NEW SESQUITERPENES FROM *RZEDOWSKIA TOLANTONGUENSIS* (CELASTRACEAE)

Antonio G. González*, Isabel L. Bazzocchi, Angel G. Ravelo, and Javier G. Luis
Instituto Universitario de Química Orgánica, Universidad de La Laguna, Tenerife, Canary Islands, Spain
Xorge A. Domínguez
Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, México

Abstract-From the aerial part and root bark of Rzedowskia tolantonguensis, six dihydro-β-agarofurane-skeleton sesquiterpenes were isolated. Five were new and identified by spectroscopic methods and chemical reactions.

In the course of our study of Celastraceae species[1,2,3] six sesquiterpenes were isolated from the aerial part and root bark of Rzedowskia tolantonguensis[4] : 1α-benzoyloxy-6β,8β,9α,15-tetracetoxy-4β-hydroxydihydro-β-agarofuran(1), 1α-benzoyloxy-9α,15-diacetoxy-4β,6β,8β-trihydroxydihydro-β-agarofuran(4), 1α-benzoyloxy-6β,9α,15-triacetoxy-8-oxo-4β-hydroxydihydro-β-agarofuran(5), 1α-benzoyloxy-6β,9α,15-triacetoxy-4β,8β-dihydroxydihydro-β-agarofuran (6), and 1α,8β-dibenzoyloxy-9α,15-diacetoxy-4β,6β-dihydroxydihydro-β-agarofuran (7), all new, and 1α-benzoyloxy-6β,9β,15-triacetoxy-4β-hydroxydihydro-β-agarofuran (8)[5]. The structure of the five new sesquiterpenes was determined by spectroscopy and chemical reactions involving four of the five products.

Hydrolysis of (1) gave three substances, one of which was identical with natural product (4); (6) when acetylated, yielded (1) and when oxidized, (5).

Compound (1) was a crystalline solid, molecular formula $C_{30}H_{38}O_{12}$; ir showed absorptions of a hydroxyl group, an ester and aromatic ring; when acetylated at r.t. with acetic anhydride in pyridine, unaltered starting material was produced and the tertiary nature of the hydroxyl group thus demonstrated; ms showed fragments suggesting the presence of a benzoate at m/z 105 and an acetate at m/z 42; ^1H nmr confirms the presence of a benzoate at 7.88 and 7.47δ (5H, m) with the geminal proton centred at 5.25δ as a double doublet (J=3.8, 12.4Hz), the methyls of four acetates at 2.36, 2.10, 1.86 and 1.52δ as singlets with geminal protons at 4.63 δ

	R_1	R_2	R_3	R_4	R_5	R_6
(1)	OAc	H	OAc	OAc	H	OAc
(2)	OH	H	OAc	OAc	H	OAc
(3)	OH	H	OAc	OAc	H	OH
(4)	OH	H	OH	OAc	H	OAc
(5)	OAc	R_2 R_3 =O	R_2 R_3 =O	OAc	H	OAc
(6)	OAc	H	OH	OAc	H	OAC
(7)	OH	H	OBz	OAc	H	OAC
(8)	OAc	H	H	H	OAc	OAC

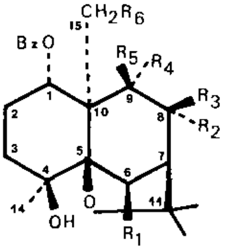

TABLE 1

	H_1	H_6	H_7	H_8	H_9	H_{15}	Ac_6	Ac_8	Ac_9	Ac_{15}
(1)	5.25dd J=3.8,12.4	6.52s	2.44d J=3.4	5.57dd J=3.4,10	6.00d J=10	4.63dd J_{AB}=13	2.10s	1.86s	1.52s	2.36s
(2)	5.27dd J=4,12	5.15d J=5.2	2.55d J=3	5.51dd J=3,10	6.05d J=10	4.64dd J_{AB}=12.7		1.87s	1.55s	2.31s
(3)	5.25dd J=4,12	5.19d J=5	2.57d J=3	5.48dd J=3,10	6.00d J=10	4.27dd J_{AB}=13		1.90s	1.58s	
(4)	5.26dd J=4,12	4.97d J=5	2.54d J=3	4.19dd J=3,10	5.85d J=10	4.65dd J_{AB}=13			1.44s	2.20s
(5)	5.37dd J=4,12.3	6.61s	2.96s		5.87s	4.67dd J_{AB}=13	2.12s		1.50s	2.05s
(6)	5.27dd J=3.7,12	6.34s	2.41d J=3	4.36dd J=3,10	5.84d J=10	4.67dd J_{AB}=13	2.11s		1.43s	2.28s
(7)	5.34dd J=4,12*	5.23d J=4.8	2.74d J=3	5.63dd J=3,10	6.25d J=10	4.68dd J_{AB}=12.7			1.52s	2.33s
(8)	5.38dd J=4,12	6.08s	2.50m		5.39d J=6	4.54dd J_{AB}=12	2.10s		1.56s	2.26s

