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

Cyclopropanes. XIX.[1] 1-Benzoyl-2-nitro-2,3,3-trimethylcyclopropane and its Reaction with Alcoholic Sodium Methoxide

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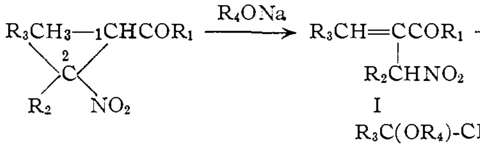
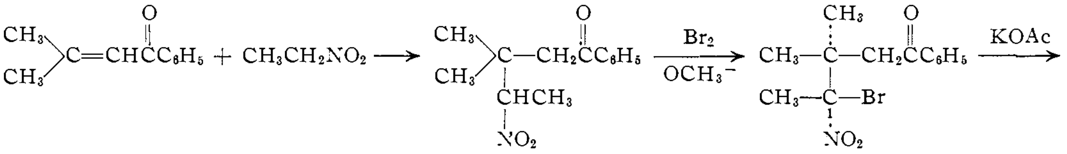
The tertiary nitrocyclopropyl ketone VI, named in the title, has been subjected to the action of basic reagents. The chief products isolated were of two types: (a) base-insoluble, nitrogen-free ketones, of which the major constituent was shown to be VII, the 1-benzoyl derivative of 2,3-dimethylbutadiene, and (b) unstable, nitrogenous, base-soluble solids, which included 3-methyl-5-phenyl-4-isoxazolone (XIII), existing almost entirely in the enolic form. A mechanism has been proposed to account for the formation of these products from VI; this involves opening of the ring at the 2,3-bond, a reverse aldol reaction, and recombination of these products to give the final products isolated.

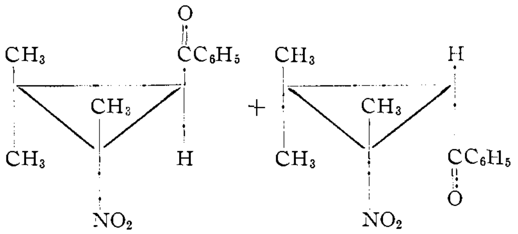
The action of basic reagents on various secondary nitrocyclopropyl ketones and tertiary nitrocyclopropyl ketones has been investigated in the preceding papers in this series.[1] Tertiary nitrocyclopropyl ketones usually react with alcoholic bases[4-6] to give unsaturated nitro ketones I and/or enol ethers of 1,4-diketones II, depending apparently on the configuration of the nitrocyclopropyl ketone. In all cases the tertiary nitrocyclopropyl ketones contained hydrogen atoms attached to carbon 1 and carbon 3 of the cyclopropane ring. It was of interest to prepare a tertiary nitrocyclopropyl ketone with only one ring hydrogen at carbon 1 and follow its reaction with alcoholic base. If the assumption that the initial step in these basic reactions is anion formation by removal of a ring hydrogen, the only position open for attack would be at carbon 1. It was hoped that the reaction of a ketone of this type could be correlated with earlier mechanisms postulated for this general reaction.[7]


I

$R_3C(OR_4)\text{-}CR_2CH_2COR_1$

The two possible isomers of 1-benzoyl-2-nitro-2,3,3-trimethylcyclopropane were synthesized by the method originally developed by Kohler. Nitroethane was added to isopropylideneacetophenone (III) to give β,β-dimethyl-γ-nitrovalerophenone (IV) in 68% yield. Alkaline bromination of IV produced the γ-bromo compound V quantitatively. Cyclization of V by action of refluxing methanolic potassium acetate gave, in 82% yield, a mixture of the two isomeric nitrocyclopropyl ketones VIa and VIb melting at 55° and 101–102°, respectively. The 55° isomer constituted 98% of the mixture. Methanolic ammonia, a reagent used for similar isomerizations,[8] converted the 101° isomer to the 55° isomer, but the 55° compound was recovered unchanged from a similar experiment. Neither of these isomers showed any nitrocarbonyl interaction in their infrared spectra.[9] The more stable 55° isomer probably has the *trans* structure VIa.


III IV V


VIa VIb

The reaction of VIa with refluxing methanolic sodium methoxide resulted in a brown solution and a precipitate of sodium nitrite. The reaction mixture was added to water. Distillation of this basic aqueous solution into 2,4-dinitrophenylhydrazine solution yielded acetone 2,4-dinitrophenylhydrazone. No acetone could be obtained from the reaction mixture before addition of water. Ether extraction of the aqueous basic mixture gave an ether solution of base-insoluble, nitrogen-free ketones. Acidification of the basic aqueous layer and ether extraction gave unstable base-soluble nitrogen-containing products in ether solution. The relative yields of the base-soluble products, the base-insoluble products, and acetone changed somewhat with conditions but did not vary greatly from 1:1.

The base-insoluble fraction was separated by chromatography over alumina. The main constituent was a liquid, nitrogen-free ketone. Analy-

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[1] Paper XVIII, L. I. Smith and Earl D. Holly, THIS JOURNAL, **78**, 1480 (1956).

[2] In part, abstracted from a thesis by W. L. Kohlhase, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, April, 1952.

[3] du Pont Post-doctoral Fellow.

[4] E. P. Kohler and P. Allen, Jr., THIS JOURNAL, **50**, 884 (1928).

[5] C. F. H. Allen and M. P. Bridges, *ibid.*, **51**, 2151 (1929).

