365. *Chalkones. The Condensation of Aromatic Aldehydes with Resacetophenone.*

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Previous statements that resacetophenone does not react with benzaldehyde and protocatechualdehyde in presence of alkali to yield the corresponding chalkones, 2 : 4-dihydroxyphenyl styryl ketone and butein respectively, are incorrect. The use of dilute alkali solution provides a convenient method for transforming these chalkones into the corresponding hydroxyflavanones.

ELLISON (J., 1927, 1720) gives m. p. 133—134° for 2 : 4-dihydroxyphenyl styryl ketone, obtained together with the isomeric 7-hydroxyflavanone (m. p. 189°) from resacetophenone and benzaldehyde in aqueous methyl-alcoholic solution, and reports that he was unable to prepare it from cinnamic acid and resorcinol in presence of zinc chloride by the method of Bargellini and Marantonio (*Atti R. Accad. Lincei*, 1908, **17**, 119), who record m. p. 175°. Shinoda and Sato (*J. Pharm. Soc. Japan*, 1928, **48**, 109) state that the preparation of polyhydroxychalkones from hydroxyacetophenones and aldehydes is beset with difficulty, and prefer to condense polyhydroxyphenols with cinnamoyl chlorides under the influence of aluminium chloride: 2 : 4-dihydroxyphenyl styryl ketone thus prepared had m. p. 151°. Mahal, Rai, and Venkataraman (J., 1935, 866) remark that resacetophenone does not react with benzaldehyde in presence of alkali to yield the chalkone; they obtained it (m. p. 151°) by debenzylation of 2-hydroxy-4-benzyloxyphenyl styryl ketone.

In view of these discrepancies we have re-examined the condensation of benzaldehyde with resacetophenone. Under Ellison's conditions 7-hydroxyflavanone (m. p. 189°) can be prepared in poor yield; 2 : 4-dihydroxyphenyl styryl ketone (m. p. 150°) can be obtained from resacetophenone and benzaldehyde by using excess of alkali at room temperature. Treatment of the chalkone with dilute sodium hydroxide solution (cf. Löwenbein, *Ber.*, 1924, **57**, 1515) then gives the flavanone in satisfactory yield.

Mahal, Rai, and Venkataraman (*loc. cit.*) obtained 7-benzyloxyflavanone (m. p. 102—104°) from 2-hydroxy-4-benzyloxyphenyl styryl ketone by treatment with phosphoric oxide in alcohol; we find, however, that a product, m. p. 126°, is obtained from the chalkone when dilute sodium hydroxide solution is used (Löwenbein, *loc. cit.*). Benzylation of 7-hydroxyflavanone gives the same product (m. p. 125—126°), which regenerates 7-hydroxyflavanone on debenzylation.

Shinoda, Sato, and Kawagoe (*J. Pharm. Soc. Japan*, 1929, **49**, 123) state that they were unable to repeat Göschke and Tambor's synthesis (*Ber.*, 1911, **44**, 3503) of butein by condensing protocatechualdehyde with resacetophenone in alcoholic alkali. We have, however, obtained the tetrahydroxychalkone from these components in alcoholic alkali by a suitable choice of conditions. Butin can be conveniently obtained from butein by treatment with dilute sodium hydroxide solution.

It is hoped to examine the possibility of the synthesis from hydroxyacetophenones and aldehydes of other hydroxy-chalkones and -flavanones.

EXPERIMENTAL.

2 : 4-*Dihydroxyphenyl Styryl Ketone from Benzaldehyde and Resacetophenone.*—A mixture of resacetophenone (5 g.), benzaldehyde (3·5 g.), alcohol (20 c.c.), and potassium hydroxide solution (75 g. in 100 c.c. of water) which had been kept for 12 hours at room temperature, diluted with water, and extracted with ether to remove unchanged benzaldehyde, gave on acidification with dilute hydrochloric acid an oil, which solidified in the refrigerator after 4 days. The dried solid (2·8 g.) crystallised from dilute alcohol and toluene (charcoal) in yellow needles, m. p. 150°, which gave a dark reddish-brown colour with alcoholic ferric chloride (Found : C, 75·0; H, 5·1. Calc. for $C_{15}H_{12}O_3$: C, 75·0; H, 5·0%).

