Octadecyl acetonedicarboxylate prepared similarly and crystallized from ethanol melts at 65.0–65.5°.

Anal. Calcd. for $C_{41}H_{80}O_5$: C, 75.40; H, 12.34. Found: C, 75.43, 75.37; H, 12.00, 11.94.

2-Acetoacetoxy-2-methyl-pentanone-4.—A solution of diacetone alcohol (300 g.) in methyl acetoacetate (1000 g.) was heated on the steam-bath for 24 hours. Fractionation through a short column yielded 1210 g. of unreacted starting materials and 54 g. of a fraction, b.p. 120–130° at 10 mm., from which 41 g. of pure acetoacetate was obtained on redistillation; b.p. 125–127° at 10 mm., $n^{25}D$ 1.4424, $\lambda_{max.}^{ethanol}$ 241.5 mμ (log ε 3.07), 306.5 mμ (log ε 2.34).

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.98; H, 8.06. Found: C, 60.22, 60.14; H, 8.19, 8.31.

Acknowledgment.—The authors wish to thank Drs. H. L. Gerhart and S. W. Gloyer for their interest in this work.

MILWAUKEE, WISCONSIN RECEIVED MARCH 31, 1951

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

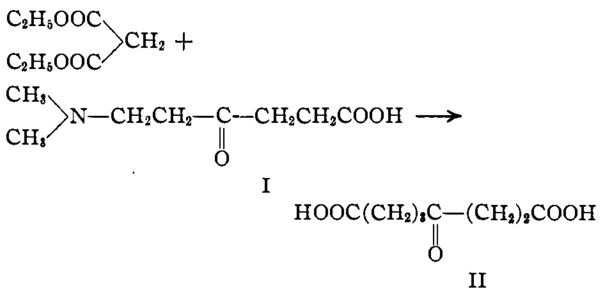
Polycyclic Compounds. II. Reactions of the Mannich Base of Levulinic Acid

BY R. M. DODSON[1] AND PAUL SOLLMAN[2]

6-Dimethylamino-4-ketocaproic acid, the Mannich base of levulinic acid, was successfully condensed with diethyl malonate to give, after hydrolysis and decarboxylation, γ-ketosuberic acid. In a similar manner, the condensation of phenylacetone with 6-dimethylamino-4-ketocaproic acid, yielded β-(4-phenyl-3-keto-1-cyclohexenyl)-propionic acid. The structure of this keto-acid was proved by its conversion to the known 4-phenylbenzoic acid and to the known *trans*-β-(4-phenylcyclohexyl)-propionic acid. A one–three shift of a double bond during the Wolff–Kishner reduction of an α,β-unsaturated ketone is reported.

The synthesis of cyclic ketones by the use of the methiodide of the Mannich base of simple ketones was developed by du Feu, McQuillin and Robinson[3] and has been extensively studied in recent years. In certain cases, the usefulness of this synthetic method would be increased if the reagent possessed an additional functional group or potential functional group. For this reason 4-keto-1,1-dimethylpiperidinium iodide and thiacyclohexan-4-one methiodide[4] have recently been used in the preparation of certain cyclic ketones instead of the more readily available Mannich base methiodides. For a similar reason, in connection with a possible synthesis of estrone, we have investigated the use of 6-dimethylamino-4-ketocaproic acid (the Mannich base of levulinic acid) for the synthesis of cyclic ketones.

In order to study the simplest possible example, one in which cyclization of the primary condensation product was improbable, 6-dimethylamino-4-ketocaproic acid (I) was condensed with diethyl malonate. The resulting product was hydrolysed and decarboxylated to γ-ketosuberic acid (II) in an over-all yield of 56%. Attempts at forming



a quaternary salt of the Mannich base (I) and simultaneously condensing it with diethyl malonate[5] resulted in a lower yield (18%) of the γ-ketosuberic acid (II).

The condensation of phenylacetone with the Mannich base of levulinic acid (I) produced a monoketo-acid (40%) which can be formulated as either IV or V depending on the direction of cyclization of the intermediate 1,5-diketone (III). Since a hydrogen attached to a methyl group is ordinarily more acidic than that attached to a methylene group, one would expect the base-catalyzed cyclization of III to yield β-(4-phenyl-3-keto-1-cyclohexenyl)-propionic acid (IV) rather than the substituted acetic acid V. That IV represented the structure of the compound obtained was established in the following ways.

