

3-(*o*-Hydroxyphenyl)-3-phenylpropiophenone or 2,4-Diphenyl-2-chromanol?

GUST.-AD. HOLMBERG and JARL AXBERG

Institutet för organisk kemi, Åbo Akademi, Åbo, Finland

The constitution of 3-(*o*-hydroxyphenyl)-3-phenylpropiophenone has been definitely established.

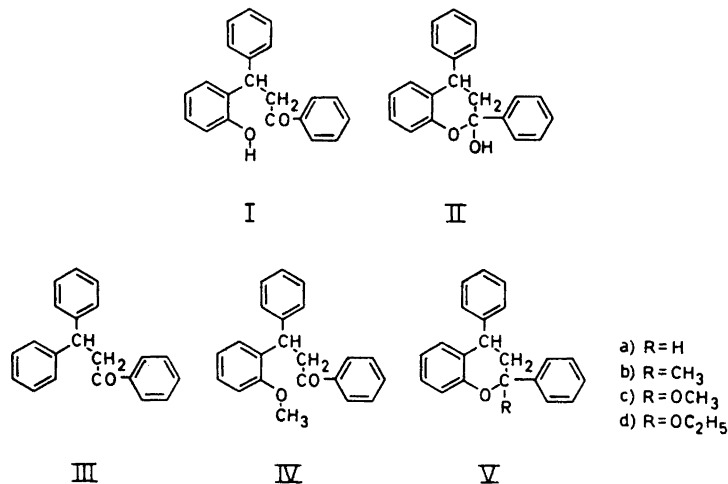
The question whether 3-(*o*-hydroxyphenyl)-3-phenylpropiophenone is an open ketone (I) or a cyclic semiketal, 2,4-diphenyl-2-chromanol (II), has not been definitely answered.

Lövenbein, Pongracz, and Spiess¹, who first prepared this compound, considered it cyclic because it was insoluble even in hot aqueous solutions of sodium or potassium hydroxides and no carbonyl derivative could be prepared. The fact that the substance was transformed to 2,4-diphenyl-2-chromene by boiling its solution in acetic acid was interpreted as evidence for the cyclic form. Geissman² established that the substance is readily soluble in methanolic potassium hydroxide and forms a semicarbazone and thus displays both phenolic and ketonic properties.

It was probable that the compound is the open ketone form, *e.g.* because Aulin-Erdtman, Björkman, Erdtman and Hägglund³ have by UV absorption measurements shown that 3-*o*-hydroxyphenylpropiophenone does not exist in the cyclic form, *i.e.* as 2-phenyl-2-chromanol. Geissman's arguments do not, however, exclude the possibility that the phenolic and ketonic characteristics result from the opening of the chroman ring during the reactions.

In order to obtain information about the constitution, the IR spectrum (Fig. 1) of the substance in a potassium bromide pellet was taken. The strong absorption in the carbonyl region at 1670 cm⁻¹ shows that the substance is a ketone at least in the solid state. This is supported by the fact that 3,3-diphenylpropiophenone (III) and 3-(*o*-methoxyphenyl)-3-phenylpropiophenone (IV) have a carbonyl band at the same frequency.

As the low solubility of 3-(*o*-hydroxyphenyl)-3-phenylpropiophenone in suitable solvents prevented an IR spectral study of the substance in solution, the UV spectrum (Fig. 3 b, continuous line) of the compound in ethanol solution was compared with the spectra of 3-(methoxyphenyl)-3-phenylpropiophenone (IV; Fig. 3 b, dotted line), 2,4-diphenylchroman (V a; Fig. 3 a), and



the two isomers of 2-methyl-2,4-diphenylchroman (V b). It was established that the spectra of 3-(*o*-hydroxyphenyl)-3-phenylpropiofenone and 3-(*o*-methoxyphenyl)-3-phenylpropiofenone almost coincided, whereas substances containing the chroman ring gave quite another type of spectrum. The curves of the latter substances have maxima and minima at the same wavelengths and in the intermediate regions they follow each other rather well. The differences in the logarithm of the molar absorptivity at the maxima and minima are collected in Table 1. The comparison clearly shows that the compound in question is a ketone even in solution, *i.e.* an equilibrium between the carbonyl and chroman form does not exist.

