Novel Indole Alkaloids from the Leaves of *Rauwolfia sumatrana* JACK. in Thailand

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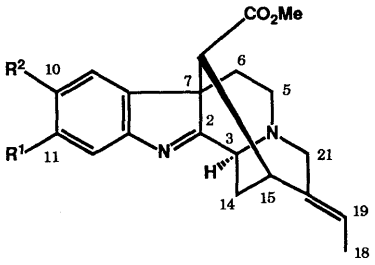
Chemical investigation of the leaves of *Rauwolfia sumatrana* JACK. collected in Thailand resulted in the isolation of three new indole alkaloids, 11-methoxystrictamine (1), rausutrine (4) and rausutranine (7), along with ten known bases, harman, tetraphyllicine, flexicorine, lanceomigine, perakine, β-carboline, peraksine, 10-hydroxystrictamine, cabufiline and compactinervine. Rausutrine (4) and rausutranine (7) are novel bis-indole alkaloids composed of an akuammilane unit and a vincorane unit, the latter of which has a unique iminoquinone function.

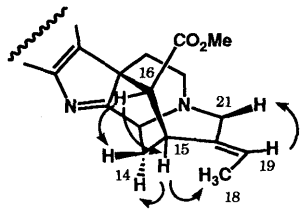
Keywords indole alkaloid; *Rauwolfia sumatrana*; Apocynaceae; rausutrine; rausutranine; dimeric indole alkaloid

The genus *Rauwolfia*, belonging to the family Apocynaceae, has been used as a medicinal plant to relieve many ills such as painful bowel complaints, and also as a tranquilizer and a hypotensive agent. *Rauwolfia sumatrana* JACK. is believed to be a general antidote to poison in Indonesia and a decoction of the bark is taken to relieve malaria in the Philippines.[1] The plants are well known to contain monoterpenoid indole alkaloids.[2] We investigated the alkaloidal constituents of this plant native to Thailand.

The ethanol extract of the leaves of *Rauwolfia sumatrana* JACK., collected in Thailand (the first collection, in February 1989) gave 26.96 g of crude alkaloids. A new alkaloid, 11-methoxystrictamine (**1**), together with six known bases, harman,[3,4] tetraphyllicine,[5,6] flexicorine (**5**),[7] lanceomigine,[8,9] perakine,[10,11] and β-carboline,[12] was separated from the crude alkaloid by a combination of column chromatography and preparative TLC. Three new bases, *i.e.*, 11-methoxystrictamine (**1**), rausutrine (**4**) and rausutranine (**7**) as well as the five known bases, harman, peraksine,[13,14] 10-hydroxystrictamine (**3**),[15] cabufiline (**6**),[16] and compactinervine[17,18] were obtained from a second collection of leaves of the same plant in April 1993. The structures of the known bases were identified by direct comparison of the spectroscopic data and the behavior on TLC in several solvent systems with those of authentic samples. The novel bis-indole alkaloids, rausutrine (**4**) and rausutranine (**7**) consisted of a vincorane-type unit, which was oxidized to an iminoquinone moiety, and an akuammilane-type unit. This is the first report of this type of dimeric indole alkaloid.

