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# PRENYLATED BENZOPYRAN DERIVATIVES FROM TWO *POLYALTHIA* SPECIES

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**Key Word Index**—*Polyalthia cerasoides*; *P. sclerophylla*; Annonaceae; stem bark; prenylated benzopyranes; chromanes.

**Abstract**—Two new benzopyran derivatives, (6*E*,10*E*)-isopolycerasoidol and polycerasoidin methyl ester, have been isolated from a methanolic extract of the stem bark of *Polyalthia cerasoides*. Their structures were established on the basis of chemical and spectral evidence. *Polyalthia sclerophylla* contains (6*E*,10*E*)-isopolycerasoidol, besides the known polycerasoidin and polycerasoidol. In addition, a known phenylpropene derivative, *trans*-asarone, has also been isolated from both species and fully characterized. Copyright © 1996 Elsevier Science Ltd

## INTRODUCTION

We recently reported the isolation and structural elucidation of two metabolites of mixed biogenesis, polycerasoidin (**1**) and polycerasoidol (**2**) from the stem bark of *Polyalthia cerasoides* [1] and determined their inhibition of the mitochondrial electron-transport chain complex [2]. In continuation of our phytochemical studies on the constituents of this species, we present the isolation and structural elucidation of two new metabolites, (6*E*,10*E*)-isopolycerasoidol (**3**) and polycerasoidin methyl ester (**4**), in addition to the known phenylpropene derivative, *trans*-asarone (**5**). Some of these compounds (**1, 2, 3** and **5**) were also identified in *P. sclerophylla*.

## RESULTS AND DISCUSSION

Polycerasoidin (**1**) and polycerasoidol (**2**) were isolated from a methanolic extract of *P. sclerophylla* stem bark and identified on the basis of their chromatographic and spectral characteristics [1]. Compound **2**, a minor component in *P. cerasoides* was the main compound in *P. sclerophylla*.

In both species, the early chromatographic fractions containing polycerasoidol (**2**) although homogeneous by TLC, were characterized, in the $^1$H-NMR spectra, by signals similar to compound **2**. An AB-system at $\delta$ 6.38 and $\delta$ 6.48 (2H, $J = 2.5$ Hz), an $ABX_2$-system at $\delta$ 2.69 (2H, *t*) and $\delta$ 1.75 (2H, *dd*), and singlets at $\delta$ 2.12 (3H) and $\delta$ 1.25 (3H), were consistent with an identically substituted chromane nucleus. Signal resonances for two olefinic protons allylically coupled with two vinyl methyl groups, as in compound **2**, and extra resonances at $\delta$ 1.82 (3H, *s*), 2.22 (2H, *ddd*) and 6.85 (1H, *dt*), were also observed, suggesting an additional isoprene unit or a mixture of compounds. The EI and CI-mass spectra gave peaks at $[M]^+$ *m/z* 358 and $[MH]^+$ *m/z* 359, respectively, and fragment ions similar to those of compound **2**. This revealed the presence of an equimolecular mixture (1:1) of polycerasoidol (**2**) and a second component (**3**) having chromatographic and spectral properties very similar to those of compound **2**, with an identical $M_r$. In particular, the mass fragmentation pattern (neglecting differences in the relative intensities of peaks) is indicative of a stereochemical, rather than structural difference; the nature of this difference was clarified after acetylation. Treatment of the mixture (**2** + **3**) overnight with acetic anhydride in pyridine gave, surprisingly, a pure compound (**3a**). However, when the acetylation was stopped at 2, 4 and 6 hr, the two main spots increased in proportion of compound **3a** by TLC (verified by the $^1$H NMR spectrum), confirming the presence of two compounds, one of which was readily isomerized upon acetylation. Preparative TLC of the reaction mixture gave pure compounds **2a** and **3a**. The identity of compound **3** was established readily by comparison of its $^1$H NMR spectrum (Table 1) with that of polycerasoidol (**2**) [1]. There was a downfield shift of the H-10 olefinic proton resonance (from $\delta$ 6.04 in compound **2** to $\delta$ 6.85 in compound **3**), a concurrent upfield shift of the resonances of the terminal vinyl methyl group (from $\delta$ 1.89 to $\delta$ 1.82) and the H-9 methylene protons (from $\delta$ 2.60 in compound **2** to $\delta$

