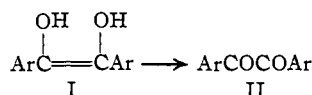


[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

## Enediols. V. Hexaisopropylstilbenediols

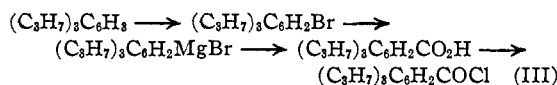
BY REYNOLD C. FUSON AND E. C. HORNING<sup>1</sup>

Stilbenediols (I) in which the aryl radicals are mesityl,<sup>2</sup> 2,6-xylyl<sup>3</sup> or 2,4,6-triethylphenyl<sup>4</sup> are stable in an inert atmosphere but are remarkably sensitive to the air. The product of autoxidation is the corresponding benzil (II). The ease of the oxidation is however, much less with the hexa-

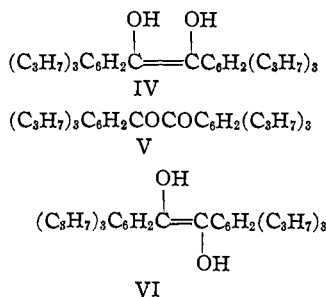


ethyl<sup>4</sup> than with the tetra-<sup>3</sup> and hexamethyl<sup>2</sup> analogs. The analogous hexaisopropylstilbenediols are still more resistant to oxidizing agents.

The new enediols were derived from 2,4,6-triisopropylbenzoyl chloride (III), the synthesis of which was carried out according to the following scheme. The starting material was 1,3,5-triisopropylbenzene



Reductive coupling with the binary mixture, Mg + MgI<sub>2</sub>,<sup>5</sup> converted the acid chloride into an enediol (IV) melting at 175–176°. It could be exposed to the air for several hours without appreciable change. In time, however, it was oxidized to the corresponding benzil (V).



An isomeric enediol was obtained by catalytic hydrogenation of the benzil in methanol. This substance was much more resistant to oxidation than was its isomer. Oxidation to the benzil, evidenced by the appearance of a yellow color,

(1) Du Pont Fellow in Chemistry, 1939–1940.

(2) (a) Fuson and Corse, THIS JOURNAL, **61**, 975 (1939); (b) Thompson, *ibid.*, **61**, 1281 (1939); (c) Fuson, McKeever and Corse, *ibid.*, **62**, 600 (1940).(3) Fuson, Scott, Horning and McKeever, *ibid.*, **62**, 2091 (1940).(4) Fuson, Corse and McKeever, *ibid.*, **61**, 2010 (1939).(5) Gomberg and Bachmann, *ibid.*, **49**, 236 (1927).

became appreciable only after several weeks. It melted at 259–260.5°.

By analogy with the *cis* and *trans* forms of other similar enediols,<sup>3</sup> this compound has been assigned the *trans* configuration (VI) while the *cis* arrangement (IV) has been assumed for the low-melting enediol.

Both forms decolorize alcoholic solutions of the blue dye, sodium 2,6-dichlorobenzeneoneindophenol, the *cis* form immediately, the *trans* form more slowly. Both are insoluble in aqueous alkali. The *cis* isomer dissolves readily in methanol and ether whereas the *trans* isomer is only slightly soluble in methanol and moderately soluble in ether. When the benzil is hydrogenated in methanol, the *cis* modification remains in solution but the *trans* isomer separates as it is formed.

It is possible to obtain both the *cis* and *trans* forms of the stilbenediol by varying the time of treatment with hydrogen in the presence of platinum. The *cis* isomer is produced initially but if the treatment is prolonged the product is the *trans* isomer. The presence of small amounts of acetic acid inhibits the formation of the *trans* compound, whereas a trace of piperidine appears to favor its formation.

The production of the *trans* enediol evidently takes place at the expense of the *cis* compound. In fact, it was found that the pure *cis* isomer could be changed to the *trans* compound by treatment with platinum and hydrogen in methanol solution. This type of conversion has been accomplished in other instances.<sup>3</sup>

The benzoin was not formed by spontaneous isomerization of the enediols but was obtained when the *cis* form was heated in a methanol solution which had been saturated with hydrogen chloride. The *trans* enediol was not affected by this treatment.

