617. *Alkyl–Oxygen Fission in Carboxylic Esters. Part XV.** 2 : 4-*Dimethoxydiphenylmethanol,* 1-(2 : 4-*Dimethoxyphenyl*)*ethanol, and* 1 : 2 : 2 : 2-*Tetra*-p-*methoxyphenylethanol.*

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The effect of the methoxy-groups on the reactivity of the alcohols named in the title has been examined.

In earlier papers of this series it was shown that conjugative electron-release by one or three *ortho-* and/or *para*-methoxyl substituents in phenylmethanols gives these compounds a high reactivity by unimolecular alkyl–oxygen heterolysis.[1] We now report a study of the reactivity of 2 : 4-dimethoxydiphenylmethanol, 1-(2 : 4-dimethoxyphenyl)ethanol, and 1 : 2 : 2 : 2-tetra-*p*-methoxyphenylethanol.

2 : 4-Dimethoxydiphenylmethanol was obtained as crystals, m. p. 49°, by hydrogenation of 2 : 4-dimethoxybenzophenone over Raney nickel, and by reaction of phenylmagnesium bromide with 2 : 4-dimethoxybenzaldehyde. Pope and Howard [2] claimed to have obtained this alcohol as a buff amorphous powder, decomposing above 130°, by the action of methyl iodide and alkali on the compound obtained by condensing resorcinol and benzaldehyde in the presence of alkali. Fabre [3] suggested that Pope and Howard's intermediate condensation product was a derivative of tetraphenylethylene. It appears, however, that this compound was 2 : 4-dihydroxydiphenylmethanol as they assumed but that this does not undergo straightforward methylation of the phenolic groups. Perhaps partial methylation of the aromatic ring takes place, as it is known to do in some polyhydroxyphenols.

1-(2 : 4-Dimethoxyphenyl)ethanol similarly was obtained by hydrogenation of 2 : 4-dimethoxyacetophenone, and by reaction of methylmagnesium iodide with 2 : 4-dimethoxybenzaldehyde.

Attempts were made to prepare the hydrogen phthalic and hydrogen succinic esters of these alcohols as a preliminary to their optical resolution. However, only neutral oils could be isolated, which were probably the dialkyl phthalates.

These two alcohols and their acetates undergo reactions which are characteristic of unimolecular alkyl–oxygen heterolysis with a facility between those of the corresponding 2- or 4-monomethoxy- and the 2 : 4 : 6-trimethoxy-compounds.[1] In analogy with the reaction of 2 : 4 : 6-trimethoxydiphenylmethanol,[4] 2 : 4-dimethoxydiphenylmethanol under acid conditions dismutates into 2 : 4 : 2′ : 4′-tetramethoxytriphenylmethane and benzaldehyde. This reaction probably proceeds by electrophilic substitution by the carbonium ion at the 1-position of un-ionised 2 : 4-dimethoxydiphenylmethanol.[4]

1 : 2 : 2 : 2-Tetraphenylethanol is fairly readily converted into its hydrogen phthalate.[5] In contrast, despite numerous attempts, it has not been possible to effect the combination of 1 : 2 : 2 : 2-tetra-*p*-methoxyphenylethanol with phthalic anhydride in the absence or presence of pyridine or triethylamine at temperatures up to 100°. From all experiments the alcohol was quantitatively recovered. Similar attempts with succinic anhydride were equally fruitless; no resolution of the alcohol through an acid ester could therefore be effected.

The decreased reactivity by the $B_{Ac}2$ mechanism on the introduction of a *p*-methoxy-group has been observed previously,[6] and derives from the inductive relay to the hydroxyl group of the increased electron density in the aromatic ring.[7]

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* Part XIV, *J.*, 1954, 3474.

[1] References are given by Davies and Kenyon, *Quart. Rev.*, 1955, **9**, 203, and by Dabby, Davies, Kenyon, and Lyons, *J.*, 1955, 3619.

[2] Pope and Howard, *J.*, 1910, **97**, 78.