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Table 1. $^1$H NMR, $\delta$ values ($J$ = Hz), of compounds **3**, **3a** and **4** ($CDCl_3$, 250 MHz)

| Position | 3 | 3a | 4 |
|---|---|---|---|
| 1 | 2.69 *t* (6.8) | 2.71 *t* (6.8) | 2.72 *t* (7.2) |
| 2 | 1.75 *dd* (6.8; 13.2) | 1.75 *dd* (6.8;13.0) | 1.60–1.80 *m* |
| 4 | 1.55–1.64 *m* | 1.54–1.66 *m* | 1.60–1.80 *m* |
| 5 | 2.03–2.11 *m* | 2.03–2.11 *m* | 2.07–2.14 *m* |
| 6 | 5.15 *dt* (7.5; 1.2) | 5.16 *br t* (7.5) | 5.14 *dt* (7.5;1) |
| 8 | 2.03–2.11 *m* | 2.03–2.11 *m* | 2.07–2.14 *m* |
| 9 | 2.22 *ddd* (7.1; 5.3; 12.1) | 2.23 *ddd* (7.8; 5.3; 12.5) | 2.55 *ddd* (15; 7.5; 1) |
| 10 | 6.85 *dt* (7.1; 1.2) | 6.85 *dt* 6.8; 1.2) | 5.92 *dt* (7.5; 1) |
| 12 | – | – | 1.89 *d* (1) |
| 13 | 1.82 *br s* | 1.82 *br s* | – |
| 14 | 1.58 *br s* | 1.59 *br s* | 1.59 *br s* |
| 15 | 1.25 *s* | 1.27 *s* | 1.26 *s* |
| 3′ | 6.38 *d* (2.5) | 6.61 *d* (2.6) | 6.44 *d* (2.9) |
| 5′ | 6.48 *d* (2.5) | 6.65 *d* (2.6) | 6.56 *d* (2.9) |
| $OCH_3$-4′ | – | – | 3.72 *s* |
| $CH_3$-6′ | 2.12 *s* | 2.13 *s* | 2.15 *s* |
| $OCOCH_3$-4′ | – | 2.25 *s* | – |
| $COOCH_3$-13 | – | – | 3.74 *s* |

2.22 in compound **3**), while the rest of the spectrum was essentially unaffected; this revealed a change in the configuration of the C-10 double bond from *Z* in polycerasoidol (**2**) to *E* in compound **3** [3–4]. The $^{13}$C NMR spectrum of the monoacetyl derivative (**3a**) (Table 2) was also in full agreement with the proposed structure because in comparison with those of other isolated prenylated benzopyran derivatives [1,5], it shows an upfield of the vinyl methyl carbon from $\delta$ values >20 (C-12 for *E,Z* isomers) to $\delta$ 11.99 (C-13 for compound **3a**), which indicate an *E*-geometry of the relevant double bond [1]. Thus, compound **3** is a novel compound structure, for which the trivial name (6*E*,10*E*)-isopolycerasoidol was assigned.

Compound **4** was obtained as oil from *P. cerasoides*. After examination of its $^1$H and $^{13}$C NMR spectral data (Tables 1 and 2), IR spectrum (absorption at 1718 $cm^{-1}$) and mass spectral fragment ions (*m/z* 386 $[M]^+$), **4** was concluded to be the methyl ester of polycerasoidin. This compound was reported before by our group as a semisynthetic product obtained after methylation of compound **1** [1]; it has now been isolated for the first time from a natural source.

Compound **5** was identified as *trans*-asarone by comparison of its physical and spectral data with the literature [6].

## EXPERIMENTAL

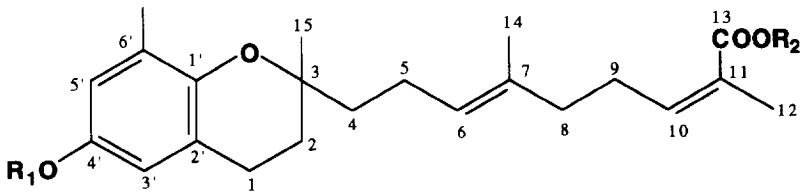
*General.* IR: film. UV: MeOH soln. $^1$H and $^{13}$C NMR: $CDCl_3$ soln; multiplicities of $^{13}$C NMR resonances determined by DEPT expts. TLC: silica gel $F_{254}$ precoated plates (Merck 5554); detection with anisaldehyde-$H_2SO_4$ or UV (254 nm).

