[Contribution from the Noyes Chemical Laboratory, University of Illinois]

REACTIONS OF BROMOMAGNESIUM ENOLATES. IV. THE BIFUNCTIONAL REAGENT DERIVED FROM 1,4-DIMESITOYLBUTANE[1]

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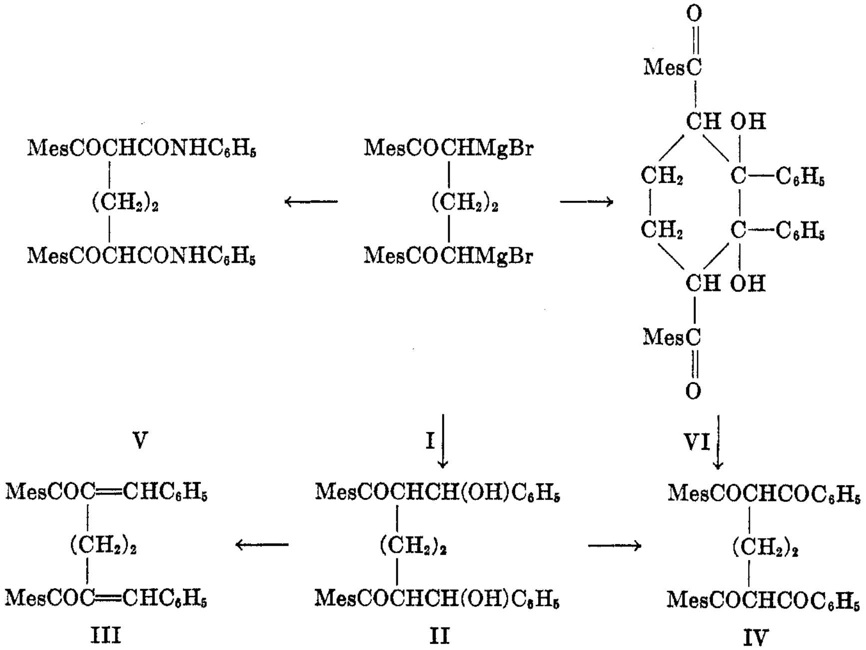
Received March 2, 1954

The complexity of the behavior of the enolates of 1,4-diketones (1) is due at least in part to the proximity of the enolizable functions. In dienolates in which these functions are separated by at least one carbon atom, the interaction between the two might not occur. In the present work the chemistry of the dienolate (I) of 1,4-dimesitoylbutane was investigated. The choice of this compound was prompted in part by the hope that it might lend itself to the formation of carbocycles.

The dienolate was produced by treating the diketone with ethylmagnesium bromide. Normal condensation reactions were realized with a number of reagents. Benzaldehyde yielded the corresponding dihydroxy diketone (II), which by dehydration was converted to the expected dibenzal diketone (III) and by chromic acid oxidation to the tetraketone (IV).



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[1] For the preceding article in this series see Fuson, Hellmann, and Friedlander, *J. Org. Chem.*, **18**, 1263 (1953).

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When *p*-chlorobenzaldehyde was used the derivatives analogous to the dihydroxy diketone (II) and the dibenzal diketone (III) were formed.

Since the reaction of a bromomagnesium enolate with phenyl isocyanate had not been recorded previously, the reaction was explored with the simple monoenolate derived from acetomesitylene. Either the mono- or the di-anilide could be obtained by regulation of the amount of phenyl isocyanate employed.

$$\mathrm{MesCOCH_2MgBr} \rightarrow \mathrm{MesCOCH_2CONHC_6H_5} \rightarrow \mathrm{MesCOCH(CONHC_6H_5)_2}$$

This behavior is completely analogous to that observed when this enolate was treated with acylating agents (2–4) and presumably involves the same mechanism. With the dienolate (I) phenyl isocyanate gave only one product, the dianilide (V) of 2,5-dimesitoyladipic acid. Carbon dioxide reacted in a similar way to give 2, 5-dimesityladipic acid.

