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STRUCTURE AND TOTAL SYNTHESIS OF (-)-MALACITANINE. AN UNUSUAL PROTOBERBERINE ALKALOID FROM *CERATOCAPNOS HETEROCARPA*

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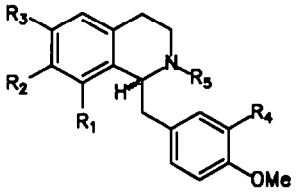
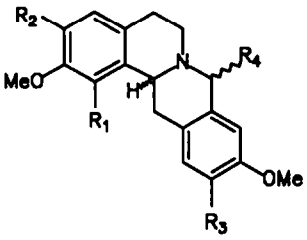
Abstract: The examination of the alkaloids present in *Ceratocapnos heterocarpa* (Papaveraceae) had led to the isolation of the new protoberberine alkaloid, (-)-malacitanine. Characteristic structural features for this alkaloid are the 1,2,10,11-substitution pattern and the hydroxymethyl group at C-8. The synthesis of (±)-malacitanine and its C-8 epimer from the benzylisoquinoline (±)-norcrassifoline has been developed. Spectroscopic data (pmr, cmr and ir) for several C-8 substituted protoberberine alkaloids are reported in connexion with the quinolizidine conformation.

Substitution at positions 2 and 3 of the protoberberine skeleton is a common feature among those alkaloids derived from the benzylisoquinoline, reticuline (**1**).[1] Among the Papaveraceae a less common biosynthetic pathway has been postulated, starting from the benzylisoquinoline crassifoline (**2**).[2,3] This pathway leads to a particular type of protoberberine alkaloids which are recognized by 1,2 substitution and are related to the cularine class of isoquinoline alkaloids.[4]

In our search for a suitable plant for studies of biosynthesis of crassifoline-derived alkaloids we examined *Ceratocapnos heterocarpa* (Papaveraceae) because it is the first plant known to contain both cularine and protoberberine alkaloids.[5,6] In the present paper we describe the isolation and structural determination of (-)-malacitanine (**3**), the first tetrahydroprotoberberine alkaloid to contain a hydroxymethyl substituent at C-8.[7] The total synthesis of racemic **3** and its C-8 epimer (**13**) is also reported.

Analysis of amorphous (-)-malacitanine (**3**), indicated a molecular formula of $C_{20}H_{23}NO_5$ in agreement with the molecular ion at m/z 358 (MH^+) observed by CIMS. The UV spectrum showed an absorption band at 284 nm that was red shifted at basic pH. The pmr of **3** contained signals for two methoxyls groups, two para and two ortho orientated aromatic protons, as well as a low field aliphatic proton in an AMX system. These data and the absence of a N-Me group suggested that **3** comprised a tetrahydroprotoberberine skeleton with a 1,2,10,11-substitution pattern.[8] The methoxyl groups were deduced to be located at C-2 and C-10 by their observed coupling



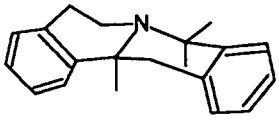


1 R_1= H R_2=R_4= OH R_3= OMe R_5= Me
2 R_1=R_4= OH R_2= OMe R_3= H R_5= Me
8 R_1=R_5= H R_2=R_3=R_4= OMe
14 R_1=R_4= OH R_2= OMe R_3=R_5= H

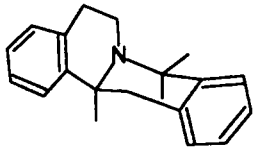
	R_1	R_2	R_3	R_4
3	OH	H	OH	α-CH_2OH
4	H	OMe	OMe	β-Me
5	H	OMe	OMe	α-Me
6	H	OMe	OMe	α-CH_2OH
7	H	OMe	OMe	β-CH_2OH
9	H	OMe	OMe	α-CO_2H
10	H	OMe	OMe	β-CO_2H
11	H	OMe	OMe	α-CO_2Me
12	H	OMe	OMe	β-CO_2Me
13	OH	H	OH	β-CH_2OH

with their ortho aromatic protons (2D-COSY). The cmr spectrum showed resonances for 20 carbon atoms, in agreement with the molecular composition. The presence of two aliphatic methines and one low field methylene indicated a hydroxymethyl group as a substituent on the quinolizidine nucleus. Confirmation of the substituent and its attachment at C-8 was deduced by EIMS. No molecular ion was recorded and the expected retro Diels Alder fragmentation pattern characteristic of tetrahydroprotoberberines[9] (usually the base peak) was scarcely observed (m/z 178, 7%). Instead, the easy loss of the substituent (M^+-31, 100%) and the stability of the fragment (m/z 326,1392, $C_{19}H_{20}NO_4$) strongly suggested its bonding with a benzylic carbon α to the nitrogen. Substitution at C-14 was excluded in view of the absence of quaternary aliphatic carbon atoms. The relative stereochemistry between C-8 and C-14 and the conformation of the quinolizidine nucleus were the next structural features to be established.

