[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Benzylation at the Terminal Methyl Group of Certain Unsymmetrical β-Diketones Through One of Two Possible Intermediate Dicarbanions

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6-Phenyl-2,4-hexanedione, 2-acetylcyclohexanone and 2-acetylcyclopentanone were treated with two molecular equivalents of potassium amide in liquid ammonia, followed by one molecular equivalent of benzyl chloride. Although each of these β-diketones could conceivably be converted into two different dicarbanions, each appeared to form only one dicarbanion, that involving the terminal methyl group, since monobenzylation occurred exclusively at this position. The structures of the alkylation products were established by independent syntheses. The theoretical and practical implications of these results are indicated.

Acetylacetone and benzoylacetone recently[2] have been alkylated with benzyl chloride at the terminal methyl group instead of at the methylene group where alkylation normally has been observed. This novel mode of alkylation was accomplished through the intermediate formation of the corresponding dicarbanion,[3] which was prepared by means of two molecular equivalents of potassium amide in liquid ammonia. The reaction may be illustrated with acetylacetone (equation 1).

$$CH_3COCH_2COCH_3 \xrightarrow[\text{liq. } NH_3]{2KNH_2} CH_3CO\overset{-}{C}HCO\overset{-}{C}H_2 \xrightarrow[2,\ NH_4Cl]{1,\ C_6H_5CH_2Cl} \underset{\text{I}}{CH_3COCH_2COCH_2CH_2C_6H_5} \quad (1)$$

The success of this mode of alkylation of acetylacetone or benzoylacetone presumably is dependent on first effecting not only the primary ionization of the relatively reactive methylene hydrogen but also the essentially complete secondary ionization of the less reactive methyl hydrogen.

A similar study now has been made of three other β-diketones which, in contrast to acetylacetone or benzoylacetone, could each be converted into two different dicarbanions. The first compound investigated was 6-phenyl-2,4-hexanedione (I) which had been obtained previously[2] in 60% yield from the benzylation of the dicarbanion of acetylacetone (see equation 1). The further treatment of this β-diketone I with two molecular equivalents of potassium amide in liquid ammonia might form dicarbanion IIa or dicarbanion IIb depending on whether a methyl or a 5-methylene hydrogen undergoes the secondary ionization.

$$\underset{\text{IIa}}{\overset{-}{C}H_2CO\overset{-}{C}HCOCH_2CH_2C_6H_5} \qquad \underset{\text{IIb}}{CH_3CO\overset{-}{C}HCO\overset{-}{C}HCH_2C_6H_5}$$

Dicarbanion IIa might be expected to give with a molecular equivalent of benzyl chloride the 1-benzyl derivative IIIa, and dicarbanion IIb the 5-benzyl derivative IIIb.

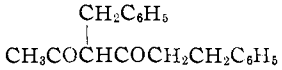
$$C_6H_5CH_2CH_2COCH_2COCH_2CH_2C_6H_5$$

IIIa

$$CH_3COCH_2COCH(CH_2C_6H_5)_2$$

IIIb

The 3-benzyl derivative IIIc or possible dibenzylation products were not expected since such derivatives were not observed in the corresponding alkylations of the dicarbanions of acetylacetone and benzoylacetone under similar conditions.



$$CH_3CO\underset{}{\overset{\overset{\displaystyle CH_2C_6H_5}{|}}{C}}HCOCH_2CH_2C_6H_5$$

IIIc

Actually the 1-benzyl derivative IIIa was mainly obtained. None of the isomeric 5-benzyl derivative IIIb or the 3-benzyl derivative IIIc was detected. Neither was any di-C-benzylation product found nor any starting β-diketone I recovered. Apparently the 1-benzyl derivative IIIa was the only β-diketone produced since, on treatment of the crude alkylation product with excess copper acetate, the almost pure copper chelate of this derivative was obtained directly in 65% yield.[4] This chelate, without purification, was converted by treatment with acid to the essentially pure β-diketone IIIa in 90% yield. The infrared spectrum of the chelate of this β-diketone gave strong bands at 6.37 and 6.57 μ, which may be considered characteristic[5] of the chelate of such a β-diketone as IIIa or IIIb but not of that of such a β-diketone as IIIc which is substituted at the 3-position. Since the infrared spectrum of the crude intermediate chelate was superimposable on that of the purified chelate prepared from the isolated β-diketone IIIa, it would appear that the crude benzylation product did not contain an appreciable amount of the 5-benzyl derivative IIIb.

