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TWO ISOMERIC BENZODIPYRANONE DERIVATIVES FROM *CALOPHYLLUM INOPHYLLUM**

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Key Word Index—*Calophyllum inophyllum*; Guttifereae; leaves; (2*S*,3*R*)-2,3-dihydro-5-hydroxy-2,3,8,8-tetramethyl-6-(1-phenylethenyl)-4H,8H-benzo [1,2-*b*:3,4-*b'*] dipyran-4-one, (2*R*,3*R*)-2,3-dihydro-5-hydroxy-2,3,8,8-tetramethyl-6-(1-phenylethenyl)-4H,8H-benzo [1,2-*b*:3,4-*b'*] dipyran-4-one; ^{13}C NMR; CD; absolute configuration.

Abstract—The new compound (2*S*,3*R*)-2,3-dihydro-5-hydroxy-2,3,8,8-tetramethyl-6-(1-phenylethenyl)-4H,8H-benzo [1,2-*b*:3,4-*b'*] dipyran-4-one along with (2*R*,3*R*)-2,3-dihydro-5-hydroxy-2,3,8,8-tetramethyl-6-(1-phenylethenyl)-4H,8H-benzo [1,2-*b*:3,4-*b'*] dipyran-4-one were isolated from the leaves of *Calophyllum inophyllum* and identified from their spectral and chemical data.

INTRODUCTION

The genus *Calophyllum* consist of 130 species of trees of which seven are found in India. *Calophyllum inophyllum*, commonly found in the coastal regions of South India, is used as a crude drug for the cure of rheumatism and skin affections [1]. Xanthones isolated from this species showed antibacterial activity [2] and 4-phenyl coumarins obtained from its leaves showed piscicidal properties [3]. Several triterpenes [4], 4-phenyl coumarins [3–8] xanthones [9–11], flavonoid glycosides [12, 13], neoflavonoids [14] and pyranoamentoflavone [14] have also been isolated from the plant. We now report the isolation, characterization and stereochemistry of the new benzo γ-pyrone derivative (**1a**) and its isomer (**1c**) from the leaves of *C. inophyllum*.

RESULTS AND DISCUSSION

A petrol extract of *C. inophyllum* on column chromatography followed by re-crystallization from $CHCl_3$–EtOH afforded the new compound (**1a**), which analysed for $C_{24}H_{24}O_4$ ($[M]^+$ *m/z* 376). The IR spectrum showed a strong band due to a chelated aromatic carbonyl group (1625 cm^{-1}), along with peaks at 785 and 700 cm^{-1}, suggesting the presence of a monosubstituted benzene ring [15]. The ^{1}H NMR spectrum (Table 1) showed a one-proton exchangeable signal at δ 12.49 characteristic of a chelated OH group and a five proton multiplet centred at δ 7.32 ascribed to the phenyl group. Other signals in the spectrum showed the presence of the following functionalities through decoupling experiments: (i) a dimethyl benzo-γ-pyrone [Ar–O–CH(Me)–CH(Me)–CO–Ar] unit, with one of the methine protons ($J_{2H,3H}$ = 3 Hz) equatorially-oriented, (ii) a 2,2-dimethyl benzo [b] pyran unit and (iii) a $>C=CH_2$ grouping.

The above data could be fitted with either structure (**1a**) or (**2**). In order to discriminate between the two structures, the compound was acetylated (Ac_2O/pyridine/DMAP/CH_2Cl_2) [16]. Since hydroxy chromones exert a significant shielding influence on *peri*-protons [17, 18], the concerned proton of the pyrone ring should have been shielded in the acetate if the structure were **2**. Actually, the pyran protons were marginally (0.03–0.05 ppm) deshielded, while the methylene protons of $>C=CH_2$ appeared shielded by 0.13 ppm and 0.07 ppm, respectively, for the lowest field and higher signals. Structures **1a** and **1b** are thus preferred for the compound and its acetate, respectively.

