

863. Reactions with Asymmetrical Diarylethylenes. Part IX.¹
A New Synthesis of 4,4'-Dialkoxy- and 4-Alkoxy-deoxybenzoins.

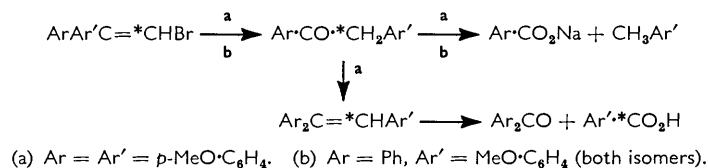
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4,4'-Dialkoxydeoxybenzoins were the main products when solutions of 1,1-di-*p*-alkoxyphenyl-2-bromoethylenes in ethylene glycol are boiled. The bromo- reacted more readily than the chloro-compounds, which also gave the deoxybenzoins. When the alkoxy-groups were replaced by chlorine, the reaction did not take place. Both isomers of 2-bromo-1-*p*-methoxyphenyl-1-phenylethylene gave 4-methoxybenzyl phenyl ketone provided that, in one case, the solution contained hydrogen bromide.

Using 1-bromo[2-¹⁴C]ethylenes led to presence of carbon-14 in the methylene group of the deoxybenzoin, which excludes an aldehyde-ketone rearrangement and mediation of a diarylacetylene.

Some new 4,4'-dialkoxydeoxybenzoins have been prepared by standard methods, and two geometrical isomers of 1,4-di-*p*-methoxyphenyl-1,4-diphenylbuta-1,3-diene isolated.

We have found that 1,1-di-*p*-alkoxyphenyl-2-bromo(or chloro)ethylenes are converted in boiling ethylene glycol into 4,4'-dialkoxydeoxybenzoins. The bromoethylenes reacted faster (within one minute) than the chloroethylenes, and from the former small quantities of 1,1-di-*p*-alkoxyphenylethylenes and 1,1,4,4-tetra-*p*-alkoxyphenylbuta-1,3-dienes were also obtained. The 2-bromo-1-*p*-methoxyphenyl-1-phenylethylene isomer of m. p. 52° gave 4-methoxybenzyl phenyl ketone, but an induction period (more than 5 min.) preceded initiation of the reaction and a trace of 1-*p*-methoxyphenyl-1-phenylethylene was also isolated. On the other hand, acidification of the ethylene glycol with hydrogen bromide was necessary to effect the reaction of the second isomer (m. p. 82°); 4-methoxybenzyl phenyl ketone was again obtained. The substituents preserved their positions, as in the rearrangement of 1,1-diaryl-2-halogenoethylenes into diarylacetylenes.¹ Using 2-bromo-1,1-di-*p*-methoxyphenyl[2-¹⁴C]ethylene or the two isomers of 2-bromo-1-*p*-methoxyphenyl-1-phenyl[2-¹⁴C]ethylene revealed inclusion of carbon-14 in the methylene group of the deoxybenzoin, as proved by the reactions shown in the Chart.



These findings exclude two possible mechanisms: (i) An aldehyde-ketone rearrangement of the type postulated² for the conversion³ of diphenyl- and di-*p*-tolyl-acetaldehyde into the corresponding deoxybenzoins, for hydrolysis of the vinyl bromide to an aldehyde followed by conversion into the deoxybenzoin would lead to inclusion of carbon-14 in the carbonyl instead of the methylene group. (ii) A rearrangement mediated by the formation of an acetylene, because 4-methoxyphenylphenylacetylene would have given¹ benzyl 4-methoxyphenyl ketone, m. p. 78°, whereas both isomers of 2-bromo-1-*p*-methoxyphenyl-1-phenylethylene gave 4-methoxybenzyl phenyl ketone of m. p. 98°, and because 2-bromo-1,1-di-*p*-methoxyphenyl[2-¹⁴C]ethylene was converted by sodium 2-hydroxyethoxide in

¹ Part VIII, *J.*, 1963, 4218.

² Ingold, "Structure and Mechanism in Organic Chemistry," Bell and Sons Ltd., London, 1953, p. 479; Collins, *Quart. Rev.*, 1960, **14**, 357.