Evidence that the alkylation product isolated had the symmetrical structure IIIa was obtained by alkaline cleavage, which produced hydrocinnamic acid and methyl β-phenylethyl ketone in yields of 99 and 86%, respectively (equation 2).

$$\text{IIIa} \xrightarrow[2,\ HCl]{1,\ KOH} C_6H_5CH_2CH_2COOH + CH_3COCH_2CH_2C_6H_5 \quad (2)$$

None of the cleavage products of the unsymmetrical β-diketone IIIb were found. Incidentally

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[1] National Science Foundation Predoctoral Fellow, 1956–1958.

[2] C. R. Hauser and T. M. Harris, THIS JOURNAL, **81**, 1154 (1959).

[3] The dicarbanion resonance form is convenient to employ for the present purpose although other resonance forms may contribute more to the structure of the dianion.

[4] On removing the β-diketone material from the crude alkylation product through the copper chelate formation, there remained an oily material which might possibly have contained O-benzylation products.

[5] R. P. Dryden and A. Winston reported at the Southeastern Regional Meeting of the American Chemical Society at Durham, N. C., Nov. 14–16, 1957, that the copper chelates of acetylacetone and similar β-diketones unsubstituted at the methylene group showed infrared bands at 6.10–6.45 and 6.52–6.60 μ, whereas chelates of their 3-substituted derivatives exhibited only the former band.

hydrocinnamic acid and methyl β-phenylethyl ketone would also be the cleavage products of one of the two possible modes of cleavage of the unsymmetrical β-diketone IIIc, but the essentially quantitative yields obtained could hardly have been realized with this structure. Further evidence against the formation of this derivative was presented above.

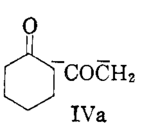
The symmetrical structure IIIa for the benzylation product of the dicarbanion of β-diketone I was confirmed by an independent synthesis involving the acylation of methyl β-phenylethyl ketone with methyl hydrocinnamate (equation 3).

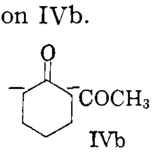
$$C_6H_5CH_2CH_2COCH_3 \xrightarrow{NaNH_2}$$

$$C_6H_5CH_2CH_2COCH_2Na \xrightarrow{C_6H_5CH_2CH_2COOCH_3} IIIa \qquad (3)$$

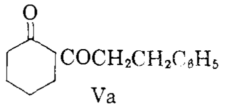
It is well known[6] that such acylations of aliphatic methyl-methylene ketones with ethyl acetate or higher aliphatic esters involve preferentially the methyl group of the ketone.

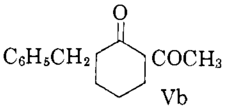
The second β-diketone studied was 2-acetylcyclohexanone, which might be converted into dicarbanion IVa or dicarbanion IVb.


IVa


IVb

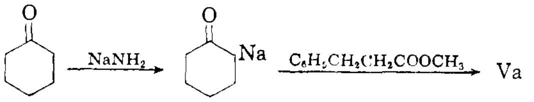
The two corresponding benzylation products from these dicarbanions would be the methyl derivative Va and the ring methylene derivative Vb, respectively.


Va


Vb

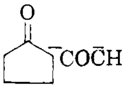
Similar to the benzylation of β-diketone I, this alkylation reaction produced mainly the terminal methyl derivative Va and apparently none of the isomeric ring methylene derivative Vb. Neither the di-C-benzylation product nor the starting 2-acetylcyclohexanone was found. Thus treatment of the crude alkylation product with excess copper acetate gave directly a 58% yield[4] of the reasonably pure copper chelate of β-diketone Va, from which the essentially pure β-diketone Va was liberated in practically quantitative yield. Moreover, the infrared spectrum of the intermediate crude copper chelate was superimposable on that of the purified chelate prepared from the isolated β-diketone.

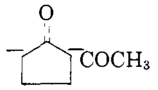
The structure of the alkylation product was established as Va by an unequivocal, independent synthesis involving the acylation of cyclohexanone with methyl hydrocinnamate (equation 4).



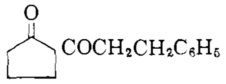
(4)

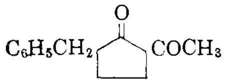
The third β-diketone studied was 2-acetylcyclopentanone, which might be converted to dicarbanion VIa or dicarbanion VIb.


