

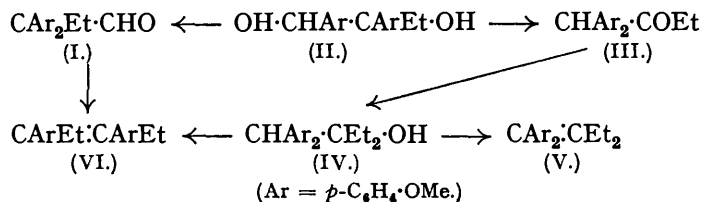
157. *New Synthesis of 4 : 4'-Dimethoxy- $\alpha\alpha'$ -diethylstilbene.*

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4 : 4'-Dimethoxy- $\alpha\alpha'$ -diethylstilbene, first obtained by Robinson *et al.* (*Nature*, 1938, 141, 247), has now been prepared by means of molecular rearrangements.

EXPERIMENTS have been carried out to prepare dimethoxystilbene derivatives by means of the so-called retropinacolinic rearrangement whereby $\alpha\alpha'$ -dimethyl- and $\alpha\alpha'$ -diethylstilbene were obtained by Meerwein (*Annalen*, 1914, 405, 174) and Lévy (*Compt. rend.*, 1921, 172, 383; *Bull. Soc. chim.*, 1921, 29, 865): the reaction of an $\alpha\alpha'$ -diphenyl- α -alkylacetaldehyde and an alkylmagnesium bromide yields a carbinol which, when distilled in the presence of a trace of dilute sulphuric acid, gives the corresponding dialkylstilbene.

An attempt was made to prepare $\alpha\alpha'$ -dianisyl- α -ethylacetaldehyde (I) according to Weill (*Bull. Soc. chim.*, 1931, 49, 1811) by refluxing $\alpha\beta$ -dihydroxy- $\alpha\beta$ -dianisylbutane (II) for a short time at the ordinary pressure and subsequent distillation. An oil was obtained which was treated with ethylmagnesium bromide, and the product distilled in the presence of dilute sulphuric acid. Only a small amount of 4 : 4'-dimethoxy- $\alpha\alpha'$ -diethylstilbene was produced. It was then found that the dehydration of (II) does not yield uniform results: after 1 minute's refluxing, (II) remains unchanged; after prolonged heating (2 hours), the amount of a low-boiling by-product increases considerably. To obtain better yields of (I), (II) was heated with 50% aqueous oxalic acid (cf. Lévy, *loc. cit.*); the product, however, was $\alpha\alpha'$ -dianisyl- β -butanone (III) (cf. Weill, *loc. cit.*), though the presence of (I) could be detected in the mother-liquor. When a mixture of equal amounts of oxalic and acetic acids was used, the yield of (III) exceeded 70%. (III) was also obtained by the action of ethylmagnesium bromide on $\alpha\alpha'$ -dianisylacetonitrile.



The difficulty of obtaining (I) and the ready formation of (III) suggested the investigation: can compounds of the type $\text{Ar}_2\text{CH}\cdot\text{C}(\text{OH})\text{Alk}_2$ be converted into stilbene derivatives? β -Hydroxy- $\alpha\alpha'$ -dianisyl- β -ethylbutane (IV) was prepared in good yield from (III) by the action of ethylmagnesium bromide. Distillation of (IV) in the presence of a trace of dilute sulphuric acid yielded an oil which slowly deposited crystals of $\alpha\alpha'$ -dianisyl- $\beta\beta$ -diethylethylene (V). The action of dehydrating agents, such as alcoholic hydrogen chloride, aqueous alkali, zinc chloride in glacial acetic acid, and phosphorus pentachloride, on (IV) gave unsatisfactory results. The action of a boiling mixture of phosphorus oxychloride and toluene (1 : 1) on (IV) yielded a mixture which could be separated into (V) and 4 : 4'-dimethoxy- $\alpha\alpha'$ -diethylstilbene (VI). The yield of (VI), however, could not be raised above 32% of the theoretical: when no toluene was used, the yield diminished (charring); when more toluene was used, the yield gradually diminished and increasing amounts of (V) were obtained. At higher temperatures charring occurred; at lower temperatures, only (V) was obtained. (V) could not be converted into (VI).

A more convenient method of preparing (IV) is as follows: 4-methoxymandelonitrile is condensed with anisole to yield $\alpha\alpha'$ -dianisylacetonitrile, which is converted into $\alpha\alpha'$ -dianisylacetic acid, the methyl ester of which gives (IV) in good yield on reaction with ethylmagnesium bromide.

