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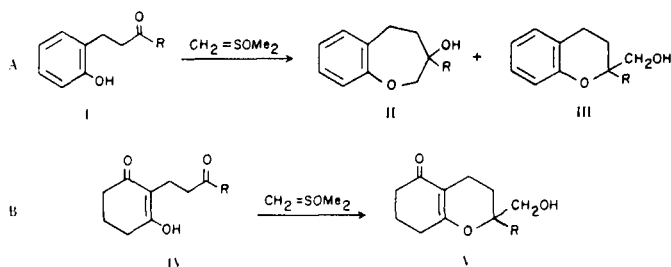
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2-Hydroxymethylchromans are the only products arising from the oxidation by *m*-chloroperbenzoic acid of the  $\beta$ -(*o*-hydroxyphenyl)olefins VI, obtained in turn from 2-(*o*-hydroxyphenyl)alkyl ketones (I) by the Wittig olefination with triphenylphosphonium methylide.

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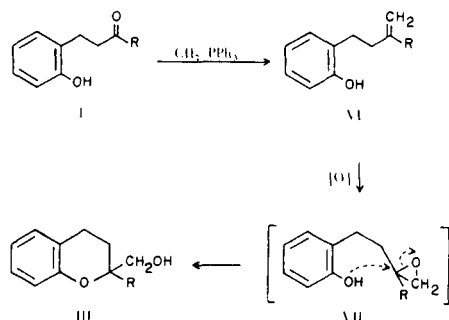
We have recently reported (1) that dimethylsulfonium or dimethyloxosulfonium methylides react with 2-(*o*-hydroxyphenyl)alkyl ketones (I) to give the corresponding 3-hydroxy-2,3,4,5-tetrahydro-1-benzooxepins (II) by the insertion of the methylene of the ylide between the carbonyl of the ketone and the phenolic oxygen. Only in certain cases, and in very low yields, are the isomeric 2-hydroxymethylchroman derivatives III isolable from this reaction. On the other hand, we have also noted (2) that the same reaction with 2-(3-oxoalkyl)cyclohexane-1,3-diones (IV) yields only the corresponding 2-hydroxymethylchroman derivatives (V). Our attempted oxidation of ring A of these derivatives (V) to the corresponding chromans (III) gave no useful results.

Scheme 1



This paper reports an alternative, efficient synthesis of 2-hydroxymethylchromans (III) starting from the readily obtainable 2-(*o*-hydroxyphenyl)alkyl ketones (I) (3). The reaction sequence involved is outlined in Scheme 2.

Scheme 2



The olefins (VI) are prepared from ketones (I) by reaction with triphenylphosphonium methylide in dimethylsulfide/tetrahydrofuran. The olefins are formed in good yield and easily separated from triphenylphosphine oxide

by chromatography on silica gel with hexane/ether (90/10) eluent. The crude product afforded by elimination of the solvent is reacted directly with *m*-chloroperbenzoic acid in chloroform at 0°. The olefin is converted quantitatively to epoxide VII. During the reaction and work-up, attack of the phenolic oxygen in epoxide VII on the quaternary epoxide carbon, through a six-membered transition state, gives 2-hydroxymethylchroman III.

There are some conflicting reports in the literature about the products arising from epoxides like VII when submitted to acid or base catalyzed ring opening. M. F. Grundon reported (4) two examples in which both acid and basic conditions brought to six-membered compounds; Grundon later reported (5) that basic promoted ring opening of the acetate of VIIa gave a one to one mixture of six- and seven-membered compounds.

Under our reaction conditions, not even a trace of the isomeric seven-membered heterocycle (II), which could arise by attack of the phenolic oxygen on the methylene carbon of the epoxide through a seven-membered transition state, is formed (6).

Epoxides VII, generated by this route, give chromans II exclusively also upon ring opening in alkaline medium (see Experimental). This fact strongly suggests that the same compounds when obtained as minor products from the reaction outlined in Scheme 1-A, do arise from the same intermediate epoxide generated from I and sulfonium methylides, while oxepins II, the major components from the same reaction, must arise from a different intermediate.

The structure of III was assigned mainly on the basis of nmr analysis. In the spectra of III, the two protons of the methylene group introduced into the molecule appear as a singlet or an AB system, depending on the substituent; in certain cases, coupling with the hydroxyl group can be seen even in deuteriochloroform. Acetylation causes the expected low field shift of both protons by approximately 0.5 ppm. Mass spectra of III show intense peaks at  $M^+$  and  $(M^+ - CH_3O)$   $m/e$  (7).

