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The Reactions of β-Hydroxychalcones and 2-Acetoxy-1,3-diarylpropan-1,3-diones with Lead Tetraacetate

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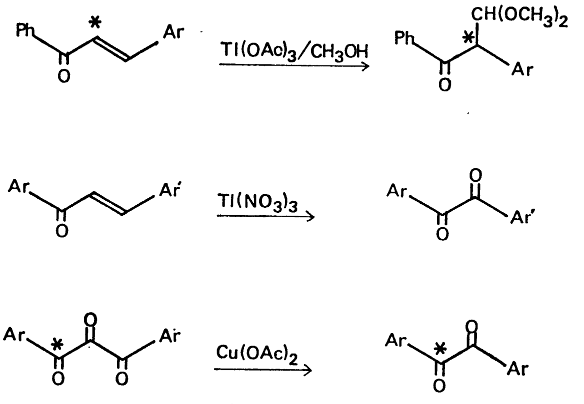
The reaction of β-hydroxychalcone with lead tetraacetate gave benzil. The reaction of 4,4′-dimethoxy-β-hydroxychalcone gave 2-acetoxy-1,3-di(*p*-methoxyphenyl)propan-1,3-dione and 4,4′-dimethoxybenzil. The reactions of 2-acetoxy-1,3-diarylpropan-1,3-diones yielded 2,2-diacetoxy-1,3-diarylpropan-1,3-diones and benzils respectively. The formation of the benzils from β-hydroxychalcones and 2-acetoxy-1,3-diarylpropan-1,3-diones has been shown to involve 1,2-aryl and 1,2-aroyl migration respectively by studies of the oxidations of ^{14}C-labelled compounds.

Carbonyl compounds react with lead tetraacetate to give α-acetoxy derivatives, and β-diketones also react to give mono- and diacetoxy compounds.[1] Our recent results on the reaction of chalcones with lead tetraacetate showed that a chalcone was oxidized to yield 2-acetoxy-1,3-diarylpropan-1,3-dione and 2,3-diacetoxy-1,3-diarylpropan-1-one.[2] This result differs from those of the oxidations of chalcones with thallium(III) acetate and with thallium(III) nitrate, which gave deoxybenzoin derivatives[3] and benzils[4] respectively (Scheme 1).



Scheme 1. Ar and Ar' refer to substituted phenyls.

A re-examination of our previous results revealed the presence of a benzil in the reaction mixture together with the acetates, suggesting that the dione could be rearranged and oxidized to the benzil.

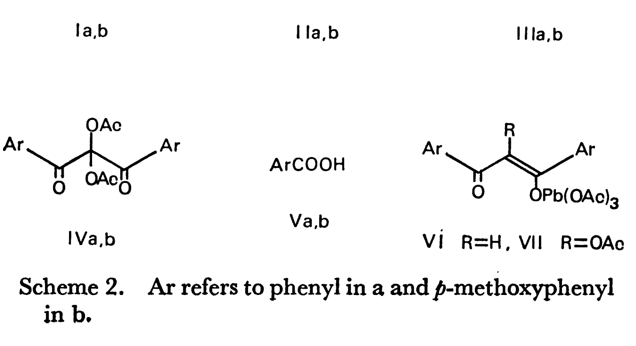
Two β-hydroxychalcones (Ia and Ib), which could be the precursors of the dione, and two 2-acetoxy-1,3-diarylpropan-1,3-diones (IIa and IIb) were prepared; the reactions of these compounds with lead tetraacetate were investigated in the hope of substantiating the rearrangement reaction.

When 4,4′-dimethoxy-β-hydroxychalcone (Ib) was oxidized with lead tetraacetate, three compounds (IIb (2%), IIIb (27%), and Vb (20%)) were obtained. The NMR spectrum of IIb ($C_{19}H_{18}O_6$; mp 96 °C) indicated the presence of two methoxy groups [δ 3.80 (s, 6H)], an acetoxy group [δ 2.30 (s, 3H)], a CH unit [δ 6.89 (s, 1H)], and two *para*-substituted phenyl groups [δ 6.91 (d, 4H) and δ 8.40 (d, 4H)]. The spectroscopic evidence suggested that the IIb has the structure of 2-acetoxy-1,3-di(*p*-methoxyphenyl)propan-1,3-dione. The structure of IIb was confirmed by the fact that the identical acetate was obtained from 2-bromo-1,3-di(*p*-methoxyphenyl)propan-1,3-dione by treating it with sodium acetate in boiling acetic acid. The NMR spectrum of IIIb showed the presence of two *p*-methoxyphenyl groups [δ 6.95 (d, 4H), δ 7.89 (d, 4H), and δ 3.85 (s, 6H)], indicating that IIIb has the structure of 4,4′-dimethoxybenzil. This was identified by comparing their IR spectrum with that of an authentic sample. Vb was shown to be anisic acid by a comparison of its melting point and its IR spectrum with those of an authentic specimen.