Several methods were tried in attempts to prepare ethers of the enediols. The only successful one involved treatment of the benzil with ethylmagnesium bromide in butyl ether and subsequent heating with methyl sulfate. The configuration of the ether obtained in this way is probably *cis*, but this has not been confirmed.

### Experimental

**2,4,6-Triisopropylbromobenzene.**—The method was similar to that used for 2,4,6-triethylbromobenzene.<sup>6</sup> The bromination required seven hours instead of five. From 102 g. of 1,3,5-triisopropylbenzene a yield of 116 g. of bromide was obtained. It boiled at 146–148° (18 mm.);  $n_D^{20}$  1.5224;  $d_4^{25}$  1.1244.

*Anal.*<sup>7</sup> Calcd. for  $C_{15}H_{23}Br$ : C, 63.58; H, 8.20. Found: C, 63.90; H, 7.88.

**2,4,6-Triisopropylbenzoic Acid.**—By the method used for the triethyl analog<sup>6</sup> 56 g. of 2,4,6-triisopropylbromobenzene gave 23 g. of 2,4,6-triisopropylbenzoic acid melting at 180–183°. The crude acid was used without further purification for the preparation of the acid chloride. Hydrolysis of a portion of the latter yielded a sample of the acid which, after recrystallization from a benzene–low-boiling petroleum ether mixture, melted at 186–187°.

*Anal.* Calcd. for  $C_{16}H_{24}O_2$ : C, 77.36; H, 9.75. Found: C, 77.07; H, 9.68.

**2,4,6-Triisopropylbenzoyl Chloride.**—The acid chloride was made by allowing the acid to stand with thionyl chloride for two days at room temperature. The yield was 92%. The chloride melted at 79–81° and boiled at 107–108° (2 mm.).

*Anal.* Calcd. for  $C_{16}H_{23}OCl$ : C, 72.06; H, 8.67. Found: C, 72.21; H, 8.80.

***cis*-2,2',4,4',6,6'-Hexaisopropylstilbenediol.**—The preparation of the enediol from the acid chloride was carried out in the usual fashion<sup>20</sup> with slight modifications. It was found possible to reduce the reaction time to ten hours without material effect on the yield, and a 5% sodium carbonate solution was used for washing in place of the potassium bicarbonate solution. From 9.9 g. of the acid chloride 3.2 g. of enediol was obtained.

The product could be recrystallized from an ether–low-boiling petroleum ether mixture, and when dry was stable for a number of hours when exposed to the atmosphere. Prolonged contact with air converted it to the benzil. The melting point in a nitrogen-filled capillary was 175–176°. Its properties were similar to those observed for the lower members of the series.

*Anal.* Calcd. for  $C_{32}H_{48}O_2$ : C, 82.69; H, 10.42. Found: C, 82.63; H, 10.25.

The alkaline extracts were combined, boiled, filtered and acidified to yield 0.15 g. of 2,4,6-triisopropylbenzoic acid.

The low-boiling petroleum ether washes were reserved for recovery of the benzil. The residues were oxidized by hydrogen peroxide or air and yielded amounts of the benzil varying from 1.0 to 1.8 g. The benzil was also obtained from oxidation of both *cis* and *trans* enediols.

**Acetylation.**—Attempts to prepare a diacetate using the *cis* enediol and acetic anhydride following the general method used for the ethyl analog<sup>4</sup> resulted in a small amount of crystalline material and some yellow oil. Recrystallization was effected first from low-boiling petroleum ether and then from methanol. The diacetate melted at 214.5–215.5°.

(6) Fuson and Corse, *THIS JOURNAL* 60, 2063 (1938).

(7) The analyses reported in this paper are microanalyses and were carried out by Mr. L. G. Fauble and Mr. W. H. Taylor.

*Anal.* Calcd. for  $C_{36}H_{52}O_4$ : C, 78.77; H, 9.56. Found: C, 79.19; H, 9.65.

When the acetylation was carried out with acetic anhydride in pyridine (using a 20% solution) the result was a diacetate which could also be recrystallized from methanol and melted at 228–230°. A mixed melting point taken with the diacetate obtained by catalytic reduction of the benzil in acetic anhydride showed no depression.