Yields and other chemico-physical data of olefins VI and 2-hydroxymethylchromans (III) are reported in Table I.

Table I

## Yields, Analytical and Spectral Data for Olefins VI and 2-Hydroxymethylchromans III

Compound	R	Yield % from I	$n_D^{20}$ or M.p., °C (solvent)	$^1\text{H Nmr}$ (deuteriochloroform), $\delta$ (ppm)			CH <sub>2</sub> -CH <sub>2</sub> (b)	M <sup>+</sup> (m/e)	Molecular Formula	Analyses Found (Calcd.) C% H%
				R	$\begin{array}{c} \text{H} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{H} \end{array}$	Ph-OH				
VIa	CH <sub>3</sub>	80	1.5296	1.78 s	4.76	5.00	2.32 2.65	162	C <sub>11</sub> H <sub>14</sub> O	81.5 8.7 (81.4) (8.7)
VIb	C <sub>2</sub> H <sub>5</sub>	78	1.5282	1.02 t, 2.06 q (e)	4.78	5.16	2.32 2.74	176	C <sub>12</sub> H <sub>16</sub> O	81.9 9.1 (81.8) (9.2)
VIc	(CH <sub>3</sub> ) <sub>3</sub> C	87	1.5238	1.06 s	4.84, 4.95	5.61	2.36 2.78	204	C <sub>14</sub> H <sub>20</sub> O	82.4 9.8 (82.3) (9.9)
VId	C <sub>6</sub> H <sub>5</sub>	97	1.5975	----	5.10, 5.31	5.72	2.80	224	C <sub>16</sub> H <sub>16</sub> O	85.9 7.0 (85.7) (7.2)
IIIa	CH <sub>3</sub>	81	1.5455	1.20 s	CH <sub>2</sub> -O	CH <sub>2</sub> OH	CH <sub>2</sub> -CH <sub>2</sub> -Ph (c)	M <sup>+</sup> , M <sup>+</sup> -CH <sub>3</sub> O	C <sub>11</sub> H <sub>14</sub> O <sub>2</sub>	74.4 7.9 (74.1) (7.9)
IIIb	C <sub>2</sub> H <sub>5</sub>	78	1.5271	0.87 t, 1.68 q (e)	3.55 d (d)	3.32	1.40-2.30, 2.60-2.86	178 147	C <sub>12</sub> H <sub>16</sub> O <sub>2</sub>	75.3 8.4 (75.0) (8.4)
IIIc	(CH <sub>3</sub> ) <sub>3</sub> C	75	39-40 (hexane)	1.01 s	3.70 s	2.26	1.65-2.00, 2.60-2.83	192 161	C <sub>14</sub> H <sub>20</sub> O <sub>2</sub>	76.1 9.1 (76.3) (9.2)
IIIId	C <sub>6</sub> H <sub>5</sub>	82	99 (benzene)	----	3.75, 3.84 (f)	2.10	1.60-2.18, 2.40-3.00	220 189	C <sub>16</sub> H <sub>16</sub> O <sub>2</sub>	80.2 6.6 (80.0) (6.7)

(a) Broad singlets for VIa and VIb, doublets ( $J = 1.5$  Hz) for VIc and VId. (b) Broad triplets. (c) Range for very complex multiplets. (d)  $J = 5.0$  Hz. (e)  $J = 7.0$  Hz. (f)  $J_{AB} = 11.5$  Hz.

## EXPERIMENTAL

Reaction of 2-(*o*-Hydroxyphenyl)ethyl Phenyl Ketone (Id) with Triphenylphosphonium Methylide.

A solution of methylsulphenyl carbanion was prepared following Corey (7) from sodium hydride (1.1 g., mineral oil dispersion - 80% sodium hydride, 0.033 mole) and dimethylsulfoxide (100 ml., RP C. Erba) in a three-necked round-bottomed flask under nitrogen by heating the mixture with mechanical stirring at 70-75° until the evolution of hydrogen ceased (about 30 minutes). The mixture was then cooled to -5°. Triphenylphosphonium iodide (12.2 g., 0.03 mole) was added in four portions and the mixture was stirred for an additional 15 minutes; 2-(*o*-hydroxyphenyl)ethyl phenyl ketone (Id) (4.1 g., 0.018 mole) in tetrahydrofuran (50 ml.) was added dropwise to the red ylide solution. Stirring was then continued for 15 minutes at -5° and for two more hours at room temperature. The reaction mixture was then poured into three times its volume of water, acidified with aqueous hydrochloric acid to pH 3-4, and extracted three times with chloroform. The combined extracts were washed three times with water, dried over anhydrous sodium sulfate and the solvent evaporated. The crude mixture of VI<sub>d</sub> and triphenylphosphine oxide was adsorbed on silica gel (50 g.) and poured into a chromatographic column. Elution with 90/10 hexane/ether gave, upon removal of the solvent 1-(2'-*o*-hydroxyphenyl)ethyl-1-phenyl ethylene (VI<sub>d</sub>) (3.9 g., 96.6% yield) as a pale yellow oil. The crude product was used in the next step with no further purification.