The formation of (VI) from (IV) is an interesting case of molecular rearrangement. According to Orékhoff and Tiffeneau (*Bull. Soc. chim.*, 1921, 29, 422) substances of the type $\text{OH}\cdot\text{CArAlk}\cdot\text{CHAR}'\cdot\text{OH}$ may be converted into aldehydes, $\text{CArAr}'\cdot\text{Alk}\cdot\text{CHO}$ (hydrobenzoin rearrangement), or ketones, $\text{CHARAr}'\cdot\text{COAlk}$ (semipinacolinic rearrangement); in the

former case the Ar' and the tertiary hydroxyl group, in the latter case the Ar and the secondary hydroxyl group, exchange places. It is very likely, however, that the hydrobenzoin rearrangement is an intermediate stage of the semipinacolinic rearrangement; indeed Weill (*loc. cit.*, p. 1819) found that (I; Ar = Ar' = anisyl, Alk = ethyl) is readily converted into (III). That would mean that in the semipinacolinic rearrangement the Ar' and the Alk group exchange places and the Ar group is not involved in the reaction. The reaction (IV) \rightarrow (VI) would then be an analogous case. By the migration of one Ar group $\text{CHAr}_2\cdot\text{CAlk}_2\cdot\text{OH}$ would be converted into the hypothetical intermediate product $\text{Ar}\cdot\text{CH}(\text{OH})\cdot\text{C}(\text{ArAlk})_2$, which would be subject to the so-called retropinacolinic rearrangement, that is, the Alk group migrates and $\text{C}(\text{ArAlk})_2$ is formed.

EXPERIMENTAL.

α -Dihydroxy- α -di-p-anisylbutane (II).—To a Grignard solution prepared from 18 g. of magnesium, 77.5 g. of ethyl bromide, and 300 c.c. of anhydrous ether, 40.8 g. of finely powdered anisoin were added in small portions. The solution was refluxed for about 4 hours and decomposed with ice and dilute hydrochloric acid, the ethereal solution washed with dilute sodium hydroxide solution and water, dried, and evaporated, and the residue crystallised from alcohol. Yield, 33.0 g.; m. p. 114—115° (cf. Weill, *loc. cit.*). Oxidation of 0.5 g. of (II) with 0.34 g. of chromic acid in acetic acid on the water-bath produced 0.35 g. of anisic acid, m. p. (after crystallisation from alcohol) 179—181°, not depressed by an authentic specimen (m. p. 183—184°).

α -Dianisyl- β -butanone (III).—(A) 50 G. of (II) were refluxed with acetic acid (210 c.c.) and oxalic acid (210 g.) for 9 hours. After evaporation of the acetic acid in a vacuum, the residue was extracted with benzene, the solution washed with dilute aqueous sodium hydroxide and water, dried, and evaporated, and the residue distilled; the fraction, b. p. 210—212°/2 mm., was crystallised from alcohol. Yield, 33.3 g.; m. p. 56—58°.

(B) To a Grignard solution prepared from 21.5 g. of magnesium, 95 g. of ethyl bromide, and 350 c.c. of anhydrous ether, 10 g. of α -dianisylacetonitrile were added in small portions with vigorous stirring. After 5 hours' refluxing the product was isolated in the usual way and distilled, and the fraction, b. p. 210—215°/2 mm., crystallised twice from alcohol. Yield, 2 g.; m. p. 52—55°, not depressed by the dianisylbutanone, prepared under (A). The semicarbazone had m. p. 193° after crystallisation from alcohol.

0.5 G. of (III), oxidised in acetic acid with 0.34 g. of chromic acid at room temperature, gave 0.4 g. of dianisyl ketone, m. p. 143—144° after one recrystallisation.

α -Dianisyl- α -ethylacetaldehyde (I).—After 10 g. of (II) had been refluxed for 2 hours and then distilled, 3.67 g. of a fraction, b. p. 190—195°/2 mm., were obtained. This fraction was assumed to contain (I) and was worked up as described below.

50 G. of (II) were refluxed with oxalic acid (210 g.) in 150 c.c. of water for 9 hours; neither (II) nor the product dissolved. The mixture was extracted with benzene, the solution washed with dilute aqueous sodium hydroxide and water, dried, and evaporated, and the residue distilled. The fraction, b. p. 210—212°/2 mm., crystallised from alcohol, yielding 10.95 g. of (III), m. p. 56—58°. The mother-liquor was evaporated to dryness, leaving 22.45 g. of an oil containing (I) and (III).

4 : 4'-Dimethoxy- α '-diethylstilbene (VI) from α -Dianisyl- α -ethylacetaldehyde (I).—The fraction (3.67 g.), b. p. 190—195°/2 mm., obtained from (II) was added to a Grignard solution prepared from 1.2 g. of magnesium, 5.1 g. of ethyl bromide, and 20 c.c. of ether, and the solution heated for 1 hour and decomposed with ice and dilute hydrochloric acid. The ethereal solution was washed, dried, and evaporated, and the residue distilled in a vacuum in the presence of a drop of dilute sulphuric acid. The fraction (2.73 g.), b. p. 185—190°/2 mm., was dissolved in alcohol (3 c.c.); the solution deposited 0.05 g. of a crystalline substance, m. p. 117—119°, not depressed by a specimen of (VI) prepared according to Robinson *et al.* (*loc. cit.*), m. p. 123—124°.

