Journal of Natural Products
Vol. 51, No. 1, pp. 155-157, Jan-Feb 1988

15α-HYDROXY-β-AMYRIN AND PATAGONIC ACID FROM *BACCHARIS MAGELLANICA* AND *BACCHARIS PATAGONICA*

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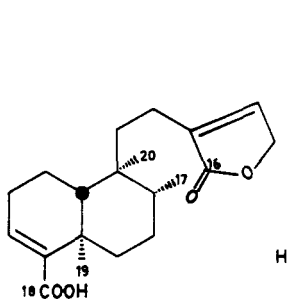
In a continuation of our phytochemical studies on the American genus *Baccharis* (Asteraceae) (1), we have examined the constituents of *Baccharis magellanica* Lam. and *Baccharis patagonica* Hook & Arn. from southern Chile. In addition to triterpenoids and aromatic compounds of common occurrence in the genus, a new neoclerodane diterpenoid **1** and a rare oleanane derivative **2** were isolated. Previous work on *B. magellanica* and *B. patagonica* from Argentina also revealed clerodanes but of different structures (2).

The combined uv and ir data of compound **1** indicated the presence of an α,β-unsaturated-γ-lactone and an α,β-unsaturated carbonyl group (λ max 212 nm, ε 8012, and absorptions at 1750 and 1685 cm^{-1}, respectively). An intense and broad absorption centered at 2955 cm^{-1} suggested the presence of a carboxylic group. The ^{1}H-nmr spectrum of **1** exhibited typical signals for a tricyclic clerodane carbon skeleton: two tertiary and one secondary methyl groups, together with two olefinic protons, one of them (δ 7.11) characteristic of an α-substituted γ-butenolide (1,3) and the other (δ 6.87) corresponding to the remaining α,β-unsaturated acid (a variable signal at δ 8.0-9.0 in the 60 MHz ^{1}H-nmr spectrum of **1** corroborated the carboxyl group). The structure depicted in **1** was in agreement with these data and was fully corroborated by the ^{13}C-nmr spectral data. The ^{13}C-nmr data also defined the relative stereochemistry at C-5 and C-10 owing to the absorption of the C-19 angular methyl carbon at δ 20.7, indicative of a *trans*-AB junction (4). The relative configuration of carbons 8 and 9 was determined by comparison of the δ values of the C-17 and C-20 methyl groups with those of other closely related clerodane diterpenes (5,6). The mass spectrum of **1** did not exhibit a molecular ion or ions corresponding to loss of CO_2H or CO_2, but it did show a prominent signal at $[M-H_2O]^+$ in a similar fashion to other diterpenic acids of very close structure (7).

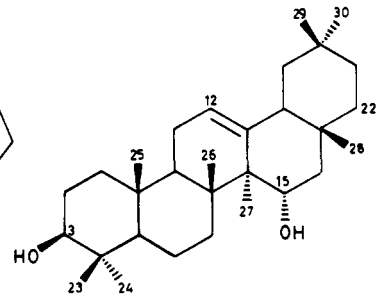
The negative molecular rotation of **1** suggests a neoclerodane absolute configuration (8) in agreement with those of other clerodane diterpenoids of known absolute configuration isolated from *Baccharis* species. Therefore, **1** was assigned as neocleroda-3,13-diene-15,16-olide-18-oic acid, for which we suggest the trivial name patagonic acid. Clerodane diterpenoids incorporating an α-substituted γ-butenolide unit are far less common than β-substituted analogs, and they are readily distinguished from each other because of the different absorptions of their β and α protons, respectively (1,3).

The ^{1}H-nmr of compound **2** $[M]^+$ 442) exhibited eight tertiary methyl groups, one olefinic proton, and two secondary equatorial hydroxyl groups, suggesting a triterpenoid with a Δ^{12}-oleanene skeleton. This assumption was supported by its mass spectrum, which showed a base peak at *m/z* 234, a characteristic retro-Diels-Alder fragment of Δ^{12}-oleanenes (9). Other prominent peaks at *m/z* 216 ($234-H_2O$) and 201 ($216-Me$) [ion **A**] indicated that one of the hydroxyl groups in **2** was located in ring D or E, most likely at C-15 or C-16.