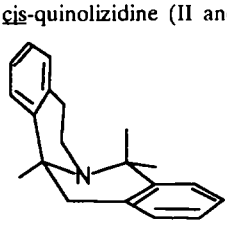
Several naturally occurring and synthetic 8-methyl protoberberines are known; all of them have a 2,3-oxygenation pattern at ring-A.[10,11] Assuming a half-chair conformation for rings B and C in solution, they may exist as an equilibrium mixture of the one B/C trans-quinolizidine (I) and two B/C cis-quinolizidine (II and III) conformers.[12,13]



I



II



III

In coralydine (**4**), the C-8 methyl group trans to the C-14 hydrogen (ß-Me) and the trans-quinolizidine conformation (I) are associated with a high field H-8 and H-14 (pmr), and a low field C-14 (cmr) together with Bohlmann bands (Table 1). In contrast, the analogous signals of its diastereoisomer, O-methylcorytenchirine (**5**) (α-Me), indicates a cis-quinolizidine conformation (II).[11,14]

Table 1. Relevant spectroscopic data for 8-substituted tetrahydroprotoberberines

	^{13}C-NMR					^{1}H-NMR			IR
	C-5	C-6	C-8	C-13	C-14	H-14	$J_{13a,14}$	$J_{13e,14}$	Bohlman bands
3	26.5	45.9	66.2	29.2	45.7	4.51	11.4	4.8	absent
5	29.2*	46.8*	58.8*	35.3*	50.0*	4.24	11.0	4.2	absent
6	28.8	46.2	66.4	31.0	50.4	4.21	11.5	4.9	absent
11	29.3	47.7	66.3	36.1	51.7	4.83	11.1	3.9	absent
13	30.0	42.7	63.7	32.7	55.7	4.20	10.0	3.6	weak
4	29.1*	46.7*	58.9*	36.0*	58.6*	3.71	11.9	3.0	2810, 2754
7	29.7	48.3	65.2	36.4	58.5	3.84	10.9	3.0	2800, 2760
12	29.1	50.4	70.8	36.5	58.1	3.68	11.2	3.1	2820, 2760

* data from ref. 23.

Comparison of pmr and cmr data for **4**, **5** and (-)-malacitanine (**3**) revealed larger differences than expected (see Table 1), which may be due to the hydroxymethyl group at C-8 and the phenolic hydroxyl at C-1.

In order to evaluate the effect of the hydroxymethyl group on the ir, pmr and cmr spectra, the related hydroxymethyl derivatives **6** and **7** were synthesized from (±)-norlaudanosine (**8**), following the Mannich approach.[15] In our hands, the more direct route, condensation of **8** with glycolaldehyde required severe reaction conditions and yields were poor. Much better results were obtained in the reaction of **8** with glyoxylic acid to give a mixture 7:3 of acids **9** and **10** (80%) that were then esterified with diazomethane. The methyl esters **11** and **12** were separated by fractional crystallization and each ester reduced to the corresponding alcohol with lithium aluminium hydride. Spectroscopic data for the ester **12** and the alcohol **7** showed a good correlation with those reported for coralydine (**4**). Consequently a ß-configuration for the substituent and a B/C trans quinolizidine conformation was assigned. Analogous consideration led us to establish for **11** and **6** the α-configuration at C-8

and a B/C cis-quinolizidine conformation (II). The higher field for C-13 in alcohol **6** as compared to O-methyl-corytenchirine (**5**) can be attributed to the larger volume of the substituent. Thus, the spectroscopic differences observed between (-)-malacitanine (**3**) and the two epimeric alcohols **6** and **7** must be due to the C-1 substituent.

