

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

The Preparation and Alkylation of 1,4-Dimesityl-3-methyl-1,2,4-butanetrione Enol

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The substitution of halogen, alkyl, phenyl or benzoyl on the 3-carbon of 1,4-diphenyl-1,2,4-butanetrione enol promotes cyclization and stabilizes the hydroxyfuranone form. The effect of these groups on the keto-enol tautomerism is obscured because of the cyclization. On the other hand, the 1,4-dimesityl compound and its bromo derivative² do not cyclize because of the excessive steric hindrance, and in these types the keto-enol reactions can be investigated without this complication. It seemed desirable to study a few more examples of this type, and the present report deals with the preparation and alkylation of the 3-methyl derivative.

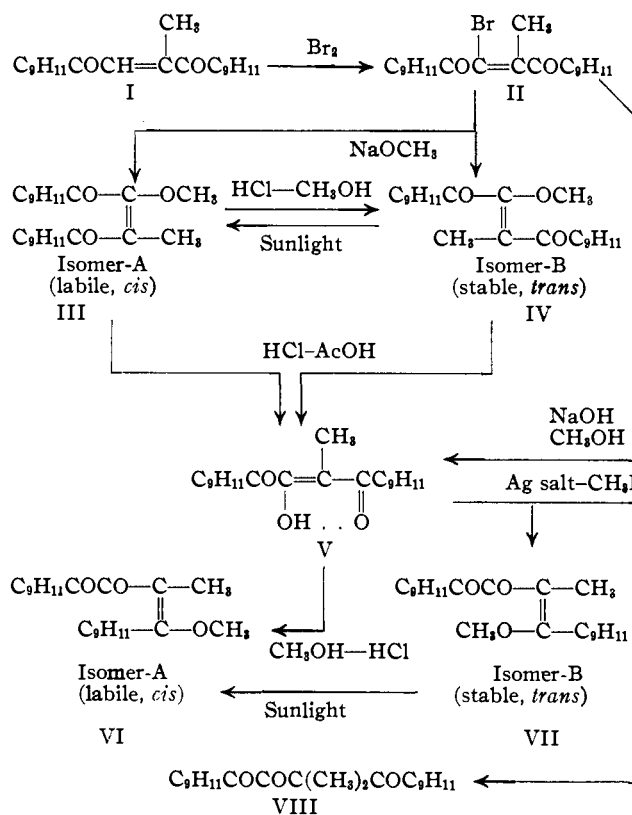
The 3-methyl triketone enol (V) was first obtained as a minor product in the alkylation of the silver salt of 1,4-dimesityl-1,2,4-butanetrione enol.³ A better method of preparation has now been devised which also demonstrates the structure of the product. This synthesis started from dimesitylmethylethylene (I) which was made from mesaconyl chloride by the Friedel-Crafts reaction. Bromination gave *cis*-bromodimesitylmethylethylene (II).⁴ The bromo compound reacted with sodium methoxide to give two enol methyl ethers which from their mode of formation must be the *cis*- and *trans*-isomers (III and IV). Acid hydrolysis of these ethers, or alkali hydrolysis of the bromo unsaturated diketone itself (II), gave the desired triketone enol (V) in good yield.

The triketone enol (V) is yellow in color, gives a red color with ferric chloride and reacts rapidly with bromine and with diazomethane. It is strongly acidic as is shown by its solubility in sodium carbonate and it gives an unstable brilliant yellow silver salt. It shows no tendency to cyclize to a hydroxyfuranone.

The methylation with diazomethane gave four isomeric compounds. Two of these proved to be

the *cis*- and *trans*-2-methyl ethers (III and IV) which were obtained as mentioned above by the action of sodium methoxide on the bromo unsaturated diketone (II). One was assigned the *cis*-configuration (III) on the basis of its instability and conversion by means of methanolic hydrogen chloride into the other which was stable and therefore was assumed to be *trans* (IV). The inversion in the opposite direction from *trans* to *cis* was accomplished by exposure to sunlight in pure methanol.