In the mass spectrum, the $[M]^+$ appeared at *m/z* 376, the base peak being at *m/z* 361 for the loss of a methyl group. The other prominent peak was at *m/z* 305 which originated from the $[M - Me]^+$ peak by loss of 56 mu. (Calc. m* 257.6, observed around 258), conceivably *via* retro-Diels–Alder cleavage of the dimethyl benzopyrone ring with expulsion of the C_4H_8 unit. Thus, compound **1a** was characterized as (2*S*,3*R*)-2,3-

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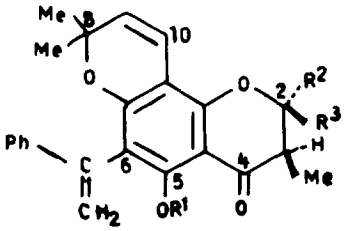
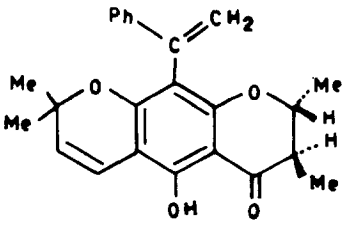


1a: $R^1 = R^2 = H$, $R^3 = Me$

1b: $R^1 = Ac$, $R^2 = H$, $R^3 = Me$

1c: $R^1 = R^3 = H$, $R^2 = Me$

1d: $R^1 = Ac$, $R^2 = Me$, $R^3 = H$



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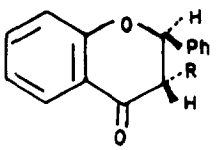

3a: R = H

3b: R = OH

dihydro-5-hydroxy-2,3,8,8-tetramethyl-6-(1-phenylethenyl)-4H,8H-benzo [1,2-*b*:3,4-*b'*] dipyran-4-one.

Compound **1c** was recrystallized from $CHCl_3$–EtOH. The molecular formula $C_{24}H_{24}O_4$, was assigned to it from the mass spectrum ($[M]^+$ *m/z* 376), which was very similar to that of **1a**, showing their isomeric nature. Most of the ^1H NMR (Table 1) signals, including acetylation shifts (shielding of $>C=CH_2$ protons in **1d** by 0.14 and 0.07 ppm) were also identical. However, the resonance position of 2-H of the pyrone ring (δ 4.25, $J = 6.5$ Hz) appeared shifted upfield by 0.38 ppm and the $J_{2H,3H}$ value was also much higher. A decoupling experiment showed the presence of a dimethyl benzo-γ-pyrone [Ar–O–CH(Me)–CH(Me)–CO–Ar] unit with the two methine protons *trans*-diaxially oriented, a 2,2-dimethyl benzo[b] pyran unit and a $>C=CH_2$ grouping.

The ^{13}C NMR spectrum of **1c** showed signals for all the 24 carbon atoms. The two methine signals at δ 115.5 and 126.1, together with methyl signals at δ 27.6 and 27.9, and also the signals at δ 77.6 (O–C<), agreed well with the presence of a 2,2-dimethyl benzo[*b*]pyran ring system [19]. The six singlets in the downfield region at δ 161.0, 159.1, 155.7, 110.9, 101.5 and 101.2, in conjunction with the carbonyl signals at δ 198.3 suggested the presence of a 5-hydroxy-7-oxy-6,8-disubstituted-benzo-γ-pyrone moiety [20]. Signals at δ 78.8 (O–CH), 45.6 (CO–CH), 19.5 (CH_3–CH–O–) and 10.0 (CH_3–CH–CO) were in agreement with the presence of 2,3-dimethyl substitution in the pyrone ring. The remaining peaks at δ 139.5(*s*) and 117.4 (*t*, $>C=CH_2$) along with those at δ 126.1, 127.8 (each accounting for two methine carbons), 126.8 (CH) and 141.6 (–C–) confirmed the presence of the Ph–C=CH_2 unit. These data confirm the structure of compound **1c** which was found to be the isomer of **1a**. Since the completion of our work, the structure of **1c** isolated from *C. tomentosum* has been reported [21]. Our data are in good agreement with those published by Babu *et al.* [21], except that the previously assigned chemical shifts for 3-H and 2-H (and those of the substituent methyl groups) need to be reversed. The ^{13}C NMR of **1c** was not given earlier. Also the absolute configuration was not determined earlier.

Table 1. ^1H NMR data of compounds **1a** and **1c** (100 MHz, $CDCl_3$)

	Chemical shifts (δ, ppm) for	
	1a	**1c**
8-Me_2	1.16(*s*)	1.12(*s*)
		1.16(*s*)
3-Me	1.22(*d*, $J = 7$ Hz)	1.22(*d*, $J = 7$ Hz)
2-Me	1.44(*d*, $J = 7$ Hz)	1.54(*d*, $J = 6.5$ Hz)
3-H	2.60(*dq*, $J = 7, 3$ Hz)	2.60(*dq*, $J = 11, 7$ Hz)
2-H	4.63(*dq*, $J = 7, 3$ Hz)	4.25(*dq*, $J = 11, 6.5$ Hz)
9-H	5.46(*d*, $J = 10$ Hz)	5.45(*d*, $J = 10$ Hz)
10-H	6.58(*d*, $J = 10$ Hz)	6.57(*d*, $J = 10$ Hz)
$=CH_2$	5.30(*d*, $J = 2$ Hz)	5.29(*d*, $J = 2$ Hz)
	5.88(*d*, $J = 2$ Hz)	5.85(*d*, $J = 2$ Hz)
–Ph	7.32(*m*)	7.30(*m*)
–OH	12.49(*s*)	12.56(*s*)

