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A SESQUITERPENE DIKETONE FROM *LIPPIA INTEGRIFOLIA*

C. A. CATALÁN*, D. I. IGLESIAS, J. A. RETAMAR†, J. B. ITURRASPE†, G. H. DARTAYET‡ and E. G. GROS‡

Instituto de Química Orgánica, Facultad de Bioquímica-Química-Farmacia, Universidad de Tucumán, Ayacucho 482, Tucumán, Argentina; †IPNAYS, Santa Fe, Argentina; ‡Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, 1428 Buenos Aires, Argentina

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Key Word Index—*Lippia integrifolia*; Verbenaceae; sesquiterpene diketone; bicyclohumulendione.

Abstract—The leaves of *Lippia integrifolia* afforded a crystalline compound that was identified as a bicyclohumulendione by means of spectroscopic methods.

Continuing with studies on the genus *Lippia* [1–4], we have isolated from the essential oil of *Lippia integrifolia* (Griseb.) Hieron. a crystalline product, $C_{15}H_{24}O_2$ (MW 236.1764), for which structure **1** is proposed on the basis of the following properties. The molecular formula together with the IR bands at 1720 and 1688 cm^{-1} indicate the presence of a bicyclosesquiterpene diketone. There are no signals of olefinic protons in the 100 MHz ^{1}H NMR spectrum or olefinic carbon atoms in the ^{13}C NMR spectrum. A double doublet at δ0.64 in the 360 MHz ^{1}H NMR spectrum (Table 1) and bands at 3030 and 1020 cm^{-1} in the IR spectrum point to a cyclopropane ring that is conjugated to one of the carbonyl groups; this assumption is confirmed by UV absorptions at 288 and 208 nm [5]. The proton at δ0.64 is coupled to two protons, one of them appearing at δ1.34 as a double doublet while the other resonates at δ1.08 as a four-fold doublet. In the 360 MHz ^{1}H NMR spectrum the first two signals show a coupling constant of 3.6 Hz with each other indicating a geminal coupling of the cyclopropane protons [6] one of which is deshielded by the keto group. The proton at δ1.08 is coupled to a proton appearing as a broadened doublet at δ1.43 and to a second proton that appears at δ1.53 as a double doublet. A similar situation has been recently reported in the literature [7]. Further, the presence of a doublet at δ2.51 coupled to a broadened doublet at δ2.02 indicates the sequence $-CO-CH_2-$. This should be connected to a methylene group attached to the cyclopropane ring through a quarternary carbon atom because the signal at δ2.02 has a long range coupling of 1.3 Hz with the one located at δ1.43. The ^{1}H NMR spectrum further shows three methyl singlets and one methyl doublet (see Table 1) also confirmed by the fully decoupled and off-resonance ^{13}C NMR spectra. Both the ^{1}H and ^{13}C NMR spectra are in agreement with a bicyclohumulendione structure different from (+)-bicyclohumulenone [8] in having an additional keto group that produces deshielding of one of the methyl groups located at C-11. The methyl group at C-4 is α-oriented because: the proton attached to C-4 is coupled to the protons at C-3 with coupling constants of 11.7 and 4.0 Hz; of the resonance value of C-4 in the ^{13}C NMR spectrum; of the plausible formation of **1** from α-humulene in its conformation CC [9] as shown in Scheme 1.

The ^{13}C NMR and high resolution mass spectra are in agreement with the proposed structure. To our knowledge, compound **1** is the first bicyclohumulene derivative found in Verbenaceae.

Table 1. ^{1}H NMR spectral data of compound **1** (360 MHz, $CHCl_3$ as int. standard).

H No.	$CDCl_3$	C_6D_6
2α	2.29 *ddd*	1.75
2β	3.15 *ddd*	2.56
3α	2.25 *ddt*	2.38
3β	1.60 *dddd*	1.15
4	2.35 *ddq*	1.85
6α	2.51 *d*	2.11
6β	2.02 *br d*	1.56
7α	1.53 *dd*	1.84
7β	1.43 *br d*	1.32
8	1.08 *dddd*	0.73
9α	1.34 *dd*	1.49
9β	0.65 *dd*	0.36
12	1.46 *s*	1.29
13	0.92 *s*	0.71
14	1.18 *s*	1.00
15	0.98 *d*	0.93

J (Hz): 2α, 2β = −16.7; 2α, 3α = 7.9; 2α, 3β = 1.4; 2β, 3α = 1.2; 2β, 3β = 11.7; 3α, 3β = −13.2; 3α, 4 = 11.7; 3β, 4 = 4.0; 4, 15 = 6.6; 6α, 6β = −19.3; 6β, 7β = 1.6; 7α, 7β = −15.2; 7α, 8 = 11.4; 7β, 8 = 2.3; 9α, 8 = 7.2; 9β, 8 = 8.7; 9α, 9β = −3.6.

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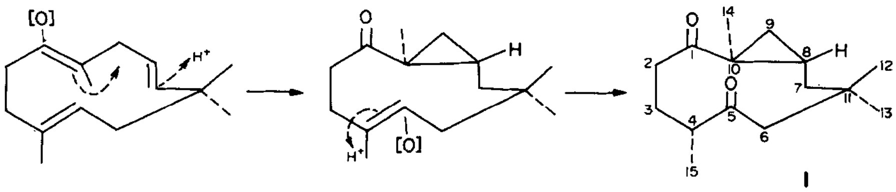
*Present address: Department of Chemistry, Stanford University, Stanford, California, U.S.A.



1

Scheme 1.

EXPERIMENTAL

General. ^{1}H NMR: 100 and 360 MHz; ^{13}C NMR: 25.2 MHz; single and double focused MS at 70 eV.

Plant material. Leaves of *L. integrifolia* were collected in Tucumán Province and a voucher specimen was deposited in the Lillo Institute, Tucumán.

Isolation of compound **1**. The leaves were air-dried and extracted as previously described [4]. Compound **1** was recrystallized several times from EtOH to give white needles, mp 183°, $[\alpha]_D^{20} - 29.1°$ ($CHCl_3$; *c* 9.6); UV λ_{max}^{EtOH} nm (ε): 288 (72), 208 (3500); IR ν_{max} cm^{-1}: 3030, 1720 (ketone), 1688 (cyclopropyl-conjugated ketone), 1020; ^{13}C NMR ($CDCl_3$–TMS): δ 17.1 (C-15), 20.3 (C-9), 21.5 (C-14), 28.9 (C-13), 29.6 (C-12), 30.4 (C-3), 31.7 (C-11), 32.3 (C-10), 35.2 (C-7), 38.6 (C-2), 46.8 (C-4 and C-8), 52.5 (C-6), 207.4 (C-1), 212.5 (C-5); MS *m/z* (rel. int.): 236.1764 $[M]^+$ (36), 221 $[M - Me]^+$ (14), 194 $[M - C_3H_6]^+$ (16), 180 $[M - C_3H_4O]^+$ and $[M - C_4H_8]^+$ (11), 109 $[C_7H_9O]^+$ (100), 69 $[C_4H_5O]^+$ (41). Calc. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.18; H, 10.34%.

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