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

Cyclopropanes. XX.[1] 1-Benzoyl-6-nitrobicyclo[3,1,0]hexane: Behavior toward Alkaline Reagents

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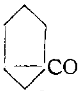
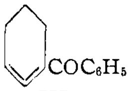
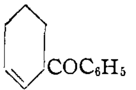
RECEIVED DECEMBER 30, 1955

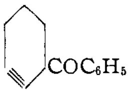
In order to examine further the hypothesis that acetylenic or allenic ketones are intermediates in the reaction between secondary nitrocyclopropyl ketones and bases, or sodiomalonic esters, whereby 1,3-diketones (or their derivatives) or α-pyrone esters are produced, respectively, the bicyclic secondary nitrocyclopropyl ketone I, named in the title, has been prepared and subjected to the action of these reagents. In this case the intermediate acetylenic or allenic ketone would of necessity contain the unsaturated system in a six-membered ring and consequently no such intermediate is likely. The products formed from I by action of the above reagents are not 1,3-diketones, their enol ethers or α-pyrones; rather, the nitrogen atom is retained in the products. The products have been identified, and a reaction scheme has been proposed to account for their formation. It is concluded that, whatever the mechanism of the reaction between secondary nitrocyclopropyl ketones and bases may be, the structural requirements for the production of enol ethers, 1,3-diketones or α-pyrones from these cyclopropanes are the same as would be required to produce acetylenic or allenic ketones as intermediates.

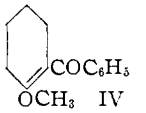
Secondary nitrocyclopropyl ketones are converted into 1,3-diketones, their enol ethers or α-pyrones by action of aqueous or alcoholic bases or of sodiomalonic ester, respectively.[3] One proposed mechanism for these reactions involves an acetylenic (or allenic) ketone as an intermediate.[4] The study reported in the present paper was designed to test further this hypothesis. A secondary nitrocyclopropyl ketone (I) so constituted that it could not be converted into an acetylenic (or allenic) ketone has been synthesized and subjected to the action of basic reagents. The acetylenic ketone derived from I would be II, and the corresponding allenic ketone would be III; the enol ethers derived from these would be IV and V, and the pyrone would have the structure VI. Although there is no conclusive proof that acetylenic or allenic bonds are incapable of existing in a six-membered ring, there does exist much evidence that the eight-membered ring is the smallest that will accommodate a triple bond and that the seven-membered ring is the smallest that will accommodate an allenic linkage.[5] Assuming that allenic or acetylenic linkages cannot exist within six-membered rings, the products formed from I by action of basic reagents cannot be derived from allenic or acetylenic intermediates. Thus, if compound I were to produce an enol ether or an α-pyrone by action of sodium methoxide or sodiomalonic ester, respectively, it could be concluded that allenic or acetylenic ketones are not necessary intermediates in either of these reactions, and it would constitute evidence of such intermediates if I, by action of these reagents, were to produce compounds differing appreciably in nature from IV, V and VI. This would not constitute proof of such intermediates, for the failure of I to produce IV, etc., could arise from other causes.

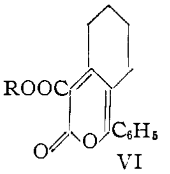

I


III


V

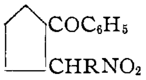

II

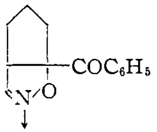

IV

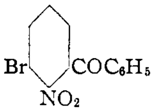

VI

The route to I involved the sequence VII, VIII and IX. Addition of nitromethane to 1-benzoylcyclopentene (VII) produced the liquid, *trans*-1-benzoyl-2-(nitromethyl)-cyclopentane (VIII, 49%). This product was a single substance, chromatographically homogeneous. That it was the *trans* isomer was indicated by the stability toward alkali. It has been shown that the reverse Michael reaction proceeds most likely *via* an E2 mechanism[6]; this is easily possible in the case of the *cis* isomer of VIII, but in the case of the *trans* isomer the reaction would require a *cis* elimination by an E2 mechanism, which, though not impossible, is energetically unlikely. Bromination of VIII in alkaline solution gave the γ-bromo compound IX as an unstable oil. This oil, subjected at once to the action of potassium acetate in ethanol, was converted into the cyclopropane I (21%).


VII


VIII, R = H
IX, R = Br


X


XI

Compound I was obtained as a single isomer melting at 103–104°, chromatographically homogeneous, and giving the proper analytical values required for $C_{13}H_{13}NO_3$. Aqueous permanganate was without action upon I; likewise bromine in chloro-

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(1) Paper XIX, L. I. Smith, W. L. Kohlhase and R. J. Brotherton, THIS JOURNAL, **78**, 2532 (1956).

(2) Abstracted from a thesis by Richard M. Scribner, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, September, 1955. Parke, Davis and Co. Fellow 1953–1954; National Science Foundation Predoctoral Fellow, 1954–1955; du Pont Summer Fellow, 1955.

(3) E. P. Kohler and L. I. Smith, THIS JOURNAL, **44**, 624 (1922).

(4) In particular, see L. I. Smith and V. E. Engelhardt, *ibid.*, **71**, 2671, 2676 (1949), and later papers.

