Pergamon

Tetrahedron, Vol. 53, No. 6, pp. 2005-2012, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(96)01183-0

The Isolation of Novel Diterpenoids, Including a C_{40} *Bis*-diterpenoid, from the Brazilian Plant *Vellozia magdalenae* (Velloziaceae)

Angelo C. Pinto*, Moacir G. Pizzolatti

Instituto de Química, Universidade Federal do Rio de Janeiro,
Cidade Universitária,
21949-970 Rio de Janeiro, RJ, Brazil

Rosângela de A. Epifanio

Instituto de Química, Universidade Federal Fluminense,
Campus do Valonguinho,
24020-150, Niterói, RJ, Brazil

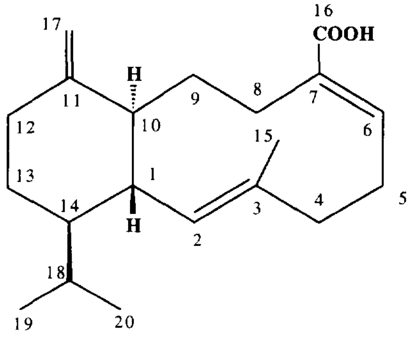
Walter Frankmölle and William Fenical

Scripps Institution of Oceanography,
University of California, San Diego,
92093-0236, La Jolla, CA, USA

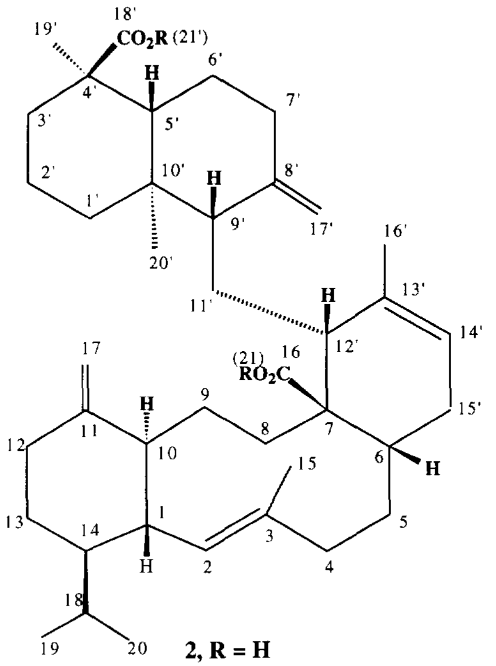
Abstract: Two new diterpenoid acids, magdalenic acid (**1**), and an unusual bis-diterpenoid diacid, bismagdalenic acid (**2**), have been isolated from the hexane extract of the Brazilian plant *Vellozia magdalenae* (Velloziaceae). Magdalenic acid is a regular diterpenoid of the uncommon eunicellan class, while bismagdalenic acid (**2**) is a *bis*-diterpene diacid apparently formed via a Diels-Alder type condensation of magdalenic acid and *cis*-ozic acid, a regular labdane diterpenoid. The structures of the new compounds were established by comprehensive spectral analysis. This is the first report of the isolation of the more commonly marine eunicellan class diterpene from a terrestrial plant, and the first report of these structural classes of diterpenoids from this chemically-prolific family of plants.

The Velloziaceae constitute a family of tropical monocotyledons with most of its 250 species occurring in Brazil. These plants grow in a characteristic ecosystem fully exposed on mountain sides in rocky or sandy soils. Although plants in the family Velloziaceae live under conditions of high solar irradiation and low water availability, they show surprising longevity.[1] The 28 Brazilian species of the family Velloziaceae studied to date have been shown to produce diterpenoids of the isopimarane,[2] clerodane,[3] cleisthantane,[4] barbacenane,[5] *ent*-kaurane, [6] rosane,[7] velloziolane[8] and totarane[9] classes.