7-*Hydroxyflavanone.*—(a) *From resacetophenone and benzaldehyde.* By Ellison's method (*loc. cit.*) the flavanone was obtained in poor yield as colourless needles, m. p. 189—190°, which gave no coloration with alcoholic ferric chloride (Found : C, 75·2; H, 5·1. Calc. for $C_{15}H_{12}O_3$: C, 75·0; H, 5·0%).

(b) *From* 2 : 4-*dihydroxyphenyl styryl ketone.* A mixture of the chalkone (1 g.) in alcohol (5 c.c.) and aqueous sodium hydroxide (15 c.c. of 1·5%) was heated under reflux for ½ hour, kept for 12 hours, diluted with water, and acidified with dilute acetic acid. The resulting precipitate separated from toluene (charcoal) in white needles (0·6 g.) giving no colour with alcoholic ferric chloride : m. p. and mixed m. p. with the product from (a) 189—190°.

(c) *From* 2-*hydroxy*-4-*benzyloxyphenyl styryl ketone.* The precipitate obtained on acidifying a mixture of the 4-benzyloxychalkone (Mahal, Rai, and Venkataraman, *loc. cit.*) (4 g.), alcohol (50 c.c.), and aqueous sodium hydroxide (60 c.c. of 1·5%) which had been heated under reflux for ½ hour and kept for 12 hours, gave on repeated crystallisation from alcohol (charcoal) 7-benzyloxyflavanone (2 g.), m. p. 126° (Found : C, 79·7; H, 5·5. Calc. for $C_{22}H_{18}O_3$: C, 79·8; H, 5·4%). A mixture of this (0·2 g.), glacial acetic acid (10 c.c.), and concentrated hydrochloric acid (15 c.c.) was heated under reflux for 30 minutes and diluted with water. The resulting precipitate separated from alcohol in white needles giving no colour with alcoholic ferric chloride and having m. p. and mixed m. p. with the product obtained from (a) 188—189°; the acetyl derivative had m. p. 98° (Ellison, *loc. cit.*, gives m. p. 98°).

Benzylation of 7-*Hydroxyflavanone.*—A mixture of 7-hydroxyflavanone (0·6 g.), benzyl chloride (3 g.), fused potassium carbonate (2 g.), and dry acetone (5 c.c.) was heated under reflux for 12 hours, the solvent evaporated, and the residue steam-distilled to remove the excess of benzyl chloride. The residual oil solidified overnight and crystallised first from alcohol and then from ether in white plates (0·15 g.), m. p. 124—125°, and 126° when mixed with the product from (c).

Condensation of Protocatechualdehyde with Resacetophenone: Preparation of Butein.—Potassium hydroxide solution (50 g. in 35 c.c. of water) was slowly added to a solution of protocatechualdehyde (5 g.) and resacetophenone (5·5 g.) in alcohol (7 c.c.) and the red mixture was heated at 100° for 10 minutes and kept out of contact with air for 12 hours. It was then diluted with an equal volume of water and acidified, with cooling, with dilute hydrochloric acid. The resulting precipitate (1·8 g.), crystallised from alcohol, had m. p. 212—213° and gave a dark purple colour with ferric chloride; the acetyl derivative had m. p. 128—129° (lit.: 210°, 213—215°; 129—131°).

Preparation of Butin.—A mixture of 1·5% sodium hydroxide solution (10 c.c.) and butein (1 g.) in alcohol (3 c.c.) which had been heated under reflux for ½ hour and kept at room temperature for 12 hours was diluted with water and acidified with dilute acetic acid. The yellow precipitate (0·5 g.) which slowly separated crystallised from water containing alcohol in needles and from water in plates. After removal of water of crystallisation by drying under reduced pressure at 130°, it had m. p. 224—226°. It gave no violet coloration with alcoholic ferric chloride; the acetyl derivative had m. p. 122—125° (lit.: 221°, 224—226°; 123—125°).

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