

equilenone (desoxyequilenin and desoxyisoequilenin) is described.

Neither compound has shown estrogenic ac-

tivity when injected into ovariectomized rats in amounts up to 500 γ .

ANN ARBOR, MICHIGAN

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

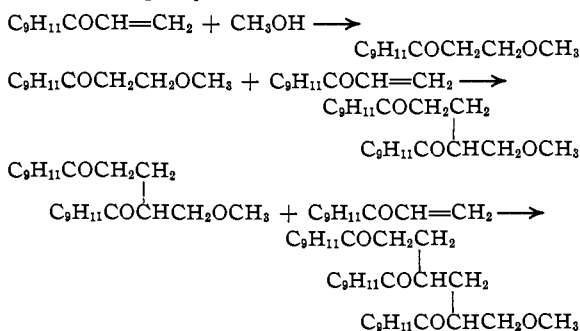
The Trimerization of Vinyl Mesityl Ketone

BY REYNOLD C. FUSON AND C. H. MCKEEVER¹

The polymerization of vinyl mesityl ketone was attempted in order to study the effect of steric hindrance on this type of reaction.

Vinyl mesityl ketone was prepared from mesitylene and β -chloropropionyl chloride by the Friedel-Crafts method. Apparently the β -chloropropionemesitylene which might have been expected spontaneously lost hydrogen chloride. The vinyl ketone absorbed bromine to give a dibromide from which it could be regained by treatment with sodium iodide. It readily decolorized a dilute solution of potassium permanganate. Reduction using Raney nickel as catalyst yielded propiomesitylene. The saturated ketone was identified by comparison of its dinitro derivative with an authentic sample.

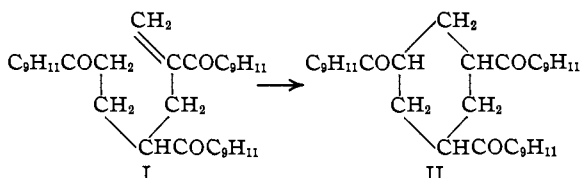
The vinyl ketone is very stable. It can be distilled undecomposed and even after years' standing exposed to the air shows no change. Polycondensation was induced, however, by heating in the presence of methanol and anhydrous potassium carbonate. The chief product was a trimer. The formation of the trimer may be pictured in the following way.



Loss of a molecule of methanol from the trimolecular condensation product would give the trimer, I.

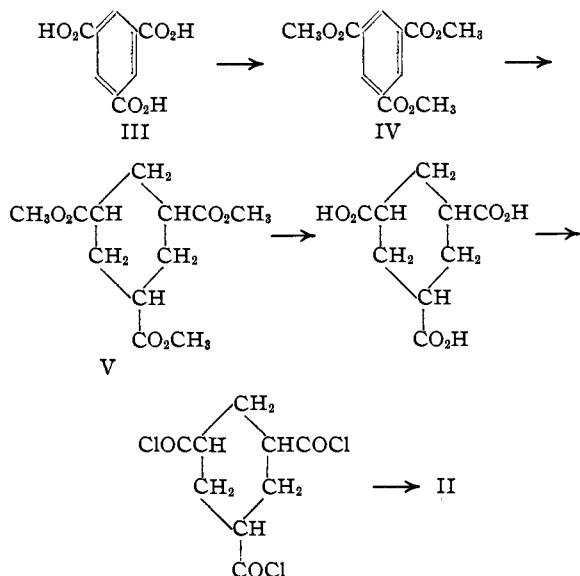
It appeared likely that the failure of the condensation to continue beyond the trimer stage might be due to cyclization. The ring closure

step would be similar in nature to the condensations proposed to explain the formation of the linear products.



The cyclic structure (II) would also account for the failure of the trimer to give tests for unsaturation.

The highly hindered character of the triketone complicated the problem of identification by methods which involved degradation. Its synthesis was therefore attempted. 1,3,5-Trimesitoylcyclohexane was made from trimesic acid by the following sequence of reactions.

