Summary

1. The two D-galaheptonic acids have been converted to amorphous ketoöctoses, designated D-gala-L-*tagato*-octose and D-gala-L-*sorbo*-octose. The former has been characterized by its crystalline phenylosazone and phenylosotriazole and the latter by its crystalline keto acetate and phenylosazone.

2. Crystalline 1-diazo-1-desoxy-*keto*-D-gala-L-*tagato*-octose hexaacetate, 1-diazo-1-desoxy-*keto*-D-gala-L-*sorbo*-octose hexaacetate and the amorphous *keto*-D-gala-L-*tagato*-octose heptaacetate are described.

3. D-Gala-L-*manno*-heptonamide dihydrate, hexaacetyl-D-gala-L-*manno*-heptonyl chloride, hexaacetyl-D-gala-L-*gluco*-heptonic acid (and its methyl ester) are described in crystalline condition.

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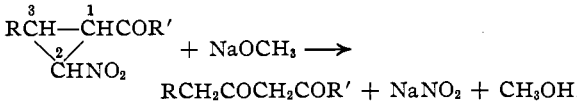
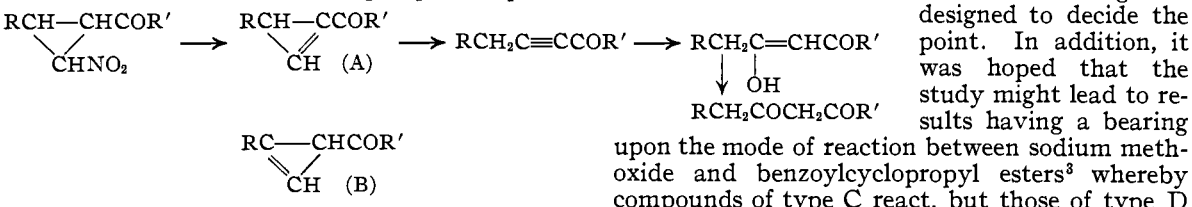
Cyclopropanes. I. The Reaction between Nitrocyclopropyl Ketones and Alkali

BY LEE IRVIN SMITH AND VAUGHN A. ENGELHARDT[1]

Kohler and his students, in a long series of researches,[2] found that nitrocyclopropyl carbonyl compounds, having one hydrogen atom attached to the carbon atom holding the nitro group, reacted with alkaline reagents to produce ultimately 1,3-dicarbonyl compounds.



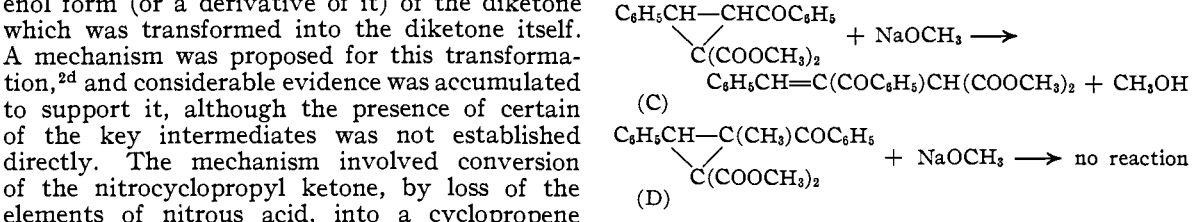
In the reaction, the ring was opened between carbon atoms 1 and 3, the nitro group was replaced



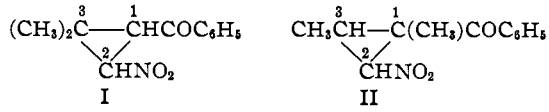
by the hydroxyl- or alkoxyl- group, giving the enol form (or a derivative of it) of the diketone which was transformed into the diketone itself. A mechanism was proposed for this transformation,[2d] and considerable evidence was accumulated to support it, although the presence of certain of the key intermediates was not established directly. The mechanism involved conversion of the nitrocyclopropyl ketone, by loss of the elements of nitrous acid, into a cyclopropene derivative and isomerization of the latter to an α,β-acetylenic ketone which, by addition of the elements of water, would lead to the enol of the 1,3-diketone.

All of the nitrocyclopropyl ketones investigated by Kohler were so constituted that there was at least one hydrogen atom attached to each of carbon atoms 1 and 3; hence, each of these, by loss of the elements of nitrous acid, could give rise to a cyclopropene of either type A, in which the double bond was conjugated with the carbonyl group, or type B, in which the double bond was not so conjugated.

One of the first problems to be solved, therefore, in a study of Kohler's mechanism is the question as to whether the double bond in the hypothetical cyclopropene must lie in the α,β- or β,γ-position to the carbonyl group; this paper is concerned with the results of an investigation designed to decide the point. In addition, it was hoped that the study might lead to results having a bearing upon the mode of reaction between sodium methoxide and benzoylcyclopropyl esters[3] whereby compounds of type C react, but those of type D are unaffected.



Two nitrocyclopropyl ketones, I and II, were synthesized: I is so constituted that loss of the elements of nitrous acid could give a cyclopropene only of type A (α,β), whereas II could give a cyclopropene only of type B (β,γ).



When the 3,3-dimethyl-2-nitro-1-cyclopropyl phenyl ketone (I) was added to methanol containing four equivalents of sodium methoxide,

(1) Abstracted from a thesis presented to the Graduate Faculty of the University of Minnesota by Vaughn A. Engelhardt, in partial fulfilment of the requirements for the Ph.D. degree, August, 1948. Presented at the 115th meeting of the American Chemical Society, San Francisco, California, March 27–April 1, 1949.