The structure of the first new alkaloid (**1**) was determined by analysis of the spectroscopic data. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **1** showed three aromatic protons, two methoxyl groups and one ethylidene side chain. The ultraviolet (UV) spectrum exhibited λ_{max} (log ε) at 228.8 (4.08) and 278.7 (3.40) nm, which suggested an aromatic substituted indolenine nucleus. The mass spectral (MS) behavior [352 (M^+, 100%), 322 (11), 293 (45), 264 (13), 210 (10) and 121 (9)] suggested that the alkaloid is a derivative of strictamine (**2**).[19,20] The FAB high-resolution (HR) MS of **1** afforded the molecular ion peak at *m/z* 353.1864 (100%) leading to the molecular formula $C_{21}H_{24}N_2O_3$. This contains one more methoxyl group than strictamine (**2**). Furthermore, the ^{1}H-NMR spectrum of **1** was very similar to that of strictamine except that the alkaloid **1** had one more methoxyl group and one less aromatic proton than those of **2**. Therefore, the alkaloid **1** is an aromatic-methoxy-substituted strictamine. Unambiguous assignments of all the carbons and protons were obtained by using ^{1}H–^{1}H correlation spectroscopy (COSY), ^{13}C–^{1}H COSY, and long-range coupling [heteronuclear multiple bond connectivity (HMBC) and correlation spectroscopy *via* long-range coupling (COLOC)] spectra. Aromatic protons displayed chemical shifts at δ 7.30 (1H, d, J=8.3 Hz), 7.19 (1H, d, J=2.4 Hz) and 6.71 (1H, dd, J=8.3, 2.4 Hz), indicating that the methoxy substitution was at C-10 or C-11 of the aromatic ring. The carbon nuclear magnetic resonance (^{13}C-NMR) spectrum of **1** was compared with those of strictamine (**2**)[20] and 10-hydroxystrictamine (**3**) (Table I). The signals of C-10 and C-12 in **1** were observed at higher field by 14.4 and 13.2 ppm, respectively, than those of strictamine (**2**), and that of C-11 in **1** is shifted to lower field (Δ 31.9 ppm) compared with that of **2**. This phenomenon can be interpreted in terms of methoxy substitution at the C-11 position on the aromatic ring. The substituted position was confirmed by HMBC and COLOC experiments, which showed three-bond correlations of the quaternary carbon (δ 138.53, C-8) to the doublet proton at δ 7.19 (H-12) having a small coupling constant (J=2.4 Hz), and the quaternary carbon (δ 55.65, C-7) to a doublet proton at δ 7.30 ppm (H-9) having a large coupling constant (J=8.3 Hz). The configurations of the ethylidene side chain and at the C-16 position were determined from the nuclear Overhauser effect (NOE) difference spectrum. As shown in Fig. 1, correlations of H-19 to H-21β, H-15 to H-18 and H-14α, and H-16 to H-15 and H-14β were observed. All of these facts led to the conclusion that **1** is 11-methoxystrictamine. The alkaloids **1** and 10-hydroxystrictamine (**3**) have the same absolute configuration as the common monoterpenoid





1: R^1=OMe, R^2=H 11-methoxystrictamine
2: R^1=R^2=H strictamine
3: R^1=H, R^2=OH 10-hydroxystrictamine

differential NOE data of **1**

Fig. 1

TABLE I. ^{13}C-NMR Data (in $CDCl_3$) for **1**, **2** and **3**

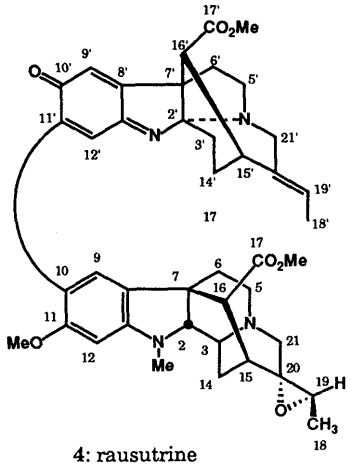
Carbon	**1**	**2**[20]	**3**
2	192.66	190.98	188.49
3	55.15	55.15	54.79
5	51.94	51.98	51.78
6	34.03	36.13	33.45
7	55.65	58.40	56.08
8	138.53	138.15	147.84
9	123.60	123.47	111.37
10	111.20	125.61	148.70
11	160.14	128.19	114.61
12	106.78	119.93	121.29
13	156.97	156.10	154.46
14	36.13	33.62	35.92
15	32.41	32.50	32.48
16	55.80	55.46	55.13
18	12.94	12.97	12.93
19	119.71	121.02	119.92
20	138.30	146.35	137.96
21	53.68	53.68	53.58
COOMe	51.56	51.55	51.60
COOMe	171.70	171.68	171.67
ArOMe	55.58	—	—

indole alkaloids as judged from their Cotton effects in the circular dichroism (CD) spectra.