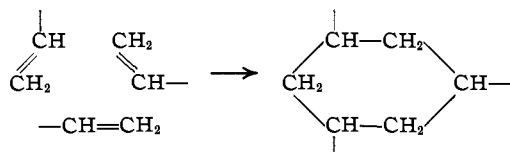


The methyl hexahydrotrimesate (V) was obtained by reducing methyl trimesate (IV) with Raney nickel under pressure. The reduced ester was purified and analyzed but the corresponding free

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acid and its acid chloride were used without purification.

The synthetic 1,3,5-trimesitylcyclohexane proved to be identical with the trimer from vinyl mesityl ketone. The result not only confirms the identity of the trimer but also supports the mechanism proposed for its formation from the vinyl ketone. In other words, it is established that three vinyl groups combine to form a cyclohexane ring.



This type of ring formation, so well known in the cyclobutane series, has apparently not been realized with a six-membered homocyclic ring. It is formally similar to the ring closure used to explain the formation of heterocyclic trimers from aldehydes and thioaldehydes.

The yield of the trimer was 65–70% of the theoretical. From the residual oil two by-products were isolated. One (m. p. 83–83.5°) was unsaturated and had a molecular weight which corresponds to a dimer of vinyl mesityl ketone. The other (m. p. 150–151°) was a trimer, presumably a stereoisomer of the one melting at 210–212°. The polycondensation of vinyl mesityl ketone resembles that of acrolein and methacrolein reported by Gilbert and Donleavy.²

Experimental

Preparation of Vinyl Mesityl Ketone.—A mixture of 54 g. of β -chloropropionic acid and 45 g. of phosphorus trichloride was heated on a steam cone for one hour. The solution was allowed to cool and 100 cc. of carbon disulfide added. The resulting solution was decanted into a 500-cc. three-necked flask and about 200 cc. of carbon disulfide and 65 g. of mesitylene were added. The solution was cooled to 10° and 70 g. of aluminum chloride was added in small portions over a period of one hour to the vigorously stirred mixture. The ice-bath was removed and the stirring continued for an additional three hours. The mixture, now dark brown, was decomposed by pouring on a mixture of 1.5 kg. of cracked ice and 200 cc. of concentrated hydrochloric acid. The carbon disulfide was evaporated and the solution extracted with three portions of benzene. The benzene extracts were washed with water, 5% sodium carbonate solution, and then water again. The benzene was removed and the light yellow oil which remained was fractionally distilled under diminished pressure. There was obtained 55 g. (63% of the theoretical amount) of an oil which boiled at 99–101° (3.5 mm.), d_{20}^{20} 0.9895, n_D^{20} 1.5290.

(2) Gilbert and Donleavy, *THIS JOURNAL*, **60**, 1737, 1911 (1938).

*Anal.*³ Calcd. for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.66; H, 8.12.

When the β -chloropropionyl chloride was added at room temperature to a mixture of mesitylene, aluminum chloride and carbon disulfide, the yield of vinyl mesityl ketone was reduced to 20 g. (25% of the theoretical amount). In this case there was obtained 20 g. of material which boiled at 200–210° (5 mm.) and melted after recrystallization from methyl alcohol at 80–81°. This compound, presumably β -mesitylpropionimesitylene, was not investigated.

Anal. Calcd. for $C_{21}H_{26}O$: C, 85.66; H, 8.90. Found: C, 85.53; H, 8.63.

Catalytic Reduction of Vinyl Mesityl Ketone.—To a solution of 5 g. of the ketone and 150 cc. of ethyl alcohol was added a small amount of Raney nickel. The reduction was run at room temperature for one hour under two atmospheres pressure. One mole of hydrogen was absorbed. The mixture was filtered and the ethyl alcohol evaporated. Distillation *in vacuo* yielded 4.3 cc. of a liquid, b. p. 119–121° (11 mm.). One gram of this liquid was nitrated according to the procedure of Fuson, Ross and McKeever.⁴ There was obtained 0.8 g. of white flakes which melted at 143.5–144.5°. Nitration of a known sample of propionimesitylene gave the same compound.⁵

Anal. Calcd. for $C_{12}H_{14}N_2O_5$: N, 10.52. Found: N, 10.53.

