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A New 30-nor Trijugin-type Limonoid, Chisotrijugin, from the Bark of *Chisocheton cumingianus* (Meliaceae)

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Abstract

A new 30-nor trijugin-type limonoid, chisotrijugin (**1**), has been isolated from the bark of *Chisocheton cuminganus* belong to the Meliaceae family. The chemical structure of **1** was elucidated by spectroscopic techniques such as UV, IR, MS, 1D and 2D NMR.

Keywords: trijugin-type limonoid, *Chisocheton cumingianus*,

Meliaceae **1. Introduction**

The genus *Chisocheton* belongs to the Meliaceae family, is consist more than 50 species and widely distributed in Nepal, India, Bhutan, Myanmar, South China, Thailand, Indonesia, Malaysia, and Papua New Guinea (Vossen and Umali, 2002). Various type of compounds have been reported from this genus such as sesquiterpenoids (Phongmaykin et al., 2008), dammarane-type triterpenoids (Phongmaykin et al., 2008; Inada et al., 1993), tirucallane-type triterpenoids (Zhang et al., 2012), apotirucallane-type triterpenoids (Yang et al., 2011) and limonoids (Yang et al., 201; Maneerat et al., 2008; Laphookhieo et al., 2008; Mohamad et al., 2009; Najmuldeen et al 2010; Najmuldeen et al., 2011; Wong et al., 2011).

In our search for novel limonoid compounds from Indonesia *Chisocheton* plants, we started our search for novel compounds from the bark of *Chisocheton cumingianus*. *C. cumingianus* is a higher plants and widely distributed in northern part of Sulawesi island in Indonesia (Heyne, 1982). The plant is known in folklore and traditional medicine in Indonesia for the treatment of fever and skin diseases (Hidayat and Hutapea, 1991; Heyne, 1982). Although secondary metabolites from other *Chisocheton* species have been reported previously, the chemical constituents of *C. cumingianus* is yet to be reported. We report herein the isolation and structure elucidation of the new limonoid compound, 30-nor trijugin-type limonoid, chisotrijugin (**1**).

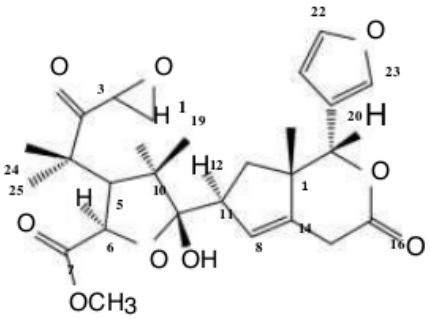

Figure. 1. Chemical structure for **1**.

2. Material and Methods

2.1 General

Melting points were measured on an electrothermal melting point apparatus IA9000 (Bibby Scientific Limited, Staffordshire, UK). Optical rotations were recorded on a Perkin-Elmer 341 polarimeter (Waltham, MA, USA). The IR spectra was recorded on a Perkin- Elmer 1760X FT-IR (Waltham, MA, USA) in KBr. Mass spectra was obtained with a Water Qtof HR-MS XEV^{otm} mass spectrometer (Santa Clara, CA, USA). ^{1}H- and ^{13}C-NMR spectra were obtained with a JEOL JNM-A-500 spectrometer (Tokyo, Japan) using TMS as an internal standard. Chromatographic separations were carried out on silica gel 60 and ODS (Merck, Darmstadt, Germany). TLC plates were precoated with silica gel GF_{254} (Merck, Darmstadt, Germany, 0.25 mm), ODS (Fujisylisia, Tokyo, Japan), and detection was achieved by spraying with 10% H_2SO_4 in ethanol, followed by heating.

2.2 Plant Material

The stem bark of *C. cumingianus* was collected in Bogor Botanical Garden, Bogor, West Java Province, Indonesia in April 2014. The plant was identified by the staff of the Bogoriense Herbarium, Bogor, Indonesia and a voucher specimen (No. Bo-1305316) was deposited at the herbarium.