(2) (a) Kohler and Engelbrecht, THIS JOURNAL, **41**, 1379 (1919). (b) Kohler and Williams, *ibid.*, **41**, 1644 (1919). (c) Kohler and Rao, *ibid.*, **41**, 1697 (1919). (d) Kohler and Smith, *ibid.*, **44**, 624 (1922). (e) Kohler and Allen, *ibid.*, **50**, 884 (1928).

(3) Kohler and Conant, THIS JOURNAL, **39**, 1404, 1699 (1917).

sodium nitrite precipitated and a neutral liquid, β-methoxy-γ-methyl-α-pentenophenone (III) was isolated. Compound III, hydrolyzed by action of hydrochloric acid in methanol, was con-

$$\text{I} + \text{NaOCH}_3 \longrightarrow (\text{CH}_3)_2\text{CHC}(\text{OCH}_3)=\text{CHCOC}_6\text{H}_5\ (\text{III}) \longrightarrow (\text{CH}_3)_2\text{CHCOCH}_2\text{COC}_6\text{H}_5\ (\text{IV})$$

verted into the 1,3 diketone IV. The identity of IV was established by an independent synthesis from ethyl isobutyrate and acetophenone; the two diketones gave the same copper enolate and the same solid enol *p*-nitrobenzoate. Identity of III was established by its conversion to IV, and by ozonolysis, whereby methyl isobutyrate and benzoic acid were produced.

When the 1,3-dimethyl-2-nitro-1-cyclopropyl phenyl ketone (II) was added to methanolic sodium methoxide, sodium nitrite precipitated and a liquid, α-methyl-β-methoxy-β-penteno-phenone (V) was produced; V, upon hydrolysis by action of hydrochloric acid in methanol was converted into the 1,3-diketone VI. Identity of VI was established by an independent synthesis from ethyl propionate and acetophenone followed by methylation of the 1-phenyl-1,3-pentanedione so produced; the two diketones, by action of hydrazine, gave the same solid pyrazole.

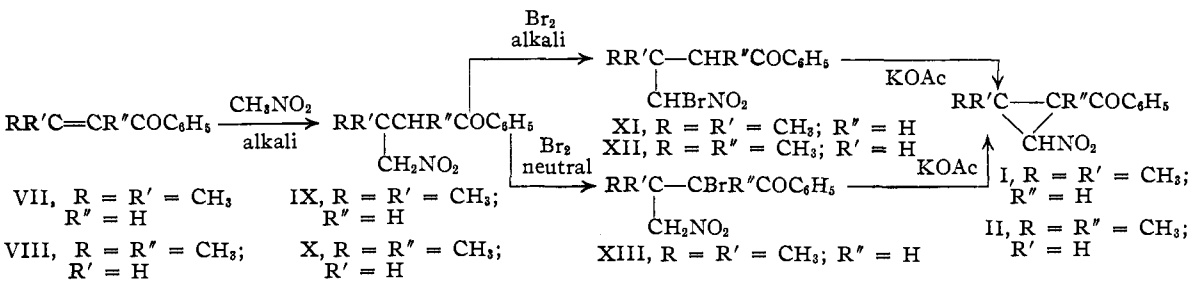
$$\text{II} + \text{NaOCH}_3 \longrightarrow \text{CH}_3\text{CH}=\text{C}(\text{OCH}_3)\text{CH}(\text{CH}_3)\text{COC}_6\text{H}_5\ (\text{V}) \longrightarrow \text{CH}_3\text{CH}_2\text{COCH}(\text{CH}_3)\text{COC}_6\text{H}_5\ (\text{VI})$$

Identity of V was established by its conversion to VI, and by ozonolysis, whereby acetaldehyde and methyl α-benzoylpropionate, identified as the solid pyrazoline, were produced. The absorption spectrum of V indicated the presence of some of the α,β-isomer, although this could not be detected chemically.

Thus it appears that the placement of the double bond in the hypothetical cyclopropene intermediate of Kohler has no effect upon the nature of the ultimate product resulting from the reaction of nitrocyclopropyl ketones with alkali—whether the double bond must lie α,β- or β,γ-, the final product is the same 1,3-diketone. However, there is one difference between the first isolable products formed from the two cyclopropanes I and II: the difference lies in the position of the double bond in the methyl enol ethers III and V. The methyl enol ether III, derived from I, has the double bond in the α,β-position to the carbonyl group. Such a difference in location of the double bond was observed previously[4] in the case of open-chained compounds derived from nitrocyclopropyl diesters. Although III would be the expected product derived by addition of the elements of methanol to the hypothetical intermediate and conjugated acetylenic ketone $(\text{CH}_3)_2\text{CHC}{\equiv}\text{CCOC}_6\text{H}_5$, ether V cannot be derived by so simple a process—here the acetylenic ketone would have to be β,γ-unsaturated, $\text{CH}_3\text{C}{\equiv}\text{CCH}(\text{CH}_3)\text{COC}_6\text{H}_5$, and addition of methanol would have to occur so as to produce entirely V. It is hardly likely that the diketone is produced first and then converted into the enol ether, for V is not the methyl enol ether of VI which would be expected as a result of a direct attack upon VI.