VIa


VIb

The two corresponding benzylation products from these dicarbanions would be the methyl derivative VIIa and the ring methylene derivative VIIb, respectively.

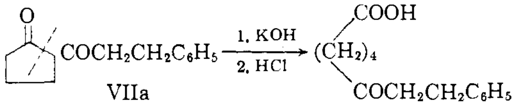

VIIa


VIIb

Similar to β-diketone I and 2-acetylcyclohexanone, 2-acetylcyclopentanone gave mainly the terminal methyl derivative VIIa and apparently none of the isomeric ring methylene derivative VIIb. However, in contrast to the two other results, treatment of the crude benzylation product with excess copper acetate produced a somewhat impure chelate from which the essentially pure β-diketone VIIa was liberated in only 72% yield. Small amounts of both lower boiling and higher boiling β-diketone material also were obtained from the decomposition of the intermediate chelate. The nature of this material is considered below.

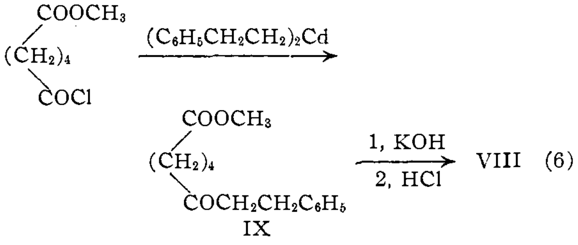
Incidentally the yield of the terminal methyl derivative VIIa isolated in two experiments was 60–62%, which is approximately the same as the yields of the terminal methyl derivatives of β-diketone I and 2-acetylcyclohexanone.

Evidence that the benzylation product isolated was the terminal methyl derivative VIIa was obtained from alkaline cleavage, which involved ring opening to form ketone-acid VIII in 60% yield (equation 5). Such ring-openings of acylcyclopentanones by alkali are well known.[7]



(5)

The ketone-acid VIII was independently synthesized from the mono-acid chloride of methyl adipate and di-β-phenylethylcadmium through ketone-ester IX (equation 6).



$$(CH_2)_4\begin{matrix}COOCH_3\\COCl\end{matrix} \xrightarrow{(C_6H_5CH_2CH_2)_2Cd} (CH_2)_4\begin{matrix}COOCH_3\\COCH_2CH_2C_6H_5\end{matrix} \xrightarrow[2,\ HCl]{1,\ KOH} VIII \qquad (6)$$

IX

The structure VIIa for the product isolated from the benzylation of 2-acetylcyclopentanone was confirmed by an independent synthesis involving an intramolecular cyclization of ketone-ester IX (equation 7).

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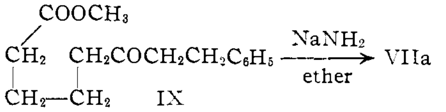
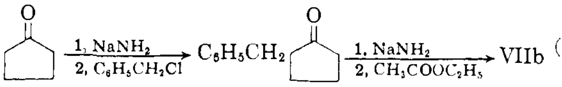
[6] See C. R. Hauser, F. W. Swamer and J. T. Adams, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 69.

[7] See C. R. Hauser, F. W. Swamer and B. I. Ringler, THIS JOURNAL, **70**, 4023 (1948); R. M. Manyik, F. C. Frostick, Jr., J. J. Sanderson and C. R. Hauser, *ibid.*, **75**, 5030 (1953).



$$\mathrm{CH_2(COOCH_3)CH_2CH_2}\text{—}\mathrm{CH_2COCH_2CH_2C_6H_5}\ (\mathrm{IX})\xrightarrow[\text{ether}]{\mathrm{NaNH_2}}\mathrm{VIIa}\qquad(7)$$

The isomeric ring methylene derivative VIIb was shown not to be present in the crude benzylation product of 2-acetylcyclopentanone by comparing the infrared spectrum of its copper chelate with that of the chelate of the crude benzylation product. This β-diketone was prepared by benzylating cyclopentanone to form the monobenzyl derivative,[8] which was then acetylated to give the β-diketone VIIb (equation 8).