First, the ultraviolet absorption spectrum of the unsaturated ketoacid, when determined in 95% ethanol, possessed a maximum at 234 mμ (log ε 4.17). This is in accord with structure IV in which the double bond possesses two β-substituents.[6] A compound corresponding to V should possess an absorption maximum at approximately 247 mμ.

Conclusive proof of structure of IV was obtained by its conversion to the known 4-phenylbenzoic acid. The Wolff–Kishner reduction of β-(4-phenyl-3-keto-1-cyclohexenyl)-propionic acid (IV) produced a mixture of olefins which contained approximately 68% of β-(4-phenyl-3-cyclohexenyl)-propionic acid (VI) and presumably 32% of β-(4-phenyl-1-cyclohexenyl)-propionic acid. Compound VI, $\lambda_{max.}$ 247 mμ (log ε 4.11) could be readily obtained from this mixture by crystallization. The ultraviolet absorption spectrum of VI is very similar to that of 1-phenylcyclohexene, $\lambda_{max.}$ 247 mμ (log ε 4.08).[7] In the conversion of IV to VI, the shift of the double bond from Δ^1 to Δ^3 was not unexpected. It has been shown that the Wolff–Kishner reduction of α,β-unsaturated ketones often

(1) G. D. Searle and Company, Chicago, Illinois.

(2) Abstracted from the Ph.D. thesis of Paul Sollman.

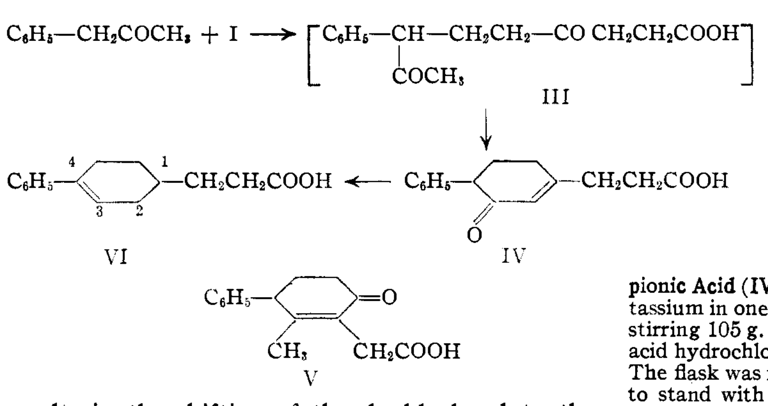
(3) E. C. du Feu, F. J. McQuillin and R. Robinson, *J. Chem. Soc.*, 53 (1937).

(4) H. M. E. Cardwell and F. J. McQuillin, *ibid.*, 708 (1949); H. M. E. Cardwell, *ibid.*, 715 (1949).

(5) For a similar but more successful reaction see N. F. Albertson, S. Archer and C. M. Suter, THIS JOURNAL, **67**, 36 (1945).

(6) R. B. Woodward, *ibid.*, **64**, 76 (1942).

(7) A. C. Cope, F. S. Fawcett and G. Munn, *ibid.*, **72**, 3399 (1950).



results in the shifting of the double bond to the adjacent position,[8] originally occupied by the carbonyl. In this case the Δ^2-olefin, which would result, would be quickly isomerized by the hot alkaline solution to the conjugated Δ^3-olefin, VI.

The mixture of olefins from the Wolff–Kishner reduction was dehydrogenated with sulfur to give 4-phenylhydrocinnamic acid. The latter in turn was oxidized to the known 4-phenylbenzoic acid.

Catalytic reduction of VI, or of the mixture of isomers from the Wolff–Kishner reduction, with platinum oxide in ethanol produced a mixture of *cis*- and *trans*-β-(4-phenylcyclohexyl)-propionic acid, from which the known *trans* isomer, m.p. 147°, was obtained in pure form by crystallization. The *trans* configuration can be definitely assigned to this isomer. It had previously been synthesized[9] from the 4-phenylcyclohexylacetic acid, m.p. 113–114°, whose configuration has since been proved to be *trans*.[10]

We are in process of investigating the reaction of 6-dimethylamino-4-ketocaproic acid with β-tetralone and with 6-methoxy-2-tetralone.