3-(*o*-Hydroxyphenyl)-3-phenylpropiofenone, however, reacts very easily as 2,4-diphenyl-2-chromanol. Addition of a relatively small quantity of hydrochloric acid to a warm alcoholic solution of the ketone leads to the formation of a ketal. In this way, 2,4-diphenyl-2-methoxychroman (V c) and 2,4-diphenyl-2-ethoxychroman (V d) were prepared. The constitution of the latter substance was established by taking the IR spectrum (Fig. 3), which exhibited no absorption bands due to carbonyl or hydroxyl groups. The UV spectrum (Fig. 2 c) of the same substance resembles those of the chromans, although the maxima and minima are displaced about 5 $m\mu$ towards shorter wavelengths.

Table 1. Values of the logarithm of the molar absorptivity ϵ at maxima and minima of UV absorption spectra of 2,4-diphenylchroman (V a) and the two isomers of 2-methyl-2,4-diphenylchroman (V b).

Compound	log ϵ at			
	245 $m\mu$ (min.)	277 $m\mu$ (max.)	281 $m\mu$ (min.)	283 $m\mu$ (max.)
V a	2.70	3.36	3.26	3.36
V b (m.p. 118–119°)	2.61	3.39	3.32	3.41
V b (m.p. 83.0–83.5°)	2.78	3.42	3.34	3.43

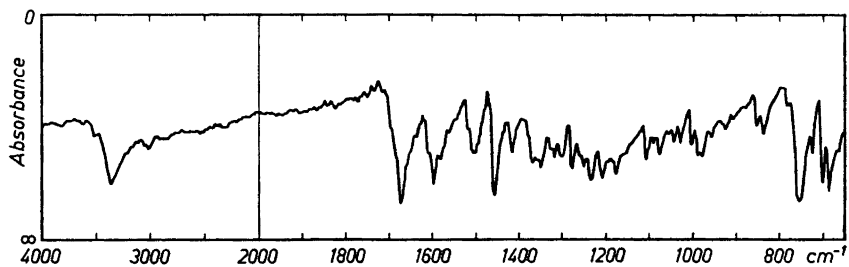


Fig. 1. IR absorption spectrum of 3-(*o*-hydroxyphenyl)-3-phenylpropiofenone in a potassium bromide pellet.

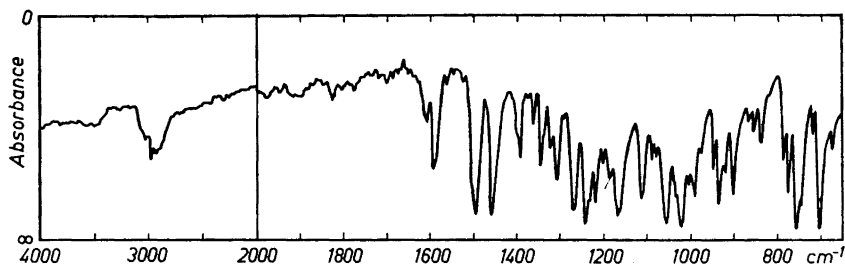


Fig. 2. IR absorption spectrum of 2-ethoxy-2,4-diphenylchroman in a potassium bromide pellet.

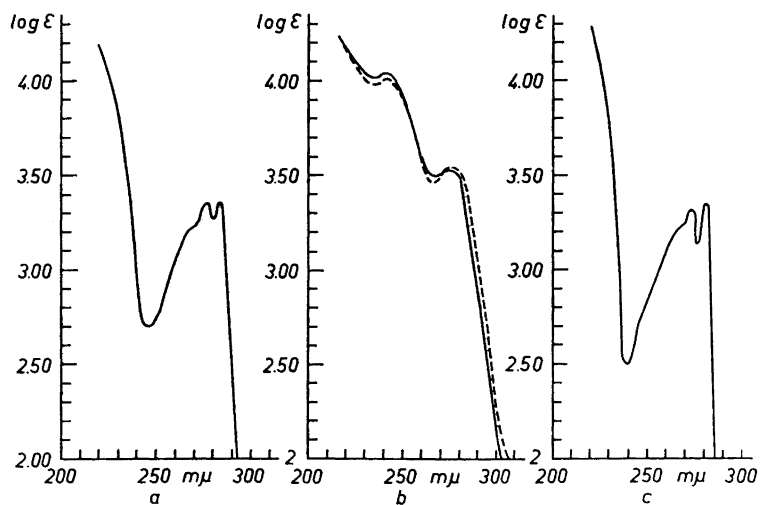


Fig. 3. UV absorption spectra of (a) 2,4-diphenylchroman, (b) 3-(*o*-hydroxyphenyl)-3-phenylpropiofenone (continuous line), and 3-(*o*-methoxyphenyl)-3-phenylpropiofenone (dotted line), and (c) 2-ethoxy-2,4-diphenylchroman.

