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ALKALOIDS FROM *VINCA MAJOR*

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Key Word Index—*Vinca major*; Apocynaceae; indolenine alkaloids; 10-methoxyperakine; vincawajine; 10-methoxyvinorine.

Abstract—Chemical investigations of the aerial parts of *Vinca major* have resulted in the isolation of two new alkaloids, 10-methoxyperakine and vincawajine. Another alkaloid, 10-methoxyvinorine, is reported for the first time from this species. The structures were determined using spectroscopic techniques.

INTRODUCTION

Vinca major is rich in indole alkaloids [1–6]. We report here the isolation and structure elucidation of two new indolenine alkaloids, 10-methoxyperakine (**1**) and vincawajine (**2**), along with 10-methoxyvinorine (**3**).

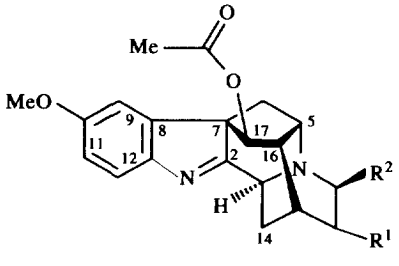
RESULTS AND DISCUSSION

The aerial parts of *V. major* were extracted with methanol. The methanolic extracts were evaporated to a gum, defatted with petrol and extracted with chloroform at various pH values. Compound **1** was isolated from the chloroform extract obtained at pH 2.5, by subjecting it first to CC and then to TLC (for details see Experimental). Its UV spectrum showed a bathochromic shift in comparison to the UV absorption of the indolenine system [7–9]. This indicated that the aromatic ring was substituted by an electron-donating group. Absorption maxima occurred at 200, 222 and 278 nm [10]. The IR spectrum showed an absorption at 1725 cm^{-1}, indicating the presence of a carbonyl group.

The mass spectrum of **1** displayed a $[M]^+$ at *m/z* 380.1687, consistent with the molecular formula $C_{22}H_{24}N_2O_4$, indicating the degree of unsaturation as 12 double bond equivalents. Another prominent peak at *m/z* 351.1708 ($C_{21}H_{23}N_2O_3$) was due to the loss of a CHO group from the $[M]^+$. The peak at *m/z* 337.1552 ($C_{20}H_{21}N_2O_3$) resulted from the loss of an acetyl group. The fragment resulting from the loss of OCOMe group appeared at *m/z* 321.1603 ($C_{20}H_{21}N_2O_2$) [11].

The ^1H NMR spectrum ($CDCl_3$, 400 MHz) gave a pattern very similar to that of perakine [11, 12] with the exception that an additional signal for a methoxy group was present at δ3.82. This suggested that the substance was a methoxy derivative of perakine. H-9 appeared as a doublet at δ7.02 ($J_{9,11}$ = 2.6 Hz). A double doublet at δ6.91 ($J_{11,9}$ = 2.6, $J_{11,12}$ = 8.5 Hz) was assigned to H-11 which was coupled both with H-9 (*meta*) and H-12 (*ortho*). H-12 appeared as a doublet at δ7.11 ($J_{12,11}$ = 8.5 Hz). The chemical shifts and splitting pattern of these signals indicated that the C-10 position was substituted. Generally when the C-10 position bears a hydroxyl or methoxy substituent in an indolenine nucleus it is the doublet showing *ortho*-coupling which is the most downfield signal in the aromatic region, while the doublet showing *meta*-coupling resonates upfield [13]. The presence of a C-10 substituent was further confirmed by the fact that the C-6β and C-16 acetoxy group showed interactions in space with the proton which was *meta*-coupled and had a relatively upfield signal as compared to the signal of the other doublet. If the substitution of the methoxy group was at C-11, then the NOE interaction would have been with an *ortho*-coupled proton.

