

[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORY OF SCHERING CORPORATION]

Cycloalkeneacetic Acids in the Perkin Reaction¹

BY ERWIN SCHWENK AND DOMENICK PAPA

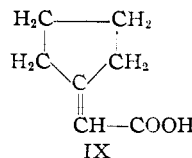
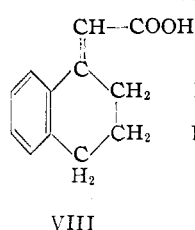
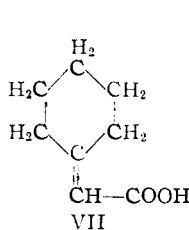
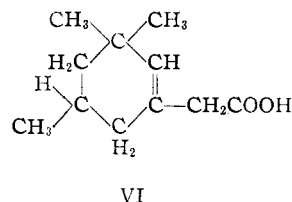
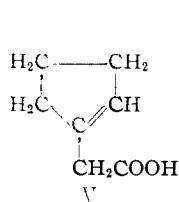
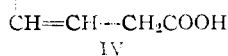
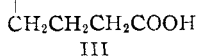
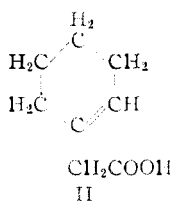
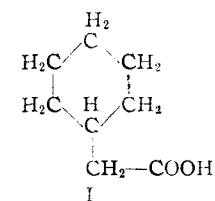
We have been interested for some time in the condensation of cyclohexaneacetic acid with aromatic aldehydes as the simplest approach to the synthesis of α -cyclohexylcinnamic acid and its derivatives. As far as could be determined from a survey of the literature, cycloalkylacetic acids have apparently not been used in the Perkin reaction.²

The first attempts at the synthesis of α -cyclohexylcinnamic acid from cyclohexaneacetic acid (I) and benzaldehyde were made in accordance with the general procedure for the preparation of α -aryl substituted cinnamic acids. In the course of these studies various reaction conditions were tried which have been used as modifications of Oglialoro's interpretation of the Perkin synthesis. From numerous experiments, including some which were carried out with aldehydes much more reactive than benzaldehyde, none of the desired α -cyclohexylcinnamic acids was obtained.³

A rather different result was obtained when in place of cyclohexaneacetic acid (I) the Δ^1 -cyclohexeneacetic acid (II) was used. This unsaturated acid in the form of the sodium or potassium salt readily underwent the Perkin reaction and good yields of α -(Δ^1 -cyclohexenyl)-cinnamic acid were obtained. This observation parallels that reported for γ -phenylbutyric acid (III) and γ -phenylisocrotonic acid (IV). Under the condi-

tion yields.⁵ As in the case of the cyclohexeneacetic acid, the β,γ -double bond in phenylisocrotonic acid exerts an activating influence on the methylene hydrogens.

This new modification of the Perkin synthesis seems to be of general applicability, since other cycloalkeneacetic acids have been found to readily undergo condensation with aldehydes. For example, Δ^1 -cyclopentene- (V) and 3,3,5-trimethyl- Δ^1 -cyclohexeneacetic acid (VI) also give good yields in this condensation. Surprisingly, the isomeric cyclohexylideneacetic acid likewise gave good yields, the reaction product being identical with that obtained from Δ^1 -cyclohexeneacetic acid. It must, therefore, be assumed that cyclohexylideneacetic acid (VII) rearranges to Δ^1 -cyclohexeneacetic acid (II) in the course of the reaction and thus provides the two necessary methylene hydrogens for the condensation. Other cycloalkylideneacetic acids, such as α -tetralideneacetic acid (VIII) and cyclopentylideneacetic acid (IX), likewise reacted smoothly.



tions of the Perkin reaction, γ -phenylbutyric acid gives only 14% of α -(β -phenylethyl)-cinnamic acid after fourteen days at 100°,⁴ whereas its unsaturated analog, γ -phenylisocrotonic acid, readily undergoes the Perkin condensation in good

