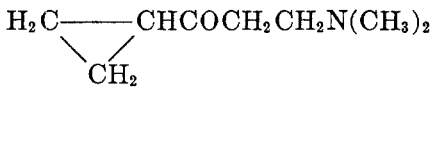
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

# CYCLOPROPANES. XIV.[1] INCIDENTAL EXPERIMENTS AND AN ATTEMPT TO SYNTHESIZE BICYCLOPROPYL

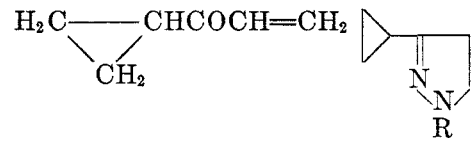
LEE IRVIN SMITH AND JOHN S. SHOWELL

*Received February 11, 1952*

The Mannich base I, derived from methyl cyclopropyl ketone, does not react with hydrazine to form a pyrazoline nor can it be converted into vinyl cyclopropyl ketone (1). However, when this base was converted into the methiodide, and the latter, without isolation, was steam distilled at *p*H 4, vinyl cyclopropyl ketone (II) was obtained as a colorless liquid boiling at 75°/60 mm. The liquid polymerized when heated; it decolorized permanganate and reacted with bromine



I



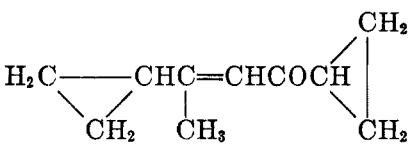
II



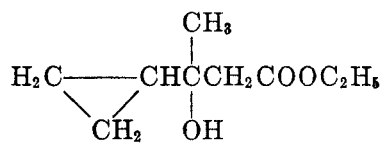
III R = H
IV R = $CSNHC_6H_5$

by addition. No oxime or semicarbazone could be obtained, and the 2,4-dinitrophenylhydrazone was polymeric. Hydrazine reacted with II with production of an unstable pyrazoline III. The pyrazoline was so unstable in air that an analytical sample could not be prepared, but a stable derivative IV was formed by reaction of III with phenyl isocyanate. Attempts to decompose the pyrazoline III and so to obtain bicyclopropyl all failed, and no organic compound of any kind could be isolated.

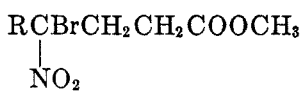
The Mannich base I, its methiodide, and the ketone II all failed to react with nitromethane. On the other hand, phenyl vinyl ketone underwent a Michael reaction with nitromethane, but the product (IX) was derived from two moles of the ketone and one of the nitro compound, and the simple 1:1 adduct could not be obtained. When β-chloropropiophenone was used instead of phenyl vinyl ketone, there was no reaction and only starting material could be recovered.



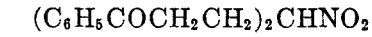
V



VI



VII R = $CH_3$
VIII R = H



IX

[1] Paper XIII, Smith and Showell, *J. Org. Chem.*, **17**, preceding paper (1952).

Ethyl β-cyclopropylacrylate and dibenzalacetone likewise failed to react with nitromethane.

Methyl cyclopropyl ketone was self-condensed in the presence of aluminum *tert*-butoxide; barium hydroxide was without action. The product V gave a 2,4-dinitrophenylhydrazone, but a Michael reaction between V and nitromethane failed.

Methyl cyclopropyl ketone underwent a Reformatsky reaction with ethyl bromoacetate and zinc, but the product VI could not be dehydrated.

Ethyl cyclopropane carboxylate failed to undergo an acyloin condensation. The ester was completely destroyed by action of sodium in xylene or in liquid ammonia, and no acyloin was obtained when the acid was subjected to the action of the binary mixture of magnesium and magnesium iodide.

Methyl γ-bromo-γ-nitrovalerate (VII) was prepared by alkaline bromination of methyl γ-nitrovalerate. Action of potassium acetate upon VII did not produce a cyclopropane; instead, the bromine atom was reductively removed and the product was methyl γ-nitrovalerate.

Methyl γ-nitrobutyrate was prepared by addition of nitromethane to methyl acrylate. The nitro ester was brominated in alkali, and the product, methyl γ-bromo-γ-nitrobutyrate (VIII) was subjected to the action of potassium acetate in methanol. No cyclopropane was formed; the bromo ester VIII was completely destroyed.