(5) A. T. Blomquist and L. H. Liu, *ibid.*, **75**, 2153 (1953); J. D. Roberts, H. E. Simmons, Jr., L. A. Carlsmith and C. W. Vaughan, *ibid.*, **75**, 3290 (1953); N. A. Domnin, *J. Gen. Chem.* (*U.S.S.R.*), **9**, 1983 (1933); **10**, 1939 (1940); **15**, 461 (1945) [*C. A.*, **34**, 4383 (1940); **35**, 3979 (1941); **40**, 4682 (1946)]; *Vestnik Leningrad Univ.*, 1, No. 3, 103 (1946) [*C. A.*, **42**, 3337 (1948)]; N. A. Domnin and V. A. Cherkasova, *J. Gen. Chem.* (*U.S.S.R.*), **17**, 2283 (1947) [*C. A.*, **42**, 4954 (1948)].

(6) (a) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, pp. 462–472; (b) Y. Amiel, A. Löffler and D. Ginsburg, THIS JOURNAL, **76**, 3625 (1954); (c) A. H. Cook and R. P. Linstead, *J. Chem. Soc.*, 958 (1934).

form was without action when the compound was shielded from strong light. The ultraviolet spectrum of I showed a maximum at 250 mμ (ϵ 15,000); the infrared spectrum (potassium bromide disc) showed a band at 1677 cm.$^{-1}$ (carbonyl), bands at 1598 and 1578 cm.$^{-1}$ (benzoyl) and at 1530 and 1373 cm.$^{-1}$ (nitro group). The infrared spectrum of a solution of I in carbon disulfide showed a sharp band at 1025 cm.$^{-1}$ (cyclopropane ring); and in Nujol there was a sharp band at 3100 cm.$^{-1}$ (cyclopropane ring).[7] Compound I showed none of the characteristic reactions of the isomeric isoxazoline oxides (X), often obtained when α-bromo-γ-nitroketones are subjected to the action of potassium acetate.[8] Thus, compound I was unaffected by action of sodium iodide in acetic acid; although action of zinc and acetic acid converted I into an oil, this oil, unlike the N-hydroxyisoxazolidines, did not form a copper derivative. Action of phosphorus pentachloride upon I at 115° produced no more chlorine than would be expected from the reagent alone at this temperature, nor any more than was produced from a known nitrocyclopropyl ketone at the same temperature. Action of hydrogen bromide upon I converted it into a γ-bromo-β-nitro ketone XI, by cleavage between C-1 and C-3, in analogy with the behavior of other secondary nitrocyclopropyl ketones.[9] Although a carbonyl derivative (2,4-DNP) of XI could be prepared, no such derivative of I could be obtained, even under forcing conditions—a behavior paralleled in steroidal cyclopropyl ketones.[10]

Although two configurations for I are possible, a *cis* and a *trans* (nitro–benzoyl relationship), the single isomer obtained was unaffected by action of methanolic ammonia, a reagent frequently used for interconversion of stereoisomeric nitrocyclopropyl ketones.[11] Compound I was recovered unchanged after its solution in dioxane had been refluxed over sodium carbonate for 12 hours, or after it had been heated with piperidine at 100° for 15 minutes.

Action of Basic Reagents upon I.—In the presence of these reagents, compound I behaved in a manner quite unlike that shown by other secondary nitrocyclopropyl ketones. Hot, aqueous potassium hydroxide slowly converted I into an intractable tar, along with some benzoic acid and approximately one-third of a mole of ammonia. Under anhydrous conditions the reaction between I and potassium hydroxide or sodium methoxide followed quite a different course. Nitrogen was not lost as ammonia, nor was it converted into nitrite as is generally the case with secondary nitrocyclopropyl ketones. Instead, the nitrogen was retained in the organic reaction products. When Compound I (2.0 g.) was subjected for ten minutes at 60° to the action of 2 *M* sodium methoxide, there resulted five products: a white solid $C_{14}H_{17}NO_4$ (360 mg.) melting at 155–157° and formulated as the N-hydroxyisoxazolidine XII; an isomeric white solid melting at 150–152° (462 mg.), formulated as the ethyl hydroxamic acid XIII; a yellow solid $C_{13}H_{12}N_2O_4$ melting at 148–149° (16 mg.), formulated as the benzoylcyclohexenone oxime XV; benzoic acid; and an unstable yellow oily solid (S) soluble in aqueous bicarbonate and weighing, together with the benzoic acid, 268 mg. Moreover, the bromonitro ketone XI under identical conditions also gave XII, XIII and the unstable oil. Compound XV may or may not have been produced by this reaction, but it was not isolated.

Both XII and XIII showed the properties of derivatives of the isoxazoline oxides, studied extensively by Kohler and his students[12] (see Experimental part). Action of sodium methoxide upon pure XIII converted it into a mixture of XII and XIII. Further hydrolysis of XII or XIII led to hydroxylamine and an unstable carboxylic acid, the former, in the basic solution, decomposed to give ammonia

$$3H_2NOH \longrightarrow N_2O + N_2 + NH_3$$ [13]

The molecular formula for compound XV suggested that it was derived by nitrosation of an isomer of I, $C_{13}H_{13}NO_3$. In keeping with this hypothesis, it was found that when the reaction mixture from I and sodium methoxide was neutralized by addition of dilute acetic acid in the presence of urea as an inhibitor of nitrosation, the yield of XV was reduced from 10 to about 1%. XV was not a nitrolic acid nor a pseudonitrole, for the color of its solution in alkali was bright yellow—not red or blue. In acetone, XV readily reduced permanganate. The ultraviolet spectrum of XV in ethanol showed maxima at 308 mμ (ϵ 48,300) and 244–246 mμ (ϵ 19,200), which suggests the presence of a benzoyl group and a nitro group conjugated with two double bonds.[14] A compound of structure XV could readily be formed by action of nitrous acid upon G (see below). XV was not produced from either XII or XIII by action of nitrous acid; hence, neither of these compounds is a precursor of XV.

