173. *The Condensation of Deoxybenzoin with Aromatic Aldehydes and Ketones. Part II. Condensation of Substituted Deoxybenzoins with Substituted Acetophenones.*

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Deoxybenzoin condenses with acetophenone in alcoholic potassium hydroxide to form a colourless compound, m. p. 200°, of unknown constitution (Klingemann, *Annalen*, 1893, **275**, 81 ; Hill, J., 1935, 1115). The reaction is remarkable in that it occurs with the loss only of four hydrogen atoms :

$$2C_{14}H_{12}O + C_8H_8O \xrightarrow{-4H} C_{36}H_{28}O_3$$

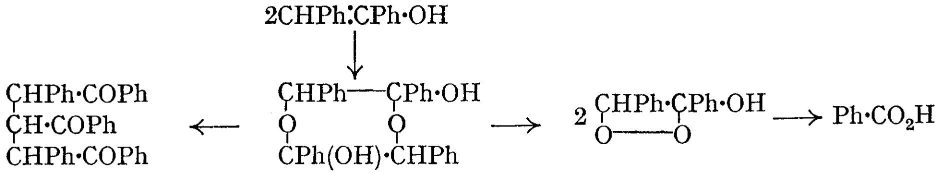
An examination of the reaction has now revealed the presence of a second, isomeric, product, m. p. 175°. Condensation also occurs between substituted compounds to give analogous products. 4-Methyl-, 4′-methyl-, 4-methoxy-, 4-chloro-, 4′-chloro-, and 4-bromodeoxybenzoin reacted similarly with acetophenone (although in the case of the last compound the amount available was too small to attempt a fractionation), as did also *p*-methyl-, *p*-methoxy-, *p*-bromo- and *p*-amino-acetophenone with deoxybenzoin.

The features of the reaction were the same in each case. Condensation was always slow (2—6 days) and access to the atmosphere was necessary. In closed flasks, little reaction occurred and in an atmosphere of hydrogen the deoxybenzoin was recovered unchanged. Where condensation occurred, there was a simultaneous formation of benzoic or substituted benzoic acid. It is apparent that the process is one of air oxidation, but that it does not involve the preliminary formation of benzoin was shown by the fact that, when this was substituted for the deoxybenzoin, reaction failed to occur.

The most acceptable explanation of the course of the reaction is the intermediate formation of an unstable oxide. Jenkins (*J. Amer. Chem. Soc.*, 1933, **55**, 1618; 1935, **57**, 2733) has found evidence for peroxide formation in ketones of type (I), which leads on standing in light and air to the formation of an aldehyde and an acid :

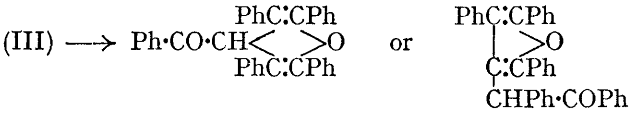
$$\text{(I.)}\quad R'\cdot CH_2\cdot COR \longrightarrow R'\cdot CH{:}C(OH)R \longrightarrow R'\cdot CHO + R\cdot CO_2H$$

If the peroxide formation is preceded by an oxide formation between two molecules of the deoxybenzoin acting in the enol-form (*i.e.*, by half oxidation), an explanation of the reaction with acetophenone offers itself. The necessary enol-form preliminary to the production of the oxide (II) will be predisposed by the presence of the alkali. The oxide, holding its oxygen loosely, will then break down either by reacting with the acetophenone present to give a *phenacylidenedideoxybenzoin* of type (III) or by further oxidation to the peroxide and thence to the acid. Such a phenacylidenedideoxybenzoin would be expected to exist as stereoisomers and in accordance with usage it is proposed to refer to the lower-melting isomer as the *iso*-derivative. Somewhat similar compounds have been obtained by other methods by Knoevenagel and Weissgerber (*Ber.*, 1893, **26**, 436) and by Kostanecki and Tambor (*Ber.*, 1896, **29**, 1495).



(III.) (II.)