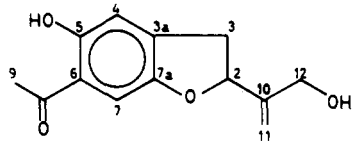
The ^{13}C-nmr spectrum of **2** was most informative because it not only confirmed the stereostructure shown in **2**, but it also ruled out another likely alternative, namely maniladiol, a 3β,16β-dihydroxy-Δ^{12}-oleanene recently iso-



1



2



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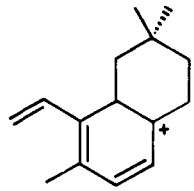

A

lated from *Baccharis heterophylla* and *Baccharis vaccinoides* of Mexican origin (10). A comparison of the ^{13}C-nmr spectra of β-amyrin (11) and compound **2** showed the expected downfield shifts for the absorptions due to C-14, C-15, and C-16, and an upfield shift (5.4 ppm) for the C-27 methyl group due to the γ-effect exerted by the α-oriented hydroxyl group at C-15. [In maniladiol, the β-hydroxyl group at C-16 shifts the C-22 methylene 7.0 ppm upfield as compared to β-amyrin (12).] Thus, compound **2** corresponds to 3β,15α-dihydroxyolean-12-ene or 15α-hydroxy-β-amyrin. This compound has previously been prepared synthetically from taraxerone (13). However, to our knowledge this is the first report of compound **2** as a natural substance.

Other compounds isolated from *B. patagonica* and *B. magellanica* in this study include the triterpenoids *Baccharis* oxide, epifriedelinol, friedelin, erythrodiol, and oleanolic acid, the sterol chondillasterol, the flavonoids acacetin and hispidulin, the coumarin scopoletin, *p*-hydroxyacetophenone, and the dihydrobenzofurane derivative **3**, 5-hydroxy-6-acetyl-2-(1-hydroxy-methylvinyl)-2,3-dihydrobenzofuran (14). These compounds were identified by comparison of their physical and spectral data with published values. The hitherto unreported ^{13}C-nmr spectrum of **3** is included in the Experimental section.

EXPERIMENTAL

PLANT MATERIALS.—*B. magellanica* was collected in Icalma (IX Región) in December and was identified by M. Mahú (Facultad de Ciencias, Universidad de Chile). *B. patagonica* was collected in Punta Arenas (XII Región) in January and was identified by E. Pisano (Universidad de Magallanes). Voucher specimens are kept at the private herbaria of Professors Mahú and Pisano.

EXTRACTION AND ISOLATION.—Aerial parts of *B. magellanica* (1.60 kg) and *B. patagonica* (2.82 kg) were extracted and worked up accord-

ing to the procedure already described (1). Aerial parts of *B. patagonica* (2.82 kg) afforded 60 mg *Baccharis* oxide, 20 mg epifriedelinol, 10 mg friedelin, 17 mg erythrodiol, 10 g oleanolic acid, 27 mg chondrillasterol, 80 mg acacetin, 60 mg scopoletin, 130 mg compound **1**, and 30 mg of the dihydrobenzofuran derivative **3**. Aerial parts of *B. magellanica* (1.60 kg) afforded 400 mg compound **2**, 220 mg hispidulin, 40 mg scopoletin, 35 mg *p*-hydroxyacetophenone, and 40 mg of compound **3**.

Patagonic acid [**1**].—Compound **1**, 130 mg, mp 100–103°, $[\alpha]_D$ −65.9° (c=2.65, $CHCl_3$); uv λ max (EtOH) 212 nm (ε 8062); ir ν max ($CHCl_3$) 3300–2700 (br), 1750, 1675, 1620, 825 cm^{-1}; ms (70 eV) *m/z* (rel. int.) 314 $[M-H_2O]^+$ (64), 299 $[314-Me]^+$ (4), 271 (7), 203 $[314-$side chain$]^+$ (16), 175 $[203-CO]^+$ (19), 153 (24), 125 (27), 105 (27), 93 (26), 87 (62), 84 (100); ^1H nmr (200 MHz, $CDCl_3$) δ 0.78 (s, 3H, H-20), 0.83 (d, 3H, J=6, H-17), 1.25 (s, 3H, H-19), 4.78 (d, 2H, J=1.4, H-15), 6.87 (t, 1H, J=3.7, H-3), 7.12 (t, 1H, J=1.4, H-14), 8.10 (bs, 1H, COOH, 60 MHz, $CDCl_3$); ^{13}C nmr (50 MHz, $CDCl_3$) δ 17.63 (t, C-1), 27.44 (t, C-2), 140.21 (d, C-3), 141.62 (s, C-4), 37.80 (s, C-5), 36.02 (t, C-6), 27.59 (t, C-7), 36.53 (d, C-8), 39.01 (s, C-9), 46.96 (d, C-10), 36.31 (t, C-11), 19.29 (t, C-12), 135.19 (s, C-13), 143.63 (d, C-14), 70.22 (t, C-15), 174.35 (s, C-16), 16.01 (q, C-17), 174.42 (s, C-18), 20.71 (q, C-19), 18.29 (q, C-20).