The application of chiroptical methods for the assignment of absolute configuration of such dimethyl benzo-γ-pyrones does not appear to have been well documented. However, CD has been used in the case of related flavanones or even 3-substituted flavanones. Opposite Cotton effects have been observed for the n–π^* transition around 320 nm and π–π^* transition around 290 nm of the arylcarbonyl chromophore, the relative signs depending on the chirality of the conjugated chromophore [22, 23]. Thus, both the flavanones **3a** (2*R*) and 3-substituted flavanones **3b** (2*S*,3*S*) with 'equivalent C-2 configuration' showed a negative maxi-

mum around 330 nm and a positive one around 280–290 nm. We therefore applied this method to **1a** and **1c**. The CD curve of the compounds showed a positive Cotton effect at around 315 nm and a negative one at around 292 nm [CD(MeOH): **1a**: $292^{-3.61}$, $315^{+1.57}$; **1c**: $292^{-3.39}$, $315^{+0.64}$]. Therefore, the absolute configuration of (**1c**) should be 2*R*,3*R*. As **1c** differ from **1a** only in the configuration of C-2, its absolute configuration has been fixed as 2*S*, 3*R*.

EXPERIMENTAL

All mps are uncorr. UV and IR spectra were recorded in MeOH and KBr pellets, respectively. ^{1}H and ^{13}C NMR were recorded at 100 MHz for ^{1}H and 25 MHz for ^{13}C. Silica gel (60–120 mesh) was used for CC and Merck Kieselgel G for TLC.

Plant material. Leaves of *C. inophyllum* L. were procured from the National Botanical Garden, Calcutta, India. A voucher specimen is deposited at the herbarium of the Department of Botany (voucher No. 37719), A.M.U. Aligarh-202002.

Extraction and isolation. Air-dried and powdered leaves (1.7 kg) were extracted ×2 with EtOH. The EtOH extract was evapd under red. pres. The dark green gummy mass (80 g) so obtained was treated with petrol (60–80°), $CHCl_3$ and MeOH. The petrol extract was concd under vacuum. The crude product (25 g) was adsorbed on silica gel. Elution of the column with petrol–benzene 4:1) afforded (**1a**) which was further recrystallized from $CHCl_3$–EtOH as needle-shaped crystals (35 mg), mp 167°. R_f 0.35 (silica gel, petrol–Me_2CO 93:7). $[\alpha]_D$ +29.5° (*c* 0.52, $CHCl_3$). UV λ_{max}^{MeOH} nm (log ε) 232 sh (4.32), 265 (4.56), 273 (4.56), 299 (3.99), 310 (3.95), 365 (3.49). IR ν_{max}^{KBr} cm^{-1}: 3400, 2950, 1645, 1625, 1595, 1460, 1445, 1418, 1392, 1350, 1315, 1292, 1262, 1245, 1195, 1130, 1120, 1028, 980, 915, 830, 785, 750, 700. MS *m/z* (rel. int.): 376 ($[M]^+$, 45, $C_{24}H_{24}O_4$), 361 $[M - Me]^+$ (100), 305 $[M - Me - C_4H_8]^+$ (89), 277 $[M^+ - Me - C_4H_8 - CO]$ (8). ^{1}H NMR in Table 1.

Further elution of the column with petrol–benzene (4:1) and recrystallization from $CHCl_3$–EtOH gave crystals of **1c** (40 mg), mp 132°*c*. R_f 0.43 (silica gel, petrol–Me_2CO, 93:7). $[\alpha]_D$ +56.1° (*c* 1.39, $CHCl_3$). UV λ_{max}^{MeOH} nm (log ε): 231 (4.41), 265 (4.60), 273 (4.60), 299 (4.04), 309 (3.97), 364 (3.50). IR ν_{max}^{KBr} cm^{-1}: 3400, 2900, 1645, 1625, 1595, 1460, 1445, 1415, 1385, 1360, 1285, 1245, 1190, 1165, 1145, 1130, 1050, 980, 920, 785, 700. MS *m/z* (rel. int.): 376 $[M]^+$, 361 (100), 305 (89), 277 (8), 161 (6), 58 (12). ^{1}H NMR in Table 1. ^{13}C NMR in text.

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