Chemical Investigation of Ceylonese Plants. Part VIII.[1] Trapezifolixanthone, a New Di-isoprenylated Xanthone from the Bark of *Calophyllum trapezifolium* Thw. (Guttiferae)

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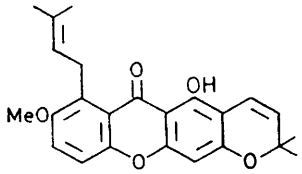
From the bark extractives of *Calophyllum trapezifolium* Thw. calabaxanthone (I), taraxerol, β-simiarenol, β-sitosterol, and a new xanthone, trapezifolixanthone (III) have been isolated. The latter has been shown to be 5,10-dihydroxy-2,2-dimethyl-12-(3-methylbut-2-enyl)pyrano[3,2-*b*]xanthen-6(2*H*)-one.

THE constituents in the heartwood extractives of *Calophyllum trapezifolium* Thw. (Guttiferae) found in India have been recently separated by Govindachari *et al.*[2] We have studied the same species from Ceylon and the bark extractives are now reported.[3]

The light petroleum extract of the bark of *C. trapezifolium* Thw. gave a yellowish white solid mixture and a gum. The solid mixture on separation on a silica gel column gave calabaxanthone[4] (I), taraxerol, β-simiarenol, and β-sitosterol which were identified by mixed m.p., spectroscopic, and t.l.c. comparison with authentic samples.



(I)

The gum was dissolved in ether and washed with cold 10% sodium carbonate solution and 10% sodium hydroxide solution. The sodium carbonate solution on working up gave a yellowish white powdery resin in high yield whose properties will be reported later. The gum obtained from the sodium hydroxide soluble fraction was separated on a silica gel column and gave a bright yellow pigment, m.p. 172°. Its u.v. and i.r. spectra indicated that it was a xanthone, and we name it trapezifolixanthone. The u.v. spectrum had an intense absorption at 292 nm (log ε 4·24). Conversion of trapezifolixanthone into tetrahydrotrapezifolixanthone caused a hypsochromic shift in the u.v. spectrum which indicated that one of the double bonds was in conjugation with the aromatic nucleus. This spectrum resembled those of dihydro-6-deoxyjacareubin[5] and related 1,3,5-trioxygenated xanthones (Table 1) suggesting that trapezifolixanthone was 1,3,5-trioxygenated.

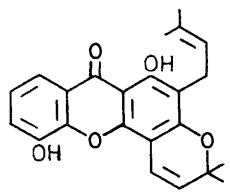
The n.m.r. spectrum indicated the presence of a chelated OH group [τ −3·25 (1H)] at C-1, and three aromatic protons appeared at τ 2·25 (1H, q) and 2·61 (2H, m). This coupling pattern is very similar to that of 6-deoxyjacareubin[4] and 1,3,5-trihydroxy-2-methoxyxanthone,[4] suggesting that three vicinal protons were located in one ring; the absence of any other aromatic signals indicated that the second aromatic ring was fully substituted. Two doublets at τ 3·24 and 4·38

TABLE 1

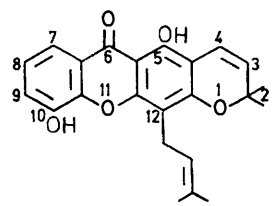
Comparison of u.v. absorption maxima

	$\lambda_{max.}$/nm (log ε)					
6-Deoxyjacareubin	243 (4·22)		270 (4·53)	296 (4·23)	310 (4·23)	370 (3·38)
Trapezifolixanthone	232 (3·90)	250 (3·85)	275sh (4·01)	292 (4·24)	315 (3·84)	380 (3·18)
Tetrahydrotrapezifolixanthone	222 (4·37)	244 (4·46)	261 (4·44)		327 (4·26)	380 (3·60)
Dihydro-6-deoxyjacareubin	222 (4·26)	244 (4·43)	255 (4·40)		320 (4·21)	365 (3·51)