Similarly, the reaction of β-hydroxychalcone (Ia) with lead tetraacetate gave IIIa (20%) and Va (10%).

When 2-acetoxy-1,3-di(*p*-methoxyphenyl)propan-1,3-dione (IIb) was oxidized with lead tetraacetate, three compounds (IIIb (10%), IVb (4%), and Vb (11%)) were isolated. The NMR spectrum of IVb ($C_{21}H_{20}O_8$; mp 145—146 °C) indicated the presence of two acetoxy groups [δ 2.14 (s, 6H)], two methoxy groups [δ 3.81 (s, 6H)], and two *p*-substituted phenyls [δ 6.38 (d, 4H) and δ 8.12 (d, 4H)], suggesting that IVb has the structure of 2,2-diacetoxy-1,3-di(*p*-methoxyphenyl)propan-1,3-dione. IIIb and Vb were identified with authentic samples. The reaction of 2-acetoxy-1,3-diphenylpropan-1,3-dione (IIa) was also carried out, giving IIIa (19%), IVa (7%), and Va (6%).

In order to establish the nature of the skeletal rearrangement of the β-hydroxychalcones and the 2-acetoxy-1,3-diarylpropan-1,3-diones, the reactions were



Scheme 2. Ar refers to phenyl in a and *p*-methoxyphenyl in b.

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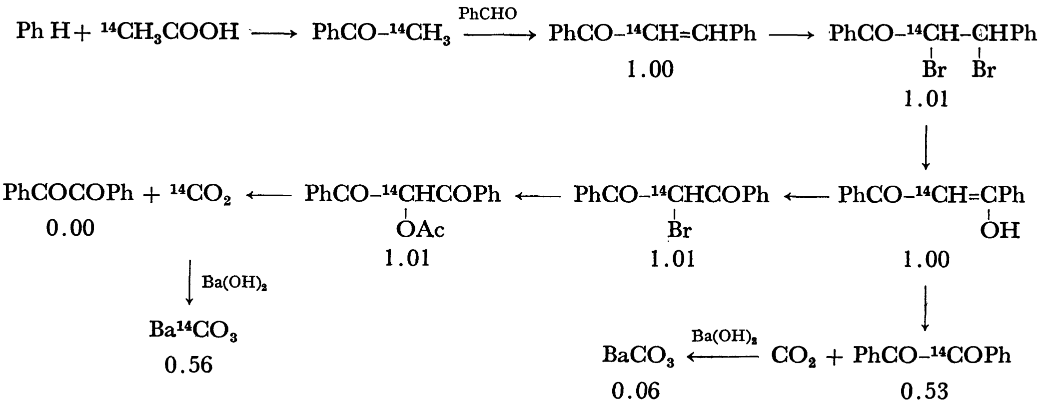

Scheme 3. Syntheses and rearrangement reactions of β-hydroxy[α-^{14}C]chalcone and 2-acetoxy-1,3-diphenyl[2-^{14}C]propan-1,3-dione (the figures under the formulae refer to the specific radioactivities of the compounds relative to chalcone).

repeated using β-hydroxy[α-^{14}C]chalcone and 2-acetoxy-1,3-diphenyl[2-^{14}C]propan-1,3-dione. When 2-acetoxy-1,3-diphenyl[2-^{14}C]propan-1,3-dione was oxidized with lead tetraacetate, inactive benzil (IIIa) and active carbon dioxide as barium carbonate were obtained (Scheme 3). The formation of the inactive IIIa from active IIa has shown clearly that a 1,2-aroyl migration took place and that then the central carbon was lost in the reaction. It has been shown that an aroyl migration is involved in the decarbonylation of 1,3-diarylpropan-1,2,3-trione with cupric acetate[5] (Scheme 1). However, evidence was not available in our case for formulating the reaction intermediate. There may be another pathway yielding carbon dioxide, since an incomplete retention of the radioactivity was observed (the specific radioactivity was 0.56 relative to that of chalcone).