2.3 Extraction and Isolation

Dried ground bark of *C. cumingianus* (2.2 kg) was extracted successively with *n*-hexane, EtOAc, and MeOH. Evaporation resulted in the crude extracts of *n*-hexane (36.9 g), EtOAc (23.6 g), and MeOH (30.0 g), respectively. The ethyl acetate extract of *C. cumingianus* (23.6 g) was subjected to vacuum liquid chromatography over silica gel using a gradient elution mixture of *n*-hexane -EtOAc (10:0-0:10) as eluting solvents to afford 9 fractions (A01 -A09) . Fraction A04 (3.8 g) was subjected to column chromatography over silica gel using a mixture of CH_2Cl_2:Me_2CO (9:1) as eluting solvents to afford 8 fractions (B01-B08). Fraction B06 (0.13 g) was subjected to column chromatography over ODS using a mixture of MeOH:Me_2CO (9:1) as eluting solvents to give **1** (5.8 mg).

2.3.1 Chisotrijugin (**1**)

White needle-like crystals; m.p (decomposed); $[\ ]^{20}_{D}$: -70 (*c* 0.1, $CDCl_3$); IR (KBr) $_{max}$ 3482, 1726, 1702, 1630, 1153, 877 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 125 MHz), see Table 1; HR-TOFMS found *m/z* 489.2124 $[M+H]^+$, (calcd. for $C_{26}H_{32}O_9$, $[M+H]^+$ *m/z* 489.2125).

3. Results and Discussion

Bark of *C. cumingianus* was grounded and successively extracted with *n*-hexane, ethyl acetate, and methanol. The ethyl acetate extract was chromatographed over a vacuum-liquid chromatographed (VLC) column packed with silica gel 60 by gradient elution. The fractions were repeatedly subjected to normal-phase and reverse-phase column chromatography to afford compounds **1** (Fig. 1). Chisotrijugin (**1**), was obtained as white needle-like crystals, m.p. (decomposed). Its molecular formula was determined as $C_{26}H_{32}O_9$, was established from the HR-TOFMS spectra (*m/z* 489.2044, $[M+H]^+$) and NMR data (Table 1). The IR spectrum suggested the presence of a hydroxyl group (3482 cm^{-1}), carbonyl ketone (1726 cm^{-1}), carbonyl ester (1702 cm^{-1}), olefinic (1630 cm^{-1}), and ether groups (1153 cm^{-1}). Twenty six carbon signals were observed in the ^{13}C NMR spectrum. The multiplicities of the carbons determined by DEPT spectra led to the attribution for five methyls, three methylenes, ten methines, eight quartenary carbons, including one ketone ($_C$ 209.0), two ester carbonyls ($_C$ 171.9 and 168.2), a β-substituted furan ($_C$ 143.1, 141,5, 120.0, 110.3), one methine olefinic ($_C$ 116.2), one quaternary carbon olefinic ($_C$ 164.8), one methoxyl group ($_C$ 52.2), three oxymethines ($_C$ 69.1, 75.6, 81. 1), and one anomeric carbons ($_C$ 107.9). The NMR spectra of **1** showed similarities to those of trijugin C (Zhang et al., 2003). The signals of the β-substituted furan ring in the ^{1}H NMR spectrum occurred at $_H$ 7.49 (H-21), 7.41 (H-23), and 6.54 (H-22) and the corresponding carbon signals at $_H$ 141.5, 143.1, and 110.3, respectively, in the HMQC spectrum. Ring D was oxidized to a C- 16 lactone, with H-17 occurring as a singlet at $_C$ 5.18 and H-15 occurring as a pair of doublets at $_H$ 1.92 and 2.76 (*J* = 6.6 Hz). The signal at $_H$ 3.85 (3H, s) showed a HMBC correlation with an ester carbonyl at $_C$ 169.9, indicating the presence methylester group at C-7. Ring A which opened was supported by the appearance of methyl doublet signal ($_H$ 1.16, d, *J*=7.2 Hz, H-19) that correlated with methine $_C$ 36.8 (H-10), 55.9 (H-5), and an anomeric carbon at $_C$ 107.9 (C-9). The presence of the double bond was deduced by the HMBC correlation between methine olefinic proton at $_H$ 6.29 (H-8) to quaternary olefinic carbon at $_C$ 164.6 (C-14), sp^3 quaternary carbon at $_C$ 39.2 (C-13), and sp^3 methine carbon at δ_C 34.1 (C-11) (Fig. 2). The presence of epoxide ring was deduced by ^{1}H-^{1}H COSY crosspeak between H-1/H-2. The relative stereochemistry at the chiral centers is suggested by comparation with previously data reported (Zhang et al., 2003). Based on the above spectral data, the structure of was determined to be as shown for **1**.

