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A New Triterpene from *Vellozia compacta*

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A triterpene not previously obtained from natural sources has been isolated from *Vellozia compacta* and its structure assigned on the basis of spectral data. For confirmation of this assignment, a partial synthesis was carried out. β-Amyrenyl acetate was oxidized and the resulting ketone reduced to a diol, which, after selective dehydration and reoxidation, furnished the natural product.

Keywords——*Vellozia compacta*; Velloziaceae; triterpene; oleanane; partial synthesis

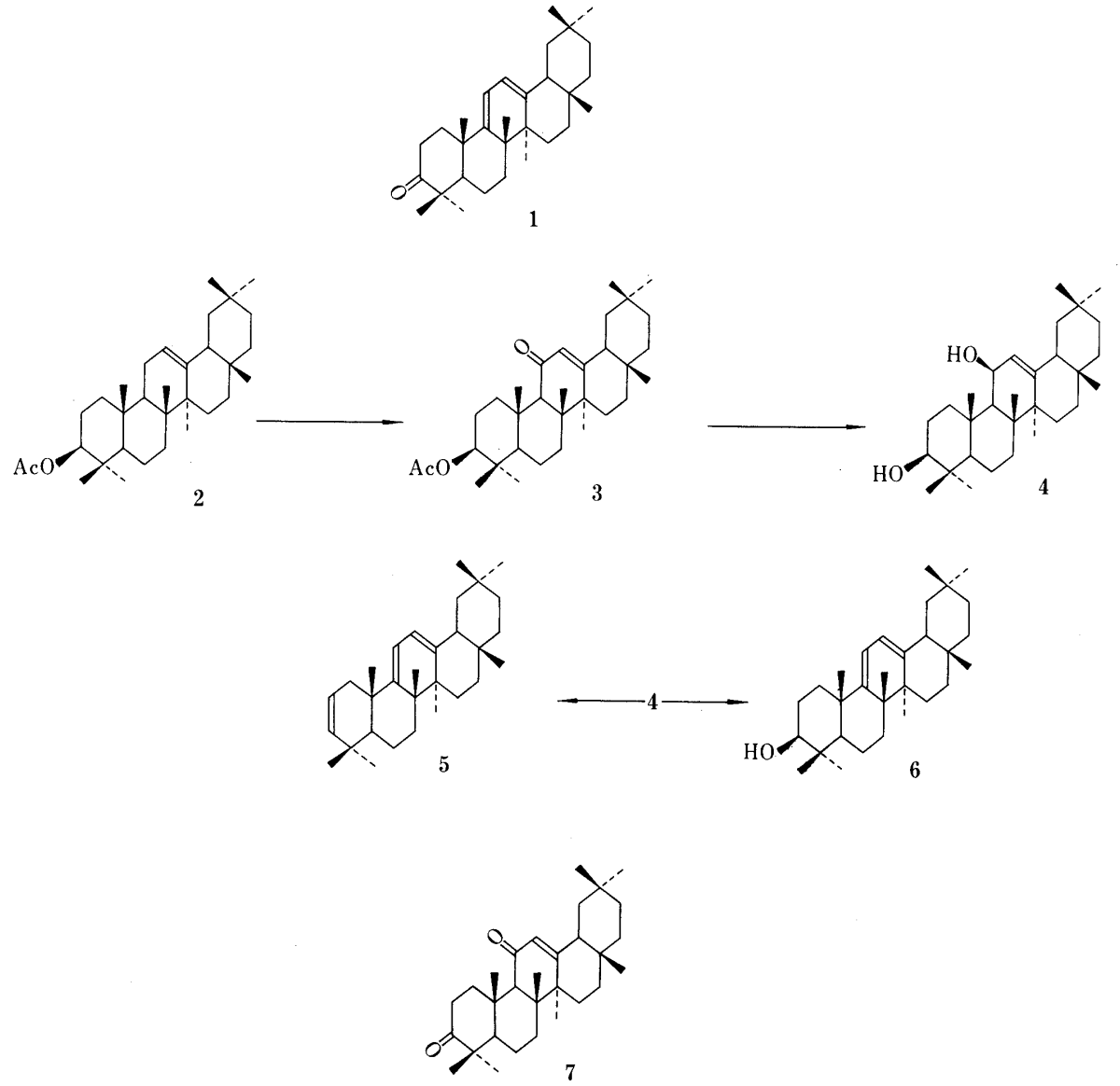
As a part of a series of studies of Brazilian plants of the genus *Vellozia*, we have examined *Vellozia compacta* MARTIUS *ex* SCHULTES and identified a number of di- and triterpenes.[1—4] In a further investigation of the hexane extract of this plant a triterpene, $C_{30}H_{46}O$, has been isolated. The infrared (IR) spectrum ($\nu = 1700\,cm^{-1}$) shows this substance to be a ketone and the ultraviolet (UV) spectrum is characteristic of a homoannular diene (λ_{max} 283; ε 8.600). The proton nuclear magnetic resonance (^{1}H-NMR) spectrum has an AB pattern ($\delta = 5.6$) indicating the presence of the structural unit ■–C=CH–CH=C–■. There were also eight singlets due to methyl groups at quaternary carbons. This fact, together with the fragmentation pattern in the mass spectrum (MS), strongly suggested an oleanane skeleton. Major fragments with masses of 255 and 269 could result from cleavage of rings B and D, respectively, in accordance with the observation of Gonzalez, Fraga and Ravelo[5] for a diene of the ursane series.