(8)

That the Claisen type of acylation represented in equation 8 involved the methylene group to form VIIb and not the methinyl group was demonstrated by the formation of the copper chelate of the product, since the methinyl derivative could not have formed a chelate. Such preferential acylations of a methylene group over a methinyl group are well known.[6]

In Table I are summarized some of the more significant absorption bands of the copper chelates of the terminal methyl derivative VIIa and the ring methyl derivative VIIb of 2-acetylcyclopentanone. Some bands are also given for 2-acetylcyclopentanone. The values given in the first column of this table were determined from the spectra of both the crude intermediate chelate and the purified chelate of VIIa, which were superimposable on one another.

TABLE I

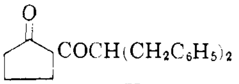
INFRARED BANDS IN μ OF THE COPPER CHELATES OF β-DIKETONES[a]

Chelate of VIIa[b]	Chelate of VIIb	Chelate of 2-acetyl-cyclo-pentanone	Chelate of VIIa[b]	Chelate of VIIb	Chelate of 2-acetyl-cyclo-pentanone
6.25s	6.25s	6.3s	10.51m	10.3w	10.54m
6.7s	6.7s	6.74s	10.89w	.....	.....
7.06s	7.1s	7.13s	.....	11.1m	.....
7.4w	7.33s	7.4w	11.75w	.....	.....
7.72s	7.72s	7.72s	12.8w	.....	12.35w
8.04w	7.98w	.....	.....	13.13m	.....
8.7w	8.57m	8.58w	13.3m	13.3m	.....
9.28w	9.22w	.....	.....	13.95m	13.75w
9.7w	9.67w	9.84w	14.32s	14.32s	.....
....	10.15w	....			

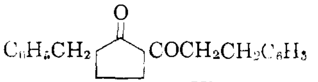
[a] S = strong, m = medium, w = weak. [b] Spectrum for both crude and pure copper chelate.

It can be seen from Table I that, while the spectra of the chelates of β-diketones VIIa and VIIb are quite similar, the latter chelate gave medium strength bands at 8.57, 11.1, 13.13 and 13.95 μ, which were not found in the spectrum of the chelate of β-diketone VIIa. Since the spectrum of the intermediate chelate obtained directly from the crude benzylation product of 2-acetylcyclopentanone was superimposable on that of the pure chelate of the terminal methyl derivative VIIa, the crude alkylation product evidently did not contain an appreciable concentration of the isomeric ring methylene derivative VIIb.

It is possible that the low boiling β-diketone material in the crude alkylation product mentioned above contained the starting 2-acetylcyclopentanone[9] and the high boiling material, the dibenzyl derivative Xa or Xb.



Xa



Xb

Although the chelate of 2-acetylcyclopentanone gave several weak infrared bands that were not observed in the spectrum of the crude chelate of VIIa (see Table I), the complete absence of the former chelate is not necessarily demonstrated since such weak bands might have escaped detection because of the low concentration of this chelate. Also, the presence of a little of the dibenzyl derivative Xa or Xb might have escaped detection in the crude intermediate chelate since, at least the chelate of the former derivative, might be expected to exhibit an infrared spectrum quite similar to that of the terminal methyl derivative VIIa.

From these results it may be concluded that only the a-series of dicarbanions (IIa, IVa and VIa) from β-diketone I, 2-acetylcyclohexanone and 2-acetylcyclopentanone undergo benzylation under the conditions employed. On the assumption that appreciable concentrations of only the a-series of dicarbanions were present in the reaction mixtures, these dicarbanions would be more weakly basic than the corresponding dicarbanions of the b-series.

Finally, the fact that such diverse structures as those studied in this investigation undergo exclusive mono-C-benzylation at the terminal methyl group suggests that preferential alkylation or other types of condensation at this position may be quite general.

Experimental[10]

Benzylation of the Dicarbanion of β-Diketone I to Form β-Diketone IIIa.—6-Phenyl-2,4-hexanedione (I) was prepared by the benzylation of the dicarbanion of acetylacetone as described previously.[2]

To a stirred solution of 0.27 mole of potassium amide in 600 ml. of liquid ammonia[2] was added 25.7 g. (0.135 mole) of β-diketone I in an equal volume of ether. The resulting dark brown solution of the dicarbanion was stirred for 30 minutes, and 17.1 g. (0.135 mole) of benzyl chloride in a little ether was then added rapidly. A vigorous reaction occurred. After 30 minutes, excess (15 g.) solid ammonium chloride was added. The ammonia was evaporated on a hot water-bath as an equal volume of ether was added. The resulting ethereal suspension was shaken with water to dis-

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[8] The yield of this derivative was low and considerable high boiling material was obtained, but this is not suprising since cyclopentanone is known to undergo facile self-condensation in the presence of base; see C. R. Hauser, B. I. Ringler, F. W. Swamer and D. F. Thompson, THIS JOURNAL, **69**, 2649 (1947); J. Mleziva, *Chem. Listy*, **51**, 2364 (1957); *Coll. Czech. Comm.*, **23**, 978 (1958).