The yellow oily solid was never obtained pure. Although material melting at 75–100° could be obtained from it, benzoic acid was always present and the oily residues decomposed to brown tars after standing for several days at room temperature. When this material was extracted with hot water, the extract, on cooling, deposited benzoic acid; the residual yellow material soon decomposed to a tar. It was possible to establish that the substance was acidic and that it contained no nitrogen; beyond this, nothing further could be done with it.

Since both I and XI gave the same products by action of alkali, the unsaturated nitro ketone G be-

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(7) (a) N. Fuson, M. L. Josien and E. Shelton, THIS JOURNAL, **76**, 2526 (1954); (b) V. A. Slabey, *ibid.*, **76**, 3604 (1954); (c) M. Fieser, W. E. Rosen and L. F. Fieser, *ibid.*, **74**, 5401 (1952); (d) L. J. Bellamy, "Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 27–28.

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

(9) (a) E. P. Kohler and H. F. Engelbrecht, *ibid.*, **41**, 1379 (1919); (b) L. I. Smith and R. E. Kelly, *ibid.*, **74**, 3300 (1952).

(10) A. Sandoval, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 2383 (1951).

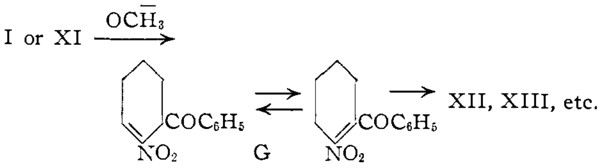
(11) L. I. Smith and E. R. Rogier, *ibid.*, **73**, 3831 (1951).

(12) E. P. Kohler, *ibid.*, **50**, 221 (1928); E. P. Kohler and G. R. Barrett, *ibid.*, **46**, 2105 (1924).

(13) J. W. Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Vol. VIII, Longmans, Green and Co., London, 1928, pp. 286–295.

(14) E. A. Braude, E. R. H. Jones and G. G. Rose, *J. Chem. Soc.*, 1104 (1947).

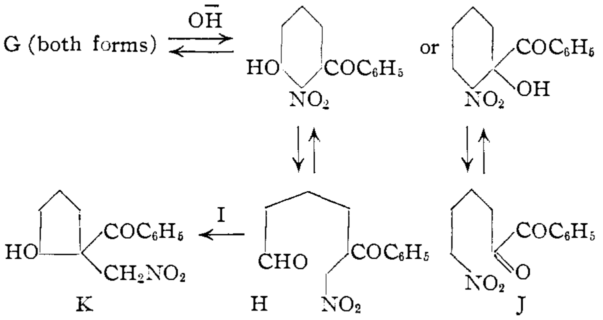
comes a reasonable intermediate because it is derivable from both I and XI.



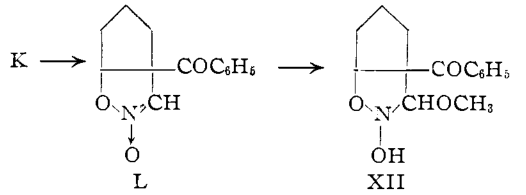
In view of the importance of G as an intermediate in the reactions of I with bases, an attempt was made to prepare G by an unequivocal synthesis, but the synthesis was unsuccessful.

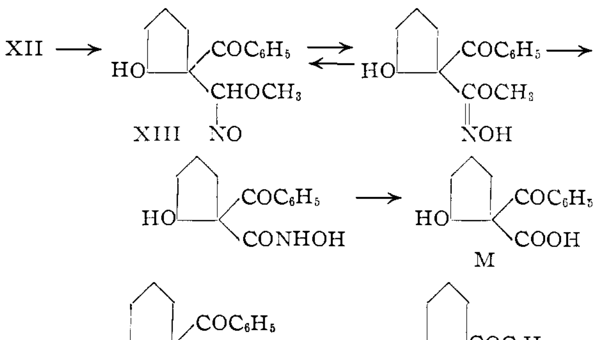
Moisture profoundly affected the course of the reaction between I and base. Unless sodium methoxide was freshly prepared from anhydrous methanol, the reaction mixture assumed a bright red color instead of the usual yellow, and yields of XII and XIII were quite variable. The presence of hydroxide ion did facilitate the rate of reaction, for compound I dissolved almost instantly in warm, methanolic potassium hydroxide and it could not be recovered even though the solution was neutralized within two minutes. But this reaction was accompanied by elimination of ammonia, yields of XII were small and no XIII could be isolated. If, then, it be assumed that G is an intermediate and that traces of hydroxide ion participate in the reaction, it becomes possible to set up a reaction sequence which accounts for the action of base upon I and XI.

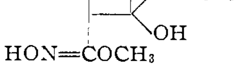
The reaction begins with opening of the ring of G by a reverse aldol condensation to form the carbonyl compounds H and J. That an aldehyde is produced in these reactions was shown by the positive Fehling test, given by XI, XII and XIII. The hydrogen atom alpha to the benzoyl group in H then participates in an aldol condensation with the aldehyde group to form the cyclopentenol K. Other aldol condensations are possible between the carbonyl groups and aci-nitro groups or hydrogen atoms alpha to the nitro groups in H and J, but these constitute either reversal of the ring opening, or lead to eight- or nine-membered rings, or else require addition to the benzoyl group instead of to the aldehyde group. K, in analogy with other compounds of this type,[12] cyclizes to the isoxazoline oxide L, which in the presence of methanol is converted into the N-hydroxyisoxazolidine XII.