The stereochemical relationship of the two isomers was demonstrated in the case of phenacylidenedideoxybenzoin and *iso*phenacylidenedideoxybenzoin by their conversion into the same cyclic derivative. By the action of sulphuric acid or dry hydrogen chloride, in glacial acetic acid both are dehydrated to a compound which may be either 4-benzoyl-2 : 3 : 5 : 6-tetraphenylpyran (IV) or 4-α-phenylphenacyl-2 : 3 : 5-triphenylfuran (V) (cf. Smith, J., 1890, **57**, 645; Dilthey, *J. pr. Chem.*, 1917, **95**, 107).



(IV.) (V.)

In view of the mechanism suggested above, an attempt was made to bring an oxide (dioxan) into reaction with acetophenone under similar conditions. A reaction occurred and the reaction mixture exhibited the characteristic features, but a product could not be isolated.

The *p*-substituted deoxybenzoins were examined in the hope that they would throw further light on the nature of the reaction, since the *p*-substituent will affect, at least, the degree of enolisation. Although the products were formed in differing yields from the various compounds employed, the differences were not such as to be accounted for so readily. The end products are the result of two competitive reactions (oxidation and condensation), both requiring the same initiation. Since the formation of the acids certainly results from a peroxide intermediate, the lack of regularity in the amount of products may be itself adduced as evidence in favour of the mechanism given. *p*-Methyl- and *p*-methoxy-acetophenone behaved like acetophenone, and *p*-bromoacetophenone gave the greatest yield of condensation product, owing no doubt to the activation of the methyl group. *p*-Aminoacetophenone, on the other hand, not only decreased the yield of condensation product, but also, apparently, inhibited the further oxidation to acid, since it provided the only case in which unchanged deoxybenzoin was recovered. In all the other cases the conversion either into acid or into condensation product was complete.

EXPERIMENTAL.

Phenacylidenedideoxybenzoin.—A solution of deoxybenzoin (5 g.) and acetophenone (3 g.) in alcohol (50 c.c.) was treated with alcoholic potassium hydroxide (2 g. in 100 c.c.) and kept at room temperature for 1 week; the yellow solution became red and, on scratching, a solid separated. This was filtered off, washed with alcohol, shaken with water to remove potassium benzoate, and crystallised from alcohol. Fractional crystallisation from alcohol yielded *phenacylidenedideoxybenzoin*, which, recrystallised from acetic acid, formed colourless needles, m. p. 199—200° (Found: C, 85·0; H, 5·5. $C_{36}H_{28}O_3$ requires C, 85·4; H, 5·5%). The alcoholic mother-liquors, after concentration, deposited a further quantity of crystals. These were repeatedly crystallised from alcohol and finally from acetic acid, which yielded colourless needles, m. p. 175°, of iso*phenacylidenedideoxybenzoin* (Found: C, 85·5; H, 6·0%).

Phenacylidenedi-(4-*methyldeoxybenzoin*).—4-Methyldeoxybenzoin and acetophenone in the same quantities and under the same conditions as above gave a solid, which was crystallised from alcohol. The product, alternately crystallised from amyl alcohol and ethyl alcohol, finally separated from the latter in colourless needles, m. p. 238—240° (Found: C, 84·5; H, 6·4. $C_{38}H_{32}O_3$ requires C, 85·0; H, 6·0%). The alcoholic mother-liquor from the first crystallisation was evaporated to one third of its volume, and the resulting solid crystallised several times from alcohol, colourless needles, m. p. 175—176°, of iso*phenacylidenedi*-(4-*methyldeoxybenzoin*) being obtained (Found: C, 85·4; H, 6·2%). The aqueous washings from the product yielded *p*-toluic acid on acidification.

