4. Proksch, P., Proksch, M., Towers, G. H. N. and Rodriguez, E. (1983) *J. Nat. Prod.* **46**, 331.
5. Proksch, P. and Rodriguez, E. (1984) *Biochem. Syst. Ecol.* **12**, 179.
6. Proksch, P., Proksch, M., Weck, W. and Rodriguez, E., *Z. Naturforsch. c* (in press).
7. Budzikiewicz, H., Laufenberg, G., Clark, C. and Proksch, P. (1984) *Phytochemistry* **23**, 2625.
8. Mitsakos, A. and Proksch, P. (1985) *Biochem. Syst. Ecol.* **13**, 257.
9. Robinson, H. (1981) *Smithson. Contrib. Botany* **51**, 48.
10. Zalkow, L. H., Ekpo, A. A., Gelbaum, L. T., Harris, R. N., Keinan, E., Novak, J. R., Ramming, C. T. and Van Derveer, D. (1979) *J. Nat. Prod.* **42**, 203.
11. Budzikiewicz, H. and Lange, E. (1985) *Org. Mass Spectrom.* **20**, 160.
12. Proksch, P. and Rodriguez, E. (1983) *Phytochemistry* **22**, 2335.
13. Bjeldanes, L. F. and Geissman, T. A. (1969) *Phytochemistry* **8**, 1293.

Phytochemistry, Vol. 24, No. 12, pp. 3071–3072, 1985.
Printed in Great Britain.

0031-9422/85 $3.00 + 0.00

BENZYL BENZOATES AND *o*-HYDROXYBENZYL FLAVANONES FROM *UVARIA FERRUGINEA*

MONTREE KODPINID, CHACHANAT THEBTARANONTH* and YODHATHAI THEBTARANONTH

Department of Chemistry, Faculty of Science, Mahidol University, Rama 6 Road, Bangkok 10400, Thailand

(*Received* 7 *March* 1985)

Key Word Index—*Uvaria ferruginea*; Annonaceae; benzyl benzoates; chamanetin; chamanetin 5-methyl ether; *o*-hydroxybenzyl flavanones; biogenesis.

Abstract—The isolation of benzyl benzoates and *o*-hydroxybenzyl flavanones from *Uvaria ferruginea*, in addition to the previously reported cyclohexene oxides, provides evidence in support of the proposed biogenetic route to these compounds via the common benzyl benzoate precursor.

Cyclohexene oxides form a small class of plant metabolites and interest in these unusual compounds has raised the question of their biogenesis. Two hypothetical pathways have been proposed, the first by Ganem and Hobbert [1] and the second by Jolad *et al.* [2]. The latter pathway postulated benzyl benzoate as the common origin of both the cyclohexene oxides and the *o*-hydroxybenzyl group in *o*-hydroxybenzyl dihydrochalcones and flavanones. In this paper we report the isolation of two benzyl benzoates and two *o*-hydroxybenzyl flavanones from *Uvaria ferruginea.* This co-isolation, in addition to the previously reported cyclohexene oxides from the same plant [3], is, to the best of our knowledge, the first observation of the co-occurrence of these three types of compounds. As can be readily seen, the implication of this observation is significant and would seem to put the Jolad *et al.* biogenetic hypothesis on firm ground.

Hexane extraction of the root of *U. ferruginea* followed by purification by CC yielded, apart from (−)-1,6-desoxysenepoxide (**1**), (−)-1,6-desoxytingtanoxide (**2**), α-senepoxide (**3**), tingtanoxide (**4**) and β-senepoxide (**5**) as previously reported [3], also benzyl benzoate (**6**) and 2-methoxybenzyl benzoate (**7**) in 0.011 and 0.016% yields, respectively. Further extraction of the plant material with chloroform gave chamanetin 5-methyl ether (**8**) [4] (0.01%). Similarly the stem of *U. ferruginea* afforded **4**–**7** from a hexane extract, while a chloroform extract yielded chamanetin (**9**) [5] (0.00057%).

The flavanone **9** and its monomethylated product **8** were identified by their spectroscopic data and by direct comparison with the natural products obtained by Professor Hufford. The structures of the compounds were also confirmed by chemical correlations. Thus treatment of either **8** or **9** with dimethylsulphate and K_2CO_3 in acetone gave the same fully methylated product **10**.

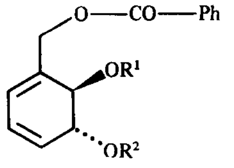
EXPERIMENTAL

^{1}H NMR: 60 MHz, TMS as int. standard; EIMS: probe 70 eV.

