NEW PRENYLFLAVANONES FROM *HERNANDIA NYMPHAEFOLIA* (PRESL) KUBITZKI

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Abstract —— Three new prenylflavanones, nymphaeol-A, -B and -C were isolated from *Hernandia nymphaefolia* (presl) Kubitzki, and the structures were assigned as I, II and III, respectively.

We have recently reported new alkaloidal components, hernagine (1,2,11-trimethoxy-10-hydroxy-N-noraporphine) and 3-cyano-4-methoxypyridine, isolated from the leaves of *Hernandia nymphaefolia* (Presl) Kubitzki (Japanese name " *Hasunoha-giri* ") collected on Ishigaki island[2]. In our further study on the constituents of this plant, we here report on the isolation and structures of three new prenylflavanones named as nymphaeol-A, -B and -C, respectively.

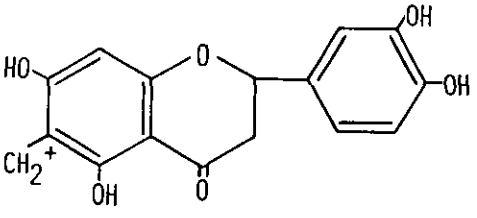
The non-basic fraction of methanol extract of the leaves was fractionated by column chromatography on silica gel. The phenolic fraction eluted with $CHCl_3$-MeOH (30:1) was submitted to preparative TLC on silica gel using $CHCl_3$-ether (1:1) to give nymphaeol-A (I, 0.6% in extract) and -B (II, 0.4% in extract).

Nymphaeol-A (I), $C_{25}H_{28}O_6$, was obtained as colorless needles, mp 168-170°, $[\alpha]_D$ -26.2° (c=0.21, $CHCl_3$), which gave purple color with MeOH-$FeCl_3$ and positive with Mg-HCl test. The IR (KBr) spectrum showed the presence of hydroxyl group (3300 cm^{-1}) and conjugated carbonyl group (1623 cm^{-1}). The UV spectra [λ_{max}^{EtOH} nm (log ε): 207 (4.69), 230 (sh, 4.43), 294 (4.29), 340 (sh, 3.63)] showed the bathochromic shift in basic medium [$\lambda_{max}^{EtOH\text{-}MeONa}$ nm (log ε): 249 (4.32), 334 (4.47)]. The salient feature of ^{1}H-NMR (acetone-d_6) spectrum is the ABX system, diagnostic for C_2 and C_3 protons of a flavanone nucleus[3]. The C_2 proton, the X part, appears as a double doublet at δ 5.33 (J_{AX}=12.4, J_{BX}=3.4 Hz) while the C_3 protons, the AB part, appears as δ 2.70 and 3.13 (J_{AB}=17.6, J_{AX}=12.4 Hz, J_{BX}=3.4 Hz). The MS spectrum showed the fragments at *m/e* 301 (M-123), 219 (base peak), 165, 136 and

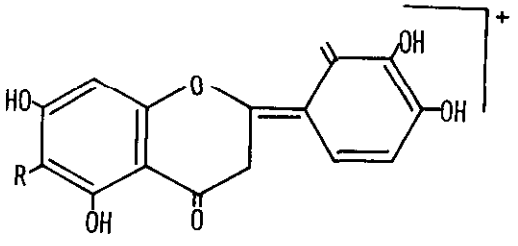
69[4-6]. The significant peak at *m/e* 301 (VII) indicates the loss of 123 mass units from the molecular ion, suggesting the presence of a geranyl (or neryl) group. The characteristic peaks at *m/e* 219 and 165 suggest the presence of two hydroxyl groups and a geranyl (or neryl) group on the ring A. The presence of geranyl (or neryl) group[4,5,7] was supported by the appearance in the ^{1}H-NMR spectrum of three methyl singlets at δ 1.59, 1.65, 1.80 (each 3H, C_{3}'',$_{8}$'',-CH_3), a broad singlet at δ 2.02 (4H, C_{5}'',$_{6}$'',-H), a broad doublet at δ 3.28 (2H, C_{1}'',-H) and a multiplet at δ 5.17 (2H, C_{2}'',$_{7}$'',-H). The possibility of geranyl group is supported by the appearance in the ^{13}C-NMR spectrum of C_{4}'', at δ 16.1 and C_{5}'', at δ 40.3, respectively[8]. The ^{1}H-NMR spectrum in pyridine-d_5 showed the *ortho*- and *meta*-coupled double doublet at δ 7.11 (1H, J=2 and 8 Hz, C_{6},-H), *ortho*-coupled doublet at δ 7.31 (1H, J=8 Hz, C_{5},-H) and *meta*-coupled doublet at δ 7.55 (1H, J=2 Hz, C_{2},-H), which indicated that the geranyl group on the ring A attached at C_6 or C_8. Acetylation of I with acetic anhydride in pyridine gave the triacetate (IV) and tetraacetate (V) as colorless syrups, respectively. The ^{1}H-NMR ($CDCl_3$) spectrum of IV shows that a signal of C_{1}'', methylene broad doublet at δ 3.23 is shifted downfield compared with that in V (δ 3.15) and the geranyl group is thus located at C_6[9]. These evidences led to the assignment of the structure (I) of nymphaeol-A devoided of the stereochemistry.