Phenacylidenedi-(4′-*methyldeoxybenzoin*).—4′-Methyldeoxybenzoin (5 g.) and acetophenone (3 g.) were treated as described above and the solid which separated was freed from potassium benzoate and boiled with a large volume of alcohol. The insoluble material crystallised from acetic acid in colourless needles, m. p. 255—256° (Found: C, 84·8; H, 6·4. $C_{38}H_{32}O_3$ requires C, 85·0; H, 6·0%). The alcohol-soluble fraction was crystallised from alcohol many times and obtained in colourless needles, m. p. 240—241°, of iso*phenacylidenedi*-(4′-*methyldeoxybenzoin*) (Found: C, 84·9; H, 6·4%).

Phenacylidenedi-(4-*methoxydeoxybenzoin*).—Treatment of 4-methoxydeoxybenzoin (10 g.) and acetophenone (6 g.) as previously described yielded a solid product (0·8 g.), which on fractional crystallisation from alcohol was separated into *phenacylidenedi*-(4-*methoxydeoxybenzoin*), colourless needles, m. p. 225° (Found: C, 80·5; H, 5·9. $C_{38}H_{32}O_5$ requires C, 80·3; H, 5·6%), and iso*phenacylidenedi*-(4-*methoxydeoxybenzoin*), colourless needles, m. p. 190° (Found: C, 80·8; H, 5·9%). The mother-liquor and aqueous washings, when acidified, yielded anisic acid, m. p. 184°.

Phenacylidenedi-(4-*chlorodeoxybenzoin*).—The reaction between 4-chlorodeoxybenzoin (5 g.) and acetophenone (3 g.) under the usual conditions was complete after 10 days. The product (2·4 g.) was fractionated from alcohol; the *phenacylidenedi*-(4-*chlorodeoxybenzoin*) so separated, on further crystallisation from alcohol, formed colourless needles, m. p. 255—256° (Found: C, 74·7; H, 4·5; Cl, 12·1. $C_{36}H_{26}O_3Cl_2$ requires C, 74·9; H, 4·5; Cl, 12·3%). iso*Phenacylidenedi*-(4-*chlorodeoxybenzoin*), separated from the reaction product above, on further crystallisation from alcohol was obtained in colourless needles, m. p. 211—212° (Found: C, 74·85; H, 4·45; Cl, 12·2%). *p*-Chlorobenzoic acid, m. p. 236°, was obtained from the residual reaction mixture and the aqueous washings on acidification.

Phenacylidenedi-(4′-*chlorodeoxybenzoin*).—4′-Chlorodeoxybenzoin (5 g.) and acetophenone (3 g.) gave 2·3 g. of solid product, which was crystallised many times from alcohol and obtained in colourless needles, m. p. 248° (Found: C, 74·7; H, 4·7; Cl, 12·0. $C_{36}H_{26}O_3Cl_2$ requires C, 74·9; H, 4·5; Cl, 12·3%). The alcoholic mother-liquor yielded, on evaporation, a further crop of crystals. These were recrystallised from alcohol, iso*phenacylidenedi*-(4′-*chlorodeoxybenzoin*) being obtained in colourless needles, m. p. 234—235° (Found: C, 74·6; H, 4·6; Cl, 12·0%). The reaction mixture and aqueous washings yielded only benzoic acid and unchanged acetophenone.

4-*Bromodeoxybenzoin.*—Dry *p*-bromobenzamide (10 g.) was added in small portions with stirring to a solution of benzylmagnesium bromide (from 30 g. of benzyl bromide) in dry ether (125 c.c.), the mixture heated and stirred for 48 hours, and the product decomposed with ice-cold dilute sulphuric acid. The solid residue left after steam distillation was crystallised twice from alcohol; p-*bromodeoxybenzoin* separated in colourless needles (3·5 g.), m. p. 115° (Found: C, 61·1; H, 4·1; Br, 28·9. $C_{14}H_{11}OBr$ requires C, 61·1; H, 4·0; Br, 29·1%).