^{1}HNMR 200 MHz, shift in δ , J in Hz.

Solvent, $CDCl_3$.

* partially overlapping with other signal.

as an AB system double doublet (J=13Hz), at 6.52δ as a singlet, as a double doublet at 5.57δ (J=3.4, 10Hz) and as a doublet at 6.00δ (J=10Hz). The benzoate group was sited on C-1α in view of the coupling constants and chemical shift of its geminal proton[6], the acetates were situated on C-6β, C-8α, C-9β and C-15 by double resonance studies and selective hydrolysis[7] leading to the derivatives (2), (3) and (4).
^{1}H nmr of (2) showed the proton on C-6 to have moved from 6.52δ to 5.15δ where it appeared as a doublet (J=5.2Hz) due to coupling with its hydroxyl proton and the disappearance of the acetate methyl at 2.10δ. ^{1}H nmr of (3) showed a shift of the AB hydroxy-methylene system from 4.63 to 4.27δ and the disappearance of the acetate methyl at 2.36δ so that the chemical shift of the acetate methyl on C-15 was established. Comparison of the ^{1}H nmr of (4) and (2) shows that the double doublet due to the proton on C-8 which had been centred at 5.51δ in (2) had moved to 4.19δ in (4) and the acetate methyl which appeared at 1.87δ in (2) is no longer to be seen in (4) so that this acetate group can be placed at C-8 and the signal that at 1.52δ in (1) may be assigned to the acetate methyl on C-9.

The stereochemistry of the sesquiterpenes was confirmed by an NOE experiment whereby in (4), the signal of the axial proton H-6 was irradiated, producing a considerable increase in the intensity of the signal at H-8 which, for a chair conformation for ring B, is only possible when there is 1,3-diaxial H6-H8 confrontation and thus established the β-equatorial position of the substituents on C-6 and C-8; the coupling constant (10Hz) between H-8 and H-9 indicates the trans-diaxial relationship between them and the acetoxy group on C-9 must therefore be α-equatorial.

Thus, the structure of (5) was determined with the carbonyl group on C-8 and the CD curve showed the expected positive Cotton effect. The structure of (6) was also established since it oxidizes to give (5).

^{1}H nmr of (7) shows two benzoate groups situated on 1α and 8β, by spectral comparison with the other products. (See Table 1)

Compound (8) proved identical to a sesquiterpene previously isolated from Orthosphenia mexicana[5] (Celastraceae).

EXPERIMENTAL

Mp's are uncorrected. Ir spectra were taken on a PE 681 spectrophotometer, ^{1}H nmr on a Bruker WP-200 SY (200MHz) (TMS as internal reference) and ms were recorded on a VG Micromass LTD-ZAB-2F and/or a HP 5930A at 70ev.

Plant Collection The plant was gathered in January 1981 in the State of Tamaulipas in northeastern México and a voucher specimen, No. 7853,is lodged with the Instituto Tecnológico y de Estudios Superiores de Monterrey,México.

Extraction and Isolation The aerial part of the plant was treated with MeOH to yield 25g of extract;n-hexane extraction of the root bark gave 34g. After repeated chromatography on silica gel,whith hexanes/ethyl acetate mixtures of increasing polarity as eluents,the following products were isolated: (1)(50mg), (4)(30mg), (5)(15mg), (6)(15mg), (7)(10mg) and (8)(15mg).

