

276. *Internuclear Cyclisation. Part IV.* The Preparation of o-Amino- α -benzylcinnamic Acid.*

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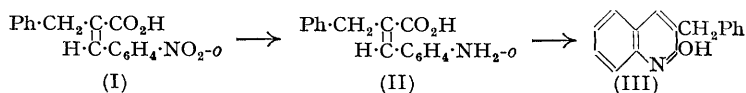
o-Amino- α -benzylcinnamic acid, prepared by the action of *o*-nitrobenzaldehyde on β -phenylpropionic acid and subsequent reduction, readily underwent cyclodehydration to give 3-benzylcarbostyryl.

THE most familiar examples of internuclear cyclisation are to be found in the Pschorr phenanthrene synthesis, in which the formation of the new internuclear bond results in the creation of a six-membered ring. In addition, there are many closely related reactions in which a new five-membered ring is formed, as in the synthesis of fluorene, fluorenone, dibenzofuran, dibenzothiophen, and carbazole derivatives (see Saunders, "The Aromatic Diazo Compounds," London, 1949, p. 258—265), by reactions which involve diazotisation and the complete elimination of the nitrogen atoms. We were therefore interested in whether analogous reactions could be applied to the formation of a new seven-membered ring, and in the first instance we considered the synthesis of a dibenzocycloheptatriene. An unsuccessful attempt to synthesise a dibenzocyclooctatetraene on similar lines has been reported by Bachman and Hoaglin (*J. Org. Chem.*, 1943, **8**, 300).

In an attempt to follow as closely as possible the established Pschorr phenanthrene synthesis attention was directed to the preparation of *o*-amino- α -benzylcinnamic acid and an examination of its properties, although it was recognised that this method of approach presented a number of special difficulties. In the first place it might not be possible to control the stereochemical configuration of the intermediate *o*-amino- α -benzylcinnamic acid in such a way that the two aromatic rings are in the *cis*-configuration, as in *o*-amino- α -phenylcinnamic acid, and secondly it is clear from scale models that the nuclear positions between which the new bond is to be formed are much less favourably placed even in the required *cis*-configuration than they are in the phenanthrene synthesis. Again, the preparative methods for α -benzylcinnamic acids are known to be much less satisfactory than the corresponding methods for α -phenylcinnamic acids because of the comparatively low reactivity of β -phenylpropionic acid in the Perkin reaction (cf. Rupe and Häussler, *Annalen*, 1913, **395**, 106; Shoppee, *J.*, 1930, 968). The α -benzylcinnamic acids also contain a three-carbon tautomeric system.

* Part III, preceding paper.

When *o*-nitrobenzaldehyde was heated with β -phenylpropionic acid and acetic anhydride in the presence of litharge (cf. Kuhn and Winterstein, *Helv. Chim. Acta*, 1928, **11**, 87) the acidic product consisted mainly of unchanged β -phenylpropionic acid and *o*-nitrocinnamic acid, but in addition α -benzyl-*o*-nitrocinnamic acid (I) was obtained in small yield. In an attempt to eliminate the formation of *o*-nitrocinnamic acid the acetic anhydride was replaced by β -phenylpropionic anhydride, but in this instance the acidic product appeared to consist solely of β -phenylpropionic acid. Reduction of α -benzyl-*o*-nitrocinnamic acid (I) with ammonia and ferrous sulphate or with ammonium sulphide gave *o*-amino- α -benzylcinnamic acid (II), which, however, was relatively unstable and readily underwent cyclodehydration to give 3-benzylcarbostyryl (III). For purposes of comparison an authentic specimen of (III) was prepared by heating 3-benzylquinoline with potassium hydroxide



at 350°. It would thus appear that in these preparations the resulting *o*-amino- α -benzylcinnamic acid has the carboxyl group and the *o*-aminophenyl group in the unwanted *cis*-configuration. The configuration of the α -benzyl-*o*-nitrocinnamic acid is not known, but rearrangement may have occurred during the reduction of the nitro-group as in the analogous example quoted by Bachman and Hoaglin (*loc. cit.*, p. 306).

EXPERIMENTAL

β -Phenylpropionic Anhydride.—A mixture of β -phenylpropionic acid (18 g.) and acetic anhydride (60 c.c.) was boiled under reflux in a Claisen flask fitted with a cold finger, containing ethylene dibromide in the first neck, and a thermometer in the second. With the bath temperature at 180° acetic acid rapidly distilled at 120°. As the rate of distillation slowed down the temperature dropped to 40°. After 5 hours the excess of acetic anhydride was removed by distillation, and *β -phenylpropionic anhydride* (12.5 g.) was collected at 165–167°/0.25 mm. as a clear liquid (Found: C, 76.0; H, 6.3. $\text{C}_{18}\text{H}_{18}\text{O}_3$ requires C, 76.5; H, 6.4%).