In a similar experiment 22.45 g. of the oil obtained from (II) by the action of acetic and oxalic acids gave 2.41 g., m. p. 123—124°, not depressed by an authentic specimen of (VI).

1 G. of this product was heated in an iron tube with a solution of potassium hydroxide (4 g.) in methyl alcohol (9 c.c.) at 200° for 7 hours. The reaction product was dissolved in water and the filtered solution treated with hydrochloric acid. The precipitate (0.86 g.), after one crystallisation from benzene, had m. p. 169—170°, not depressed by authentic 4 : 4'-dihydroxy- α '-diethylstilbene.

α -Dianisylacetic Acid.—Anisaldehyde cyanohydrin (25 g.), anisole (25 g.), and 73% sulphuric acid (90 c.c.) were heated at 80° for a few minutes, the product poured into water, and

the dianisylacetonitrile filtered off and washed with much alcohol. Yield, 25 g.; m. p. 154—155°. 25 G. of the nitrile were heated with 100 c.c. of 20% methyl-alcoholic potassium hydroxide in an iron tube at 115—120° for 3 hours (at lower temperatures the reaction proceeds very slowly; cf. Bistrzycki *et al.*, *Ber.*, 1911, **44**, 2606). The methyl alcohol was distilled off, the residue dissolved in water, and the filtered solution treated with hydrochloric acid, giving 25.5 g. of α -dianisylacetic acid, m. p. 113—114°.

The methyl ester was prepared by refluxing 59.5 g. of the acid with 75 c.c. of methyl alcohol containing 1 c.c. of concentrated sulphuric acid for 3 hours. It crystallised on cooling, and after being washed with methyl alcohol and with water had m. p. 71—72°. The ethyl ester had m. p. 68—69°.

β -Hydroxy- α -dianisyl- β -ethylbutane (IV).—(A) 58.8 G. of (III) were added in small portions to a Grignard solution prepared from 15.5 g. of magnesium, 70 g. of ethyl bromide, and 250 c.c. of ether, and the mixture refluxed for 2 hours and then decomposed with ice and dilute hydrochloric acid. The ethereal solution was washed, dried, and evaporated. The residue (61.2 g.), crystallised from ethyl alcohol (65 c.c.), gave 50.7 g. of (IV), m. p. 83—84°. A sample crystallised twice from ethyl alcohol melted at 87—88°.

(B) Methyl dianisylacetate (50 g.) was treated in exactly the same way. The residue (51.5 g.) obtained from the ethereal solution was crystallised from ethyl alcohol (55 c.c.), giving 35.5 g., m. p. 83—84°, not depressed by (IV) prepared under (A).

Oxidation of (IV) (0.5 g.) with chromic acid (0.34 g.) in acetic acid on the water-bath gave dianisyl ketone (0.4 g.), m. p. 142—144° after crystallisation from alcohol.

Dehydration of (IV). (i) 2 G. were distilled in the presence of a drop of dilute sulphuric acid. The main fraction, b. p. 210°/3 mm., was dissolved in alcohol; after a few days a small amount of a crystalline substance, m. p. 86—88°, separated.

(ii) 2 G. were heated in a sealed tube with 10 c.c. of alcoholic hydrogen chloride for 1 hour. The product was poured into water and the precipitate filtered off and recrystallised from alcohol. Yield, 1.25 g.; m. p. 90—92°, depressed by (IV) but not by the substance, m. p. 86—88°, obtained under (i).

0.5 G. of this substance, oxidised with 0.34 g. of chromic acid in acetic acid on the water-bath, gave 0.4 g. of dianisylketone, proving that no molecular rearrangement had taken place. The substance is obviously α -dianisyl- β -diethylethylene (V). 4:4'-Dimethoxy- α '-diethylstilbene (VI) yielded under identical conditions only anisic acid, m. p. 184°.

4:4'-Dimethoxy- α '-diethylstilbene (VI).—2 G. of (IV) were dissolved in 6 c.c. of toluene, and the solution gradually added to a boiling mixture of 6 c.c. of toluene and 12 c.c. of phosphorus oxychloride. When the reaction was completed, the solution was decomposed with ice-water, washed with dilute aqueous sodium hydroxide and water, dried, and evaporated. The residue was dissolved in 2 c.c. of methyl alcohol; on cooling, a crystalline substance (0.69 g., m. p. 108—115°) was deposited, which was quickly filtered off; the mother-liquor soon deposited a second crop of crystals, which were found to be (V), m. p. 88—90°. The first crop, recrystallised from alcohol, gave 4:4'-dimethoxy- α '-diethylstilbene (0.6 g.), m. p. 123—125°, not depressed by an authentic specimen.