The effect of substitution at C-1 is well documented and its interaction with C-13 tends to favour the cis-II form in the conformational equilibrium with the trans-I form. Consequently the Bohlmann bands are weaker or absent[16], the chemical shift of C-6, C-13 and C-14 moves to high field (cmr)[17], while the H-14 is deshielded (pmr).[12]

Taking these arguments into consideration seemed likely that (-)-malacitanine would have a α-hydroxymethyl group in a B/C cis-fused protoberberine conformation. To strengthen this conclusion the total synthesis of (±)-malacitanine (**3**) and its epimer **13** was undertaken. (±)-Norcrassifoline (**14**) was prepared by the Reissert approach according to the procedure previously described.[5] As expected, the phenolic activation at the cyclization step allowed a straightforward route. Condensation of **14** with glycolaldehyde under mild conditions gave an excellent yield (94%) of two epimeric alcohols in a 3:2 ratio.[18] The major product was shown to be identical with **3**.

Spectroscopic data for the minor alcohol, epimalacitanine (**13**) agree with a ß-CH_2OH, existing in solution as an equilibrium mixture of the cis-(II) and the trans-(I) quinolizidine conformations, as suggested by the upfield displacement noted for C-6 due to γ-gauche interactions.

By analogy with related systems[19], the high field C-5 (cmr) displacement indicates that (-)-malacitanine has the α-CH_2OH configuration, in a cis-(II)-conformation in equilibrium with the cis-(III) conformation.

It is well established that levorotation in protoberberine alkaloids is related to the S configuration at C-14.[8] Moreover, many examples indicate that a second chiral centre does not change the sign of the optical rotation.[10,11b,20,21,22] On these grounds the (8S,14S)- absolute configuration is proposed for (-)-malacitanine (**3**).

From what is known of the biosynthesis of other protoberberines[1], it is likely that the biosynthesis of (-)-malacitanine is from a 7,8-substituted benzylisoquinoline like (S)-norcrassifoline, with the introduction of two carbon atoms on the nitrogen before the cyclization step. This possibility is now being investigated in our laboratory.

EXPERIMENTAL

All mp's are uncorrected. IR spectra were recorded in chloroform solution with a Perkin-Elmer 883 spectrometer. UV spectra were recorded with a HP-5482A spectrophotometer. Optical rotations were measured at 18-20°C with a Perkin-Elmer mod. 241 polarimeter. Low resolution mass spectra in the electron impact (EIMS) or chemical ionization (CIMS) modes were recorded with a HP-5988; high resolution spectra were obtained with a Kratos MS 50 apparatus. ^1H and ^{13}C-NMR spectra were recorded using a Bruker WP 200 SY spectrometer. Proton chemical shifts are referenced to the residual chloroform signal (δ 7.24) and carbon chemical shifts to the solvent ($^{13}CDCl_3$= 77ppm). The multiplicity of ^{13}C resonances was determined by INEPT experiments. The 2D NMR and NOE data were analysed using Bruker's microprograms. TLC were performed on silicagel 60 F 254 plates and column chromatography was carried out on silicagel 60 (70-230 mesh).

(-)-Malacitanine (3)

The air-dried and powdered plant (3 Kg) was extracted with hot MeOH. Acid-base fractionation of the

extract gave a crude alkaloid fraction (33.7 g), that was dissolved in $CHCl_3$-MeOH. The soluble portion (27.2 g) was separated by column chromatography (silicagel) and the fraction eluted with CH_2Cl_2-EtOAc 1:5, was further purified by preparative TLC to give (-)-malacitanine (45 mg). Amorphous powder, mp 116-118°C; $[\alpha]_D$ -87.3° (c 0.05, MeOH); UV λ_{max} nm MeOH (log ϵ): 206 (4.80), 226sh (4.18), 284 (3.76); +NaOH: 208 (5.05), 242sh (4.12), 288 (3.93); IR ν_{max} cm^{-1} ($CHCl_3$): 3546 (O-H); CIMS (CH_4) m/z: 358 $[M+H]^+$; EIMS m/z (rel.int.): 326.1392 $[M-31]^+$ (100) (calc. for $C_{19}H_{20}NO_4$: 326.13922), 310 (20), 178 (7); ^{1}H-NMR ($CDCl_3$) δ ppm: 6.73 (d, 1H, J= 8.5 Hz, H-3), 6.63 (d, 1H, J= 8.5 Hz, H-4), 6.61 (s, 1H, H-9), 6.54 (s, 1H, H-12), 4.51 (dd, 1H, J= 4.8 and 11.4 Hz, H-14), 3.84 (s, 6H, 2xOCH_3), 3.77-3.58 (m, 3H, H-8 and CH_2O), 2.98 (dd, 1H, J= 4.8 and 17 Hz, H-13eq), 2.74 (dd, 1H, J= 11.4 and 17 Hz, H-13ax), 3.26-2.67 (m, 4H, CH_2-CH_2); ^{13}C-NMR ($CDCl_3$) δ ppm: 145.3, 144.6, 144.2, 141.8 (C-1, C-2, C-10, C-11), 127.1, 126.9, 125.3, 124.4 (C-4a, C-8a, C-12a, C-14a), 119.7, 114.5, 109.4, 109.1 (C-3, C-4, C-9, C-12), 66.2 (C-8), 63.5 (CH_2OH), 56.2, 56.0 (2xOCH_3), 45.9 (C-6), 45.7 (C-14), 29.2 (C-13), 26.5 (C-5); Anal. calc. for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92. Found: C, 67.34; H, 6.47; N, 3.71.