3-(*o*-Hydroxyphenyl)-3-phenylpropiofenone was prepared according to Löwenbein, Pongracz, and Spiess¹ by addition of salicylideneacetophenone to a solution of phenylmagnesium bromide in ether. 3,3-Diphenylpropiofenone was synthesized by a modification of Kohler's original method from benzylideneacetophenone and phenylmagnesium bromide. 3-(*o*-Methoxyphenyl)-3-phenylpropiofenone was obtained in the same way from phenylmagnesium bromide and *o*-methoxybenzylideneacetophenone. The latter substance was prepared by condensation of acetophenone with *o*-methoxybenzaldehyde, for the preparation of which an improved and simplified method has been worked out. 2,4-Diphenylchroman was obtained by catalytic hydrogenation of 2,4-diphenylchromene. 2-Methyl-2,4-diphenylchroman was prepared by ring closure of crude 4-(*o*-hydroxyphenyl)-2,4-diphenyl-2-butanol, which was obtained by allowing 3-(*o*-hydroxyphenyl)-3-phenylpropiofenone to react with methylmagnesium iodide. Two isomers were isolated.

EXPERIMENTAL

3,3-Diphenylpropiofenone. A solution of benzylideneacetophenone (10.4 g) in dry ether (80 ml) was gradually added to the Grignard reagent prepared from bromobenzene (19.63 g), magnesium (3.00 g), and dry ether (60 ml). The mixture was gently refluxed for 15 min before the reaction products were decomposed with a mixture of hydrochloric acid (15 ml), water (60 ml), and ice (about 200 g). After addition of more ether and a small quantity of benzene in order to obtain a clear solution, the organic phase was separated and washed with water and potassium hydrogen carbonate solution. Most of the ether was evaporated and steam was led through the residue until the small quantity of biphenyl formed during the reactions had been removed. The residue solidified on cooling and was isolated by filtration. The solid was dissolved in hot ethanol (200 ml) and on cooling the solution 3,3-diphenylpropiofenone (10.17 g), m.p. 93.5–94.5°, crystallized. After recrystallization from ethanol, it melted at 94.5–95.0°.

3-(o-Methoxyphenyl)-3-phenylpropiofenone. *o*-Methoxybenzaldehyde was prepared in the following way. Salicylaldehyde (25 g; 21.4 ml) was dissolved in an equivalent quantity (46 ml) of an aqueous potassium hydroxide solution containing 0.25 g KOH/ml. Dimethyl sulphate (19.5 ml) was added and the mixture was agitated for half an hour on a shaking machine. More potassium hydroxide solution (23 ml) and dimethyl sulphate (10 ml) were added and the shaking was continued for half an hour. Potassium hydroxide (11.5 ml) and dimethyl sulphate (5 ml) were again added and the mixture was shaken for half an hour. Two batches were combined. Potassium hydroxide (40 ml) was added and the mixture heated on a boiling water bath for about half an hour to hydrolyze any excess of dimethyl sulphate. After the mixture had cooled, the organic phase was taken up into ether. The ether phase was washed with a small volume of very dilute hydrochloric acid. After drying the phase with sodium sulphate, the ether was evaporated and the residue distilled under reduced pressure. The yield of pure *o*-methoxybenzaldehyde b.p. 117.5–118.0°/14 mm, was 83.6% (43.65 g).

Acetophenone (15.12 g) and *o*-methoxybenzaldehyde (16.71 g) were mixed in a separatory funnel and a solution of sodium (2.86 g) in absolute ethanol (115 ml) was added to the mixture. After three hours, the oil that had formed was separated. On addition of water (10 ml), another quantity of the oil separated which was combined with the first one. The oil was shaken with a dilute hydrochloric acid solution and the organic material was taken up into ether. After separation and drying of the ether solution, the solvent was evaporated. When the residue was treated with ligroin containing a small amount of ether, the substance solidified. The *o*-methoxybenzylideneacetophenone thus obtained melted at 61.5–62.5°.

