Tetrahedron, 1966, Vol. 22, pp. 3209 to 3211. Pergamon Press Ltd. Printed in Northern Ireland

FLAVANOID EPOXIDES—II

A NEW SYNTHESIS OF 4-HYDROXY-3-PHENYLCOUMARINS

M. GEOGHEGAN, W. I. O'SULLIVAN and E. M. PHILBIN
Department of Chemistry, University College, Belfield, Dublin 4, Ireland

(*Received* 20 *April* 1966; *accepted for publication* 23 *May* 1966)

Abstract—Aurone epoxides on treatment with BF$_3$-etherate yield the corresponding 4-hydroxy-3-phenylcoumarins.

IN A preliminary report[1] it was shown that aurone epoxides undergo ring expansion on treatment with alkali to form flavonols, whereas, under the influence of BF$_3$-etherate or of conc sulphuric acid they yield 4-hydroxy-3-phenylcoumarins (benzotetronic acids). Thus 6-methoxyaurone epoxide[2](Ic) gave 7-methoxyflavonol with the former reagent and 4-hydroxy-7-methoxy-3-phenylcoumarin(IIc) with the latter. The work has since been extended to include the aurone epoxides (I; a, b, d) which with BF$_3$ give the corresponding 4-hydroxy-3-phenylcoumarins (II; a,[3]b,[4]d) in high yields. These coumarins showed UV and IR absorption patterns consistent with the assigned structures (see Table 1). Coumarin IId was also synthesized by condensation of pyrogallol-1,2-dimethyl ether with diethyl phenylmalonate using the method described by Mentzer *et al.*[3,4]

TABLE 1. ABSORPTION SPECTRA OF 4-HYDROXY-3-PHENYLCOUMARINS

Compound	λ_{max}(mμ)(MeOH)	λ_{max}(μ)(CHCl$_3$)		λ_{max}(μ)(KBr)	
		OH	C=O	OH	C=O
IIa	288 (infl.). 313 (log ε 3·76, 4·07)	2·83	5·89 5·83 (infl.)	3·2	5·98
IIb	288 317 (log ε 3·87, 4·13)	2·84	5·86, 5·93	3·2 (broad)	5·95 6·01, 6·06
IIc	287 (infl.) ,320 (log ε 3·68, 4·25)	2·86	5·9	3·2 (broad)	6·03
IId	316 (log ε 4·24)	2·88	5·88	3·08 (broad)	6·03

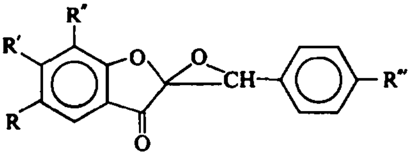
The rearrangement of aurone epoxides into 4-hydroxycoumarines involves benzoyl migration and is analogous to the formation of 2-phenylcyclohexan-1,3-dione from 2-benzylidenecyclopentanone epoxide.[5]

---

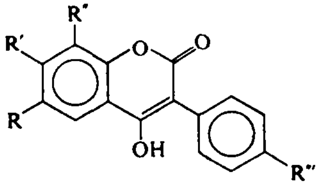
[1] M. Geoghegan, W. I. O'Sullivan, T. S. Wheeler and E. M. Philbin, *IUPAC Abstracts* **A**, 80 (1963).
[2] M. Geoghegan, W. I. O'Sullivan, E. M. Philbin and T. S. Wheeler, *Tetrahedron* **22**, 3209 (1966).
[3] C. Mentzer, D. Molho and P. Vercier, *Bull. Soc. Chim. Fr.* 749 (1949).
[4] P. Vercier, D. Molho and C. Mentzer, *Bull. Soc. Chim. Fr.* 1248 (1950).
[5] H. O. House and R. L. Wasson, *J. Amer. Chem. Soc.* **78**, 4394 (1956).

Recently another example of this type of rearrangement has been recorded[6] where the coumaranone epoxide (V) was converted into 3,3-diphenylchroman-2,4-dione (VI).

In the early stages of the work it was thought that the acid (m.p. 202–203°) isolated from the product of the reaction of aurone epoxide (Ic) with conc sulphuric acid might be 6-methoxy-2-phenylbenzofuran-3-carboxylic acid (III) since it has spectral characteristics[7] similar to those noted for compounds of this type. However, comparison of the acid with 6-methoxy-2-phenylbenzofuran-3-carboxylic acid (III) or with the isomeric 6-methoxy-3-phenylbenzofuran-2-carboxylic acid (IV), which also had m.p. 202–203°[8], showed it to be neither, and it was subsequently identified as 4-hydroxy-7-methoxy-3-phenylcoumarin (IIc).

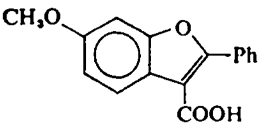


I

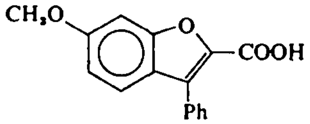


II

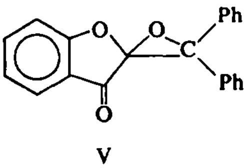
(a; R = R′ = R″ = R‴ = H)
(b; R = CH_3; R′ = R″ = R‴ = H)
(c; R′ = OCH_3; R = R″ = R‴ = H)
(d; R′ = R″ = OCH_3; R = R‴ = H)



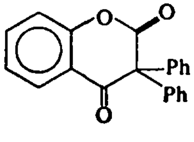
III



IV



V



VI

EXPERIMENTAL

M.ps are uncorrected. UV spectra: 95% EtOH on a Bausch and Lomb Spectronic 505 spectrometer. IR spectra: Beckman IR-5 spectrometer.