[3] Fabre, *Ann. Chim.* (*France*), 1922, **18**, 82.

[4] Kenyon and Mason, *J.*, 1952, 4964.

[5] Ellison and Kenyon, *J.*, 1954, 779.

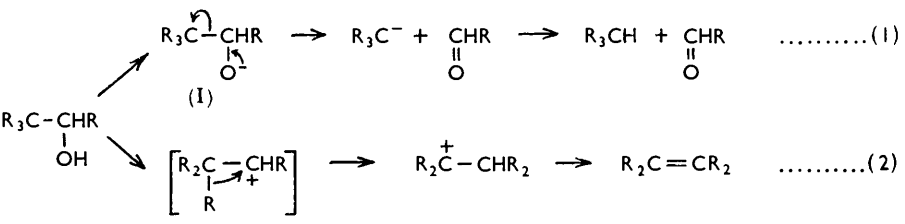
[6] Balfe, Kenyon, and Thain, *J.*, 1951, 386.

[7] Davies and Kenyon, *Quart. Rev.*, 1955, **9**, 203.

In marked contrast, acetic anhydride in pyridine solution converts the alcohol quantitatively into its acetate; acetic acid at room temperature is without action. This non-reaction with cyclic acid anhydrides but ready reaction with acyclic anhydrides has already been observed with di-*p*-methoxyphenylmethanol [8] and with 2 : 4 : 6-trimethoxydiphenylmethanol.[4]

A method which is used for the preparation of hydrogen phthalates of alcohols of low reactivity under the above conditions, or of high tendency to dehydration, consists in converting the alcohols into their potassio-derivatives which are then added to phthalic anhydride. In the present case this method also was unsuccessful since the potassio-derivative instead of reacting with the acid anhydride underwent scission, after addition of water, to tri-*p*-methoxyphenylmethane and *p*-anisaldehyde. The same products were obtained when the alcohol or its acetate was treated with alcoholic potassium hydroxide (cf. 1 : 2 : 2 : 2-tetraphenylethanol [8]), and probably result from the formation of the alkoxy-anion (I) which decomposes according to equation (1). This reaction is the reverse of the carbonyl addition reaction of metal triarylmethyls to aldehydes by which, for example, 1 : 2 : 2 : 2-tetraphenylethanol has been prepared.[9]

By an analogous reaction, *p*-methoxyphenyl tri-*p*-methoxyphenylmethyl ketone with alcoholic potassium hydroxide gives, less readily, tetra-*p*-methoxyphenylmethane and *p*-anisic acid *via* the anion $Ar_3C{\cdot}CAr(OH){\cdot}O^-$.



(R = *p*-methoxyphenyl)

1 : 2 : 2 : 2-Tetra-*p*-methoxyphenylethanol is not appreciably more reactive by alkyl–oxygen heterolysis than the corresponding unsubstituted alcohol.[5] It still does not react with boiling methyl, ethyl, or *tert.*-butyl alcohol over long periods, and does not give a sulphone with sodium toluene-*p*-sulphinate in aqueous acetone. Under acid conditions alkyl–oxygen heterolysis does occur, but is always accompanied by migration of an aryl-group and, as in the case of the unsubstituted alcohol, only the tetra-arylethylene (equation 2) is isolated.

EXPERIMENTAL

2 : 4-*Dimethoxybenzophenone.*—The Friedel–Crafts reaction between benzoyl chloride and 1 : 3-dimethoxybenzene in carbon disulphide solution in the presence of aluminium chloride or titanium tetrachloride gave 2 : 4-dimethoxybenzophenone as prisms (from aqueous alcohol), m. p. 82° (yield : $AlCl_3$ catalyst, 80%; $TiCl_4$ catalyst 86%). Pfeiffer and Loewe,[10] and König and Kostanecki,[11] report m. p. 82° and 87—88°, respectively.