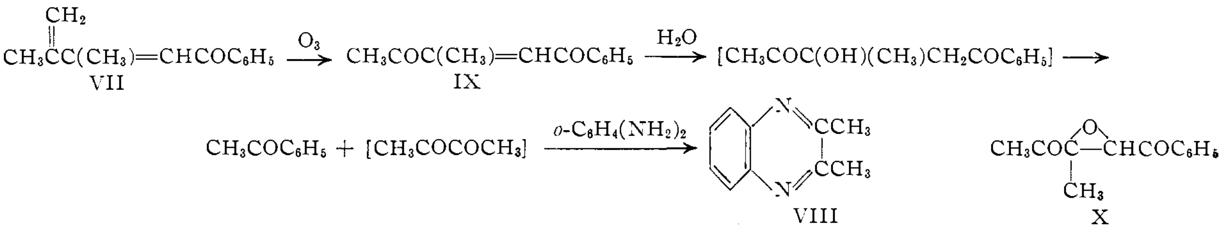
[6] L. I. Smith and J. S. Showell, *J. Org. Chem.*, **17**, 827 (1952).

[7] L. I. Smith and V. A. Engelhardt, THIS JOURNAL, **71**, 2676 (1949).

[8] E. P. Kohler and L. I. Smith, *ibid.*, **44**, 624 (1922).

[9] This absence of nitrocarbonyl interaction in the infrared spectra has been observed previously; L. I. Smith and E. R. Rogier, *ibid.*, **73**, 3831 (1951); L. I. Smith and E. D. Holly, *ibid.*, **78**, 1472 (1956).

sis showed its empirical formula to be $C_{13}H_{14}O$. The ultraviolet spectrum of this compound showed a maximum at 288 mμ which suggested the presence of a stronger conjugated system than a simple α,β-unsaturated phenyl ketone. The carbonyl stretching frequency in the infrared spectrum was at 1656 cm.$^{-1}$ which indicated at least α,β-unsaturation. Action of potassium permanganate upon $C_{13}H_{14}O$ resulted in the recovery of about one-third of the theoretical amount of benzoic acid. Hydrogenation of the unknown ketone over platinum gave a saturated ketone with the absorption of two moles of hydrogen. The infrared spectrum and the 2,4-dinitrophenylhydrazone of this saturated ketone were identical with those from an authentic sample of β,γ-dimethylvalerophenone (XII). Therefore the unsaturated ketone $C_{13}H_{14}O$ is 1-benzoyl-2,3-dimethylbutadiene (VII). Ozonolysis of this compound gave benzoic acid (31%), formaldehyde (18%), a neutral solid carbonyl compound, $C_{12}H_{12}O_3$, and a liquid which made up the major portion of the product. This liquid analyzed as a mixture of $C_{12}H_{12}O_2$ and the solid $C_{12}H_{12}O_3$. The reaction of this liquid mixture with *o*-phenylenediamine gave acetophenone and 2,3-dimethylquinoxaline (VIII), indicating the presence of biacetyl. The biacetyl must have been produced during the reaction with *o*-phenylenediamine, since the original ozonolysis product yielded no biacetyl when it was distilled under reduced pressure. The structure of the compound $C_{12}H_{12}O_2$ was probably IX. Acetophenone and biacetyl conceivably could have been produced by the addition of water followed by a reverse aldol reaction as shown. The properties of the solid, $C_{12}H_{12}O_3$ suggest that it may have structure X.



β,γ-Dimethylvalerophenone (XII) was prepared by action of diphenylcadmium on 3,4-dimethylvaleroyl chloride. The chloride was prepared from 3,4-dimethylvaleric acid (XI) which in turn was synthesized unequivocally from methyl isopropyl ketone and zinc ethylbromoacetate followed by dehydration of the product, saponification of the resulting unsaturated ester, and hydrogenation of the acid.

$$CH_3COCH(CH_3)_2 + ZnBrCH_2COOC_2H_5 \longrightarrow$$

$$(CH_3)_2C(OH)(CH_3)CH_2COOC_2H_5 \xrightarrow[3,\ H^+]{\substack{1,\ -H_2O\\ 2,\ OH^-}}$$

$$(CH_3)_2CHC(CH_3){=}CHCOOH \xrightarrow[Pt]{H_2}$$

$$\underset{XI}{(CH_3)_2CH(CH_3)CH_2COOH} \xrightarrow[2,\ (C_6H_5)_2Cd]{1,\ SOCl_2}$$

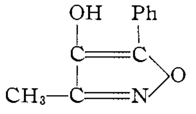
$$(CH_3)_2CHCH(CH_3)\underset{C_6H_5CO}{CH_2}$$

XII

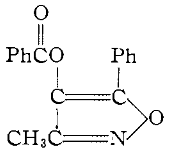
The base-soluble product from the reaction of VIa with refluxing methanolic sodium methoxide consisted of a nitrogen-containing solid shown to be 3-methyl-5-phenylisoxazolone (XIII) and an oil which was a mixture of benzoic acid and unidentified products. XIII was extremely unstable, decomposing into benzoic acid and an oil with an almond odor. The rate of decomposition was slower under nitrogen or under reduced pressure. The acidity of the hydrogen of the enolic hydroxyl group was comparable with that of carboxylic acids, since XIII was soluble in 5% sodium bicarbonate. XIII reacted with bromine in carbon tetrachloride (no hydrobromic acid evolved) and with 2% potassium permanganate. It reacted with approximately one mole of hydrogen at room temperature and atmospheric pressure over a platinum oxide catalyst. No identifiable oxidation or reduction products were recovered. There was no reaction with 2,4-dinitrophenylhydrazine reagent or with ferrous hydroxide. Action of ferric chloride produced an olive-green color. The reaction of XIII with diazomethane yielded an oil which could not be crystallized, but benzoyl 3-methyl-5-phenylisoxazolone (XIV), was obtained by action of benzoyl chloride upon the sodium salt of XIII.