*α -Benzyl-*o*-nitrocinnamic Acid.*—(a) A mixture of β -phenylpropionic acid (10 g.), *o*-nitrobenzaldehyde (10 g.), acetic anhydride (17 g.), and litharge (7.5 g.) was heated under reflux for 4 hours. The mixture was poured into water (300 c.c.) which was then boiled. The supernatant liquid was decanted from the red oil, which had separated on cooling, and the oil was extracted with boiling aqueous sodium carbonate. Acidification gave a pale brown precipitate consisting of β -phenylpropionic acid, *o*-nitrocinnamic acid, and α -benzyl-*o*-nitrocinnamic acid. By fractional crystallisation from aqueous alcohol *α -benzyl-*o*-nitrocinnamic acid* (0.78 g.) was obtained as the most soluble acid constituent; it separated in diamond-shaped crystals, m. p. 194–196° (Found: C, 67.8; H, 4.75; N, 4.9. $\text{C}_{16}\text{H}_{13}\text{O}_4\text{N}$ requires C, 67.8; H, 4.6; N, 4.95%). (b) In a subsequent experiment, in which a mixture of β -phenylpropionic acid (12.5 g.), β -phenylpropionic anhydride (12.5 g.), *o*-nitrobenzaldehyde (12.5 g.), and litharge (9.2 g.) was heated at 150° for 4 hours, only β -phenylpropionic acid was isolated from the acidic product, which was free from nitrogenous acids.

*Reduction of α -Benzyl-*o*-nitrocinnamic Acid.*—(a) A solution of α -benzyl-*o*-nitrocinnamic acid (1.5 g.) in excess of aqueous ammonia was added to a boiling solution of ferrous sulphate (10 g.) in water (100 c.c.) with vigorous stirring. Ammonia (90 c.c.; *d* 0.88) was slowly added while the mixture was boiled under reflux for 20 minutes. The hot mixture was filtered and neutralised with hydrochloric acid. Recrystallisation of the white precipitate from alcohol gave products of variable melting point, which indicated that the amine was being readily converted into 3-benzylcarbostyryl by loss of water. The 3-benzylcarbostyryl (0.12 g.) was finally obtained in small needles, m. p. 193–194° (Found: C, 81.6; H, 5.6; N, 5.9. $\text{C}_{16}\text{H}_{13}\text{ON}$ requires C, 81.7; H, 5.5; N, 6.0%). (b) Hydrogen sulphide was passed for 6 hours into a solution of α -benzyl-*o*-nitrocinnamic acid (0.5 g.) in ammonia solution (25 c.c.; *d* 0.88) and water (50 c.c.) at 0°. After the excess of ammonia and hydrogen sulphide had been boiled off, the hot solution was filtered. Addition of acetic acid gave a yellow precipitate which was dissolved in excess of dilute hydrochloric acid, and the hot solution again filtered to remove sulphur. Careful addition of dilute ammonia solution precipitated *o*-amino- α -benzylcinnamic acid (0.38 g.), which separated from alcohol, with one molecule of water of crystallisation, in small needles, m. p. 182–183° (Found: C, 69.8; H, 6.2; N, 5.4. $\text{C}_{16}\text{H}_{15}\text{O}_2\text{N}\cdot\text{H}_2\text{O}$ requires C, 70.3; H,

6.3; N, 5.2%). The amino-group could be diazotised and the product coupled with alkaline β -naphthol. Subsequent repeated recrystallisation of the amine resulted in its gradual conversion into 3-benzylcarbostyryl.

3-Benzylcarbostyryl.—A mixture of 3-benzylquinoline (1 g.), prepared by Borsche's method (*Annalen*, 1937, 532, 141), and potassium hydroxide (1 g.), which had been dried at 350°/0.05 mm. for an hour, was heated in a copper tube at 350° for 3 hours. The cooled product was extracted with water, and the aqueous extract made neutral with hydrochloric acid. The resulting brown precipitate (0.01 g.) was dissolved in alcohol and the solution boiled with charcoal. 3-Benzylcarbostyryl separated from the filtered solution in small needles, m. p. 193—194° undepressed on admixture with the compound obtained as above from *o*-amino- α -benzylcinnamic acid.

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