As part of a continuing study of the secondary metabolite chemistry of this family, we report here the results of chemical studies of *Vellozia magdalenae* collected at Santa Maria Madalena, Rio de Janeiro State, Brazil. This investigation led to the isolation of two unusual diterpenoids, magdalenic acid (**1**), a diterpene acid of the eunicellan class, and bismagdalenic acid (**2**), a bis-diterpene diacid composed of both eunicellan and labdane diterpene components. Terpenoids of the eunicellan class have previously only been isolated from marine invertebrates, and in particular from numerous soft corals.[10]



1



2, R = H

3, R = (CH_3)

The condensation of two diterpenes forming a C_{40} *bis*-diterpenoid is rare, but several examples have been observed. Compounds of this type can be dimers formed by two units of the same C_{20} skeleton, or *bis*-diterpenoids produced by the coupling of two different C_{20} skeletons. The dimeric diterpenes reported are the C_{40} cembranoids, methyl chlorosarcophytoate and methyl sartortuoate, isolated from the soft corals *Sarcophyton glaucum* and *Sarcophyton tortuosum*,[11] the dimeric totarane, maytenone, isolated from *Maytenus dispermus*,[12] and the dimeric atisine alkaloid, staphisine, isolated from the seeds of *Delphinium staphisagria*.[13] An example of a *bis*-diterpene composed of two different C_{20} skeletons, is acutifloric acid, a labdane-kaurane composite isolated from *Xylopia acutiflora*.[14] On structural grounds, the majority of these *bis*-diterpenes appear to be derived from a classical Diels-Alder reaction of a diterpenoid diene with an activated dienophile-containing diterpenoid precursor. This also appears to explain the origin of bismagdalenic acid (**2**) isolated and described here.

Vellozia magdalenae was collected at Santa Maria Madalena (Rio de Janeiro, Brazil) during September, 1989. The dried plant was subsequently extracted with *n*-hexane to give a crude extract from which magdalenic acid (**1**) and bismagdalenic acid (**2**) were isolated by standard chromatographic methods. Magdalenic acid (**1**) [mp. 193-195 °C, λ_{max} (MeOH) 236 nm (e 3400)], was obtained as colorless crystals as 0.009 % of the plant dry weight. The molecular formula $C_{20}H_{30}O_2$ was deduced by HRFABMS in combination with ^{13}C NMR analysis. The IR spectrum of **1** revealed absorbances assigned to a carboxylic acid functionality (3200-2700 (br) and 1700 cm^{-1}) and to olefinic bonds (1650 and 890 cm^{-1}). The ^1H NMR spectrum of **1** showed broadened signals at 25 °C, greatly complicating measurement of the coupling constants for most proton signals (Table 1). This situation could not be significantly improved by varying the temperature, however maximal sharpening was observed at 28 °C in $CDCl_3$. Thus all NMR experiments were performed under these conditions. The ^1H NMR data indicated the presence of four olefinic protons (δ 6.90, 5.14, 4.68 and 4.60), an olefinic methyl group (δ 1.55, singlet) and an isopropyl group (two doublets at δ 0.64 and 0.88). On the basis of ^{13}C and HMQC NMR experiments, it was deduced that three methyl, seven methylene (1 sp^2 and 6 sp^3), six methine (4 sp^3 and 2 sp^2) and four quaternary sp^2 carbons (one from the acid carbonyl) were present in the molecule. The above data illustrated that magdalenic acid is a bicyclic diterpene with a different carbon skeleton from those previously reported from plants of the family Velloziaceae.

The planar structure of magdalenic acid was assigned by comprehensive 2D NMR experiments involving ^1H-COSY experiments and HMQC (1-bond) and HMBC (2- and 3-bond) heterocorrelation measurements. These measurements allowed all protons and their respective carbons to be confidently assigned (Table 1). The relative stereochemistry of **1** was determined by interpretation of a 2D NOESY ^1H NMR experiment. As illustrated by the conformation of **1** shown in Figure 1, the olefinic hydrogen at C-2 (δ 5.14) showed strong nOe correlations with the protons at C-14 (δ 1.33) and C-10 (δ 1.66), but showed no correlations to protons at either C-1 (δ 1.90) or C-15 (δ 1.55). Strong correlations were observed between protons at C-1 (δ 1.90) and those at C-15 (δ 1.55) and the C-20 methyl group (δ 0.64). These observations confirmed the *trans*-diaxial bridgehead configuration (C-1 to C-10) of magdalenic acid and illustrated that protons at C-20, C-1, and C-15 were on the top face of the molecule. These nOe results can only be explained by the overall molecular geometry as defined below for this metabolite. No data were obtaineed to define the absolute stereochemistry of **1**.