³ Daniloff and Venus-Danilova, *Ber.*, 1926, **59**, 1032.

ethylene glycol into di-*p*-methoxyphenylacetylene.⁴ This acetylene was converted in boiling ethylene glycol containing hydrogen bromide into 4,4'-dimethoxydeoxybenzoin. The products of fusion of this ketone with sodium hydroxide, namely, methyl *p*-tolyl ether and sodium *p*-anisate revealed the presence of carbon-14 in both the carbonyl and the methylene groups (cf. above). However, the isotope tracer was not equally distributed amongst the methylene and carbonyl groups, indicating a probable partial isotope effect (however, Burr⁵ claimed that there was no isotope effect when water was added to diphenylacetylene labelled with carbon-14).

Conversion of the halogenoethylenes into deoxybenzoin did not take place in non-hydroxylated solvents such as phenetole (b. p. 170°) and methyl benzoate (b. p. 199°); comment on this finding and other possibilities for mechanism of the rearrangement are postponed.

2-Bromo-1,1-di-*p*-chlorophenylethylene failed to undergo the reaction (of. the effect of substituting chlorine for alkoxy in previously reported reactions^{1,6}), even when ethylene glycol was acidified with hydrogen bromide.

Reaction of the two isomers of 2-bromo-1-*p*-methoxyphenyl-1-phenylethylene and of 1-*p*-methoxyphenyl-1-phenylethylene in boiling acetic acid was very sluggish, but it was catalysed by hydrogen bromide, giving the two geometrical isomers of 1,4-di-*p*-methoxyphenyl-1,4-diphenylbuta-1,3-diene with m. p. 165° and 215°. The butadiene of m. p. 215° was previously reported⁷ as a by-product in the preparation of 1-*p*-methoxyphenyl-1-phenylvinylmagnesium bromide.

Some new di-*p*-alkoxydeoxybenzoin have been prepared by reduction of 4,4'-dialkoxybenzoin with alcoholic stannous chloride⁸ and by addition of water to diarylacetylenes in boiling ethylene glycol containing hydrobromic acid.

EXPERIMENTAL

Reactions of 1,1-Diaryl-2-halogenoethylenes in Ethylene Glycol.—(a) 1,1-Di-*p*-alkoxyphenyl-2-bromoethylenes. The procedure is exemplified as follows: (i) A solution of 2-bromo-1,1-di-*p*-methoxyphenylethylene (2 g.) in ethylene glycol (50 c.c.) was refluxed for 1 min., diluted with water, and extracted with ether. Ether was distilled off and the residue was treated with boiling alcohol, whereby a trace of 1,1,4,4-tetra-*p*-methoxyphenylbuta-1,3-diene separated first (m. p. and mixed m. p.⁹ 206—207°). On cooling, the alcoholic mother-liquors deposited a fraction, m. p. 135°, whence, on recrystallisation from alcohol, 1,1-di-*p*-methoxyphenylethylene (0.1 g.), m. p. and mixed m. p. 142°, separated. The fraction which crystallised on longer cooling gave, on recrystallisation from alcohol, 4,4'-dimethoxydeoxybenzoin (0.7 g.), m. p. and mixed m. p.¹⁰ 110—111° (Found: C, 74.8; H, 6.1. Calc. for C₁₆H₁₆O₃: C, 75.0; H, 6.2%).

Similarly were obtained the following: (ii) 2-Bromo-1,1-di-*p*-ethoxyphenyl-ethylene (2 g.) gave 1,1,4,4-tetra-*p*-ethoxyphenylbuta-1,3-diene (0.2 g.), m. p. and mixed m. p.⁹ 206° 1,1-di-*p*-ethoxyphenylethylene (0.1 g.), m. p. and mixed m. p. 142°, and 4,4'-diethoxydeoxybenzoin (0.45 g.), m. p. and mixed m. p.¹⁰ 103—104° (Found: C, 75.7; H, 6.9. Calc. for C₁₈H₂₀O₃: C, 76.1; H, 7.0%). (iii) 2-Bromo-1,1-di-*p*-propoxyphenylethylene (2.0 g.) gave 1,1,4,4-tetra-*p*-propoxyphenylbuta-1,3-diene (0.5 g.), m. p. and mixed m. p.⁹ 198°, 1,1-di-*p*-propoxyphenylethylene (0.12 g.) m. p. and mixed m. p. 134°, and 4,4'-di-*p*-propoxydeoxybenzoin (0.4 g.), m. p. 117—118° (from alcohol) (Found: C, 76.8; H, 7.5. C₂₀H₂₄O₃ requires C, 76.9; H, 7.7%). (iv) 2-Bromo-1,1-di-*p*-isopropoxyphenylethylene (2.0 g.) gave 1,1,4,4-tetra-*p*-isopropoxyphenylbuta-1,3-diene (0.4 g.), m. p. and mixed m. p.⁹ 186—187°, 4,4'-di-isopropoxydeoxybenzoin (0.4 g.) m. p. 114—115° (from alcohol) (Found: C, 76.6; H, 7.5%). (v) 2-Bromo-1,1-di-*p*-butoxyphenylethylene (2 g.) gave 1,1,4,4-tetra-*p*-butoxyphenylbuta-1,3-diene, m. p.