Since there is only one possible location for the diene system in this skeleton we conclude that our triterpene has the structure **1**.

The ketone group must be at C-3 from biogenetic considerations and this was confirmed by comparing the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum with those of known triterpenes[6] (Table I).

A ketone reported to have the structure **1** was prepared by Picard and Spring[7] from β-amyrenyl benzoate, but since there was some controversy[7,8] about one of the reactions involved, it was decided to carry out an alternate synthesis for confirmation of this structure. β-Amyrenyl acetate **2** was oxidized to the ketone **3**; this reaction was analogous to that carried out by Spring and collaborators[7] using chromic acid and the corresponding benzoate. However with *tert*-butyl chromate, the desired ketone was obtained in a much better yield (85—90%).[10]

The reduction of the ketone group of **3** was even more difficult than expected. Sodium borohydride under mild conditions had no effect, and under forcing conditions it removed the protecting acetate group, leaving the ketone unchanged. However, with lithium aluminum hydride, the diol **4** was obtained in good yield. The reduction was stereospecific, since thin



layer chromatography (TLC) showed that a single product had been formed. The angular methyl groups at C-8 and C-10 inhibit the approach of the reagent from the β side of the molecule, so that resulting hydroxyl group must be β (axial). Since this hydroxyl group is *trans* to the axial hydrogen at C-9, it was anticipated that dehydration would be more readily effected at this part of the molecule than in ring A. The first attempt at dehydration using phosphorus oxychloride and pyridine at 0 °C resulted in elimination of both hydroxyl groups to yield the olefin **5**.

No rearrangement of ring A took place under these conditions since the ^{1}H-NMR spectrum showed the presence of four olefinic hydrogens and the absence of methyl groups linked to an olefinic carbon. Finally it was found that the use of dilute hydrochloric acid to separate the aluminum salts in the preparation of the diol **4**, furnished sufficient acid to catalyze the desired dehydration. The alcohol **6** obtained in this way was treated with Jones reagent at 0 °C to form **1**, which was identical to the natural product.

The ease with which the dehydration of **4** occurred suggests that the biogenesis of **1** also involves the formation of **4** from β-amyrin, followed by dehydration and oxidation as in our laboratory synthesis. Evidence that oxidation at C-11 takes place in these plants is furnished by the isolation of the diketone **7** from *Vellozia glabra*.[11]

TABLE I. ^{13}C Chemical Shifts of Compounds **1**, **3** and β-Amyrin[a)]