Preparation of α,β -Dibromopropionimesitylene.—To a solution of 5 g. of vinyl mesityl ketone and 15 cc. of carbon tetrachloride was added dropwise at 5° a solution of 4.8 g. of bromine and 5 cc. of carbon tetrachloride. The mixture was poured into water, and the carbon tetrachloride layer separated and washed with 5% sodium hydroxide, then with water, and dried over calcium chloride. When the solvent was removed, there remained 9 g. of a solid which recrystallized from methyl alcohol in long white needles; m. p. 78.5–79.5°.

Anal. Calcd. for $C_{12}H_{14}OBr_2$: C, 43.15; H, 4.22; Br, 47.85. Found: C, 43.10; H, 4.20; Br, 47.95.

Action of Sodium Iodide on α,β -Dibromopropionimesitylene.—Three-tenths of a gram of α,β -dibromopropionimesitylene was treated with sodium iodide as described by Fuson, Ross and McKeever.⁴ The iodine color appeared rather slowly. There was obtained four drops of light yellow halogen-free oil which possessed the characteristic penetrating odor of vinyl mesityl ketone. This oil was reconverted to the dibromide by treatment with bromine.

Action of Methylmagnesium Iodide on Vinyl Mesityl Ketone.—Ten grams (0.057 mole) of the ketone was added dropwise, with stirring, to the Grignard reagent obtained from 1.524 g. (0.063 atom) of magnesium and 8.95 g. (0.063 mole) of methyl iodide. After the addition was complete, the solution was refluxed for two hours, then decomposed by pouring into 100 cc. of ice water acidified with hydrochloric acid. The ether layer was separated, washed with water and dried over anhydrous

(3) The analyses in this paper are microanalyses and were carried out by Mr. L. G. Fauble, Mr. W. H. Taylor and Miss Mary S. Kreger.

(4) Fuson, Ross and McKeever, *THIS JOURNAL*, **61**, 414 (1939).

(5) This compound was first prepared by Dr. C. H. Fisher.

sodium sulfate. The ether was removed and the oil distilled *in vacuo*. There was obtained 4 cc. of a liquid which boiled at 120–121° (7 mm.) and 3 g. of residue which could not be distilled. One-half gram of this compound was nitrated in the usual manner.⁴ There was obtained 0.5 g. of white needles, m. p. 133–135°.

n-Butyromesitylene was prepared by the Friedel-Crafts method from *n*-butyryl chloride and mesitylene and a sample nitrated. The dinitro derivative crystallized from ethyl alcohol as long white needles, m. p. 133–135°.

Anal. Calcd. for $C_{13}H_{16}O_2N_2$: N, 10.00. Found: N, 10.02.

The melting point of a mixture of these dinitro derivatives was not depressed.

Preparation of β -Chloropropiomesitylene.—Fifteen grams of the ketone was stirred vigorously for seventy-two hours with 120 cc. of concentrated hydrochloric acid. The solution was diluted with water and extracted with ether. The ether extracts were washed with water, then dilute sodium hydroxide solution and finally with several more portions of water. The solution was dried over anhydrous sodium sulfate, the solvent removed under diminished pressure and the remaining oil distilled *in vacuo*. There was obtained 6 g. of the starting material, b. p. 103–105° (4.5 mm.), and 8 g. of a pale yellow liquid, b. p. 123–126° (2 mm.). On cooling and scratching the sides of the container this latter compound completely solidified. It was recrystallized from low-boiling petroleum ether; m. p. 46.5–47.5°.

Anal. Calcd. for $C_{14}H_{18}OCl$: C, 68.42; H, 7.18; mol. wt., 211. Found: C, 68.65, 68.58; H, 6.96, 7.15; mol. wt. (in boiling chloroform), 216.9, 217.7.

The low-boiling fraction was identified as vinyl mesityl ketone by converting it to the dibromide.

Attempts to Polymerize Vinyl Mesityl Ketone.—A mixture of 5 g. of vinyl mesityl ketone and 0.2 g. of benzoyl peroxide was heated to 90° for nine hours. The solution darkened slightly but did not become viscous. When it was distilled *in vacuo* there was recovered 4.5 g. of vinyl mesityl ketone. The same result was obtained when ascaridole was used as the catalyst.