*Plant material. Polyalthia cerasoides* (Roxb.) Bedd. and *P. sclerophylla* Hk. f. et Th were collected in December 1992 in the National Park of Varirata, located in the Central Province of Papua New Guinea. Voucher specimens are deposited in the Herbarium of the University of Papua New Guinea.

*Extraction and isolation of* Polyalthia cerasoides. Dried and powdered stem bark (550 g) [1] were macerated with MeOH at room temp. The concd MeOH extract (A) was partitioned between $CH_2Cl_2$ and 50% aq. MeOH. The $CH_2Cl_2$-soluble portion (B, 4.70 g) was washed with 5% aq. KOH, yielding a $CH_2Cl_2$ extract (C, 4.05 g) and an aq. fr. After neutralization, the aq. fr. extracted with $CH_2Cl_2$ gave 0.51 g of a further $CH_2Cl_2$ extract (extract D). Flash CC on silica gel (Merck 9385) was carried out on the C extract and developed with hexane containing gradually increasing amounts of $CH_2Cl_2$. Fr. 3 eluted with hexane was rechromatographed on silica gel (hexane–EtOAc, 9:1) to give compound **5** (85 mg) and **4** (23 mg). Extract D was subjected to 60H silica gel CC (Merck 7736) and eluted with $CH_2Cl_2$–EtOAc 3:2; frs 50–60 were combined yielding 15 mg of a **2** + **3** equimolecular mixt.

*Extraction and isolation of* Polyalthia sclerophylla. Dried and powdered stem bark (498 g) was macerated with MeOH at room temp. The concd MeOH extract (A) was partitioned between hexane and 50% aq. MeOH. After removal of the hexane fr. (2.8 g, B), the aq. MeOH soln was partially evapd under red. pres. and extracted with $CH_2Cl_2$. The $CH_2Cl_2$-soluble portion was dried and concd (6.0 g, C) and fractionated by 60H silica gel CC (Merck 7736), eluting with hexane–EtOAc (3:2), yielding frs 46–51 (**5**, 90 mg), frs 64–66 (**1**, 68 mg), frs 73–140 (**2**, 1700 mg) and frs 141–200 (**2** + **3** mixt. 156 mg). Prep. TLC of the **2** + **3** mix. (15 mg) after three developments using hexane–EtOAc (3:2) yielded 3 mg of compound **3**.

(6*E*,10*E*)-3,6′-*Dimethyl*-3-(7,11-*dimethylnonanoic*-6,10-*dienyl*)-*chroman*-4-*ol or* (3E,7E)-2,8-*dimethyl*-2-(4,8-*dimethylnonanoic*-3,7-*dienyl*)-*chroman*-6-*ol* ((6E,10E) *isopolycerasoidol*) (**3**). Oil. UV $\lambda_{max}$ EtOH nm (log $\epsilon$): 234 (3.55), 294 (3.38). EI-MS *m/z* (rel.

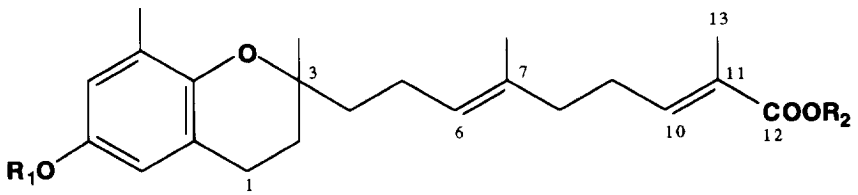


**1**: $R_1$= $CH_3$; $R_2$= H: **polycerasoidin**

**2**: $R_1$= $R_2$= H: **polycerasoidol**

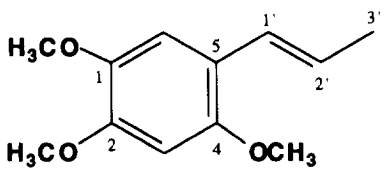
**2a**: $R_1$= Ac; $R_2$= H

**4**: $R_1$= $R_2$= $CH_3$: **polycerasoidin methyl ester**



**3**: $R_1$= $R_2$= H: **(6*E*,10*E*) isopolycerasoidol**

**3a**: $R_1$= Ac; $R_2$= H



**5**: ***trans*-asarone**

int.): 358 $[M]^+$ (100), 340 (12), 203 (11), 192 (17), 191 (11), 189 (17), 177 (66), 175 (50), 137 (72), 121 (22), 93 (12), 91 (9), 79 (10), 55 (6). $^1$H NMR (250 MHz, $CDCl_3$): Table 1.

