NOVEL QUASSINOIDS FROM *EURYCOMA LONGIFOLIA*

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A new 1, 2-seco-1-nor-6(5-10)-*abeo*-picrasan-2, 5-olide skeleton quassinoid named eurylactone and two new C_{19}- and C_{20}-skeleton quassinoids were isolated from the woods of *Eurycoma longifolia* (Simaroubaceae). Their structures were established by spectroscopic means.

KEYWORDS eurylactone; quassinoid; *Eurycoma longifolia*; Simaroubaceae

Crude extracts of *Eurycoma longifolia* (Simaroubaceae), one of the famous folk medicines in Southeast Asia, have been shown to exhibit antimalarial and cytotoxic activities.[1] During a survey of novel cytotoxic antitumour compounds from *Eurycoma longifolia*, we earlier reported on various quassinoids,[2] squalene-type[3] and tirucallane-type[4] triterpenes. As a result of our further fractionation efforts, a new 1, 2-seco-1-nor-6(5-10)-*abeo*-picrasan-2, 5-olide skeleton quassinoid, named eurylactone (**1**), and two new C_{19}- and C_{20}-skeleton quassinoids (**2** and **3**) were isolated from the *n*-butanol extract of the woods. In this communication, the structural elucidation of compounds **1** - **3** is reported.

The methanolic extract of the woods of *E. longifolia*[4] was successively partitioned into methylene chloride, *n*-butanol and water, and the *n*-butanol layer was subjected to Diaion HP-20. The fractions eluted with 40% methanol were further separated by silica gel chromatography using methylene chloride - methanol and ethyl acetate - methanol solvent system to give compounds **1** - **3** (**1**: 0.035%, **2**: 0.44%, **3**: 0.036% yield from the *n*-butanol extract).

Eurylactone (**1**),[5] mp 210-212°C from ethyl acetate, $[\alpha]_D$ +62.4° (c 0.17, MeOH), was shown to have a norpicrasane skeleton, $C_{19}H_{22}O_9$, by high resolution mass spectrum. In the NMR spectra, the presence of an exomethylene (^{1}H: δ 5.58 and 6.06; ^{13}C: δ 149.22 and 119.28), a δ-lactone (^{13}C: δ 173.58) and an 11β,20-epoxy (^{1}H: δ 3.90 and 4.58, ^{13}C: δ 68.62) moiety indicated the similarity to eurycomanone[6] except for A and B rings. The IR (1742cm^{-1}) and UV (213nm, ε 12700) spectra indicated the presence of an α,β-unsaturated γ-lactone. In this group, an α-proton at δ 5.97 was long-range coupled with both a lactonic proton at δ 5.16 and a methyl proton at δ 2.56 attached to β-position on the α,β-unsaturated γ-lactone. Furthermore, methylene protons (δ 2.40 and 3.04) at C-6 were only coupled with a proton (δ 5.11) at C-7. These data suggested that **1** possesses 1,2-seco-1-nor-6(5-10)-*abeo*-picrasan-2,5-olide skeleton, which has been known only in shinjulactone B[7] and yadanziolide.[8]

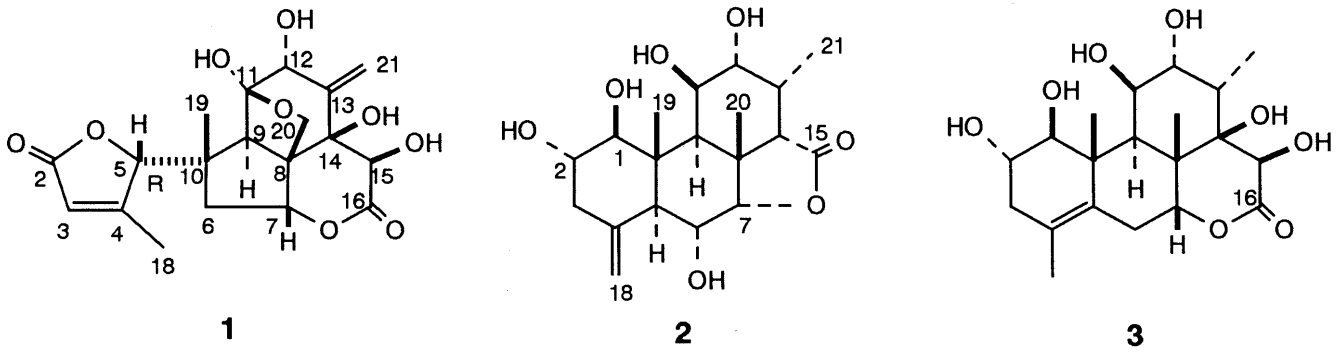

Fig. 1

Using a combination of homo- and heteronuclear two-dimensional NMR techniques (^{1}H-^{1}H COSY, HMQC and HMBC spectra), complete assignments of the ^{1}H and ^{13}C signals of **1** were successfully performed (see Ref. and Table 1). The stereostructure was corroborated by the NOE relationships observed in phase-sensitive NOESY spectrum (Fig. 3). The configuration at C-5 can be interpreted to be R by the NOE's between H-9 and H-18 and between H-5 and H-6α, considering the biosynthesis of quassinoids, which was also confirmed by X-ray analysis (Fig. 2).[9]