**2,2',4,4',6,6'-Hexaisopropylbenzoin.**—One gram of the *cis* enediol treated as usual<sup>4</sup> with methanol saturated with hydrogen chloride yielded 0.6 g. of the benzoin, which was recrystallized from methanol. The melting point was 126.5–127.5°.

*Anal.* Calcd. for  $C_{32}H_{48}O_2$ : C, 82.69; H, 10.42. Found: C, 82.80; H, 10.54.

The *trans* enediol was maintained under reflux with a solution of hydrogen chloride in methanol for fifteen hours without appreciable effect. The enediol did not go into solution and was recovered unchanged.

**Benzoin Acetate.**—The benzoin acetate was prepared by the action of acetic anhydride on the benzoin, using the method employed for the *cis* enediol. The product was recrystallized from methanol; m. p. 114–115.5°.

*Anal.* Calcd. for  $C_{34}H_{50}O_3$ : C, 80.56; H, 9.95. Found: C, 80.54; H, 10.08.

**2,2',4,4',6,6'-Hexaisopropylbenzil.**—Oxidation of an ethereal solution of 0.75 g. of the *cis* enediol by shaking for a few minutes with an aqueous solution of sodium hypiodite followed by recrystallization of the product from methanol resulted in 0.6 g. of the yellow benzil; m. p. 155–156°.

*Anal.* Calcd. for  $C_{32}H_{46}O_2$ : C, 83.04; H, 10.03. Found: C, 83.24; H, 10.21.

***trans*-2,2',4,4',6,6'-Hexaisopropylstilbenediol.**—Reduction of the benzil in methanol using a platinum catalyst resulted in the formation of the *trans* enediol. This was only very slightly soluble in methanol and was precipitated from the solution as it was formed. Filtration of an ether solution of the product removed the catalyst, and recrystallization was effected from ether–low-boiling petroleum ether. The melting point in a nitrogen-filled capillary was 259–260.5°.

*Anal.* Calcd. for  $C_{32}H_{48}O_2$ : C, 82.69; H, 10.42. Found: C, 82.46; H, 10.51.

The *trans* enediol was very much less soluble in the solvents employed than was the *cis* enediol. It was fairly stable with respect to autoxidation, but in the course of a number of weeks a gradual oxidation was observed, evidenced by the appearance of a yellow color. It decolorized alcoholic solutions of 2,6-dichlorobenzeneoneindophenol slowly while the *cis* enediol was effective immediately. It was insoluble in aqueous alkali, as was the *cis* form.

**Acetylation.**—The acetylation of the *trans* enediol was accomplished by the method used for the *cis* enediol. The resulting diacetate was recrystallized several times from methanol and melted at 214.5–215.5°; a mixed melting point with the diacetate prepared from the *cis* enediol by the use of acetic anhydride showed no depression.

**Oxidation of the *trans* Enediol.**—To a combination of 15 cc. of ether and 15 cc. of 5% sodium hydroxide solution was added 0.4 g. of the *trans* enediol and 2 g. of iodine. The mixture was stirred with a high speed stirrer for forty

minutes, the aqueous layer removed, and the treatment repeated on the ethereal layer. The ether solution was separated and washed several times with water. After drying over a little calcium chloride the ether was removed and the residue recrystallized from methanol; yield, 0.35 g. of the benzil.

A mixture of 25 cc. of 95% ethanol, 3 cc. of 20% sodium hydroxide solution, 2 cc. of 30% hydrogen peroxide solution and 0.45 g. of the *trans* enediol was stirred with a high speed stirrer for thirty minutes. The mixture was poured into water and extracted with ether. After washing, drying, and removing the ether the residue was recrystallized from methanol; yield, 0.35 g. of the benzil.

**Reduction in Acetic Anhydride.**—When the benzil was reduced in acetic anhydride according to the method of Thompson<sup>2b</sup> there was obtained a diacetate which could be recrystallized from methanol and melted at 231–232.5°.

*Anal.* Calcd. for  $C_{30}H_{42}O_4$ : C, 78.77; H, 9.56. Found: C, 78.99; H, 9.60.