A solution of this *o*-methoxybenzylideneacetophenone (7.65 g) in dry ether (50 ml) was gradually added to a Grignard reagent prepared from bromobenzene (10.09 g), magnesium (1.54 g), and dry ether (50 ml). After the mixture had been gently refluxed for 15 min, it was cooled and the reaction products decomposed with a mixture of hydro-

chloric acid (10 ml), water (50 ml), and ice (200 g). When the substance that had separated was filtered and recrystallized from ethanol, pure 3-(*o*-methoxyphenyl)-3-phenylpropio-phenone (5.65 g), m.p. 123.5–124.0°, was obtained. (Found: C 83.75; H 6.37. Calc. for $C_{22}H_{20}O_2$: C 83.51; H 6.37.)

The phases in the filtrate obtained when the crude product was isolated were separated. The organic phase was washed with water and sodium hydrogen carbonate solution and dried with sodium sulphate. When the solvent was evaporated and the residue treated with ethanol, another sample (3.33 g) of the same substance was obtained, the total yield being 85.9 % of theory.

2,4-Diphenylchroman. 2,4-Diphenylchromene (4.90 g) prepared from 3-(*o*-hydroxyphenyl)-3-phenylpropio-phenone according to Löwenbein, Pongracz and Spiess¹ was dissolved in ethyl acetate (100 ml) and hydrogenated at room temperature and atmospheric pressure in the presence of "Pd-catalyst A"⁵ (2.00 g). When the theoretical amount of hydrogen had reacted, the catalyst was removed by centrifugation and the solvent evaporated under reduced pressure. The crystals remaining were treated with ethanol and recrystallized from acetic acid. The yield of 2,4-diphenylchroman, m.p. 144.5–145.5°, was nearly quantitative. (Found: C 88.22; H 6.36. Calc. for $C_{21}H_{18}O$: C 88.08; H 6.33.)

2-Methyl-2,4-diphenylchroman. 3-(*o*-Hydroxyphenyl)-3-phenylpropio-phenone (8.00 g) was gradually added to a Grignard reagent prepared from methyl iodide (9.47 g), magnesium (1.60 g), and dry ether (65 ml). The reaction mixture was gently warmed for half an hour before it was added to a mixture of ice (200 g) and ammonium chloride (25 g). After addition of more ether, the organic phase was separated and dried with sodium sulphate. The solvent was removed and the residue dissolved in acetic acid (50 ml). The temperature of the mixture was brought to the boiling point and a small quantity (10 drops) of sulphuric acid was added. The mixture was allowed to cool and next morning the solvent was evaporated under reduced pressure at room temperature. Water and ether were added to the residue and the organic phase was separated, washed with a dilute sodium hydroxide solution, and dried with sodium sulphate. The solvent was evaporated and the residue treated with hot ethanol. The substance that first separated was recrystallized twice from ethanol, giving the higher melting isomer of 2-methyl-2,4-diphenylchroman, m.p. 118–119°. (Found: C 88.00; H 7.00. Calc. for $C_{22}H_{20}O$: C 87.96; H 6.71.)

The lower melting isomer, which crystallized less rapidly from ethanol, was isolated by fractional recrystallization from the mother liquors. In the pure state it melted at 83.0–83.5°. (Found: C 88.08; H 6.98. Calc. for $C_{22}H_{20}O$: C 87.96; H 6.71.)

2,4-Diphenyl-2-methoxychroman. Hydrochloric acid (1.5 ml) was added to a hot solution of 3-(*o*-hydroxyphenyl)-3-phenylpropio-phenone (2.00 g) in methanol (50 ml). When the solution had cooled, white crystals of 2,4-diphenyl-2-methoxychromane were filtered. After recrystallization from methanol, the pure compound melted at 107.0–107.5°. (Found: C 83.71; H 6.33. Calc. for $C_{22}H_{20}O_2$: C 83.51; H 6.37.)

2,4-Diphenyl-2-ethoxychroman was obtained in the same way when ethanol was used instead of methanol. After recrystallization from ethanol, it melted at 125–126°. (Found: C 83.47; H 6.72. Calc. for $C_{23}H_{22}O_2$: C 83.60; H 6.71.)

The elementary analyses were carried out by Dr A. Bernhardt, Mühlheim. The IR spectra were taken by Mr B. C. Fogelberg, M.Sc., Centrallaboratorium Ab., Helsingfors, and the UV spectra by Mr B. Skrifvars, M.Sc., Institutet för analytisk och oorganisk kemi vid Åbo Akademi.

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