Another downfield proton resonating as a doublet at δ4.16 ($J_{3\alpha,14\alpha}$ = 9.2 Hz) was assigned to the C-3 methine proton as it showed cross-peaks in the ^1H–^1H COSY spectrum with H-14α, the latter resonating as a multiplet



	R^1	R^2
1	βCHO	Me
2	βCH_2-OCOMe	Me
3	=\	H

at δ1.75. The geminal H-14β was assigned to the multiplet at δ1.61, because it showed a coupling in the COSY spectrum with the C-15 proton at δ2.86 (triplet, $J_{15\alpha,16\alpha}$ = 5.40 Hz, $J_{15\alpha,14\beta}$ = 5.38 Hz) which in turn gave cross-peaks with a 'triplet-like' signal at δ2.45 ($J_{16\alpha,5\alpha}$ = 5.8 Hz, $J_{16\alpha,15\alpha}$ = 5.5 Hz). These two 'triplets' were assigned to H-15 and H-16, respectively.

H-16 showed a cross-peak in the COSY spectrum with the double doublet at δ3.60 for H-5α ($J_{5\alpha,6\alpha}$ = 11.9 Hz, $J_{5\alpha,16\alpha}$ = 6.0 Hz). The latter was also coupled with the H-6β methylene proton. H-6β resonated as a double doublet at δ2.74 ($J_{6\beta,5\alpha}$ = 11.9 Hz, $J_{6\beta,6\alpha}$ = 4.9 Hz) and showed cross-peaks in COSY with its geminal proton resonating as a doublet at δ1.67 ($J_{6\alpha,6\beta}$ = 4.2 Hz), as well as with H-5. H-17 showed a fairly downfield signal at δ4.97 because it was vicinal to an acetoxy group which exerted a deshielding neighbouring effect. The Me-18 protons at δ1.29 appeared as a doublet (J = 6.7 Hz), while H-19 appeared as a multiplet at δ3.31. The aldehydic, acetoxy methyl and the C-10 methoxy protons appeared as three separate singlets at δ9.83, 2.17 and 3.82, respectively. These assignments were made after taking into consideration the COSY spectrum (Table 1) and comparison with other closely related alkaloids [2, 7, 11].

The ^{13}C NMR spectrum ($CDCl_3$, 100 MHz, Table 2) of **1** indicated the presence of 22 carbon resonances. These values were similar to those of closely related compounds [14–16]. The multiplicity assignments were made using DEPT with the last polarization pulse angle θ = 45°, 90° and 135° [17, 18]. A HMQC experiment served to establish the one bond ^{13}C–^{1}H connectivities (Table 2). These spectral studies led to structure **1**, corresponding to the structure of perakine [7–11] with an additional methoxy group at C-10.

Compound **2** was isolated by CC and repeated prep. TLC of the extract obtained at pH 2.5 (see Experimental). Its UV spectrum was similar to that of **1**, with absorption maxima at 282, 227 and 204 nm [10] showing a bathochromic shift from the normal indolenine nucleus, indicative of the presence of a methoxy or hydroxyl substituent on the benzene ring [7–10]. The absorption at 1730 cm^{-1} in the IR spectrum suggested that an ester carbonyl function was present.

The mass spectrum of **2** displayed a $[M]^+$ at m/z 424 which was confirmed by a FD mass spectrum. The HR mass spectrum established its exact mass as 424.1999, corresponding to the molecular formula $C_{24}H_{28}N_2O_5$, giving the degree of unsaturation as 12 double bond equivalents. In the EI mass spectrum, the base peak was at m/z 365.1833, representing the loss of an OCOMe group. Another intense peak at m/z 381.1806 was due to the loss of an acetyl fragment. A significant peak resulted from the loss of CH_2OCOMe moiety at m/z 351.1721.

The ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **2** showed the presence of only three protons in the aromatic region. The most downfield of these was a doublet at δ7.51 for the C-12 proton ($J_{12,11}$ = 8.5 Hz). The H-9 proton also resonated as a doublet at δ7.00 ($J_{9,11}$ = 2.5 Hz). The most upfield signal in the aromatic region was H-11 which resonated as a double doublet at 6.90 ($J_{11,12}$ = 8.5 Hz, $J_{11,9}$ = 2.6 HZ). In accordance with the reasoning in the case of the preceding compound (**1**), it was clear from the chemical shifts that there was a substituent at C-10. In the NOESY spectrum of **2**, the methyl protons of the C-17 acetoxy group showed a cross-peak with the proton at δ7.0, which is the *meta*-coupled proton. The interaction in space would have been with an *ortho*-coupled proton if C-11 (and not C-10)