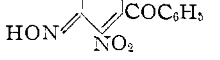
Hydrolysis of XII would lead to an α-nitroso ether or oximido ester XIII, isomeric with and closely related to XII and showing many of the properties of XII; further hydrolysis of XIII would lead to hydroxylamine and an unstable carboxylic acid M.







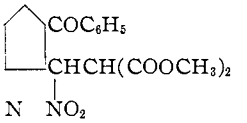
XIV



XV

Benzoic acid, always found among the products resulting by action of alkali upon I or XI, could arise easily by cleavage of XIII or M. The alternative structure for XIII, represented by XIV, though more closely related to a known oximido ester,[12] was eliminated because XIII produced no benzoic acid when it reacted with periodic acid.

Action of Sodiomalonic Ester upon I.—Unlike the secondary nitrocyclopropyl ketones previously studied, compound I by action of methanolic sodiomalonic ester produced no α-pyrone VI, but gave instead a 44% yield of compound VIII. This curious reaction is difficult to interpret; although a typical 1,4-addition of the reagent to I could readily produce such a substance as N, which in turn could lose the elements of malonic ester, the product would then be an unsaturated nitroketone, and not the saturated compound VIII. It is not clear why a reduction should occur during the reaction between I and methanolic sodiomalonic ester, whereas no such reduction occurs when sodium methoxide alone is used. The bromonitroketone XI was also subjected to the action of methanolic sodiomalonic ester in the hope that if G were first formed it would be converted into the α-pyrone. The product was a light yellow oil having the approximate composition $C_{11}H_{12}O_2$; comparison of the properties and the spectrum of this compound with those of an authentic α-pyrone ester showed that whatever the substance was, it was not an α-pyrone. Thus, action of sodium methoxide upon the cyclopropane I or its derivative XI gave the same products, but action of sodiomalonic ester upon the two compounds gave different products.



N

The results of this investigation show that, whatever the mechanism of the reaction may be, the structural requirements necessary to produce 1,3-diketones (or their derivatives) by action of basic reagents upon secondary nitrocyclopropyl ketones are the same as those which would be required to produce acetylenic or allenic ketones as intermediates in this reaction.

Experimental Part[15]

1-Benzoylcyclopentene (VII).[16]—Aluminum chloride (266 g., 2 moles) was added (90 minutes) portionwise to a stirred and cooled (0–5°) solution of benzoyl chloride (283 g., 2 moles) and cyclopentene (147 g., 2.2 moles) in carbon disulfide (800 cc.). The mixture was stirred for ten minutes longer[17] and then added cautiously to ice (3 kg.). The amorphous solid was removed[18] and set aside. The organic solution was removed, and the aqueous phase was extracted with chloroform. The combined organic solutions were washed successively with water containing 1% pyridine, aqueous bicarbonate (5%) and dried (magnesium sulfate). The solvents were removed under reduced pressure, the residue was combined with the amorphous solid previously removed, and the whole was refluxed in petroleum ether (200 cc., b.p. 70–110°) and pyridine (80 cc.). The pyridine salts (70 g.) were removed, and the filtrate was washed successively with water, hydrochloric acid (5%), water and aqueous bicarbonate. The solution was dried (magnesium sulfate), solvents were removed under reduced pressure, and the residue was fractionated through a short column packed with glass helices. The main fraction (181 g., 53%) was a yellow oil boiling at 100–110° (0.7 mm.) and having $n^{25}\text{D}$ 1.5660.

The oxime, recrystallized from alcohol, melted at 138–142°; its spectrum in the infrared showed the presence of a double bond and a hydroxyl group.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.48. Found: C, 77.19; H, 7.19; N, 7.69.

The 2,4-dinitrophenylhydrazone was oily but, after everal crystallizations from alcohol, it melted at 165–167°; he value in the literature is 162–163°.[19]

There are numerous reports in the literature of rearrangements—partial or complete—occurring during reactions between olefins and acid chlorides when aluminum chloride is used as a catalyst. It was important for preparation of the cyclopropane I, that the specimen of VII be free from rearranged products, or that rearranged products, if present, did not interfere. Because of the wide boiling range of the above product (10° (1 mm.)), its conversion to an oxime and a 2,4-DNP which were purified with difficulty and the presence in the infrared spectrum of extraneous bands besides those expected for VII, this compound was prepared once *via* an alternate synthesis which eliminated the use of acid catalysts. 1-Cyclopentenecarboxylic acid, m.p. 120–121°,[6c] was prepared from cyclopentanone *via* the bisulfite addition product, the cyanohydrin and 1-cyanocyclopentene, although failure was encountered in the dehydration of the cyanohydrin by action of thionyl chloride and phosphorus oxychloride had to be used. The crude acid (43 g., 0.38 mole) was stirred while thionyl chloride (65 g., 0.55 mole) was added dropwise (12 minutes) to the solid. After the exothermic reaction subsided, the mixture was warmed (50°) for one hour, excess thionyl chloride was removed under reduced pressure, and the black residue was fractionated through a Vigreux column (6 in.).

