

## **Tomentonone, a New Xanthonoid from the Stem Bark of *Calophyllum tomentosum***

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TOMENTONONE, A NEW XANTHONOID FROM THE STEM BARK  
OF *CALOPHYLLUM TOMENTOSUM*

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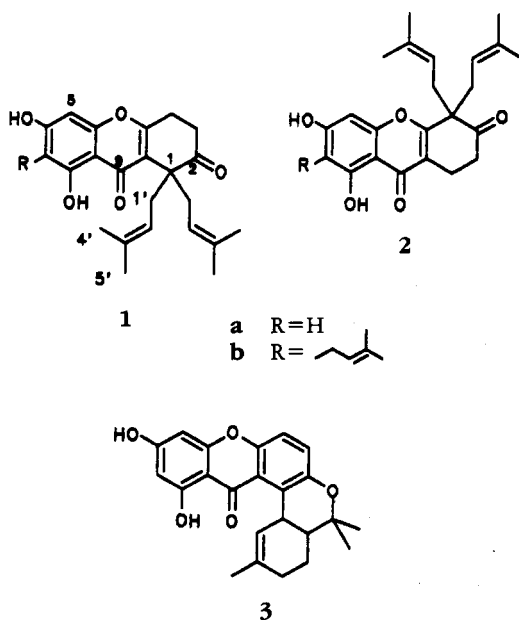
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**ABSTRACT.**—A new xanthonoid, tomentonone [**1a**], together with zeyloxanthone [**1b**], calozeyloxanthone [**3**], and five other hydroxylated xanthenes, was isolated from the bark of *Calophyllum tomentosum*. The structure of **1a** has been established as [1,2,3,4-tetrahydro-6,8-dihydroxy-1,1-bis(3-methylbut-2-enyl)-xanthen-2,9-dione] by spectroscopic and chemical methods.

Xanthenes, in spite of their restricted occurrence in the plant kingdom, are reported to possess antileukemic, antitumor, antiulcer, antimicrobial, antihepatotoxic, and CNS-depressant activities (1–3). Plants belonging to the family Guttiferae are known to elaborate prenylated xanthenes in addition to simple oxygenated xanthenes (4). In our search for bioactive compounds, phytochemical investigation of the stem bark of *Calophyllum tomentosum* T. Anders (Guttiferae) was undertaken. Isolation of betulinic acid, friedelin, taraxerone, sitosterol, and calabaxanthone from the bark of *C. tomentosum* has been described in the literature (5–7). Herein we report the isola-

tion and characterization of tomentonone [**1a**], a new xanthonoid, along with two rare prenylated xanthonoids, zeyloxanthone (syn. wightianone) [**1b**] and calozeyloxanthone [**3**], and several other compounds.

The stem bark of *C. tomentosum* was extracted successively with *n*-hexane and  $\text{CHCl}_3$ . In addition to friedelin and sitosterol, two compounds [**1b**] and [**3**] were isolated from the *n*-hexane extract. Spectroscopic and chemical studies of **1b** and **3** suggested that these were prenylated xanthenoids. The physical and chemical data of the former compound were identical to those of zeyloxanthone (syn. wightianone). Zeyloxanthone, isolated



from *C. zeylanicum* (9), was assigned the structure **1b** by Sultanbawa *et al.* However, Dean *et al.* isolated the same compound (wightianone) from *C. wightianum* but revised the structure from **1b** to **2b** (10,11). Neither group provided unequivocal evidence for their assignment. Therefore, a reinvestigation on the structure was carried out and definitive proof for structure **1b** has been obtained (12). Compound **3** was also a complex xanthonoid. Its molecular formula ( $C_{23}H_{22}O_5$ ) and  $^1H$ -nmr data were suggestive of the presence of a  $C_{10}$  isoprenoid unit in addition to the xanthone moiety. Based on spectral studies (ir, uv and  $^1H$  nmr) **3** was characterized as calozeoyloxanthone: the only other presently known source of **3** is *C. zeylanicum* (8).

Six compounds were isolated from the  $CHCl_3$  extract. These included a new xanthonoid, tomentonone [**1a**], and five known xanthonones which were characterized as 2-hydroxyxanthone (13), 3-hydroxyxanthone (13), euxanthone (14), 1,5-dihydroxyxanthone (14), and 1,3,5-trihydroxy-2-methoxyxanthone (15), by comparison of their chemical and physical properties (mp, uv, nmr, ms) with those reported in the literature.