In the same way olefins VI<sub>a-c</sub> were prepared; these were also used in the crude state after elution from the column. Yields and spectroscopic data used for product identification are reported in Table I.

Reaction of 1-(2'-*o*-Hydroxyphenyl)ethyl-1-phenyl Ethylene (VI<sub>d</sub>) with *m*-Chloroperbenzoic Acid.

To a solution of olefin VI<sub>d</sub>, prepared as described above, in chloroform (1.1 g., 5.0 mmoles in 15 ml.) was added dropwise a solution of *m*-chloroperbenzoic acid in chloroform (1.1 g., 5.8 mmoles in 15 ml.) with stirring and cooling to 0°. The mixture was left at 0° for one hour and at room temperature for two additional hours, washed with aqueous sodium bicarbonate (three times with 10 ml.), and dried over sodium sulfate. Removal of the solvent at reduced pressure afforded a crude oil which crystallized on standing. Crystallization from benzene gave 2-hydroxymethyl-2-phenylchroman (III<sub>d</sub>) (yield, 0.89 g., 81.6%), m.p. 99°.

In the same way compounds III<sub>a-c</sub> were prepared. They were purified by silica gel chromatography using hexane containing 8% ethyl ether for their elution.

When *m*-chloroperbenzoic acid was added to solutions of olefins VI in chloroform or methylene chloride in the presence of

excess of sodium carbonate, under efficient mechanical stirring, compounds III were obtained in comparable yields.

Yields and spectroscopic data used for product identification are reported in Table I.

## 2-Acetoxyethyl-2-phenylchroman.

A solution of 2-hydroxymethyl-2-phenylchroman (III<sub>d</sub>) (0.5 g., 2.0 mmoles), acetic anhydride (5 ml.) and glacial acetic acid (3 ml.) was refluxed three hours. Alcohol (10 ml.) was added and the resulting solution was refluxed for five additional minutes. The residue after the removal of the solvent at reduced pressure was poured into ice-water (50 g.) and the pH adjusted to neutral. The mixture was extracted with chloroform (twice with 15 ml.); the combined extracts were dried over sodium sulfate and the solvent evaporated to give 2-acetoxyethyl-2-phenylchroman (yield, 0.54 g., 95%), m.p. 77° (from hexane); ir (nujol): 1735 and 1235 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 2.0 (s, CH<sub>3</sub>O), 2.16-2.76 (m, CH<sub>2</sub>-CH<sub>2</sub>), 4.36 (s, CH<sub>2</sub>O).

Anal. Calcd. for C<sub>18</sub>H<sub>18</sub>O<sub>3</sub>: C, 76.6; H, 6.4. Found: C, 76.7; H, 6.4.

## 2-Acetoxyethyl-2-methylchroman.

This compound was prepared by the previous procedure, yield 96%, oil, n<sub>D</sub><sup>20</sup> = 1.5212; ir (nujol): 1750, 1235 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 1.30 (s, CH<sub>3</sub>C); 1.60-2.10 (m, PhCH<sub>2</sub>-CH<sub>2</sub>), 2.05 (s, CH<sub>3</sub>CO), 2.76 (t, J = 7 Hz, CH<sub>2</sub>Ph), 4.08 and 4.18 (AB, J<sub>AB</sub> = 7.0 Hz, CH<sub>2</sub>O).

Anal. Calcd. for C<sub>13</sub>H<sub>16</sub>O<sub>3</sub>: C, 70.89; H, 7.3. Found: C, 70.7; H, 7.3.

## REFERENCES AND NOTES

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- (6) Glc analysis of the crude reaction products.
- (7) The fragmentation patterns of 2-hydroxymethylchromans (III) and of the isomeric 3-hydroxy-1-benzooxepins (II) will be the object of a detailed study.
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