## EXPERIMENTAL PART

*Vinyl cyclopropyl ketone* (II). Methyl iodide (36 g., 0.25 mole) was added dropwise and with cooling (Dry Ice) to a solution of the Mannich base I (1) (65 g., 0.23 mole) in ether (200 cc.). The mixture was allowed to warm gradually to room temperature; a white solid mass separated. The entire reaction mixture was added to an aqueous solution of potassium acid phthalate (50 g., 0.25 mole, in 600 cc. of water) and then was steam-distilled until no more organic material appeared in the distillate. Hydroquinone (0.1 g.) was added to the distillate, which was then saturated with sodium chloride. The organic layer was removed, and the aqueous layer was extracted with ether (300 cc.). The organic layers were combined, dried (magnesium sulfate), hydroquinone (0.1 g.) was added, the solvent was removed, and the residual oil was distilled. The distillate, a colorless liquid with a sharp odor, weighed 11.4 g. (51%) and boiled at 63–65°/60 mm. The analytical sample boiled at 65°/60 mm., and had $n_D^{21}$ 1.4560.

*Anal.* Calc'd for $C_6H_8O$: C, 75.00 H, 8.39.
Found: C, 74.3; H, 8.75.

The ketone II immediately decolorized bromine in carbon tetrachloride with no evolution of hydrogen bromide, and gave an immediate precipitation of manganese dioxide with permanganate. Apparently the ketone was completely destroyed by action of permanganate, for no cyclopropane carboxylic acid could be isolated from the product. The ketone polymerized to a viscous oil when it was heated in the absence of a stabilizer. A precipitate was formed with 2,4-dinitrophenylhydrazine, but this solid was apparently a polymer for it was insoluble in all the common solvents. Action of semicarbazide upon II resulted in a similar product.

Several attempts were made to add nitromethane to II by action of both catalytic and equivalent amounts of sodium methoxide, but the only material that could be isolated from the product was the ketone II.

The methiodide of I, prepared from 28.3 g. (0.1 mole) of I as described above, was dissolved in dry methanol (150 cc.) and the solution was added with stirring to a solution of

nitromethane (6.1 g., 0.1 mole) and sodium methoxide (from 2.4 g. sodium) in dry methanol (50 cc.). The solution was allowed to stand overnight at room temperature, then was acidified with dilute acetic acid (4 cc. of acid, 500 cc. of water) and extracted with benzene (200 cc.). The extract was dried (magnesium sulfate) and the solvent was removed. No volatile material could be obtained from the residue when an attempt was made to distill it under reduced pressure. The experiment was repeated several times, changing the order of mixing the reagents, but the result was always the same. When the Mannich base I was substituted for the methiodide in these experiments, the only isolable product was unchanged I.

*3-Cyclopropylpyrazoline* (III). The ketone II (31 g., 0.36 mole) was added dropwise and with stirring to hydrazine (43 g., 95%, 1.35 moles). During the addition, the mixture refluxed spontaneously; after the addition was completed, the mixture was warmed on a steam-bath for 15 minutes. Excess hydrazine was removed under reduced pressure and the residue was quickly distilled. The distillate (21 g., 52%), a colorless liquid with an ammoniacal odor, boiled at 83–84°/5–8 mm. It was unstable in air, becoming yellow and evolving a gas. The liquid solidified in a refrigerator at −15°; the solid, which melted at 5° (dec.) could be stored indefinitely as long as it was protected from air and kept in the dark. The analytical sample boiled at 81–82°/3–4 mm., and had $n_D^{25}$ 1.5136; it was obtained by distilling the material through a column (8 cm.) packed with glass helices and taking a center cut.

*Anal.* Calc'd for $C_6H_{10}N_2$: C, 65.42; H, 9.15.

Found: C, 66.30; 68.61; H, 8.26, 9.78.

The pyrazoline was difficult to burn in the combustion train. The substance immediately decolorized permanganate, and reacted with bromine in carbon tetrachloride with no evolution of hydrogen bromide. In air, it decomposed slowly with effervescence; a drop of the liquid, placed on a filter paper, soon puffed with formation of a white cloud of smoke and production of very penetrating fumes.

*3-Cyclopropyl-1-pyrazolylthiocarbanilide* (IV) was obtained from III and phenyl isothiocyanate. The derivative, crystallized from ethanol, formed long white needles melting at 123–124°.

*Anal.* Calc'd for $C_{13}H_{15}N_3S$: C, 63.63; H, 6.16.

Found: C, 63.89; H, 6.29.

The pyrazoline III (5.5 g.) and copper filings (3 g.) were placed in a 50-cc. flask connected in series with a Dry-Ice trap and a gas trap. The liquid was refluxed for six hours and the evolved nitrogen (110 cc.) was collected. The residue in the flask, when distilled, gave unchanged III (2.8 g., 51%). There was no organic material in the Dry-Ice trap. Thus, no bicyclopropyl was formed, but the experiment demonstrated that the pyrazoline III was quite stable in the absence of air. In a second experiment, the pyrazoline (21 g., 0.19 mole) was dropped on to platinized asbestos at 160°. The volatile material (3 g.) was ammonia; it evaporated completely at room temperature.

