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Friedelin, a Triterpenoid Pentacyclic from the Leaves of *Calophyllum soulattri* Burm.f. (Guttiferae)

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Abstrak

Kajian kimia daun Bitanggur (*Calophyllum soulatri* Burm.f.) menghasilkan triterpenoid cincin lima friedelin (I). Penetapan struktur senyawa hasil isolasi dilakukan dengan data-data spektroskopi seperti spektrofotometer inframerah, ^{1}H dan ^{13}C RMI dan spektroskopi masa.

Keywords: *Calophyllum soulattri* Burm.f., Guttiferae, pentacyclic triterpenoid, friedelin.

Introduction

Most of the known constituents reported from *Calophyllum* species (Guttiferae) were derived from xantone, coumarin, chalchon, biflavonoid and triterpen derivate (Gunasekera *et all*, 1975; Cao, *et al*, 1997; Chihiro, *et al*, 1999). A famous anti-HIV compound calanolide from *Calophyllum inophyllum* is now in clinical trial to be use as future AIDS drug (Tsutomu, 2000). Gunasekera *et all* (1977) who investigate *C. cuneifolium* Thw. and *C. soulattri* Burm.f. led to identify several compounds from the bark and timber of *C. cuneifolium* such as calaba-xanthone, trapezifolixanthone, 6-deoxyjacareubin, 1,6-dihydroxy-5-metho-xyxanthone, 1,7-dihydroxy xanthone,1-hydroxy-5-methoxyxanthone, 1,3,5-trihydroxy-2-(3-methylbut-2-enyl)xanthon, taraxerol, simiaren-3β-ol, friedelin, β-sitosterol and isoapetalic acid. While from *C. soulattri* they found soulattrolide and taraxerone together with taraxerol, 1,3,5-trihydroxy-2-(3-methyl-but-2-enyl)xanthon and β-sitosterol.

In West Sumatra-Indonesia, *Calophyllum soulattri* is endemic plant in the Pinang-Pinang village forest. Traditionally, the bark of plant is used for fish poison and the leaves is used for arthritis illness or making 'jamu' for horses if animal being unwell (Burkill, 1966). However, the information of chemistry of this plant is still limited. We reported previously a biflavonoid amentoflavon as flavonoid constituent from the leaves of this plant. In this study, we describe the isolation of a pentacyclic triterpenoid friedelin (I) and reported firstly from the leaves of this plant.

MATERIALS AND METHODS

General: Melting point was determined on Fisher melting point apparatus and uncorrected. Infrared spectrum was recorded as potassium bromide disc using a Biorad FTIR instrument. ^{1}H and ^{13}C NMR spectra were determined in $CDCl_3$ on a Bruker spectrometer at 500 and 125 MHz, respectively. An EI spectrum was obtained on Micromass Quatro II mass spectrometer. Column chromatography was performed on silica gel G (Merck, 7743) and TLC on silica gel with indicator at 254 nm (PolyGram Sil G/UV_{254}).

Plant materials: The leaves of *Calophyllum soulattri* were collected from Pinang-Pinang region, West Sumatra Indonesia in 2004. Identification of *C. soulattri* was done in Herbarium Biology-FMIPA, the University of Andalas (ANDA).

Extraction and purification: The fresh leaves (5.2 Kg) of *Calophyllum soulattri* were chopped into small pieces, and then extracted with methanol for 3 days. Extraction was repeated twice more and the combined extracts were concentrated *in vacuo* to about 1 L. The methanolic extract was triturated with hexane and then with ethyl acetate, successively, to separate non-polar and semi polar compounds. Water fraction was extracted with n-buthanol. All fraction were evaporated *in vacuo* to give a residue; 28.7 g, 16.7 g and 48.6 g, for hexane, ethyl acetate and n-butanol respectively.