Synthesis of (±)-9 and (±)-10

The hydrochloride of (±)-norlaudanosine (**8**, 3.79 g, 0.01 mol) and 40% glyoxylic acid (35 ml, 0.2 mol) were refluxed for 1 h. The reaction mixture was diluted with water, extracted with CH_2Cl_2 and dried over Na_2SO_4. Solvent elimination afforded a solid residue (2.7 g, 80%) consisting of a mixture of acid **9** and acid **10** in the ratio 7:3 (^{1}H-NMR). The two products appeared to be inseparable by preparative TLC and flash chromatography.

Acid (±)-9: ^{1}H-NMR ($CDCl_3$) δ ppm: 7.05, 6.56, 6.52, 6.48 (four s, 4H, aromatic protons), 5.20 (m, 1H, H-14), 4.82 (br s, 1H, H-8); ^{13}C-NMR ($CDCl_3$) δ ppm: 171.0 (C=O), 66.7 (C-8), 53.0 (C-14), 45.9 (C-6), 32.7 (C-13), 26.4 (C-5).

Acid (±)-10: ^{1}H-NMR ($CDCl_3$) δ ppm: 7.12, 6.70, 6.62, 6.52 (four s, 4H, aromatic protons), 4.58 (br s, 1H, H-8), 4.17 (m, 1H, H-14); ^{13}C-NMR ($CDCl_3$) δ ppm: 170.8 (C=O), 70.6 (C-8), 58.3 (C-14), 51.0 (C-6), 34.4 (C-13), 27.6 (C-5).

Synthesis of (±)-11 and (±)-12

The mixture of acids **9** and **10** (1.3 g) dissolved in methanol was treated with excess of an ethereal solution of diazomethane to give a quantitative yield of methyl esters **11** and **12**. Anal. calc. for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.53; N, 3.39. Found: C, 66.95; H, 6.69; N, 3.38. The isomers were separated by repeated crystallization from MeOH-ether.

Ester (±)-11: Pale yellowish crystals, mp 108°C (MeOH+ether); UV λ_{max} nm MeOH (log ϵ): 206 (4.86), 228sh (4.30), 282 (4.24); IR ν_{max} cm^{-1} ($CHCl_3$): 1729 (C=O); EIMS m/z (rel.int.): 413 (M^+, 0.4), 354 (M^+-59, 100); ^{1}H-NMR ($CDCl_3$) δ (ppm): 6.75 (s, 1H, H-9), 6.69 (s, 1H, H-1), 6.64 (s, 1H, H-12), 6.59 (s, 1H, H-4), 4.83 (dd, 1H, J= 3.9 and 11.1 Hz, H-14), 4.71 (s, 1H, H-8), 3.86, 3.85, 3.84, 3.83 (4s, 3H each, 4xOCH_3), 3.71 (s, 3H, $COOCH_3$), 3.16 (dd, 1H, J= 3.9 and 16 Hz, H-13eq), 2.78 (dd, 1H, J= 11.1 and 16 Hz, H-13ax), 3.2-2.7 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ (ppm): 172.3 (CO), 148.8, 147.7, 147.6 (C-2, C-3, C-10 and C-11), 129.9, 127.1, 126.2, 122.9 (C-4a, C-8a, C-12a and C-14a), 111.6, 109.8, 109.2 (C-1, C-4, C-9 and C-12), 66.3 (C-8), 56.1, 55.9 (4xOCH_3), 52.1 ($COOCH_3$), 51.7 (C-14), 47.7 (C-6), 36.1 (C-13), 29.3 (C-5).