*4-Nitro-1,7-diphenyl-1,7-heptandione* (IX). A solution of sodium methoxide (from sodium, 1.32 g., 0.057 gram-atom) in methanol (25 cc.) was added rapidly (five minutes) and with stirring to a solution of nitromethane (3.1 g., 0.05 mole) and phenyl vinyl ketone (2) (6 g., 0.045 mole) in methanol (50 cc.) at 35–40°. The solution was stirred at room temperature for two hours, cooled, and acidified with acetic acid (3.5 cc.). The white solid (2 g., m.p. 131–133°) was removed; the mother liquor, when concentrated, yielded a second crop (0.5 g.). The material, when crystallized from aqueous acetone, melted at 134–135°.

*Anal.* Calc'd for $C_{19}H_{19}NO_4$: C, 70.15; H, 5.89.

Found: C, 69.74, 70.04; H, 6.00, 5.96.

A solution of nitromethane (6.6 g.) in methanol (25 cc.) was added to a solution of potassium acetate (19 g., freshly fused) and β-chloropropioophenone (3) (24 g.) in methanol (100 cc.). The solution was made basic (litmus) by addition of sodium methoxide, and was then refluxed for two hours. The cooled solution was acidified with acetic acid (4 cc.) and poured into water (200 cc.). The white solid (22 g. m.p. 54–59°) was β-chloropropiophenone.

*1,3-Dicyclopropyl-2-butene-1-one* (V). Methyl cyclopropyl ketone (84 g., 1 mole) and aluminum *tert*-butoxide (110 g. 0.45 mole) (4) were stirred and heated at 115–120° in dry

xylene (300 cc.) for 16 hours. Water (30 cc.) was added and the mixture was stirred and refluxed for 30 minutes. The precipitate of aluminum hydroxide was removed by centrifuging and was extracted with ether (1 l.), also with centrifuging. The ether extract was combined with the viscous xylene solution, the solvents were removed under reduced pressure, and the residue was distilled. The product (25 g. 33%) boiled at 117–127°/23–30 mm. Redistillation gave a center cut boiling at 111.5–112.5°/15 mm.

*Anal.* Calc'd for $C_{10}H_{14}O$: C, 79.94; H, 9.39.

Found: C, 80.35; H, 9.55.

The self-condensation of methyl cyclopropyl ketone failed when barium hydroxide was used as the catalyst. The ketone decolorized bromine in carbon tetrachloride with no evolution of hydrogen bromide. The 2,4-dinitrophenylhydrazone, recrystallized from ethanol, was orange-red and melted at 87–91°.

*Anal.* Calc'd for $C_{16}H_{18}N_4O_4$: C, 58.10; H, 5.46.

Found: C, 58.3; H, 5.69.

The ketone failed to give an adduct with nitromethane by the action of either catalytic or equivalent amounts of sodium methoxide.

*Ethyl 2-hydroxy-2-cyclopropylbutyrate* (VI). A portion (30 cc.) of a solution of ethyl bromoacetate (31.1 g., 0.168 mole) and methyl cyclopropyl ketone (15 g., 0.168 mole) in a mixture of benzene (80 cc.) and toluene (70 cc.) was added to zinc shavings (10.3 g., 0.168 gram-atom). The mixture was warmed on a steam-bath and the reaction was initiated by addition of a crystal of iodine. The balance of the solution was then added with stirring at such a rate that the reaction mixture refluxed smoothly. The mixture was then heated for two hours and allowed to stand overnight. The cooled (0°) mixture was acidified with sulfuric acid (6 *N*), the organic layer was removed, dried (magnesium sulfate), the solvents were removed, and the residue was distilled. The distillate (12.8 g., 44%) boiled at 80–88°/7 mm.; the analytical sample, a center cut, boiled at 85.5–86.5°/7 mm.

*Anal.* Calc'd for $C_8H_{16}O_3$: C, 62.80; H, 9.33.

Found: C, 63.6; H, 9.45.

Attempts to dehydrate VI by the action of hydrogen chloride, thionyl chloride in pyridine, acetic anhydride and sodium acetate, iodine in benzene, and 85% formic acid, all failed.