[9] Since this β-diketone was prepared by the boron fluoride-catalyzed acetylation of cyclopentanone with acetic anhydride, it might have contained a little acetylacetone resulting from the self-condensation of the anhydride; see ref. 6, p. 101.

[10] Melting points were taken on a Fisher–Johns melting point apparatus. Infrared spectra were produced with a Perkin–Elmer Infracord by the potassium bromide pellet method. Elemental analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

solve the inorganic salts, and the two layers were separated. The aqueous layer was extracted with ether, and the ethereal extracts combined with the original ethereal layer. The ethereal solution was dried over Drierite and the solvent removed. The liquid residue was treated with an excess of a hot, filtered, aqueous solution of copper acetate, and the mixture filtered. The filtrate was blue because of the presence of excess copper acetate. The solid on the funnel was washed with water until the filtrate was colorless, followed by petroleum ether (b.p. 30–60°) until the washings again came through the filter cake essentially colorless. The precipitate was dried by drawing air through the funnel to give 27.1 g. (65%) of the blue copper chelate of 1,7-diphenyl-3,5-heptanedione, m.p. 188–191°.

This copper chelate was suspended in ether, and the suspension was shaken with 12 *M* hydrochloric acid until the solid had disappeared. The two layers were separated and the aqueous layer was extracted with ether. The ethereal solutions were combined, washed with water, and dried over Drierite. The solvent was removed, and the residue was distilled *in vacuo* to give 22.0 g. (90% from the chelate, 59% over-all yield) of 1,7-diphenyl-3,5-heptanedione (IIIa), b.p. 188–193° at 1 mm. An analysis was made on a mid-fraction, b.p. 189° at 1 mm., $n^{25}D$ 1.5685. This β-diketone gave a red enol test with ethanolic ferric chloride.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.13; H, 7.18.

A sample of β-diketone IIIa was reconverted to the copper chelate (blue) which, after recrystallization from benzene and petroleum ether (b.p. 30–60°), melted at 190.5–193.5°. The infrared spectra of a sample of this product and of the crude chelate obtained directly from the reaction mixture as described above were identical, giving strong bands at 6.37, 6.57 and 6.85 μ.

Anal. Calcd. for $C_{38}H_{38}O_4Cu$: C, 73.35; H, 6.15; Cu, 10.21. Found: C, 73.52; H, 6.17; Cu, 10.37.

Alkaline Cleavage of β-Diketone IIIa.—A solution of 10 g. of β-diketone IIIa and 3 g. of potassium hydroxide in 60 ml. of 80% ethanol was refluxed on the steam-bath for 12 hr. The solvent was removed. Water and ether were added to the residue. After shaking the mixture, the ethereal and aqueous (alkaline) layers were separated and worked up as described below.

The ethereal solution was dried, and the solvent removed. The residue was treated with semicarbazide hydrochloride and sodium acetate to give 6.3 g. (86%) of the semicarbazone of methyl β-phenylethyl ketone, m.p. 138–142° and 141–144° after one recrystallization from benzene and petroleum ether (b.p. 30–60°). The latter melting point was not depressed on admixture of the semicarbazone with an authentic sample (m.p. 142–145°) of the compound.

The aqueous layer of the reaction product obtained as described above was saturated with carbon dioxide and the mixture washed with ether to remove any unreacted β-diketone IIIa. The aqueous solution then was acidified with cold dilute hydrochloric acid, and the resulting mixture was extracted with ether. The ethereal solution was dried and the solvent removed to give 5.3 g. (99%) of hydrocinnamic acid, m.p. 47–49°. This melting point was not depressed on admixture with an authentic sample of hydrocinnamic acid, m.p. 48–50°.