Ester (±)-12: Yellowish crystals, mp 166°C (MeOH+ether); UV λ_{max} nm MeOH (logϵ): 206 (4.24), 230sh (3.65), 286 (3.36); IR ν_{max} cm^{-1} ($CHCl_3$): 2820 and 2760 (Bolhmann bands), 1727 (C=O); EIMS m/z (rel.int.): 413 (M^+, 0.2), 354 (M^+-59, 100); ^{1}H-NMR ($CDCl_3$) δ (ppm): 6.72 (s, 1H, H-1), 6.67 (s, 2H, H-9 and H-12), 6.58

(s, 1H, H-4), 4.41 (s, 1H, H-8), 3.86, 3.85, 3.84, 3.80 and 3.79 (5s, 3H each, 4xOCH_3+$COOCH_3$), 3.68 (dd, 1H, J= 3.1 and 11.2 Hz, H-14), 3.19 (dd, 1H, J= 3.1 and 15.5 Hz, H-13eq), 3.00 (dd, 1H, J= 11.2 and 15.5 Hz, H-13ax), 3.24-2.57 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ (ppm): 173.4 (C=O), 148.5, 147.9, 147.8, 147.6 (C-2, C-3, C-10 and C-11), 129.0, 127.3, 126.9, 123.2 (C-4a, C-8a, C-12a and C-14a), 111.7, 111.4, 108.7, 108.3 (C-1, C-4, C-9 and C-12), 70.8 (C-8), 58.1 (C-14), 56.1, 56.0, 55.9 (4xOCH_3), 52.6 ($COOCH_3$), 50.4 (C-6), 36.5 (C-13), 29.1 (C-5).

Synthesis of (±)-6

A solution of ester **11** (413 mg, 1 mmol) in dried THF (20 ml) was added to a stirred solution of lithium aluminium hydride (3 mmol) in THF (25 ml) at room temperature. After 4h the reaction was quenched by the addition of water (0.2 ml), 15% KOH (0.2 ml) and water (0.6 ml). The solid was filtered and washed with CH_2Cl_2. The combined filtrates were dried (Na_2SO_4), and the solvent evaporated. Alcohol **6** (72%), was obtained as pale yellowish crystals, mp 92°C (MeOH); UV λ_{max} nm MeOH (log ϵ): 206 (4.88), 228sh (4.32), 286 (3.96). IR ν_{max} cm^{-1} ($CHCl_3$): 3440 (O-H); EIMS m/z (rel.int.): 354 (M^+-31, 100); ^{1}H-NMR ($CDCl_3$) δ (ppm): 6.63 (s, 1H, H-4), 6.58 (s, 2H, H-1 and H-9), 6.55 (s, 1H, H-12), 4.21 (dd, 1H, J= 11.5 and 4.9 Hz, H-14), 3.85 (s, 9H, 3xOCH_3), 3.83 (dd, 1H, J= 10.8 and 5.0 Hz, H-8), 3.82 (s, 3H, OCH_3), 3.68 (dd, 1H, J= 10.8 and 5.0 Hz, CH_2O), 3.54 (t, 1H, J= 10.8 Hz, CH_2O), 2.98 (dd, 1H, J= 11.5 y 17.0 Hz, H-13ax), 2.70 (dd, 1H, J= 4.9 and 17.0 Hz, H-13eq), 3.35-2.6 (m, 4H, CH_2-CH_2); ^{13}C-NMR ($CDCl_3$) δ (ppm):148.4, 148.2, 148.1, 147.6 (C-2, C-3, C-10 and C-11), 129.7, 125.1, 124.4 (C-4a, C-8a, C-12a and C-14a), 111.9, 111.5, 109.8 (C-1, C-4, C-9 and C-12), 66.4 (C-8), 63.7 (CH_2OH), 56.1, 55.9 (4xOCH_3), 50.4 (C-14), 46.2 (C-6), 31.0 (C-13), 28.8 (C-5).
Anal. calc. for $C_{22}H_{27}NO_5$: C, 68.55; H, 7.06; N, 3.63. Found: C, 68.56; H, 7.20; N, 3.57.