All of the preliminary experiments on the cycloalkene and cycloalkylidene acetic acids were carried out with the anhydrous potassium salts of the acids. These metal salts are quite disagreeable to prepare because of their hygroscopic and soapy character. This difficulty was overcome by making use of the observations of Kalnin⁶ and of Bakunin and Peccerillo⁷ who, after making extensive studies of the Perkin reaction in the preparation of α -aryl substituted cinnamic acids, concluded that in the presence of metallic salts or organic amines, the condensation of the free aryl acetic acids and aromatic aldehydes proceeds quite well. In particular, alkali acetates, such as potassium acetate, and tertiary

(1) Presented in abstract before the Division of Organic Chemistry, American Chemical Society Meeting, New York, September 11, 1944.

(2) "Organic Reactions," The Perkins Reaction, Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 224.

(3) The only condensation products isolated from these experiments were cinnamic acids which were obtained in yields of approximately 10-15%.

(4) Rupe, *Ann.*, **395**, 106, 411 (1913).

(5) Thiele, *ibid.*, **306**, 154 (1899).

(6) P. Kalnin, *Helv. Chim. Acta*, **11**, 977 (1928).

(7) Bakunin and Peccerillo, *Gazz. Chim. Ital.*, **65**, 1145 (1935).

aliphatic amines, such as triethylamine, have been reported to be excellent catalysts for the condensation of two reactive components. It has been found possible to bring about the Perkin condensation of cycloalkeneacetic acids and aromatic aldehydes with either of these two substances in yields approximately equal to or better than those obtainable by using the alkali salts of the acids. Triethylamine proved to be more effective as a catalyst in the condensation of cycloalkene acetic acids than either potassium acetate or the potassium salts of the acids.

Since acetic anhydride may be used for the dehydration of cycloalkanol acetic acids, it was of interest to determine whether or not the usual reaction conditions would effect the concurrent dehydration and condensation of cyclohexanol-acetic acids. The anhydrous potassium cyclohexanol-1 acetate and benzaldehyde in acetic anhydride afforded none of the Δ^1 -cyclohexenyl-cinnamic acid. However, in the presence of triethylamine or potassium acetate as catalysts, the free cyclohexanol-1-acetic acid and benzaldehyde gave a fairly good yield of the condensation product. Since large amounts of acetic acid are known to have a deleterious effect on the course of the Perkin synthesis,⁸ triethylamine was used in an amount sufficient to neutralize not only the cyclohexanolacetic acid but also the acetic acid which resulted from the dehydration. Attempts to distill out of the reaction mixture acetic acid which results from the dehydration of the cycloalkanol-acetic acid proved unsuccessful.

Using the conditions for the condensation of the cycloalkanolacetic acid, it has been found possible to condense ethyl cyclohexanol-1-acetate with benzaldehyde. The yields obtained by this procedure were rather poor and this reaction was not further investigated.

The arylcycloalkeneacrylic acids described in this paper were subjected to hydrogenation studies, the results of which have not as yet been published. It may be pointed out here that these compounds resist hydrogenation in a low-pressure hydrogenator⁹ but are readily reduced with Raney's alloy and aqueous alkali.^{10,11}

Experimental

Preparation of Intermediates

1. Ethyl cyclohexanol-1-acetate was prepared conveniently in 4-mole quantities according to the procedure of Natelson and Gottfried.¹² In place of the zinc foil, as suggested by these authors, it has been found that granular zinc, purified by washing rapidly with 2% hydrochloric acid followed by water, alcohol, and absolute ether, gives consistently good yields of the product with a minimum

(8) "Organic Reactions," The Perkin Reaction, Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 239.

(9) Compare W. Baker and H. Sansbury, *J. Soc. Chem. Ind.*, **62**, 192 (1943).