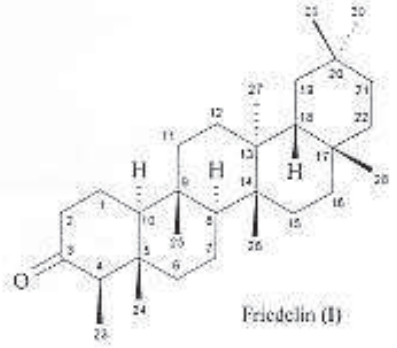
Sixteen gram of ethyl acetate fraction were chromatographed on column chromatography using silica gel G (150 g on 3 x 60 cm column) and then eluted successively with hexane, hexane-ethyl acetate and ethyl acetate-methanol mixes of increasing polarity progressively. Each fractions collected were spotted on TLC plate and then eluted with n-hexane-ethyl acetate (1:4) or ethyl acetate-methanol (1:9). The spots with similar Rf value on TLC were combined and evaporated the solvent to give ten sub-fractions (CS-Et-01 – CS-Et-10). Sub-fraction from CS-Et-05 to Cs-Et-07 showed a yellow pale precipitate and then crystallized with methanol to afford 450 mg of biflavonoid amentoflavon.

The minor compound from these fraction (CS-Et-02 and CS-Et-03; named CS-Et-23) showed green-violet spot on TLC with vanillin - sulfuric acid. The combined sub fractions (2,1 g) were chromatographed on silica gel (30g on 2 x 30 cm column) and n-hexane-ethyl acetate gradient solvent system were used as solvent elution. After collecting each fraction and then monitored on TLC, the spots giving positive reaction with vanillin - sulfuric acid were combined. One major spot was collected (CS-Et23-15-19) and crystallized using acetone-methanol to give a pale crystalline powder (150 mg), m.p. 262-263°C.

RESULTS AND DISCUSSION

The ethyl acetate extract of the leaves of *Calophyllum soulattri* was partitioned over Silica gel column using hexane with increasing polarity by ethyl acetate as solvent system. From previous work, we obtained a biflavonoid amentoflavon as a major component from the ethyl acetate fraction of *C. soulattri*. Indeed, apart of flavonoid containing-fraction, a second major band was observed when the TLC plat of this fraction was treated with vanillin-sulfuric acid reagent. Thus, indicating this extract contains also triterpenoid compound. Pursue our work on this extract lead us to isolate a pale cristalin powder (I), m.p 262-263 °C (ref. 263 °C). IR υ_{max}^{KBr} cm^{-1}: 1777 (C=O stretching), 2927 and 1390 (C-H stretching and C-H bending, respectively). The MS spectrum showed a molecular ion peak at *m/z* 246.0.

The ^{1}H NMR of (I) (Fig.1) revealed signals for seven singlet of methyls at δ 1.18 (H-28),1.05 (H-27), 1.01 (H-26), 1.00 (H-30), 0.96 (H-29),0.87 (H-25) and 0.73 (H-24), a doublet of methyl at δ (ppm) 0.88 (d, J = 6.64 Hz, H-23). a methine proton(CH) at δ 2.25 (q, J = 6.64 Hz, H-4), and methylene protons (CH_2) at δ (ppm) 2.40 (ddd, J = 13.96, 5.26, 2.06 Hz, H-2) and δ 2.31 (ddd, J = 13.96, 7.09, 1.15 Hz, H-2), respectively. There is no vinylic signal observed.



Friedelin (I)

The ^{13}C of NMR spectra showed a total of 30 carbon atoms were observed including one of ketone carbon at δ=213.23 ppm. The remaining of 29 carbons was characterized by DEPT spectra (spectra not shown) indicating the present of 8 methyl groups along with 11 of CH_2, 4 of CH and 6 of quaternary carbons (minus C=O). These data showed that compound (I) seemed to be friedelin (Akihisa *etal*., 1992). The ^{13}C NMR data (Tab.1) was identical with those reported in literature for friedelin (Mahato and Kundu, 1994). Therefore, the molecular formula of (I) was determined as $C_{30}H_{50}O$, which correspond with a molecular ion (M^+, *m/z*) = 426.0.