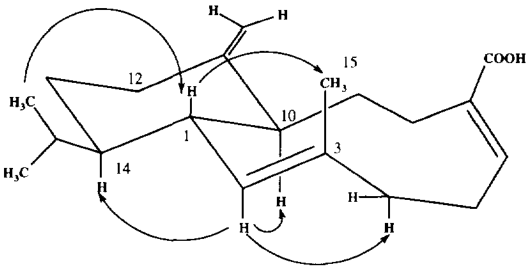


Figure 1. Observed Nuclear Overhauser Enhancements for Magdalenic Acid (**1**)

Bismagdalenic acid (**2**) was isolated as an amorphous, cream-colored solid (0.022 % dry weight) which, because of its polar, diacid functionality, showed awkward, broadened spectral characteristics. The molecular formula $C_{40}H_{60}O_4$ was suggested by LRMS data ($[M]^+$ 604 amu) derived from the free diacid, and later confirmed by HRMS analysis of the corresponding dimethyl ester (**3**) produced by diazomethane esterification. The HRFAB mass spectra of the dimethyl ester derivative showed a prominent molecular ion $[M+H]^+$ at 633.4863 amu which analyzed for $C_{42}H_{65}O_4$ (calc. 633.4883) indicating that the compound was composed of two diterpenoid acid residues. The structure elucidation of bismagdalenic acid utilized the more soluble dimethyl ester derivative which showed well resolved NMR signals.

The ^1H NMR data of **3** showed signals for six olefinic hydrogens (δ 5.27, 5.04, 4.90, 4.68, 4.64 and 4.58), two methoxy groups (δ 3.62 and 3.46), four methyl groups (δ 1.75, 1.47, 1.10 and 0.70) and an isopropyl group (δ 0.84 and 0.64, both doublets). The ^{13}C NMR spectrum, in combination with DEPT and HMQC experiments, showed the presence of eight methyl, fifteen methylene (13 sp^3, 2 sp^2), ten methine (8

Table 1. NMR Data for Magdalenic Acid (1)*

#C	δ^1H	δ^{13}C$^+$	HMBC^{++} ^{2}J(#C)	HMBC^{++} ^{3}J(#C)	^{1}H-^{1}H-COSY (#H)
1	1.90 (1H, dd, 10.2, 4.0)	51.2	2, 10, 14	3, 9, 11, 13	2, 10, 14
2	5.14 (1H, br m)	130.1			1, 15
3		132.3			
4a	1.74 (1H, m)	32.2			4b, 5a
4b	2.57 (1H, br m)				4a
5a	2.20 (1H, br m)	29.7	4, 6	3, 7	4a, 4b, 5b, 6
5b	2.60 (1H, m)				5a
6	6.90 (1H, dd, 9.7, 6.2)	140.9			5a, 5b
7		135.3			
8a	2.19 (1H, br m)	27.3	9	10, 16	8b, 9a
8b	2.38 (1H, br m)		7	10	8a
9a	0.72 (1H, m)	29.7			9b, 8a, 10
9b	2.40 (1H, br m)			1	9a
10	1.66 (1H, dd, 10.2, 9.1)	49.9	1, 9, 11	2, 8, 12, 14, 17	1, 9a
11		153.6			
12a	1.98 (1H, dt, 12.8, 3.6)	37.4	11, 13	17	12b, 13a, 13b
12b	2.35 (1H, br m)		11	17, 14	12a, 13a, 13b
13a	1.08 (1H, br m)	26.6	12, 14		12a, 12b, 13b, 14
13b	1.72 (1H, m)				12a, 12b, 13a, 14
14	1.33 (1H, br m)	48.2			1, 13a, 13b
15	1.55 (3H, br s)	21.6	3	2, 4	
16		173.5			
17a	4.60 (1H, br t, 1.0)	104.5		10, 12	10, 12a, 12b
17b	4.68 (1H, br q, 1.0)			10, 12	10, 12a, 12b
18	1.76 (1H, br dsep, 7.0, 2.8)	28.7	14, 19, 20	13	19, 20
19	0.84 (3H, d, 7.0)	21.6	18	14, 20	18
20	0.64 (3H, d, 7.0)	15.6	18	14, 19	18

* Spectra were recorded at 500 MHz at 28°C in $CDCl_3$; $^+$ Assignments by DEPT and HMQC experiments; $^{++}$ τ value for the HMBC experiment was 6 Hz. HMBC assignments were made by observation and by interpretation of the overall data.