The acid chloride weighed 45.2 g. (90%), and boiled at 56° (29 mm.). The acid chloride (43 g., 0.33 mole) dissolved in benzene (50 cc.) was added, with stirring, to a solution of diphenylcadmium (0.5 mole) in benzene (150 cc.). The solution was refluxed for one hour, and then the product was isolated in the usual manner. The product, fractionally distilled, gave as the main fraction a yellow oil (20 g., 34%) boiling at 115–118° (0.06 mm.), and having $n^{25}\text{D}$ 1.5767. The 2,4-DNP melted sharply at 166–167° and there was no depression in melting point when it was mixed with the 2,4-DNP (m.p. 165–167°) of VII prepared *via* the Friedel–Crafts reaction. Moreover, both specimens of VII, when converted into the cyclopropane I, gave the same product, although VII prepared by the second method gave better yields of I by about 10%.

1-Benzoyl-2-(nitromethyl)-cyclopentane (VIII).—A solution of nitromethane (170 g., 2.8 moles) and VII (121 g., 0.7 mole) in dry methanol (300 cc.) was refluxed and stirred while a solution of sodium methoxide in methanol (from sodium 18.5 g., 0.8 gram atom; methanol, 300 cc.) was slowly (two hours) added. The red solution was cooled and poured into ice-water (1.5 l.) containing acetic acid (70 cc.) and urea (20 g.). The organic layer was removed and the aqueous phase was extracted once with chloroform (500 cc.). The combined organic material was washed successively with aqueous bicarbonate (5%, four 200-cc. portions), water and hydrochloric acid (1%). The solution was dried (magnesium sulfate), the solvent was removed, and the residue was fractionated. The main fraction, a yellow oil, boiled at 168–173° (0.5 mm.), and weighed 80 g. (49%). The analytical sample boiled at 130–132° (0.08 mm.), and had $n^{25}\text{D}$ 1.5485.

Anal. Calcd. for $C_{13}H_{15}NO_3$: C, 66.92; H, 6.48; N, 6.01. Found: C, 67.34, 66.96; H, 6.41, 6.77; N, 6.16.

The 2,4-dinitrophenylhydrazone, after three crystallizations from ethanol, melted at 139–140°.

Anal. Calcd. for $C_{19}H_{19}N_5O_6$: C, 55.20; H, 4.65. Found: C, 55.34; H, 4.94.

The semicarbazone, after two crystallizations from methanol, melted at 146–147°.

Anal. Calcd. for $C_{14}H_{18}N_4O_3$: C, 57.92; H, 6.25; N, 19.30. Found: C, 57.92; H, 6.63; N, 19.36.

Attempts to prepare a phenylhydrazone or an oxime of VIII were unsuccessful.

1-Benzoyl-2-(bromonitromethyl)-cyclopentane (IX).—A solution of sodium ethoxide (from sodium, 7.9 g., 0.34 gram atom, and dry ethanol, 150 cc.) was slowly added, with stirring and cooling (0°), to a solution of the nitroketone VIII (80 g., 0.34 mole) in dry ethanol (150 cc.). This solution of the aci-nitro compound was allowed to stand for five minutes and was then added dropwise (one hour) and with stirring and cooling (10°) to a solution of bromine (57 g., 0.35 mole) in dry ethanol (200 cc.). Cooling was discontinued; the solution was stirred for 30 minutes and then poured into water (2 l.) containing hydrochloric acid (10 cc.). The mixture was extracted with chloroform (two 300-cc. portions) and the combined extracts were washed successively with water, aqueous bisulfite (5%), aqueous bicarbonate (5%) and water. The solution was dried (Drierite) and the solvent was removed under reduced pressure while the temperature was kept below 45°. The residue, a red oil, weighed 109 g. (109%). The oil was quite unstable and had to be used directly in the next step. It could not be purified by distillation and no solid derivative could be obtained.

1-Benzoyl-6-nitrobicyclo[3,1,0]hexane (I).—The above bromonitroketone IX (109 g.) and potassium acetate (160 g., freshly fused) were dissolved in dry ethanol (1 l.) and the solution was refluxed for 15 hours. The cooled solution was poured into water (4 l.) and allowed to stand for one hour. The black, tarry material was removed and the filtrate was extracted with chloroform (two 300-cc. portions). The extract was washed successively with water and aqueous bicarbonate (5%), dried (magnesium sulfate) and the solvent was removed under reduced pressure. The residue, together with the black material previously removed, was refluxed for 30 minutes with successive 1-l. portions of petroleum ether (b.p. 60–68°) until the petroleum ether, after removal and cooling overnight in a refrigerator, no longer deposited crystals of I. In most cases this required

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[15] Microanalyses by Miss C. C. Chuen, J. H. Cooley, D. D. Davis, O. A. Runquist, O. Romanus, J. S. Swenson and Mrs. T. Y. Lee.

[16] R. C. Fuson, R. Johnson and W. Cole, THIS JOURNAL, **60**, 1594 (1938).

[17] In this preparation, the time the reaction mixture is allowed to stand after addition of aluminum chloride is critical. The yield of product varied between 0 and 49% when the mixture was allowed to stand for longer periods of time than ten minutes.

[18] This solid was 1-benzoyl-2-chlorocyclopentane. After four crystallizations from petroleum ether and one from aqueous methanol, the material melted at 92–95°. The yield was often as high as 10%. It was inert to the action of permanganate in acetone, reacted slowly with hot alcoholic silver nitrate, and evolved hydrogen chloride when heated to 80–90°. *Anal.* Calcd. for $C_{12}H_{13}OCl$: C, 69.06; H, 6.28. Found: C, 69.01, 69.19; H, 6.70, 6.50.