Finally, the dienolate reacted with benzil to give a dihydroxy diketone corresponding to the expected cyclohexane derivative (VI). This product was obtained in two forms, presumably stereoisomeric. Isomer A melted at 212° and isomer B at 219°. The structure of isomer B was established by oxidative cleavage with periodic acid, which converted it to the tetraketone (IV) mentioned earlier.

EXPERIMENTAL

Preparation of the dienolate (I) *from 1,4-dimesitoylbutane.* A Grignard reagent was prepared from 0.80 g. of magnesium turnings and an excess of ethyl bromide in 100 ml. of dry ether under an atmosphere of nitrogen. When the magnesium had disappeared, the mixture was diluted with 100 ml. of dry benzene, and a solution of 3.0 g. of 1,4-dimesitoylbutane in 50 ml. of dry benzene was added. When the resulting clear, pale yellow solution was heated gently under reflux, with stirring, for 4 hours, a colorless precipitate of the dienolate gradually formed. This suspension was cooled in an ice-bath and treated with various reagents (still under nitrogen) as described below.

Reaction of the dienolate with benzaldehyde. To a cold suspension of the dienolate was added dropwise a solution of 4.0 g. of freshly purified benzaldehyde in 25 ml. of dry benzene. When the addition was complete, the mixture was heated gently under reflux, with stirring, for 5 hours. The resulting mixture, which had gradually become bright yellow, then was cooled in an ice-bath and decomposed by pouring into iced 20% hydrochloric acid. After the ether-benzene layer had been washed three times with water and dried over sodium sulfate, the solution was evaporated to a small volume with a water pump. A large volume of low-boiling petroleum ether was added and the solution was refrigerated. After several hours the crude 2,5-dimesitoyl-1,6-diphenyl-1,6-hexanediol (II) was deposited as a colorless solid; yield 2.7 g. (57%); m.p. 113–116°. Recrystallization from ether-petroleum ether (2:1) gave colorless plates; m.p. 116–117°.

Anal.[3] Calc'd for $C_{38}H_{42}O_4$: C, 81.10; H, 7.52.
Found: C, 81.06; H, 7.66.

Dehydration of the dihydroxy diketone (II). A mixture of 0.3 g. of the diol, 10 ml. of 95% ethanol, and 3 ml. of concentrated hydrochloric acid was heated on the steam-bath for 1½ hours. The copious white precipitate of 1,4-dibenzal-1,4-dimesitoylbutane (III), recrystallized from ethanol-benzene, melted at 216–217°.

Anal. Calc'd for $C_{38}H_{22}O_2$: C, 86.65; H, 7.27.
Found: C, 86.48; H, 7.41.

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[3] The microcombustions were carried out by Mrs. L. Chang, Mrs. Esther Fett, Miss K. Pih, and Mr. Joseph Nemeth.

This compound was made also by condensing 1,4-dimesitoylbutane with benzaldehyde in the presence of sodium ethoxide or potassium hydroxide.[4] A mixture of 10 g. of 1,4-dimesitoylbutane, 100 ml. of absolute ethanol, and 5 g. of potassium hydroxide was heated under reflux, with stirring, for 30 minutes; 10 g. of benzaldehyde was added rapidly and the heating was continued for one hour. The dibenzal derivative, isolated by conventional procedures, was recrystallized from an ethanol-benzene solution; m.p. 217°; yield 6.4 g. (42%).

Anal. Calc'd for $C_{38}H_{38}O_2$: C, 86.65; H, 7.27.
Found: C, 86.31; H, 7.40.

Comparison of infrared spectra[5] and a mixture melting point determination showed the two products to be identical.

Oxidation of the diol (II). To a solution of 1.0 g. of the dienolate-benzaldehyde adduct (II) in 10 ml. of glacial acetic acid was added in several portions a solution of 1.1 g. of chromic anhydride in 10 ml. of glacial acetic acid and 3 ml. of water. After the solution had been allowed to stand at room temperature for 45 minutes, a precipitate of needle-shaped crystals appeared in the brown solution. The tetraketone (IV) was washed with acetic acid and then with water. It crystallized from ethanol in pale yellow needles; m.p. 201–203°.