(*J* 10 Hz) and a singlet at 8·51 (6H) indicated the presence of a 2,2-dimethyl-2*H*-pyrano-ring. Further the presence of a 2-methylbut-2-enyl group was indicated by two singlets at τ 8·12 (3H) and 8·27 (3H) for two olefinic methyl groups, a multiplet at 4·73 (1H) due to a vinylic proton, and a doublet at 6·51 for the methylene group. The presence of two hydroxy-groups in trapezifolixanthone was indicated by the formation of a dimethyl ether which gave two singlets for the two methoxy-groups at τ 5·98 (3H) and 6·02 (3H). Based on the oxygenation pattern of 6-deoxyjacareubin and on the same arguments as for calabaxanthone[4] and osajaxanthone,[5] trapezifolixanthone could be formulated with the 2,2-dimethyl-2*H*-pyrano-ring being fused [3,2-*b*] (III) or [2,3-*c*] (II) to the xanthen system. If it had structure (II) the 2-methylbut-2-enyl side chain



(II)



(III)

should be adjacent to the chelated OH group and ought to ring-close to form a dihydropyran type of compound on warming with formic acid.[6] However, trapezifolixanthone failed to cyclise under these conditions and hence we conclude that it has structure (III).

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This structure was further confirmed by determining the n.m.r. spectrum of trapezifolixanthone diacetate and observing the chemical shift differences for C-3 and C-4 protons with respect to the parent compound (Table 2).

TABLE 2

Chemical shift (τ value) differences

	4-H	3-H
Trapezifolixanthone	3·24	4·38
Trapezifolixanthone acetate	3·53	4·29
Diamagnetic ($\Delta\tau$/p.p.m.)	+0·29	
Paramagnetic ($\Delta\tau$/p.p.m.)		−0·09

The positive diamagnetic shift and a negative paramagnetic shift supported a linearly fused 2,2-dimethyl-2*H*-pyrano-ring.[7]

The trapezifolixanthone structure has been synthesised by Jain and the natural product provided by us has been shown to be identical with the synthetic compound.*

6-Deoxyjacareubin has been isolated from the timber of *Calophyllum brasiliense* Camb.,[8] *C. inophyllum* L.,[9] *C. scribilitifolium* Hend and Wyatt Smith,[10] *C. fragrans* Ridley,[11] *C. calaba* L.,[4] *C. bracteatum* Thw.,[4] *C. neoebudicum* Guillaumin,[12] and *C. cuneifolium* Thw.[13] but the isoprenylated 6-deoxyjacareubin (or trapezifolixanthone) has been isolated from the bark alone of *C. trapezifolium* Thw. and *C. cuneifolium* Thw.[13] This is the third di-isoprenylated xanthone recorded to date from the bark of the *Calophyllum* species. It appears that the di-isoprenylated xanthones are specific constituents in the bark of the *Calophyllum* species.

EXPERIMENTAL

U.v. spectra were recorded with a Unicam 8000B spectrophotometer. I.r., n.m.r., and mass spectral data were obtained from the Universities of Osaka, Sheffield, and Aberdeen. Analytical and preparative t.l.c. (p.l.c.) were carried out with silica gel G (Merck). M.p.s were determined on a Kofler hot stage apparatus. Elemental analyses were carried out at the C.S.I.R.O., Microanalytical Service, Melbourne.

The plant material was obtained from Hantane, Kandy.

Bark Extractives of Calophyllum trapezifolium *Thw.*—Powdered bark (12 kg) was extracted with cold light petroleum (b.p. 60—80°). On concentration of the extract a yellowish white solid (0·20 g) and a gum were obtained. The solid was chromatographed on a silica gel (30—70 mesh; 10 g) column prepared with light petroleum and eluted with light petroleum and increasing amounts of benzene and then chloroform.