Table 1. Coupling interactions in COSY 45° spectra of **1**–**3**

	1		**2**		**3**	
H	δ	Coupled H	δ	Coupled H	δ	Coupled H
3	4.16	H-14α (1.75)	4.32	—	4.17	H-14α (1.91)
5	3.61	H-6β (2.74), H-16 (2.45)	3.85	H-6β (2.79), H-16 (2.45)	3.38	H-6β (2.70), H-16 (2.41)
6α	1.67	H-6β (2.74)	1.73	H-6β (2.79)	1.67	H-6β (2.70)
6β	2.74	H-6α (1.67), H-5 (3.61)	2.79	H-6α (1.73), H-5 (3.85)	2.70	H-6α (1.67), H-5 (3.38)
9	7.02	H-11 (6.91)	7.0	H-11 (6.9)	7.02	H-11 (6.89)
11	6.91	H-9 (7.02), H-12 (7.51)	6.9	H-9 (7.0), H-12 (7.51)	6.89	H-9 (7.02), H-12 (7.50)
12	7.51	H-11 (6.91)	7.51	H-11 (6.9)	7.50	H-11 (6.89)
14α	1.75	H-3 (4.16), H-14β (1.61)	2.03	H-3 (4.32)	α,β = 1.91	H-3 (4.17), H-15 (3.25)
14β	1.61	H-14α (1.75), H-15 (2.86)	1.66	H-14α (2.03), H-15 (2.45)	—	—
15	2.86	H-14β (1.61), H-16 (2.45)	2.45	H-16 (2.48), H-6α (1.66)	3.25	H-14α,β (1.91), H-16 (2.41)
16	2.45	H-15 (2.86), H-5 (3.61)	2.48	H-15 (2.45), H-5 (3.85)	2.41	H-5 (3.38), H-15 (3.25)
17	4.97	—	4.93	—	5.03	—
18	1.29	H-19 (3.31)	1.44	H-19 (2.79)	1.66	H-19 (5.29), H-21 (3.5)
19	3.31	H-18 (1.29), H-20 (2.15)	2.79	H-18 (1.44), H-20 (1.69)	5.29	H-18 (1.66)
20	2.15	H-19 (3.31)	1.69	H-19 (2.79), H-21 (4.16)	—	
21	—	—	4.16	H-20 (1.69)	3.52	H-18 (1.66), H-19 (5.29)
OCOMe	—	—	2.06	—	—	—
OCOMe	2.17	—	2.16	—	2.16	—
OMe	3.82	—	3.80	—	3.81	—
CHO	9.83	—	—	—	—	—

Table 2. ^1H and ^{13}C NMR data and ^1H–^{13}C connectives (HMQC) of **1–3** in $CDCl_3$