Experimental Part[5]

The route *via* which the nitrocyclopropyl ketones I and II were synthesized paralleled that used by Kohler in the synthesis of nitrocyclopropanes, as follows



β,β-Dimethylacryloyl Chloride.[6]—The acid (20 g., 0.2 mole) was mixed with thionyl chloride (20 cc., 0.3 mole); the solution, after standing for two and one-half hours, was warmed on the steam-bath for an hour and the product was distilled. It boiled at 59–61° (30 mm.), and weighed 19.1 g. (81%).

Isopropylideneacetophenone (VII).[7]—A solution of dimethylacryloyl chloride (160 g., 1.35 moles) in dry benzene (1400 cc.) was cooled (0°) and stirred while aluminum chloride (190 g., 1.42 moles) was added portionwise over a period of thirty minutes. The mixture was stirred for an hour, cooling was discontinued and hydrogen chloride was removed under reduced pressure (150 mm.). The mixture was then heated to 40° under this pressure for three and one-half hours, after which it was cooled and added, with stirring, to ice (1 kg.). The organic layer was removed and washed successively with hydrochloric acid (10%), water, and then with aqueous sodium carbonate (10%) until the alkaline extracts no longer gave senecioic acid when acidified. The solution was dried (Drierite), the solvent was removed by distillation and the residue was fractionated. Two fractions were collected: (a) the ketone VII (75 g., 35%) boiling at 104–106° (5 mm.), $n^{23}\text{D}$ 1.5579 and (b) β-methyl-β-phenylbutyrophenone $(\text{CH}_3)_2\text{C}(\text{C}_6\text{H}_5)\text{CH}_2\text{COC}_6\text{H}_5$,[8] (80 g., 25%) boiling at 162–164° (5 mm.), $n^{20}\text{D}$ 1.5710. The dibromide of VII, crystallized from methanol, melted at 78–79°.[9]

Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{OBr}_2$: C, 41.28; H, 3.78. Found: C, 41.54; H, 3.90.

(4) Kohler and Darling, THIS JOURNAL, **52**, 424 (1930).

(5) Microanalyses by R. W. Amidon, J. Buckley, W. H. Hunter, and S. A. Sundet.

(6) v. Auwers, *Ann.*, **421**, 41 (1920).

(7) Darzens, *Compt. rend.*, **189**, 766 (1929).

(8) Kohler and Engelbrecht, THIS JOURNAL, **41**, 1379 (1919).

(9) Kohler, *Am. Chem. J.*, **42**, 397 (1909), reported the m. p. as 81°.

The saturated ketone was inert to potassium permanganate in acetone.

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 86.30; H, 7.73.

The semicarbazone of the saturated ketone, recrystallized from alcohol, melted at 178.5–179°.

Anal. Calcd. for $C_{18}H_{21}ON_3$: C, 73.19; H, 7.17. Found: C, 73.16; H, 7.37.

β,β-Dimethyl-γ-nitrobutyrophenone (IX).—The ketone VII (75 g., 0.47 mole) and nitromethane (31.5 g., 0.52 mole) in dry ethanol (225 cc.) were refluxed and stirred while a solution of sodium ethoxide (1.4 g. of sodium, 25 cc. of ethanol) was added. The mixture was refluxed for twenty-two hours, then cooled and neutralized with acetic acid (4 cc.). Ethanol was removed under reduced pressure, the residual oil was dissolved in benzene, washed with water and dried (sodium sulfate). The solvent was removed by distillation and the residue, when distilled, formed a clear, pale yellow oil (79 g., 76%) boiling at 155–158° (4 mm.), $n^{21.5}D$ 1.5282.

Anal. Calcd. for $C_{12}H_{15}O_3N$: C, 65.14; H, 6.83. Found: C, 65.39; H, 6.72.

The semicarbazone, crystallized from ethanol, melted at 163–164°.

Anal. Calcd. for $C_{13}H_{18}O_3N_4$: C, 56.10; H, 6.52. Found: C, 55.81; H, 6.86.

β,β-Dimethyl-γ-bromo-γ-nitrobutyrophenone (XI).—A solution of sodium methoxide (2.3 g. of sodium, 30 cc. of dry methanol) was slowly added, with stirring, to the nitroketone IX (20 g., 0.09 mole), while the temperature was not allowed to exceed 5°. After fifteen minutes, the solution of the aci-nitro compound was added dropwise and with stirring to a cold (0°) solution of bromine (5 cc., 0.1 mole) in dry chloroform (30 cc.). Cooling was discontinued and the solution was stirred for thirty-five minutes, after which the solution was washed successively with water, aqueous sodium bisulfite (0.4 g. in 10 cc.), aqueous sodium bicarbonate (10%), and water. The solution was dried (Drierite) and the solvent was removed under reduced pressure. The residue, a clear yellow oil, weighed 25.1 g. (92.5%). The substance decomposed when attempts were made to distill it under reduced pressure (4 mm.), hence the crude material was used directly in the next step.

The semicarbazone, crystallized from aqueous acetic acid, melted with decomposition at 159°.

Anal. Calcd. for $C_{13}H_{17}O_3N_4Br$: C, 43.71; H, 4.80. Found: C, 43.81; H, 5.05.

β,β-Dimethyl-α-bromo-γ-nitrobutyrophenone (XIII).—Liquid bromine (9.8 g., 0.61 mole) was added dropwise (forty-five minutes) to a solution of the nitro ketone IX (12.2 g., 0.055 mole) in dry chloroform (25 cc.). The solution was then stirred for an hour and evaporated to dryness under reduced pressure. The residue, which solidified when rubbed with ethanol, was crystallized from ethanol when it formed clusters of prisms (15.9 g., 96%) melting at 87–88°. The substance gave no reaction with alcoholic silver nitrate or aqueous potassium permanganate.