A mixture of nitromethane (1.65 g.) and ethyl β-cyclopropylacrylate (5) (4 g.) was added dropwise and with stirring to a solution of sodium ethoxide (from 1.62 g. of sodium) in ethanol (35 cc.). The solution was stirred for ten minutes, acidified with acetic acid (4 cc.), poured into water, and extracted with benzene (100 cc.). The extract was dried (magnesium sulfate), the solvent was removed, and the residue was distilled. The only product was ethyl β-cyclopropylacrylate (1.5 g., 35%). When the order of addition was reversed and the ester was added to an alkaline solution of nitromethane, the ester was recovered in 90% yield.

A solution of sodium methoxide (6.5 g.) in methanol (75 cc.) was added dropwise and with stirring to a solution of dibenzalacetone (23.4 g., 0.1 mole) and nitromethane (16 g., 0.25 mole) in methanol (400 cc.). The temperature was maintained at 35° for 45 minutes; the mixture was poured into water (1.5 l.) and the solid was removed. It was unchanged dibenzalacetone (22 g., 94%), m.p. and mixture m.p. 54–58°.

Ethyl cyclopropanecarboxylate (15 g., 0.11 mole) was added, quickly and with stirring, to a suspension of sodium powder (23 g., 1 mole) in ether (300 cc.); the mixture was stirred for one hour, but there was no evidence of any reaction. More ester (57 g., 0.39 mole) was added and stirring was continued for an hour, but no reaction occurred. Ethanol (100 cc.) was added in portions over several hours. The mixture was acidified with aqueous sulfuric acid, the ether layer was removed, and the aqueous layer was extracted with ether (500 cc.). The combined ether solutions were dried (magnesium sulfate) and the solvent was removed. The residue was a viscous oil which gave a negative test for the carbonyl group with 2,4-dinitrophenylhydrazine.

Attempts were made to bring about the acyloin condensation of the ester by action of

sodium in liquid ammonia, according to the procedure of Kharasch, Sternfield, and Mayo (6). The only product from 28.5 g. (0.25 mole) of the ester was 6 g. of recovered ester; no other product could be found. Solid iodine (97 g., 0.38 mole) was added portionwise to a suspension of magnesium (20 g., 0.82 gram-atom) in ether (100 cc.) and benzene (200 cc.). Cyclopropanecarboxylic acid (21.5 g., 0.25 mole) was slowly added. After the initial reaction subsided, the mixture was refluxed for five days in an inert atmosphere. The suspended solids were removed and the filtrate was poured into water and acidified with aqueous sulfuric acid. The organic layer, on evaporation, left no residue. The solids were suspended in water (50 cc.), acidified with aqueous sulfuric acid, and the solution was extracted with ether (500 cc.). Removal of the solvent and distillation of the residue gave cyclopropanecarboxylic acid (5 g., 25%) as the only product.

*Methyl γ-bromo-γ-nitrovalerate* (VII). A solution of sodium methoxide (from 13.8 g., 0.6 gram-atom of sodium) in methanol (75 cc.) was added to a solution of methyl γ-nitrovalerate (7) (93 g., 0.56 mole) in chloroform (50 cc.), and the resulting suspension was added with cooling (−20°) and stirring to a solution of bromine (96 g., 0.6 mole) in chloroform (100 cc.). The solution was stirred for one hour at room temperature, then washed successively with water, aqueous sodium bisulfite, aqueous sodium bicarbonate, and water, dried (magnesium sulfate), and the solvent was removed. The residue, when distilled, gave VII (104 g., 78%) boiling at 105–114°/1–2 mm. The analytical sample boiled at 106–110°/0.4 mm.; $n_D^{28}$ 1.4750.

*Anal.* Calc'd for $C_6H_{10}BrNO_4$: C, 30.02; H, 4.20.

Found: C, 30.0; H, 4.17.

On standing, the bromo ester developed an orange color, slowly in the dark, rapidly in sunlight. With potassium iodide in acetone, there was immediate liberation of iodine. When the above bromination was attempted in neutral solution in chloroform and in the presence of ultraviolet light, there was no reaction; addition of benzoyl peroxide had no effect and the unchanged ester was recovered.

The bromo ester VII (60 g., 0.25 mole) and potassium acetate (150 g., 1.53 mole, freshly fused) were dissolved in methanol (600 cc.) and the solution was refluxed for 72 hours. Potassium bromide was removed and solvent was removed from the filtrate under reduced pressure. The residue was added to water (300 cc.) and extracted with ether (750 cc.). The extract was washed with aqueous sodium bicarbonate and water, dried (magnesium sulfate), the solvent was removed, and the residue was flash distilled. The product (21 g., 54%), a colorless liquid, boiled at 75–98°/0.65–2.2 mm.; $n_D^{21}$ 1.440. This liquid was fractionally distilled through a column (50 cm.) packed with glass helices. The bulk (15 g.) of the material boiled at 55–68°/0.35 mm. From this, there was isolated a fraction (7.95 g.) boiling at 59–62°/0.3 mm.; $n_D^{20}$ 1.4394. This was methyl γ-nitrovalerate. No cyclopropane could be found in the product.