sp^3, 2 sp^2) groups and nine non-protonated carbon atoms (3 sp^3, 6 sp^2 - including 2 ester carbonyls). These data indicated that the two diterpene units were composed of different carbon skeletons, and that one was probably a eunicellan diterpenoid similar to magdalenic acid (**1**). Comprehensive NMR measurements (Table 2), involving HMBC (J = 6 and 10 Hz), DQF COSY, nOe and ROESY experiments provided the data needed to make all carbon and proton assignments, which fully defined the 3-dimensional structure of bismagdalenic acid ester (**3**). Interestingly, bismagdalenic acid appears to be formed by a Diels-Alder type condensation between magdalenic acid (**1**) and the known diterpenoid ozic acid.[15]

The relative stereochemistry of bismagdalenic acid (**3**) was established by nOe difference experiments and ROESY data. The nuclear Overhauser enhancements observed for the protons at C-2, C-10, and C-4, and between C-1, C-15 and C-20 of the eunicellan component of the molecule illustrated the same overall stereochemistry as in magdalenic acid (**1**) (Figure 2). The strong nOe observed between the methyl group protons at C-19' (δ 1.10) and C-20' (δ 0.70), confirmed their 1, 3-diaxial relationship within the *trans*-diaxial labdane skeleton. The relative stereochemistry of the ozic acid portion of the molecule was illustrated by nOe correlations of the methine proton at C-12' (δ 2.64), and by correlations of the C-20' methyl protons (δ 0.70) (Figure 2). The C-12' proton showed strong nOe enhancements to the C-6 proton (δ 1.95), to one of the C-11' protons (δ 1.77) and to one of the C-17' exo-olefinic protons (δ 4.66). In addition, the C-20' methyl group protons (δ 0.70) showed nOe enhancements to one of the C-11' protons (δ 1.77) and to the C-16' methyl protons (δ 1.47), which are in close proximity beneath the molecule. The correlation of two distinct proton sets in the ozic acid component (C-17' and C-20') with the proton at C-12', the nOe correlation with the proton at C-6, and the correlation of the C-4 proton with the C-6 proton, provided a series of linkages which related the relative stereochemistry of the two diterpenoid components.

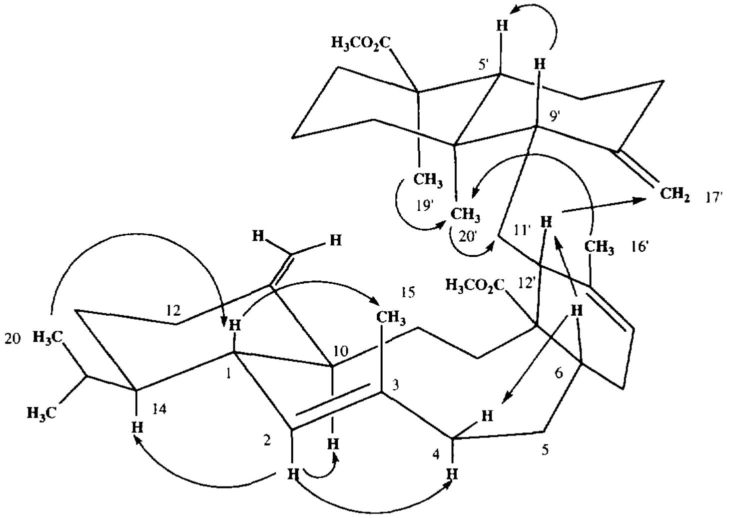


Figure 2. Observed Nuclear Overhauser Enhancements for Bismagdalenic Acid Dimethyl Ester (**3**)

Magdalenic acid (**1**) is the first example of a eunicellan based diterpenoid to be isolated from a terrestrial plant. Bismagdalenic acid (**2**) is apparently formed from a Diels-Alder type reaction of ozic acid (a labdane