Trimerization of Vinyl Mesityl Ketone.—A mixture of 10 g. of the ketone, 50 cc. of methyl alcohol and 1 g. of anhydrous potassium carbonate was refluxed on a steam cone for sixteen hours. After about three hours a white solid began to precipitate from the solution. The reaction mixture was allowed to cool, acidified with dilute hydrochloric acid and filtered. The solid was washed thoroughly with small portions of cold methyl alcohol and dried; yield 7 g. It crystallized from absolute alcohol as small white needles, m. p. 210–212°. This compound failed to decolorize dilute potassium permanganate or absorb bromine in carbon tetrachloride solution.

Anal. Calcd. for $C_{36}H_{42}O_3$: C, 82.72; H, 8.10; mol. wt., 522. Found: C, 82.42; H, 8.27; mol. wt. (in boiling chloroform), 517.

The filtrates and mother liquor were poured into water, extracted with ether and the ether extracts washed with water and dried over calcium chloride. The ether was removed and the residue distilled *in vacuo*. About 0.5 g. of thick light yellow oil, b. p. 236–242° (3 mm.), was ob-

tained. This compound solidified after two days. It was recrystallized from methyl alcohol and melted at 83–83.5°.

Anal. Calcd. for $C_{24}H_{28}O_2$: C, 82.72; H, 8.10; mol. wt., 348. Found: C, 82.84; H, 8.05; mol. wt. (Rast), 339, 344.

It decolorized dilute potassium permanganate immediately and also a solution of bromine in carbon tetrachloride.

The residue from the distillation was dissolved in acetone. When the solvent was allowed to evaporate there remained a small amount of solid which was recrystallized from methyl alcohol. After several recrystallizations the melting point was 150–151°. This compound failed to decolorize dilute potassium permanganate or bromine solutions.

Anal. Calcd. for $C_{36}H_{42}O_3$: C, 82.72; H, 8.10; mol. wt., 522. Found: C, 82.88; H, 8.23; mol. wt. (Rast), 517, 521.

If the reaction mixture was refluxed for only eight hours the yields of high-melting trimer, dimer and low-melting trimer were 4 g., 2.5 g. and 1.7 g., respectively.

Synthesis of 1,3,5-Trimesitoylcyclohexane

A. Preparation of Methyl Trimesate.—A solution of 27 g. of trimesic acid, 250 cc. of methyl alcohol and 5 cc. of concentrated sulfuric acid was refluxed for one-half hour. Two-thirds of the methyl alcohol was removed by distillation, dried over anhydrous potassium carbonate and poured back into the reaction chamber. This process was repeated. When the reaction mixture was allowed to cool there precipitated a large amount of white needles which were removed by filtration and dissolved in 300 cc. of ether. The filtrate was poured into water and extracted with ether. The ether solutions were combined, washed thoroughly with 10% potassium bicarbonate solution, then with water and dried. The ether was removed and the solid ester recrystallized from methyl alcohol. There was obtained 22 g. of long white needles which melted at 144–145°. Five grams of trimesic acid was recovered from the potassium bicarbonate extracts.

B. Preparation of Methyl Hexahydrotrimesate.—To a solution of 15 g. of methyl trimesate and 40 cc. of dioxane was added one-fourth teaspoonful of Raney nickel. The mixture was reduced in a bomb at 175° under 2750 pounds pressure. The reduction was complete in two hours. The reaction mixture was diluted with acetone, filtered, the solvents were removed and the residue was distilled *in vacuo*. There was obtained 1 cc. of forerun, 12 cc. of almost colorless oil, b. p. 162–165° (2.5 mm.), and almost no residue. When redistilled the oil came over at 163–164° (2.5 mm.).

Anal. Calcd. for $C_{12}H_{18}O_6$: C, 55.80; H, 7.02. Found: C, 55.86; H, 7.00.

The product appeared to be a mixture of the stereoisomeric forms of methyl hexahydrotrimesate. After standing for two days the oil partially crystallized as colorless needles which, after recrystallization from low-boiling petroleum ether or methanol, melted at 42–44°.

C. Preparation of the Triketone.—Eight grams of methyl hexahydrotrimesate was refluxed with 100 cc. of

(6) Von Pechmann, *Ann.*, **264**, 296 (1891).