15α-Hydroxy-β-amyrin [**2**].—Compound **2**, 400 mg, mp 230–232° (crystallized from MeOH/H_2O), $[\alpha]^{20}_D$ +68.4° (c=1.12, $CHCl_3$); ir λ max (KBr) 3300, 2950, 1440, 1350 cm^{-1}; ms (70 eV) *m/z* 442 $[M]^+$ (7), 424 $[M-H_2O]^+$ (8), 406 $[M-2H_2O]^+$ (7), 234 $[M-C_{14}H_{24}O]^+$ (100), 216 $[M-C_{14}H_{26}O_2]^+$ (50), 208 $[M-C_{16}H_{26}O]^+$ (6), 201 $[M-C_{15}H_{29}O_2]^+$ (34); ^1H nmr (200 MHz, $CDCl_3$) δ 0.78 (s, $2CH_3$), 0.87, 0.89, 0.92, 0.97, 0.98, 1.20 (s, $6CH_3$), 3.20 (dd, J=5.40, 10.3, H-3), 4.17 (dd, J=5.0, 11.4, H-15), 5.23 (t, J=3.6, H-12); ^{13}C nmr (50 MHz, $CDCl_3$) δ 38.8 (t, C-1), 27.4 (t, C-2), 79.1 (d, C-3), 38.9 (s, C-4), 55.4 (d, C-5), 18.5 (t, C-6), 31.1 (t, C-7), 40.1 (s, C-8), 47.0 (d, C-9), 37.5 (s, C-10), 23.7 (t, C-11), 122.5 (d, C-12), 143.7 (s, C-13), 44.0 (s, C-14), 66.2 (d, C-15), 37.1 (t, C-16), 32.8 (s, C-17), 49.3 (d, C-18), 46.1 (t, C-19), 30.7 (s, C-20), 33.4 (t, C-21), 35.8 (t, C-22), 28.3 (q, C-23), 15.7 (q, C-24), 15.7 (q, C-25), 17.0 (q, C-26), 21.6 (q, C-27), 27.3 (q, C-28), 34.3 (q, C-29), 24.1 (q, C-30).

5-Hydroxy-6-acetyl-2-(1-hydroxymethylvinyl)-2,3-dihydrobenzofuran [**3**].—^{13}C nmr (50 MHz, $CDCl_3$) 83.73 (d, C-2), 36.01 (t, C-3), 137.62 (s, C-3a), 108.25 (d, C-4), 158.32 (s, C-5), 118.15 (s, C-6), 114.79 (d, C-7), 151.77 (s, C-7a), 181.44 (s, C-8), 26.87 (q, C-9), 108.25 (s, C-10), 112.93 (t, C-11), 63.25 (t, C-12).

ACKNOWLEDGMENTS

We thank Professor D.B. MacLean, McMaster University, Canada, for nmr and ms measurements. This research was supported by DIB (Universidad de Chile), FONDECYT, and the Organization of American States.

LITERATURE CITED

1. A. Givovich, A. San-Martín, and M. Castillo, *Phytochemistry*, **25**, 2829 (1986).
2. C. Zdero, F. Bohlmann, R.M. King, and H. Robinson, *Phytochemistry*, **25**, 2841 (1986).
3. F. Bohlmann and U. Fritz, *Phytochemistry*, **17**, 1769 (1978).
4. J.L. Cough, J.P. Guthrie, and J.B. Stothers, *J. Chem. Soc., Chem. Commun.*, 979 (1972).
5. G. Savona, B. Bruno, F. Piozzi, O. Servettaz, and B. Rodriguez, *Phytochemistry*, **23**, 849 (1984).
6. H. Wagner, R. Seitz, H. Lotter, and W. Herz, *J. Org. Chem.*, **13**, 3339 (1978).
7. U.C. Pandey, A.K. Singhal, N.B. Bama, R.P. Sharma, J.N. Barnah, K. Watanabe, P. Kulanthaivel, and W. Herz, *Phytochemistry*, **23**, 391 (1984).
8. D. Rogers, G.G. Dunal, D.J. Williams, S.V. Ley, G.A. Sim, B.S. Joshi, and K.R. Rabindramath, *J. Chem. Soc., Chem. Commun.*, 97 (1979).
9. L. Ogunkoya, *Phytochemistry*, **20**, 121 (1981).
10. F.J. Arriaga-Giner, E. Wollenweber, I. Schober, P. Dostal, and S. Braun, *Phytochemistry*, **25**, 719 (1986).
11. S.A. Knight, *Org. Magn. Reson.*, **6**, 603 (1974).
12. H.C. Ling, M.L. King, M-H. Su, G.L. Chen, and C.T. Wang, *J. Chin. Chem. Soc. (Taipei)*, **28**, 95 (1981).
13. W.H. Hui and M.M. Li, *Phytochemistry*, **15**, 1313 (1976).
14. F. Bohlmann and C. Zdero, *Chem. Ber.*, **109**, 1450 (1976).

Received 2 June 1987