(10) Schwenk, Papa, Whitman and Ginsberg, *J. Org. Chem.*, **9**, 175 (1944).

(11) Schwenk and Papa, *ibid.*, in press.

(12) Natelson and Gottfried, *THIS JOURNAL*, **61**, 970 (1939).

amount of inconvenience; average yield, 70%, b. p. 88–92° (2–3 mm.)^{12a}

2. Ethyl cyclopentanol-1-acetate was prepared from cyclopentanone *via* the Reformatsky reaction; yield, 55%; b. p. 89–93° (4 mm.).

3. 6-Methoxy- α -tetralideneacetic acid was obtained from 6-methoxy- α -tetralone¹³ and ethyl bromoacetate *via* the Reformatsky reaction.¹⁴ The hydroxy ester split out water on distillation, even when the distillation was conducted in a low vacuum. The distillate, which boiled at 165–170° (1 mm.), was saponified and the crude acid after recrystallization from petroleum ether melted at 80°. *Anal.* Calcd. for C₁₃H₁₄O₃: C, 71.52; H, 6.47. Found: C, 71.35; H, 6.67.

Since the elimination of water can take two courses, the product obtained is either 6-methoxy-3,4-dihydro- α -naphthaleneacetic acid or the isomeric 6-methoxy- α -tetralideneacetic acid. It has been found that the acid which is obtained readily hydrogenated with Raney's alloy and aqueous alkali to the known 6-methoxy- α -tetralylacetic acid melting at 84°.¹⁵ On the basis of our reduction studies with cyclohexene- and cyclohexylideneacetic acid,¹⁰ it has been assumed that its structure corresponds to the tetralidene compound.

4. Cyclohexeneacetic acid was prepared by a modification of the procedure of Natelson and Gottfried.¹² Anhydrous hydrogen chloride was bubbled through ethyl cyclohexanol-1-acetate while heating at 100°. The reaction product was then fractionated, and that portion which came over between 80–82° (2 mm.) was collected. The distillation residue was again treated with hydrogen chloride and the fractionation repeated; average yield, 80%; b. p. 80–82° (2 mm.).

5. Cyclohexylideneacetic acid was obtained from ethyl cyclohexanol-1-acetate by refluxing with acetic anhydride¹⁶ for three hours, followed by saponification with alcoholic potassium hydroxide; yield, 68%; m. p. 90–92° from petroleum ether.

6. Cyclohexaneacetic acid was obtained by reducing the cyclohexylideneacetic acid with nickel-aluminum alloy and aqueous alkali.¹⁰

7. Cyclohexanol-1-acetic acid resulted from the ethyl ester by saponification with alcoholic potassium hydroxide; recrystallized from petroleum ether, m. p. 64–65°.

8. Cyclopenteneacetic acid was obtained from ethyl cyclopentanol-1-acetate by dehydration with thionyl chloride. The dehydration product was contaminated with cyclopentylideneacetic acid and only after numerous recrystallizations from petroleum ether was the pure cyclopenteneacetic acid obtained. It melted at 50–51°. ¹⁷ Rather poor yields of this preparation were obtained because of the unlimited solubility of the acid in all the solvents which were tried.

9. Cyclopentylideneacetic acid resulted from cyclopentanol-1-acetic acid on dehydration with acetic anhydride. Recrystallization from petroleum ether gave the pure acid melting at 60–61°. ¹⁷ When this substance

(12a) This description of a modified procedure was received on June 18, 1945 while the article was in press.

(13) The 6-methoxy- α -tetralone was prepared from tetralin by sulfonation, alkali fusion, and oxidation in accordance with the known methods (Schroeter, *Ann.*, **426**, 119 (1922); Burnop, Elliott and Linstead, *J. Chem. Soc.*, 731 (1940)). It has been recommended that the oxidation mixture be steam distilled for twenty hours with superheated steam in order to secure good yields of pure 6-methoxy- α -tetralone. However, it was found that by simply diluting the chromic acid oxidation with an equal volume of butyl ether and then diluting with ten volumes of water, excellent separation of the 6-methoxy- α -tetralone is effected. The yield of purified ketone by this procedure is 65–70%.

