

NEW PRENYLFLAVANONES FROM *HERNANDIA NYMPHAEFOLIA* (PRESL) KUBITZKI

Kenichi Yakushijin, Kenichi Shibayama, Hiroyuki Murata¹ and
Hirosi Furukawa*

Faculty of Pharmacy, Meijo University, Yagoto, Tempaku, Nagoya
468, Japan

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 island². 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.

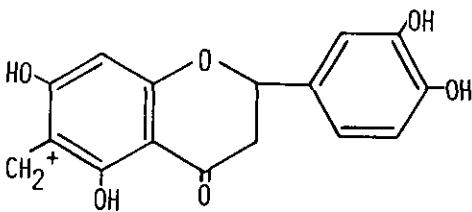
The non-basic fraction of methanol extract of the leaves was fractionated by column chromatography on silica gel. The phenolic fraction eluted with CHCl₃-MeOH (30:1) was submitted to preparative TLC on silica gel using CHCl₃-ether (1:1) to give nymphaeol-A (I, 0.6% in extract) and -B (II, 0.4% in extract).

Nymphaeol-A (I), C₂₅H₂₈O₆, was obtained as colorless needles, mp 168-170°, [α]_D -26.2° (c=0.21, CHCl₃), which gave purple color with MeOH-FeCl₃ 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 [λ_{max}^{EtOH-MeONa} nm (log ε): 249 (4.32), 334 (4.47)]. The salient feature of ¹H-NMR (acetone-d₆) spectrum is the ABX system, diagnostic for C₂ and C₃ protons of a flavanone nucleus³. The C₂ proton, the X part, appears as a double doublet at δ 5.33 (J_{AX}=12.4, J_{BX}=3.4 Hz) while the C₃ 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

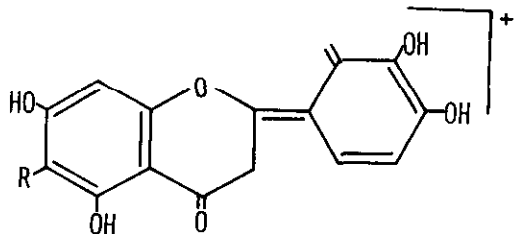
69⁴⁻⁶. The significant peak at m/e 301 (VII) indicates the loss of 123 mass units from the molecular ion, suggesting the presence of a geranyl (or neryl) group. The characteristic peaks at m/e 219 and 165 suggest the presence of two hydroxyl groups and a geranyl (or neryl) group on the ring A. The presence of geranyl (or neryl) group^{4,5,7} was supported by the appearance in the ¹H-NMR spectrum of three methyl singlets at δ 1.59, 1.65, 1.80 (each 3H, C_{3,,8,,}-CH₃), 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 ¹³C-NMR spectrum of C_{4,,} at δ 16.1 and C_{5,,} at δ 40.3, respectively⁸. The ¹H-NMR spectrum in pyridine-d₅ 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 C₆ or C₈. Acetylation of I with acetic anhydride in pyridine gave the triacetate (IV) and tetraacetate (V) as colorless syrups, respectively. The ¹H-NMR (CDCl₃) 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 C₆⁹. These evidences led to the assignment of the structure (I) of nymphaeol-A devoided of the stereochemistry.

Nymphaeol-B (II), C₂₅H₂₈O₆, was obtained as colorless amorphous solid, mp 48-52°; IR ν_{\max}^{KBr} cm⁻¹: 3300 (OH), 1623 (C=O); UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ϵ): 215 (4.51), 230 (4.32), 290 (4.22); $\lambda_{\max}^{\text{EtOH-MeONa}}$ nm (log ϵ): 217 (4.55), 250 (4.06), 328 (4.44); MS m/e : 300, 153 (base peak), 123, 69; ¹H-NMR (acetone-d₆) 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, C₂-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,,}-CH₃), 2.00 (4H, C_{5,,6,,}-H), 3.54 (2H, C_{1,,}-H), 5.10 (2H, C_{2,,7,,}-H). In the ¹H-NMR spectrum in pyridine-d₅, the presence of *meta*-coupled doublets (J=2 Hz) at δ 6.43 and 6.47 indicated that the A ring was unsubstituted at C₆ and C₈. 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 ¹H-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 ¹³C-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°, $\text{C}_{30}\text{H}_{36}\text{O}_6$, $[\alpha]_D -14^\circ$ ($c=0.2$, CHCl_3); IR $\nu_{\text{max}}^{\text{CHCl}_3} \text{ cm}^{-1}$: 3360 (OH), 1630 (C=O); UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm ($\log \epsilon$): 209 (4.66), 233 (sh, 4.26), 294 (4.12); $\lambda_{\text{max}}^{\text{EtOH-MeONa}}$ nm ($\log \epsilon$): 210 (4.69), 251 (4.05), 334 (4.32); $^1\text{H-NMR}$ (CDCl_3) δ : 2.69 (1H, dd, $J=3.2$ and 17.2 Hz, $\text{C}_{3\text{eq}}\text{-H}$), 3.09 (1H, dd, $J=12.4$ and 17.2 Hz, $\text{C}_{3\text{ax}}\text{-H}$), 5.44 (1H, dd, $J=3.2$ and 12.4 Hz, $\text{C}_2\text{-H}$), 5.92 (1H, s, $\text{C}_6\text{-H}$), 6.74 (1H, d, $J=8$ Hz, $\text{C}_6\text{-H}$), 6.91 (1H, d, $J=8$ Hz, $\text{C}_5\text{-H}$); geranyl and γ,γ -dimethylallyl: 1.56, 1.64, 1.74, 1.80 (15H, $\text{C}_{3,,8,,3,,}\text{-CH}_3$), 2.02 (4H, $\text{C}_{5,,6,,}\text{-H}$), 3.36 (4H, $\text{C}_{1,,1,,}\text{-H}$), 5.11 (3H, $\text{C}_{2,,7,,2,,}\text{-H}$). 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 $^1\text{H-NMR}$ (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) $\text{R}=\text{H}$, m/e 300 (M^+-124)