Phenacylidenedi-(4-bromodeoxybenzoin).—4-Bromodeoxybenzoin (2 g.) and acetophenone (1·5 g.), reacting in the usual way, gave a product (0·3 g.), which was washed with water and crystallised twice from alcohol. No attempt was made to fractionate it; m. p. 248° (Found: C, 65·4; H, 4·3. $C_{36}H_{26}O_3Br_2$ requires C, 64·9; H, 4·0%). The aqueous washings yielded *p*-bromobenzoic acid, m. p. 251°, on acidification.

p-*Methylphenacylidenedideoxybenzoin.*—Deoxybenzoin (3 g.) and methylacetophenone (2 g.) in alcohol (30 c.c.) were treated as in previous cases. The product which separated was crystallised first from acetone and finally from alcohol and obtained in colourless needles, m. p. 217° (Found: C, 85·8; H, 6·3. $C_{37}H_{30}O_3$ requires C, 85·1; H, 5·75%). The acetone mother-liquor deposited a second compound, which was crystallised from alcohol many times and obtained in long colourless needles, m. p. 196—197°, of iso-p-*methylphenacylidenedideoxybenzoin* (Found: C, 84·9; H, 5·8%).

iso-p-*Methoxyphenacylidenedideoxybenzoin.*—Deoxybenzoin (3 g.) and *p*-methoxyacetophenone (2 g.) gave after 2 days a solid, which was washed with alcohol and water successively and recrystallised from alcohol, forming colourless needles, m. p. 190—191° (Found: C, 82·4; H, 5·7; OMe, 5·5. $C_{37}H_{30}O_4$ requires C, 82·5; H, 5·6; OMe, 5·75%). The reaction mixture deposited a further quantity of solid on standing, which was treated as before. It crystallised from alcohol in colourless needles, m. p. 209°, of p-*methoxyphenacylidenedideoxybenzoin* (Found: C, 82·5; H, 5·75; OMe, 5·7%).

p-*Bromophenacylidenedideoxybenzoin.*—Deoxybenzoin (5 g.) and *p*-bromoacetophenone (3 g.) were treated with alcoholic potash in the usual manner. The solid which separated from the deep red solution overnight was filtered off and washed with alcohol and water. It was fractionated first from acetone and then from glacial acetic acid. The less soluble fraction was crystallised from alcohol and acetic acid successively and obtained in colourless crystals, m. p. 231° (Found: C, 73·1; H, 4·8; Br, 13·8. $C_{36}H_{27}O_3Br$ requires C, 73·6; H, 4·6; Br, 13·6%). The more soluble fraction crystallised from acetic acid in colourless needles, m. p. 213—215°, of iso-p-*bromophenacylidenedideoxybenzoin* (Found: C, 73·8; H, 4·6; Br, 13·8%).

p-*Aminophenacylidenedideoxybenzoin.*—Deoxybenzoin (5 g.) and *p*-aminoacetophenone (3 g.) were treated as already described. A small quantity of solid that separated after 4 days proved to be potassium benzoate. After further standing, the reaction mixture was treated with water and the small amount of solid product thus obtained was twice crystallised from alcohol. It was purified by alternate crystallisation from benzene and alcohol and obtained in colourless needles, m. p. 205° (Found: C, 82·8; H, 6·0. $C_{36}H_{29}O_3N$ requires C, 82·6; H, 5·6%). The alcoholic mother-liquors yielded deoxybenzoin on concentration.

Dehydration of Isomeric Phenacylidenedideoxybenzoins.—(a) Phenacylidenedideoxybenzoin (0·5 g.), suspended in glacial acetic acid (8 c.c.), was treated with a stream of hydrogen chloride until all the solid had dissolved (5 mins.). The stream was continued for a further 15 minutes, and the solution was kept for 12 hours before being poured into water. The cream-coloured precipitate was crystallised first from dilute alcohol and finally from glacial acetic acid, forming colourless needles, m. p. 118—119° (Found: C, 88·3; H, 5·3. $C_{36}H_{26}O_2$ requires C, 88·2; H, 5·3%).

(b) Phenacylidenedideoxybenzoin (0·5 g.) in glacial acetic acid (20 c.c.) was kept with concentrated sulphuric acid (4 c.c.) for 24 hours. The solution was then poured into water and treated as in (a), yielding the same product.

Treatment of the *iso*-derivative by either of these methods resulted in the formation of the same compound.

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