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A chromene acid from *Calophyllum cordato-oblongum*

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Abstract

A new chromene acid, isocordato-oblongic acid, was isolated from the sodium carbonate soluble fraction of the *n*-hexane extract of the stem bark of *Calophyllum cordato-oblongum*. © 1999 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Calophyllum cordato-oblongum (local name: Kalu Keena) is a rare endemic plant that grows in the lowland, evergreen, wet zone forests in Sri Lanka (Dassanayake & Fosberg, 1980). Four xanthones, five pyranocoumarins, a chromene acid and three triterpenoids have been reported from the stem wood, stem bark (Gunasekara, Jayatilaka, Selliah, & Sultanbawa, 1977), leaves (Dharmaratne, Sotheeswaran, Balasubramaniam, & Waight, 1985), twigs and buds (Dharmaratne, Sajeevani, Marasinghe, & Ekanayake, 1998) of this plant. Recently HIV-1 reverse transcriptase inhibitory activity of some of the above pyranocoumarins were reported from this species (Dharmaratne, Wanigasekera, Mata-Greenwood, & Pezzuto, 1998).

Calophyllum is a rich source of chromene acids (bark acids) and they were first reported only from the stem bark of various *Calophyllum* species (Samaraweera, Sotheeswaran, & Sultanbawa, 1983). Later they were isolated from the leaves of several *Calophyllum* species (Gunatilaka, De Silva, Sotheeswaran, Balasubramaniam, & Wazeer, 1984; Bandara, Dharmartne, Sotheeswaran, & Balasubramaniam, 1986). Most of these acids possess a phloroglucinol ring system and in some cases a modified phloroglucinol ring system, such as the cyclohexadienone system in calozelanic acid (Gunatilaka et al., 1984). In this communication, we report on the isolation and structure elucidation of a new chromene acid, isocordato-oblongic acid (**1**), from the *n*-hexane extract of the stem bark of *C. cordato-oblongum*. The known cordato-oblongic acid was also isolated from the *n*-hexane extract.

2. Results and discussion

The *n*-hexane extract (25 g) of the stem bark of *cordato-oblongum* was dissolved in Et_2O and washed with 10% Na_2CO_3 soln. The aq. Na_2CO_3-soluble fraction was separated and acidified with 4 N HCl acid and subsequently extracted with Et_2O. The ethereal layer was thoroughly washed with distilled water, dried over anhydrous sodium sulphate and evaporated to give a yellow solid (6.7 g, 26.8%). TLC gave an elongated streaking spot showing the presence of more than one compound. Further purification of this fraction by CC (silica gel, hexane–EtOAc), gave a pale yellow solid which was suspected to be a mixture of cordato-oblongic acid (Gunasekara et al., 1977) and some unidentified products. A part of the above mixture (30 mg) was methylated using an ethereal soln of CH_2N_2 to give two products. Separation of these products using PTLC (silica gel, hexane–EtOAc) yielded 16 mg (54%) of a low polarity product and 6 mg (20%) of a polar product. The above reaction was repeated and more of the polar product was isolated for further studies. Treatment of the Na_2CO_3-soluble fraction of the *n*-hexane extract, in MeOH with 2 N HCl under reflux for 45 min, gave two products which were identical to the CH_2N_2 methylation products.

The less polar product (**2**) from the above reactions

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had an $[M]^+$ of m/z 374 with m/z 375 $[M+1]^+$ as the base peak and the IR spectra showed the presence of carbonyl (ester) and olefinic groups. The ^1H NMR data (Table 1) of **2** suggested that the 3H singlet at δ 3.60 was due to an ester methyl group. Further comparison Table 1 of the ^1H NMR data of **2** with those of the methyl ester of cordato-oblongic acid (Gunasekara et al., 1977) and the m.p. 89–90°C, suggested that compound **2** was cordato-oblongic acid methyl ester. The minor product, which was more polar than **2**, also had an $[M]^+$ of m/z 374 with m/z 375 $[M+1]^+$ as the base peak.