For comparative purposes, the closely related isomer of XIII, 3-phenyl-5-methylisoxazolone (XV), was prepared[10] by reduction and diazotization of 3-phenyl-4-nitro-5-methylisoxazole. An attempt to utilize a similar procedure for the preparation of XIII was unsuccessful.

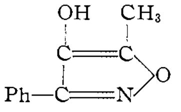
The infrared spectra of XIII, XIV and XV were obtained. The spectrum of XIII has no absorption characteristic of the nitro group, but has a very weak carbonyl band at 1640 cm.$^{-1}$. The hydroxyl group is represented by a broad band 2500–3400 cm.$^{-1}$ and a double band at 2640 and 2700 cm.$^{-1}$. There is no apparent absorption in the 1640 or 2500–3400 cm.$^{-1}$ regions in the spectrum of the benzoate XIV. Therefore, these absorption



XIII



XIV



XV

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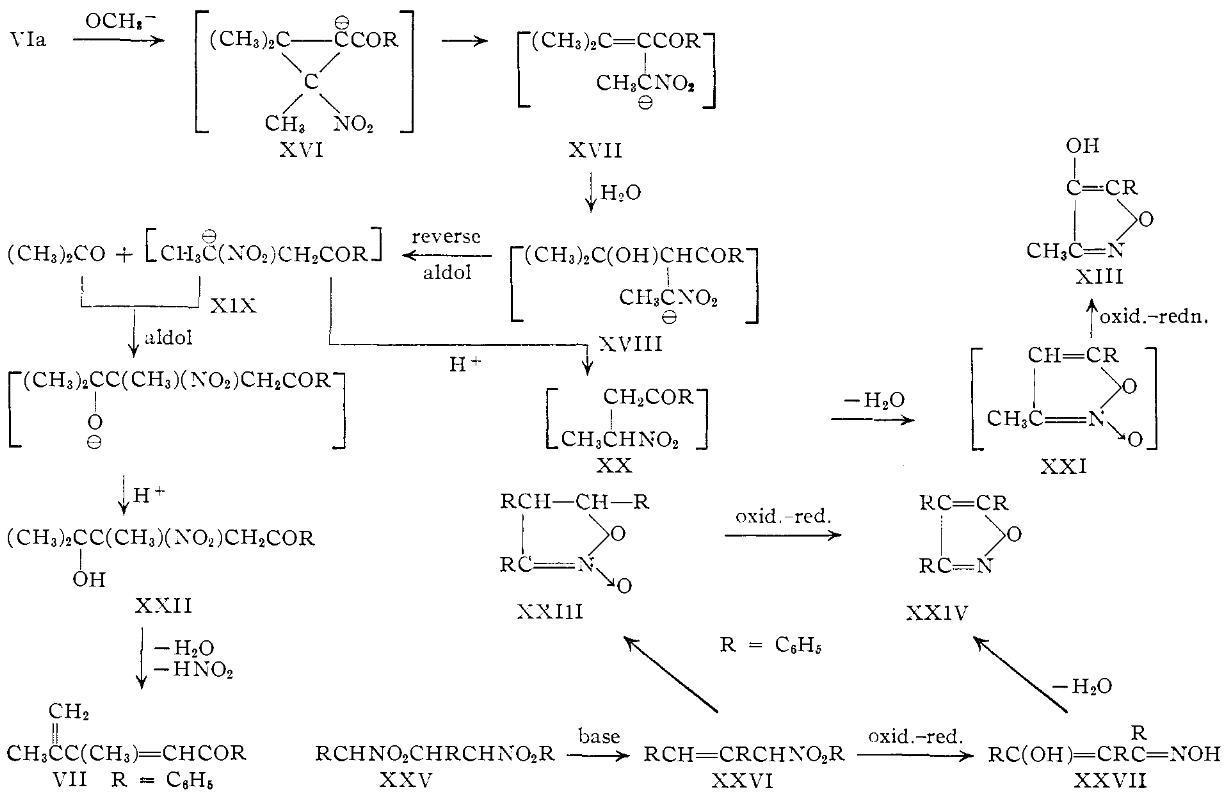
[10] A. Quilico, *et al.*, *Gazz. chim. ital.*, **76**, 87 (1946), reported the following behavior and reactions of XV: solubility in alkali and carbonates, decomposition in air and light to benzonitrile (the decomposition of XIII gives no acetonitrile) and an oil (almond odor), reaction with ferric chloride solution to give an olive-green color, formation of an oily derivative with diazoethane, and formation of a solid benzoate, m.p. 67–68°, with benzoyl chloride.



bands in XIII must arise from the keto–enol system in this molecule. The carbonyl absorption is so weak that XIII must exist almost exclusively in the enol form. The double bond region of the infrared spectrum of XIII shows two more weak bands at 1575 and 1600 cm.$^{-1}$. The C=C and C=N absorption in cyclic conjugated systems has been found to be somewhat unpredictable in other cases.[11] The isomer XV has an infrared absorption pattern similar to that of XIII. The carbonyl absorption at 1640 cm.$^{-1}$ is much more intense. However, the hydroxyl band, though similar, is slightly weaker and the double band is less well defined. This is consistent with the structures of the isomers, since the presence of a phenyl group in the 5-position as in XIII would be expected to increase the amount of the enol form in this case compared with XV. The isomer XV shows weak absorption at 1575 cm.$^{-1}$.