The other two of the four isomeric methylation products were shown also to be enol ethers by the



facile acid hydrolysis to the enol (V). By difference they must be the structurally isomeric *cis*- and *trans*-4-methyl ethers (VI and VII). The *cis*-*trans* relationship was confirmed by the inversion of one (the stable) into the other (the labile) by the action of sunlight; unfortunately, inversion in the opposite direction was not accomplished. We are assuming tentatively that the labile form

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(2) (a) Lutz and Wood, THIS JOURNAL, 60, 705 (1938); (b) Lutz and Terry, J. Org. Chem., 7, 274 (1942).

(3) Lutz and Terry, *ibid.*, 7, 320 (1942).

(4) Lutz and Terry, THIS JOURNAL, 64, 2426 (1942).

is that one which has the mesityl and mesityl-glyoxyl groups on the same side of the molecule, namely, VI.

One striking fact was observed in this series, namely, that the enol (V) reacted readily and quantitatively with methanolic hydrogen chloride to give the *labile* 4-methyl ether (VI). This type of reaction does not take place with dimesitylbutanetrione enol itself (the diphenyl analogs all give the alkoxyfuranones under these conditions). There is analogy for direct etherification of a strongly acidic enolic hydroxyl in the case of hydroxynaphthoquinone, where etherification to 2-methoxy-*p*-naphthoquinone takes place under these conditions.⁵ In the case in hand it is perhaps surprising that the *labile* 4-methyl ether should be the one formed.

The formation of all of the four possible isomeric ethers in the reaction between the enol (V) and diazomethane calls to mind the formation of three of the four possible isomeric ethers in the similar methylation of the dimesitylbutanetrione enol itself.³ It is clear from these results that there is no simple stereochemical relation between the products of methylation and the presumably chelated enols from which they were made.

Alkylation of the silver salt of the enol (V) was of interest because it was expected to produce results closer to those obtained in the case of dimesitylbutanetrione silver enolate than to those obtained in the case of the diphenyl analog. The dimesityl triketone silver enolate underwent chiefly oxygen-alkylation at the 4-oxygen whereas the diphenyl analog was found to undergo mainly carbon-alkylation. The results in the present case were approximately as predicted. Dimesitylmethylbutanetrione silver enolate reacted with methyl iodide to give a mixture of carbon and oxygen-alkyl derivatives. The carbon-alkyl derivative (VIII) was obtained in a yield of 30%. The oxygen-alkyl derivative was obtained in 65% yield and was the expected 4-enol methyl ether, but it was the stable stereoisomer-B (VII).

In summary of the alkylation results it may be said that diazomethane reacts with the enol to give all four 2- and 4-enol ethers; methanolic hydrogen chloride gives the *labile* 4-enol ether; and the silver salt with methyl iodide gives the stable 4-enol ether along with a lesser but sizeable yield of the carbon-alkyl derivative. The marked tendency to react at the 4-oxygen is noteworthy.

(5) Fieser, *THIS JOURNAL*, **48**, 2922 (1928).

Experimental

1,4-Dimesityl-3-methyl-1,2,4-butanetrione Enol (V).—A suspension of 4.5 g. of the *cis*-2-enol methyl ether (III) in 40 cc. of concd. acetic acid, 10 cc. of concd. hydrochloric acid and 5 cc. of water was stirred vigorously at room temperature for three hours. The solution became bright yellow, and 4.25 g. (98%) of bright yellow needles separated (m. p. 120–122°). When the reaction mixture was refluxed the yields were smaller and a larger amount of non-crystalline material formed. Repeated crystallizations from methanol brought the melting point to 124.5–125°.

Anal. Calcd. for $C_{23}H_{26}O_3$: C, 78.86; H, 7.5. Found: C, 78.40, 78.81; H, 7.23; 7.39.

Alternative preparations are as follows.

(a) A suspension of 1.5 g. of the *cis*-bromo unsaturated diketone (II) in 75 cc. of 90% methanol and 1.5 g. of sodium hydroxide was refluxed for ten minutes after solution was complete. The purple solution was acidified with dilute hydrochloric acid, diluted with water and extracted several times with ether. The ether extract was shaken four times with 25-cc. portions of 5% sodium hydroxide. Acidification of the alkaline solution and extraction with ether removed the enol which was isolated as a partly crystallized residue upon evaporation of the solvent. Crystallization from ethanol gave 0.8 g. (64%).

In a similar experiment using 80% methanol and refluxing for one hour, largely non-crystalline material was obtained along with a 30% (by weight) yield of a colorless solid which upon repeated crystallization from ethyl acetate melted at 234° (it contained no halogen). *Anal.* C, 81.98; 81.73; H, 6.90; 6.77. This compound has not been investigated.