**Catalytic Conversion.**—One gram of the *cis* enediol obtained from the coupling of the acid chloride with the binary mixture was shaken in 30 cc. of methanol with a platinum catalyst in an atmosphere of hydrogen. The time of shaking varied from twenty-four to thirty hours and the yields from 0.2 to 0.4 g. of the *trans* enediol. Addition of a few drops of piperidine did not increase the amount of conversion.

**Catalytic Effects.**—Several interesting effects have been observed in the catalytic hydrogenation of the benzil with a platinum catalyst. It is possible to follow the effects qualitatively without difficulty. The benzil and its solutions are yellow. The *cis* enediol is quite soluble in methanol, while the *trans* enediol precipitates from methanol as it is formed. Thus reduction to a clear, colorless solution indicates complete reduction of the benzil to the *cis* enediol. The latter compound has been isolated from solutions of this type. Reduction to a colorless solution containing a suspension of fine white needles indicates complete reduction of the benzil, the solid material being *trans* enediol, and any *cis* enediol present remains in solution. From mixtures of this type the *trans* enediol was always obtained simply by filtration. The catalyst was removed as described previously.

It was found that acetic acid, in relatively small amounts, exerted an influence on the course of the reduction. When 1 g. of the benzil was reduced in 30 cc. of methanol containing 3 cc. of glacial acetic acid the product was a colorless and clear or only very slightly opalescent solution. From one such solution there was obtained 0.4 g. of the *cis* enediol, along with some benzil occasioned by oxidation during the experimental operations of isolating the enediol. Prolonging the period of catalytic contact after reduction was complete seemed to be without effect.

When the amount of acetic acid was reduced to three

drops, the other quantities remaining the same, the formation of the *trans* enediol was retarded but not suppressed. One such solution, with a catalytic contact period extending for several hours after reduction was completed, yielded 0.5 g. of *trans* enediol.

During attempts to obtain only the *trans* enediol, in which the acetic acid was of course omitted, it was observed that the addition of a drop or two of piperidine seemed to accelerate formation of the *trans* enediol during the primary reduction period. In no case, however, whether piperidine was used or not, was quantitative reduction to the *trans* enediol observed. Colorless solutions, indicating complete reduction and containing suspended *trans* enediol, invariably turned yellow a few minutes after filtration. This was caused by the presence of *cis* enediol; methanol in contact with the *trans* enediol does not undergo this change.

The best results were obtained when one gram of benzil in 30 cc. of methanol, to which one or two drops of piperidine was added, was reduced and a catalytic contact period of several hours was allowed after reduction. Under such conditions the yield of the *trans* enediol was about 0.8 g. The solutions again turned yellow, indicating the presence of the *cis* form. Prolongation of the catalytic contact period to fifteen hours did not increase the yield.

It was not possible to transform the *cis* enediol obtained by reduction with the aid of acetic acid to the *trans* enediol by continued shaking with fresh catalyst after an excess of piperidine (5 cc.) was added to the solution in which reduction had taken place.

**2,2',4,4',6,6'-Hexaisopropylstilbenediol Dimethyl Ether.**—The Grignard reagent from 6 cc. of ethyl bromide and 2.43 g. of magnesium was prepared in 50 cc. of *n*-butyl ether in an atmosphere of nitrogen. To this solution was added 10 g. of 2,2',4,4',6,6'-hexaisopropylbenzil. The mixture was stirred for one-half hour, warmed, and 27 cc. of methyl sulfate was added slowly. At the end of the addition the mixture was heated to a reflux temperature and then allowed to stand overnight. After treatment with 100 cc. of 20% hydrochloric acid the mixture was subjected to steam distillation. From the residue there was obtained 8.4 g. of the ether. Recrystallization was effected from a methanol-benzene mixture; the melting point was 178.5–179.5°.

*Anal.* Calcd. for  $C_{34}H_{52}O_2$ : C, 83.00; H, 10.55. Found: C, 83.09; H, 10.53.

### Summary

Hexaisopropylbenzil has been reduced to the corresponding stilbenediol which exists in *cis* and *trans* modifications. These substances are much more resistant to oxidation than are other known enediols.

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