⁴ Tadros, Sakla, and Ishak, *J.*, 1958, 4210.

⁵ Burr, jun., *J. Amer. Chem. Soc.*, 1953, 75, 1990.

⁶ Tadros, *J.*, 1954, 2966.

⁷ Hurd and Webb, *J. Amer. Chem. Soc.*, 1927, 49, 546.

⁸ Apitzsch, *Ber.*, 1907, 40, 1803.

⁹ Tadros and Aziz, *J.*, 1951, 2553.

¹⁰ Wiechell, *Annalen*, 1894, 279, 337.

and mixed m. p.¹¹ 185—186°, 1,1-di-*p*-butoxyphenylethylene (0.12 g.), m. p. and mixed m. p. 125°, and 4,4'-*dibutoxydeoxybenzoin* (0.5 g.), m. p. 118—119° (from alcohol) (Found: C, 77.3; H, 8.0. C₂₂H₂₈O₃ requires C, 77.6; H, 8.2%).

(b) 1,1-Di-*p*-alkoxyphenyl-2-chloroethylenes.—Repeating experiment (a) with 2-chloro-1,1-di-*p*-methoxyphenylethylene (2.0 g.) and heating for 30 min. gave 4,4'-dimethoxydeoxybenzoin (0.7 g.), m. p. and mixed m. p. 110—111° (from alcohol). Similarly 2-chloro-1,1-di-*p*-ethoxyphenylethylene (2.0 g.) gave 4,4'-diethoxydeoxybenzoin (0.6 g.), m. p. and mixed m. p. 103—104°.

(c) *Isomers of 2-bromo-1-p-methoxyphenyl-1-phenylethylene*.¹² (i) 2-Bromo-1-*p*-methoxyphenyl-1-phenylethylene, m. p. 52° (2.0 g.) was refluxed in ethylene glycol (30 c.c.) for 15 min., cooled, diluted with water, and extracted with ether. The ether was removed and the residue was recrystallised from alcohol. 4-Methoxybenzyl phenyl ketone that separated had m. p. and mixed m. p.¹³ 98° (1.1 g.) (Found: C, 79.7; H, 6.1. Calc. for C₁₅H₁₄O₂: C, 79.6; H, 6.2%). 1-*p*-Methoxyphenyl-1-phenylethylene was separated by steam-distilling the alcoholic mother-liquors and, recrystallised from alcohol, had m. p. and mixed m. p. 75° (0.1 g.). (ii) The isomer of m. p. 82° (2.0 g.) was recovered unchanged after being boiled in ethylene glycol for 5 hr. (iii) Experiment (ii) was repeated with ethylene glycol (30 c.c.) containing hydrogen bromide (6.0%) and heating for 15 min.; 4-methoxybenzyl phenyl ketone (1.1 g.) was then obtained (m. p. and mixed m. p. 98°).

[¹⁴C]Methyl iodide.—Material from a 0.5 mc ampoule was diluted with 50 c.c. of normal methyl iodide.

1,1-Di-*p*-methoxyphenyl[2-¹⁴C]ethylene.—4,4'-Dimethoxybenzophenone (16.0 g.) was added to a Grignard reagent from magnesium (3.0 g.) and [¹⁴C]methyl iodide (21.3 g.) in ether (200 c.c.). Decomposition with aqueous ammonium chloride and extraction with ether gave 1,1-di-*p*-methoxyphenyl[2-¹⁴C]ethylene (13.5 g.), m. p. 142° (from alcohol).