Anal. Calc'd for $C_{38}H_{38}O_4$: C, 81.69; H, 6.86.
Found: C, 81.67; H, 6.79.

Reaction of the dienolate with p-chlorobenzaldehyde. The reaction was carried out as described in the benzaldehyde experiment, except that the period of reflux was only 5 hours. After the same work-up procedure, refrigeration of the petroleum ether solution caused a viscous, tan oil to separate. The supernatant liquid was decanted and returned to the refrigerator, where it soon began to deposit crystals. After two days, 1.1 g. of colorless crystals was collected; m.p. 142–145°. The oil was taken up in an ether-petroleum ether solution and again chilled. Additional crops of crystals were obtained until the total yield of diol was 3.14 (58%). Recrystallization from ether-petroleum ether produced crystals which melted at 146–147°.

Anal. Calc'd for $C_{36}H_{40}Cl_2O_4$: C, 72.26; H, 6.38; Cl, 11.23.
Found: C, 72.05; H, 6.58; Cl, 11.05.

Dehydration of 1,6-di(p-chlorophenyl)2,5-dimesitoyl-1,6-hexanediol. A solution of a small amount of the diol in an ethanol-hydrochloric acid mixture was boiled vigorously for 15 minutes. The reaction proceeded as in the case of II; the very pale yellow precipitate (m.p. 235–240°) was recrystallized from ethanol-benzene; m.p. 258–259°.

Anal. Calc'd for $C_{36}H_{36}Cl_2O_2$: C, 76.63; H, 6.09; Cl, 11.91.
Found: C, 76.86; H, 6.00; Cl, 11.67.

Carbonation of the dienolate. A suspension of the dienolate was poured through a glass wool plug into a hydrogenation bottle (4). The bottle was placed in a shaker, solid carbon dioxide was packed around it, and gaseous carbon dioxide was admitted at 40 p.s.i. After 4 hours, the contents were poured into iced hydrochloric acid, washed with cold water, and then extracted twice with cold 5% sodium carbonate solution. The combined carbonate solution was carefully neutralized with dilute hydrochloric acid, and the organic material was taken up in ether. The ethereal layer was separated, low-boiling petroleum ether was added, and the solution refrigerated. After several days at 0°, 2,5-dimesitoyladipic acid separated in colorless needles; m.p. 110–118°. Recrystallization from ether-petroleum ether gave colorless needles; m.p. 115–118°.

Reaction of the dienolate with phenyl isocyanate. To a cooled suspension of the dienolate made from 3.0 g. of dimesitoylbutane was added the theoretical amount (1.9 ml.) of phenyl isocyanate dissolved in 30 ml. of dry benzene. After the reaction mixture had been heated for 5 hours, it was worked up in the usual manner. Chilling the ethereal solution caused the

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[4] This experiment was performed by Dr. Richard F. Heitmiller.

[5] The infrared spectra reported in this paper were recorded and interpreted by Miss Helen Miklas, Mrs. Rosemary Hill, and Mr. James Brader.

separation of 0.58 g. (12%) of the dianilide (V) of 2,5-dimesitoyladipic acid as pale orange crystals which, after recrystallization from ethanol-benzene, melted at 217–218°.

Anal. Calc'd for $C_{38}H_{40}N_2O_4$: C, 77.52; H, 6.85; N, 4.76.
Found: C, 77.51; H, 6.99; N, 4.75.

Reaction of acetomesitylene enolate with phenyl isocyanate. A suspension of the enolate prepared in ether from 0.80 g. of magnesium, an excess of ethyl bromide, and 2.8 g. (2.9 ml.) of acetomesitylene, was heated for 3 hours and cooled. A solution of 3.9 ml. of phenyl isocyanate in 30 ml. of dry benzene was then added dropwise. The reaction, which appeared to be quite rapid, produced a copious gray precipitate, which changed little in appearance when the mixture was heated overnight under reflux.

The mixture was then cooled and decomposed with iced 2% hydrochloric acid. The ether solution was washed several times with water, dried, and condensed by evaporation to a small volume. Most of the product solidified, leaving a small amount of brown oil. Removal of the oil by washing with methanol left 3.58 g. (21%) of colorless crystals; m.p. 141–145°. Recrystallization of the dianilide from methanol-ethanol raised the melting point to 147–148°.