*Anal.* Calc'd for $C_6H_{11}NO_4$: C, 44.71; H, 6.88; N, 8.69.

Calc'd for $C_6H_9NO_4$ (cyclopropane): C, 45.38; H, 5.70; N, 8.80.

Found: C, 45.26; 45.28; H, 7.15, 7.19; N, 8.65.

The infrared spectra of this material and that of methyl γ-nitrovalerate were identical.

*Methyl γ-bromo-γ-nitrobutyrate* (VIII). A solution of sodium methoxide (from 2.3 g., 0.1 gram-atom, of sodium) in methanol (40 cc.) was added to a solution of methyl γ-nitrobutyrate (8) (14.5 g., 0.1 mole) in chloroform (40 cc.), and the resulting slurry was added, dropwise and with stirring, to a solution of bromine (17.6 g., 0.11 mole) in chloroform (40 cc.) at −20°. The solution was stirred for one hour at room temperature, then washed successively with water, aqueous sodium bisulfite (10%), and water, dried (magnesium sulfate) and the solvent was removed. The residue, when distilled, gave VIII (13.2 g., 60%) boiling at 112–114°/1–2 mm.; $n_D^{25}$ 1.4732. The analytical sample, a colorless liquid, was a center cut boiling at 118–119°/1.4 mm.; $n_D^{27}$ 1.4760.

*Anal.* Calc'd for $C_5H_8BrNO_4$: C, 26.56; H, 3.57.

Found: C, 26.8; H, 3.98.

The bromo ester gave a pink color with potassium iodide in acetone.

A solution of the bromo ester VIII (28 g., 0.13 mole) and potassium acetate (80 g., 0.82

mole, freshly fused) in dry methanol (150 cc.) was refluxed for 70 hours. Potassium bromide was removed, and solvent was removed from the filtrate under reduced pressure. The residue was added to water (100 cc.) and extracted with ether (300 cc.). The extract was washed with aqueous sodium bicarbonate and water, dried (magnesium sulfate), and the solvent was removed. A very small amount (0.39) of residue remained; this had $n_D^{25}$ 1.4387 and was unchanged VIII. There was no other ether-soluble material. When the experiment was repeated, but with a shorter (seven hours) period of reflux and somewhat more (1 mole) potassium acetate, VIII was recovered in 50% yield and no other organic material could be isolated.

SUMMARY

1. Vinyl cyclopropyl ketone II has been prepared from methyl cyclopropyl ketone *via* the methiodide of the Mannich base I. The vinyl ketone II has been converted into 3-cyclopropylpyrazoline III by action of hydrazine, but pyrolysis of the pyrazoline III gave no bicyclopropyl.

2. The Mannich base I, its methiodide, and the vinyl ketone II did not react with nitromethane.

3. Methyl cyclopropyl ketone has been condensed with itself to give the $\alpha,\beta$-unsaturated ketone V, and with ethyl bromoacetate in a Reformatsky reaction to give the $\beta$-hydroxy ester VI, but the hydroxy ester could not be dehydrated.

4. Methyl $\gamma$-bromo-$\gamma$-nitrovalerate VII and methyl $\gamma$-bromo-$\gamma$-nitrobutyrate VIII did not give cyclopropanes when subjected to the action of potassium acetate in methanol.

MINNEAPOLIS 14, MINNESOTA

## REFERENCES

(1) SMITH AND ROGIER, *J. Am. Chem. Soc.*, **73**, 3842 (1951).
(2) MANNICH AND HEILNER, *Ber.*, **55**, 336 (1922).
(3) HALE AND BRITTON, *J. Am. Chem. Soc.*, **41**, 845 (1919).
(4) WAYNE AND ADKINS, *J. Am. Chem. Soc.*, **62**, 3401 (1940).
(5) SMITH AND ROGIER, *J. Am. Chem. Soc.*, **73**, 3835 (1951).
(6) KHARASCH, STERNFIELD, AND MAYO, *J. Org. Chem.*, **5**, 362 (1940).
(7) KLOETZEL, *J. Am. Chem. Soc.*, **70**, 3571 (1948).
(8) LEONARD AND FELLEY, *J. Am. Chem. Soc.*, **72**, 2542 (1950).