202. *Stilbenecarboxylic Acids.*

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The preparation of the undermentioned stilbenecarboxylic acids is described :
Monocarboxylic : 3- and 4- (4 methods).
Dicarboxylic : α : 4, α : 4′, 4 : 4′ (3 methods).
Tricarboxylic : α : 4 : 4′.

By means of 10% potassium hydroxide–ethylene glycol solution, cyanides resistant to the standard processes are readily hydrolysed.

Although stilbenecarboxylic acids are desirable intermediates for many purposes, until recently only the 2- and 2 : 2′-acids had been described, and these were obtained by rather indirect processes (Gabriel and Posner, *Ber.*, 1894, **27**, 2503; Ruggli and Meyer, *Helv. Chim. Acta*, 1922, **5**, 28). More recently Hager, van Arendouk, and Shoule (*J. Amer. Chem. Soc.*, 1944, **66**, 1982) have described the preparation of stilbene-2 : 4′- and -4 : 4′-dicarboxylic acids from the corresponding cyanides, although the hydrolysis presented considerable difficulty.

Three general routes are available for stilbenecarboxylic acids, *viz.*, condensation of the appropriate phenylacetic acid or benzyl cyanide with a benzaldehyde, (ii) coupling of a diazotised aminobenzoic acid with cinnamic acid according to the method of Meerwein, Büchner, and van Emster (*J. pr. Chem.*, 1939, **152**, 237), or (iii) from the nitrostilbene *via* the amine and cyanide. Pfeiffer, Behr, Kübler, and Rüping (*ibid.*, 1929, **121**, 85) have described the preparation of α : 4-dicyanostilbene from *p*-cyanobenzyl cyanide and benzaldehyde. In a similar way α : 4 : 4′-*tricyanostilbene* was prepared from *p*-cyanobenzyl cyanide and *p*-cyanobenzaldehyde, α : 4′-*dicyanostilbene* from benzyl cyanide and *p*-cyanobenzaldehyde, 4 : 4′-dicyanostilbene from *p*-cyanophenylacetic acid and *p*-cyanobenzaldehyde, and 4-cyanostilbene from *p*-cyanophenylacetic acid and benzaldehyde and, also, from phenylacetic acid and *p*-cyanobenzaldehyde. Most of these cyanides were resistant to hydrolysis by the usual methods (cf. Fosdick and Urbach, *J. Amer. Chem. Soc.*, 1947, **69**, 504), but it was found that they could all be converted easily into the corresponding acids by boiling them with a 10% solution of potassium hydroxide in ethylene glycol. The resultant *stilbene*-α : 4- and -α : 4′-*dicarboxylic acids* were converted into *stilbene*-4-*carboxylic acid* by heating them with quinoline and basic copper carbonate (Bergmann and Schapiro, *J. Org. Chem.*, 1947, **12**, 57); similarly the α : 4 : 4′-*tricarboxylic acid* was converted into stilbene-4 : 4′-dicarboxylic acid.

Meerwein's method (*loc. cit.*) applied to *p*-aminobenzoic acid provided a much more satisfactory method of preparation of stilbene-4-carboxylic acid. Similarly, from diazotised *m*-aminobenzoic acid, *stilbene*-3-*carboxylic acid* was obtained in good yield. It was not found possible, however, to prepare stilbene-2-carboxylic acid by a similar reaction from anthranilic acid.

4 : 4′-Dicyanostilbene has been prepared from dibenzyl by Bance, Barber, and Woolman (*J.*, 1943, 1). This was found to be a much more economical method than that of Lamb and White (*J.*, 1939, 1256). From this dicyano-compound stilbene-4 : 4′-dicarboxylic acid was obtained more conveniently than described above.

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* It is noteworthy that there is a discrepancy between our evaluation of $\Delta C_{p_1} - \Delta C_{p_2}$ and that in the paper of Wynne-Jones and Rushbrooke. In the first place an arithmetical error makes their value too small by a factor of 2. Furthermore, to represent the temperature variation of the dielectric constant of water they choose an equation used by Everett and Wynne-Jones (*loc. cit.*) to represent Kockel's data (*Ann. Physik*, 1925, **87**, 417); this equation, which gives a value of $\Delta C_{p_1} - \Delta C_{p_2}$ about two-fifths of that calculated here, does not agree with the recent data of Wyman and Ingalls (*J. Amer. Chem. Soc.*, 1398, **60**, 1182) whose results we have used.

EXPERIMENTAL.