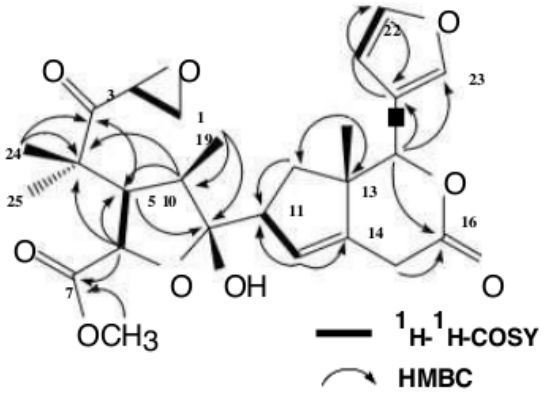

Figure. 2. Selected ^{1}H-^{1}H COSY and HMBC Correlations for **1**.

Usually tetranortriterpenoid with an open ring B have an 8(30) double bond. Trijugin class compounds have a rare contracted ring C and Connolly and co-workers (Purushothaman et al., 1987) was postulated that the trijugin may be formed by ring C contraction occurring by a Pinacol–Pinacolone rearrangement of a 9(11)-dihydroxy precursor and anticipated more detailed examination of such compounds would be necessary. In pentanortriterpenoid **1**, C-30 has been removed by further oxidation of the 8(30) double bond. A continued with cleavage ether bridge at 1(14) to form a double bond at 8(14). The cleavage of ring A at 1(10) and formed an epoxide ring at 1(2) have not been described before. The oxidation of C-6 of tetranortriterpenoids with a lactone ring D and an opened ring B had been reported (Zhang et al., 2003).

4. Conclusion

The bark of *C. cumingianus* produce a new 30-nor trijugin-type limonoid, and was named chisotrijugin (**1**). This investigation indicate that Indonesian *Chisocheton* plants can produce an unique structure due to the environmetal condition.

Table 1. NMR data (500 MHz for ^{1}H and 125 MHz for ^{13}C, in $CDCl_3$) for **1**

carbon position	**1**	
	^{13}C NMR	^{1}H NMR
	δc (mult.)	δ_H (Integral, mult., *J*=Hz)
1	46.9 (t)	2.45 (1H, dd, 5.8, 8.2)
		2.65 (1H, dd, 3.6, 5.8)
2	69.1 (d)	1.41 (1H, d, 3.6)
3	209.0 (s)	-
4	48.0 (s)	-
5	55.9 (d)	2.29 (1H, dd, 3.8, 6.2)
6	75.6 (d)	4.83 (1H, d, 3.8)
7	171.9 (s)	-
8	116.2 (d)	6.29 (1H, d, 3.2)
9	107.9 (s)	-
10	36.8 (d)	3.30 (1H, m)
11	34.1 (d)	2,66 (1H, m)
12	27.3 (t)	1.91 (1H, dd, 2.5, 14.3)
		2.10 (1H, d, 14.3)
13	39.2 (s)	-
14	164.6 (s)	-
15	24.8 (t)	1.92 (1H, d, 15.6)
		2.76 (1H, d, 15.6)
16	168.2 (s)	-
17	81.1 (d)	5.18 (1H, s)
18	17.7 (q)	1.09 (3H, s)
19	11.8 (q)	1.16 (3H, d, 7.2)
20	120.0 (s)	-
21	141.5 (d)	7.49 (1H, d, 4.8)
22	110.3 (d)	6.45 (1H, d, 4.8)
23	143.1 (d)	7.41 (1H, s)
28	29.5 (q)	1.38 (3H, s)
29	23.2 (q)	0.99 (3H, s)
OCH_3	52.2 (q)	3.69 (3H, s)

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