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ALKALOIDS OF KOPSIA JASMINIFLORA FROM THAILAND

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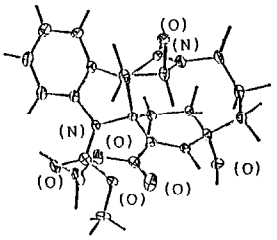
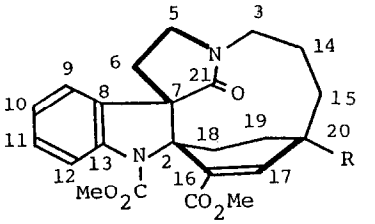
Abstract: Kopsijasminilam, deoxykopsijasminilam, and 14,15-dehydrokopsijasminilam, isolated from Kopsia jasminiflora Pitard, were found to form a novel skeletal group of Kopsia alkaloids. New alkaloids, kopsijasmine and jasminiflorine, together with two known alkaloids were also isolated.

A study of the alkaloid constituents was made on Kopsia jasminiflora Pitard (Family Apocynaceae, subfamily Plumerioideae, tribe Rauvolfieae), a species on which no chemical report has been published. From the methanol extract of the leaves collected at Chiang Mai province of Thailand two known and five new alkaloids were obtained. Among the new alkaloids three were found to be novel class of Kopsia alkaloids.

Compound I[1)] showed the UV spectrum characteristic to N-acylated indoline chromophore. The ^{1}H-NMR spectrum, though revealed some readily assignable functional groups such as $N_{(a)}$-methoxycarbonyl (δ3.79 & 3.81, rotamers), aromatic ring protons (δ7.12(H-9), δ7.06(H-10), δ7.23(H-11), and δ7.50 & 7.94(H-12, rotamers)), and a conjugated methyl ester (δ3.77(CO_2Me) and 7.04(H-17)), strongly suggested a hitherto unencountered type basic skeleton. At this stage X-ray structural analysis was carried out.

The crystal of compound I had the following crystal data: triclinic, P_1, a=10.108(2), b=15.118(2), c=7.221(1) Å, α =99.84(1), β =108.81(2), γ =80.09(1). Intensity data of 4039 reflections, $F(o) > 3\sigma F(o)$, were measured on a four circles diffractometer. The structure was solved by the direct method and the result was refined by block-diagonal least squares calculations to an R value of 0.062. The ORTEP drawing is shown below. Compound I, now named kopsijasminilam (I), turned out to be the first example of D/E seco Kopsia alkaloids.





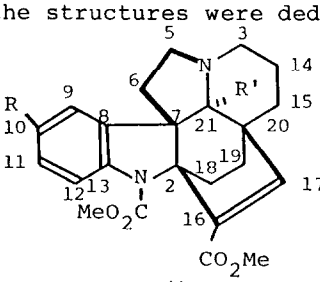
I R=OH
II R=H
III R=OH
Δ^{14}

In the ^{1}H-NMR spectrum of kopsijasminilam (I) a highly deshielded signal is observed at δ4.10, which is ascribable to H-3α suffering from deshielding anisotropic effect caused by C-21 amide carbonyl group. Other protons adjacent to nitrogen were observed at δ3.00(H-3β), δ2.88(H-5α), and δ3.50(H-5β). The ^{13}C-NMR data are shown in Table 1. Based on these and other spectroscopic data, structures of two additional closely related alkaloids, compound II and compound III, were elucidated as described below.

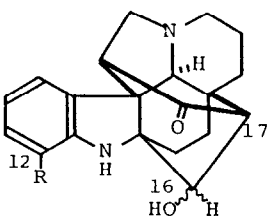
Compound II[2] showed the ^{1}H-NMR signals due to the methylenes on C-3(δ 3.02(H-3β) and δ4.15(3α)) and C-5 (δ2.87(H-5α) and δ3.56(H-5β)) at almost the same positions as kopsijasminilam (I). The ^{13}C-NMR (Table 1) indicated this compound to be 20-deoxykopsijasminilam (II). The C-20 signal was found at δ33.0 as a doublet. The signal due to C-18 was observed at δ30.4, at a position shifted downfield by 4.1 ppm from I owing to the relief from the γ-gauche effect of the hydroxyl group at C-20 of I.

Compound III[3] possessed one double bond in the molecule of kopsijasminilam (I). The ^{1}H-NMR spectrum of III showed two olefinic protons, H-14 and H-15, at δ 5.44 and δ5.80, respectively. The characteristic H-3 α signal moved further downward to δ4.94 in this compound. These findings, together with ^{13}C-NMR spectral data (Table 1), indicated the structure to be Δ^{14}-kopsijasminilam (III). Catalytic reduction of III (H_2/Pd-C, atmospheric pressure) afforded kopsijasminilam (I) as expected.

Two additional new alkaloids, compound IV and compound V, were isolated and the structures were deduced as follows.