15% sodium hydroxide until the ester completely dissolved. The solution was acidified with dilute hydrochloric acid and evaporated to dryness. It was ground to a fine powder and, after drying for twenty-four hours over phosphorus pentoxide, was treated with 30 cc. of thionyl chloride. The reaction mixture was allowed to stand overnight at room temperature, then warmed to 60° for three hours. The excess thionyl chloride was removed and the fluffy solid transferred to a 250-cc. three-necked flask. Fifty grams of mesitylene and 50 cc. of carbon disulfide were added and stirring was started; then 25 g. of aluminum chloride was introduced in small portions over a period of thirty minutes. The reaction mixture, a thick dark red paste, was diluted with an additional 50 cc. of carbon disulfide and stirred vigorously for two hours. It was decomposed by pouring upon a mixture of 500 g. of ice and 50 cc. of concentrated hydrochloric acid. The carbon disulfide was evaporated, the solution extracted with 250 cc. of benzene and the benzene extracts were washed thoroughly with water, 10% potassium bicarbonate and again with water. The benzene and mesitylene

were removed at diminished pressure. There remained a tan solid which was washed with methyl alcohol then crystallized from absolute alcohol. The 1,3,5-trimesitylcyclohexane crystallized in long white needles and melted at 210–212°; yield, 4.5 g. The melting point of a mixture of this compound and the trimer of vinyl mesityl ketone showed no lowering.

Summary

Vinyl mesityl ketone has been prepared from mesitylene and β -chloropropionyl chloride by the Friedel-Crafts method.

It is remarkably stable and fails to undergo polymerization in the presence of peroxides.

However, when heated in the presence of methanol and potassium carbonate it trimerizes to 1,3,5-trimesitylcyclohexane. The structure of the triketone has been proved by synthesis.

URBANA, ILLINOIS

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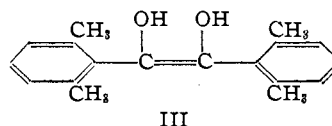
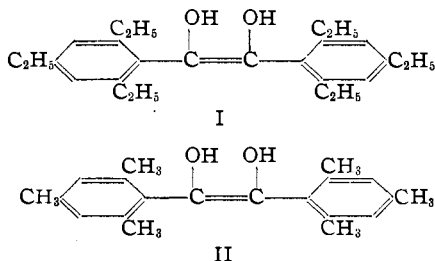
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Enediols. IV. *cis-trans* Isomerism

BY REYNOLD C. FUSON, S. L. SCOTT, E. C. HORNING¹ AND C. H. MCKEEVER²

Stilbenediols might be expected to exist in *cis* and *trans* modifications. Of those known up to now one (I), that from hexaethylbenzil, has been isolated in a single form³ while the other (II), derived from mesityl, has been reported to exist in two forms.⁴ Thompson^{4b} recognized these two forms as geometrical isomers. The fact that these enediols are stable in the absence of oxygen, showing no tendency to rearrange spontaneously to the corresponding benzoin, is in keeping with Thompson's interpretation.

It has now been possible to confirm the correctness of this idea and to extend it to the hexaethyl (I) and tetramethyl (III) analogs.



Each of the three is now known in two modifications. By analogy with other *cis-trans* compounds, it seems highly probable that of a given pair the lower melting compound possesses the *cis* configuration and the higher melting form has the *trans* arrangement. Accordingly, these designations will be used in describing the enediols.

The method for making them is essentially that of Thompson.^{4b} It has been found that catalytic hydrogenation can be used to prepare either form at will. Whether the product is the *cis* or the *trans* form of the enediol, depends only on the duration of the treatment with platinum and hydrogen. If the hydrogenation is interrupted as soon as the yellow color of the benzil has disappeared the product is the *cis* compound. If the process is sufficiently prolonged the *trans* compound is produced.

Apparently the *cis*-enediol, always produced initially, slowly isomerizes in the presence of the catalyst and hydrogen to yield the corresponding *trans*-enediol. In fact, the pure *cis* modification can be transformed to the corresponding *trans*

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

(2) Röhm and Haas Research Assistant.

(3) Fuson, Corse and McKeever, *THIS JOURNAL*, **61**, 2010 (1939).

(4) (a) Fuson and Corse, *ibid.*, **61**, 975 (1939); (b) Thompson, *ibid.*, **61**, 1281 (1939); (c) Fuson, McKeever and Corse, *ibid.*, **62**, 600 (1940).