Isolation of calabaxanthone, taraxerol, β-sitosterol, and β-simiarenol. Elution with benzene gave calabaxanthone (0·120 g, 0·001%), m.p. 172° (lit.,[4] 172°); taraxerol, m.p. 279—280° (lit.,[14] 279—280°); and β-sitosterol, m.p. 135° (lit., 136—137°). Further elution with benzene–chloroform gave β-simiarenol, m.p. 209° (lit.,[15] 210°). These compounds were identical with authentic samples by mixed m.p., i.r., and t.l.c. comparison.

The gum was dissolved in ether and washed with ice-cold 10% sodium carbonate solution, 10% sodium hydroxide, and with water. The sodium carbonate solution was acidified with ice-cold dilute HCl solution, extracted with ether, and the extract was washed, dried ($MgSO_4$), and evaporated to give a brownish yellow resin. Further work on this is in hand.

On working up the sodium hydroxide extract in a similar way, a gum (4 g) was obtained.

Isolation of trapezifolixanthone (III). The foregoing gum (4 g) was separated on a silica gel column (30—70 mesh; 100 g) prepared in light petroleum (b.p. 60—80°). On elution with benzene it gave yellow crystals (from benzene) of *trapezifolixanthone* {*5,10-dihydroxy-2,2-dimethyl-12-(3-methylbut-2-enyl)pyrano*[3,2-b]*xanthen-6*(2H)*-one*} (1·01 g, 0·01%), m.p. 171—172°, which gave a positive $FeCl_3$ test (Found: C, 73·05; H, 5·8%; M^+, 378. $C_{23}H_{22}O_5$ requires C, 73·0; H, 5·7%; *M*, 378), $\lambda_{max.}$ (EtOH–$AlCl_3$) 237 (log ε 4·08), 255 (4·02), 280 (3·90), 304 (4·16), 309 (4·18), and 357 nm (3·88); no shifts with NaOAc or NaOAc–H_3BO_3, $\nu_{max.}$ (Nujol) 3200, 2920, 1650, 1624, 1584, 1560, 1376, 1340, 1292, 1246, 1220, 1210, 1163, 1140, 1129, 1106, 1076, 1052, 1025, 1000, 974, 944, 912, 881, 866, 850, 835, 789, 766, 749, and 722 cm^{-1}, τ ($CDCl_3$, 100 MHz) 2·25 (1H, q, *J* 8 and 3 Hz, 7-H), 2·61 (2H, m, 8- and 9-H), 3·24 (1H, d, *J* 10 Hz, 4-H), 3·60—4·00 (1H, m, 10-OH), 4·38 (1H, d, *J* 10 Hz, 3-H), 4·73 (1H, m, :CH), 6·51 (2H, d, *J* 7 Hz, $ArCH_2$), 8·12 and 8·27 (6H, s, :CMe_2), and 8·51 (6H, s, CMe_2), τ [$(CD_3)_2SO$, 60 MHz] −3·25 (1H, s, 5-OH), *m/e* 378 (67%), 364 (70), 363 (100), 335 (28), 323 (19), 308 (9), 307 (21), 303 (8), 295 (10), 281 (5), 279 (5), 154 (5), 28 (8), and 18 (37).

Trapezifolixanthone Diacetate.—Trapezifolixanthone (25 mg), pyridine (5 ml), and acetic anhydride (1 ml) was warmed on a water-bath for 5 h. The usual work-up and crystallisation from light petroleum (b.p. 60—80°) gave pale yellow crystals of trapezifolixanthone diacetate (23 mg), m.p. 166—167°, τ ($CDCl_3$, 100 MHz) 3·53 (1H, d, *J* 10 Hz, 4-H), 4·29 (1H, d, *J* 10 Hz, 3-H), 1·92 (1H, q, *J* 8 and 2 Hz, 7-H), 2·60 (1H, q, *J* 8 and 2 Hz, 9-H), 2·75 (1H, t, *J* 8 Hz, 8-H), 4·82 (1H, t, *J* 7 Hz, :CH), 6·54 (2H, d, *J* 7 Hz, $ArCH_2$), 7·53 (3H, s, 5-OAc), 7·62 (3H, s, 10-OAc), 8·20 and 8·33 (each 3H, s, :CMe_2), and 8·55 (6H, s, CMe_2), *m/e* 462 (1%), 420 (40), 405 (100), 377 (14), 363 (36), 335 (5), 305 (6), 303 (7), 139 (6), 137 (6), 109 (9), 81 (10), 69 (14), 57 (13), 55 (14), 43 (40), 42 (44), and 28 (76). A satisfactory elemental analysis was not obtained.