[19] W. Baker and P. G. Jones, *J. Chem. Soc.*, 787 (1951).

ten portions of the solvent. The solids were combined and crystallized twice from petroleum ether (Norite), when they formed white needles melting at 101–102° (17 g., 21%). The analytical sample melted at 103–104°.

Anal. Calcd. for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06; mol. wt., 231. Found: C, 67.51, 67.75; H, 6.02, 5.86; N, 6.29; mol. wt. (Rast), 226.

A solution of I in acetone was unaffected by action of permanganate; a solution of I in chloroform was unaffected by action of bromine. No carbonyl derivative of I could be prepared, even under forcing conditions.[10]

1-Benzoyl-2-nitro-3-bromocyclohexane (XI).—A solution of the cyclopropane (I, 500 mg.) in acetic acid (8 cc.) and acetic anhydride (2 drops) was cooled (0°) and saturated with hydrogen bromide. The solution was allowed to stand for three hours at room temperature, then was poured into water (100 cc.) and extracted with chloroform (four 20-cc. portions). The combined extracts were washed with aqueous bicarbonate (10%), then with water, dried (magnesium sulfate) and the solvent was removed under reduced pressure. The residue weighed 596 mg. (88%), and after three crystallizations from petroleum ether–benzene (1:1) the white crystals melted at 116.8–117.2°. No stereoisomers could be found.

Anal. Calcd. for $C_{13}H_{14}NO_3Br$: C, 50.00; H, 4.52; N, 4.49. Found: C, 50.22; H, 4.52; N, 4.41.

The bromo compound XI was inert to action of sodium iodide in acetone (50°, six minutes), and to hot, alcoholic silver nitrate. A few crystals of an orange 2,4-DNP melting at 176–183° after crystallization from ethanol–ethyl acetate, resulted when an alcoholic solution of XI was subjected to the reagent for two weeks. The derivative decomposed at the melting point with evolution of gas.

Action of Sodium Methoxide upon I.—Numerous experiments showed that unless the conditions of this reaction were carefully defined, unstable oils were the major products and little or no solid material resulted. The following procedure represents what appeared to be the optimum conditions for production of solid material. Freshly cut sodium (2.3 g.) was dissolved in methanol (50 cc.), which had been carefully dried.[20] To this solution, under dry nitrogen, was added all at once the cyclopropane I (2.0 g.). The container was loosely sealed and kept for *exactly* ten minutes in an oil-bath at 60°, with gentle agitation until the mixture became homogeneous. The solution was then cooled in an ice-bath while a cold (0°) solution of acetic acid (20 cc.) and urea (2 g.) in water (100 cc.) was added with stirring. After ten minutes, cold, dilute, sulfuric acid was added until the yellow solution became colorless. The solution was saturated with magnesium sulfate and extracted with ether (reagent grade, three 100-cc. portions), and the aqueous layer was discarded. The combined ether solutions were extracted with aqueous bicarbonate (5%) until the aqueous layer remained colorless. The orange bicarbonate extracts = W; the light yellow ethereal solution = Y.

The aqueous bicarbonate solution (W) was acidified with cold, dilute sulfuric acid and extracted with ether. The extract was washed with water, dried (magnesium sulfate) and the solvent was removed under reduced pressure. The residue was a yellow solid (S in the text) (268 mg.) melting at 75–100°.

The ethereal solution Y was washed with water and then shaken with aqueous copper acetate (2%, two 100-cc. portions each containing a drop of acetic acid). The green solid (Z) was removed; the filtrate Y was washed with water containing a trace of bicarbonate, dried (magnesium sulfate) and the solvent was removed under reduced pressure at a temperature always below 30°. The residue was a yellow oil (AA).

The solid Z was washed with water and ethanol and dried in a vacuum desiccator over phosphorus pentoxide. It then weighed 815 mg. and was moss-green in color. Unlike true chelate compounds, Z did not melt below 300°, nor was it soluble in common organic solvents except for a slight solubility in chloroform. Z (500 mg.) was finely ground in an agate mortar, added to dry ether (100 cc.), and a vigorous stream of hydrogen sulfide was passed through the suspension for 30 minutes. The copper sulfide was removed, and the ethereal filtrate was evaporated under reduced pressure. The light brown, solid residue (360 mg.), after crystallization from benzene, gave 208 mg. of white crystals melting at 154–155°. This was 4-benzoyl-2-hydroxy-3-methoxy-4,5-cyclopentanoisoxazolidine (XII). The analytical sample melted at 155–157°.

Anal. Calcd. for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.32; OCH_3 (one), 11.78. Found: C, 63.99; H, 6.58; N, 5.44[21]; OCH_3, 11.39.[22]

The isoxazolidine contained one methoxyl group, formed an insoluble copper compound, slowly produced ammonia by action of aqueous base, slowly reacted with permanganate, slowly gave a positive Fehling test, gave an amber color with ferric chloride, showed two active hydrogen atoms, and no addition in the Grignard analysis, was insoluble in aqueous bicarbonate and could be recovered unchanged when its cold solution in alkali was acidified within three to five minutes. Action of periodic acid upon XII gave only tar and water-soluble products, some of which were aldehydes or ketones, and the periodic acid was reduced to iodine. The infrared spectrum of XII showed no bands characteristic of the nitro group, but there were bands which may arise from NH, OH, secondary amide, benzoyl and phenyl groups.