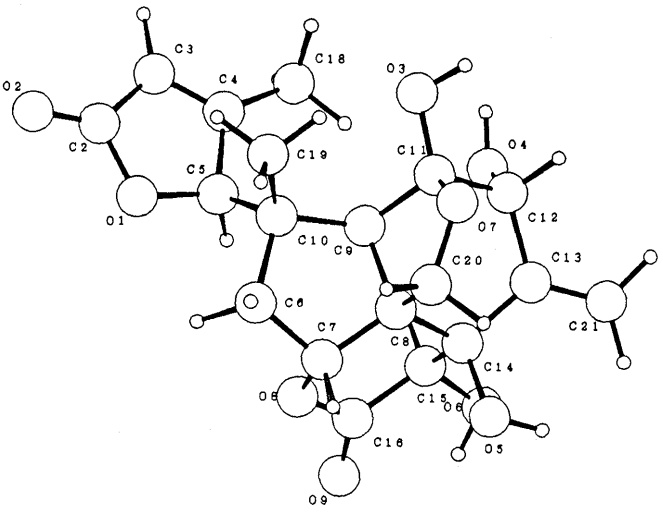

Fig. 2. Molecular Structure of Eurylactone **1**

Biogenetically, eurylactone seems to be derived from a picrasane-type derivative, such as 14, 15β-dihydroxy-klaineanone,[2] which is a similar biosynthetic route from ailantone to shinjulactone B.[7]

Compound **2**,[10] mp 145-147°C from ethyl acetate, $[\alpha]_D$ +68.6° (c 1.8, MeOH), was shown to have a longilactone-type C_{19}-skeleton,[2] $C_{19}H_{28}O_7$, by high resolution mass spectrum. The spectroscopic data about the A ring were different from those of longilactone;[2] *i.e.* **2** shows no UV absorption band ascribable to an α,β-unsaturated ketone and the presence of an exomethylene group in NMR spectra (^{1}H: δ 5.30 and 5.43; ^{13}C: δ 141.72 and 110.34). In ^{1}H-^{1}H COSY spectrum, H-1 (δ 3.84) attached to a hydroxyl-bearing carbon was coupled with H-2 (δ 4.11) also attached to a hydroxyl-bearing carbon, which was also coupled with methylene protons (δ 2.84 and 2.21). Then, the exomethylene protons were long-range coupled with both the above methylene and a proton (δ 2.72) ascribable to H-5. These couplings and the NOE relationship (Fig. 3) indicated the partial structure of the A ring as in Fig. 1. The other ^{1}H and ^{13}C-NMR data were consistent with those of longilactone.[2]

Compound **3**,[11] mp 148-150°C from toluene, $[\alpha]_D$ +93.7° (c 0.19, MeOH), was shown to have the klaineanone-type C_{20}-skeleton, $C_{20}H_{30}O_8$, by high resolution mass spectrum. The spectroscopic data of B, C and D rings were almost identical with those of 14, 15β-dihydroxyklaineanone.[2] In ^{1}H NMR spectrum, the coupling sequence from H-1 to H-3 in ring A was similar to that of **2**; however, a methyl signal (δ 1.76) on a double bond was observed. The H-6 methylene protons were only coupled with H-7, and, in ^{13}C-NMR, two quaternary carbons (δ 124.70 and 131.99) ascribable to a double bond were newly observed. Therefore, the structure **3** with the double bond at C-4 in ring A was deduced as shown in Fig. 1. The stereostructure was established as shown in Fig. 3 by NOE relationship.

Pharmacological activities of compounds **1** - **3** are now under investigation.

Table 1 ^{13}C-NMR Data of Compounds **1** - **3** [Pyridine-d_5, 125MHz]

Carbon	1	2	3
C-1		82.64	82.90
C-2	172.59	73.46	67.66
C-3	119.09	44.66	41.09
C-4	170.03	141.72	124.70
C-5	92.15	52.55	131.99
C-6	46.14	64.23	28.47
C-7	82.75	87.11	70.89
C-8	63.04	43.59	47.08
C-9	47.98	42.99	46.61
C-10	47.43	44.47	44.50
C-11	110.20	72.79	74.40
C-12	82.75	75.33	82.81
C-13	149.22	27.38	36.62
C-14	77.92	56.28	77.57
C-15	71.94	177.14	77.89
C-16	173.58		176.10
C-18	16.19	110.34	14.22
C-19	18.38	13.61	16.11
C-20	68.62	21.25	19.77
C-21	119.28	14.77	19.64