(14) Burnop, Elliott and Linstead, *J. Chem. Soc.*, 731 (1940); J. Hoch, *Bull. soc. chim.*, [5] **5**, 273 (1938).

(15) Haberland, *Ber.*, **69**, 1380 (1936), gives m. p. 87° for this compound.

(16) Compare "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, pp. 13–14.

(17) Harding and Hawthorth, *J. Chem. Soc.*, **97**, 492 (1910)

was recrystallized from petroleum ether, it was necessary to freeze the petroleum ether solution in an acetone-carbon dioxide mixture in order to precipitate the acid.

10. 3,3,5-Trimethylcyclohexanone was prepared in 81% yield by the chronic acid oxidation¹⁸ of the commercially available 3,3,5-trimethylcyclohexanol.

11. Ethyl 3,3,5-trimethylcyclohexanol-1-acetate was obtained from 3,3,5-trimethylcyclohexanone and ethyl bromoacetate in accordance with the usual Reformatsky procedure, using a mixture of benzene and toluene as solvents; average yield, 58%; b. p. 125–129° (10 mm). The ester, without further purification, was saponified with alcoholic alkali and the 3,3,5-trimethylcyclohexanol-1-acetic acid, which was isolated in the usual manner, melted at 109–114°. Recrystallized from water, the acid melted at 115.5–116.5°.

Anal. Calcd. for $C_{11}H_{20}O_3$: C, 65.95; H, 10.08, neut. equiv., 200. Found: C, 66.11; H, 10.26, neut. equiv., 200.8.

12. The anhydrous potassium salts of the cycloalkyl- and cycloalkeneacetic acids were prepared by dissolving the acids in methyl alcohol, adding a concentrated solution of potassium hydroxide in methanol until faintly alkaline to phenolphthalein, and evaporating to dryness. The cakes of potassium salts were then ground up in a mortar and dried at 110°.

Procedures for Condensations

The two following methods were used for condensing the cycloalkene and the cycloalkylideneacetic acids with aromatic aldehydes:

(a) The condensations were carried out in an atmosphere of nitrogen in a three-necked flask equipped with stirrer, thermometer, and condenser carrying a calcium chloride tube. One-tenth of a mole of the anhydrous potassium salt of the cycloalkene- or cycloalkylideneacetic acid, 0.1 mole of aldehyde, and 0.5 mole of acetic anhydride were heated at 100–110° (internal temperature) for approximately twelve to fifteen hours. The reaction mixture was then cooled to 60°, and the excess acetic anhydride cautiously decomposed with water. After pouring the mixture on ice, the semi-solid product was extracted with ether. The ether extracts, after washing free of acetic acid, were extracted with 5% Na_2CO_3 . The sodium carbonate extracts were freed of ether and while hot were neutralized with hydrochloric acid. The neutral solution was treated with decolorizing carbon, heated for one-half hour, filtered and acidified. The crude condensation products were usually sufficiently pure for further synthetic work. However, they may be purified further by recrystallization from an aqueous solution of acetone or alcohol. The ether-sodium carbonate method of purification has been applied to all the condensation products in order to remove the small amounts of decarboxylated material which are formed in the reaction.

(b) One-tenth of a mole of the cycloalkene- or cycloalkylideneacetic acid, 0.1 mole of aldehyde, 0.1 mole of anhydrous triethylamine, and 0.5 mole of acetic anhydride were heated for ten to fifteen hours at 105–110°. The reaction mixture was then worked up as described under method (a). Under similar conditions, it has been found that anhydrous potassium acetate will also promote the condensation of these acids with aromatic aldehydes.

Condensation Products

The letters (a) and (b) following the percentage yields indicate the condensation procedure which was used.