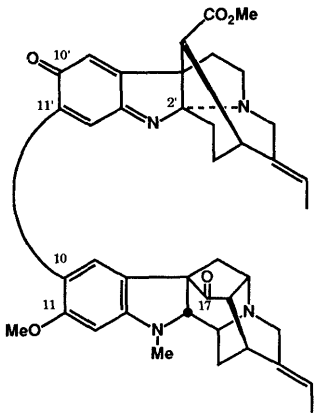
The new dark-red indole alkaloid (**4**), named rausutrine, displayed absorption at λ_{max} (log ε) 277.9 (4.23) nm in the UV spectrum. The ^{1}H-NMR spectrum showed the signals attributable to four isolated protons on the aromatic system, three methoxyl, one *N*-methyl, one ethylidene and one *C*-methyl groups. Upon $NaBH_4$ reduction in methanol, **4** gave a colorless compound, which, in turn, underwent spontaneous oxidation in air to afford the starting material. This phenomenon has been reported[7,21] as diagnostic of iminoquinone-type alkaloids having a C_6H_5–N–C–N function. This assignment was also supported by the chemical shift of the carbon between the two nitrogen atoms at δ 104.0. The electron impact (EI)-MS of rausutrine (**4**) displayed a peak at *m/z* 722 (M^++2, 16%). This M^++2 ion formed by a thermal *in situ* hydrogenation of the iminoquinone was observed in the spectra of flexicorine (**5**)[7] and vincarubine[21] as well. The FAB HR-MS of **4** showed the molecular ion [M+2H+H^+] at *m/z* 723.3751 (100%) leading to the chemical formula $C_{42}H_{51}N_4O_7$, corresponding to the molecular formula $C_{42}H_{48}N_4O_7$. These data showed that rausutrine (**4**) was a dimeric indole alkaloid having an iminoquinone moiety in the molecule which was similar to that of flexicorine (**5**). A non-iminoquinone unit in **4** displayed one aromatic methoxyl, one carbomethoxyl, one indoline *N*-methyl, one *C*-methyl (δ 1.26, 3H, d, J=5.9 Hz) and one methine (δ 3.04, 1H, q, J=5.9 Hz) groups. These facts showed that the non-iminoquinone unit of **4** was of akuammilane type, being identical to that of cabufiline (**6**), which possesses an epoxy group at the C19–20 position. Unambiguous assignments of all the carbons and protons were obtained by using H–H-COSY, phase-sensitive heteronuclear single quantum coherence (PHSQC), and HMBC spectra. The connected position between the akuammilane unit at C-10 and the iminoquinone unit at C-11′ was determined from the HMBC spectrum, which showed the correlations between C-10 and H-12′ as well as C-11′ and H-9. This assignment was supported in part by a phase-sensitive rotating frame nuclear Overhauser effect spectroscopy (PROESY) experiment, which showed correlations of H-12 with an aromatic methoxyl group and an *N*-methyl group. The configurations of C-16, C-16′ and C-19′ in **4** were confirmed by a PROESY experiment, as shown in Fig. 2. NOE was observed between H-18 and both H-15 and the methyl group of carbomethoxy as well as between H-19 and H-21β. Therefore, the configuration of the epoxide moiety can be assumed to be 19(*R*) and 20(*R*).

The ^{13}C-NMR spectra of flexicorine (**5**) and cabufiline (**6**) were re-assigned by using PHSQC and HMBC experiments. Some reported[7,16] positions were interchanged. The stereochemistry of the epoxide moiety in cabufiline (**6**) was not described in the literature.[16] The PROESY experiment on cabufiline (**6**) gave the same result regarding the configuration at the C19–20 position as in the case of **4**.

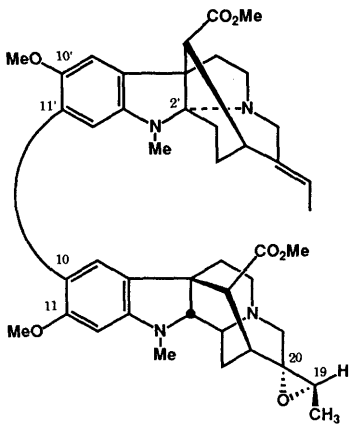
The third new alkaloid, rausutranine (**7**), the red indole alkaloid, exhibited a similar ^{1}H-NMR spectrum to that of **4**, except that it had one methoxyl group less than **4**. This was supported by the EI-MS, which displayed a peak at *m/z* 708 (M^++2, 16%), and the FAB HR-MS (+KI), which afforded the molecular peak [M+2H+H^+] at *m/z* 709.3606 (75%) and another intense peak at 747.3170 (100%), leading to the chemical formulae $C_{41}H_{49}N_4O_7$ and $C_{41}H_{48}KN_4O_7$, respectively. Thus, the molecular formula of **7** was $C_{41}H_{46}N_4O_7$. The ^{13}C-NMR spectrum