Independent Synthesis of β-Diketone IIIa.—To a stirred suspension of 0.3 mole of sodium amide in 500 ml. of ether was added 44.4 g. (0.3 mole) of methyl β-phenylethyl ketone, followed after 15 minutes by 24.6 g. (0.15 mole) of methyl hydrocinnamate according to the general sodium amide-method B.[11] After stirring for 4 hours at room temperature, the reaction mixture was poured into iced hydrochloric acid. The ethereal layer was washed with sodium bicarbonate solution, dried, and the solvent removed. The residue was treated with hot, filtered, aqueous copper acetate to precipitate the copper chelate which, after thorough washing with water and with petroleum ether (b.p. 30–60°), was decomposed with hydrochloric acid to give 12.0 g. (35%) of 1,7-diphenyl-3,5-heptanedione (IIIa), b.p. 187–189° at 1 mm., $n^{25}D$ 1.5680.

A sample of this product was reconverted to its copper chelate (blue) which, after recrystallization from benzene and petroleum ether (b.p. 30–60°), melted at 191–192°. This melting point was not depressed by admixture with a sample of the copper chelate of β-diketone IIIa obtained from the benzylation of β-diketone I as described above. The infrared spectra of the two samples were superimposable.

Benzylation of the Dicarbanion of 2-Acetylcyclohexanone to Form β-Diketone Va.—2-Acetylcyclohexanone was prepared by the acylation of cyclohexanone with acetic anhydride by means of boron fluoride in acetic acid.[12] To a stirred solution of 0.4 mole of potassium amide in 600 ml. of liquid ammonia[2] was added 28 g. (0.2 mole) of 2-acetylcyclohexanone in an equal volume of ether. After 30 minutes a considerable amount of white precipitate had formed, and the dicarbanion formation was assumed to be complete. To the stirred suspension was added 25.2 g. (0.2 mole) of benzyl chloride over a 10-minute period. After 30 minutes excess (25 g.) ammonium chloride was added and the ammonia replaced with ether. The ethereal suspension was washed with water, dried, and the solvent removed. The residue was treated with hot, filtered, aqueous coppper acetate to give, after washing with methanol and petroleum ether (b.p. 30–60°), 30 g. (58%) of the copper chelate of β-diketone Va (green), m.p. 175–180°. One recrystallization of a small portion of the product from acetone and methanol raised the melting point to 181–182°.

The unrecrystallized copper chelate was decomposed with hydrochloric acid in practically quantitative yield to 2-hydrocinnamoylcyclohexanone (Va), m.p. 41.5–42°, colorless needles. Further recrystallization did not raise the melting point. This β-diketone gave a violet enol test with ethanolic ferric chloride.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.48; H, 7.66.

A sample of the β-diketone Va was reconverted to the green copper chelate which, after recrystallization from acetone and methanol, melted at 183–184°. The infrared spectrum of this chelate and that of the crude chelate prepared as described above were superimposable, giving strong bands at 6.35, 6.77 and 7.10 μ.

Anal. Calcd. for $C_{30}H_{34}O_4Cu$: C, 69.01; H, 6.56; Cu, 12.17. Found: C, 69.24; H, 6.40; Cu, 12.36.

Independent Synthesis of β-Diketone Va.—To a stirred suspension of 0.4 mole of sodium amide in 500 ml. of ether was added 39.2 g. (0.4 mole) of cyclohexanone, followed after 10 minutes by 32.8 g. (0.2 mole) of methyl hydrocinnamate in a little ether according to the general sodium amide-method B.[11] After stirring for 6 hr., the reaction mixture was poured into iced hydrochloric acid. The ethereal layer was washed with water, dried and the solvent removed. The residue was treated with an excess of hot, filtered, aqueous copper acetate solution, and the mixture was allowed to cool to room temperature. The green precipitate of the copper chelate was collected on the Büchner funnel, washed with a little ethanol and sucked dry in air. The chelate was was decomposed with dilute hydrochloric acid to give 11.4 g. (24%) of 2-hydrocinnamoylcyclohexanone (Va) (colorless needles), m.p. 41–42°. This melting point was unchanged by recrystallization from petroleum ether (b.p. 30–60°). Admixture of a sample of this product with that obtained from the benzylation of the dicarbanion of 2-acetylcyclohexanone did not depress the melting point.

A sample of this β-diketone was reconverted to the green copper chelate, m.p. 183–184°. Admixture of a sample of this chelate with that obtained by chelating the product obtained from the benzylation of the dicarbanion of 2-acetylcyclohexanone did not depress the melting point, and their infrared spectra were superimposable.