1. α -(Δ^1 -Cyclohexenyl)-cinnamic acid was obtained from Δ^1 -cyclohexeneacetic acid and benzaldehyde, yield 42% (a); 55% (b). Recrystallized from a mixture of acetone and water, m. p. 156–157°. Calcd. for $C_{16}H_{18}O_2$: C, 78.90; H, 7.07. Found: C, 78.60; H, 7.16. This sub-

stance was also obtained from the isomeric cyclohexylideneacetic acid, yield 44% (a); 53% (b).

2. α -(Δ^1 -Cyclohexenyl)-*p*-hydroxycinnamic acid was obtained from Δ^1 -cyclohexeneacetic acid and *p*-hydroxybenzaldehyde; yield 62% (a); 69% (b); recrystallized from acetone-water, m. p. 194–195°. Calcd. for $C_{16}H_{18}O_3$: C, 73.73; H, 6.61. Found: C, 73.43; H, 6.78. Using the cyclohexylideneacetic acid, yield 54% (a); 62% (b).

The α -(Δ^1 -cyclohexenyl)-*p*-hydroxycinnamic acid also has been obtained by condensing cyclohexanol-1-acetic acid with *p*-hydroxybenzaldehyde. Fifteen and eight tenths grams (0.1 mole) of cyclohexanolacetic acid, 12.2 g. (0.1 mole) of *p*-hydroxybenzaldehyde, 30 g. (0.3 mole) of triethylamine, and 53 g. (0.5 mole) of acetic anhydride were heated for ten to fifteen hours at 105–110° (internal temperature). The reaction mixture was then worked up as described under (a), and the crude yield of the substituted cinnamic acid amounted to 13.7 g. (56%) melting at 184–188°. Recrystallization from acetone and water gave a melting point of 194–195°. When the amount of triethylamine used was only that required for the condensation, then the yields obtained were of the order of 30–50%.

3. α -(Δ^1 -Cyclopentenyl)-*p*-hydroxycinnamic acid was prepared from Δ^1 -cyclopenteneacetic acid and *p*-hydroxybenzaldehyde in a yield of 55% (a); recrystallized from acetone-water, m. p. 183° (dec.). Calcd. for $C_{14}H_{16}O_3$: C, 73.01; H, 6.12. Found: C, 72.49; H, 6.12. The cyclopentylideneacetic acid gave a 36% yield (a).

4. α -(6-Methoxy-3,4-dihydro- α -naphthyl)-*p*-hydroxycinnamic acid resulted from the condensation of 6-methoxy- α -tetralidene acetic acid with *p*-hydroxybenzaldehyde in a crude yield of 47% (b); recrystallized from a mixture of acetone and water, m. p. 186° (dec.). Calcd. for $C_{20}H_{18}O_4$: C, 74.54; H, 5.64. Found: C, 74.44; H, 5.41.

5. α -(Δ^1 -Cyclohexenyl)-piperonylacrylic acid was prepared from Δ^1 -cyclohexeneacetic acid and piperonal, using triethylamine as the condensation catalyst. It was obtained in a crude yield of 66%, melting at 170–175°. Recrystallization from a mixture of acetone and water gave pale yellow needles melting at 186–187°. Calcd. for $C_{18}H_{18}O_4$: C, 70.15; H, 5.93. Found: C, 70.55; H, 5.74.

6. α -(Δ^1 -Cyclohexenyl)-3,4-dimethoxycinnamic acid was prepared from Δ^1 -cyclohexeneacetic acid, veratraldehyde and triethylamine, in a crude yield of 56% melting at 180–186.5°. Recrystallization from a mixture of acetone and water gave long, pale yellow needles melting at 190–191°. Calcd. for $C_{17}H_{20}O_4$: C, 70.83; H, 6.94. Found: C, 70.66; H, 7.22.