Nymphaeol-B (II), $C_{25}H_{28}O_6$, was obtained as colorless amorphous solid, mp 48-52°; IR ν_{max}^{KBr} cm^{-1}: 3300 (OH), 1623 (C=O); UV λ_{max}^{EtOH} nm (log ε): 215 (4.51), 230 (4.32), 290 (4.22); $\lambda_{max}^{EtOH\text{-}MeONa}$ nm (log ε): 217 (4.55), 250 (4.06), 328 (4.44); MS *m/e*: 300, 153 (base peak), 123, 69; ^{1}H-NMR (acetone-d_6) δ: 2.65 (1H, dd, J=3.2 and 17.2 Hz, C_{3eq}-H), 3.17 (1H, dd, J=12.6 and 17.2 Hz, C_{3ax}-H), 5.61 (1H, dd, J=3.2 and 12.6 Hz, C_{2}-H), 5.97 (2H, s, $C_{6,8}$-H), 6.81 (1H, d, J=8 Hz, C_{6},-H), 6.98 (1H, d, J=8 Hz, C_{5},-H), geranyl: 1.56, 1.62, 1.70 (each 3H, C_{3}'',$_{8}$'',-CH_3), 2.00 (4H, C_{5}'',$_{6}$'',-H), 3.54 (2H, C_{1}'',-H), 5.10 (2H, C_{2}'',$_{7}$'',-H). In the ^{1}H-NMR spectrum in pyridine-d_5, the presence of *meta*-coupled doublets (J=2 Hz) at δ 6.43 and 6.47 indicated that the A ring was unsubstituted at C_6 and C_8. Furthermore, the substitution pattern of two hydroxyls and a geranyl group on B ring was assigned as follows: The *ortho*-coupled doublets (J=8 Hz) at δ 6.81 and 6.98 in ^{1}H-NMR spectrum of II, showed the presence of 1,2,3,4-substituted ring B. And in the MS spectrum, the fragment peak at *m/e* 300, the loss of 124 mass units from the molecular ion, for a fragment VIII suggested the location of a geranyl moiety. Furthermore, this substitution pattern on B ring was also supported by the chemical shifts of carbons on ring B in ^{13}C-NMR spect-

rum of II. From these data, the structure of nymphaeol-B was assigned as II. The phenolic fraction eluted with $CHCl_3$ was submitted to preparative TLC on silica gel using $CHCl_3$-ether (1:1) to give nymphaeol-C (III, 10% in extract): mp 77-81°, $C_{30}H_{36}O_6$, $[\alpha]_D$ -14° (c=0.2, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3360 (OH), 1630 (C=O); UV λ_{max}^{EtOH} nm (log ε): 209 (4.66), 233 (sh, 4.26), 294 (4.12); $\lambda_{max}^{EtOH-MeONa}$ nm (log ε): 210 (4.69), 251 (4.05), 334 (4.32); ^{1}H-NMR ($CDCl_3$) δ: 2.69 (1H, dd, J=3.2 and 17.2 Hz, C_{3eq}-H), 3.09 (1H, dd, J=12.4 and 17.2 Hz, C_{3ax}-H), 5.44 (1H, dd, J=3.2 and 12.4 Hz, C_2-H), 5.92 (1H, s, C_6-H), 6.74 (1H, d, J=8 Hz, C_6,-H), 6.91 (1H, d, J=8 Hz, C_5,-H); geranyl and γ,γ-dimethylallyl: 1.56, 1.64, 1.74, 1.80 (15H, $C_{3''}$,$_{8''}$,$_{3'''}$,-CH_3), 2.02 (4H, $C_{5''}$,$_{6''}$,-H), 3.36 (4H, $C_{1''}$,$_{1'''}$,-H), 5.11 (3H, $C_{2''}$,$_{7''}$,$_{2'''}$,-H). From these data, nymphaeol-C was also belong with the flavanone having four hydroxyls, a geranyl and a γ,γ-dimethylallyl group. The MS spectrum of III showed the fragments at *m/e* 368, 221, 165 (base peak), 123, 69. The significant peak at *m/e* 368 (IX) indicates the loss of 124 mass units from the molecular ion, which was similar to the fragment VIII in nymphaeol-B (II); we assumed that the position of geranyl group and γ,γ-dimethylallyl group were thus located at C_2, and C_8. In addition, the similarities of three methyl singlets of geranyl group in the ^{1}H-NMR (acetone-d_6) spectrum of nymphaeol-B (δ 1.56, 1.62, 1.70) and -C (δ 1.56, 1.61, 1.70) supported the assignment of the structure of nymphaeol-C as III.