2 : 4-*Dimethoxydiphenylmethanol.*—The above ketone (20 g.) in absolute ethanol (200 c.c.) containing Raney nickel (*ca.* 0·5 g.) was shaken in an atmosphere of hydrogen until absorption of gas was complete (12 hr.; 1990 c.c. at 20°. Calc., 1985 c.c.). 2 : 4-*Dimethoxydiphenylmethanol* was isolated as fine thread-like crystals (from light petroleum) (20 g.), m. p. 49° (Found : C, 73·4; H, 6·4. $C_{15}H_{16}O_3$ requires C, 73·7; H, 6·5%). The ketone was recovered after treatment with zinc dust and sodium hydroxide in ethanol for 6·5 hr. on the steam-bath.

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[8] Balfe, Kenyon, and Thain, *J.*, 1952, 790.
[9] Schlenk and Ochs, *Ber.*, 1916, **49**, 608.
[10] Pfeiffer and Loewe, *J. prakt. Chem.*, 1937, **147**, 293.
[11] König and Kostanecki, *Ber.*, 1906, **39**, 4027.

From the Grignard reaction between 2 : 4-dimethoxybenzaldehyde[12] (27 g.) and phenylmagnesium bromide (bromobenzene, 27 g.; magnesium, 4·5 g.), 2 : 4-dimethoxydiphenylmethanol (5 g.), m. p. 49°, was isolated and much of the aldehyde (20 g.), m. p. 71°, was recovered.

Pope and Howard's Reactions.—The reaction between resorcinol and benzaldehyde under Pope and Howard's conditions[2] gave a brown amorphous solid which darkened in air. It was readily soluble in aqueous sodium hydroxide and was reprecipitated on acidification; it darkened at 180° and softened and decomposed at about 200°. Attempts to methylate this supposed 2 : 4-dihydroxydiphenylmethanol with methyl iodide or methyl sulphate in the presence of potassium hydroxide gave a brown amorphous product which was insoluble in alkali, and darkened and decomposed above 180°. Pope and Howard report decomposition above 130°.

2 : 4-*Dimethoxydiphenylmethyl Acetate.*—2 : 4-Dimethoxydiphenylmethanol (1 g.), acetic anhydride (1 c.c.), and pyridine (2 c.c.) after 1 hr. at 100° yielded the *acetate*, m. p. 72—73° (from light petroleum) (Found : C, 71·1; H, 6·3. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%). The acetate, m. p. and mixed m. p. 73°, was also obtained in good yield when water was added to a solution of the alcohol (0·2 g.) in acetic acid (2 c.c.), which had been stored overnight.

Bis-2 : 4-*dimethoxydiphenylmethyl Ether.*—2 : 4-Dimethoxydiphenylmethanol was recovered after 6 hr. at 55°, or 1 hr. at 110°, but after 10 min. at 210° the alcohol (0·2 g.) yielded the *ether* (recrystallised from butanol once, and from aqueous acetone twice) (0·1 g.), m. p. 190° (Found : C, 76·3; H, 6·5. $C_{30}H_{30}O_5$ requires C, 76·1; H, 6·4%).

2 : 4-*Dimethoxydiphenylmethyl* p-*Tolyl Sulphone.*—After 2 hr. at room temperature a solution of the alcohol (0·24 g.) and sodium toluene-*p*-sulphinate (0·19 g.) in acetic acid (1 c.c.) was diluted with water, yielding the *sulphone*, prisms (from methanol) (0·3 g.), m. p. 137° (Found : C, 68·9; H, 5·8; S, 8·4. $C_{22}H_{22}O_4S$ requires C, 69·1; H, 5·8; S, 8·4%). A similar reaction mixture prepared from the acetate, next day yielded the same sulphone, m. p. and mixed m. p. 137°.