Table 2. NMR Data for Bismagdalenic Acid Dimethyl Ester (**3**)*

#C	**δ^1H (#H, m, *J*)**	**δ^{13}C$^+$**	**HMBC^{++}**		**DQFCOSY**
			^{2}J(#C)	**^{3}J(#C)**	**(#H)**
1	1.95 (1H, m)	51.9	2, 10, 14	3, 9	2, 14
2	5.04 (1H, d, 10.9)	130.2	1, 3	10, 4, 14, 15	1, 15
3		136.4			
4a	1.67 (1H, m)	34.8		2, 6, 15	4b
4b	2.38 (1H, m)		3, 5	2, 6, 15	4a, 5b
5a	1.67 (1H, m)	39.5	6	15'	5b
5b	2.11 (1H, m)		4, 6	3, 7, 15'	4b, 5a
6	1.95 (1H, m)	29.7	5, 7, 15'	4, 16	15b'
7		54.7			
8a	1.56 (1H, m)	36.4	7, 9	10, 16, 12'	8b, 9b
8b	1.98 (1H, m)		9	16	8a
9a	1.17 (1H, m)	25.6	10	7	9b
9b	1.93 (1H, m)			11, 7	9a
10	1.42 (1H, m)	52.4	1, 9, 11	2, 8, 17	1, 9a, 9b
11		153.5			
12a	1.98 (1H, m)	37.3	11, 13	17	12b, 13a, 13b
12b	2.38 (1H, m)		11, 13	10, 14, 17	12a, 13a, 13b
13a	1.08 (1H, m)	26.7	12, 14		12a, 12b, 13b, 14
13b	1.72 (1H, m)		14		12a, 12b, 13a,14
14	1.33 (1H, m)	48.3			1, 13a, 13b
15	1.75 (3H, br s)	23.0	3	2, 4	2
16		177.1			
17a	4.58 (1H, br s)	103.4	11	10, 12	17b
17b	4.68 (1H, br s)			10, 12	17a
18	1.74 (1H, m)	29.3			19, 20
19	0.84 (3H, d, 6.9)	21.5	18	14, 20	18
20	0.64 (3H, d, 6.9)	16.0	18	14, 19	18
21	3.46 (3H, s)	50.8	16		
1a'	1.00 (1H, m)	37.7	10'		1b', 2'
1b'	1.55 (1H, m)		2', 10'	5'	*1a'
2'	1.55 (2H, m)	18.6	3'	4'	*1a', 3b'
3a'	1.51 (1H, m)	36.9	4'	1', 5', 19'	3b'
3b'	1.72 (1H, m)			5', 18'	2', 3a'
4'		47.8			
5'	1.87 (1H, dd, 12.3, 0.9)	50.2	4', 6', 10'	1', 7',9',18',19',20'	6a', 6b'
6a'	1.20 (1H, m)	27.0		8'	5', 6b', 7a', 7b'
6b'	1.42 (1H, m)		5', 7'	10'	5', 6a',7a', 7b'
7a'	1.95 (1H, m)	37.8	8'	5', 17'	6a', 6b', 7b'
7b'	2.30 (1H, d, 11.7)		6', 8'	5', 9', 17'	6a', 6b', 7a'
8'		148.1			
9'	1.67 (1H, m)	53.5	8', 10', 11'	5', 12', 17', 20'	11a', 17a'
10'		39.0			
11a'	1.35 (1H, m)	25.2	9', 12'	8', 10', 13', 7	9', 11b', 12'
11b'	1.77 (1H, m)		9', 12'		11a', 12'
12'	2.64 (1H, dd, 11.9, 3.3)	43.6	11', 13', 7	14', 16', 6, 8,16	11a', 11b'
13'		138.7			
14'	5.27 (1H, br s)	122.9	15'	12', 16', 6	15a', 16'
15a'	2.00 (1H, m)	33.3	14', 6	13', 5, 7	14', 15b'
15b'	2.58 (1H, m)				6, 15a', 16'
16'	1.47 (3H, br s)	24.6	13'	12', 14'	14', 15b'
17a'	4.64 (1H, s)	107.9	8'	7', 9'	9', 17b'
17b'	4.90 (1H, s)		8'	7', 9'	17a'
18'		179.3			
19'	1.10 (3H, s)	16.6	4'	3', 5', 18'	
20'	0.70 (3H, s)	14.9	10'	1', 5', 9'	
21'	3.62 (3H, s)	51.8	18'		

* Spectra were recorded at 500 MHz in $CDCl_3$; $^+$Assignments by DEPT and HMQC experiments; $^{++}$ τ values for the HMBC experiments were 6 and 10 Hz; Assignments were made by observation and by interpretation of the overall data. Underlined or starred signals may be interchanged.

diterpenoid) and magdalenic acid. The stereochemistry determined above by nOe methods, and in particular the all *cis* relationship of the protons at C-6, and -12' and the -CO_2CH_3 group at C-7, indicates that the ozic acid diene precursor must have been the $\Delta^{13'-14'}$ = *cis* isomer.[15] The new structure types presented here represent a significant extension of the biosynthetic capability of terrestrial plants of the family Velloziaceae.