Benzylation of the Dicarbanion of 2-Acetylcyclopentanone to Form β-Diketone VIIa.—2-Acetylcyclopentanone was prepared by the acylation of cyclopentanone with acetic anhydride by means of boron fluoride in acetic acid.[12]

To a stirred solution of 0.4 mole of potassium amide in 500 ml. of liquid ammonia[2] was added 25.2 g. (0.2 mole) of 2-acetylcyclopentanone in an equal volume of ether. There was formed in the stem of the addition funnel a white precipitate[13] which was washed into the reaction mixture with ether. The resulting suspension of the dicarbanion was stirred for 30 minutes, and 25.3 g. (0.2 mole) of benzyl chloride in an equal volume of ether then was added. After stirring for 30 minutes longer, excess (25 g.) ammonium chloride was added, and the ammonia replaced with ether.

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[11] See ref. 6, p. 122.

[12] See ref. 6, p. 131.

[13] This precipitate was presumably the ammonium salt or complex of 2-acetylcyclopentanone; see note 7 of ref. 2.

The ethereal suspension was washed with water, dried, and the solvent removed. The residue was treated with hot, filtered, aqueous copper acetate to give 42.9 g. (87%) of the copper chelate of 2-hydrocinnamoylcyclopentanone (green), m.p. 167–170°. Recrystallization of a small portion of the material from benzene and petroleum ether (b.p. 30–60°) raised the melting point to 168–171°.

The copper chelate was decomposed with hydrochloric acid to give 27.1 g. (72% based on the chelate, 62% over-all yield) of 2-hydrocinnamoylcyclopentanone (VIIa), b.p. 129–134° at 0.8 mm. A forerun was obtained that was too low boiling to be collected at 0.8 mm. Also some high boiling material remained in the distillation flask after the major fraction had distilled. An analysis was made on a mid-fraction, b.p. 131° at 0.8 mm., n^{26}_{D} 1.5501.[14] This β-diketone gave a cherry-red enol test with ethanolic ferric chloride.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.98; H, 7.29.

A sample of β-diketone VIIa was reconverted to its copper chelate (green) which, after recrystallization from benzene and petroleum ether (b.p. 30–60°), melted at 175–176°. The infrared spectrum of this purified copper chelate was essentially the same as that of the crude copper chelate obtained from the benzylation of 2-acetylcyclopentanone as described above.

Anal. Calcd. for $C_{28}H_{30}O_4Cu$: C, 68.06; H, 6.13; Cu, 12.86. Found: C, 68.06; H, 6.14; Cu, 13.03.

Cleavage of β-Diketone VIIa to Form Ketone-acid VIII.—To a solution of 2 g. of potassium hydroxide in 50 ml. of 50% methanol was added 5.5 g. of β-diketone VIIa. The reaction mixture was heated for 16 hr. on the steam-bath. The solvent was removed. After cooling, water and ether were added and the two layers were carefully separated. The ether layer left essentially no residue on evaporation and was discarded. The aqueous layer was acidified with hydrochloric acid, and the liberated organic acid taken up in ether. Evaporation of the solvent left an oil which crystallized on trituration with petroleum ether (b.p. 30–60°). Recrystallization from ether and petroleum ether gave 3.5 g. (60%) of 8-phenyl-6-oxo-octanoic acid (VIII), m.p. 50–53° and 52–54° after another recrystallization from the same solvent pair.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.89; H, 7.81.

Independent Synthesis of Keto-acid VIII.—Di-β-phenylethyl-cadmium was prepared by a procedure similar to that described by Cason and Prout for diisoamylcadmium.[15]

To a stirred solution of 7.7 g. (0.32 mole) of magnesium turnings and 100 ml. of anhydrous ether was added 61 g. (0.33 mole) of β-phenylethyl bromide (b.p. 104–106° at 20 mm.) at such a rate as to maintain reflux. After 90 minutes, 32.3 g. (0.176 mole) of anhydrous (free-flowing) cadmium chloride was introduced. The ether was distilled as an equal volume of benzene was added.

To the resulting suspension of the cadmium reagent was added 38.5 g. (0.216 mole) of the acid chloride of monomethyl adipate (b.p. 71–73° at 1 mm.), which was prepared from monomethyl adipate and excess thionyl chloride (4 hours at room temperature), the excess thionyl chloride being removed on the steam bath with an aspirator.[16] After stirring and refluxing for 90 minutes, the reaction mixture was poured into iced hydrochloric acid, and the two layers were separated. The benzene layer was combined with an ether extract of the aqueous layer, and the resulting solution was dried over Drierite. The solvents were removed, and the residue was distilled *in vacuo* to give 31.9 g. (60%) of the methyl 8-phenyl-6-oxo-octanoate (IX), b.p. 133–137° at 0.3 mm. An analysis was made on a mid-fraction, b.p. 124° at 0.2 mm., n^{24}_{D} 1.5009.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.52; H, 8.10.