α : 4-Dicyanostilbene, from *p*-cyanobenzyl cyanide and benzaldehyde, recrystallised from alcohol in plates, m. p. 145° (Pfeiffer, Behr, Kübler, and Rüping, *loc. cit.*, give needles, m. p. 147°). Heated at 140° for 1½ hours with a mixture of equal volumes of sulphuric acid, acetic acid, and water, it furnished *α-cyanostilbene-*4*-carboxylic acid* together with other compounds from which it was freed with considerable difficulty. This acid was best prepared by hydrolysis with hydrogen chloride in ethyl alcohol solution and saponification of the resultant ester. It formed long hair-like needles, m. p. 245° (Found : N, 6·0; equiv., 249. $C_{16}H_{11}O_2N$ requires N, 5·6%; equiv., 251), and dissolved in sulphuric acid at 100° to give a bright crimson solution from which an orange-yellow indonesulphonic acid was precipitated by water.

Stilbene-α : 4*-dicarboxylic Acid.*—(*a*) α-Cyanostilbene-4-carboxylic acid (1·0 g.) was hydrolysed by heating it for 3 hours under reflux at 140—160° with 10 c.c. of 10% potassium hydroxide–ethylene glycol solution. The resultant *stilbene-α* : 4*-dicarboxylic acid* crystallised in needles from aqueous alcohol, m. p. 225° (Found : equiv., 133. $C_{16}H_{12}O_4$ requires equiv., 134).

(*b*) Homoterephthalic acid (9·0 g.), mixed with benzaldehyde (5·5 g.) and piperidine (5 drops), was heated 3 hours at 150—160°. The deep red product was crystallised from glacial acetic acid and then from aqueous alcohol; yield, 5·4 g.; m. p. 225°.

Decarboxylation. Stilbene-α : 4-dicarboxylic acid (2·0 g.) was heated with quinoline (20 c.c.) and basic copper carbonate (2·0 g.). Reaction began at 145° and was apparently complete in 45 minutes. Heating was continued for a further 15 minutes, and the quinoline removed by steam. Acidification of the residue yielded stilbene-4-carboxylic acid, m. p. 245°.

α : 4*'-Dicyanostilbene.*—*p*-Cyanobenzaldehyde (2·0 g.), mixed with benzyl cyanide (2·0 g.) and piperidine (5 drops), was heated at 150° for 1 hour. The product, which solidified on standing, was recrystallised from ethyl alcohol. α : 4*'-Dicyanostilbene* forms fine needles, m. p. 172° (Found: N, 11·9. $C_{16}H_{10}N_2$ requires N, 12·2%).

Stilbene-α : 4*'-dicarboxylic Acid.*—α : 4'-Dicyanostilbene (1·0 g.) was heated with 10% potassium hydroxide–ethylene glycol (10 c.c.) solution for 4 hours. The resultant *stilbene-α* : 4*'-dicarboxylic acid* crystallised from alcohol; m. p. 293° (Found : equiv., 132. $C_{16}H_{12}O_4$ requires equiv., 134). This acid was readily decarboxylated to stilbene-4-carboxylic acid by the quinoline–copper carbonate method.

α : 4 : 4*'-Tricyanostilbene.*—*p*-Cyanobenzaldehyde (5·2 g.) was heated with *p*-cyanobenzyl cyanide (5·6 g.) at 140°, and piperidine (3 drops) was added to the molten mixture, which immediately solidified. The red mass was recrystallised from piperidine, giving α : 4 : 4*'-tricyanostilbene* as pale yellow needles, m. p. 302—303°; yield, 6·5 g. (Found : C, 79·8; H, 3·7; N, 16·8. $C_{17}H_9N_3$ requires C, 80·0; H, 3·5; N, 16·5%).

*α-Cyanostilbene-*4 : 4*'-dicarboxylic acid* was obtained by heating the tricyano-compound with sulphuric acid–acetic acid for 8 hours at 140°, and also by alkaline hydrolysis of ethyl α-cyanostilbene-4 : 4'-dicarboxylate (obtained by 18 hours' alcoholysis of the tricyano-compound with hydrogen chloride and ethyl alcohol). It formed a white powder insoluble in the usual organic solvents (Found : N, 4·67; equiv., 147·1. $C_{17}H_{11}O_4N$ requires N, 4·77%; equiv., 146·5).

Stilbene-α : 4 : 4*'-tricarboxylic acid,* obtained by heating α-cyanostilbene-4 : 4'-dicarboxylic acid (1·5 g.) at 150—160° for 4 hours with 10% potassium hydroxide–ethylene glycol solution (10 c.c.), crystallised from acetic acid as small plates, m. p. 286—288° (Found : equiv. 103. $C_{17}H_{12}O_6$ requires equiv., 104). It was readily decarboxylated to stilbene-4 : 4'-dicarboxylic acid.

