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# SHORT REPORT

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## A NEW COMPOUND FROM *UVARIA RUFAS*

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### Abstract

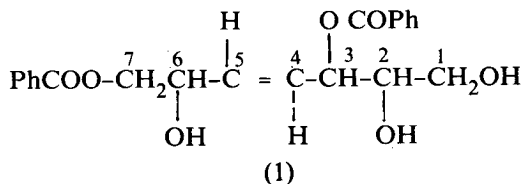
*Extraction of the leaves of Uvaria rufas Blume with dichloromethane-methanol followed by quick column chromatography gave a new compound. Spectroscopic studies revealed that it is (E)-3,7-bisbenzoyloxyhept-4-en-1,2,6-triol.*

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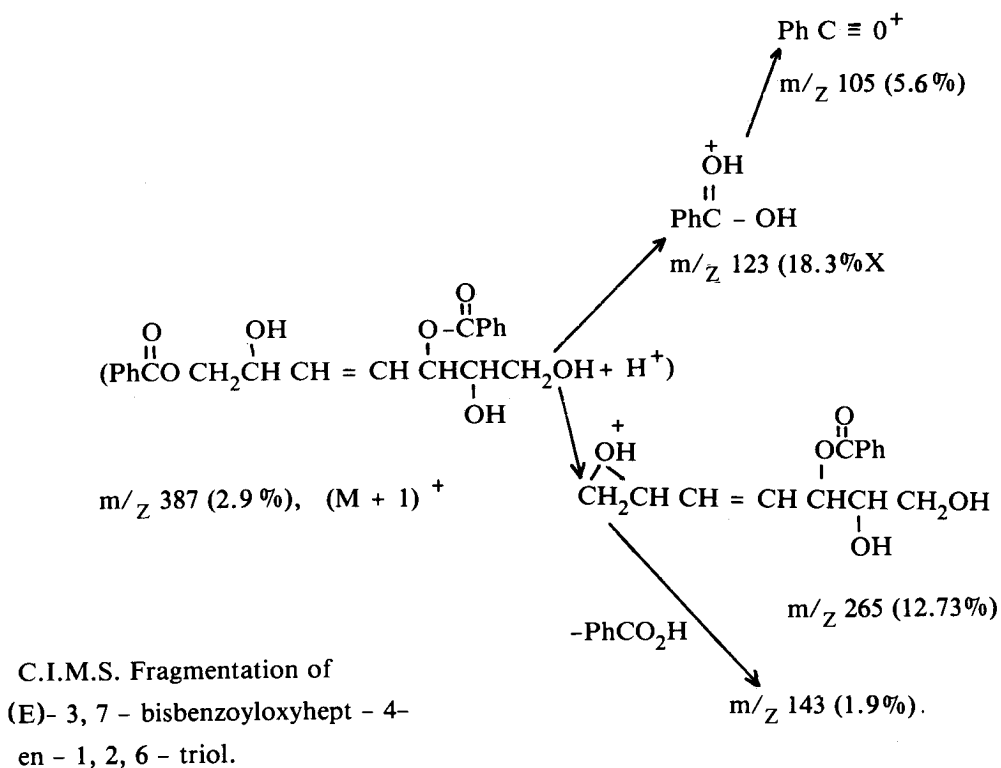
Our interest in *Uvaria* spp. (family Annonaceae) began when it was reported that two 3-benzylhydrochalcones isolated from *U. acuminata* exhibited activity in the P-388 (3 PS) lymphocytic leukemia test system<sup>1</sup> and that C-benzylflavones isolated from *U. chammae* proved to be cytotoxic. In addition to these results, several species have yielded a variety of cyclohexene derivatives related to crotepoxide<sup>3,4,5,6</sup>.

Previous work on *U. rufas* revealed that the bark contained three flavonoids but no cyclohexene derivatives. The present work was undertaken in order to determine whether any cyclohexene derivatives were present in other parts of the plant.

Extraction of the dried leaves of *U. rufas* with dichloromethane-methanol followed by chromatographic separation gave a new substance which is shown to have the *acyclic* structure (1), (E)-3,7-benzoyloxyhept-4-en-1,2,6-triol.