Experimental[11]

γ-Ketosuberic Acid (II).—To a mixture of 12.57 g. (0.060 mole) of 6-dimethylamino-4-ketocaproic acid hydrochloride[12] and 9.61 g. (0.060 mole) of diethyl malonate was added a cold solution of 0.123 mole of sodium ethoxide (prepared from 2.83 g. of sodium) in 50 ml. of absolute ethanol. This reaction mixture was kept at room temperature for 12 days and on the second, fourth and sixth days an additional 0.0035 mole of sodium ethoxide was added (2 ml. of a solution made by dissolving 1.00 g. of sodium in 25 ml. of absolute ethanol). In all 0.1335 mole of sodium ethoxide was used, 0.0135 mole in excess of that required to neutralize the acids present. After 12 days the mixture was acidified with concentrated hydrochloric acid, the solvent was removed under reduced pressure, and water was added. The organic layer was separated and the aqueous layer was extracted with ether. This ether solution was added to the organic product, and the resulting solution was dried with sodium sulfate, then evaporated. The 13.6 g. of light yellow oil remaining was heated under reflux for 12 hours with 30 ml. of dilute (1:1) hydrochloric acid. The solvent was removed under reduced pressure. The residue, on crystallization from a mixture of acetone and petroleum ether, b.p. 60–68°, yielded 6.36 g. (56%) of γ-ketosuberic acid, m.p. 128–133°. Crystallization of this material from water and decolorization of the aqueous solution with charcoal gave 5.36 g. of pure keto-acid, m.p. 133–134°; reported[13] m.p. 130–132°.

Anal. Calcd. for $C_8H_{12}O_5$: C, 51.05; H, 6.43; neut. equiv., 94.1. Found: C, 51.35; H, 6.58; neut. equiv., 94.9.

γ-Ketosuberic acid semicarbazone, m.p. 160–163° (dec.), was prepared in the usual way and crystallized from dilute alcohol. The melting point of the compound varies with the rate of heating.

Anal. Calcd. for $C_9H_{15}N_3O_5$: C, 44.07; H, 6.17. Found: C, 43.95; H, 6.19.

β-(4-Phenyl-3-keto-1-cyclohexenyl)-propionic Acid (IV).—To a solution of 41 g. (1.05 moles) of potassium in one liter of *t*-butyl alcohol at 18° was added with stirring 105 g. (0.50 mole) of 6-dimethylamino-4-ketocaproic acid hydrochloride[12] and 67 g. (0.50 mole) of phenylacetone. The flask was flushed with nitrogen, stoppered, then allowed to stand with occasional shaking in an ice-chest at 12° for 66 hours. The reaction mixture was then acidified with 100 ml. of concentrated hydrochloric acid, and the solvent was removed under reduced pressure. The semi-solid mass, which separated on the addition of 200 ml. of water, was collected on a Büchner funnel. The filtrate from this was extracted with four 50-ml. portions of ether. The semi-solid material was dissolved in 280 ml. of a 7% sodium hydroxide solution, and the resulting solution was extracted with the ether extract obtained above. From this ether extract, 7.3 g. of phenylacetone, b.p. 106–107° (20 mm.), was recovered. The alkaline solution was acidified with 40 ml. of concentrated hydrochloric acid, and the precipitate was collected by filtration. Crystallization of this material from ethyl acetate yielded 43.4 g. (40% yield when allowance is made for the recovered phenylacetone) of the keto-acid IV, m.p. 128–131°. A second crystallization from dilute dioxane gave 41.0 g. of keto-acid, m.p. 130–131°.

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.74; H, 6.60; neut. equiv., 244. Found: C, 73.62; H, 6.86; neut. equiv., 240.

β-(4-Phenyl-3-keto-1-cyclohexenyl)-propionic acid semicarbazone, m.p. 193–195° (dec.), was easily purified by crystallization from dilute alcohol.

Anal. Calcd. for $C_{16}H_{19}N_3O_3$: C, 63.77; H, 6.35. Found: C, 63.84; H, 6.42.

β-(4-Phenyl-3-cyclohexenyl)-propionic Acid (VI).—A solution of 8.00 g. of the keto-acid IV, 7.00 g. of potassium hydroxide and 5.0 ml. of 85% hydrazine hydrate in 50 ml. of diethylene glycol was heated under reflux with an oil-bath for two hours. Then water was distilled from the solution until the internal temperature had risen to 195°. The resulting solution was heated under reflux for 20 hours. It was then diluted with 60 ml. of water and the *p*H lowered to about 8 by the addition of 14 ml. of dilute (1:1) hydrochloric acid. The solution was extracted with ether and treated with carbon. After filtration and acidification with 16 ml. of dilute (1:1) hydrochloric acid, the solution deposited 6.2 g. of material, m.p. 95–100°. This material after crystallization from petroleum ether, b.p. 90–100°, then from dilute ethyl alcohol (Norit), weighed 3.44 g., m.p. 109–114°. It apparently was a mixture of approximately 68% of VI and an isomer presumably having the double bond in the original position. The ultraviolet absorption spectrum of this mixture in 95% alcohol showed $\lambda_{max.}$ 247 mμ (ε 8,800).