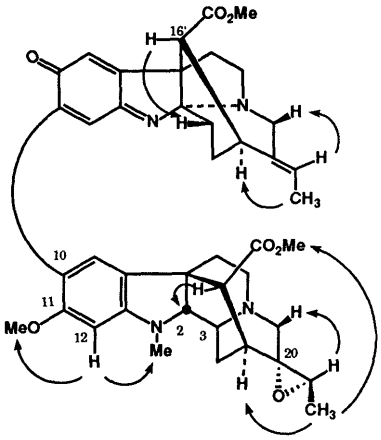
4: rausutrine



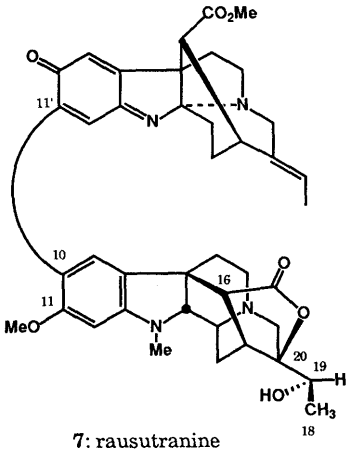
5: flexicorine



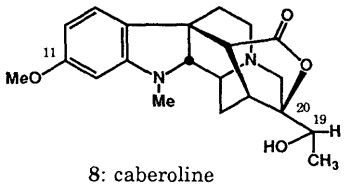
6: cabufiline



selected NOE data of 4



7: rausutranine



8: caberoline

Fig. 2

of **7** displayed a very similar pattern to that of **4**, except for one carbon less than in **4** (Table II). The signal of C-20 (δ 90.64) in **7** was observed at lower field by 24.7 ppm as compared with the corresponding signal of **4**. The signals of two ester carbonyl groups were observed at δ 177.04 and 172.74, the latter of which was assigned as a carbonyl of a carbomethoxy group in the vincorane moiety. All these data were reminiscent of carberoline (**8**)[16] for the akuammilane unit, in which the carboxyl group at the C-17 position is condensed with the C-20 position of the epoxide ring in **4**, resulting in the formation of the 5-membered lactone ring. The connected position of these two monomers was the same as that of **4**, which was confirmed by the correlations in the HMBC and PROESY spectra. Biogenetically, rausutranine (**7**) might be derived from rausutrine (**4**), so the configurations at C-19 and C-20 in **7** could be assumed to be (*R*) and (*S*), respectively. The CD spectra of **4** and **7** showed very similar Cotton curves, implying that they have the same absolute configuration.

Experimental

The instruments used in this study were as follows; UV spectra were taken on a Hitachi UV3400 spectrophotometer in MeOH solutions; NMR spectra were recorded at 500 MHz for ^{1}H and 125 MHz for ^{13}C on JEOL JNM-GSX 500 and JNM A500 spectrometers; MS were recorded on a JEOL JMS-HX 101 spectrometer; CD spectra were measured with a JASCO J-500A in MeOH. TLC was performed on Merck Silica gel 60 GF_{254} plates, and the detection of compounds was accompanied by exposure to UV light or by spraying a solution of Ce(IV)$(NH_4)_2SO_4$. Column chromatography was carried out on Merck Silica gel 60, 230—400 mesh for flash chromatography and on a pre-packed column (Kusano CPS-HS-221-05) for medium-pressure column chromatography (MPLC). Abbreviations used are: singlet (s), doublet (d), triplet (t), multiplet (m), shoulder (sh).

Extraction of the Alkaloidal Fraction Dried, coarsely powdered leaves (7.4 kg, the first collection) collected in February 1989 in Thailand were moistened with 25% NH_4OH and allowed to stand overnight. They were then macerated with ethanol (25 l) for 3 d, three times, and filtered. The combined filtrate was concentrated to a syrupy mass under reduced pressure, mixed with 10% HCl (3 × 400 ml) and filtered. The acidic filtrate was washed with portions of hexane (2 × 600 ml), then made basic (pH 7) with 25% NH_4OH and extracted with $CHCl_3$ (4 × 600 ml). The combined $CHCl_3$ extract was washed with water, dried over anhydrous Na_2SO_4 and evaporated to yield the crude alkaloids (RA) 26.96 g.