Anal. Calcd. for $C_{12}H_{14}O_3NBr$: C, 48.04; H, 4.70. Found: C, 48.10; H, 5.01.

3,3-Dimethyl-2-nitro-1-cyclopropyl Phenyl Ketone (I). A. From XI.—The γ-bromo compound XI (25.1 g., 0.082 mole) was dissolved in a solution of potassium acetate (24.6 g., 0.25 mole, freshly fused) in dry methanol (90 cc.). The solution was allowed to stand at room temperature for fifteen hours, potassium bromide was removed, and the filtrate was refluxed until no more potassium bromide separated (thirteen hours). Methanol was removed under reduced pressure, the crystalline residue was washed with water and recrystallized from ethanol, when it formed clusters of prisms (13.8 g., 75%) melting at 65.5–66.6°.

Anal. Calcd. for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98. Found: C, 65.59; H, 6.01.

B. From XIII.—The α-bromo compound XIII (15 g., 0.05 mole) was mixed with a solution of potassium acetate (14.7 g., 0.15 mole) in dry methanol (90 cc.). Potassium bromide separated immediately and heat was evolved; after twenty minutes, potassium bromide was removed and the filtrate was refluxed for eight hours. Methanol was removed under reduced pressure and water was added to the semi-solid residue. The residue was extracted with benzene, the extract was dried (Drierite) and the solvent was removed under reduced pressure. The residual oil (11.4 g.) could not be induced to crystallize. A portion (6 g.) of it, distilled under a pressure of 0.2 mm., gave two fractions: (a) bath temperature 80–115°, 1.2 g., (b) bath temperature 115–180°, 2.5 g. Fraction a solidified on cooling and, when recrystallized from ethanol, melted at 65.5–66.5°, alone or when mixed with I prepared from the γ-bromo compound.

Anal. Calcd. for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98. Found: C, 65.52; H, 6.04.

Fraction b solidified to a brittle, orange glass, apparently a polymer. The cyclopropane I was soluble in ethanol, methanol, and ether, and insoluble in water. It contained nitrogen, but no halogen; the ferrous hydroxide test for the nitro group was positive. No reaction was observed between I and (a) bromine in carbon tetrachloride, (b) aqueous-acetone solution of potassium permanganate; or when an alcoholic solution of I was refluxed with zinc dust for several hours. These properties, together with the synthesis from the two bromo compounds, serve to establish the structure of I. The compound gave no phenylhydrazone or 2,4-dinitrophenylhydrazone; a semicarbazone was formed, but it could not be purified. The oxime, formed from I and hydroxylamine hydrochloride in pyridine and ethanol, and crystallized several times from aqueous ethanol, melted at 121.5–123°.

Anal. Calcd. for $C_{12}H_{14}O_3N_2$: C, 61.52; H, 6.02. Found: C, 61.52; H, 6.13.

This oxime (0.5 g.) when hydrolyzed by action of a mixture of warm hydrochloric acid (1 cc.), water (1 cc.) and formalin (40%, 0.35 cc.) gave 0.3 g. of the cyclopropane I, m. p. and mixed m. p., 64–66°.

γ-Bromo-β-nitroisocaprophenone $(CH_3)_2CBrCHNO_2$-$CH_2COC_6H_5$.—The cyclopropyl ketone I (11 g., 0.05 mole) was added portionwise, with stirring, to acetic acid (50 cc.) which had been saturated with hydrogen bromide at 0°. The solution solidified; more acetic acid (20 cc.) was added, and the mixture was stirred for one hour and poured into ice water. The solid was removed, washed free of acid with water, and crystallized from ethanol. The resulting needles (11.5 g., 76%) melted at 112–113°. The substance contained both nitrogen and halogen, and gave a precipitate of siliver bromide with alcoholic silver nitrate.

Anal. Calcd. for $C_{12}H_{14}O_3NBr$: C, 48.04; H, 4.70. Found: C, 48.03; H, 4.85.

β-Methoxy-γ-methyl-α-pentenophenone (III).—The cyclopropane I (8.5 g., 0.039 mole) was added, with stirring, to a solution of sodium methoxide (3.6 g. of sodium, 40 cc. of dry methanol). Sodium nitrite separated and the temperature rose to 60°; the solution was stirred until the temperature dropped to 30° (seventy minutes). Ice water (100 cc.) was added and the solution was extracted three times with ether. The combined extracts were washed with aqueous sodium bicarbonate (5%) until neutral (litmus), dried (Drierite), and evaporated. When distilled, the residual oil gave a clear yellow distillate (3.8 g., 48%) boiling at 141–143° (8 mm.) (117–119°) (3 mm.) and having $n^{25}D$ 1.5482.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.43; H, 7.90. Found: C, 76.64; H, 8.12.