*Stilbene-*4 : 4*'-dicarboxylic Acid.*—4 : 4'-Dicyanostilbene (5·0 g.) was heated at 160—170° with potassium hydroxide–ethylene glycol solution (50 c.c.) until evolution of ammonia was complete (3 hours), poured into water, and the free acid liberated with dilute sulphuric acid. The liquid containing the gelatinous precipitate was left on a hot plate for several hours to facilitate filtration. Stilbene-4 : 4'-dicarboxylic acid (Found : equiv., 135. Calc. : equiv., 134) is a white amorphous powder insoluble in the usual organic solvents, including nitrobenzene, dioxan, and phenol, but easily converted into stilbene by heating with lime. Stilbene-2 : 4'-dicarboxylic acid, m. p. 296°, was obtained in the same way from the readily-available 2 : 4'-dicyanostilbene (Bance, Barber, and Woolman, *loc. cit.*).

*Stilbene-*4 : 4*'-dicarboxylic Chloride.*—Stilbene-4 : 4'-dicarboxylic acid (2·0 g.) was heated for 12 hours with thionyl chloride (10 c.c.). Excess of thionyl chloride was evaporated off and the last traces removed over soda-lime in vacuum desiccator. The residue was crystallised twice from benzene–light petroleum, and the *chloride* formed a white powder, m.p. 223—224° (Found: Cl, 23·4. $C_{16}H_{10}O_2Cl_2$ requires Cl, 23·2%).

*Anilide of Stilbene-*4 : 4*'-dicarboxylic Acid.*—Stilbene-4 : 4'-dicarboxylic chloride (1·0 g.) was heated for several minutes with a few c.c. of aniline, and the *anilide* precipitated by dilute hydrochloric acid. It crystallised from nitrobenzene in small hair-like needles, m. p. 316—317° (Found: N, 6·66. $C_{28}H_{22}O_2N_2$ requires N, 6·7%).

4-Cyanostilbene was prepared by condensation of equimolecular proportions of *p*-cyanophenylacetic acid and benzaldehyde or phenylacetic acid and *p*-cyanobenzaldehyde at 160—170° in the presence of a few c.c. of piperidine; it formed fine needles, m. p. 115°, from alcohol or 80% acetic acid.

*Stilbene-*4*-carboxylic Acid.*—(a) *Hydrolysis of* 4*-cyanostilbene.* 4-Cyanostilbene (2·5 g.) was heated at 160—170° with 10% potassium hydroxide–ethylene glycol solution until evolution of ammonia was complete (2 hours). Yield, 2·6 g.; m. p. 245°.

(b) *Meerwein reaction.* The hydrochloride of 4-aminobenzoic acid (25 g.) was suspended in a mixture of concentrated hydrochloric acid (25 c.c.) and water (40 c.c.), and diazotised with a solution of sodium nitrite (11 g.) in water (20 c.c.). The diazo-solution was filtered, and sodium acetate (35 g.) stirred in. When solution was complete, cinnamic acid (22 g.) in acetone (200 c.c.) was added and the ice-bath removed. 5 Minutes later, cupric chloride (6·5 g.) dissolved in water (20 c.c.) was added. The mixture was well stirred and the temperature allowed to rise slowly to 17° during 1 hour. Sitrring was then continued for a further 2 hours at 30°. The acetone was removed by steam, and the *stilbene-*4*-carboxylic acid* which had separated was recrystallised twice from glacial acetic acid, yielding a fine crystalline powder, m. p. 244—245° (yield 60%) (Found : equiv., 223. $C_{15}H_{12}O_2$ requires equiv., 224).

*Stilbene-*3*-carboxylic Acid.*—Procedure and quantities were the same as for the isomeric 4-acid, except that after 1 hour's stirring to room temperature the mixture was then stirred for 3 hours at 23—25°. After this time evolution of gas was complete, and two layers had formed. The upper layer was a dark green oil, and the lower layer a bright green water–acetone mixture.

The acetone was removed by steam, and the oily layer, which solidified on cooling, was recrystallised twice from glacial acetic acid. Further recrystallisation from benzene or aqueous alcohol gave *stilbene*-3-*carboxylic acid* as small, fine crystals, m. p. 194—195° (Found: equiv., 225. $C_{15}H_{12}O_2$ requires equiv., 224).

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[*Received, July* 21*st*, 1947.]