7. α -(Δ^1 -Cyclohexenyl)-*p*-nitrocinnamic acid was obtained by the condensation of Δ^1 -cyclohexeneacetic acid, *p*-nitrobenzaldehyde and triethylamine. The crude condensation product was obtained in a yield of 54% and melted at 134–144°. After two recrystallizations from a mixture of benzene and petroleum ether, the substance was obtained in the form of brilliant, yellow needles melting at 183–184°. Calcd. for $C_{16}H_{16}O_4N$: N, 5.13. Found: N, 5.14.

8. α -(Δ^1 -Cyclohexenyl)-3-pyridylacrylic acid was obtained from 3-pyridinealdehyde,¹⁹ Δ^1 -cyclohexeneacetic acid, and triethylamine. The crude condensation product was obtained in a yield of 52% and melted at 147–152°. Recrystallization from a mixture of methanol and water gave a product which separated in long, fine white needles, m. p. 159.5–160°. Calcd. for $C_{14}H_{18}O_2N$: C, 73.32; H, 6.59. Found: C, 72.93; H, 6.50.

9. α -(Δ^1 -Cyclohexenyl)-furylacrylic acid was prepared from freshly distilled furfural, Δ^1 -cyclohexeneacetic acid, and triethylamine. The yield of crude product was 56%, m. p. 142–146°. Recrystallized from a mixture of acetone and water, the substituted acrylic acid melted at 151.5–152°. Calcd. for $C_{18}H_{14}O_3$: C, 71.52; H, 6.47. Found: C, 70.85; H, 6.37.

10. α -(3,3,5-Trimethyl- Δ^1 -cyclohexenyl)-*p*-hydroxycinnamic acid was prepared from 3,3,5-trimethyl-

(18) The procedure of L. T. Sandborn for the oxidation of menthol was applied to this trimethylcyclohexanol (*Organic Syntheses*, Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., p. 340).

(19) M. Hartman and W. Bosshard, *Helv. Chim. Acta*, **24**, 281 (1941).

Δ^1 -cyclohexeneacetic acid and *p*-hydroxybenzaldehyde in a crude yield of 49% melting at 172–176° (b). From 3,3,5-trimethylcyclohexanol-1-acetic acid the yield of condensation product was 38%; recrystallized from aqueous methanol, m. p. 181–182°. Calcd. for $C_{18}H_{22}O_3$: C, 75.48; H, 7.75. Found: C, 75.00; H, 7.82%.

Acknowledgment.—The authors wish to express their appreciation to Miss Hilda Hankin, Miss Anna Strauss, and Mr. Peter Hirschler for their technical assistance.

Summary

1. Cycloalkeneacetic acids have been found to readily undergo the Perkin condensation with aromatic aldehydes in good yields.

2. The isomeric cycloalkylideneacetic acids likewise give good yields in the Perkin reaction. The condensation of these acids must be pre-

ceded by a shift of the double bond into the alicyclic ring.

3. The condensation of these acids can be carried out by using the alkali metal salts of the acids or by using the free acids with molecular proportions of triethylamine or anhydrous potassium acetate as catalysts. The yields which were obtained by these two modifications were of approximately the same order, those condensations in which triethylamine was used giving usually slightly better yields.

4. It has been found that the cycloalkanol-1-acetic acids likewise undergo the Perkin condensation with aromatic aldehydes, the condensation being preceded by the dehydration of the tertiary alcohol.

BLOOMFIELD, NEW JERSEY

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF SMITH COLLEGE]

A Low Pressure Method for Wolff-Kishner Reduction

BY MILTON D. SOFFER, MARY BARNS SOFFER AND KENNETH W. SHERK

The best established general methods for the direct conversion of carbonyl compounds to their methylene analogs are the Clemmensen reduction and the reaction of Kishner¹ and Wolff.² While both of these methods usually give good results, certain limitations^{3,4,5} in the Clemmensen reaction, particularly in the case of high molecular weight aliphatic ketones^{3,4} have led to a renewed interest³ in the alternative method. One disadvantage of the latter is that it usually is carried out in the presence of a volatile alcohol, imposing the requirement of a high-pressure apparatus^{3,6,7} or the disadvantage of a bomb-tube⁸ technique.