The three products (acetone, 1-benzoyl-2,3-dimethylbutadiene (VII) and 3-methyl-5-phenylisoxazolone (XIII)) isolated from the reaction of VIa with sodium methoxide are all unique in this series. It has been assumed in all previous cases that the initial step in the reaction was removal of a hydrogen atom from the ring. The formation of the above products can also be explained by the following reaction sequence commencing with removal of the ring hydrogen atom to give XVI and ring opening of the 2–3 bond to give XVII. Acetone is produced in aqueous basic solution, since it could not be isolated from the reaction mixture previous to addition of water. Addition of water to XVII yields XVIII which can undergo a reverse aldol reaction resulting in the formation of acetone and the anion XIX. Acidification of XIX would give the intermediate nitro ketone XX. This compound, by loss of water, can give the isoxazole oxide XXI which undergoes internal oxidation–reduction to the isoxazolone XIII. The acetone produced by the reverse aldol reaction of XVIII can in turn undergo an aldol reaction with anion XIX to give the hydroxynitroketone XXII on acidification. Loss of water and nitrous acid from XXII leads to the dienone VII.

Internal oxidation–reduction reactions such as XXI to XIII have been reported previously in connection with related nitrogen containing compounds. For example, triphenylisoxazoline oxide (XXIII) gives triphenylisoxazole (XXIV) quantitatively by action of aqueous alcoholic sodium hydroxide.[12] In a related case, the saturated nitro compound XXV loses nitrous acid in basic solution to give the α,β-unsaturated nitro compound XXVI, a portion of which undergoes internal oxidation–reduction to dibenzoylphenylmethane monooxime (XXVII).[13] The remainder of XXVI rearranges to the isoxazoline oxide XXIII. Both XXIII and XXVII give XXIV on further reaction with base.

Experimental Part[14]

Isopropylideneacetophenone (III) was prepared as previously described.[15] The ultraviolet spectrum of III in 95% ethanol had a maximum at 262 mμ (log ϵ 4.16) and a minimum at 228 mμ (log ϵ 3.43). The 2,4-dinitrophenyl-

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[11] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 228.

[12] E. P. Kohler and G. R. Barrett, THIS JOURNAL, **46**, 2106 (1924).

[13] D. E. Worrall, *ibid.*, **57**, 2299 (1935).

[14] Microanalyses by J. H. Cooley, B. K. Davis, J. R. Holum, C. B. Koons, R. F. Lange, T. Y. Lee, O. Romanus and E. L. Wheeler.

[15] L. I. Smith and R. E. Kelly, THIS JOURNAL, **74**, 3307 (1952).

hydrazone of III has not been previously reported. It was obtained as flat orange needles which melted without decomposition at 172–173.5° (uncor.) after several recrystallizations from ethanol. Maxima at 223 mμ (log ε 4.34) and 381 mμ (log ε 4.44) occurred in the ultraviolet spectrum of a 95% ethanol solution of this derivative; there was a minimum at 316 mμ (log ε 3.53).

Anal. Calcd. for $C_{17}H_{16}O_4N_4$: C, 59.99; H, 4.74; N, 16.47. Found: C, 60.39; H, 5.01; N, 16.51.

Attempts to prepare a semicarbazone from III yielded only a compound (m.p. 179–182°) which analyzed for an equimolar mixture of semicarbazide and the normal semicarbazone.

Anal. Calcd. for $C_{13}H_{20}O_2N_6$: C, 53.46; H, 6.90; N, 28.78. Found: C, 53.5; H, 7.19; N, 30.35.

β,β-Dimethyl-γ-nitrovalerophenone (IV).—The general procedure was that used in earlier work[15] carried out in these laboratories. A solution of sodium ethoxide (from 0.35 g. sodium 0.015 gram-atom) in anhydrous ethanol (15 cc.) was added in several portions to a hot solution of isopropylideneacetophenone (24.02 g., 0.150 mole) and nitroethane (12 g., 0.160 mole) in anhydrous ethanol (70 cc.). The mixture was refluxed and stirred for 36 hours, cooled, and neutralized by addition of acetic acid (0.91 g., 0.015 mole). Ethanol was removed under reduced pressure, and the resulting slurry was extracted with ether. Removal of the ether and distillation of the residual oil yielded an initial fraction (7.83 g.) boiling at 75–141° (0.5–0.6 mm.) followed by the β,β-dimethyl-γ-nitrovalerophenone (21.3 g.) boiling at 141–151° (0.55 mm.), 161–166° (2.5 mm.). The first fraction was a mixture of IV and biphenyl carried over from the preparation of III; the yield of IV was 68%, corrected for the biphenyl content (9–10%) of III. Redistillation of the second fraction yielded IV as a light yellow liquid (n^{20}_{D} 1.5288) which boiled at 130° (0.12 mm.). The ultraviolet spectrum (in 95% ethanol) had maxima at 243 mμ (log ε 4.10), 280 mμ (log ε 3.06) and 330 mμ (log ε 2.09); minima occurred at 275 mμ (log ε 3.03) and 320 mμ (log ε 1.86).

Anal. Calcd. for $C_{13}H_{17}O_3N$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.50; H, 7.04; N, 5.94.

Use of sodium methoxide as the catalyst for the addition of nitroethane to III gave a 62% yield of IV; diethylamine did not catalyze the addition.

β,β-Dimethyl-γ-nitrovalerophenone did not decolorize permanganate but did react with bromine, with the evolution of hydrogen bromide. The ketone slowly oxidized ferrous hydroxide, indicating the presence of a nitro group. The semicarbazone melted at 190.5–191°, after recrystallization from 95% ethanol.