EXPERIMENTAL SECTION

Plant Extraction and Isolation: Samples of *Vellozia magdalenae* were collected in Santa Maria Madalena (Rio de Janeiro, Brazil) in September, 1989. The stems, roots and leaves were air dried (790 g), cut into small pieces and extracted with *n*-hexane. The crude extract was concentrated *in vacuo* to afford 15.4 g of a brownish residue which was then filtered through a KOH-impregnated silica gel column using *n*-hexane, dichloromethane and lastly methanol. The KOH-silica gel was prepared by adding 400 ml of 5% aqueous solution of KOH in 300 g of silica gel 60 and heating the mixture overnight at 105 °C.[3] The methanol fraction obtained from the method described above afforded a residue after evaporation that was redissolved in ethyl ether and further extracted with an aqueous 5% solution of NaOH. The aqueous phase was neutralized with HCl and extracted with ethyl ether. The organic phase was dried with Na_2SO_4 and evaporated under vacuum. The resulting carboxylic acid residue was chromatographed using silica gel and eluting with a gradient of ethyl acetate in *n*-hexane to afford 70 mg of magdalenic acid (**1**) and 180 mg of bismagdalenic acid (**2**).

Magdalenic acid (1). White crystals from *n*-hexane, mp. 193-195 °C; which showed the following spectral characteristics: $[\alpha]_D$ = -40° (c 0.16, $CHCl_3$); UV (MeOH): λ_{max} = 236 nm (log ε = 3.53); LRFABMS (NBA matrix): $[M+H]^+$ *m/z* = 303 (50 %), 302 (34), 301 (32), 285 (19), 259 (30), 257 (35), 220 (19), 219 (14), 179 (16), 178 (14), 173 (16), 165 (23), 161 (26), 159 (19), 157 (17), 155 (38), 152 (26), 149 (19), 145 (31), 143 (23), 141 (24), 139 (42), 138 (61), 137 (91), 123 (58), 105 (100) ; IR (KBr): 3200-2700, 2960, 1700, 1650, 1300, 1240, 890 cm^{-1}.

Bismagdalenic Acid (2). The acid was isolated as an amorphous, cream colored solid which showed the following spectral characteristics: $[\alpha]_D$ = +0.5° (c 1.0, MeOH); IR (film): 3413, 3000, 1641, 600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.69 (3H, d, J = 7 Hz), 0.73 (3H, s), 0.89 (3H, d, J = 7 Hz), 1.16 (3H, s), 1.54 (3H, s), 1.81 (3H, s), 4.61 (1H, bs), 4.68 (1H, bs), 4.74 (1H, bs), 4.95 (1H, bs), 5.10 (1H, bd, J = 6 Hz), 5.34 (1H, bs) plus numerous unresolved bands (36H); ^{13}C NMR (75 MHz, $CDCl_3$): 14.9, 16.0, 16.3, 18.6, 21.6, 23.2, 24.8, 25.4, 25.7, 26.9, 27.0, 29.3, 29.4, 33.5, 34.8, 36.5, 36.9, 37.4, 37.7, 37.8, 38.8, 39.6, 43.7, 47.5, 48.3, 49.8, 51.7, 52.3, 53.5, 54.4, 103.4, 107.9, 122.8, 130.0, 136.3, 138.6, 147.7, 153.2, 183.1, 185.1; LREIMS: $[M]^+$ *m/z* = 604 amu for $C_{40}H_{60}O_4$.

Conversion of Bismagdalenic Acid (2) to Dimethyl Ester 3. A solution of bismagdalenic acid (60 mg) in 5 ml dry diethyl ether was treated with excess freshly prepared diazomethane in dry ether at room temperature. The resulting solution was stirred for 30 min and allowed to evaporate until colorless. Removal of remaining solvent under vacuum provided the corresponding dimethyl ester **3** in quantitative yield (62 mg). The dimethyl ester was further purified by recrystallization from hexane.