The compound exhibited ultraviolet absorption maxima at 228, 272 and 278 nm, and strong hydroxyl and carbonyl infrared absorption. The chemical ionization mass spectrum contained a  $(M + 1)^+$  peak at  $m/z$  387, indicating the molecular formula,  $C_{21}H_{22}O_7$ . Further analysis of the fragmentation pattern indicated the presence of 2-benzoyl groups [ $m/z$  265 and 143 corresponding to  $(M + H^+) - PhCO_2H$  and  $(M+H^+) - 2PhCO_2H$  respectively]. Other major peaks present resulted from the presence of the benzoic acid moiety.



The 400 MHz  $^1\text{H}$ -NMR spectrum shows (Fig. 1) three broad signals upfield, which disappeared on  $\text{D}_2\text{O}$  exchange. Furthermore, the signals at 3.64, 3.74, 3.88 and 4.56 became properly resolved, indicating that the protons responsible for these resonances were attached to the same carbons as the hydroxyl groups. In the exchanged spectrum (Fig. 1 a), the multiplet at  $\delta$  3.64 and 3.74 can be assigned to  $(\text{H}-1)_2$  since a  $J_{\text{gem}}$  of 11.2 Hz is present in each, as well as  $J_{\text{vic}}$  of 5.8 and 3.2 Hz to H-2 ( $\delta$  3.8) respectively. H-2 is coupled to H-3 ( $\delta$  5.54) with  $J_{2,3}$  6.0 Hz. The chemical shift of H-3 and the absence of OH coupling allows a benzyloxy group to be located at C-3. C-4 and C-5 support a *trans* disubstituted olefinic bond ( $J_{4,5}$  15.5 Hz), with H-4 resonating as a doublet of doublet of doublets,  $J_{4,5} = 15.7$  Hz,  $J_{4,3}$  6.5 Hz and  $J_{4,6}$  1.0 Hz. H-5 resonates as a doublet of doublets, with vicinal coupling with H-6 ( $J_{5,6}$  6.5 Hz). Finally, H-6 is coupled in turn to  $(\text{H}-7)_2$  ( $J_{6,7a}$  6.0 Hz,  $J_{6,7b}$  4.0 Hz), which resonate at  $\delta$  4.34 ( $\text{H}_a-7$ ) and 4.42 ( $\text{H}_b-7$ ) ( $J_{7a,7b}$  11.3 Hz);  $(\text{H}-7)_2$  is clearly associated with a second benzoate group. The protons of the aromatic rings give rise to the usual characteristic downfield patterns.

The chemical shift nonequivalence of  $(\text{H}-1)_2$  and  $(\text{H}-7)_2$  is due to the intrinsic asymmetry present. Double irradiation experiments confirms the coupling relationships of the protons and thus the total connectivity pattern.