IV R=H R'=H
VIII R=OMe R'=H
IX R=OMe R'=OH
X R=OMe R'=OH N-Oxide



V R=OMe 16β-OH
VI R=H 16β-OH
VII R=H 16α-OH

Compound IV[4] showed the UV spectrum superimposable to that of (I), thus indicating the chromophores of $N_{(a)}$-methoxycarbonyl indoline and acrylic ester. The ^{1}H-NMR spectral data of the non-aromatic moiety and the mass spectral fragments were remarkably analogous to those of a reported compound VIII derived from natural kopsidasine (IX) or kopsidasine N-oxide (X) by Homberger and Hesse.[5] The ^{13}C-NMR of IV (Table 1) strongly supported the

C	I	II	III	IV	V
2	69.2[a]	69.5	68.9[a]	71.1	65.5
3	42.3	42.9	40.8	47.3	48.5
5	43.9	44.0	45.2	50.2[a]	54.7
6	32.9[b]	32.4	31.6	39.0	55.4
7	60.3	61.3	65.0[b]	62.5	60.6
8	130.5	130.4	129.5[c]	135.2	130.6
9	124.9	124.4,124.9	124.3	122.1	110.4
10	123.6	123.3	123.6	123.6	117.3
11	128.7	128.5,128.6	128.8	127.4	121.5
12	115.4	115.3	115.6	115.2	146.4
13	140.6	140.9	140.8	142.0	138.8
14	22.5	22.6	124.9[c]	16.1	17.8
15	41.3	31.4	138.8[b]	26.0	35.7
16	130.1	-----	130.1	-----	70.9
17	145.7	148.0,148.6	142.9	143.4[a]	59.1
18	26.3	29.3,30.4	26.6	38.2	31.6
19	31.2[b]	23.9	29.7[a]	32.3	29.5
20	69.4[a]	33.0	68.2	34.0	35.4
21	172.0	172.0	172.3	69.0	67.0
C-C=O	166.5	166.9	166.5	166.1	214.9
N-C=O	153.4	153.2	153.3	-----	
O-Me	52.3	51.8	52.2	51.8	53.7
O-Me	52.8	52.0	52.8	52.2	

a),b),c) : Assignments may be interchanged.

Table 1. ^{13}C-NMR (67.5MHz, $CDCl_3$)

elucidated structure. The name of kopsijasmine was given to compound IV (IV).

Compound V[6] (jasminiflorine) was found to have a 12-methoxy indoline chromophore by the UV spectrum and the ^{1}H NMR spectrum (δ 3.85(OMe), δ 6.76(H-11), δ 6.85(H-10), and δ 6.97(H-9)). The IR absorption at 1725 cm^{-1} and ^{13}C-NMR signal at δ 214.8(s) indicated the ketonic group of the type of fruticosine - fruticosamine. These and other spectral data demonstrated the structure shown above. The orientation of the hydroxyl group at C-16 was deduced to be β on the basis of the coupling constant (J=6.6 Hz) between 16-H and 17-H.[7]

Along with the above new alkaloids two more bases were isolated and were shown to be fruticosine (VI)[7] and fruticosamine (VII)[7] through comparison of the spectral data with those given in the literature.[7]

ACKNOWLEDGEMENT: This work has been financially supported by Grants-in-Aid for Overseas Scientific Survey and for General Scientific Research from the Ministry of Education, Science and Culture of Japan.

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1) Compound I (kopsijasminilam)(I): mp 245-246 °C, $[\alpha]_D$ -220° ($CHCl_3$), $C_{23}H_{26}N_2O_6$. MS m/z: 426(M^+,70), 408(43), 394(32), 339(100), 42(45). IR(KBr) 3450, 1720, 1700, 1690 cm^{-1}. UV(MeOH) 208, 247, 280, 290 nm. ^{1}H-NMR(270MHz, $CDCl_3$)δ: 1.61-2.35(8H), 2.48(1H,ddd,J=15.3,15.3,5.6Hz), 2.88(1H,dd,J=9.6, 9.6Hz), 3.00(1H,dd,J=14.2,4.6Hz), 3.50(1H,ddd,J=11.4, 11.4,11.4Hz), 3.67(1H,br.s), 3.79 & 3.81(each s, 6H altogether), 4.10(1H,dd,J=13.8, 11.9Hz), 7.04(1H,s), 7.06(1H,dd,J=7.3, 7.3Hz), 7.12(1H,d,J=6.3Hz), 7.23(1H,t-like), 7.50(d-like) & 7.94(br)(1H).