(b) The action of methyl iodide on the dimesitylbutanetrione silver enolate in isopropyl ether (refluxing for two hours) gave the carbon-methyl derivative (V) in 7% yield.

(c) Hydrolysis of the *cis*-2-enol methyl ether by means of saturated methanolic hydrogen chloride gave the enol (V) in 81% yield.

The enol (V) gave a deep maroon color with alcoholic ferric chloride. It is soluble in aqueous sodium carbonate.

The sodium enolate did not crystallize from a methanol solution. It proved to be quite soluble in water and alcohol, in contrast to the sodium salt of the parent dimesitylbutanetrione enol. The silver salt (bright yellow) was precipitated from an aqueous or methanolic solution of the sodium salt by the addition of silver nitrate; it darkened rapidly on standing and was black within twenty minutes.

Hydroxylamine in pyridine or in methanol was without action, as also was semicarbazide and 2,4-dinitrophenylhydrazine in ethanol.

Methylation by Diazomethane.—Two grams of the enol (V) was added to 50 cc. of ether containing 0.4 g. of diazomethane. After the vigorous reaction subsided the solution was allowed to stand overnight and was washed with dilute hydrochloric acid and with water. Upon evaporation of the ether in a current of dry air, an oil was obtained from which digestion with ethanol produced a crystalline precipitate (0.72 g. or 44%) which proved to be the main product, the 2-enol methyl ether-A (*cis*) (III) (described under this

compound). A second fraction (0.18 g., 9%) was then obtained and shown to be the *trans*-2-enol methyl ether (IV) (described under that compound). Upon standing the filtrate deposited a third compound (yield 15%) which was found to be the *cis*-4-enol methyl ether (VI) (described under that compound). Careful manipulation of the residues produced a fourth and more soluble isomer in a 30% yield. This was obtained from 90% ethanol and was shown to be the 4-enol methyl ether-B (*trans*) (VII) (described under that compound).

Alkylation of the Silver Enolate with Methyl Iodide.—A methanol solution of 1.2 g. of the enol (V) and one equivalent of sodium methoxide was treated with 3.5 cc. of methyl iodide. The mixture was stirred mechanically and maintained at 0°. An aqueous solution (65 cc.) of 2% silver nitrate was added slowly and stirring was continued for three hours while the mixture was allowed to come to room temperature. The mixture was then heated on a water-bath at 60° for one hour, filtered from silver iodide, diluted with water and extracted with ether. The ether solution was shaken three times with 20-cc. portions of 10% sodium hydroxide which removed the unchanged enol present (0.34 g. was recovered). Evaporation of the ether gave a bright yellow solid which was washed with methanol; yield 0.58 g. (65%). This proved to be the 4-enol methyl ether-B (*trans*) (VII). From the methanol solution 0.3 g. (37%) of bright yellow crystals of the dimethyltriketone (VIII) was isolated (see that compound).

***cis*-1,4-Dimesityl-3-methyl-1,2,4-butanetrione 2-Enol Methyl Ether (III).**—This compound was obtained as described under the methylation of the enol with diazomethane (yield 44%). It was obtained in better yield as follows.

A mixture of 2.5 g. of *cis*-bromodimesitylmethylethylene (II) and 50 cc. of methanol containing 2 g. of dissolved sodium was stirred for two hours at room temperature. The colored solution was concentrated and diluted with water slowly; 0.22 g. (12%) of pale yellow crystals separated and was identified as the *trans*-2-enol methyl ether-B (described below). Further concentration of the filtrate produced 1.08 g. (58%) of a more soluble and colorless product. This was recrystallized repeatedly from methanol and melted at 134.5–135°. This latter compound was obtained in almost quantitative yield by exposing a methanol solution of the *trans*-isomer-B (V) to the action of sunlight for eight hours.

Anal. Calcd. for $C_{24}H_{28}O_3$: C, 79.12; H, 7.74; OCH_3 , 8.5. Found: C, 78.93; H, 7.63; OCH_3 , 8.79, 8.44.

Hydrolysis of 4 g. in a mixture of concd. acetic acid, 10 cc. of concd. hydrochloric acid and 5 cc. of water, at room temperature (three hours) or under refluxing for fifteen minutes, gave nearly quantitative yields of the enol (V).