Anal. Calcd. for $C_{14}H_{20}O_3N_4$: C, 57.52; H, 6.90; N, 19.16. Found: C, 57.42; H, 7.35; N, 18.73.

γ-Bromo-β,β-dimethyl-γ-nitrovalerophenone (V).—A methanol solution of the sodio-derivative of IV was prepared from 117.6 g. (0.50 mole) of IV and sodium methoxide (from 250 cc. of anhydrous methanol and 11.60 g. of sodium, 0.50 gram-atom). This solution was added over an eight-minute period to a cooled (below −20°) and stirred solution of bromine (80.4 g., 0.50 mole) in chloroform (300 cc.). The mixture was then allowed to attain room temperature, after which it was diluted with water (300 cc.). The aqueous layer was removed, and washed with chloroform (three 50-cc. portions). The combined chloroform extracts were washed successively with 60-cc. portions of 2% sodium bisulfite, 2% sodium bicarbonate, and water (four portions) and then dried over magnesium sulfate. Removal of the solvent left the crude V as a pale green oil (166 g., theory 157 g.). A portion was prepared for analysis by drying it under 0.03 mm. overnight.

Anal. Calcd. for $C_{13}H_{16}O_3NBr$: C, 49.69; H, 5.13; N, 4.46. Found: C, 49.94; H, 5.39; N, 4.23.

Evidence that the bromine atom in V was attached to the carbon holding the nitro group[16] was obtained by boiling a sample in ethanolic potassium iodide. In seven hours 61% of the theoretical amount of iodine was liberated.

1-Benzoyl-2-nitro-2,3,3-trimethylcyclopropane (VIa and VIb).—The crude bromo compound (V, 86 g., 0.273 mole) was added to a hot solution of freshly fused potassium acetate in anhydrous methanol (600 cc.), and the mixture was refluxed for 12 hours. Most of the salts were precipitated by dilution with ether (500 cc.) and removed by filtration. The solvents were removed from the filtrate under reduced pressure. The resulting slurry was mixed with water (500 cc.) and extracted with ether (one 150-cc. portion and three 50-cc. portions). The combined ether extracts were washed with water (three 20-cc. portions) and dried over magnesium sulfate. Removal of the ether left an orange oil (61.8 g., 97%) that readily crystallized once crystals of VI had been obtained.

Recrystallization of the crude product from a mixture of methanol (175 cc.) and water (15 cc.) gave VIa (45.9 g., 76%) as white needles, m.p. 55.2–55.7°. The filtrate, when concentrated and carefully cooled, gave 3.57 g. of a mixture of VIa and VIb, m.p. 49.5–92°. After two additional recrystallizations from methanol, the lower melting isomer from the first crop melted at 55.4–55.7°; the sample could be remelted several times at the same temperature. About 0.5 g. of the higher melting isomer VIb was obtained from the second crop of crystals (3.57 g.) by either fractional crystallization from aqueous methanol or by fractional sublimation *in vacuo*. The lower melting isomer was the more volatile. After four recrystallizations from aqueous methanol the higher melting isomer melted at 99–100°. After several additional recrystallizations from methanol the compound melted at 101–102°; after solidification the sample remelted at 78–80°.

Anal. Calcd. for $C_{13}H_{15}O_3N$: C, 66.93; H, 6.48; N, 6.01. Found: VIa, C, 66.5; H, 6.77; N, 6.27. VIb, C, 67.42; H, 6.59; N, 6.15.

Neither VIa nor VIb decolorized permanganate. The 55° isomer did not react with bromine, ozone or phosphorus pentachloride. Failing to evolve chlorine when mixed with phosphorus pentachloride indicated that the compound was not the isomeric isoxazoline oxide.[17] The lower melting isomer slowly oxidized ferrous hydroxide, indicating the presence of a nitro group. Lack of sufficient material prevented running many of these qualitative tests on the 101° isomer.

The ultraviolet absorption spectra of VIa and VIb in 95% ethanol were very similar. For the 55° isomer maxima were observed at 249 mμ (log ε 4.17) and 330 mμ (log ε 2.28). Corresponding maxima in the spectrum of the 101° isomer occurred at 248 mμ (log ε 4.13) and 330 mμ (log ε 2.49). Inflection points occurred in both spectra at 280 mμ, and minima were observed at 320 mμ (log ε 1.74 for the 55° isomer and 2.20 for the 101° isomer). Infrared spectra of the two isomers were essentially identical, except for the presence of three additional weak bands in the spectrum of the 101° isomer at 723, 912 and 1595 cm.$^{-1}$. There were also bands at 863, 1000, 1026 (Nujol) and at 869 cm.$^{-1}$ (CCl_4) in the infrared spectrum of the 55° isomer; there was a band at about 870 cm.$^{-1}$ (CCl_4) in the spectrum of the 101° isomer.

The 2,4-dinitrophenylhydrazone of the 55° isomer was obtained as fine needles, m.p. 201.5–202.5° dec. (uncor.) after five recrystallizations from a mixture of ethyl acetate, ethanol and water.

Anal. Calcd. for $C_{19}H_{19}O_6N_5$: C, 55.20; H, 4.64; N, 16.93. Found: C, 55.2; H, 4.65; N, 16.65.

The ultraviolet absorption spectrum of the 2,4-dinitrophenylhydrazone (in 95% ethanol) obtained from the 55° isomer showed maxima at 222 mμ (log ε 4.39) and 370 mμ (log ε 4.43), with a minimum at 307 mμ (log ε 3.58).