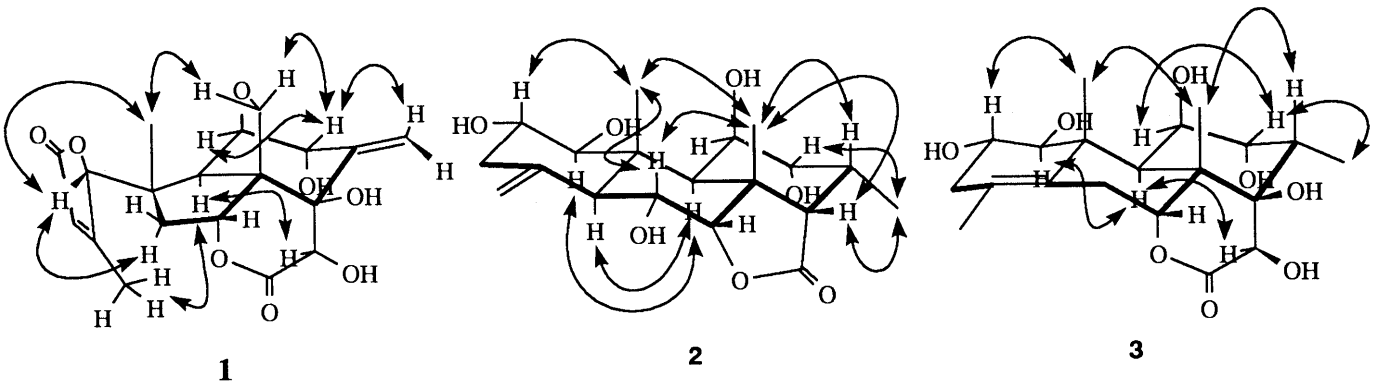

Fig. 3. NOE Enhancements of Compounds **1-3**
Arrows show NOE relationship.

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5) ^{1}H-NMR (Pyridine-d$_5$, 400MHz): δ 5.97 (t, J 1.5, H-3), 5.16 (brs, H-5), 2.40 (dd, J 4.8, 16.2, H-6β), 3.04 (d, J 16.2, H-6α), 5.11 (d, J 4.8, H-7), 3.90 (s, H-9), 4.81 (s, H-12), 5.68 (s, H-15), 2.56 (brs, H-18), 1.59 (s, H-19), 3.90 and 4.58 (each d, J 8.7, H-20), 5.58 and 6.06 (d, J 1.5, H-21). HI-MS *m/z* 394.1263 Calcd. for $C_{19}H_{22}O_9$, Found 394.1264.

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9) Crystal data: $C_{19}H_{22}O_9$, M_r=394.4, orthorbombic, space group $P2_12_12_1$, z=4, a=11.283(6), b=17.753(9), c=8.804(5)Å, V=1763.5Å^3, Dx=1.485 gcm^{-3}, Data were measured on Philips PW 1100 diffractometer using graphite-monochromated Cu-Kα radiation with the ω-2θ scan technique. The structure was solved by direct methods and block-diagonal-matrix least-squares refinement gave R=0.0553, for 1880 reflections in the 2θ range 6^o through 156^o.

10) ^{1}H-NMR (Pyridine-d$_5$, 400MHz): δ 3.84 (d, J 8.1, H-1), 4.11 (ddd, J 5.8, 12.0, 8.1, H-2), 2.84 (dd, J 5.8, 12.0, H-3e), 2.21 (t, J 12.0, H-3a), 2.72 (d, J 11.3, H-5), 4.63 (dd, J 11.3, 3.5, H-6), 4.49 (d, J 3.5, H-7), 2.59 (d, J 1.6, H-9), 5.77 (brt, J 3.6, H-12), 2.78 (ddq, J 2.8, 5.5, 7.4, H-13), 2.46 (d, J 5.5, H-14), 5.30 and 5.43 (each brs, H-18), 1.58 (s, H-19), 1.90 (s, H-20), 1.74 (d, J 7.4, H-21). HI-MS *m/z* 368.1835 Calcd. for $C_{19}H_{28}O_7$, Found 368.1864.

11) ^{1}H-NMR (Pyridine-d$_5$, 400MHz): δ 3.98 (d, J 9.8, H-1), 4.16 (ddd, J 5.3, 9.8, 10.5, H-2), 2.44 (dd, J 5.3, 16.5, H-3e), 2.35 (dd, J 10.5, 16.5, H-3a), 2.75 (brd, J 15.0, H-6e), 2.98 (dd, J 3.6, 15.0, H-6a), 4.92 (dd, J ??, 3.6, H-7), 2.55 (d, J 2.2, H-9), 5.64 (ddd, J 2.2, 2.8, 5.3, H-11), 4.40 (ddd, J 2.8, 2.9, 4.3, H-12), 3.12 (dq, J 2.9, 7.3, H-13), 5.79 (s, H-15), 2.14 (s, H-20), 1.76 (s, H-18), 2.01 (s, H-19), 1.80 (d, J 7.3, H-21), 6.28 (d, J 5.3, OH-11), 6.94 (d, J 4.3, OH-12). HI-MS *m/z* 398.1940 Calcd. for $C_{20}H_{30}O_8$, Found 398.1924.

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