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.22; H, 7.88. Found: C, 78.26; H, 8.02.

The isomer possessing the conjugated double bond (VI) was obtained from the above mixture by crystallizations from petroleum ether, b.p. 100–140°, dilute dioxane, and finally dilute acetic acid; m.p. 119–120°; $\lambda_{max.}$ 247 mμ (ε 12,900) in 95% alcohol.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.22; H, 7.88. Found: C, 77.98; H, 8.11.

Similar results were obtained when the semicarbazone of IV was treated with a solution of sodium in diethylene glycol under similar conditions.

4-Phenylhydrocinnamic Acid.—Dehydrogenation of 4.60 g. of the mixture of olefinic acids, m.p. 100–112°, obtained from a Wolff–Kishner reduction of IV, was accomplished by heating it with 1.28 g. of sulfur for one hour at 180–190° and an additional 20 minutes at 200–210°. The resulting material was treated with 100 ml. of 1% sodium hydroxide solution to convert the 4-phenylhydrocinnamic acid into its

(8) G. Lardelli and O. Jeger, *Helv. Chim. Acta*, **32**, 1817 (1949).

(9) C. D. Nenitzescu and J. Gavat, *Ber.*, **70B**, 1883 (1937).

(10) L. F. Fieser, M. T. Leffler and co-workers, This Journal, **70**, 3186 (1948).

(11) Microanalyses by Messrs. Errede and Wheeler. Melting points were taken on a Fisher–Johns melting point apparatus.

(12) C. Mannich and M. Bauroth, *Ber.*, **57**, 1108 (1924).

(13) N. J. Leonard and W. E. Goode, This Journal, **72**, 5404 (1950).

relatively insoluble sodium salt. The suspension was filtered; from the filtrate 0.55 g. of an impure acid, m.p. 135–140°, was obtained. The precipitate, which contained the relatively insoluble sodium 4-phenylhydrocinnamate, was extracted with 250 ml. of hot water. On acidification of this extract 2.23 g. of 4-phenylhydrocinnamic acid[14] separated, which after one crystallization from petroleum ether, b.p. 60–68°, melted at 147–149° (1.85 g.). Recrystallization of this compound from a mixture of benzene and petroleum ether raised the melting point to 151–152°.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.6; H, 6.24. Found: C, 79.5; H, 6.41.

4-Phenylhydrocinnamamide,[14] m.p. 196–197°, was prepared by converting the acid to the acid chloride with thionyl chloride and treating this acid chloride with concentrated ammonium hydroxide.

Anal. Calcd. for $C_{15}H_{15}NO$: C, 80.0; H, 6.71. Found: C, 80.2; H, 6.80.

4-Phenylbenzoic acid, m.p. 227–228°, was obtained by the oxidation of 4-phenylhydrocinnamic acid with alkaline potassium permanganate. It was also converted to methyl 4-phenylbenzoate, m.p. 116–117°, by a Fischer esterification. These compounds are reported[15] to melt at 228° and 117.5°, respectively.

***trans*-β-(4-Phenylcyclohexyl)-propionic Acid.**—Hydrogenation of 1.40 g. of β-(4-phenyl-3-cyclohexenyl)-propionic acid (VI) in 50 ml. of ethyl alcohol using a platinum oxide catalyst stopped after the absorption of one molar equivalent of hydrogen. The product, 1.37 g., m.p. 90–95°, was precipitated from the alcohol by the addition of water. Repeated crystallization of this material from petroleum ether, b.p. 90–100°, yielded the pure *trans*-β-(4-phenylcyclohexyl)-propionic acid, m.p. 146–147°. This compound is reported[9] to melt at 145.5°. The hydrogenation of the mixture of olefins obtained from the Wolff–Kishner reduction of IV proceeded in the same manner. The material, m.p. 96–104°, remaining after removal of some of the pure *trans*-acid by crystallization, was analyzed in order to prove that it was isomeric. The ultraviolet absorption spectrum of this material possessed no maximum at 247 mμ.

Anal. Calcd. for $C_{15}H_{20}O_2$: C, 77.53; H, 8.68. Found: C, 77.82; H, 8.42.

Acknowledgment.—The authors are indebted to the Research Corporation for a grant in support of this research.