Isomerization of Cyclopropanes.—The higher melting isomer VIb (m.p. 101–102°, 0.1 g.) was added to ammoniacal methanol (5 cc., saturated at 0°). After five days at 4° and eight hours at room temperature, the methanol and ammonia were removed under reduced pressure leaving a solid (0.1 g.) melting at 40–52°. The mixed melting point of this material (recrystallized from methanol, m.p. 55.5–56.5°) and the lower melting cyclopropane isomer VIa was 54–56°

Treatment of the lower melting isomer VIa in an identical manner resulted in the quantitative recovery of starting material.

The General Reaction of 1-Benzoyl-2-nitro-2,3,3-trimethylcyclopropane (VIa) with **Alcoholic Sodium Methoxide.**—In a typical reaction the cyclopropane (6.22 g., 0.0267 mole) was added to methanolic sodium methoxide (from sodium 0.69 g., 0.0267 mole and methanol 27 cc.), and the solution was refluxed for ten minutes. A noticeable

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(16) E. P. Kohler, This Journal, **38**, 889 (1916).

(17) E. P. Kohler and G. R. Barrett, *ibid.*, **48**, 1770 (1926).

exothermic reaction occurred with the deposition of solid sodium nitrite. The cooled brown solution was added to water (100 cc.), and the mixture was distilled on a water-bath into a solution of 2,4-dinitrophenylhydrazine. The resulting orange solid represented a 30-35% yield of acetone 2,4-dinitrophenylhydrazone, m.p. 125–127°. The mixed melting point of this compound and authentic acetone 2,4-dinitrophenylhydrazone was 124–126.5°.

The aqueous basic mixture was extracted three times with 50-cc. portions of ether. The combined extracts were dried over magnesium sulfate, and the ether was removed under reduced pressure to give a mixture of nitrogen-free ketones (approximately 2 g., 40% yield).

The aqueous basic layer was acidified by the addition of acetic acid (1.2 g.), and extracted with three 50-cc. portions of ether. The combined extracts were dried over magnesium sulfate, and the solvent was removed under reduced pressure. The residue was a mixture of nitrogen-containing, base-soluble products (approximately 2 g., 40% yield).

1-Benzoyl-2,3-dimethylbutadiene (VII).—The base-insoluble, nitrogen-free fraction (4.3 g.) from the reaction of VIa with sodium methoxide was chromatographed on an alumina column (27 × 3.5 cm.). The mixture was eluted with petroleum ether and benzene. A total of 3.9 g. of material was recovered from the column, and one combined fraction (1.88 g., n^{25}_{D} 1.5693) was distilled through a spiral wire column. The main fraction (0.65 g.) distilled at 91–94° (0.3 mm.) and had n^{25}_{D} 1.5797.

Anal. Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.57; mol. wt., 186. Found: C, 83.82, 84.00; H, 7.63, 7.72; mol. wt. (cryoscopic), 190.

The 2,4-dinitrophenylhydrazone of VII, after four crystallizations from ethyl acetate-ethanol, formed an orange powder which melted at 163–165°.

Anal. Calcd. for $C_{19}H_{18}O_4N_4$: C, 62.28; H, 4.96; N, 15.29. Found: C, 62.32; H, 5.30; N, 14.94.[18]

The ultraviolet absorption spectrum of a solution of this derivative in 95% ethanol showed maxima at 215 mμ (log ε 4.48) and 363 mμ (log ε 4.46); a minimum occurred at 299 mμ (log ε 3.61).

Reduction of 1-Benzoyl-2,3-dimethylbutadiene (VII).—The dienone (2.28 g.) was reduced in absolute alcohol (15 cc.) at room temperature over platinum oxide (0.068 g.). After the theoretical pressure drop (approximately six hours), the product was isolated. The infrared spectrum of this compound was identical with that of β,γ-dimethylvalerophenone (XII). The 2,4-dinitrophenylhydrazone of this reduced product melted at 141–144° alone or when mixed with an authentic specimen.

Ozonolysis of 1-Benzoyl-2,3-dimethylbutadiene (VII).—A dilute mixture of ozone in oxygen was passed for 35 minutes through a cooled (below −20°) solution of the dienone (1.84 g., 0.0099 mole, n^{20}_{D} 1.5870) in ethyl bromide (100 cc.) for 35 minutes. This was equivalent to 0.0103 mole of ozone. The solution was then concentrated to a volume of 15 cc. by passing a current of dry air over the surface. The concentrate was then added to a vigorously stirred mixture of zinc dust (1 g.) and water (50 cc.) containing traces of hydroquinone and silver nitrate. Stirring was continued at room temperature for three hours and at 50° for one-half hour.

The mixture containing the decomposed ozonide was extracted with chloroform (three 20-cc. portions). The combined extracts were washed with water and dried over magnesium sulfate; removal of the solvent at room temperature (1 mm.) left 1.15 g. of a pale yellow oil (A). The solvent, which was caught in a Dry Ice trap, yielded a trace of an orange precipitate when treated with 2,4-dinitrophenylhydrazine. The aqueous layer left from the chloroform extraction was diluted with ethanol (6 cc.), and about two-thirds of the solvent was removed by distillation. Addition of an ethanol solution of 2,4-dinitrophenylhydrazine sulfate to the distillate gave 0.33 g. of formaldehyde 2,4-dinitrophenylhydrazone, m.p. 155–158°. The aqueous residue left from the distillation was acidified with dilute sulfuric acid and extracted with ether (four 20-cc. portions). Removal of the ether left 0.38 g. of benzoic acid (31% of theory), m.p. 118–120° alone or when mixed with an authentic specimen. The acidified aqueous solution was distilled to dryness, and an additional 0.04 g. of formaldehyde 2,4-dinitrophenylhydrazone was obtained from the distillate. The total weight (0.37 g.) of the 2,4-dinitrophenylhydrazone represented an 18% yield of formaldehyde. The derivative melted at 161–162° after several recrystallizations from methanol; it did not depress the melting point of an authentic specimen and showed the proper elemental analysis.