2) Compound II (deoxykopsijasminilam)(II): mp 192-195 °C, $C_{23}H_{26}N_2O_5$, $[\alpha]_D$ -210° ($CHCl_3$). MS m/z 410(M^+,81), 378(78), 323(100), 59(54). IR(KBr)

1720, 1710, 1690 cm^{-1}. UV(MeOH) 210(4.62), 243(4.25), 282(3.47), 289(3.43) nm. ^{1}H-NMR(270MHz, $CDCl_3$) δ:1.5-2.3(10H), 2.87(1H,dd,J=7.1, 7.1Hz), 2.90(1H,m), 3.02(1H,dd,J=13.2, 4.6Hz), 3.56(1H,br.), 3.64(s) & 3.83(s)(3H), 3.76(3H,s), 4.15(1H,dd,J=12.8, 12.8Hz), 7.06(1H,dd,J=7.6, 7.6Hz), 7.14(1H,d,J=7.1Hz), 7.23(1H,t-like), 7.26(1H,s, overlapped with $CHCl_3$ signal), 7.51(d,J=7.9Hz) & 7.95(d,J=7.9Hz)(1H).

3) Compound III (Δ^{14}-kopsijasminilam) (III): amorphous powder. High Resolution MS: 424.1632(M^+) (Calcd. for $C_{23}H_{26}N_2O_5$; 424.1632). MS m/z 424(M^+,68), 406(7), 365(7), 338(24), 337(100), 259(7), 167(9), 115(8), 59(15). UV(MeOH) 209, 242, 281, 290 nm. ^{1}H-NMR(270MHz, $CDCl_3$)δ: 1.92(1H,ddd,J=14.4,9,7,9.7Hz), 1.90 - 2.15(4H,m), 2.32(1H,m), 2.40(1H,m), 2.65(1H,ddd,J=16.6, 14.0, 6.4Hz), 2.90(1H,m), 2.96(1H,dd,J=9.5, 9.5Hz), 3.37(1H,dd,J=17.2, 6.8Hz), 3.40(1H,m), 3.72 & 3.80 (each s, 6H altogether), 4.94(1H,ddd,J=17.4, 2.7, 2.7Hz), 5.44(1H,dd,J=12.5,6.1Hz), 5.80(1H,dd,J=12.5,2.7Hz), 6.82(1H,s), 7.06(2H), 7.24(1H), 7.52(d,J=7.9Hz) & 7.98(d,J=8.6Hz)(1H).

4) Compound IV (kopsijasmine) (IV): mp 199-202 C, $[\alpha]_D$ -202°($CHCl_3$. High Resolution MS: 394.1885(M^+) (Calcd. for $C_{23}H_{26}N_2O_4$; 394.1890). MS m/z :394(M^+,100), 393(20), 379(31), 363(12), 336(20), 335(66), 307(19), 282(19) 275(19), 226(21), 59(12). ^{1}H-NMR (270MHz, $CDCl_3$)δ: 1.2-1.4(3H), 1.46(1H,ddd,J=13.3,13.3,3.5Hz), 1.60(1H,ddd,J=13.3,9.1,9.1Hz), 1.45 - 1.65(1H,m), 1.70 - 1.90(2H,m), 2.05(1H,br.d,J=13.1Hz), 2.47(1H,dd,J=13.7, 6.8Hz), 2.58(1H,ddd,J=8.6,8.6,6.8Hz), 2.68(1H,dd,J=2.7,2.7Hz), 3.05(2H,br,d,J=6.7Hz), 3.33(1H,s), 3.74 & 3.79 (br.s and s, 6H altogether), 6.85(1H,br.s), 7.03(1H,dd,J=7.0, 7.3Hz), 7.20(1H,dd,J=7.0, 7.0Hz), 7.29(1H,d,J=7.2Hz), 7.50(br) & 7.91(br) (1H).

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6) Compound V (jasminiflorine) (V): mp 230-233° C, $[\alpha]_D$ -55.3°($CHCl_3$). High Resolution MS: 352.1784 (Calcd. for $C_{21}H_{24}N_2O_3$; 352.1785). UV(EtOH) 210(4.50), 245(3.84), 291(3.37) nm. MS m/z 352(M^+,100), 323(90), 254(17), 253(10), 210(9), 124(60). IR(KBr) 3500-3300, 1730 cm^{-1}. ^{1}H-NMR(270MHz, $CDCl_3$) δ: 1.1-1.5(5H,m), 1.78(1H,dd,J=11.5, 3.3Hz), 1.87(1H,ddd,J=12.8, 9.6, 9.6 Hz), 2.20(1H,ddd,J=11.5, 9.9, 9.9Hz), 2.41(1H,d,J=4.6Hz), 2.58(1H,d,J=6.6Hz), 2.84(1H,d,J=10.6Hz),2.85-2.90(2H,br), 3.22(1H,s), 3.59(1H,dd,J=11.6,4.6Hz), 3.85(3H,s), 4.20(1H,d,J=6.6Hz), 6.76(1H,dd,J=8.0, 1.0Hz), 6.86(1H,dd,J=8.0, 8.0Hz), 6.96(1H,dd,J=7.3, 1.0Hz).

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