The IR spectra of **1** showed the presence of carbonyl (ester) and olefinic groups. The UV spectra of **1** indicated the presence of a chromanone–chromene type chromophore, which is common to cordato-oblongic acid and other chromene acids reported from a considerable number of *Calophyllum* species worldwide (Samaraweera et al., 1983; Gunatilaka et al., 1984; Dharmaratne et al., 1998). The ^1H NMR data (Table 1) of **1** suggested that the 3H singlet at δ 3.60 was due to an ester methyl group. However, further comparison (Table 1) of the ^1H NMR data of **1** with those of the methyl ester of cordato-oblongic acid (**2**), suggested that **1** was a stereoisomer of **2**. Mass spectral data further supported the proposed structure. A careful comparison of the ^1H NMR data (Table 1) of **1** and **2**, clearly indicated that there were significant differences in coupling constants of the multiplets due to the protons at C-7 and C-8 in these two acid esters. The proton (H-7) in the vicinity of the 7-CH_3 group and H-8 of **1** appeared at δ 2.54 as a doublet of a quartet (dq) with coupling constants of 3.3 and 7.5 Hz, while the analogous proton of **2** appeared at δ 2.54 as a doublet of a quartet (dq) with coupling constants of 7.01 and 11.07 Hz. Concurrently, the proton (H-8) in the vicinity of the 8-CH_3 group and H-7 of **1** appeared at δ 4.54 as a doublet of a quartet with coupling constants of 3.3 and 6.6 Hz, while the analogous proton of **2** appeared at δ 4.14 as a doublet of a quartet with coupling constants of 6.26 and 12.51 Hz. Considering the relatively higher coupling constants of 11 and 12.5 Hz, a *trans*-diaxial arrangement for H-7 and H-8 has been proposed for cordato-oblongic acid (**2**) (Dassanayake & Fosberg, 1980). However, the comparable protons of **1** showed coupling constants of 3.3 Hz each for the signals of H-7 and H-8. These lower coupling constants represent either axial–equatorial or equatorial–equatorial arrangement for H-7 and H-8. Hence a *cis* arrangement can be proposed for the relative configuration of the protons at C-7 and C-8 of compound **1**, in contrast to the *trans* arrangement of the cordato-oblongic acid methyl ester. Thus, the two bark acids present in the initial extract are cordato-oblongic acid (**2**) and isocordato-oblongic acid (**1**). This is the first report of the occurrence of isocordato-oblongic acid in nature. The ^{13}C NMR and the DEPT spectra of **1**, further support the proposed structure (**1**).

Table 1
^1H NMR data of compounds **1** and **2** ($CDCl_3$) (coupling constants (Hz) are given in parentheses)

H	1	2
3-H	5.473 d ($J=10$)	5.4 d ($J=10$)
4-H	6.603 d ($J=10$)	6.6 d ($J=10$)
5-OH	12.389 s	12.45 s
7-H	2.537 dq ($J=3.3$, 7.5)	2.54 dq ($J=7.01$, 11.07)
8-H	4.535 dq ($J=3.3$, 6.6)	4.14 dq ($J=6.26$, 12.51)
7-Me	1.16 d ($J=6.9$)	1.27 d ($J=7.09$)
8-Me	1.40 d ($J=6.6$)	1.21 d ($J=6.99$)
11-H	3.81 m ($J=7.2$, 10.5, 14.4)	3.79 m ($J=7.23$, 14.59)
11-Me	1.26 d ($J=7.5$)	1.51 d ($J=6.28$)
12-H_2	2.743 ($J=7.5$, 15.3)	2.745 ($J=7.59$, 15.38)
2-Me_2	1.45	1.46 s
COOMe	3.60	3.60 s

3. Experimental

3.1. General

M.p.s: uncorr.; ^1H NMR: 200 or 400 MHz, $CDCl_3$, with TMS as int. standard.

3.2. Plant material

Calophyllum cordato-oblongum Thw. was identified and collected in June 1996 from the Kanneliya forest in the Southern Province of Sri Lanka by Mr. Shantha Ekenayake (Institute of Fundamental Studies, Kandy). The plant specimen was compared with the herbarium specimens (specimen No. 24771) at the Royal Botanic Gardens, Peradeniya, Sri Lanka.

3.3. Isocordato-oblongic acid methyl ester (1)

UV λ_{max} (MeOH) nm ($\log \varepsilon$): 304.0 (3.961), 317.8 (3.962), 336.2 sh (3.33), 363.6 (3.49); IRν_{max} (Nujol) cm^{-1}: 3424, 1737, 1622, 1574, 1286, 1240, 1197, 1160, 1129, 1014, 806, ^{13}C NMR $CDCl_3$ (75.5 MHz): 201.1 (C-6), 173.5 (C-5), 159.7 (C-13), 159.3 (C-10a), 157.2 (C-9a), 125.6 (C-3), 115.7 (C-4), 111.1 (C-5a), 102.7 (C-4a), 101.3 (C-10), 78.1 (C-2), 76.1 (C-8), 51.2 (OCH_3), 44.3 (C-7), 39.5 (C-12), 28.3, 28.2 (Me_2-2), 25.7 (C-11), 19.2 (Me-11), 16.3 (Me-8), 9.3 (Me-7); CIMS m/z (rel. int.): 375 $[M+1]^+$(100), 374 $[M]^+$, 359(7), 343(3).

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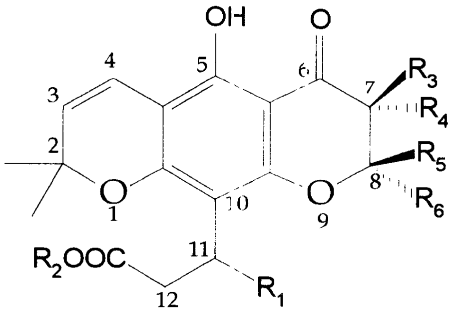

	R_1	R_2	R_3	R_4	R_5	R_6
1. Isocordato-oblongic acid methyl ester	CH_3	CH_3	CH_3	H	CH_3	H
2. Cordatro-oblongic acid methyl ester	CH_3	CH_3	CH_3	H	H	CH_3

Structure 1

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