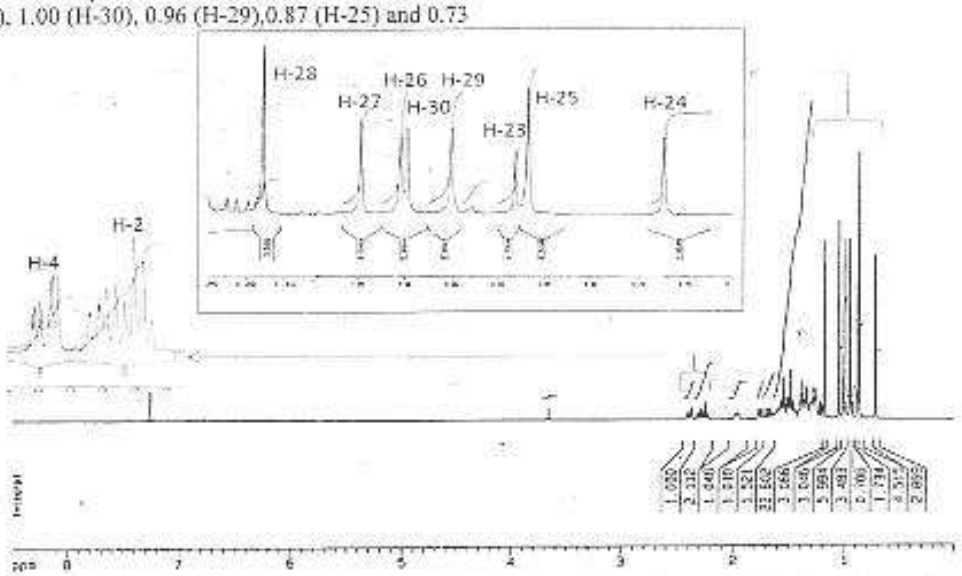


Fig. 1. ^{1}H NMR spectra of compound (I) in $CDCl_3$ (insert region 0.7 - 1.2 and 2.2 - 2.45 ppm)

Table 1. ^{13}C NMR of triterpenoid isolated from *Calophyllum soulattri* in $CDCl_3$, δ (ppm)

No.of C	Comp (I)	Friedelin (Mahato, 1994)	Exp
1	22.27	22.3	CH_2
2	41.52	41.5	CH_2
3	213.23	213.2	C=O
4	58.22	58.2	CH
5	42.14	42.1	C
6	41.28	41.3	CH_2
7	18.23	18.2	CH_2
8	53.09	53.1	CH
9	37.44	37.4	C
10	59.47	59.4	CH
11	35.62	35.6	CH_2
12	30.49	30.5	CH_2
13	39.69	39.7	C
14	38.29	38.3	C
15	32.41	32.4	CH_2
16	36.00	36.0	CH_2
17	29.99	30.0	C
18	42.78	42.8	CH
19	35.33	35.3	CH_2
20	28.16	28.1	C
21	32.76	32.7	CH_2
22	39.24	39.2	CH_2
23	6.81	6.8	CH_3
24	14.65	14.6	CH_3
25	17.93	17.9	CH_3
26	20.25	20.2	CH_3
27	18.65	18.6	CH_3
28	32.08	32.1	CH_3
29	35.01	35.0	CH_3
30	31.77	31.8	CH_3

Friedelin is a triterpenoid common in plant Kingdom and this compound was isolated for the first time from *Harungana madagascariensis* Lam. ex Poir (Clusiaceae). The stereochemistry of this terpenoid was deduced after its crystal structure established in 1989 and then reinvestigate again by Declercq *et al.* in 1991. The distribution of (I) in the plant Kingdom mainly in the family of Celastraceae, Guttiferae and Flacourtiaceae (Gunatilaka, 1984). From *Calophyllum* species, friedelin has been reported from *Calophyllum innophyllum* (Ali, *et al.*, 1999; Yimdjo, *et al.* 2004), *C. gracilipes* (Cao, *et al.*, 1997), *C. lankaensis*, *C. thwaitesii* (Dhamaratne, *etal.*, 1984), *C. calaba* (Gunatilaka, *et al.*, 1984), *C. amoenum* (Banerji, *et al.*, 1977) and *C. cuneifolium* (Gunasekera, *et al.*, 1977), but none mentioned before from *C. soulattri*.

Despite of this compound found in many medicinal plants, several bioassays has been done. It seem that friedelin has no effect on antimicrobial activity, antioxidant, cytotoxic test and antiulcerogenic (Yang, *et al.*, 2006, Subhadhirasakul and Pechpongs, 2005; Queiroga, *et al.*, 2000). However, extract Bamboo containing rich in friedelin was reported to have vasodilator effect (Jiao, *et al.*, 2007) and friedelin derivates have potential cytotoxic effect to insect and mammalian cell (Moiteiro, *et al.*, 2006)

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