Alkylation of 1 : 3-*Dimethoxybenzene.*—A solution of the alcohol (0·1 g.) and 1 : 3-dimethoxybenzene (0·1 g.) in ethanol (2 c.c.) containing 5N-sulphuric acid (1 drop) was boiled for 5 min. After 1 hr. at room temperature, 2 : 4 : 2′ : 4′-tetramethoxytriphenylmethane was isolated as needles (recrystallised from ethanol) (0·1 g.), m. p. 124°. It was identified by its mixed m. p. (124°) with the product (m. p. 124°) which was isolated after 3 weeks from a solution of benzaldehyde (1·06 g.) and 1 : 3-dimethoxybenzene (2·76 g.) in ethanol (20 c.c.) containing 5N-sulphuric acid (2 drops). Kauffman and Kieser[13] report m. p. 122°; as they describe, it gives a bright orange solution in concentrated sulphuric acid.

Dismutation of the Alcohol under Acid Conditions.—A solution of 2 : 4-dimethoxydiphenylmethanol (0·5 g.) in ethanol (20 c.c.) containing 5N-sulphuric acid (2 drops) after 3 weeks was diluted with water, 2 : 4 : 2′ : 4′-tetramethoxytriphenylmethane, m. p. and mixed m. p. 124°, being precipitated. The mother-liquors yielded benzaldehyde 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 237°.

1-(2 : 4-*Dimethoxyphenyl*)*ethanol.*—The Grignard reaction between 2 : 4-dimethoxybenzaldehyde (23 g.) and methylmagnesium iodide (methyl iodide, 11 g.; magnesium, 4 g.) was carried out below 5°. 1-(2 : 4-*Dimethoxyphenyl*)*ethanol* (23 g., 90%) was isolated as needles, m. p. 44°; the m. p. was not raised when the product was recrystallised from ether–light petroleum [Found : C, 66·1; H, 7·6%; *M* (Rast), 183. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·7%; *M*, 182]. The same compound, m. p. and mixed m. p. 44°, was obtained in almost quantitative yield by the hydrogenation of 2 : 4-dimethoxyacetophenone in ethanol over Raney nickel. The ketone was recovered after its attempted reduction with aluminium *iso*propoxide or sodium and moist ether; reaction with sodium and alcohol, or zinc and sodium hydroxide, or aluminium amalgam and water, gave a resin.

This alcohol (2 g.), pyridine (5 c.c.), and acetic anhydride (5 c.c.), after storage overnight, were poured into iced water, yielding the acetate, b. p. 127°/2 mm.

Bis-1-(2 : 4-*dimethoxyphenyl*)*ethyl Ether.*—During one year the alcohol gradually liquefied, and then resolidified. Washing with light petroleum left needles (60%), m. p. 101—102°, which gave the *ether*, m. p. 110—111° after recrystallisation from ethanol (Found : C, 69·9; H, 7·6. $C_{20}H_{26}O_5$ requires C, 69·3; H, 7·5%). From the petroleum extract a liquid, b. p. 110°/1 mm., was recovered (5%) which decolorised bromine in chloroform, and was oxidised by alkaline

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[12] Dimroth and Zoeppritz, *Ber.*, 1902, **35**, 993.

[13] Kauffman and Kieser, *Ber.*, 1912, **45**, 2333.

potassium permanganate to 2 : 4-dimethoxybenzoic acid, m. p. 109 (Robinson and Venkataraman [14] report m. p. 109°). The liquid was therefore 2 : 4-dimethoxystyrene.

1-(2 : 4-*Dimethoxyphenyl*)*ethyl* p-*Tolyl Sulphone*.—A solution of the alcohol (0·45 g.) and sodium toluene-*p*-sulphinate (0·45 g.) in acetic acid (4 c.c.) was diluted next day with water, yielding the *sulphone* (recrystallised from methanol; 0·6 g.) as prisms, m. p. 135° (Found : S, 9·6. $C_{17}H_{20}O_4S$ requires S, 10·0%). By a similar procedure the acetate (0·22 g.) gave the same sulphone (0·20 g.), m. p. 135°.