(14) An acid, m.p. 145°, and amide, m.p. 196°, presumably identical with those reported here were prepared by C. Willgerodt and T. Scholtz [*J. prakt. Chem.*, [2] **81**, 382 (1910)] by the action of ammonium polysulfide on phenylpropiophenone. The phenylpropiophenone was prepared by the acylation of biphenyl with propionyl chloride and, therefore, should be the *p*-isomer. They claimed, however, to have oxidized the phenylpropiophenone to 3-phenylbenzoic acid, m.p. 160–161°.

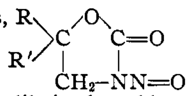
(15) H. C. Gull and E. B. Turner, *J. Chem. Soc.*, 491 (1929); W. Schlenk and T. Wieckel, *Ann.*, **368**, 295 (1909).

MINNEAPOLIS, MINNESOTA RECEIVED MARCH 14, 1951

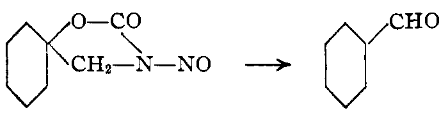
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY]

New Reactions Involving Alkaline Treatment of 3-Nitroso-2-oxazolidones[1]

BY MELVIN S. NEWMAN AND ABRAHAM KUTNER[2]

The preparation of a series of substituted 3-nitroso-2-oxazolidones,  , mainly from ketones RCOR′, is described. On treatment with alkali these compounds decompose readily in the cold to yield aldehydes, ketones, acetylenes and vinyl ethers. When the R groups are aliphatic, aldehydes, RR′CHCHO, are formed. This constitutes a new general method for going from RCOR′ to RR′CHCHO. When the R groups are phenyl, diphenylacetylene is formed. Thus a new general method for going from ArCOAr to ArC≡CAr is at hand although its generality is yet to be established. When one R is aliphatic and one is phenyl, a mixture of disubstituted acetylene and ketone is obtained. When the alkaline decomposition is carried out in absolute alcohols, vinyl ethers are obtained. A mechanism involving a transitory unsaturated carbonium ion, RR′C=C$^+$H, is proposed to account for the products isolated.

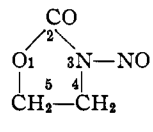
In a previous communication[3] it was shown that 3-nitroso-1-oxa-3-azaspiro[4,5]decan-2-one (I) is converted to hexahydrobenzaldehyde on treatment with alkali.



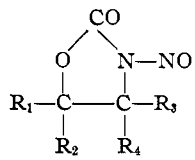
I

Further studies on this type of compound have revealed a number of interesting new reactions which include, in addition to further examples of the aldehyde synthesis as above, the following: (1) formation of diaryl acetylenes; (2) formation of ketones; (3) formation of vinyl ethers. Although our work is far from complete we believe publication at this time is desirable because of the possible utility of these reactions to other workers.

In 1905 Gabriel[4] noted that *n*-nitrosoöxazolidone (II) yielded nitrogen and a small amount of acetylene on treatment with alkali. He also obtained small amounts of acetylene and propyne from nitroso derivatives of oxygen containing heterocyclic amides.[4] We have been unable to find any other references pertinent to this study.



II



III

The compounds herein discussed are of the general formula III. They were made by nitrosation of the corresponding oxazolidones which, in turn, were made by one of two general methods: (1) the rearrangement of β-hydroxyacid azides[5]; and (2) the cyclization of β-aminoalcohols with phosgene,[6] urea[7] or diethyl carbonate.[8] Method

(1) This work was supported by a grant from the Research Corporation. It formed part of the Ph.D. thesis of A. K., O. S. U., 1950.

(2) Hercules Powder Co., Wilmington, Del.

(3) M. S. Newman, THIS JOURNAL, **71**, 378 (1949).

(4) S. Gabriel, *Ber.*, **38**, 2405 (1905).

(5) (a) R. Baltzly and J. S. Buck, THIS JOURNAL, **62**, 164 (1940); (b) W. S. Ide and R. Baltzly, *ibid.*, **70**, 1048 (1948); (c) W. J. Close, *ibid.*, **73**, 95 (1951).

(6) H. L. Crowther and R. McCombie, *J. Chem. Soc.*, **103**, 27 (1913).

(7) J. M. Stratton and F. J. Wilson, *J. Roy. Tech. Coll. (Glasgow)*, **3**, 21 (1933), *C. A.*, **27**, 3203 (1933).

(8) A. H. Homeyer, U. S. Patent 2,399,118, *C. A.*, **40**, 4084 (1946).