	1		**2**		**3**	
C	δC	δH	δC	δH	δC	δH
1	—	—	—	—	—	—
2	182.64	—	166.4	—	170.0	—
3	56.5	4.16 (*d*, J = 9.2 Hz)	59.5	4.32 (*bs*)	55.7	4.17 (*t*, $J_1 = J_2$ = 5.5 Hz)
4	—	—	—	—	—	—
5	56.2	3.61* (*dd*, J = 6.0, 11.9 Hz)	57.2	3.85 (*m*)	58.3	3.38 (*bt*, $J_1 = J_2$ = 5.1 Hz)
6	37.9	α 1.67 (*d*, J = 4.2 Hz)	36.1	α 1.73 (*m*)	37.2	α 1.67 (*d*, J = 11.7 Hz)
		β 2.74* (*dd*, J = 4.9, 11.9 Hz)		β 2.79 (*dd*, J = 4.25, 12.45 Hz)		β 2.70 (*dd*, J = 5.1, 11.7 Hz)
7	64.1	—	64.3	—	64.3	—
8	136.5	—	—	—	136.8	—
9	111.5	7.02 (*d*, J = 2.6 Hz)	111.2	7.0 (*d*, J = 2.5 Hz)	111.1	7.02 (*d*, J = 2.7 Hz)
10	144.9	—	149.9	—	150.1	—
11	113.7	6.91 (*dd*, J = 2.6, 8.5 Hz)	113.1	6.9 (*dd*, J = 2.6, 8.5 Hz)	113.0	6.89 (*dd*, J = 8.4, 2.7 Hz)
12	123.7	7.51 (*d*, J = 8.5 Hz)	121.8	7.51 (*d*, J = 8.5 Hz)	121.3	7.50 (*d*, J = 8.4 Hz)
13	156.2	—	158.4	—	158.2	—
14	26.2	α 1.75 (*m*)	21.7	α 2.03 (*m*)	26.5	α, β = 1.91 (*t*, $J_1 = J_2$ = 3.9 Hz)
		β 1.61 (*m*)		β 1.66 (*m*)		
15	22.5	2.86 (*t*, J = 5.5 Hz)	26.6	2.45 (*m*)	27.4	3.25 (*m*)
16	49	2.45 (*t*, J = 5.8, 5.5 Hz)	48.9	2.48 (*m*)	48.9	2.41 (*bdd*, J = 6.1, 6.1 Hz)
17	77	4.97 (*s*)	77.6	4.93 (*s*)	77.6	5.03 (*s*)
18	18	1.29 (*d*, J = 6.7 Hz)	17.2	1.44 (*bs*)	13.0	1.66 (*d*, J = 6.6 Hz)
19	41	3.31 (*m*)	38.2	2.79 (*m*)	116.4	5.3 (*q*, J = 6.6 Hz)
20	48	2.15 (*m*)	41.9	1.69 (*m*)	137.8	—
21	—	—	62.7	4.16 (*ddd*, J = 8.7, 11.45, 20.15 Hz)	54.0	3.52 (*m*)
– OCOMe		—	169.9	—	—	—
– COMe	—	—	20.8	2.06 (*s*)	—	—
OCOMe	169	—	170.8	—	180.8	—
OCOMe	21	2.17 (*s*)	21.0	2.16 (*s*)	21.1	2.16 (*s*)
OMe	57	3.82 (*s*)	55.7	3.80 (*s*)	56.1	3.81 (*s*)
CHO	201	9.83 (*s*)	—	—	—	—

was the site of substitution. The C-10 methoxy resonated as a singlet at δ3.80. The multiplet at δ3.85 for H-5 showed connectivities in the ^1H–^1H COSY spectrum with a 2H multiplet at δ2.45 and a double doublet at δ2.79. A two-proton multiplet for H-15 and H-16 at δ2.48 showed connectivities in the COSY spectrum with the H-5 proton (δ3.85), as well as with the multiplet at δ1.66 for H-14β. The double doublet at δ2.79 was assigned to H-6β proton, since it showed cross-peaks with H-5 and its geminal partner proton resonating at δ1.73.

H-14α at δ2.03 partly overlapped with the singlet of the C-23 acetoxy methyl protons at δ2.06, but it was shifted in pyridine-d_5 to δ1.94: it still showed connectivities in the COSY spectrum (in pyridine-d_5) with H-14β and H-15 at δ1.6 and δ2.45, respectively. The methyl protons of the other acetoxy group resonated as a singlet at δ2.16. A doublet of double doublets at δ4.1 was assigned to the C-21 methylene protons which were connected to the multiplet for H-20 at δ1.69.

A broad singlet at δ4.32 for H-3 showed connectivity with H-14β at δ2.03. A downfield singlet at δ4.93 was assigned to C-17H. The C-18 methyl protons resonated as a broad 3H singlet at δ1.44. This broad singlet was connected in the COSY spectrum to the double doublet at δ2.79 which integrated for two protons. The ^1H NMR spectrum in pyridine-d_5 showed a double doublet at δ2.80 and an additional upfield multiplet at δ2.56 (separated in pyridine-d_5 from the overlapping signal at δ2.79 in $CDCl_3$). The latter was connected to the C-18 protons in the COSY spectrum (recorded in pyridine-d_5). This signal was therefore assigned to the C-19 proton. These proton connectivities led to a perakine-type structure. The assignments of these protons were further confirmed from the ^1H–^1H COSY interactions (Table 1) [2, 7, 11, 18].

The ^{13}C NMR spectrum ($CDCl_3$, 125 MHz, Table 2) indicated the presence of 23 carbon resonances, one carbon less than the molecular formula $C_{24}H_{28}N_2O_5$, one of the quaternary carbons (C-8) being too weak to be discernible from the noise. The multiplicity assignments were made using DEPT with the last polarization pulse angle $\theta = 45°$, 90° and 135° [17, 18]. A HMQC experiment served to establish the one-bond connectivities.