The enol ether (III) was recovered unchanged after (a) exposure to sunlight for six hours in chloroform containing a trace of iodine; and (b) treatment with alcoholic sodium acetate under reflux for seven hours.

Treatment of 0.5 g. of the compound for five days with saturated methanolic hydrogen chloride gave two crystalline fractions. The first (0.3 g.) was the *trans*-isomer-B (IV), and the second (0.15 g.) the enol (V).

***trans*-1,4-Dimesityl-3-methyl-1,2,4-butanetrione 2-Enol Methyl Ether-B (IV).**—This compound was obtained as

described above in 12% yield by the action of sodium methoxide on the *cis*-bromo unsaturated diketone (II), and in 9% yield by the action of diazomethane on the enol (V). It was obtained also in 60% yield by the action of saturated methanolic hydrogen chloride on the *cis*-isomer-A (III) at room temperature for five days (as described above). The *trans*-isomer-B was purified by repeated crystallizations from ligroin, 85% methanol, and methanol; pale yellow crystals of m. p. 156.5–157°.

Anal. Calcd. for $C_{24}H_{28}O_3$: OCH_3 , 8.52. Found: OCH_3 , 8.48.

Hydrolysis of 0.5 g. by a mixture of 10 cc. of concd. acetic acid, 3 cc. of concd. hydrochloric acid and 2 cc. of water at room temperature for three hours gave 0.3 g. (6%) of nearly pure enol (V).

***cis*-(?) -1,4-Dimesityl-3-methyl-1,2,4-butanetrione 4-Enol Methyl Ether-A (VI).**—A solution of 0.45 g. of the enol (V) in saturated methanolic hydrogen chloride was allowed to stand for five days at room temperature. Evaporation in an air stream gave 0.44 g. (92%) of product which was crystallized repeatedly from methanol and obtained as colorless prisms of m. p. 142°.

Anal. Calcd. for $C_{24}H_{28}O_3$: C, 79.12; H, 7.74; OCH_3 , 8.52. Found: C, 78.25; H, 7.99; OCH_3 , 8.33.

This compound was obtained also in 15% yield in the methylation of the enol with diazomethane, as described above. It was also obtained by the action of sunlight for seven hours on a methanol solution of the *trans*-isomer-B (VII).

Hydrolysis of 0.25 g. by 25 cc. of concd. acetic acid, 4 cc. of concd. hydrochloric acid and 3 cc. of water under reflux for fifteen hours gave 0.2 g. (83%) of nearly pure enol (V). Treatment of the ether (VI) with methanolic potassium hydroxide under reflux for five hours was without effect. This ether was not changed by exposure to sunlight for six hours in chloroform containing a trace of iodine.

***trans*-(?) -1,4-Dimesityl-3-methyl-1,2,4-butanetrione 4-Enol Methyl Ether-B (VII).**—This isomer was prepared as described above by the action of methyl iodide on the silver enolate and also by the action of diazomethane on the enol. Upon repeated crystallization from methanol it was obtained as pale yellow needles of m. p. 119.5–120°.

Anal. Calcd. for $C_{24}H_{28}O_3$: C, 79.12; H, 7.74; OCH_3 , 8.52. Found: C, 78.57; H, 8.09; OCH_3 , 8.79.

Hydrolysis of 0.25 g. in the concd. acetic-hydrochloric acid-water mixture (refluxing for one and one-half hours) gave 0.21 g. (81%) of nearly pure enol (V). The compound was recovered unchanged after treatment with (a) methanolic potassium hydroxide (refluxing for ten hours) and (b) saturated methanolic hydrogen chloride (for three days at room temperature).

1,4-Dimesityl-3,3-dimethylbutanetrione-1,2,4 (VIII).—This bright yellow compound was obtained as described above in the methylation of the silver enolate of (V) by methyl iodide. Repeated crystallizations from ethanol brought the melting point to 132.5–133°.

Anal. Calcd. for $C_{24}H_{28}O_3$: C, 79.12; H, 7.74; OCH_3 , 0. Found: C, 79.28, 79.41; H, 7.60, 7.85; OCH_3 , 0.

The compound was recovered unchanged when treated with (a) the concd. acetic-hydrochloric acid-water mixture