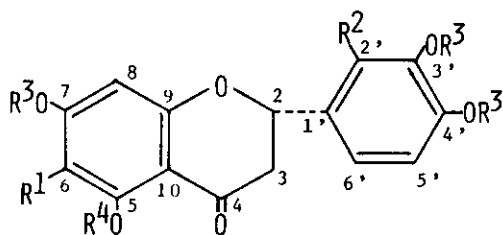
(IX) $\text{R}=\text{P}$, m/e 368 (M^+-124)

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

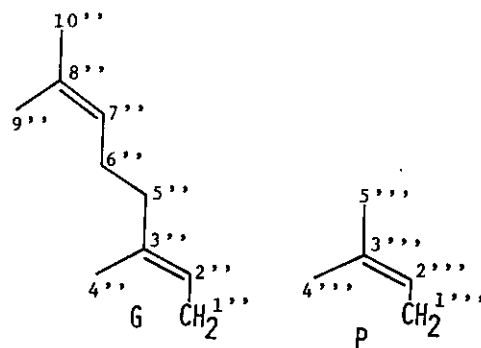
Comparison of the ^{13}C -NMR chemical shifts of eriodictyol (in DMSO-d_6)¹⁰, nymphaeol-A (in acetone- d_6), nymphaeol-B (in acetone- d_6) and nymphaeol-C (in acetone- d_6)

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) R¹=G, R²=R³=R⁴=H
- (II) R²=G, R¹=R³=R⁴=H
- (III) R¹=P, R²=G, R³=R⁴=H
- (IV) R¹=G, R²=R⁴=H, R³=Ac
- (V) R¹=G, R²=H, R³=R⁴=Ac
- (VI) R²=G, R¹=H, R³=R⁴=Ac



The absolute configuration of nymphaeol-A, -B and -C were determined as (-)-2S-flavanones by the CD spectra¹¹. 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).

References

1. Present address: 12-cho, Ibusuki, Kagoshima 891-04, Japan.
2. K. Yakushijin, S. Sugiyama, Y. Mori, H. Murata and H. Furukawa, Phytochemistry, in press.
3. J. Massicot and J. -P. Marthe, Bull. Soc. Chim. France, 1962, 1962; R. Hansel, D. Ohlendorf and A. Pelter, Z. Naturforsch., 1970, 25B, 989.
4. A. Ueno, M. Ichikawa, T. Miyase, S. Fukushima, Y. Saiki and K. Morinaga, Chem. Pharm. Bull. (Tokyo), 1973, 21, 1734.
5. T. Nomura and T. Fukai, Heterocycles, 1978, 9, 1295.
6. H. Audier, Bull. Soc. Chim. France, 1966, 2892.
7. G. Cardillo, L. Merlini and R. Mondelli, Tetrahedron, 1968, 24, 497.
8. M. Kozawa, N. Morita, K. Baba and K. Hata, J. Pharm. Soc. Japan, 1978, 98, 210; T. Nomura, T. Fukai, J. Uno and T. Arai, Heterocycles, 1978, 9, 1543.
9. F. Bohlmann, C. Zdero, R. M. King and H. Robinson, Phytochemistry, 1979, 18, 1246; F. Bohlmann and W. -R. Abraham, ibid., 1979, 18, 1851.
10. H. Wagner and V. M. Chari, Tetrahedron Lett., 1976, 1799.
11. W. Gaffield, Tetrahedron, 1970, 26, 4093.
12. J. W. Clark-Lewis, Aust. J. Chem., 1968, 21, 2059.

Received, 26th November, 1979