Anal. Calc'd for $C_{25}H_{24}N_2O_3$: C, 74.98; H, 6.04; N, 7.00.
Found: C, 74.96; H, 6.52; N, 6.99.

When the reaction was run with an equimolar amount of phenyl isocyanate, the monoanilide was obtained (2.75 g.; 57%); m.p. 84–88°. After recrystallization from methanol, it melted at 97–99°.

Anal. Calc'd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98.
Found: C, 76.83; H, 6.91; N, 5.22.

Reaction of the dienolate with benzil. To a cold suspension of the dienolate made from 3.0 g. of dimesitoylbutane was added dropwise 1.80 g. of benzil dissolved in 30 ml. of dry benzene and the resulting orange-brown mixture was heated under reflux for 5 hours. The reaction mixture was then worked up with iced hydrochloric acid in the usual manner. The resulting ethereal solution was dried and condensed by evaporation to a small volume. Low-boiling petroleum ether was added and the mixture was refrigerated. After several days a solid was obtained which, when recrystallized from ethanol-benzene, gave 0.25 g. (5%) of colorless needles; m.p. 211–213° (Isomer A).

Anal. Calc'd for $C_{38}H_{40}O_4$: C, 81.39; H, 7.19.
Found: C, 81.14; H, 7.08.

When benzil was used in a ratio of two moles to one of the enolate, the product of the reaction, after recrystallization, melted at 217–219° (Isomer B); yield 37%. A mixture of Isomers A and B melted at 195–210°.

Anal. Calc'd for $C_{38}H_{40}O_4$: C, 81.39; H, 7.19.
Found: C, 81.53; H, 7.43.

After these crystals were collected, about 0.5 g. of lower-melting crystals were obtained from the mother liquor. On recrystallization, these melted at 133–138°. The infrared spectrum and melting point indicate that this product is benzoin (m.p. 137°), produced by reduction of the excess benzil.

The infrared spectra of the two isomers showed the following bands when observed in 5% solution in chloroform:

Isomer A		Isomer B	
3525 cm^{-1}	wk.	3500 cm^{-1}	med., broad
3270	med.	1681	strong
1682	strong	1658	med., shoulder

The bands in the 3200–3500 $cm.^{-1}$ region are attributed to O—H stretching vibrations, while those in the 1600 $cm.^{-1}$ region are due to carbonyl absorption. Both isomers showed bands at 1615 $cm.^{-1}$ and 857 $cm.^{-1}$, attributable to the mesityl group, and at 698 $cm.^{-1}$, attributable to the mono-substituted benzene nucleus.

Oxidation of Isomer B with periodic acid. The glycol was treated with periodic acid according to a modification of a method of Reichstein and von Euw (5). To a solution of 0.25 g. of the glycol in 25 ml. of purified dioxane was added a solution of 0.20 g. of periodic acid in 10 ml. of dioxane and 3 ml. of water. The solution, maintained at 65–75° for 5 hours, turned bright orange. It was then reduced to about half the original volume by evaporation, and the inorganic precipitate was removed. The filtrate was taken up in ether, and the solution, after being extracted several times with water, was washed with sodium bicarbonate solution and with water, and dried. It was then evaporated nearly to dryness on the steam-bath and the residue was taken up in ether-petroleum ether; 0.15 g. (60%) of colorless crystals separated; m.p. 117–123°. After recrystallization from ether-petroleum ether, the compound melted at 124–126°. Comparison of infrared spectra and a mixture melting point determination showed this product to be identical to the tetraketone (IV). When this reaction was conducted at room temperature for 3 days, starting material was recovered.

SUMMARY

The bifunctional bromomagnesium enolate of 1,4-dimesitoylbutane has been prepared and treated with a number of reagents. Normal addition products have been obtained with benzaldehyde, phenyl isocyanate, and carbon dioxide. A cyclization has been effected with benzil.

The monofunctional enolate from acetomesitylene yields both mono- and di-substituted derivatives when treated with phenyl isocyanate.

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