The substance was insoluble in aqueous sodium hydroxide (10%), gave a red color with alcoholic ferric chloride, decolorized aqueous permanganate, decolorized a solution (2%) of bromine in carbon tetrachloride, and did not react with aqueous copper acetate. The methoxy compound (3.65 g., 0.018 mole) in ethyl bromide (70 cc.) was subjected at −20 to −30° for two hours to a current of ozonized oxygen (5.6%). The solution was concen-

trated to 20 cc. in a current of dry air and was then added to a boiling mixture of water (70 cc.), zinc dust (1.2 g.), a few crystals of hydroquinone and a few drops of aqueous silver nitrate. Water (50 cc.) was removed by distillation, the zinc sludge was removed, and the filtrate, when cooled, deposited benzoic acid, m. p. 122°. The total amount of benzoic acid obtained by filtration and extraction of the filtrate and the zinc sludge was 1 g. (46%). The aqueous distillate (50 cc.) was saturated with potassium carbonate, extracted with ether, and the extract was dried (Drierite). Removal of the solvent and distillation of the residue gave a distillate of methyl isobutyrate (0.87 g., 48%), b. p., 88–89° (760 mm.), $n^{20}D$ 1.3831. The ester was hydrolyzed and the acid was identified as the *p*-phenylphenacyl ester, m. p., 88–89°, alone or when mixed with an authentic specimen.

4-Methyl-1-phenyl-1,3-pentanedione (IV).—The methoxy compound III (0.8 g.) was refluxed with methanol (4 cc.) and hydrochloric acid (0.6 cc.) for seventy-five minutes. The solution was diluted with water, extracted with ether, and the extract was washed with aqueous sodium bicarbonate (10%) until neutral. The solvent was evaporated, the residue was dissolved in methanol (3 cc.) and the solution was shaken with a hot, aqueous solution of cupric acetate monohydrate (0.6 g.). The copper enolate (0.9 g.) was removed and crystallized twice from aqueous methanol, when it formed an olive green solid melting at 163–164° (dec.).

Anal. Calcd. for $C_{24}H_{26}O_4Cu$: C, 65.21; H, 5.93. Found: C, 65.45; H, 6.16.

The copper enolate (1.5 g.) suspended in ether (20 cc.) was shaken with sulfuric acid (5 cc., 20%) until the ether layer was colorless. The ether layer was washed with aqueous sodium bicarbonate and then with water until neutral (litmus) and dried (Drierite). The solvent was removed and the residual liquid was distilled. The distillate (0.9 g.) boiled at 121–122° (5 mm.), and had $n^{27}D$ 1.5696. The diketone reacted with *p*-nitrobenzoyl chloride in the presence of pyridine to give a *p*-nitrobenzoate which melted at 115.5–116.5° after crystallization from aqueous ethanol.

Anal. Calcd. for $C_{19}H_{17}O_5N$: C, 67.25; H, 5.05. Found: C, 67.17; H, 5.34.

The diketone IV was prepared from acetophenone (21 g., 0.175 mole), ethyl isobutyrate (40.5 g., 0.35 mole) and solid sodium methoxide following the general procedure of Adkins, *et al.*,[10] and purified *via* the copper enolate. The diketone boiled at 118–120° (5 mm.)[11]; the yield was poor.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.58; H, 7.40.

The copper enolate, crystallized from methanol, melted at 163° (dec.) alone or when mixed with the copper enolate obtained via the methoxy compound III; similarly, the *p*-nitrobenzoate melted at 115.5–116.5°, alone or when mixed with the *p*-nitrobenzoate obtained via the methoxy compound III.

The method of Blaise and Herman,[12] involving a Friedel–Crafts reaction between tiglyl chloride and benzene, does not produce the ketone VIII in such a form that it can be purified. The route finally chosen, and which gave pure VIII in good yield, involved the following steps

$$C_6H_5COCH_2CH_3 \xrightarrow[Na + NaOEt]{HCOOEt} HOCH{=}C(CH_3)COC_6H_5 \underset{HCl}{\overset{Me_2NH\cdot HCl}{\rightleftharpoons}} (CH_3)_2NCH{=}C(CH_3)COC_6H_5 \xrightarrow[61\%]{CH_3MgI} VIII\ 70\%$$

68%

α-Hydroxymethylenepropiophenone.—Dry ethanol (9.2 g., 0.2 mole) was added dropwise and with stirring to a cooled (5°) suspension of powdered sodium (46 g., 2 moles) in dry ether (500 cc.). A solution of propiophenone (268 g., 2 moles) in ethyl formate (188 g., 2.5 moles) was then added, with stirring and at such a rate that the temperature was maintained below 10°. Then dry ethanol (82.8 g., 1.8 moles) was added gradually and the mixture was stirred for half an hour at 0° and three and one-half hours at room temperature. Sufficient ice water was added to dissolve the solid material, and the ether layer was removed (from this there was recovered 73.2 g. of propiophenone). The alkaline aqueous layer was acidified with hydrochloric acid and the solid was removed and dried for forty-eight hours in a vacuum desiccator over solid potassium hydroxide. The solid weighed 222 g. (68.5%) and melted at 118–119°, the value given in the literature.[13]

α-Dimethylaminomethylenepropiophenone.—The above hydroxymethylene compound (233.6 g., 1.44 moles) was dissolved in a solution of sodium ethoxide (33.2 g. of sodium, 800 cc. of dry ethanol). Dimethylamine hydrochloride (128 g., 1.57 moles) was added; the flask was stoppered and allowed to stand at room temperature for sixty-eight hours. Sodium chloride was removed, and alcohol was removed from the filtrate by distillation. Water was added to the residue and the whole was extracted several times with ether. The combined extracts were washed with aqueous sodium hydroxide (10%) until a test portion, on acidification, gave no precipitate of the hydroxymethylene compound (32.7 g. recovered). The ether solution was then washed with water, dried (Drierite), the solvent was removed; and the residue was distilled. The product (167 g., 61%), a clear yellow liquid, boiled at 169–172 (5 mm.) and had $n^{26}D$ 1.6175. When warmed briefly with dilute hydrochloric acid, the substance was rapidly converted into the hydroxymethylene compound.