In the present work, the use of a large amount of a non-volatile solvent provides a feasible method for effecting large scale conversions in the liquid phase and obviates the requirement for any

special apparatus. Our experiments were confined to reactions in solution which appeared to be more general and direct than the variations involving alkaline fusion⁹ of the dry hydrazone^{1,10} or semicarbazone.^{11,12} The reactions were usually carried out by refluxing a mixture of the carbonyl compound and a solution of sodium and excess hydrazine hydrate in mono-, di- or triethylene glycol. The temperature of the reaction mixture could be varied by changing the proportion of excess hydrazine in relation to the amounts of the less volatile glycol and its sodium derivative. The desired substance was easily isolated as the only water insoluble reaction product. Good yields were obtained with a series of representative ketones, and the method has already been used in another laboratory, as an improvement over the Clemmensen alternative, for successful reduction of two aliphatic keto acids, *i. e.*, 5-keto-8-methylnonanoic acid and 5-keto-10-methylundecanoic acid.^{13,13a}

(9) These methods do not require pressure apparatus but involve the isolation of the intermediate carbonyl derivatives.

(10) Rabe and Jantzen, *Ber.*, **54**, 928 (1921).

(11) Cook and Linstead, *J. Chem. Soc.*, 956 (1934).

(12) Ruzicka and Goldberg, *Helv. Chim. Acta*, **18**, 672 (1935), used sodium benzylate in benzyl alcohol to decompose the semicarbazone.

(13) The yields obtained by reaction in diethylene glycol were 92 and 80%, respectively. Private communication from Dr. I. F. Fieser, Harvard University, who will report full experimental details later.

(13a) Since this paper was submitted the method has been applied with excellent results to the reduction of another keto-acid in the course of a separate work in this Laboratory. 10-Keto-12-phenyldodecanoic acid, m. p. 72°, gave 12-phenyldodecanoic acid, m. p. 60–60.5°, in quantitative yield by similar treatment at 170° for ninety hours. Although we have not attempted to determine the minimum decomposition times for these reactions, it appears that shorter heating periods would suffice in most cases.—(Received June 28, 1945.)

(1) Kishner, *J. Russ. Phys.-Chem. Soc.*, **43**, 582 (1911); *C. A.*, **6**, 347 (1912).

(2) Wolff, *Ann.*, **394**, 86 (1912).

(3) Herr, Clarke, Rowland, Whitmore and Schiessler, "Higher Hydrocarbons. III. The Wolff-Kishner Reaction." Abstracts of Papers, 107th meeting, American Chemical Society, April 4th, 1944.

(4) Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, 1941, p. 420.

(5) Martin, *THIS JOURNAL*, **58**, 1438 (1936); The Clemmensen Reduction, "Organic Reactions," John Wiley and Sons, Inc., New York, 1942, p. 155.

(6) High pressure catalytic hydrogenation is open to the same objection and is further limited because the reaction normally proceeds to the methylene stage only in the case of aryl carbonyl compounds [Adkins, "Reactions of Hydrogen," the University of Wisconsin Press, Madison, Wis., 1937; Fieser and Hershberg, *THIS JOURNAL*, **59**, 1028, 2331 (1937)]. The last limitation also applies to the low pressure method of I'apa, Schwenk and Whitman involving nickel-aluminum and aqueous alkali [*J. Org. Chem.*, **7**, 587 (1942)].

(7) A very promising alternative method involving low-pressure hydrogenolysis of an intermediate carbonyl thiacetal has been reported recently by Wolfroni and Karabinos [*THIS JOURNAL*, **66**, 909 (1944)].

(8) Fieser, ref. 4, p. 424.