Dried coarsely powdered leaves (2.6 kg, the second collection) collected in April 1993 in Thailand were extracted by the same procedure as described above to give the crude alkaloids (RB) 6.97 g.

Separation of Alkaloids Crude RA 8.5 g was chromatographed over a silica gel column (300 g) packed in EtOAc, and eluted in 50 ml fractions. Elution was performed with EtOAc 500 ml, EtOAc–MeOH (8 : 2) 1500 ml, EtOAc–MeOH (6 : 4) 800 ml and MeOH 400 ml. Fractions were analyzed by TLC and pooled according to their composition. Harman (3.6 mg, 0.04% of RA) was found in fractions 5—8, (**1** 39 mg, 0.46% of

TABLE II. ^{13}C-NMR Data for **4**, **5**, **6**, and **7**

Carbon	4[a]	5[b]	6[c]	7[a]
2	79.24	79.77	78.51	78.68
3	47.08	51.11[d]	46.42	46.00
5	50.11	54.36	49.36	50.40
6	33.29	35.63	33.51	33.94
7	42.53	59.11	41.86	40.28
8	131.79	122.08	131.46	133.59
9	123.92	125.49	123.86	122.44
10	115.03	116.80	118.02	115.79
11	157.59	159.88	156.22	157.30
12	94.18	95.78	94.92	94.82
13	155.72	157.82	153.88	155.31
14	33.65	32.23	32.61	30.17
15	39.27	29.55	39.08	32.22
16	53.88	51.32	53.03	48.44
17	173.20	214.52	173.13	177.04
18	15.70	12.99	15.55	17.25
19	65.69	117.52	64.31	68.83
20	65.91	137.80	65.61	90.64
21	55.78	56.05	55.15	53.82
COOMe	51.55	—	51.20	—
ArOMe	55.89	56.39	55.49	56.10
NMe	33.58	34.20	34.13	34.19
2′	103.95	105.00	97.26	104.01
3′	27.75	28.67	19.88	27.73
5′	53.80	54.40	54.52	53.79
6′	40.93	42.06	40.90	40.93
7′	56.75	58.10	56.82	56.79
8′	157.97	159.88	136.10	158.08
9′	123.29	124.86	110.03	123.25
10′	187.35	188.74	148.89	187.14
11′	144.91	146.74	127.19	145.01
12′	130.61	131.35	108.20	131.21
13′	164.51	166.34	142.93	164.44
14′	26.73	27.31	25.46	26.72
15′	35.73	36.92	34.13	35.72
16′	50.30	51.10[d]	50.31	50.31
17′	172.73	174.19	173.36	172.74
18′	13.72	14.15	13.33	13.75
19′	122.94	124.63	121.09	122.94
20′	139.30	140.16	139.66	139.33
21′	59.15	59.88	57.58	59.11
COOMe′	51.89	52.40	51.51	51.87
ArOMe′	—	—	56.57	—
NMe′	—	—	27.57	—

a) In $CDCl_3$. *b*) In CD_3OD. *c*) In DMSO-d_6. *d*) These signals may be interchangeable.

RA), perakine (16 mg, 0.19% of RA) and β-carboline (1 mg, 0.01% of RA) in fractions 9—19, and tetraphyllicine (12 mg, 0.14% of RA), **5** (12.2 mg, 0.14% of RA) and lanceomigine (5.8 mg, 0.07% of RA) in fractions 22—29. Crude RB 3.0 g was chromatographed over a silica gel column (100 g) packed in EtOAc, and eluted in 50 ml fractions. Elution was performed with 10% MeOH/EtOAc 700 ml, 20% MeOH/EtOAc 500 ml, 30% MeOH/EtOAc 500 ml, 40% MeOH/EtOAc 500 ml, 50% MeOH/EtOAc 700 ml and MeOH 1000 ml. Fractions were analyzed by TLC and pooled according to their composition. Alkaloids **1** (56.0 mg, 1.86% of RB), **7** (18.4 mg, 0.61% of RB), harman (3.8 mg, 0.13% of RB), and peraksine (27.7 mg, 0.92% of RB) were found in fractions 12—20, while **4** (2.8 mg, 0.09% of RB), **3** (2.8 mg, 0.09% of RB), **6** (3.3 mg, 0.11% of RB), and compactinervine (1.1 mg, 0.04% of RB) were in fractions 21—25. The mixture of alkaloids was purified by a combination of column chromatography, preparative TLC and MPLC.