Trapezifolixanthone Dimethyl Ether.—Trapezifolixanthone (0·10 g) was refluxed with calcined potassium carbonate (4 g), dimethyl sulphate (2 ml), and dry acetone (100 ml) for 16 h. The mixture was cooled, filtered, and the filtrate was concentrated. The residue was treated with ammonia (2 ml) and water (100 ml) to precipitate *trapezifolixanthone dimethyl ether* as a white solid, m.p. 110—111° (from ethanol), $\nu_{max.}$ (KBr) 2893, 1647, 1593, and 1575 cm^{-1}

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(Found: C, 74·05; H, 6·55%; M^+, 406. $C_{25}H_{26}O_5$ requires C, 73·9; H, 6·45%; M, 406), τ [$(CD_3)_2CO$, 100 MHz] 2·29 (1H, s, 7-H), 2·72 (2H, m, 8- and 9-H), 3·27 (1H, d, J 10 Hz, 4-H), 4·15 (1H, d, J 10 Hz, 3-H), 4·67 (1H, t, J 8 and 8 Hz, :CH), 5·98 (3H, d, 5-OMe), 6·40 (2H, d, J 7 Hz, $ArCH_2$), 8·16 and 8·34 (each 3H, s, $:CMe_2$), and 8·50 (6H, s, CMe_2), *m/e* 406 (65%), 391 (100), 377 (24), 363 (28), 361 (24), 335 (16), 322 (15), 320 (21), 295 (10), 203 (8), 188 (15), 168 (12), 169 (11), 151 (17), 115 (13), 108 (12), 77 (25), 55 (21), 41 (58), and 28 (24).

Tetrahydrotrapezifolixanthone.— Trapezifolixanthone (0·0509 g) was dissolved in 95% ethanol (100 ml) and hydrogenated over palladised charcoal until hydrogenation was complete (t.l.c. monitoring). The mixture was filtered and the filtrate on concentration yielded yellow needles of *tetrahydrotrapezifolixanthone* {3,4-*dihydro*-5,10-*dihydroxy*-2,2-*dimethyl*-12-(3-*methylbutyl*)*pyrano*[3,2-b]-*xanthen*-6(2H)-*one*}, m.p. 160—161° (Found: M^+, 382. $C_{23}H_{26}O_5$ requires M, 382), τ ($CDCl_3$, 100 MHz) −3·09 (1H, 5-OH), 2·26 (1H, q, J 6, 7, and 7 Hz, 7-H), 2·74 (2H, complex, 8- and 9-H), 7·24 (4H, t, J 7 and 7 Hz, 2 × $ArCH_2$), 8·15 (2H, t, J 7 and 7 Hz, 3-H), 8·3—8·6 (3H, complex, CH_2CHMe_2), 8·61 (6H, s, CMe_2), and 9·00 (6H, d, J 6 Hz, $CHMe_2$).

Treatment of Trapezifolixanthone with Formic Acid.[5]— Trapezifolixanthone (20 mg) in formic acid (1 ml) was heated on a water-bath for 2 h and the mixture was poured into ice–water and extracted with ether. The ether extract was washed with sodium carbonate solution, water, dried ($MgSO_4$), and evaporated. The residue was crystallised from benzene, m.p. 171—172°, and was identical with trapezifolixanthone by mixed m.p., i.r., and t.l.c.

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