Synthesis of (±)-7

Alcohol **7** was prepared from **12** using the procedure described above. Amorphous powder, mp 80°C. UV λ_{max} nm MeOH (log ϵ): 206 (4.85), 228sh (4.35), 286 (4.07).IR ν_{max} cm^{-1} ($CHCl_3$): 3450 (O-H), 2800 and 2760 (Bolhmann bands). EIMS m/z (rel.int.): 354 (M^+-31, 100). ^{1}H-NMR ($CDCl_3$) δ (ppm): 6.77 (s, 1H), 6.67 (s, 1H, H-12), 6.64 (s, 1H), 6.62 (s, 1H), 4.13 (dd, 1H, J= 3.0 y 10.6 Hz, CH_2O), 3.88, 3.86, 3.85, 3.84 (4s, 3H each, 4xOCH_3), 3.84 (m, 1H, J= 3.0 y 10.9 Hz, H-14), 3.83 (m, 1H, H-8), 3.79 (m, 1H, CH_2O), 3.45-3.38 (m, 1H, H-6), 3.16 (dd, 1H, J= 3.0 y 15.3 Hz, H-13eq), 3.10 (m, 1H), 2.84 (dd, 1H, J= 10.9 y 15.3 Hz, H-13ax), 2.75-2.60 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ (ppm): 148.2-147.7 (C-2, C-3, C-10 and C-11), 129.3, 128.2, 126.8, 126.7 (C-4a, C-8a, C-12a and C-14a), 111.6, 111.4, 109.4, 109.1 (C-1, C-4, C-9 and C-12), 65.2 (C-8), 64.2 (CH_2OH), 58.5 (C-14), 56.2-55.9 (4xOCH_3), 48.3 (C-6). 36.4 (C-13), 29.7 (C-5)
Anal. calc. for $C_{22}H_{27}NO_5$.½H_2O: C, 66.93; H, 7.15; N, 3.55. Found: C, 66.70; H, 6.90; N, 3.48.

Synthesis of (±)-malacitanine (3) and (±)-13

A mixture of norcrassifoline[5] (200 mg), glycolaldehyde (600 mg) and 2.5M HCl (16 ml), was stirred at 60 °C under argon, for 2 hours. The mixture was then basified (NH_4OH), extracted with $CHCl_3$ and dried (Na_2SO_4). Solvent evaporation afforded a solid residue (213 mg, 94%) consisting of a mixture of the two alcohols **3** and **13** in the ratio 3:2 (^{1}H-NMR), which were separated by preparative TLC (CH_2Cl_2-MeOH, 20:1). The major isomer (faster moving on TLC) was identified as (±)-malacitanine (**3**).The minor isomer (±)-epimalacitanine (**13**). Yellowish amorphous powder mp 114°C. UV λ_{max} nm MeOH (log ϵ): 206 (4.75), 228sh (4.06), 286 (3.56). IR ν_{max} cm^{-1} ($CHCl_3$): 3544 (O-H), 2818 and 2760 (Bolhmann bands). EIMS m/e (%): 326 (M^+-31, 100). ^{1}H-NMR

($CDCl_3$) δ (ppm): 6.73 (d, 1H, J= 8.3 Hz, H-3), 6.65 (s, 1H, H-12), 6.63 (d, 1H, J= 8.3 Hz, H-4), 6.59 (s, 1H, H-9), 4.24 (dd, 1H, J= 3.8 and 10.5 Hz, CH_2O), 4.20 (dd, 1H, J= 3.6 and 10 Hz, H-14), 4.08 (dd, 1H, J= 3.8 and 4.1 Hz, H-8), 3.83 (dd, 1H, J= 4.1 and 10.5 Hz, CH_2O), 3.86 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.60 (dd, 1H, J= 3.6 and 16 Hz, H-13eq), 2.67 (dd, 1H, J= 10 and 16 Hz, H-13ax), 3.20-2.58 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ (ppm): 145.4, 144.5, 144.4, 142.6 (C-1, C-2, C-10 and C-11), 129.9, 128.3, 125.7, 124.8 (C-4a, C-8a, C-12a and C-14a), 119.4, 114.5, 109.2, 107.9 (C-3, C-4, C-9 and C-12), 63.7 (C-8), 62.7 (CH_2OH), 56.3, 56.1 (2 OCH_3), 55.7 (C-14). 42.7 (C-6), 32.7 (C-13), 30.0 (C-5).

Anal. calc. for $C_{20}H_{23}NO_5.½H_2O$: C, 65.50; H, 6.60; N, 3.82. Found: C, 65.54; H, 6.30; N, 3.74.

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