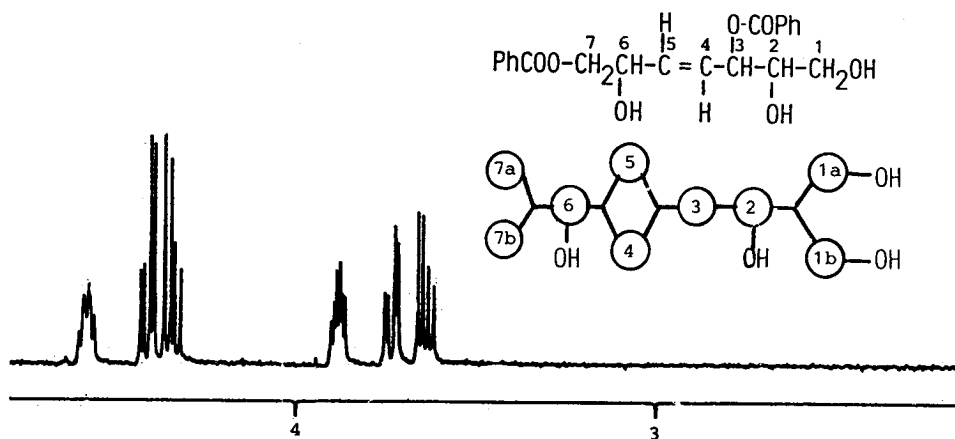
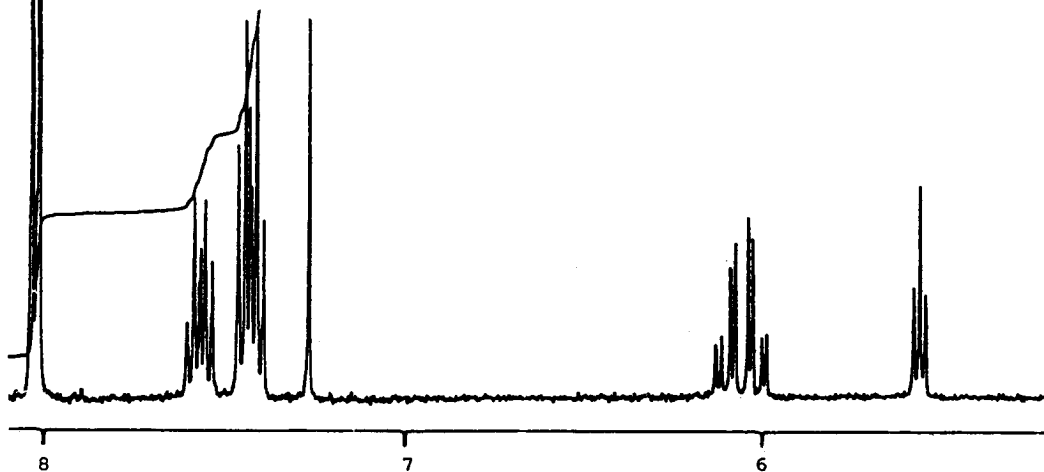
The noise-decoupled 100.62 MHz  $^{13}\text{C}$ -NMR spectrum (fig. 2) showed, in addition to peaks from the two benzoate groups, signals from four oxygenated carbons and one olefinic pair. The  $^1\text{H}$ -coupled spectrum revealed the full multiplicities of the signals and confirmed the presence of  $2x-\text{CH}_2\text{O}$ - and  $3x-\dot{\text{C}}\text{H}-\text{O}$ - groups, and  $1x-\text{CH}=\text{CH}$ - group, having the appropriate  $J_{\text{CH}}$  coupling constant values.

The determination of the absolute stereochemistry of (1) is in hand and the result will be reported elsewhere.

Melting point were determined on an Electrothermal melting point apparatus and is uncorrected. Nuclear magnetic resonance spectra were obtained with a Bruker WM-400 operating at 400 MHz for protons and 100.62 MHz for Carbon-13. The C.I. mass spectrum was measured with an A.E.I. MS-30 spectrometer using methane as the ionizing gas. Infrared spectrum was recorded on a JASCO DS-701 G Spectrophotometer and ultraviolet spectrum was measured with a Hitachi 124 Spectrophotometer.

A voucher specimen of the plant material (PS 241) has been deposited in the Herbarium of the Biology Department at the Prince of Songkla University, Hat Yai, Thailand.

Milled air-dried leaves (800g) of *Uvaria rufas* collected beside the rubber plantation opposite the Prince of Songkla University, Hat Yai, Thailand, were extracted for 24 hours twice with dichloromethane-methanol (2 : 1, 10 l). The extract was concentrated under reduced pressure. The green residue containing some residual water was extracted with dichloromethane (5  $\times$  200 ml). The combined dichloromethane extracts were dried with sodium sulfate and evaporated to give a dark green gum (20g).