(VII) *m/e* 301 (M^+-123)



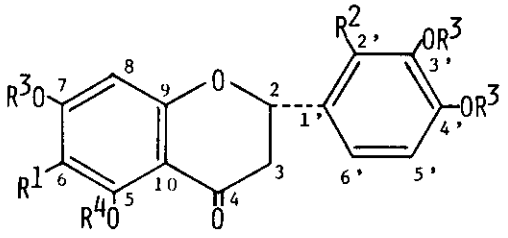
(VIII) R=H, *m/e* 300 (M^+-124)
(IX) R=P, *m/e* 368 (M^+-124)

These structures of nymphaeol-A, -B and -C were also supported by the ^{13}C-NMR spectra indicated in the next page.

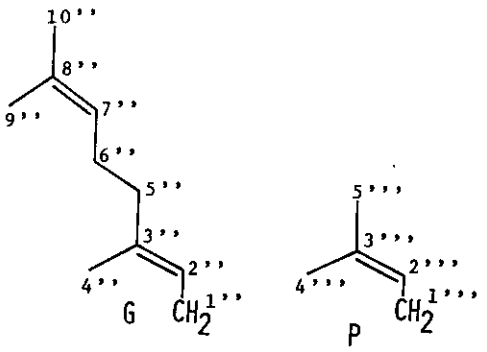
Comparison of the ^{13}C-NMR chemical shifts of eriodictyol (in DMSO-d_6)[10], nymphaeol-A (in acetone-d_6), nymphaeol-B (in acetone-d_6) and nymphaeol-C (in acetone-d_6)

	Chemical shift (ppm)				Chemical shift (ppm)			
Carbon No.	Eriodic.	Nym.-A	Nym.-B	Nym.-C	Carbon No.	Nym.-A	Nym.-B	Nym.-C
2	78.3	79.5	77.0	76.9	1''	21.4	25.1	25.1
3	42.2	43.4	43.1	43.3	2''	123.2	123.8	123.7
4	196.2	196.5	197.0	197.0	3''	134.3	135.0	135.0
5	163.4	161.7	164.8	161.8	4''	16.1	16.3	16.3
6	95.7	108.6	96.6	108.7	5''	40.3	40.3	40.2
7	166.6	164.7	167.0	164.4	6''	27.2	27.2	27.2
8	94.8	95.0	95.6	95.0	7''	124.7	124.7	124.6
9	162.8	161.3	164.2	161.8	8''	131.0[b]	131.4	131.3
10	101.7	102.5	102.8	102.7	9''	17.6	17.6	17.8
1'	129.4	130.9[b]	129.4	129.5	10''	25.7	25.7	25.7
2'	114.2	114.2	127.3	127.1	1'''	–	–	21.5
3'	145.1[a]	145.4[c]	143.7	143.6	2'''	–	–	123.3
4'	145.6[a]	145.8[c]	145.2	145.1	3'''	–	–	130.7
5'	115.3	115.7	113.2	113.2	4'''	–	–	17.8
6'	117.8	118.6	118.2	118.1	5'''	–	–	25.7

Values with the same superscript could be interchanged.



(I) R^1=G, R^2=R^3=R^4=H
(II) R^2=G, R^1=R^3=R^4=H
(III) R^1=P, R^2=G, R^3=R^4=H
(IV) R^1=G, R^2=R^4=H, R^3=Ac
(V) R^1=G, R^2=H, R^3=R^4=Ac
(VI) R^2=G, R^1=H, R^3=R^4=Ac



The absolute configuration of nymphaeol-A, -B and -C were determined as (-)-2S-flavanones by the CD spectra[11]. Since the 2-aryl group in (-)-nymphaeol-A (I) is equatorial ($J_{2,3ax}$=12.4 Hz)[12] the positive Cotton effect at 330 nm ($\Delta\epsilon$ +0.49) and the negative Cotton effect at 293 nm ($\Delta\epsilon$ -3.58) allows the assignment of the S configuration at C-2 in (-)-nymphaeol-A (I). Similarly, nymphaeol-C (III) indicated the positive Cotton effect at 333 nm ($\Delta\epsilon$ +0.55) and the negative Cotton effect at 292 nm ($\Delta\epsilon$ -6.41). The absolute configuration of nymphaeol-B (II) was established by the measurement of CD spectrum [335 nm ($\Delta\epsilon$ +1.30) and 306 nm ($\Delta\epsilon$ -2.39)] of its tetraacetate (VI).

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