4-Hydroxy-7-methoxy-3-phenylcoumarin (IIc). BF_3-etherate (1·0 ml) was added to a soln of 6-methoxyaurone epoxide (0·5 g) in dry ether (100 ml) and the mixture was heated under reflux for ½ hr. The ethereal soln was washed with water and extracted with 5% $NaCO_3$aq. Acidification of the $NaCO_3$ extract precipitated 4-hydroxy-7-methoxy-3-phenylcoumarin (0·45 g) which crystallized from dil. AcOH aq in needles, m.p. 202–203°. The m.p. was not depressed on admixture with an authentic sample.[8]

---

[6] A. Schonberg and K. Junghans, *Chem. Ber.* **99**, 531 (1966).

[7] B. Cummins, D. M. X. Donnelly, J. F. Eades, H. Fletcher, F. O. Cinneide, E. M. Philbin, J. Swirski, T. S. Wheeler and R. K. Wilson, *Tetrahedron* **19**, 499 (1963).

[8] T. R. Seshadri, P. E. Subramani and S. Varadarajan, *J. Sci. Ind. Research (India)* **11B**, 56 (1952).

The following three coumarins were obtained from I(a, b and d) by procedures similar to those described in the above reaction.

4-Hydroxy-7,8-dimethoxy-3-phenylcoumarin (IId). 6,7-Dimethoxyaurone epoxide (0·1 g) gave yellow needles (0·098 g) of *4-hydroxy-7,8-dimethoxy-3-phenylcoumarin*, m.p. 218–220°. (Found: C, 68·6; H, 5·0; OCH_3, 21·0. $C_{17}H_{14}O_5$ requires: C, 68·5; H, 4·7; OCH_3, 21·2%.) For comparison a sample of this coumarin was also prepared by heating a mixture of pyrogallol-1,2-dimethyl ether[9] (10 g) and diethyl phenylmalonate (10 g) under reflux for 8 hr. The solid obtained on cooling crystallized from MeOH in platelets of 4-hydroxy-7,8-dimethoxy-3-phenylcoumarin, m.p. and mixed m.p. 219–220°.

4-Hydroxy-3-phenylcoumarins (IIa *and* IIb). The product of alkaline H_2O_2 oxidation of aurone (0·5 g; containing 50% of aurone epoxide as estimated by titration[1]) on treatment with BF_3-etherate yielded IIa which separated from dil. AcOH in yellow needles (0·25 g), m.p. 238–239° (lit.[3] m.p. 239°). (Found: C, 75·3; H, 4·2. Calc. for $C_{15}H_{10}O_3$: C, 75·6; H, 4·2%.)

The product of alkaline H_2O_2 oxidation of 5-methylaurone (0·5 g) containing 60% Ib as estimated by titration[1] on treatment with BF_3-etherate yielded IIb which separated from dil. AcOH in yellow needles (0·3 g) m.p. 195° (lit.[4] m.p. 195°). (Found: C, 75·8; H, 4·7 Calc. for $C_{16}H_{12}O_3$: C, 76·2; H, 4·8%.)

Reaction of epoxide (Ic) *with sulphuric acid.* A soln of 6-methoxyaurone epoxide (0·2 g) in conc. H_2SO_4 (10 ml) was kept at room temp for ½ hr and then poured onto a mixture of ice and water. The precipitate which separated was taken up in ether and the soln extracted with 5% Na_2CO_3aq. Treatment of the Na_2CO_3 extract with dil. HCl precipitated an acid which separated from MeOH in platelets, m.p. 202–203°. This m.p. depressed on admixture with a sample of either III (prepared as described below) or IV (m.p. 202–203° (lit.[8] m.p. 203°), λ(KBr) 6·0(broad)μ) but remained constant when mixed with 4-hydroxy-7-methoxy-3-phenylcoumarin.

6-Methoxy-2-phenylbenzofuran-3-carboxylic acid (III). A mixture of 2′-hydroxy-4′-methoxychalcone (5 g), 2N NaOH (100 ml), H_2O_2 (25 ml; 6%) and MeOH (100 ml) was kept at room temp for 3 days. The mixture was acidified and extracted with ether. The ethereal soln was washed with sat NaClaq and extracted with 5% Na_2CO_3 aq. Acidification of the latter extract gave *6-methoxy-2-phenylbenzofuran-3-carboxylic acid*, which crystallized from AcOH aq in yellow needles (0·3 g) m.p. 180–182°. 229, 318 mμ (log ε 4·05, 4·26), λ(KBr), 5·96, 6·02 μ. (Found: C, 71·3; H, 4·6. $C_{16}H_{12}O_4$ requires: C, 71·7; H, 4·5%.)

---

[9] J. Herzig and J. Pollak, *Ber. Dtsch. Chem. Ges.* **36**, 661 (1903).