Anal. Calcd. for $C_{12}H_{15}ON$: C, 76.15; H, 7.99. Found: C, 75.45; H, 8.04.

α-Methyl-α-butenophenone (VIII).—The above dimethylamino compound (115.6 g., 0.61 mole) in dry ether (200 cc.) was added dropwise (one hour) and with stirring to a cooled (0°) solution of methylmagnesium iodide (from methyl iodide, 149 g., 1.05 moles, magnesium 23 g., 0.95 g. atom, dry ether, 450 cc.). Stirring was continued for another forty minutes, when the mixture solidified. The mass was broken up and added gradually, with stirring, to hydrochloric acid (165 cc.) and ice. The layers were separated; the aqueous layer was extracted with ether, the combined ether solutions were washed with aqueous sodium bicarbonate and then with water, and dried (Drierite). Ether was removed, and the residue was distilled. The product (69.2 g., 71%) boiled at 99–102° (6 mm.), and had $n^{29.5}D$ 1.5402, $n^{19.5}D$ 1.5460.

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.22; H, 7.69.

The *p*-nitrophenylhydrazone, crystallized several times from ethanol, melted at 124–125° (dec.).

Anal. Calcd. for $C_{17}H_{17}O_2N_3$: C, 69.13; H, 5.80. Found: C, 68.83; H, 6.00.

α,β-Dimethyl-γ-nitrobutyrophenone (X).—A solution of nitromethane (31.5 g., 0.52 mole) and the ketone VIII (75 g., 0.47 mole) in dry ethanol (240 cc.) was refluxed and stirred while sodium ethoxide (sodium, 1.2 g., dry ethanol, 30 cc.) was added. The mixture was stirred and refluxed for twenty-one hours, then cooled and neutralized with acetic acid (3 cc.). Most of the solvent was removed by distillation under reduced pressure; water was added to the residue and the whole was extracted with ether. The combined extracts were dried (Drierite), the solvent

(10) Sprague, Beckham and Adkins, THIS JOURNAL, **56**, 2665 (1934).

(11) Styles, *Ber.*, **20**, 2181 (1887), prepared this compound, but gives no experimental data. He gives the b. p. as 170° (26 mm.).

(12) Blaise and Herman, *Ann. chim. phys.*, [8] **23**, 529 (1911).

(13) Claisen and Meyerowitz, *Ber.*, **22**, 3277 (1889).

was removed, and the residue oil was distilled. A small forerun (20 g., b. p., 92–158° (6 mm.)) was followed by a clear, straw-colored liquid (65.7 g., 63.5%) boiling at 158° (6 mm.), $n^{23}D$ 1.5289. The substance, on standing, became deep reddish-purple in color.

Anal. Calcd. for $C_{13}H_{15}O_3N$: C, 65.14; H, 6.83. Found: C, 65.25; H, 7.10.

γ-Bromo-α,β-dimethyl-γ-nitrobutyrophenone (XII).—The nitroketone X (18.5 g., 0.084 mole) was cooled (0°) and stirred while a solution of sodium methoxide (sodium, 2 g., dry methanol, 30 cc.) was added. The solution of the sodium derivative was then added, with stirring, to a solution of bromine (4.7 cc., 0.092 mole) in dry chloroform (30 cc.) at 5°. Cooling was discontinued, chloroform (10 cc.) was added, and the solution was stirred for thirty minutes. The solution was washed successively with water, aqueous sodium bisulfite, aqueous sodium bicarbonate (10%), and water. The solution was dried (Drierite) and the solvent was removed under reduced pressure. The residual oil (22.8 g.) could not be distilled; it decomposed explosively when a portion of it was heated under reduced pressure.

1,3-Dimethyl-2-nitro-1-cyclopropyl Phenyl Ketone (II).—The crude bromo compound XII (91.7 g., 0.31 mole) was dissolved in dry methanol (300 cc.) containing potassium acetate (92.5 g., freshly fused), and the solution was refluxed for forty-three hours. Potassium bromide was removed, and methanol was removed from the filtrate by distillation under reduced pressure. Water was added to the residual oil and the purple solid was removed, washed with ethanol, and crystallized from ethanol (100 cc.). The material still retained a purple tinge, which was removed by washing the solid with small portions of ether. The colorless solid (20.5 g., 31%) then melted at 85–86°.

Anal. Calcd. for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98. Found: C, 65.99; H, 6.19.

A purple oil (38.4 g.) was recovered from the mother liquors and from the aqueous residues by ether extraction; this oil could not be induced to crystallize, nor could it be separated into pure materials by distillation.

The oxime, prepared from the ketone and hydroxylamine hydrochloride in pyridine and ethanol, and recrystallized from alcohol (Norit), melted at 178–179.5° (dec.).

Anal. Calcd. for $C_{12}H_{14}O_3N_2$: C, 61.52; H, 6.02. Found: C, 61.42; H, 6.16.