*Acetylation of mixture* **2** + **3**. Treatment of an equimolecular mixt. of **2** + **3** (15 mg) with $Ac_2O$–pyridine for 6 hr at room temp. and conventional work-up, gave the monoacetate derivatives **2a** and **3a**, which were purified by prep. TLC yielding compounds **2a** (1.5 mg) and **3a** (7 mg). Acetylation of **2** + **3** (5 mg) by $Ac_2O$–pyridine overnight at room temp. furnished pure **3a** (4.8 mg).

*Compound* **3a**. Oil. $[\alpha]_D$ MeOH − 2° (*c* 1.0) IR $\nu_{max}$ $cm^{-1}$: 3300, 2924, 2850, 1755, 1684, 1473, 1366, 1283, 1204, 1131. UV $\lambda_{max}$ (EtOH) nm (log $\epsilon$): 212 (4.27), 280 (3.40); EI-MS *m/z* (rel. int.): 400 $[M]^+$ (45), 372 (8), 358 (100), 340 (18), 258 (12), 219 (21), 203 (15), 191 (21), 177 (51), 137 (48), 121 (23). $^1$H NMR (250 MHz, $CDCl_3$): Table 1. $^{13}$C NMR (62.5 MHz, $CDCl_3$): Table 2.

*Compound* **4** (*polycerasoidin methyl ester*). Oil. $[\alpha]_D$ MeOH − 3.12° (c 1.6) UV $\lambda_{max}$ EtOH nm (log $\epsilon$): 234 (3.35), 293 (3.08). IR and EI-MS see [1]. $^1$H NMR (250 MHz, $CDCl_3$): Table 1. $^{13}$C NMR (62.5 MHz, $CDCl_3$): Table 2.

Trans-*asarone* (**5**). IR $\nu_{max}$ $cm^{-1}$: 2930, 2847, 1606, 1580, 1511, 1460, 1208, 1122, 1034, 965 UV $\lambda_{max}$ EtOH nm (log $\epsilon$): 258 (3.82), 312 (4.08). EI-MS *m/z* (rel. int.): 208 $[M]^+$ (100), 193 (42), 165 (24), 137 (12), 105 (8), 91 (13), 77 (11), 69 (15), 65 (8). $^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ 6.93 (1H, *s*, H-6), 6.64 (1H, *dd*, $J$ = 15.8 Hz and 1.5 Hz, H-1′), 6.48 (1H, *s*, H-3), 6.10 (1H, *dq*, $J$ = 6.5 Hz and 15.8 Hz, H-2′), 1.87 (3H, *dd*, $J$ = 6.5 Hz and 1.5 Hz, $CH_3$-3′), 3.86, 3.84 and 3.80 (*s*, 3H each, 3-$OCH_3$). $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 150.5 (C-4), 148.6 (C-2), 143.2 (C-1),

Table 2. $^{13}C$ NMR spectral data of compounds **3a** and **4** ($CDCl_3$, 63 MHz)

| Position | [3a] | [4] |
|---|---|---|
| 1 | 22.3 | 22.6 |
| 2 | 30.9 | 31.4 |
| 3 | 75.8 | 75.3 |
| 4 | 39.6 | 39.6 |
| 5 | 22.1 | 22.1 |
| 6 | 125.2 | 124.9 |
| 7 | 133.9 | 134.3 |
| 8 | 38.0 | 39.1 |
| 9 | 27.4 | 28.0 |
| 10 | 144.5 | 143.2 |
| 11 | 127.3 | 126.7 |
| 12 | 173.8 | 20.6 |
| 13 | 12.0 | 168.3 |
| 14 | 15.8 | 15.7 |
| 15 | 24.2 | 24.0 |
| 1′ | 144.5 | 146.3 |
| 2′ | 120.9 | 120.9 |
| 3′ | 119.1 | 110.9 |
| 4′ | 149.4 | 152.1 |
| 5′ | 121.1 | 114.7 |
| 6′ | 127.3 | 127.2 |
| $OCH_3$-4′ | – | 55.6 |
| $CH_3$-6′ | 16.1 | 16.2 |
| $OCOCH_3$-4′ | 170.4 | – |
| $OCOCH_3$-4′ | 21.1 | – |
| $COOCH_3$-13 | – | 51.2 |

124.9 (C-1′), 124.2 (C-2′), 118.9 (C-5) 109.7 (C-6), 97.4 (C-3), 18.7 (C-3′), 56.6, 56.4 and 56.0 (3-$OCH_3$). See also ref. [6].

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