Anal. Calcd. for $C_7H_6O_4N_4$: C, 40.01; H, 2.88; N, 26.67. Found: C, 40.77; H, 3.26; N, 26.51.

Yellow oil A was distilled at 0.001 mm. (oil-bath at 70–100°), giving 0.52 g. of a yellow oil (B, n^{20}_{D} 1.5513); about 0.16 g. of low boiling material was lost during the distillation. The orange gum (0.47 g.) left in the flask was triturated with ethanol; about 0.05 g. of a white solid remained undissolved. This white solid melted at 166–168° (Fisher–Johns apparatus) after one recrystallization from 85% methanol and at 169–170° after three additional recrystallizations. This recrystallized sample melted at 161° (uncor.) in a capillary. This solid was insoluble in aqueous alkali and was not affected by action of alkaline hydrogen peroxide or permanganate. It gave no color with ferric chloride but did form a 2,4-dinitrophenylhydrazone (m.p. 185–207° dec.). The analytical data and chemical properties suggest that the white solid may be the oxido-ketone X.

Anal. Calcd. for $C_{12}H_{12}O_3$: C, 70.63; H, 5.93. Found: C, 70.71; H, 6.13.

Oil B was redistilled (below 0.006 mm.); the elemental analysis of the distillate (n^{20}_{D} 1.5518) suggested that it was a mixture of the compounds $C_{12}H_{12}O_2$ and $C_{12}H_{12}O_3$.

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.67; H, 6.44. Calcd. for $C_{12}H_{12}O_3$: C, 70.63; H, 6.13. Found: C, 73.31; H, 6.50.

The distillate (0.32 g.) from B was mixed with *o*-phenylenediamine (0.145 g., 0.0013 mole) and dissolved in 0.3 cc. of methanol. A dark red color appeared immediately, but no solid separated. Also, no solid separated after addition of three drops of water and cooling at −20° for two days. Addition of acetic acid (15 drops), heating at 90° for one hour, and further cooling for seventeen days gave no solid. The red-brown solution was then diluted with water (4 cc.) and extracted with ether (five 6-cc. portions). The ether extract was washed with 2% hydrochloric acid (three 2-cc. portions), dilute aqueous sodium bicarbonate, and water. Removal of the ether left 0.27 g. of red oil having the odor of acetophenone. It yielded a 2,4-dinitrophenylhydrazone (m.p. 240.6–241.3°, uncor., after four recrystallizations) that was found by analysis and mixed melting point to be the derivative of acetophenone.

Anal. Calcd. for $C_{14}H_{12}O_4N_4$: C, 56.00; H, 4.03. Found: C, 56.19; H, 4.07.

The dilute hydrochloric acid extracts obtained from the *o*-phenylenediamine reaction were combined, made alkaline, and extracted with ether. Removal of the ether from the dried extract left 0.10 g. of solid which yielded white needles (m.p. 104–105°) upon sublimation *in vacuo*. This material was shown to be 2,3-dimethylquinoxaline (VIII) by comparison with an authentic sample prepared from biacetyl by the method of Gabriel and Sonn.[19]

3-Methyl-5-phenylisoxazolone (XIII).—The base-soluble, nitrogen-containing fraction (1.85 g.) from the reaction of VIa with sodium methoxide was recrystallized from benzene or benzene–petroleum ether to give XIII, 0.63 g., m.p. 77–80°.

Anal. Calcd. for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.33; H, 4.93; N, 7.94.

The remaining material from this base-soluble fraction could not be completely identified, but benzoic acid was isolated in substantial amounts by extraction. The isoxazolone XIII is very unstable decomposing in light and air to benzoic acid and an unidentifiable oil. Impure samples decompose more rapidly, but the decomposition rate is slower under vacuum or in a nitrogen atmosphere. There was no reaction between XIII and ferrous hydroxide or 2,4-nitrophenylhydrazine solution. Ferric chloride solution produced an olive-green color, and the addition of copper acetate solution[20] resulted only in a slight color change from blue to blue green. XIII was soluble in sodium bicarbonate

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(18) We thank Mr. James Kerns, of General Mills, Inc., for the determination of nitrogen.

(19) S. Gabriel and A. Sonn, *Ber.*, **40**, 4850 (1907).

(20) E. P. Kohler and A. H. Blatt, THIS JOURNAL, **50**, 504 (1928), isolated a solid copper salt of 3,4-diphenylisoxazolone. However no attempts to prepare the copper salt of a 4-isoxazolone have been recorded.

and could be titrated to a phenolphthalein end-point. Equivalent weight determinations of XIII in 50% ethanol-water solution gave values for its molecular weight of 177 and 180 (calculated for XIII, 175). XIII reacted with bromine in carbon tetrachloride with no evolution of hydrogen bromide. It also gave a brown precipitate with 2% potassium permanganate. Hydrogenation of XIII at room temperature and pressure over a platinum oxide catalyst resulted in the consumption of 1.2 equivalents of hydrogen. Apparently the addition of the second hydrogen molecule is much more difficult than the first.