Tomentonone [**1a**] is a bright yellow crystalline solid (mp 218°). Its high-resolution mass spectrum ( $[M]^+ = 382.1777$ ) suggested a molecular formula of  $C_{23}H_{26}O_5$  (calcd 382.1780). Uv spectra of **1a** in conjunction with shift reagents ( $AlCl_3$ ,  $NaOAc$ ) indicated a reduced xanthone system possessing two phenolic hydroxyl groups, with the chelated one being assigned at C-8 while the other was assigned to C-6. The appearance of two bands at  $1660\text{ cm}^{-1}$  and  $1700\text{ cm}^{-1}$  in the ir spectrum, was indicative of a xanthone carbonyl and a saturated carbonyl functionality. The  $^1H$ -nmr spectrum of **1a** showed a low-field signal at  $\delta$  13.15 for a chelated hydroxyl group. Two signals (1H each, d,  $^4J = 2\text{ Hz}$ ) at  $\delta$  6.31 and  $\delta$  6.27 accounted for two meta-coupled protons. Two triplets (2H each) at  $\delta$  2.84

and  $\delta$  2.56 could be assigned to a  $-CH_2CH_2-CO-$  system. The signals at  $\delta$  4.80 (2H, t) for two vinylic protons, at  $\delta$  3.12 and  $\delta$  2.68 (each 2H, q) for two methylene groups, and at  $\delta$  1.46 and  $\delta$  1.56 (each 6H, s) for four methyl groups, revealed the presence of two identical prenyl substituents. This was confirmed by the mass spectral fragmentation of **1a**, which exhibited ions at  $m/z$  313  $[M-69]^+$  (base peak) representing a loss of a  $C_5H_9$  unit, and at  $m/z$  258  $[M-69-55]^+$  due to a further loss of a  $C_4H_7$  fragment.

In addition to the two prenyl groups, the  $^{13}C$ -nmr spectrum indicated the presence of two carbonyls, two aromatic methines, two methylenes, and six other quaternary carbons (Table 1). A critical analysis of spectral data showed remarkable similarity with those of zeyloxanthone (wightianone) (9,10). In the  $^1H$ - $^1H$  COSY nmr spectrum, the methylene protons of the *gem*-diprenyl moiety displayed cross-peaks with the adjacent vinylic protons, which in turn showed COSY interactions with the methyl resonances. The expected interactions between the two adjacent methylene groups

TABLE 1.  $^{13}C$ - and  $^1H$ -Nmr Data of **1a** in  $CDCl_3$ .

Carbon No.	$^{13}C$	$^1H$	
	$\delta$ (ppm)	$\delta$ (ppm)	$J_{HH}$ (Hz)
1	55.3 s		
2	217.0 s		
3	26.8 t	2.56 t	7.7
4	37.9 t	2.84 t	7.7
4a	162.7 s		
5	93.4 d	6.27 d	2.0
6	153.4 s		
7	99.3 dd	6.31 d	2.0
8	157.6 s		
8a	105.5 s		
9	180.4 s		
9a	117.3 s		
10a	162.1 s		
1'	35.4 t	3.12 dd 2.68 dd	13.8, 7.3 13.8, 5.9
2'	119.7 d	4.80 t	7.6
3'	134.9 s		
4'	17.8 s	1.56 s	
5'	25.9 s	1.46 s	

of the cyclohexenone ring were also observed. Based on the data presented above, **1a** and **2a** are two possible structures for tomentonone. Though the COSY interactions were useful in the precise assignment of  $^1\text{H}$ -nmr resonances, the ambiguity regarding the structures still persisted. Proof for **1a** was provided by deuterium-exchange nmr experiments. A critical examination of the structures reveals that in **1a**, both the methylene groups at positions 3 and 4 are activated due to carbonyl groups at positions 2 and 9, respectively, and are thus exchangeable, while in **2a** only the methylene group adjacent to the non-conjugated carbonyl is labile.