Bismagdalenic Acid Dimethyl Ester (3). White crystals from hexane, mp. 62-63° C; UV (MeOH): λ_{max} = 222 nm (log ε = 3.76); IR (KBr): 3100, 2960, 1725, 1660, 1450, 1290, 1000, 895, 705, 670 cm^{-1}; LRFABMS

(NBA matrix) : $[M+H]^+$ *m/z* = 633 (25 %), 632 (13), 573 (17), 513 (4), 275 (14), 227 (7), 211 (7), 201 (11), 199 (11), 189 (21), 187 (19), 185 (14), 183 (11), 181 (12), 177 (18), 175 (37), 173 (28), 171 (19), 163 (34), 161 (27), 159 (31), 157 (22), 149 (21), 147 (34), 145 (37), 143 (25), 133 (43), 131 (41), 129 (25), 123 (30), 121 (100); HRFABMS (NBA matrix): $[M+H]^+$ *m/z* = 633.4863 amu, for $C_{42}H_{63}O_4$ calc. 633.4883; NMR data: see Table 2.

ACKNOWLEDGMENTS

This work was supported by grants from CNPq, Brazil and from the U. S. National Science Foundation, under grants CHE 93-22776 (Chemistry Division) and INT 94-03032 (Division of International Programs) to WF. The authors are grateful to Dr. Nanuza L. Menezes (IB-USP) for the identification of *Vellozia magdalenae* and for maintaining a voucher specimen.

REFERENCES

1. Gilbert, B. *Pontif. Accad. Sci. Ser. Varia* **1977**, 41, 225.
2. Pinto, A. C. and Borges, C. *Phytochemistry* **1983**, 22, 2011.
3. Pinto, A. C.; Antunes, O. A. C.; Rezende, C. M.; Correia, C. R. D. *Phytochemistry* **1995**, 38, 1269.
4. Pinto, A. C.; Epifanio, R. de A.; Pizzolatti, M. G. *Phytochemistry* **1992**, 31, 4241.
5. Pinto, A. C.; Frechiani, M. C.; Tinant, B.; Declerq, J-P.; Meerssche, M. V. *J. Chem.. Soc., Chem. Commun.* **1985**, 446.
6. Pinto, A. C.; Pinchin, R.; Prado, S. K. *Phytochemistry* **1983**, 22, 2017.
7. Pinto, A. C.; Scofield, T. C. V.; Braz F^o, R. *Tetrahedron Lett.* **1983**, 24 , 5043.
8. Pinto, A. C.; Gonçalves, M. L. A.; Braz F^o, R.; Neszmelyi, A.; Lukacs, G. *J. Chem. Soc., Chem. Commun.* **1982**, 293.
9. Pinto, A. C.; Zocher, D. H. T.; Rezende, C. M.; Gottlieb, H. E. *Nat. Prod. Lett.* **1995**, 6, 209.
10. Kennard, O.; Wilson, D. G.; Riva di Sanseverino, L.; Tursch, B.; Bosmans, R.; Djerassi, C. *Tetrahedron Lett.* **1968**, 2897.
11. Kusumi, T.; Igari, M.; Ishitsuka, M. O.; Ichikawa, A.; Itezono, Y.; Nakayama, N.; Kakisawa, H. *J. Org. Chem.* **1990**, 55, 6286; Jingyu, S.; Kanghou, L.; Tangsheng, P.; Cun-heng, H.; Clardy, J. *J. Am. Chem. Soc.* **1986**, 108, 177; Jingyu, S.; Kanghou, L.; Tangsheng, P.; Longmei, Z.; Qitai, Z.; Xiuyum, L. *Sciencia Sinica, Ser. B* **1988**, 31, 1172.
12. Falshaw, C. P. and King, T. J. *J. Chem. Soc., Perkin Trans. I* **1983**, 1749.
13. Pelletier, S. W.; Kapadi, A. H.; Wright, L. H.; Page, S. W.; Newton, M. G. *J. Am. Chem. Soc.* **1972,** 94, 1754.
14. Hasan, C. M.; Healey, T. M.; Waterman, P. G. *Phytochemistry* **1985**, 24, 192.
15. Bevan, C. W.; Eklong, W. K.; Okogun, D. E. U. *Chem. Commun.* **1966**, 44.; Bevan, C. W.; Eklong, W. K.; Okogun, D. E. U. *J. Chem. Soc. C.* **1968**, 1063.

(*Received in USA* 19 *September* 1996; *revised* 16 *December* 1996; *accepted* 18 *December* 1996)