3-Methyl-4-benzoyl-5-phenylisoxazolone (XIV).—The isoxazolone XIII (0.04 g.) was dissolved in sodium hydroxide (15 cc., 0.0418 *N*). Benzoyl chloride (0.05 g.) was added, and the mixture was allowed to stand for 30 minutes. A 5% sodium bicarbonate solution (15 cc.) was added to dissolve excess benzoic acid, and the resulting solid was filtered. Recrystallization from methanol gave XIV, m.p. 78.5–80°.

Anal. Calcd. for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 72.95; H, 5.01; N, 5.01.

Ethyl 3-Hydroxy-3,4-dimethylvalerate.—A solution of benzene (600 cc.), toluene (200 cc.), ethyl bromoacetate (167 g.) and methyl isopropyl ketone (86 g.) was prepared. Approximately 100 cc. of this solution was added to granular zinc (71.5 g. of 20 mesh) previously washed with 5% hydrochloric acid. A crystal of iodine was added, and the mixture was heated almost to the boiling point before a vigorous reaction commenced; the remainder of the solution was then added. The total addition required three hours with alternate heating and cooling. After an additional hour at reflux temperature, the solution was cooled and poured into sulfuric acid (120 cc.) and ice (1000 g.). The benzene-toluene layer was separated, and the aqueous portion was extracted with 100 cc. of benzene. The combined benzene-toluene layer was dried over magnesium sulfate, and the solvent was removed under reduced pressure. The remaining liquid was distilled at 12 mm. to give ethyl 3-hydroxy-3,4-dimethylvalerate (87.5 g., 56%), $n^{25}D$ 1.4298.

Dehydration of Ethyl 3-Hydroxy-3,4-dimethylvalerate.—A mixture of the hydroxy ester (73.5 g.), phosphorus pentoxide (85.2 g.), and dry benzene (150 cc.) was refluxed for 2.5 hours. The tarry solid was discarded, water (200 cc.) was added, and the benzene layer was separated. The benzene was dried over magnesium sulfate, and the solvent was removed under reduced pressure to give 46 g. (70%) of what is probably a mixture of the α,β- and β,γ-unsaturated esters.

Saponification of the Unsaturated Esters.—The mixture of the unsaturated esters (46 g.) and a solution of potassium hydroxide (42 g.) in 120 cc. of water was refluxed for 1.5 hours. The basic solution was cooled and extracted with two 100-cc. portions of ether from which 2–3 g. of the unchanged ester was recovered. The aqueous layer was acidified with dilute hydrochloric acid and extracted with three 100-cc. portions of ether. This combined ether extract was dried over magnesium sulfate, and the ether was removed to give 34 g. of the α,β- and β,γ-unsaturated acids, $n^{25}D$ 1.4450. This mixture was distilled at 1.5 mm., and the fraction boiling at 83–94°, $n^{25}D$ 1.4510, was used in the following experiment.

3,4-Dimethylvaleric Acid (XI).—Hydrogenation at room temperature of the unsaturated acid (5.06 g.) over a platinum oxide catalyst (150 mg.) in 95% ethanol gave 4.24 g. (83% yield) of XI, $n^{25}D$ 1.4245.[21,22]

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.83. Found: C, 64.80; H, 10.93.

3,4-Dimethylvaleramide.—The acid XI (1.31 g.) was refluxed for one hour with thionyl chloride (5 cc.) and the mixture was then poured into excess ammonium hydroxide and allowed to stand overnight at 5°. The solid was removed and crystallized from benzene, when it melted at 137–139°. Adkins[21] reported a melting point of 138–138.5° for this compound; Huston and Agett[22] reported 95.5°.

β,γ-Dimethylvalerophenone (XII).—The acid XI (4.8 g.) was added to thionyl chloride (8 cc.). The mixture was allowed to stand at room temperature for 15 minutes followed by 30 minutes on the steam-bath. Excess hydrochloric acid and thionyl chloride were removed under reduced pressure, and the remaining 3,4-dimethylvaleroyl chloride was used in the following step. The acid chloride in 50 cc. of dry benzene was added dropwise (15 minutes) to a benzene solution of diphenylcadmium prepared by a previously described method[15] from 7.33 g. (0.04 mole) of anhydrous cadmium chloride and phenylmagnesium bromide. The mixture was warmed gently for 30 minutes and poured into sulfuric acid (20 cc.) and ice (300 g.). The benzene layer was separated, and the aqueous layer was extracted with 75 cc. of benzene. The combined benzene layers were dried over magnesium sulfate, and the solvent was removed under reduced pressure. Distillation of the remaining product gave initial fractions (total 2.5 g.) containing some biphenyl and a final fraction (1.69 g.). Redistillation of this latter fraction gave β,γ-dimethylvalerophenone (b.p. 83–87° at 0.5 mm., $n^{25}D$ 1.5103).

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.11; H, 9.47. Found: C, 82.28; H, 9.69.

β,γ-Dimethylvalerophenone 2,4-dinitrophenylhydrazone, after crystallization from ethyl acetate, melted at 144–144.5°.

Anal. Calcd. for $C_{22}H_{19}N_4O_4$: C, 61.61; H, 5.99; N, 15.13. Found: C, 61.86; H, 5.85; N, 15.37.

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[21] H. Adkins and J. L. R. Williams, *J. Org. Chem.*, **17**, 980 (1952), prepared this compound by formylation of 2,3-dimethylbutadiene followed by oxidation to XI, $n^{25}D$ 1.4255.

[22] R. C. Huston and A. H. Agett, *ibid.*, **6**, 130 (1941), also prepared XI by the Grignard reaction of ethylene oxide and 2-bromo-3-methylbutane followed by oxidation. No refractive index was reported.