On the other hand, the oxidation of Ia gave radioactive IIIa (the relative specific radioactivity was 0.53) and carbon dioxide (the relative specific radioactivity was 0.06 on barium carbonate). This may indicate that there are at least two pathways which equally lead to benzil: one must involve a 1,2-aryl migration in such a reaction intermediate as VI (Scheme 2), thus yielding the radioactive IIIa, while the other is one *via* IIa, giving the inactive IIIa.

The formation of IIb, IVa, and IVb can be explained by assuming enol intermediates (VI and VII) that are known to be involved in the reaction of ketones with lead tetraacetate.[1] Both IVa and IVb are stable and, therefore, "end products" in the oxidation. This conclusion was confirmed by a separate experiment.

Experimental

All the NMR spectra were recorded for the deuteriochloroform solution with a Hitachi R 24 NMR spectrometer, with tetramethylsilane as the internal reference. The IR spectra were recorded for the chloroform solution with a JASCO IRA-1 grating spectrometer, while the UV spectra were measured for the methanol solution with a Hitachi EPS-3T spectrophotometer. The melting points were determined with a Yanagimoto hot-stage apparatus and were uncorrected. The radioactivity measurements were recorded, for samples crystallized to a constant specific activity, with an Aloka liquid scintillation spectrometer. The scintillator consisted of 0.4% DPO and 0.1% POPOP (Dojindo Chemicals, Kumamoto) dissolved in toluene. Barium carbonate samples were suspended in a gel made up with 4% W/V CAB-O-SIL (Beckmann Instruments Inc,. U.S.A.). Sample counts were repeated twice; the maximum observed error was within ±0.5%.

β-Hydroxychalcone (Ia). β-Hydroxychalcone (Ia) (mp 78 °C) was prepared by the method described in the literature.[6]

4,4′-Dimethoxy-β-hydroxychalcone (Ib). 2-Bromo-1,3-di(*p*-methoxyphenyl)propan-1,3-dione[7] (1 g) was stirred with zinc powder (3 g) in acetic acid (30 ml) at room temperature for an hour. After the removal of insoluble materials by filtration, water (15 ml) was added to the filtrate. The precipitates were collected and recrystallized from methanol, giving Ib (580 mg, 74%); mp 112—113 °C (lit.[8] mp 114 °C).

*2-Acetoxy-1,3-di(*p*-methoxyphenyl)propan-1,3-dione (IIb).* A mixture of 2-bromo-1,3-di(*p*-methoxyphenyl)propan-1,3-dione (2.2 g), anhydrous sodium acetate (4.0 g), and acetic acid (50 ml) was heated under reflux for 5 hr. The reaction mixture was then poured into water and extracted with chloroform. The chloroform was evaporated *in vacuo*, and the residue was allowed to crystallize from ethanol, thus giving colourless prisms (1.3 g, 62%), mp 96 °C, ν_{max}: 1760 and 1690 cm^{-1}; λ_{max} (ε): 291 nm (24700). Found: C, 66.37; H, 5.48%. Calcd for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30%.

2-Acetoxy-1,3-diphenylpropan-1,3-dione (IIa). IIa was obtained in a 65% yield in the manner described above (mp 92—93 °C (lit,[9] mp 90—95 °C)).