The yellow oil (AA) was triturated with benzene. There appeared a few crystals; more crystals were obtained by slowly adding a mixture of benzene–petroleum ether (15 cc., 3:1). The solid, after crystallization from benzene–petroleum ether weighed 478 mg. and melted at 144–148°. When this material was slowly recrystallized from benzene, there appeared on top of the white, feathery crystals a few dense clusters of yellow prisms. The white (XIII) and yellow (XV) solids were separated manually; the white material (XIII) constituted the major portion of fraction AA. The yellow solid, after three crystallizations from benzene, weighed 16 mg., and melted at 148–149°. This was pure 2-nitro-3-benzoylcyclohex-2-enone oxime (XV). Unless XV was purified extensively, it decomposed to a yellow oil on storage for a few weeks.

Anal. Calcd. for $C_{13}H_{12}N_2O_4$: C, 59.97; H, 4.66; N, 10.80. Found: C, 60.02, 60.07, 60.17; H, 4.97, 4.93, 4.90; N, 11.30, 11.30, 10.92.

The infrared spectrum of XV showed a rather broad band at 3320 $cm.^{-1}$ which could indicate an hydroxyl group, or which, taken together with bands at 1660 and 1518 $cm.^{-1}$, could indicate a secondary amide. The meager supply of R made a detailed investigation impossible.

The white material (XIII), 1-benzoyl-2-hydroxycyclopentane-1-ethyl hydroxamic acid, was crystallized three times from benzene–petroleum ether (3:1) when it melted at 150–152° with slight sintering at 142°. A mixture of XII and XIII melted at 147–150°.

Anal. Calcd. for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.32; OCH_3 (one), 11.78; mol. wt., 263. Found: C, 64.04; H, 6.72; N, 5.38[21]; OCH_3, 11.45[22]; mol. wt. (Rast), 295.

XIII possessed in general properties very similar to those of XII. It contained one methoxyl group, did not form a copper compound. Compared with XII, XIII reacted more rapidly with base to produce ammonia, gave the Fehling test more rapidly, gave no color with ferric chloride, was inert toward permanganate, could not be recovered from its solution in bases, showed the same behavior as XII toward periodic acid. The infrared spectrum of XIII showed many bands different from those in the spectrum of XII, but the bands most readily interpreted in the spectrum of XII are also present in the spectrum of XIII, though generally shifted to somewhat lower frequencies. These properties of XIII are also the properties of derivatives of the isoxazoline oxides.

XIII reacted with cold, aqueous nitrous acid to produce a yellow oil which contained a few white crystals melting at 138–139°. This substance was insoluble in aqueous bicarbonate and was unaffected by action of permanganate, but the amount was too small for further investigation. When XIII (63 mg.) was mixed with aqueous sodium hydroxide (5 cc., 0.03 *M*) at 0°, the aqueous phase became yellow. The mixture was centrifuged immediately and the clear yellow supernatant liquid was removed and acidified

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(20) H. Lund and J. Bjerrum, *Ber.*, **64**, 210 (1931).

(21) We wish to thank Mr. James Kerns, of General Mills, Inc., for this C, H and N analysis.

(22) Clark Microanalytical Laboratories.

with dilute hydrochloric acid. The resultant gummy solid was removed, triturated with ether–petroleum ether (5 cc., 1:1), and the extract was removed and evaporated. There remained a white solid (5 mg.) which, recrystallized from benzene, melted at 148–150°. The infrared spectrum of this compound was identical with that of XV—even though this compound was white and XV was yellow. Unfortunately, a sample of XV was no longer available for a determination of the mixed melting point.

Action of Sodium Methoxide upon XI.—The bromonitroketone XI (150 mg.) was subjected to action of methanolic sodium methoxide (10 cc., 3.0 *M*) in the same manner as described above for I. The products were benzoic acid and an unstable oil in the bicarbonate-soluble fraction; in the alkali-insoluble fraction, a white solid identical with XIII and a compound which formed a copper derivative identical with Z. Identities were established by comparison of the infrared spectra, and by mixed melting point determinations in the case of the solids.

Action of Sodiomalonic Ester upon I.—The cyclopropane I (2.0 g.) was added to a solution prepared from methyl malonate (2.7 g., 0.025 mole) and methanolic sodium methoxide (from sodium, 0.46 g., and methanol, 20 cc.). The solution was maintained at 60°; within ten minutes a bright red color appeared. After 1.5 hours the solution was cooled and added dropwise to a solution of acetic acid (5 cc.) in water (100 cc.). The solution was extracted with chloroform and the extract was washed with water and aqueous bicarbonate, and dried (magnesium sulfate). The solvent was removed under reduced pressure and the residue was fractionated, giving a middle fraction (0.8 cc.) of a yellow oil. Redistillation gave 0.4 cc. of yellow oil having $n^{25}\text{D}$ 1.5338. This was compound VIII.

Anal. Calcd. for $C_{13}H_{15}NO_4$: C, 66.92; H, 6.48. Found: C, 67.16; H. 6.74.

The 2,4-DNP melted at 139–140°, alone or when mixed with the 2,4-DNP of VIII prepared from VII.

Anal. Calcd. for $C_{19}H_{19}N_5O_6$: C, 55.20; H, 4.65; N, 16.94. Found: C, 55.64; H, 4.65; N, 16.86.