Fig.1a.  $^1\text{H-NMR}$  Spectrum in  $(\text{CDCl}_3 + \text{D}_2\text{O})$ Fig.1  $^1\text{H-NMR}$  Spectrum in  $\text{CDCl}_3$  (upfield)Fig.1  $^1\text{H-NMR}$  Spectrum in  $\text{CDCl}_3$  (downfield)

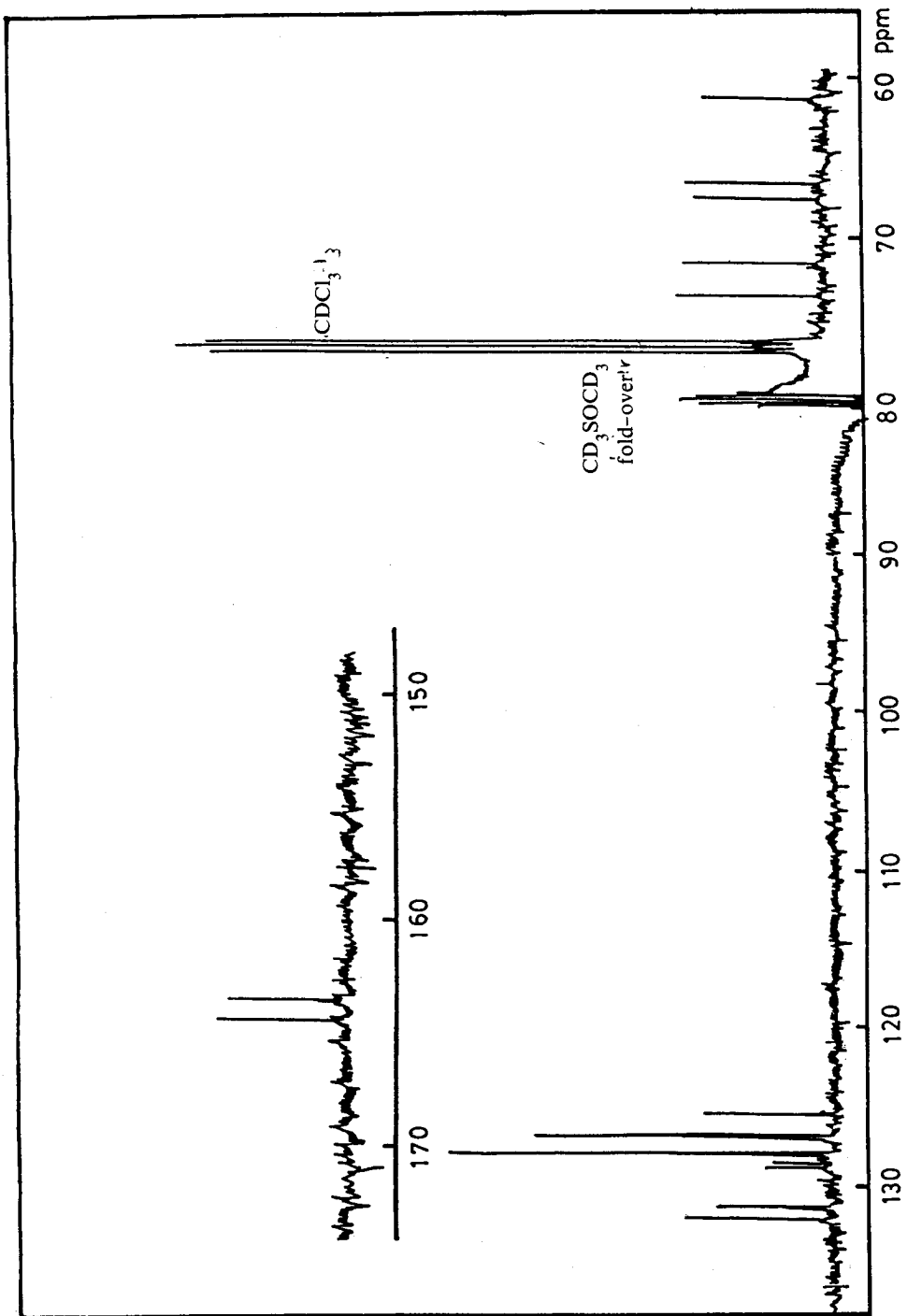


Fig.2.  $^{13}\text{C}$ -NMR Spectrum in  $\text{CDCl}_3 + \text{CD}_3\text{SOCD}_3$

