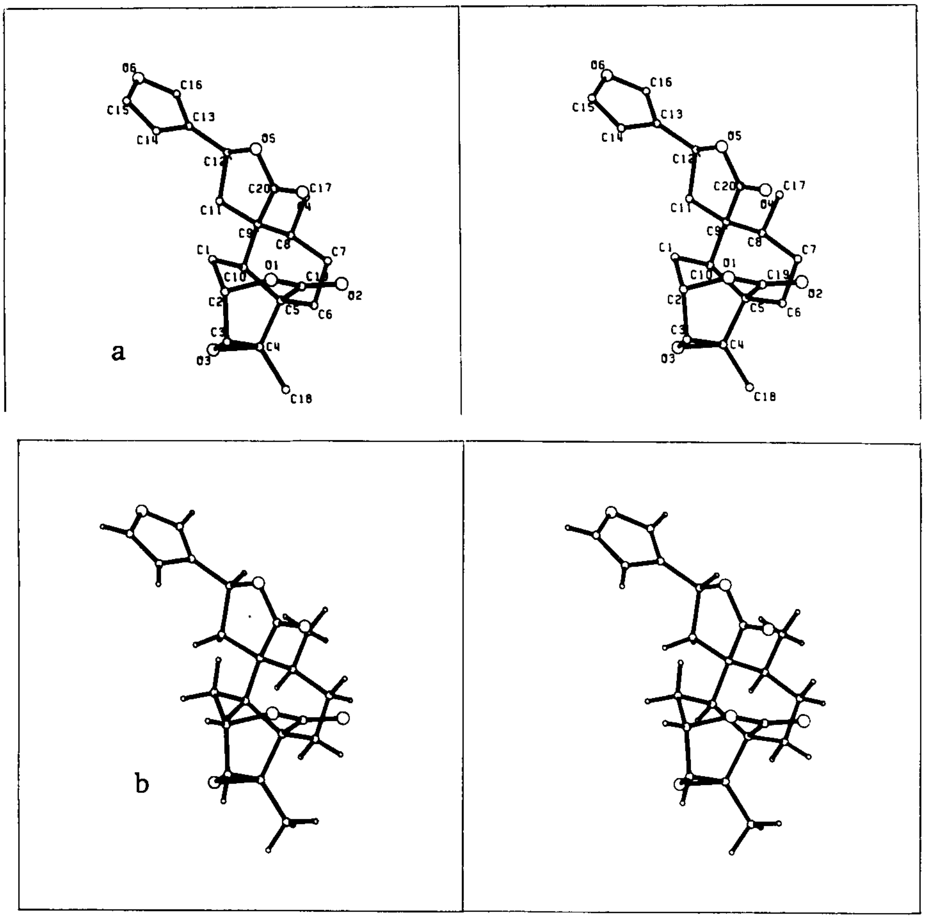


Fig. 1. Stereoscopic view of bartemidiolide (**1**): (a) with numbering; (b) with hydrogens.

Table 1. ^{13}C NMR spectral data for compound **1**

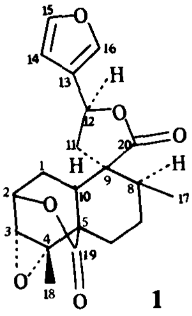
C	δ	C	δ
1	26.4 t^a	11	41.9 t
2	75.5 d	12	71.8 d
3	59.9 d	13	124.8 s
4	63.5 s	14	107.8 d
5	47.0 s	15	143.9 d
6	26.8 t^a	16	139.5 d
7	29.3 t	17	17.2 q^c
8	40.9 d^b	18	16.0 q^c
9	53.6 s	19	173.0 s
10	39.9 d^b	20	176.2 s

^{a,b,c}Interchangeable.

transform mode, in CDCl$_3$, TMS as int. standard. Assignment of the carbon spectrum was aided by using data provided in ref. [7, 8] and by single frequency off-resonance decoupled spectra which afforded signal multiplicities. IR: KBr. X-ray single crystal analysis was made using 3D intensity data, collected on a computer controlled Enraf-Nonius (CAD-4) diffractometer (CuKα = 1.5418 Å) by ω-2θ technique ($\theta < 77°$) at room temp. The crystallographic data, bond lengths, bond angles and dihedral angles are available as supplementary material.

Isolation procedure. Air-dried, finely ground aerial parts of *B. artemisioides* H. and A. (4.65 kg) collected near El Durazno Alto, San Luis, Argentina and classified by Ing. David L. Anderson (voucher specimen bearing flowers deposited at the Herbario de la Universidad Nacional de San Luis, No. 2907 INTA V.M.) were extracted twice with CHCl$_3$. The solvent was evapd under red. pres. the residue (580 g) taken up in MeOH which after the addition of water (10, 20 and 30%) was partitioned between *n*-hexane, CCl$_4$ and CHCl$_3$, respectively. The CHCl$_3$ solution was evapd (red. pres.) and the residue (186 g) chromatographed on silica gel 60 H, using C$_6$H$_6$ and different mixtures of C$_6$H$_6$–EtOAc: the combination 9:1 yielded compound **1** (980 mg).

Bartemidiolide (**1**). Mp. 224–225° (from MeOH), $[\alpha]_D^{25}$ +84.4° (CHCl$_3$ *c* 0.7); IR ν_{max}cm^{-1} 3150, 3080, (epoxide), 1760 (γ-lactone), 1750 (δ-lactone), 1500, 1450 (C=C), 1270 (epoxide), 1050, 860 (C=C), 830 (epoxide), 750; MS (HR) *m/z* (rel. int.): 314.153 [M $-$ CO$_2$]$^+$ (27), 290.978 [M $-$ C$_4$H$_3$O (cleavage of bond C-12 to C-13)]$^+$ (2.0), 299.114 (5.8), 247.127 [M $-$ CO$_2$ $-$ C$_4$H$_3$O]$^+$ (2.5), 266.961 (4.2), 220.108 [M $-$ C$_7$H$_6$O$_3$]$^+$ (cleavage of bonds C-9 to C-11 and to C-20) (46.0), 187.091 (11.5), 177.088 (13.6), 175.106 (42.6), 161.099 (20.7), 159.087 (18.3), 133.029 (19.6), 123.092 (44.0), 67.054 [C$_4$H$_3$O (furan)]$^+$ (22.6), MW [M]$^+$ 358.131, C$_{20}$H$_{22}$O$_6$ requires: 358.141.



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