2-Bromo-1,1-di-*p*-methoxyphenyl[2-¹⁴C]ethylene.—The product from bromine (6.4 g., 0.04 mole) and 1,1-di-*p*-methoxyphenyl[2-¹⁴C]ethylene (9.6 g., 0.04 mole) in ether (200 c.c.) was washed with 5% aqueous sodium hydroxide, followed by water, and after recovery was heated on the water-bath with sodium hydroxide (3 g.) in alcohol (60 c.c.) for 30 min. The mixture was diluted with water and cooled, and the precipitate was filtered off and washed with water. Recrystallisation from alcohol gave 2-bromo-1,1-di-*p*-methoxyphenyl[2-¹⁴C]ethylene (10.8 g.), m. p. 84°.

Experiments with Labelled 4,4'-Dimethoxydeoxybenzoin.—(i) *Preparations*. This was as for the unlabelled deoxybenzoin.

(ii) 1,1,2-Tri-*p*-methoxyphenyl[2-¹⁴C]ethylene. Labelled 4,4'-dimethoxydeoxybenzoin (3.2 g.) was added to the Grignard reagent¹⁴ from magnesium (0.6 g.) and *p*-bromoanisole (4.7 g.) in ether (50 c.c.), and the mixture was refluxed for 3 hr. with stirring. Stirring was further continued for 4 hr. at room temperature and the whole was set aside overnight. Decomposition with aqueous ammonium chloride and extraction with ether gave 1,1,2-tri-*p*-methoxyphenyl[2-¹⁴C]ethylene (3.1 g.), m. p. 100—101° (from alcohol).

1,1,2-Tri-*p*-methoxyphenyl[2-¹⁴C]ethylene (0.5 g.) and potassium permanganate (0.7 g.) in acetone (25 c.c.) were heated for 2 hr., then filtered while hot, and the manganese dioxide was washed with hot acetone. The acetone was distilled off and the residue boiled with water and collected. Recrystallisation from alcohol gave 4,4'-dimethoxybenzophenone (0.25 g.), m. p. and mixed m. p. 142—143° (Found: C, 74.1; H, 6.0. Calc. for C₁₅H₁₄O₃: C, 74.4; H, 5.8%), having radioactivity 0.0082 μc/mmmole. After being washed with acetone, the manganese dioxide was boiled with water and filtered off. The filtrate was acidified with dilute hydrochloric acid, and the precipitated *p*-anisic acid was recrystallised from dilute alcohol from which (0.11 g.) separated, with m. p. and mixed m. p. 179—180° (Found: C, 63.5; H, 4.8. Calc. for C₈H₈O₃: C, 63.2; H, 5.3%), and radioactivity 1.141 μc/mmmole.

(iii) *Fusion with sodium hydroxide*. Powdered, labelled 4,4'-dimethoxydeoxybenzoin (0.5 g.) was added to fused sodium hydroxide (2.0 g.) in a platinum crucible fitted with an air-condenser. The mixture was heated by a direct flame for a further 40 sec., left to cool, and treated with a little water, and the whole was extracted with ether. The aqueous solution was

¹¹ Tadros and Sakla, *J.*, 1957, 3210.

¹² Stoermer and Simon, *Ber.*, 1904, 37, 4163.

¹³ Oréckhoff and Tiffeneau, *Bull. Soc. chim. France*, 1925, 37, 1410.

¹⁴ Carter and Hey, *J.*, 1948, 150.

acidified with dilute hydrochloric acid, and the precipitated *p*-anisic acid was filtered off, washed with water, and recrystallised from dilute alcohol (m. p. and mixed m. p. 178—180°) (Found: C, 63·8; H, 5·2. Calc. for C₈H₈O₃: C, 63·2; H, 5·3%); its radioactivity was 0·030 μc/mmole. Evaporating the ethereal extract gave an oil that was steam-distilled, and the distillate was extracted with ether and dried (Na₂SO₄). Methyl *p*-[¹⁴C]tolyl ether was obtained on removal of the solvent and was dried (CaCl₂) (Found: C, 78·2; H, 8·8. Calc. for C₉H₁₀O: C, 78·7; H, 8·2%); it had radioactivity 0·8474 μc/mmole.

Degradation of 4,4'-Dimethoxydeoxybenzoin obtained from Di-p-methoxyphenyl[¹⁴C]acetylene.—(a) *Preparation of di-p-methoxyphenyl[¹⁴C]acetylene.* 2-Bromo-1,1-di-*p*-methoxyphenyl[2-¹⁴C]-ethylene (1·595 g.) and a solution of sodium (0·23 g.) in ethylene glycol (15 c.c.) were boiled for 3 hr. Di-*p*-methoxyphenyl[¹⁴C]acetylene (0·8 g.) was obtained with m. p. and mixed m. p. 142—143° (from alcohol).

