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%.

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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 preceded 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.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF SMITH COLLEGE]

A Low Pressure Method for Wolff–Kishner Reduction

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The best established general methods for the direct conversion of carbonyl compounds to their methylene analogs are the Clemmensen reduction and the reaction of Kishner[1] 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 interest[3] 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-tube[8] 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 fusion[9] 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]

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(1) Kizhner, *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 Papa, 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 Wolfrom and Karabinos [THIS JOURNAL, **66**, 909 (1944)].

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

(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. L. 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.)

Experimental

Reduction of 1-Phenyleicosanone-3.[3,14]—In an all-glass apparatus, 1.5 ml. (0.03 mole) of 100% hydrazine hydrate (Edwal Laboratories) and 2.00 g. of the ketone (0.0054 mole), m. p. 56–57°, were added to a solution prepared from 5 g. of sodium and 100 ml. of diethylene glycol (Eastman Kodak Co. Pract.), and the mixture, protected with calcium chloride and soda-lime, was refluxed in an air-bath for fifty hours. During this period the temperature of the liquid mixture fell from 191 to 181°. After dilution with water, extraction with benzene or petroleum ether, and washing in turn with water, dilute hydrochloric acid, and again with water, the extract was dried over anhydrous magnesium sulfate. Removal of solvent left the crude hydrocarbon m. p. 39–40° in quantitative yield. One recrystallization from 95% ethanol gave 1.49 g. (78%) of 1-phenyleicosane,[14] m. p. 41.5–42.5°.

In one run, with the same amount of ketone, 5.0 g. of sodium, and 1.0 ml. of hydrazine hydrate, triethanolamine (Pract.) was substituted for diethylene glycol. In this case, after a reaction period of twenty-five hours at 203-199°, the pure hydrocarbon was obtained after two recrystallizations in only 32% yield.

In another case, with octyl alcohol (185 ml.) as the solvent, 10 g. of the ketone (0.027 mole) was used with 2.0 ml. (0.04 mole) of hydrazine hydrate, and 3.7 g. of sodium. After eighteen hours of refluxing at 185-180°, the product was isolated by extraction with benzene as before. Removal of solvent at reduced pressure and crystallization from ethanol gave 8.0 g. (83%) of material melting at 38-41°, and 6.5 g. (68%) of the pure product.

Preliminary experiments with the Clemmensen reaction in water and in dilute alcohol gave unsatisfactory results, probably because of the insolubility of the ketone in aqueous media. In both cases the only product which could be isolated in a pure condition was unchanged starting material. Much better results were obtained by the modification of Mikeska, Smith and Lieber.[15] A solution of 10.0 g. of the ketone in 150 ml. of toluene was refluxed with concentrated hydrochloric acid and 50 g. of amalgamated zinc for forty hours, while gaseous hydrogen chloride was allowed to bubble through the reaction mixture. Distillation of the recrystallized product, 7.3 g. (76%), m. p. 38.5-39.5°, gave 6.53 g. (68%) of relatively pure material, m. p. 39.5-42°. In another experiment, where the toluene layer was not in actual contact[15] with the zinc amalgam, no reduction had taken place after refluxing for seventy-two hours.

Reduction of 1,14-Diphenyltetradecadione-3,12.—Three experiments were carried out with 3.0 g. of ketone (m. p. 67-67.5°) (0.0077 mole), 1.0 ml. (0.02 mole) of hydrazine hydrate, 5 g. of sodium and 100 ml. of the glycol. A reaction in triethylene glycol (Pract.) after twenty-five hours at 210-190° and recrystallization as before gave 1.67 g. (60%) of 1,14 diphenyltetradecane,[16] m. p. 38–38.5°. As in the previous case, reaction in triethanolamine gave much poorer results. In one run after fifty hours at 225–176° only 5% of the pure product was obtained.

The best results with this diketone were obtained in a larger run under different conditions, with a greater excess of hydrazine. In this case 42 g. (0.11 mole) of starting material was used with 50 ml. (1.0 mole) of hydrazine hydrate, 35 g. of sodium and 1100 ml. of diethylene glycol. The mixture was refluxed (180°) for one hundred and eighteen hours. The yield of purified hydrocarbon was 28.5 g. (73%).

Reduction of Octanone-2.—A reaction with 12.8 g. (0.1 mole) of the ketone (Eastman Pract.), 9 ml. (0.18 mole) of hydrazine hydrate, 20 g. of sodium and 400 ml. of diethylene glycol was carried out at 170–156° for sixty-eight hours. The neutral fraction, after extraction with ether and the previously described treatment, and removal of ether through a short column, was crude hydrocarbon, b. p. 124-132°. Redistillation over sodium gave 8.55 g. (75%) of *n*-octane, b. p. 124.5–125.5°, n^{21}_D 1.401.[17a]

Reduction of Propiophenone.—The treatment was the same as that described for octanone-2, using 0.1 mole of ketone and 8 ml. (0.16 mole) of hydrazine hydrate. The product, b. p. 154-160°, isolated as before after forty-nine hours of refluxing at 193-175°, was redistilled over sodium; yield of *n*-propylbenzene, 9.47 g. (79%), b. p. 156–158° n^{20}_D 1.491.[17b]

Reduction of 2,6-Dimethylheptanone-4.—The reaction, carried out as described for propiophenone, gave 8.95 g. (70%) of 2,6-dimethylheptane, b. p. 131–133°, n^{22}_D 1.398.[17c]

Summary

By the use of glycols or high-boiling alcohols as the reaction medium, the Wolff–Kishner reduction may be carried out in the liquid phase at atmospheric pressure, obviating the isolation of an intermediate hydrazine derivative and the use of bomb tubes or high pressure apparatus. The method has been applied successfully to several representative ketones and three long chain keto acids.

NORTHAMPTON, MASS. RECEIVED MAY 9, 1945

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(14) Schiessler, *et al.*, *Proc. Am. Petroleum Inst.*, **23**, 111, 15 (1942).

(15) Mikeska, Smith and Lieber, *J. Org. Chem.*, **2**, 501 (1938).

(16) This hydrocarbon and the preceding ketone were prepared previously in a separate work, which is still in progress and will be reported on later.

(17) "Beilsteins Handbuch" lists the following constants: (a) b. p. 125-125.6°; n^{20}_D 1.4028; (b) b. p. 158°; n^{20}_D 1.4925; (c) b. p. 133°, $n^{17.6}_D$ 1.3988.