The total green gum was separated by quick column chromatography using silica gel (Merck GF<sub>254</sub>) as the adsorbant and eluting with light petroleum, light petroleum-benzene, benzene, benzene-dichloromethane, dichloromethane, dichloromethane-acetone, then acetone. The eluants were examined on silica gel thin layer chromatography and the fractions with similar constituents were combined. The fraction eluted with dichloromethane-acetone contained a pale yellow solid. Repeated recrystallization from ethyl acetate-ether (six times) gave colourless needles of m.p. 117-117° C;  $[\alpha]_D - 22^\circ$  (CHCl<sub>3</sub>, 0.2M). Found C65.1, H5.7%; C<sub>21</sub>H<sub>22</sub>O<sub>7</sub> requires C65.3, H5.7%. C.I.M.S., m/z: Found M+H<sup>+</sup>, 387.5(2.8), C<sub>21</sub>H<sub>22</sub>O<sub>7</sub>+H<sup>+</sup> requires 387; 371 (0.9), 370 (4.5), 369 (19.6), 251 (2.0), 266 (1.8), 265 (12.7), 249 (1.4), 248 (1.6), 247 (10.3), 231 (1.0), 229 (2.7), 217 (1.6), 165 (5.1), 143 (1.9), 125 (3.5), 124 (1.5), 123 (18.2), 107 (1.1), and 105 (5.6);  $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$  (log $\Sigma$ ) 228 (4.657), 272 (3.455) and 2.78 nm (3.391);  $\nu_{\text{max}}$  (KBr) 3500 cm<sup>-1</sup> (s), 3250 (br), 1740 (s), 1700 (s), 1600 (s), 1325 (s), 1285 (br), 1130 (br), 1020 (s) and 700 (br); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) 2.3 (broad s, 1H, OH), 2.8 (broad s, 1H, OH), 2.9 (broad s, 1H, OH), 3.64 (broad m, 1H, H-1), 3.74 (broad m, H, H-1), 3.88 (broad s, 1H, H-2), 4.34 (dd, 1H, J=11, and 6.0 Hz, H<sub>a</sub>-7), 4.42 (dd, 1H, J=11.3 and 4.0 Hz, H<sub>b</sub>-7), 4.56 (broad s, 1H, H-6), 5.54 (dd, 1H, J=6.0 and 6.5 Hz, H-3), 6.01 (dd, 1H, J=15.5 and 5 Hz, H-5), 6.07 (1H, dd, J=15.5 and 6.5 Hz, H-4), 7.41 (m, 4H, m-ArH), 7.60 (m, 2H, p-ArH), 8.01 (d, 4H, o-ArH); <sup>1</sup>H-NMR (CDCl<sub>3</sub> + D<sub>2</sub>O) 3.64 (1H, dd, J=11.2 and 5.8 Hz, H-1), 3.74 (1H, dd, J=11.2 and 3.2 Hz, H-1), 3.88 (1H, m, H-2), 4.56 (1H, m, H-6), the rest of the spectrum remained the same. <sup>13</sup>C-NMR (CDCl<sub>3</sub> + CD<sub>3</sub> SOCD<sub>3</sub>) (<sup>1</sup>J<sub>-CH</sub>, Hz) 61.22 (141.6), C-1; 66.57 (145.8), C-7; 67.46 (141.0), C-6; 71.71 (143.4), C-2; 73.73 (148.5), C-3; 125.44 (159.8), C-4 (a); 126.87 (164.3), C-2', -6' (b); 126.94 (164.3), C-2'', -6'' (b); 128.03 (165.0), C-3', -3'', -5', -5''; 128.65, C-1' (c); 128.94, C-1'' (c); 131.46 (162.8), C-4' (d); 131.53 (162.8), C-4'' (d); 132.67 (157.5), C-5 (a); 163.60 (C=O), 164.50 (C=O). [assignments for pairs (a), (b), (c) and (d) may be interchanged].

### Acknowledgement

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### บทคัดย่อ

ได้สกัดใบของ *Uvaria rufas* Blume ด้วย ไดคลอโรมีเทน-เมธานอลตามด้วยโครมาโตกราฟี ในคอลัมน์ ได้สารใหม่ซึ่งคุณสมบัติทางโครมาโตกราฟี แสดงว่าเป็น (E)-3,7-bisbenzoyloxyhept-4-en-1,2,6-triol.