11-Methoxystrictamine (1) Colorless amorphous powder. UV λ_{max}^{MeOH} nm (log ε): 228.8 (4.08), 278.7 (3.40). CD (*c*=0.000455, MeOH), $\Delta\varepsilon^{24.5}$ (nm): 0 (213), −3.00 (219), −20.65 (238), 0 (250), +10.66 (276), 0 (346). EI-MS *m/z* (%): 352 (M^+, 100), 322 (11), 293 (45), 264 (13), 210 (10), 121 (9). ^{1}H-NMR ($CDCl_3$) δ: 7.30 (1H, d, *J*=8.3 Hz, H-9), 7.19 (1H, d, *J*=2.4 Hz, H-12), 6.71 (1H, dd, *J*=8.3, 2.4 Hz, H-10), 5.49 (1H, q, *J*=7.1 Hz, H-19), 4.66 (1H, d, *J*=4.9 Hz, H-3), 4.04 (1H, br d, *J*=16.9 Hz, H-21α), 3.83 (3H, s, Ar-OCH_3), 3.72 (3H, s, $COOCH_3$), 3.67 (1H, ddd, *J*=14.4, 14.4, 6.1 Hz, H-6), 3.50 (1H, br s, H-15), 3.10 (1H, d, *J*=16.9 Hz, H-21β), 2.70 (1H, dd, *J*=13.6, 5.8 Hz, H-5), 2.68 (1H, ddd, *J*=13.6, 5.4, 2.7 Hz, H-14), 2.58 (1H, ddd, *J*=14.2, 14.2, 4.9 Hz, H-5), 2.07 (1H, d, *J*=3.9 Hz, H-16), 1.97 (1H, dd, *J*=14.4, 4.9 Hz, H-6), 1.73 (1H, dd, *J*=13.6, 2.9 Hz, H-14), 1.54 (3H, dd, *J*=7.1, 2.7 Hz, H-18). ^{13}C-NMR Table I. FAB HR-MS Calcd for $C_{21}H_{25}N_2O_3$ $(M+H)^+$: 353.1865. Found 353.1864.

Rausutrine (4) Dark red amorphous powder. UV λ_{max}^{MeOH} nm (log ε): 277.9 (4.23). CD (*c*=0.000156, MeOH), $\Delta\varepsilon^{23}$: 0 (240), +5.24 (257), +0.19 (301), +0.58 (310), 0 (322), −4.86 (355), −2.72 (394), −3.89 (418), 0 (470), EI-MS *m/z* (%): 722 (M^++2, 16), 704 (12), 210 (8), 137 (14), ^{1}H-NMR (CD_3OD): δ 6.87 (1H, s, H-9), 6.25 (1H, s, H-12), 4.10 (1H, d, *J*=5.1 Hz, H-3), 3.77 (3H, s, Ar-OMe), 3.74 (1H, ddd, *J*=13.7, 13.7, 4.9 Hz, H-5α), 3.70 (3H, s, 17-OMe), 3.47 (1H, d, *J*=15.6 Hz, H-21α), 3.04 (1H, q, *J*=5.9 Hz, H-19), 2.95 (1H, d, *J*=3.9 Hz, H-16), 2.74 (3H, s, N-CH_3), 2.70 (1H, br s, H-15), 2.68 (1H, ddd, *J*=15.2, 13.7, 6.1 Hz, H-6β), 2.64 (1H, m, H-14), 2.61 (1H, s, H-2), 2.51 (1H, dd, *J*=13.7, 6.1 Hz, H-5β), 2.25 (1H, d, *J*=15.6 Hz, H-21β), 1.73 (1H, dd, *J*=15.2, 5.4 Hz, H-6α), 1.62 (1H, m, H-14), 1.26 (3H, d, *J*=5.9 Hz, H-18), 7.30 (1H, s, H-12′), 6.57 (1H, s, H-9′), 5.43 (1H, q, *J*=6.6 Hz, H-19′), 4.02 (1H, d, *J*=15.6 Hz, H-21′α), 3.79 (3H, s, 17′-OMe), 3.76 (1H, br s, H-15′), 3.01 (1H, d, *J*=15.6 Hz, H-21′β), 2.82 (1H, ddd, *J*=12.7, 8.3, 4.4 Hz, H-5′α), 2.76 (1H, d, *J*=1.4 Hz, H-16′), 2.70 (1H, m, H-5′β), 2.70 (1H, m, H-3′α), 2.53 (1H, m, H-6′β), 1.94 (1H, dd, *J*=14.7, 7.8 Hz, H-6′α), 1.86 (2H, m, H-14′), 1.64 (3H, dd, *J*=6.9, 1.7 Hz, H-18′), 1.34 (1H, ddd, *J*=15.7 11.0, 8.6 Hz, H-3′β). FAB HR-MS (+KI) Calcd for $C_{42}H_{51}N_4O_7$ $(M+2+H)^+$ 723.3758, Found 723.3751, Calcd for $C_{42}H_{50}KN_4O_7$ $(M+2+K)^+$ 761.3317, Found 761.3329.