Comparison with literature values [14–16] and consideration of the HMQC interactions and other data presented above, led to structure **2** for the substance, which was named vincawajine.

10-Methoxyvinorine (**3**) was isolated as an amorphous solid and identified on the basis of its spectral data [2]. Little spectral data was reported previously. We report here its ^{13}C NMR data and ^{1}H–^{13}C one bond connectivities for the first time (Table 2). The UV spectrum of **3** exhibited absorption maxima at λ_{max} 201, 223 and 279 nm indicating a substituted indolenine nucleus [7–10]. The IR spectrum ($CHCl_3$) of the alkaloid showed intense absorptions at ν_{max} 2925 (C-H), 1735 (ester carbonyl) and 1560 (C = C) cm^{-1}. The HREI mass spectrum of **3** showed a $[M]^+$ peak at *m/z* 364.1792 corresponding to the molecular formula $C_{22}H_{24}N_2O_3$, indicating 12 degrees of unsaturation. A peak in the mass spectrum at *m/z* 349.1551 was due to the loss of a methyl group from the $[M]^+$. The peak at *m/z* 321.1610 ($C_{20}H_{21}N_2O_3$) represented the loss of an acetyl group $[M - 43]^+$. Other prominent peaks were at *m/z* 305 ($C_{20}H_{21}N_2O$), 265 ($C_{17}H_{17}N_2O$), 212 ($C_{13}H_{12}N_2O$), 198 ($C_{12}H_{10}N_2O$) and 183 ($C_{11}H_5N_2O$) [11].

The ^{1}H NMR data ($CDCl_3$, 400 MHz) of **3** are presented in Tables 1 and 2, its ^{13}C NMR spectral data ($CDCl_3$, 100 MHz) and ^{1}H–^{13}C one bond connectivities in Table 2. The C-18 methyl protons showed NOE with H-15α, whereas H-19 showed NOE with the C-21 methylene protons, thereby establishing the '*Z*' orientation of the ethylidene moiety. These studies confirmed that **3** is 10-methoxyvinorine [2, 3].

EXPERIMENTAL

General. IR spectra were measured in $CHCl_3$, UV spectra in MeOH. ^{1}H NMR were measured in $CDCl_3$ at 400 MHz, with TMS as int. standard. ^{13}C NMR spectra were measured at 100 and 125 MHz with TMS as int. standard. TLC was performed on Merck precoated silica gel GF-254 plates. CC was carried out on Merck silica gel 60(70–230 mesh size).

Plant material. Vinca major subsp. *hirsuta* collected from hilly areas in Turkey and identified by Prof. Semra Kurucu at the University of Ankara, Turkey. A voucher specimen is deposited at the herbarium of the faculty of Pharmacy, Ankara University, Ankara, Turkey (AEF No. 16652).

Extraction. Dried aerial parts (16 kg) were crushed and then extracted with MeOH. The MeOH extracts were filtered and concd to a gum under vacuum, acidified with 10% HOAc to pH 2.5 and extracted with petrol (50 l) to remove fatty materials. The alkaloids were then extracted from the defatted aq. layer into $CHCl_3$. This crude fr. obtained at pH 2.5 was dried with Na_2SO_4, concd and weighed (119.2 g). All the alkaloids resulted from CC of this fr. It was subjected to CC on silica gel (1500 g), (GF-70, 230 mesh size) which was successively eluted with petrol, petrol–$CHCl_3$, $CHCl_3$ and $CHCl_3$–MeOH mixts of increasing polarity. A fr. (1.5 g) which was obtained from the column on elution with $CHCl_3$–MeOH (97:3) was again subjected to CC (30 g of silica gel GF-254). Elution of the column was done with petrol, petrol–$CHCl_3$, $CHCl_3$ and $CHCl_3$–MeOH mixts of increasing polarity. A fr. eluted with $CHCl_3$–MeOH (99:1) was then subjected to prep. TLC on silica gel using Me_2CO–petrol–MeOH (6:3:1) to afford a band which contained 2 alkaloids. This band was again subjected to prep. TLC on silica gel using the same solvent system. This process afforded **1** (0.003 g, 19×10^{-6}% yield). A fr. eluted with $CHCl_3$–MeOH (19:1) was subjected to repeated TLC on silica gel GF-254 using benzene–Me_2CO (1:4) to give 15 mg of **2** (9×10^{-5}% yield). Another fr. eluted with $CHCl_3$–MeOH (24:1) was purified by prep. TLC on silica gel GF-254 using petrol–Me_2CO (3:2) to afford 20 mg of pure **3** (12×10^{-3}% yield).