Extraction and separation. Ground, air-dried roots of *U. ferruginea* (3 kg), collected from Khonkhaen University campus, Khonkhaen Province, Northeast Thailand, were extracted with hexane (8 l.) at room temp. for 7 days, after which the extract was

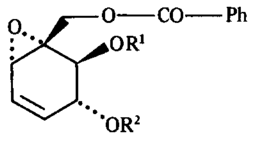
---

*Author to whom correspondence should be addressed.



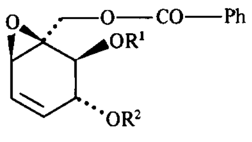
1 R^1 = R^2 = COMe

2 R^1 = COMe, R^2 = COPh

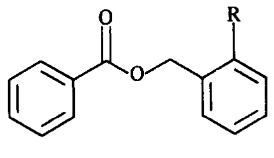


3 R^1 = R^2 = COMe

4 R^1 = COMe, R^2 = COPh

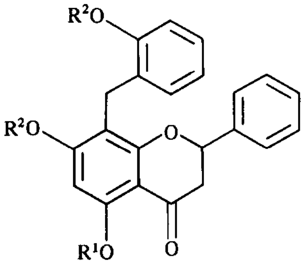


5 R^1 = R^2 = COMe



6 R = H

7 R = OMe



8 R^1 = Me, R^2 = H

9 R^1 = R^2 = H

10 R^1 = R^2 = Me

filtered, concd and chromatographed on a short silica gel column using EtOAc–hexane (1:20) as eluant to give a total of seven fractions. After further purification by prep. TLC (silica gel) using EtOAc–hexane (1:10) each fraction yielded a pure compound, listed together in order of decreasing R_f value as follows: **6** (336 mg), **7** (465 mg), **2** (200 mg), **1** (150 mg), **4** (2.6 g), **5** (1.5 g) and **3** (125 mg).

The identification of **6** and **7** was carried out by comparison of their spectroscopic data with those of authentic samples obtained earlier from another plant [6], whereas the identification of **1–5** was accomplished as previously reported [3].

The plant residue remaining after extn with hexane was further extd with $CHCl_3$ (5 l.) at room temp. for 3 days, then filtered and the extract concd to give a dark-brown viscous liquid. This material was kept at 0° for 2 days by which time a brown solid had ppted. The solid was collected and recrystallized × 2 from Me_2CO using decolourizing charcoal to yield colourless needles of chamanetin 5-methyl ether (**8**).

Hexane (8 l.) extraction of the ground dried stems of *U. ferruginea* (3 kg) at room temp. for 7 days followed by chromatographic sepn in the same manner as already described led to the isolation of **4** (105 mg), **5** (78 mg), **6** (50 mg), and **7** (34 mg), while $CHCl_3$ extn of the remaining plant residue gave a small amount of crude material, which, after chromatography on a short silica gel column with 30% EtOAc in hexane as eluant, yielded chamanetin (**9**).

Chamanetin 5-methyl ether (**8**). Colourless needles (312 mg), mp 226–227° (lit. [4] mp 226–227°): spectroscopic properties identical to those reported in lit. [4]. (Found: C, 73.21; H, 5.56. Calc. for $C_{23}H_{20}O_5$: C, 73.40; H, 5.32%.)

Chamanetin (**9**). Colourless needles from $CHCl_3$ (171 mg), mp 207–209° (lit. [5] mp 210–211°): spectroscopic properties identical to those reported in lit. [5]. (Found: C, 72.70; H, 5.08. Calc. for $C_{22}H_{18}O_5$: C, 72.93; H, 4.97%.)

Methylation of **8** *and* **9**. The compounds when methylated using Me_2SO_4–K_2CO_3–Me_2CO both yielded the same product, viz. chamanetin trimethyl ether (**10**), identical in all respects to that reported in lit. [5].

Acknowledgements—We sincerely thank Professor C. D. Hufford of the University of Mississippi, U.S.A. for the supply and comparison of samples. Support from the International Foundation for Science (to C.T.) is gratefully acknowledged.

REFERENCES

1. Ganem, B. and Holbert, G. W. (1977) *Bioorg. Chem.* **6**, 393.
2. Jolad, S. D., Hoffmann, J. J., Schram, K. H., Cole, J. R., Tempesta, M. S. and Bates, R. B. (1981) *J. Org. Chem.* **46**, 4267.
3. Kodpinid, M., Sadavongvivad, C., Thebtaranonth, C. and Thebtaranonth, Y. (1983) *Tetrahedron Letters* **24**, 2019.
4. El-Sohly, H. N., Lasswell, W. L., Jr. and Hufford, C. D. (1979) *J. Nat. Prod.* **42**, 264.
5. Lasswell, W. L., Jr. and Hufford, C. D. (1977) *J. Org. Chem.* **42**, 1295.
6. Kodpinid, M., Sadavongvivad, C., Thebtaranonth, C. and Thebtaranonth, Y. (1984) *Phytochemistry* **23**, 199.