Rausutranine (7) Dark red amorphous powder. UV λ_{max}^{MeOH} nm (log ε): 209.6 (4.45), 278.4 (4.31). CD (*c*=0.000368, MeOH), $\Delta\varepsilon^{23}$: 0 (210), −16.06 (220), 0 (240), +6.38 (255), 0 (322), −6.38 (355), −4.32 (390), −4.73 (415), 0 (512), EI-MS *m/z* (%): 708 (M^++2, 16), 368 (3), 338 (9), 279 (9), 211 (7), 129 (12), ^{1}H-NMR ($CDCl_3$): δ 7.15 (1H, s, H-9), 6.29 (1H, s, H-12), 3.96 (1H, d, *J*=4.4 Hz, H-3), 3.77 (3H, s, Ar-OMe), 3.63 (1H, q, *J*=6.3 Hz, H-19), 3.33 (1H, d, *J*=8.1 Hz, H-16), 3.29 (1H, ddd, *J*=14.2, 7.1, 2.7 Hz, H-5α), 3.26 (1H, d, *J*=16.6 Hz, H-21α), 3.08 (1H, dd, *J*=8.1, 4.2 Hz, H-15), 2.75 (3H, s, N-CH_3), 2.71 (1H, dd, *J*=14.2, 7.4 Hz, H-5β), 2.68 (1H, d, *J*=16.6 Hz, H-21β), 2.64 (1H, s, H-2), 2.10 (1H, dd, *J*=14.2, 4.2 Hz, H-14α), 1.91 (1H, ddd, *J*=15.4, 7.1, 2.7 Hz, H-6β), 1.72 (1H, dd, *J*=14.2, 4.4 Hz, H-14β), 1.49 (1H, dd, *J*=15.4, 7.4 Hz, H-6α), 1.27 (3H, d, *J*=6.3 Hz, H-18), 7.32 (1H, s, H-12′), 6.57 (1H, s, H-9′), 5.43 (1H, q, *J*=6.9 Hz, H-19′), 4.03 (1H, br d, *J*=15.7 Hz, H-21′α), 3.79 (3H, s, 17′-OMe), 3.77 (1H, br s, H-15′), 3.02 (1H, d, *J*=15.3 Hz, H-21′β), 2.82 (1H, ddd, *J*=12.7, 12.7, 4.4 Hz, H-5′α), 2.78 (1H, d, *J*=1.5 Hz, H-16′), 2.73 (1H, m, H-3′α), 2.71 (1H, dd, *J*=12.7, 8.6 Hz, H-5′β), 2.53 (1H, ddd, *J*=14.4, 11.3, 8.6 Hz, H-6′β), 1.94 (1H, dd, *J*=14.4, 8.1 Hz, H-6′α), 1.87 (2H, m, H-14′), 1.64 (3H, dd, *J*=6.8, 2.7 Hz, H-18′), 1.37 (1H, ddd, *J*=15.7, 11.0, 7.6 Hz, H-3′β). FAB HR-MS (+KI) Calcd for $C_{41}H_{49}N_4O_7$ $(M+2+H)^+$ 709.3601, Found 709.3606, Calcd for $C_{41}H_{48}KN_4O_7$ $(M+2+K)^+$ 747.3160, Found 747.3170.

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