10-Methoxyperakine (**1**). $[\alpha]_D$ − 43° $CHCl_3$ 0.003 g (100 ml^{-1}). UV λ_{max}^{MeOH} nm (log ε): 201 (4.183), 225 (3.982), 277 (3.725). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2874 (C-H), 1725 (C = O). EIMS *m/z* (rel. int.) 380 $[M]^+$ (56), 365 (4), 351 (19), 337 (10), 321 (13), 281 (13), 226 (21), 198 (36); HRMS *m/z* (formulae, calc. value) 380.1743 ($C_{22}H_{24}N_2O_4$, 380.1735), 365.1606 ($C_{22}H_{23}NO_4$, 365.1625), 351.1716 ($C_{21}H_{23}N_2O_3$, 351.1708), 337.1541 ($C_{20}H_{21}N_2O_3$, 337.1552), 321.1599 ($C_{20}H_{21}N_2O_2$, 321.1602), 281.1332 ($C_{17}H_{17}N_2O_2$, 281.1289), 226.1060 ($C_{14}H_{14}N_2O$, 226.1106), 198.0802 ($C_{12}H_{10}N_2O$, 198.0793). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, Table 2): 1.29 (*d*, 3H, $J_{18,19}$ = 6.7 Hz, H-18), 1.61 (*m*, 1H, H-14α), 1.67 (*d*, $J_{6\alpha,6\beta}$ = 4.2 Hz, H-6α), 1.65 (*m*, 1H, H-14β), 2.15 (*m*, 1H, H-20), 2.17 (*s*, 3H, OCOMe), 2.28 (*m*, 1H, H-20), 2.45 (*t*, 1H, $J_{16\alpha,15\alpha}$ = 5.5 Hz, $J_{16,5}$ = 5.8 Hz, H-16), 2.74 (*dd*, 1H, $J_{6\beta,5\alpha}$ = 11.9 Hz, H-6β), 2.86 (*t*, 1H, $J_{15\alpha,16\alpha}$ = 5.40 Hz, $J_{15\alpha,14\beta}$ = 5.38 Hz, H-15), 3.31 (*m*, 1H, H-19), 3.60 (*dd*, 1H, $J_{5\alpha,16\alpha}$ = 6.0 Hz, $J_{5\alpha,6\beta}$ = 11.9 Hz, H-5α), 3.82 (*s*, 3H, OMe), 4.16 (*d*, 1H, $J_{3,14\alpha,\beta}$ = 9.2 Hz, H-3), 4.97 (*s*, 1H, H-17), 6.91 (*dd*, 1H, $J_{11,9}$ = 2.6 Hz, $J_{11,12}$ = 8.5 Hz, H-11), 7.02 (*d*, 1H, $J_{9,11}$ = 2.6 Hz, H-9), 7.51 (*d*, 1H, $J_{12,11}$ = 8.5 Hz, H-12). ^{13}C NMR ($CDCl_3$, 100 MHz, δ) and HMQC: Table 2.