Deuteration of tomentonone (see Experimental) resulted in the sequential exchange of methylene protons. The progress of deuteration was monitored by  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectroscopy. The C-3 protons exchanged with deuterium within 11 min as evident from the disappearance of the proton signal at  $\delta$  2.56. As a result, the triplet at  $\delta$  2.84 collapsed into a singlet in the  $^1\text{H}$ -nmr spectrum. The  $^{13}\text{C}$ -nmr resonance at  $\delta$  26.8 due to C-3 (a triplet) was depleted due to coupling and loss of nOe and was barely distinguishable from the background noise. On prolonged treatment, the deuteration at C-4 was also observed at a slower rate. After 29 h, the methylene protons at  $\delta$  2.84 (a singlet now) at the C-4 position showed a 81% reduction of its signal intensity. The corresponding carbon signal,  $\delta$  37.9, was unobservable due to weak intensity. Thus, spectroscopic data in conjunction with isotopic exchange studies unambiguously established the structure of tomentonone as [1,2,3,4-tetrahydro-6,8-dihydroxy-1,1-bis(3-methylbut-2-enyl)-xanthen-2,9-dione] [**1a**].

Tomentonone is the second naturally occurring xanthonoid of its kind.

## EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mps were determined on a Fisher-Johns mp apparatus and are uncorrected. The uv spectra were recorded

using MeOH as solvent on a Shimadzu spectrophotometer (model 240S). The ir spectra were scanned on a Perkin-Elmer spectrophotometer (model 783). Ms were recorded on a Shimadzu GCMS-QP1000A spectrometer. The high-resolution ms was recorded on a VG micromass 7070H spectrometer (EI 70 eV), using a VG data system. The nmr experiments were carried out on a Bruker AM-500 Ft-nmr spectrometer operating at 500 MHz for  $^1\text{H}$ . COSY and NOESY nmr experiments were performed with 256  $t_1$  and 1K  $t_2$  points. The time-domain data were zero-filled to 512 points along the  $t_1$  axis. The data were multiplied by sine bell window functions along the  $t_2$  and  $t_1$  axes respectively, prior to respective Fourier transformations.

PLANT MATERIAL.—*Calophyllum tomentosum* T. Anders was collected from Agumbe, Karnataka, India, and identified by Dr. V. Abraham, Bhabha Atomic Research Centre (BARC). A voucher specimen (No. 1516) has been deposited in the Herbarium of the Landscape and Cosmetic Maintenance Section, BARC.

EXTRACTION AND ISOLATION.—The dried and powdered stem bark (600 g) of *C. tomentosum* was extracted (Soxhlet) successively with *n*-hexane and  $\text{CHCl}_3$ . The extracts were concentrated under reduced pressure. The *n*-hexane extract when fractionated by cc over Si gel, using gradient elution (*n*-hexane,  $\text{CHCl}_3$ , EtOAc, and MeOH), followed by repeated prep. tlc and crystallization, yielded a triterpene, friedelin (200 mg), mp 260° (lit. (7) 261°); a steroid, sitosterol (150 mg), mp 138°; and the two known prenylated xanthonoids, zeyloxanthonone [**1b**] and calozeyloxanthonone [**3**].

*Tomentonone* [**1a**].—Yellow crystalline solid, mp 218° (yield 40 mg, 0.006%); hrms,  $m/z$  [ $\text{M}$ ]<sup>+</sup> 382.1777, ( $\text{C}_{23}\text{H}_{26}\text{O}_5$  requires 382.1780); uv (MeOH)  $\lambda$  max (log  $\epsilon$ ) 232, 251, 292 nm (4.22, 4.26, 3.92); +  $\text{AlCl}_3$  265, 312, 369 nm (4.37, 4.00, 3.75); +  $\text{AlCl}_3/\text{HCl}$  264, 312, 366 nm (4.37, 4.01, 3.75); +  $\text{NaOAc}$  261, 324 nm (4.23, 3.89); +  $\text{NaOAc}/\text{H}_3\text{BO}_3$  251, 293 nm (4.24, 3.88); +  $\text{NaOMe}$  266, 331 nm (4.32, 3.99); ir (KBr)  $\nu$  max 3200, 2940, 1700, 1660, 1520, 1460, 1285, 1165, 880, and 840  $\text{cm}^{-1}$ ; ms  $m/z$  382 [ $\text{M}$ ]<sup>+</sup> (20), 313 (100), 258 (52), 217 (20), 153 (25), 69 (75), and 41 (85);  $^1\text{H}$  and  $^{13}\text{C}$  nmr, see Table 1.

Deuteration of **1a**.—Compound **1a** (4 mg) was dissolved in  $\text{CD}_3\text{OD}$  (0.3 ml) in an nmr (5 mm) tube, the air was flushed out with argon and  $\text{CD}_3\text{ONa}$  (100 mmol) was added. Progress of deuteration was monitored by  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectroscopy.

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