Action of Sodiomalonic Ester upon XI.—The bromonitro ketone XI (1.0 g., 0.0032 mole) was refluxed with sodiomethyl malonate (0.012 mole) in methanol (20 cc.) for 1.5 hours. The bright red solution was processed as described above. The product was a light yellow oil (450 mg.) which was neither compound VIII nor a pyrone ester.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 75.01; H, 6.88. Found: C, 74.66; H, 7.07; N, none.

The ultraviolet spectrum of this oil (in ethanol) showed a maximum at 215 mμ (*E* 1%, 1 cm. 3.56 × 10³), whereas the spectrum of the known 3-carbethoxy-4-ethyl-5-methyl-6-phenyl-α-pyrone[23] showed a maximum at 327 mμ (ε 1.20 × 10⁴). Likewise, the infrared spectrum of this oil showed none of the bands characteristic of an α-pyrone ester.

An attempt was made to synthesize 1-benzoyl-2-nitro-2-bromocyclohexane in the hope that it could be converted into the unsaturated nitro ketone G. 2-Benzoylcyclohexanone was prepared as described in the literature[24]; it was planned to prepare the monoöxime of the diketone and convert the oxime into an α-bromonitro group.[25] Unfortunately, only the isoxazole, m.p., 64°, resulted from the action of hydroxylamine upon the diketone.

An attempt was also made to prepare the bicycloheptyl homolog of I, *viz.*, 1-benzoyl-7-nitrobicyclo[4,1,0]heptane, in order to compare its behavior toward alkali with that of I. The synthetic route was analogous to that used for synthesis of I. 1-Benzoylcyclohexene,[26] however, could not be condensed with nitromethane in a Michael reaction in spite of numerous attempts under varied conditions.

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[23] L. I. Smith and R. E. Kelly, THIS JOURNAL, **74**, 3305 (1952).

[24] C. R. Hauser, B. J. Ringler, F. W. Swamer and D. F. Thompson, *ibid.*, **69**, 2649 (1947).

[25] D. C. Iffland and T.-F. Yen, *ibid.*, **76**, 4083 (1954).

[26] R. E. Christ and R. C. Fuson, *ibid.*, **59**, 895 (1937)

MINNEAPOLIS 14, MINNESOTA

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

Synthesis and Alkaline Hydrolysis of a β,γ-Dibromo Ketone: 3,4-Dibromo-1-phenyl-2-benzyl-2,3-dimethyl-1-butanone

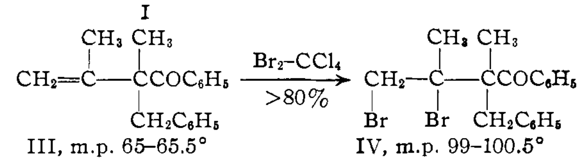
BY LEE IRVIN SMITH AND JOHN R. HOLUM[1]

RECEIVED FEBRUARY 10, 1956

The first simple open-chain β,γ-dibromo ketone, named in the title, has been synthesized, and its behavior upon hydrolysis has been studied. Alkaline hydrolysis of IV was accompanied by loss of the elements of water, and resulted in formation of a cyclic hemi-acetal VIII. Formation of VIII, which is also a vinyl ether, involved no rearrangement of the carbon skeleton of IV. The cyclic form of VIII may, in solution, exist in equilibrium with the open-chain isomer IX.

This report contains a description of the synthesis and properties of 3,4-dibromo-1-phenyl-2-benzyl-2,3-dimethyl-1-butanone (IV), a representative of a class of substances, simple open-chain β,γ-dibromo ketones, hitherto unknown. In particular, the reaction of IV with alkali has been studied.

The synthetic route to IV was



$$CH_2{=}C(CH_3){-}CH(CH_3)COC_6H_5 + C_6H_5CH_2Br \xrightarrow[48\%]{KO\textit{t}\text{-}Bu}$$

I

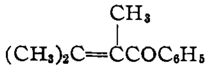
$$CH_2{=}C(CH_3){-}C(CH_3)(CH_2C_6H_5)COC_6H_5 \xrightarrow[>80\%]{Br_2\text{-}CCl_4} CH_2Br{-}CBr(CH_3){-}C(CH_3)(CH_2C_6H_5)COC_6H_5$$

III, m.p. 65–65.5° IV, m.p. 99–100.5°

The sample of I, prepared according to Cologne and Chambion,[2] was not a pure substance but contained also (in undetermined and probably considerable amounts) the α,β-unsaturated isomer α,β-dimethylcrotonophenone (VI). Cologne and Cham-

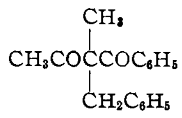
$(CH_3)_2CClCHCH_3COC_6H_5$

V



$$(CH_3)_2C{=}C(CH_3)COC_6H_5$$

VI



$$CH_3COC(CH_3)(CH_2C_6H_5)COC_6H_5$$

VII

bion reported that the reaction between trimethylethylene and benzoyl chloride in the presence of stannic chloride led to the chloro ketone V which, by action of hot dimethylaniline, was converted into the α,β-unsaturated ketone VI. In our hands, the product of these reactions was a mixture of I and

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[1] Abstracted from a thesis by John R. Holum presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, August, 1954. National Science Foundation Pre-doctoral Fellow, 1952–1954.

[2] J. Cologne and J. Chambion, *Bull. soc. chim.*, 1001 (1947).