The cyclopropane II (1.1 g.) was recovered unchanged when subjected, at 0° for two hours, to the action of acetic acid (8 cc.) saturated with hydrogen bromide. When the time was increased to two days, the product was an oil from which no pure material could be isolated. The cyclopropane did not reduce an aqueous acetone solution of potassium permanganate.

β-Methoxy-α-methyl-β-pentenophenone (V).—The cyclopropane II (15 g., 0.7 mole) was added, with stirring, to a solution of sodium methoxide (sodium, 6.3 g., dry methanol, 70 cc.). The temperature rose to 48°, the ketone dissolved, and sodium nitrite separated. The solution was stirred for two and one-half hours, cooled, and the sodium nitrite was removed. The filtrate was diluted with water and extracted with ether. The combined extracts were washed with water until neutral (litmus), dried (Drierite), and the solvent was removed. Distillation of the residual oil gave a colorless liquid (10.7 g., 77%) which boiled at 133.5–135.5 (8 mm.), and had $n^{20}D$ 1.5287.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.43; H, 7.90. Found: 76.37; H, 8.02.

The methoxy compound V decolorized permanganate, and reacted by addition with a solution of bromine in carbon tetrachloride. There was no reaction with aqueous cupric acetate. The aqueous residues from the preparation of V were acidified and extracted with ether; the ether extract contained no product.

The methoxy compound V (3.5 g., 0.017 mole) in ethyl bromide (60 cc.) was subjected for two and one-half hours to the action of ozonized oxygen (5%) at −20 to −30°. Ethyl bromide (45 cc.) was removed in a current of dry air and the remaining solution was added dropwise to a boiling mixture of water (70 cc.) and zinc dust (1.2 g.), containing a little hydroquinone and a few drops of aqueous silver nitrate, contained in an apparatus arranged for downward distillation, with the receiver cooled in an ice-bath. Ethyl bromide was removed from the distillate, washed with water, and the water was added to the aqueous layer of the distillate. Evaporation of the ethyl bromide left 0.2 g. of oily material. The aqueous portion of the distillate was added to a solution of dimedon (2.7 g.) in ethanol (12 cc.) and water (48 cc.) containing piperidine (4 drops). The solution was saturated with sodium acetate and set aside in a refrigerator overnight. The solid (0.9 g., equivalent to acetaldehyde, 34%) was removed and crystallized from methanol, when it melted at 140.5–141.5° alone or when mixed with an authentic specimen of the dimedon derivative of acetaldehyde. The residue of zinc dust and water remaining in the distilling flask was extracted with ether. The combined extracts were added to the oily material remaining after evaporation of ethyl bromide, the whole was dried (Drierite) and the solvent was removed. The residual oil gave a pale yellow distillate (1.8 g.) boiling at 121° (8 mm.), and having $n^{20}D$ 1.5252. This material was impure methyl α-benzoylpropionate, identified by conversion, by action of hydrazine, into 3-phenyl-4-methylpyrazolone-5, m. p., 212–215° (dec.), alone or when mixed with an authentic specimen of the pyrazolone prepared from ethyl α-benzoylpropionate.[14]

Anal. Calcd. for $C_{10}H_{10}ON_2$: C, 68.94; H, 5.79. Found: C, 69.24; H, 6.06.

Although the results of ozonolysis of V indicated only the β,γ-unsaturated ketone, the absorption spectrum in the ultraviolet of V in ethanol showed a rather intense band at 245 mμ, and a weak band at 315 mμ, indicating the presence of some of the α,β-form.[15]

2-Methyl-1-phenyl-1,3-pentanedione.—The methoxy compound V (1.2 g., 0.006 mole) was refluxed with methanol (1.5 cc.) and hydrochloric acid (0.5 cc.) for five minutes; the solution was diluted with water and extracted with ether. The extracts were washed with aqueous sodium bicarbonate (5%) until neutral (litmus), then with water, and dried (Drierite). Ether was removed and the residue, on distillation, gave 2-methyl-1-phenyl-1,3-pentanedione (0.9 g., 80%) boiling at 128° (3 mm.), and having $n^{22}D$ 1.5266.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.31; H, 7.59.

The diketone formed a copper enolate melting at 173–175° (dec.) and was converted in 77% yield into 3-ethyl-4-methyl-5-phenylpyrazole, m. p. and mixed m. p. 100.5–101.5°, by action of hydrazine hydrate (80%).

1-Phenyl-1,3-pentanedione.—Sodium amide (0.9 mole)[16] was suspended in dry ether; acetophenone (54 g., 0.45 mole) in dry ether (50 cc.) was added with stirring. After ten minutes, ethyl propionate (91.8 g., 0.9 mole) was added and the mixture was stirred and refluxed for two hours, when it was almost completely solid. The product was added to ice-water (400 cc.), the mixture was acidified with hydrochloric acid (50%) and extracted with ether. The combined extracts were washed with aqueous sodium bicarbonate (5%), then with water, and dried (Drierite). Ether was removed by distillation, and then unchanged starting materials were removed by distillation at 120° (5 mm.). Distillation of the residue gave the diketone (48.2 g., 61%) boiling at 120–122° (5 mm.), and having $n^{20}D$ 1.5837. The copper enolate, crystallized twice from methanol, melted at 151°.[17]

(14) v. Auwers and Mauss, *J. prakt. Chem.*, **110**, 221 (1925), give the m. p. as 213–214.5°.

(15) Menschick, Page and Brossert, *Ann.*, **495**, 225 (1932).

(16) Adams, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y. 1942, p. 99.