C	1	3	β-Amyrin
1	37.0[b)]	38.7	28.7
2	34.5	23.4	27.3
3	217.3	80.5	79.0
4	47.2	38.0	38.8
5	51.7	54.9	55.3
6	19.1	18.4	18.4
7	31.2	32.6	32.8
8	40.6	43.3	38.8
9	152.1	61.5	47.7
10	38.1	36.9	37.0
11	117.3	201.4	23.6
12	120.4	127.9	121.8
13	147.2	170.2	145.1
14	42.9	45.3	41.8
15	27.2	26.4	26.2
16	25.6	26.4	27.0
17	32.1	32.3	32.5
18	45.6	47.5	47.4
19	46.8	45.0	46.9
20	31.6	31.0	31.1
21	34.5	34.4	34.8
22	37.7[b)]	36.4	37.2
23	26.8	28.0	28.2
24	21.2	16.6	15.5
25	20.5	15.7	15.6
26	19.9	17.3	16.9
27	25.2	23.5	26.0
28	28.7	28.7	28.4
29	33.1	33.0	33.3
30	23.6	23.5	23.7
COO	—	170.6	—
CH_3	—	21.2	—

a) The δ values are in ppm downfield from TMS; the solvent was $CDCl_3$.
b) These assignments may be reversed.

Experimental

The ^{13}C-NMR spectra were obtained using a Varian XL-100-12 spectrometer (25.2 MHz, spectral width 5 kHz, acquisition time 0.8 s, flip angle 45° and internal ^2H pulse lock). Tetramethylsilyl (TMS) was the internal standard for ^1H-NMR. Melting points are uncorrected (Kofler apparatus).

Isolation of 1——*Vellozia compacta* was collected in the Serra do Cipó in the state of Minas Gerais, Brazil. Stems, roots and leaf sheaths were cut into small pieces and extracted with hexane, and the extract was concentrated *in vacuo*. The crude concentrate was chromatographed on silica gel (Merck, 0.05—0.20 mm); elution with 1% AcOEt in hexane provided **1**, which was recrystallized from hexane. mp 206—208 °C.

$$[\alpha]^{25}=\frac{373}{589}\ \frac{393}{578}\ \frac{463}{546}\ \frac{998}{436}\ \frac{2338}{365}\ \text{nm}\quad (c=1.07,\ CHCl_3).$$

UV $\lambda_{max}^{CH_2Cl_2}$ 283 nm (ε=8560). IR ν_{max}^{KBr} cm^{-1}: 1700, 830. ^1H-NMR (100 MHz, $CDCl_3$) δ: 0.90 (6H, s), 1.00 (3H, s), 1.02 (3H, s), 1.04 (3H, s), 1.08 (3H, s), 1.20 (3H, s), 1.28 (3H, s), 2.5 (2H, m), 5.51 (1H, d, J=6 Hz), 5.63 (1H, d, J=6 Hz). MS *m/e* (%): 422 (100, M^+), 407 (11), 324 (1), 269 (27), 255 (31), 171 (20), 145 (20), 143 (18), 133 (37), 118 (28), 95 (48), 69 (63), 55 (70), 41 (95).

β-Amyrenyl Acetate (2)——A solution of β-amyrin (175 mg) in acetic anhydride (freshly distilled from CaC_2) was treated with a catalytic quantity (10 mg) of 4-dimethylaminopyridine and the reaction mixture was allowed to stand for 12 h at room temperature. Excess acetic anhydride was distilled off *in vacuo* and the residue was dried to

constant weight in a vacuum desiccator over sodium hydroxide, giving 192 mg (100%) of product, which was crystallized from ethyl acetate–acetic acid. mp 237—240 °C.

11-Keto-β-amyrenyl Acetate (3)——*tert*-Butyl chromate[12] (2.4 ml) was added to a solution of **2** (127 mg) in carbon tetrachloride (12 ml), acetic acid (4 ml) and acetic anhydride (2 ml). This solution was heated at reflux temperature for 6 h then cooled and diluted with chloroform (30 ml). The mixture was washed with water (20 ml), oxalic acid solution (3 × 20 ml, 5%) and saturated sodium bicarbonate solution (20 ml), then dried over sodium sulfate. The solvents were evaporated off and the residue was crystallized from acetic acid. The purified product (115 mg, 88%) had mp 262 °C. IR ν_{max}^{KBr} cm^{-1}: 1740, 1690. ^{1}H-NMR (100 MHz, $CDCl_3$) δ: 2.06 (3H, s), 4.52 (1H, dd, J=10 and 6 Hz), 5.56 (1H, s).