(b) *Conversion of the acetylene into 4,4'-dimethoxydeoxybenzoin.* A solution of the acetylene (0·5 g.) in ethylene glycol (13·5 c.c.) containing *ca.* 48% hydrobromic acid (1 c.c.) was refluxed for 3 hr. 4,4'-Dimethoxy[¹⁴C]deoxybenzoin (0·35 g.) separated from alcohol with m. p. and mixed m. p. 110—111°.

(c) Fusion of the deoxybenzoin as above gave *p*-anisic acid, m. p. and mixed m. p. 178—180°, and methyl *p*-tolyl ether (oil), that had radioactivity 0·6263 and 0·3134 μc/mmole, respectively.

Experiments with Labelled 2-Bromo-1-p-methoxyphenyl-1-phenylethylenes.—Labelled 4-methoxybenzyl phenyl ketone was obtained as above from both isomers of 2-bromo-1-*p*-methoxyphenyl-1-phenyl[2-¹⁴C]ethylene. It separated from alcohol with m. p. and mixed m. p. 98°. Fusion with sodium hydroxide as above gave benzoic acid and methyl *p*-tolyl ether having radioactivity 0·00738 for benzoic acid and 0·348 μc/mmole for the ether from the isomer of m. p. 52°, and 0·00616 for benzoic acid and 0·306 μc/mmole for the ether from the isomer of m. p. 82°.

4,4'-Dialkoxydeoxybenzoin.—(1) Di-*p*-methoxyphenylacetylene (0·5 g.), ethylene glycol (13·5 c.c.), and *ca.* 48% hydrobromic acid (1·0 c.c.) were refluxed for 3 hr. The mixture was cooled, diluted with water, and filtered. The residue recrystallised from alcohol, giving 4,4'-dimethoxydeoxybenzoin (0·3 g.).

Similarly were obtained in good yield: 4,4'-diethoxy-, m. p. and mixed m. p. 103—104°, 4,4'-dipropoxy-, m. p. and mixed m. p. 117—118°, 4,4'-di-isopropoxy-, m. p. and mixed m. p. 114—115°, and 4,4'-dibutoxy-deoxybenzoin, m. p. and mixed m. p. 118—119°. The 4,4'-diisopropoxydeoxybenzoin was partly dealkylated and required realkylation.

(2) 4-Propoxybenzaldehyde (24·7 g.), alcohol (27 c.c.), and potassium cyanide (6·5 g.) in water (20 c.c.) were refluxed for 2 hr. on the water-bath (cf. Bössler¹⁵). More potassium cyanide (6·5 g.) was then added and heating continued for a further 3 hr. The mixture was cooled, and the precipitate was filtered off, washed with water, and recrystallised from alcohol from which 4,4'-dipropoxybenzoin (12·0 g.), m. p. 80—81°, separated (Found: C, 73·3; H, 7·2. C₂₀H₂₄O₄ requires C, 73·2; H, 7·3%). Similarly prepared were 4,4'-di-isopropoxy-, m. p. 112—113° (Found: C, 72·9; H, 7·1%), and 4,4'-dibutoxy-benzoin, m. p. 86—87° (Found: C, 74·3; H, 7·6. C₂₂H₂₈O₄ requires C, 74·2; H, 7·9%).

(3) 4,4'-Diethoxybenzoin¹⁶ (3·0 g., 0·01 mol.), stannous chloride dihydrate (3·358 g.), and concentrated hydrochloric acid (10 c.c.) in alcohol (25 c.c.) were heated for 3 hr. on the water-bath (cf. ref. 8). The mixture was diluted with cold water and the precipitate was filtered off, washed with water, and then recrystallised from alcohol, giving 4,4'-diethoxydeoxybenzoin (2·5 g.), m. p. and mixed m. p. 103—104°. Similarly were prepared: 4,4'-di-propoxy-, m. p. and mixed m. p. 117—118°, 4,4'-di-isopropoxy-, m. p. and mixed m. p. 114—115°, and 4,4'-dibutoxy-deoxybenzoin, m. p. and mixed m. p. 118—119°.

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¹⁵ Bössler, *Ber.*, 1881, **14**, 323; Mason and Dryfoos, *J.*, 1893, 1293.

¹⁶ Weissberger, Strasser, Mainz, and Schwarze, *Annalen*, 1930, **478**, 112.