(17) Andre, *Compt. rend.*, **152**, 1489 (1912), reported a value of 152°.

2-Methyl-1-phenyl-1,3-pentanedione.—The above diketone (46 g., 0.25 mole) in dry ether (250 cc.) was added dropwise, with stirring, to a suspension of powdered sodium (6 g., 0.25 g. atom) in dry ether (80 cc.) at 0°. The mixture was stirred for three hours at 0°; ether was removed under reduced pressure and the residue was dissolved in dry acetone (300 cc.). The solution was stirred while methyl iodide (0.5 mole) was added dropwise; after addition was complete, the mixture was stirred for one and one-half hours and then allowed to stand overnight. Excess methyl iodide and acetone were removed by distillation under reduced pressure, water was added, and the whole was extracted with ether. The extract was dried (Drierite), ether was removed, and the residue was distilled. The product (35.1 g., 71%), a pale yellow liquid, boiled at 128–130° (5 mm.), and had $n^{20}D$ 1.5268, $n^{22}D$ 1.5261.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.61; H, 7.69.

The diketone formed a copper enolate which, crystallized from methanol, was olive-green and melted at 173–175° (dec.), but there was always a small amount that remained unmelted and no feasible way was found to purify the substance.

3-Ethyl-4-methyl-5-phenylpyrazole.—Hydrazine hydrate (80%, 1.2 cc.) was added, with cooling and shaking, to the above diketone (2.4 g., 0.013 mole). Ethanol was added dropwise until the mixture became homogeneous; the solution was refluxed for five minutes, then cooled and diluted with water. The resulting heavy oil (2.1 g., 89%) solidified on standing in a refrigerator overnight. The product was crystallized three times from aqueous alcohol, when it melted at 100.5–101.5°, alone or when mixed with the pyrazole prepared from the diketone resulting from hydrolysis of V.

Anal. Calcd. for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58. Found: C, 77.25; H, 7.72.

Summary

1. Two new nitrocyclopropyl ketones, each representing a new type of these substances, have been synthesized. One of these, 3,3-dimethyl-2-nitro-1-cyclopropyl phenyl ketone (I), has no hydrogen attached to the number 3 carbon atom of the ring; the other, 1,3-dimethyl-2-nitro-1-cyclopropyl phenyl ketone (II), has no hydrogen attached to the number 1 carbon atom of the ring.

2. Both of the new nitrocyclopropanes have been converted into 1,3-diketones by reaction with sodium methoxide; hence, if the reaction involves intermediate cyclopropenes formed by loss of the elements of nitrous acid, it is immaterial whether the double bond in the cyclopropene lies in the α,β- or β,γ- position to the carbonyl group. However, the precursors of the diketones, the methyl enol ethers, do differ in the two cases: from I, with no hydrogen attached to C-3 of the ring, the β-methoxy ketone is unsaturated at the α,β-position; from II, with no hydrogen attached to C-1 of the ring, the β-methoxy ketone is unsaturated at the β,γ- position.

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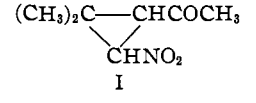
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

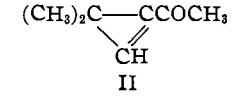
Cyclopropanes. II.[1] An Aliphatic 2-Nitro-1-cyclopropyl Ketone. Mechanism of the Reaction between Nitrocyclopropyl Ketones and Alkali

BY LEE IRVIN SMITH AND VAUGHN A. ENGELHARDT[2]

In the previous paper,[1] it was shown that in the transformation of a nitrocyclopropyl ketone into a 1,3-diketone by action of alkali, the position of the double bond in the hypothetical cyclopropene intermediate was immaterial; whether the nitrocyclopropane was so constituted that the intermediate cyclopropenyl ketone possessed the double bond in the α,β- or β,γ-position to the carbonyl group, the ultimate product was a 1,3-diketone. In all the nitrocyclopropyl ketones previously studied, there was always at least one aromatic group present as a substituent and, in addition, the ring held directly a carbonyl or carbalkoxyl group. To explore the possible effects of these two groupings upon the reaction with alkali, a purely aliphatic nitrocyclopropyl ketone, I, has been prepared. This substance is of the type which could give only an α,β-cyclopropene ketone, II, by loss of the elements of nitrous acid.



I



II

The preparation of I followed the conventional route established by Kohler and his students[3]; nitromethane was added to mesityl oxide to give the nitro ketone III, which, when brominated in alkaline solution, gave the liquid γ-bromo compound IV. When IV was subjected to the action of potassium acetate in methanol, the elements of hydrobromic acid were eliminated and a compound $C_7H_{11}O_3N$ resulted. In contrast with all the other γ-nitro ketones so far studied, III is a methyl ketone, and the possible compounds formed by ring closure of the bromo compound IV derived from III exceed in number those possible when the ketone is a phenyl- or *t*-butyl ketone. *A priori*, it cannot be taken for granted that bromination of III, even though in

(1) Paper I, Smith and Engelhardt, THIS JOURNAL, **71**, 2671 (1949).

(2) Abstracted from a thesis presented to the Graduate Faculty of the University of Minnesota by Vaughn A. Engelhardt, in partial fulfilment of the requirements for the Ph.D. degree, August, 1948. Presented at the 115th meeting of the American Chemical Society, San Francisco, California, March 27–April 1, 1949.

(3) For example, Kohler and Smith, THIS JOURNAL, **44**, 624 (1922).