Reduction of 11-Keto-β-amyrenyl Acetate——Sodium borohydride (300 mg) was added to a solution of the ketone **3** (110 mg) in 2-methoxyethanol (4 ml) and dimethylformamide (5 ml), and the reaction mixture was stirred at 50 °C for 16 h. Dilution with water precipitated a solid whose IR spectrum showed a single carbonyl peak (1671 cm^{-1}). This substance, after reaction with acetic anhydride, yielded the ketone **3**.

A solution of **3** (84 mg) in dry tetrahydrofuran (THF) (10 ml) was added to a suspension of lithium aluminum hydride (30 mg) in THF (5 ml). The mixture was stirred at reflux temperature for 8 h, then cooled. Water was added slowly to the reaction mixture, forming a flocculent precipitate which was washed with small portions of ether (4 × 15 ml). The combined ether solution was washed with water, dried over sodium sulfate and concentrated, finally *in vacuo*. The residual solid, **4**, (62 mg, 80%) was characterized by TLC (single spot) and IR: ν_{max}^{KBr} cm^{-1}: 3225 (br), no carbonyl peaks.

Dehydration of 4——A solution of **4** (40 mg) in dry pyridine (1.5 ml) was stirred at 0 °C while phosphorus oxychloride (1 ml) was added dropwise. After an hour, water was added carefully with continued cooling. The reaction mixture was diluted with chloroform and the solution washed with water, dried and concentrated to yield **5** as an oil. ^{1}H-NMR (100 MHz, $CDCl_3$) δ 4.3—4.6 (4H, m), CH_3 peaks as for compound **1**.

Oleana-9(11),12-dien-3-β-ol (6)——The reduction of **3** with lithium aluminum hydride was carried out at described for the preparation of **4** except that the precipitate formed by adding water to the reaction mixture was dissolved by the addition of a small amount of concentrated hydrochloric acid. The product was then extracted with chloroform and the solution was dried and concentrated. TLC showed the presence of a small amount of impurity, but the major product was **6**.[13] ^{1}H-NMR (100 MHz, $CDCl_3$) δ: 0.82 (3H, s), 0.88 (3H, s), 0.90 (6H, s), 1.00 (3H, s), 1.04 (3H, s), 1.16 (3H, s), 1.20 (3H, s), 3.23 (1H, dd, J=9 and 5 Hz), 5.40 (1H, d, J=5 Hz), 5.57 (1H, d, J=5 Hz).

Oxidation of 6——Jones' reagent was added a drop at a time to a solution of **6** (20 mg) in acetone (5 ml) at 0 °C until the red-orange color persisted. Excess bisulfite was immediately added and the product extracted with chloroform. The residue remaining after evaporation of the chloroform was recrystallized from hexane to yield **1**, whose spectral properties (IR, ^{1}H-NMR, and UV) were identical with those of the natural product. The mp's of the two samples of **1** were identical and the mixture melting point was undepressed.

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References and Notes

1) A. C. Pinto, A. J. R. Silva, L. M. U. Mayer and R. Braz Filho, *Phytochemistry*, **18**, 2036 (1979).
2) A. C. Pinto, *An. Acad. Brasil. Ciênc.*, **52**, 473 (1980).
3) A. C. Pinto, L. M. M. Valente, R. S. da Silva, W. S. Garcez and P. P. da S. Queiroz, *An. Acad. Brasil. Ciênc.*, **53**, 73 (1981).
4) A. C. Pinto and C. Borges, *Phytochemistry*, **22**, 2011 (1983).
5) A. G. Gonzalez, B. M. Fraga and A. G. Ravelo, *An. Quim.*, **68**, 1433 (1972).
6) F. W. Wehrli and T. Nishida, *Fortschritte d. Chem. Org. Naturst.*, **36**, 1 (1979).
7) C. W. Picard and F. S. Spring, *J. Chem. Soc.*, **1940**, 1198.
8) J. H. Beynon, K. S. Sharples and F. S. Spring, *J. Chem. Soc.*, **1938**, 1233.
9) L. Ruzicka, G. Muller and H. Schellenberg, *Helv. Chim. Acta*, **22**, 758 (1939).
10) In a forthcoming communication, oxidations of other terpenoid compounds in good yields with this reagent will be described.
11) Manuscript in preparation.
12) K. Block, *Helv. Chim. Acta*, **36**, 1611 (1953).
13) This substance was described in ref. 7 as having a melting point of 213.5—214.5 °C.