Vincawajine (**2**). $[\alpha]_D$ − 10.9° $CHCl_3$ 0.009 g (100 ml^{-1}). UV λ_{max}^{MeOH} nm (log ε): 204 (0.0257), 227 (0.02219), 282 (0.0129). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2926 (C-H), 1730 (C =O). EIMS *m/z* (rel. int.) 424 $[M]^+$ (58), 381 (8), 365 (100), 351 (7), 226 (9), 198 (6); HRMS *m/z* (formulae, calc. value) 424.1999 ($C_{24}H_{28}N_2O_5$, 424.1998), 381.1806 ($C_{22}H_{25}N_2O_4$, 381.1814), 365.1833 ($C_{22}H_{25}N_2O_3$, 365.1865), 351.1721 $C_{21}H_{23}N_2O_3$, 351.1708), 226.1086 ($C_{14}H_{14}N_2O$, 226.1106), 198.0813 ($C_{12}H_{10}N_2O$, 198.0793). ^{1}H NMR ($CDCl_3$, 500 MHz, δ, Table 2): 1.44 (*m*, 3H, H-18), 1.66 (*m*, 1H, H-14α), 1.69 (*m*, 1H, H-20), 1.73 (*m*, 1H, H-6α), 2.03 (*m*, 1H, H-14β), 2.06 (*s*, 3H, OCOMe), 2.16 (*s*, 3H, OCOMe), 2.45 (*m*, 1H, H-15), 2.48 (*m*, 1H, H-16), 2.79 (*dd*, 1H, $J_{6\beta,6\alpha}$ = 4.25, $J_{6\beta,5\alpha}$ = 12.45 Hz, H-6β), 2.79 (*m*, 1H, H-19), 3.80 (*s*, 3H, OMe), 3.85 (*m*, 1H, H-5), 4.32 (*bs*, 1H, H-3), 4.93 (*s*, 1H, H-17), 4.16 (*ddd*, 2H, $J_{21\alpha,20\beta}$ = 8.7 Hz, $J_{21\beta,21\alpha}$ = 11.45 Hz, $J_{21\alpha,21\beta}$ = 20.15 Hz, H-21), 6.90 (*dd*, 1H, $J_{11,9}$ = 2.6 Hz, $J_{11,12}$ = 8.5 Hz, H-11), 7.02 (*d*, 1H, $J_{9,11}$ = 2.5 Hz, H-9), 7.5 (*d*, 1H, $J_{12,11}$ = 8.5 Hz, H-12). ^{13}C NMR ($CDCl_3$, 125 MHz, δ) and HMQC: Table 2.

10-Methoxyvinorine (**3**). $[\alpha]_D$ + 23.5° ($CHCl_3$, 0.2 g 100 ml^{-1}). UV λ_{max}^{MeOH} nm (log ε): 201 (4.619), 223 (4.502),

279 (4.238). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2925 (C-H), 1785 (C = O) and 1590 (C = C). EIMS *m/z* (rel. int.) 364 $[M]^+$ (100), 349 (5), 321 (76), 305 (50), 265 (6), 212 (15), 198 (45), 183 (13); HRMS *m/z* (formulae, calc. value) 364.1792 ($C_{22}H_{24}N_2O_3$, 364.1786), 321.1610 ($C_{20}H_{21}N_2O_3$, 321.1602), 305.1646 ($C_{20}H_{21}N_2O$, 305.1653), 265.1349 ($C_{17}H_{17}N_2O$, 265.1340), 212.0977 ($C_{13}H_{12}N_2O$, 212.0949), 198.0793 ($C_{12}H_{10}N_2O$, 198.0793), 183.0335 ($C_{11}H_5NO_2$, 183.0320); ^1H NMR ($CDCl_3$, 400 MHz, δ, Table 2): 1.66 (*d*, 3H, $J_{18,19}$ = 6.6 Hz, H-18), 1.67 (*d*, 1H, $J_{6\alpha,6\beta}$ = 11.7 Hz, H-6α), 1.91 (*bt*, 2H, H-14α, β), 2.16 (*s*, 3H, OCOMe), 2.41 (*bdd*, 1H, $J_1 = J_2$ = 6.1 Hz, H-16), 2.70 (*dd*, 1H, $J_{6\beta,6\alpha}$ = 5.1 Hz, H-6β), 3.25 (*m*, 1H, H-15), 3.38 (*bt*, 1H, H-17), 3.52 (*m*, 2H, H-21α, β), 4.17 (*t*, 1H, $J_{3,14\alpha}$ = 5.5 Hz, H-3), 5.29 (*q*, 1H, $J_{19,18}$ = 6.6 Hz, H-19), 6.89 (*dd*, 1H, $J_{11,12}$ = 8.4 Hz, $J_{11,9}$ = 2.7 Hz, H-11), 7.02 (*d*, 1H, $J_{9,11}$ = 2.7 Hz, H-9), 7.50 (*d*, 1H, $J_{12,11}$ = 8.4 Hz, H-12); ^{13}C NMR ($CDCl_3$, 100 MHz, δ); HMQC: Table 2.

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