Attempted Preparation of Acid Esters of 2 : 4-*Dimethoxydiphenylmethanol and* 1-(2 : 4-*Dimethoxyphenyl*)*ethanol*.—The alcohols were separately mixed with phthalic anhydride (1 mol.) and a slight excess of pyridine, diluted with benzene or dioxan, and heated at 40°, 50°, 60°, or 70° for 10 min. to 6 hr. The products were decomposed with ice and dilute hydrochloric acid, and were neutral oils. Similar results were obtained when succinic anhydride or 3-nitrophthalic anhydride were substituted for phthalic anhydride, and when a benzene solution of phthalic anhydride and the potassium salt of the alcohols was heated under reflux for 1—3 hr.

1 : 2 : 2 : 2-*Tetra*-p-*methoxyphenylethanol*.—The alcohol was prepared by two procedures: (*a*) By Bachman's method [15] modified in two respects. Instead of adding solid *p*-methoxyphenyl tri-*p*-methoxyphenyl ketone to ethylmagnesium bromide it was added as a solution–suspension in benzene, and heating of the resultant reaction mixture was omitted. This resulted in the yield of alcohol being increased from 60% to 88%. (*b*) By the interaction of tri-*p*-methoxyphenylacetaldehyde and *p*-methoxyphenylmagnesium bromide. Each procedure gave a very good yield of the required alcohol, prisms, m. p. and mixed m. p. 144—146°. The ketone was recovered quantitatively when attempts were made to reduce it with zinc dust and alkali or with aluminium *iso*propoxide.

The alcohol was oxidised with chromic oxide in acetic acid to regenerate the ketone (67%), and by potassium permanganate in acetic acid to give 4 : 4′-dimethoxybenzophenone. Oxidation with acetone and aluminium *tert.*-butoxide gave, surprisingly, tri-*p*-methoxyphenylethylene glycol (63%), m. p. and mixed m. p. 175—176°.

1 : 2 : 2 : 2-*Tetra*-p-*methoxyphenylethyl Acetate*.—A solution of the alcohol (0·47 g.) in pyridine (2 g.) and acetic anhydride (0·54 g.), heated at 90° for several hr., yielded the *acetate* (0·4 g.), prisms (from aqueous acetone), m. p. 144—145° (mixed with the original alcohol the m. p. was depressed by some 20°) (Found : C, 74·7; H, 6·3. $C_{32}H_{32}O_6$ requires C, 75·0; H, 6·3%)

Scission of the Alkoxy-anion.—(a) *From the acetate*. A solution of the acetate (1 g.) in ethanol (30 c.c.) containing N-potassium hydroxide (2 c.c.) was gently heated for 15 min. Next day crystals separated, and a further crop (total 0·57 g., 88%) on dilution : each had m. p. 51—52° either alone or mixed with tri-*p*-methoxyphenylmethane.[16] From the acidified filtrate the 2 : 4-dinitrophenylhydrazone of *p*-anisaldehyde was prepared, m. p. and mixed m. p. 253—254° (0·44 g., 69%).

(b) *From the alcohol*. By a similar procedure the alcohol yielded tri-*p*-methoxyphenylmethane (90%) and *p*-anisaldehyde (75%).

Non-reactivity of the Acetate.—(a) *With alcohols*. The acetate was recovered after being heated under reflux for many hours with methanol, ethanol, or *tert.*-butyl alcohol.

(b) *With sodium toluene*-p-*sulphinate*. Solutions of the acetate and sulphinate in aqueous acetone, with or without a few drops of acetic acid, after evaporation during several days yielded the unchanged acetate.

Rearrangement of the Carbonium Ion.—The alcohol was (*a*) heated with acetic acid on the steam-bath for 10 min., (*b*) left at room temperature for several hr. in acetic acid containing a trace of sulphuric acid, and (*c*) triturated with cold formic acid. Each experiment yielded tetra-*p*-methoxyphenylethylene almost quantitatively, m. p. and mixed m. p. 183—184°. The same product was obtained after 1 day from a solution of the acetate in acetone containing a trace of hydrochloric acid.

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[14] Robinson and Venkataraman, *J.*, 1929, 61.

[15] Bachman, *J. Amer. Chem. Soc.*, 1933, **55**, 3857.

[16] Baeyer and Villiger, *Ber.*, 1902, **35**, 1189.