1α-Benzoyloxy-6β,8β,9α,15-tetracetoxy-4β-hydroxydihydro-β-agarofuran (1) mp 210-212°C (hexane-ethyl acetate); ir $\nu_{max}^{CHCl_3}$cm^{-1}: 3680, 3002, 2945, 2920, 2845, 1730, 1595, 1445,1380, 1365, 1335,1240, 1170, 1105,1085, 1035, 860; ^{1}H nmr(200MHz) δ:1.31 (3H, s), 1.52 (6H, s), 1.67 (3H, s), 1.86 (3H, s), 2.10 (3H, s), 2.36 (3H, s), 2.44 (1H, d, J=3.4Hz), 2.67 (1H, s), 4.45, 4.81 (2H, d_{AB}, J=13Hz), 5.25 (1H, dd,J=3.8Hz, J=12.4Hz), 5.57 (1H, dd,J=3.4Hz,J=10Hz), 6.00 (1H, d, J=10Hz), 6.52 (1H, s), 7.47 (3H, m), 7.88 (2H, m); ms m/z: 575 (M^+-15)(1), 530 (4), 488 (5), 470 (1), 428 (1), 246 (5), 164 (8), 149 (5), 105 (100). Calc. $C_{30}H_{38}O_{12}$: mol wt, 590.2399. Found: mol wt, 590.2363(High resolution ms).

A solution of (1) (34mg)(0.057mmol) in MeOH (4ml) was treated with $NaHCO_3$ 0.1M (2ml) and heated under reflux for 4 h. After work-up and chromatography, (2)(15mg), (3)(3mg) and (4)(5mg) were obtained.

1α-Benzoyloxy-8β,9α,15-triacetoxy-4β,6β-dihydroxydihydro-β-agarofuran (2) mp 186-188°C (hexane-ethyl acetate); ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3520, 3400, 3030, 2950, 1740, 1730, 1365, 1275, 1230, 1100, 1095, 1030, 960, 710; ^{1}H nmr (200MHz) δ: 1.55 (3H, s), 1.58 (3H, s), 1.62 (3H, s), 1.87 (3H, s), 2.31 (3H, s), 2.55 (1H, d, J=3Hz), 3.08 (1H,s) 4.37, 4.91 (2H, d_{AB}, J=12.7Hz), 5.15 (1H, d, J=5.2Hz), 5.35 (1H, d, J=5.2Hz, OH), 5.27 (1H, dd, J=4.0Hz,J=12.0Hz), 5.51 (1H, dd, J=3.0Hz,J=10.0Hz), 6.05(1H,d,J=10Hz), 7.47 (3H, m), 7.87 (2H, m); ms m/z: 533 (M^+-15) (1), 488 (5), 428 (1), 413 (1), 315 (1), 306 (2), 246 (6), 213 (1), 189 (20), 164 (61), 149 (35), 105 (77).

1α-Benzoyloxy-8β,9α-diacetoxy-4β,6β,15-trihydroxydihydro-β-agarofuran (3) amorphous powder;ir$\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3520, 3410, 2940, 2920, 2840, 1735, 1710, 1595, 1445, 1365, 1275, 1090, 1070, 1030, 960; ^{1}H nmr (200MHz)δ:1.58(3H,s),1.60(3H,s), 1.70(3H,s), 1.72 (3H, s), 1.90 (3H, s), 2.57 (1H, d, J=3.0Hz), 3.12 (1H, s), 4.18, 4.32 (2H,d_{AB}, J=13.0Hz), 5.19 (1H, d, J=5Hz), 5.37 (1H, d,J=5.0Hz,OH), 5.25 (1H, dd, J=4.0Hz, J=12.0Hz), 5.48 (1H, dd, J=3.0Hz,J=10.0Hz),6.00(1H,d,J=10Hz),7.47(3H,m),7.87(2H,m); ms m/z:

491 (M^+-15) (1), 488 (3), 446 (3), 413 (2), 366 (1), 324 (1), 306 (3), 279 (6), 246 (11), 234 (14), 189 (10), 164 (27), 149 (100), 105 (100).