Oxidation of β-Hydroxychalcones (Ia and Ib) and 2-Acetoxy-1,3-diarylpropan-1,3-diones (IIa and IIb). A mixture of the substrate (1 mmol), lead tetraacetate (2 mmol for Ia and Ib, and 1 mmol for IIa and IIb), and acetic acid (10 ml) was heated at 100 °C for 3 hr. After the removal of the acetic acid *in vacuo*, the residue was triturated with water and extracted with benzene. The benzene solution was then washed with aqueous sodium carbonate, from which two acids (Va and Vb) were obtained after acidification with concentrated hydrochloric acid. After the removal of the benzene *in vacuo*, the residue was separated on tlc. β-Hydroxychalcone (Ia) yielded IIIa (mp 95 °C (lit,[10] mp 95 °C)) and Va (mp 122 °C). 4,4′-Dimethoxy-β-hydroxychalcone (Ib) gave IIb (mp 96 °C), IIIb (mp 132 °C (lit,[11] mp 133 °C)), and Vb (mp 185 °C). The oxidation of IIa gave IIIa (mp 95 °C), Va (mp 122 °C), and 2,2-diacetoxy-1,3-diphenylpropan-1,3-dione (IVa) (mp 171—172 °C); ν_{max}: 1780 and 1710 cm^{-1}; λ_{max} (ε): 259 nm (22600); δ: 7.2—8.2 (m, 2×

C_6H_5) and 2.14 (s, 2×OAc) (Found: C, 67.13, H, 4.58%. Calcd for $C_{19}H_{16}O_6$: C, 67.06; H, 4.75%). IIb gave IIIb (mp 132 °C), Vb (mp 185 °C), and 2,2-diacetoxy-1,3-di(*p*-methoxyphenyl)propan-1,3-dione (IVb) (mp 145—146 °C); ν_{max}: 1770 and 1700 cm^{-1}; λ_{max} (ε): 299 nm (28100) (Found: C, 63.00; H, 5.07%. Calcd for $C_{21}H_{20}O_8$: C, 62.99; H, 5.04%).

[α-^{14}C]Chalcone. [Me-^{14}C]Acetophenone was prepared by the method described in the literature[3] using sodium [2-^{14}C]acetate (250 μCi, Radiochemical Centre, Amersham, England). [α-^{14}C]Chalcone (mp 55—57 °C) (specific radioactivity: 4.00 μCi/mmol) was prepared by the method described in "Organic Syntheses"[12] in a 76% yield.

[α-^{14}C]Chalcone Dibromide. To a solution of [α-^{14}C]-chalcone (5.0 g) dissolved in benzene (20 ml), we added bromine (3.84 g) at 0 °C. The precipitates (mp 147 °C; 7.25 g; 82%; specific radioactivity, 4.03 μCi/mmol) were used without further purification.

β-Hydroxy[α-^{14}C]chalcone. [α-^{14}C]Chalcone dibromide (7.10 g) was treated with sodium methoxide,[6] thus giving β-hydroxy[α-^{14}C]chalcone (mp 76—77 °C (ethanol); 2.67g; 62%; specific radioactivity, 4.00 μCi/mmol).

2-Bromo-1,3-diphenyl[2-^{14}C]propan-1,3-dione. β-Hydroxy-[α-^{14}C]chalcone (1.48 g) was treated with bromine (1.27 g) in chloroform (10 ml) at 0 °C for an hour to give 2-bromo-1,3-diphenyl[2-^{14}C]propan-1,3-dione (mp 88—89 °C (benzene–light petroleum); 1.56 g; 78%; specific radioactivity, 4.03 μCi/mmol).

2-Acetoxy-1,3-diphenyl[2-^{14}C]propan-1,3-dione. This compound was prepared from 2-bromo-1,3-diphenyl[2-^{14}C]-propan-1,3-dione in the manner described previously (mp 92—93 °C; 51%; specific radioactivity, 4.05 μCi/mmol).

Oxidations of Radioactive Ia and IIa. Radioactive Ia (224 mg) was oxidized with lead tetraacetate (1.33 g) in acetic acid (10 ml) under conditions identical with those described above to give radioactive IIIa (mp 95 °C; 14.2 mg; 7%; specific radioactivity, 2.11 μCi/mmol), Va (mp 122 °C; 6.5 mg; 5%; specific radioactivity, 0.03 μCi/mmol), and carbon dioxide, the latter being later converted to barium carbonate (6.8 mg; specific radioactivity, 0.23 μCi/mmol). The oxidation of the radioactive IIa (282 mg) with lead tetraacetate (444 mg) gave IIIa (mp 95 °C; 32 mg, 14%; specific radioactivity, 0.00 μCi/mmol) and carbon dioxide, which was trapped as barium carbonate (42 mg; 21%; specific radioactivity, 2.25 μCi/mmol).

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