Saponification of 1.2 g. of the ketone-ester IX was carried out in a solution of 1 g. of potassium hydroxide in 50 ml. of water to give 0.7 g. (62%) of ketone-acid VIII, melting at 50–53° and at 53–54° after recrystallization from ether and petroleum ether (b.p. 30–60°). The melting point of this product was not depressed on admixture with a sample of the ketone-acid VIII prepared as described above.

Independent Synthesis of β-Diketone VIIa.—To a stirred suspension of 0.5 mole of sodium amide in ether[11] was added an ethereal solution of 12.4 g. (0.05 mole) of ketone-ester IX. After stirring for 4 hr. the reaction mixture was poured into iced hydrochloric acid. The layers were separated, and the aqueous layer was extracted with ether. The ethereal solutions were combined, and the solvent removed. The residue was treated with hot aqueous copper acetate to form the copper chelate. The chelate was washed with petroleum ether (b.p. 30–60°) and decomposed by shaking with aqueous hydrochloric acid. The resulting mixture was extracted with ether. The ethereal solution was dried and the solvent removed. The residue was distilled *in vacuo* to give 6.1 g. (56.5%) of 2-hydrocinnamoylcyclopentanone (VIIa), b.p. 126–132° at 0.7 mm. The β-diketone was reconverted to the copper chelate by treatment with copper acetate. Admixture of this chelate (m.p. 174–176°) with the chelate of β-diketone VIIa produced by the benzylation of the dicarbanion of 2-acetylcyclopentanone did not depress the melting point, and their infrared spectra were superimposable (see Discussion).

Synthesis of β-Diketone VIIb.—To a stirred suspension of 0.835 mole of sodium amide in 600 ml. of liquid ammonia[11] was added 70 g. (0.835 mole) of cyclopentanone, followed after 15 minutes by 56 g. (0.445 mole) of benzyl chloride. The reaction mixture was stirred for 30 minutes and excess ammonium chloride (40 g.) then was added. The liquid ammonia was evaporated as an equal volume of ether was added. The ether suspension was washed with water, dried and the solvent removed. Three distillations of the residue gave 17.3 g. (22% based on benzyl chloride) of 2-benzylcyclopentanone, b.p. 79–89° at 0.25 mm. (reported[17] b.p. 144–146° at 16 mm.). Much high-boiling material remained in the distillation flask.

To a stirred solution of 0.2 mole of potassium amide in ether was added 16.8 g. (0.097 mole) of 2-benzylcyclopentanone, followed after 5 minutes by 18 g. (0.2 mole) of ethyl acetate. After stirring for 3 hr. the reaction mixture was poured into iced hydrochloric acid. The two layers were separated, and an ether extract of the aqueous layer was combined with the ethereal layer. The ethereal solution was dried and the solvent removed. The residue was treated with hot aqueous copper acetate, and the precipitated chelate (green) was collected and washed with water followed by petroleum ether (b.p. 30–60°). The chelate was decomposed with hydrochloric acid to give 8.2 g. (26%) of 2-acetyl-5-benzylcyclopentanone (VIIb), b.p. 119–121° at 0.6 mm., n^{25}_{D} 1.5503. This product gave a red enol test with ethanolic ferric chloride.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.78; H, 7.59.

This β-diketone was reconverted to its green copper chelate, which melted with decomposition at 212–215° after recrystallization from benzene and petroleum ether (b.p. 30–60°). The infrared spectrum of the chelate was distinguishable from that of the chelate of β-diketone VIIa (see Discussion).

Anal. Calcd. for $C_{28}H_{30}O_4Cu$: C, 68.06; H, 6.13; Cu, 12.86. Found: 67.94; H, 5.99; Cu, 13.09.

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(14) The refractive index did not change appreciably over the boiling range of 129–134°.

(15) See J. Cason and F. S. Prout, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 601.

(16) See J. Cason, *ibid.*, p. 169.

(17) D. A. Duff and C. K. Ingold, *J. Chem. Soc.*, 87 (1934).