1α-Benzoyloxy-9α,15-diacetoxy-4β,6β,8β-trihydroxydihydro-β-agarofuran (4) mp 278-281°C (hexane-ethyl acetate);ir$\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3520, 3400, 3020, 3000, 2940, 1740, 1730, 1600, 1365, 1275, 1230, 1045, 960, 860, 710; ^{1}H nmr (200MHz) δ: 1.44 (3H, s), 1.57 (3H, s), 1.58 (3H, s), 1.72 (3H, s), 2.20 (3H, s), 2.43(1H,d,J=4.8Hz), 2.54 (1H, d, J=3.0Hz), 3.07 (1H, s), 4.19 (1H, dd, J=3.0Hz,J=10.0Hz), 4.39, 4.92 (2H, d_{AB}, J=13.0Hz), 4.97 (1H, d, J=5.0Hz), 5.32 (1H, d, J=5.0Hz,OH), 5.26 (1H, dd, J=4.0Hz,J=12.0Hz), 5.85 (1H, d, J=10.0Hz), 7.48 (3H, m), 7.94 (2H, m); ms m/z : 491 (M^+-15) (2), 488 (2), 466 (1), 428 (1), 413 (1), 351 (2), 324 (3), 306 (1), 264 (2), 263 (2), 246 (5), 231 (4), 213 (6), 202 (8), 164 (24), 147 (5), 105 (100). Calc. $C_{25}H_{31}O_{10}$ (M^+-15): mol wt, 491.1914. Found: mol wt, 491.1900 (High resolution ms).

1α-Benzoyloxy-6β,9α,15-triacetoxy-8-oxo-4β-hidroxydihydro-β-agarofuran (5) mp 224 - 226°C (hexane/ethyl acetate); ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 3010, 2940, 2870, 1738, 1598, 1445, 1380, 1366, 1335, 1265, 1215, 1170, 1105, 1078, 1050, 1005, 965; ^{1}H nmr (200 MHz) δ: 1.37 (3H, s), 1.50 (3H, s), 1.58 (3H, s), 1.61 (3H, s), 2.05 (3H, s), 2.12 (3H, s), 2.96 (1H, s), 4.27, 5.05 (2H, d_{AB}, J=13.0Hz), 5.37 (1H, dd, J=4.0Hz,J=12.3 Hz), 5.87 (1H, s), 6.61 (1H, s), 7.50 (3H, m), 7.96 (2H, m); ms m/z : 546 (M^+) (2), 531 (1), 530 (2), 504 (6), 488 (5), 444 (10), 413 (6), 343 (9), 281 (18), 218 (42), 205 (33), 149 (98), 105 (100). Calc. $C_{28}H_{34}O_{11}$: mol wt, 546.2104. Found: mol wt, 546.2098 (High resolution ms).

1α-Benzoyloxy-6β,9α,15-triacetoxy-4β,8β-dihydroxydihydro-β-agarofuran (6) mp 142-145°C (hexane/ethyl acetate); ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3670, 3590, 3010, 3000, 2920, 2850, 1738, 1598, 1448, 1380, 1365, 1335, 1275, 1230, 1170, 1108, 1092, 1043, 965 ; ^{1}H nmr (200 MHz) δ: 1.30 (3H, s), 1.43 (3H, s), 1.52 (3H, s), 1.73 (3H, s), 2.11 (3H, s), 2.28 (3H, s), 2.41 (1H, d, J=3.0Hz), 2.73 (1H, s), 4.36 (1H, dd, J=3.0Hz,J=10.0Hz), 4.49, 4.86 (2H, d_{AB}, J=13.0Hz), 5.27 (1H, dd, J=3.7Hz,J=12.0Hz), 5.84 (1H, d, J=10.0Hz), 6.34 (1H, s), 7.50 (3H,m), 7.96 (2H, m); ms m/z : 533(M^+-15) (2), 530 (3), 515 (2), 488 (7), 470 (1), 428 (2), 413 (2), 384 (1), 366 (1), 351 (1), 324 (3), 306 (2),246 (7), 202 (9), 164 (25), 151 (13), 105 (100). Calc. $C_{27}H_{33}O_{11}$ (M^+-15): mol wt, 533.2022. Found : mol wt, 533.1996 (High resolution ms).

Acetylation of (6) 7mg (0.010mmol) of (6), treated with acetic anhydride in pyridine was extracted in the usual way to yield 6mg of (1).

Oxidation of (6) 4mg(0.007mmol) of (6) were treated with 2 drops of Jones'reagent to give 2.5mg of (5).

1α,8β-Dibenzoyloxy-9α,15-diacetoxy-4β,6β-dihydroxydihydro-β-agarofuran (7) mp 202-204ºC (benzene-ethyl acetate); ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 3300, 3020, 2930, 1735, 1725, 1598, 1448, 1365, 1310, 1280, 1230, 1105, 1065, 1025, 960, 945, 710; ^{1}H nmr(200MHz) δ: 1.52 (3H, s), 1.56 (3H, s), 1.63 (3H, s), 1.78 (3H, s), 2.23 (3H, s), 2.74 (1H, d, J=3Hz), 3.07 (1H, s), 4.41, 4.95 (2H, d_{AB}, J=12.7Hz), 5.23 (1H, d, J=4.8Hz), 5.36 (1H, d, J=4.8Hz, OH), 5.34 (1H, dd, J=4Hz)(partially overlapping with doublet at 5.36), 5.63 (1H, dd, J=3Hz, J=10Hz), 6.25(1H, d, J=10Hz), 7.39 (6H, m), 7.78 (2H, m), 7.88 (2H, m); ms m/z: 595 (M^+-15) (1), 592 (1), 579 (1), 550 (3), 534 (1), 488 (4), 458 (1), 428 (2), 413 (3), 306 (4), 246 (16), 202 (16), 164 (38), 149 (42), 105 (100). Calc. $C_{33}H_{36}O_{10}$ (M^+-18): mol wt, 592.2305. Found:mol wt,592.2304 (Hrms).

1α-Benzoyloxy-6β,9β,15-triacetoxy-4β-hydroxydihydro-β-agarofuran (8) mp 188-190ºC (benzene-ethyl acetate); ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3630, 3530, 3010, 2920, 1725, 1595, 1445, 1365, 1275, 1090; ^{1}H nmr (200MHz) δ: 1.31 (3H, s), 1.50 (3H, s), 1.53 (3H, s),1.55 (3H, s), 2.09 (3H, s), 2.24 (3H, s), 2.50 (1H, m), 4.44, 4.62 (2H, d_{AB}, J=12Hz), 5.38 (1H, dd, J=4Hz, J=12Hz), 5.39 (1H, d, J=6Hz), 6.07 (1H, s), 7.50 (3H, m), 8.02 (2H, m); ms m/z: 517 (M^+-15) (1), 490 (2), 472 (2), 430 (1), 412 (3), 350 (1), 308 (2), 293 (2), 290 (2), 267 (4), 248 (6), 202 (6), 159 (4), 127 (5), 105 (94). Calc. $C_{27}H_{33}O_{10}$ (M^+-15): mol wt, 517.2032. Found: mol wt, 517.2073 (Hrms).

ACKNOWLEDGEMENTS

This research has been subsidized by CAICYT Grant No. 0694-84 and by the AIETI Foundation.

REFERENCES

1 A.G. González, B.M. Fraga, C.M. González, A.G. Ravelo, E. Ferro, X.A. Domínguez, M.A. Martínez, J. Fayos, A. Perales and M.L. Rodríguez, Tetrahedron Letters, 1983, 24, 3033.

2 A.G. González, I.L. Bazzocchi, E.A. Ferro, A.G. Ravelo, J.G. Luis and M.A. Aguilar, Biochemical Systematics and Ecology (in press, ms 0811).

3 A.G. González, E.A. Ferro and A.G. Ravelo, Heterocycles, 1986, 24, 1295.

4 F. González-Medrano, Boletin de la Sociedad Botánica de Mexico, 1981, 41, 41.

5 A.G. González, C.M. González and A.G. Ravelo, Heterocycles, (submitted for publication).

6 C.R. Smith, Jr., R.W. Miller, D. Weisleder, W.K. Rohwedder, N. Eickman and J. Clardy, J. Org. Chem., 1976, 41, 3264.

7 R.L. Baxter, L. Crombie, D.J. Simmonds and D.A. Whiting, J.C.S. Perkin I, 1979, 12, 2972.

Received, 9th June, 1986