dried over sodium sulfate and fractionated to give a liquid with the following physical properties: b. p. 224–225° at 753 mm.; $n^{20}D$ 1.4571; d^{20}_4 0.9475; yield, 16 g.

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.17; H, 10.27.

This product, however, was difficult to obtain free from hydroxyester as this latter compound apparently formed an azeotropic mixture with the unsaturated ester.

Ethyl α,α,2-Trimethylcyclopentaneacetate.—In glacial acetic acid, 16 g. of ethyl α,α,2-trimethylcyclopentene-1-acetate rapidly consumed the calculated quantity of hydrogen at atmospheric pressure in the presence of Adams platinum catalyst. Fractionation following removal of the catalyst and solvent gave a liquid with the following physical properties: b. p. 225–226° at 750 mm.; $n^{20}D$ 1.4468; d^{20}_4 0.9327; yield, 14 g.

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.50; H, 11.18.

α,α,2-Trimethylcyclopentaneacetic Acid.—A mixture of 14 g. of ethyl α,α,2-trimethylcylopentaneacetate and 28 cc. of concentrated hydrochloric acid was heated in a sealed tube for twenty-four hours at 140–150°, diluted to twice its volume and extracted with ether. The ether layer was extracted with dilute sodium hydroxide, and, upon acidification of the alkaline layer with dilute hydrochloric acid, the organic acid separated and was extracted with benzene. The benzene layer was dried with sodium sulfate and fractionated to obtain the liquid acid, b. p. 256–257° at 743 mm.; $n^{20}D$ 1.4612; d^{20}_4 0.9843; yield, 10 g.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.40; H, 10.56.

α,α,2-Trimethylcyclopentaneacetanilide.—Prepared by the same procedure employed in the preparation of 1-isopropylcyclohexanecarboxanilide, α,α,2-trimethylcyclopentaneacetanilide was recrystallized from alcohol in the form of colorless microscopic needles and melted at 102–103°.

Anal. Calcd. for $C_{16}H_{23}ON$: N, 5.71. Found: N, 5.82.

Summary

1. *dl*-1,2,2-Trimethylcyclohexanecarboxylic acid, 1-isopropylcyclohexanecarboxylic acid, 1-isopropyl-2-methylcyclopentanecarboxylic acid, and α,α,2-trimethylcyclopentaneacetic acid have been synthesized and characterized. These acids were not identical with the $C_{10}H_{18}O_2$ acid isolated from California petroleum by Shive, Horeczy, Wash and Lochte and obtained by Roberts and Bailey in degrading the $C_{16}H_{25}N$ base also isolated from California petroleum.

2. New general methods of synthesis of 1-alkylcycloalkanecarboxylic acids and 1,2-dialkylcycloalkanecarboxylic acids have been developed.

AUSTIN, TEXAS RECEIVED JULY 18, 1941

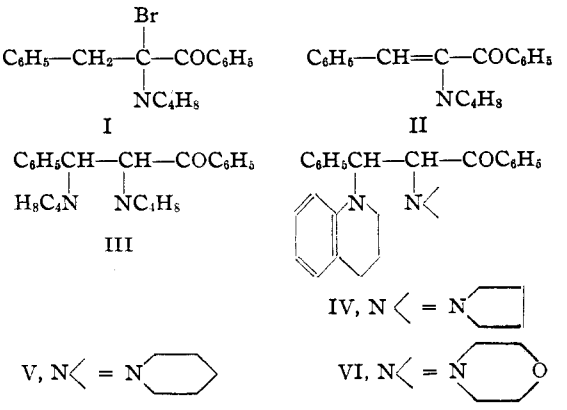
[CONTRIBUTION FROM AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

α,β-Unsaturated Aminoketones. V. Reaction of Pyrrolidine and Tetrahydroquinoline with Bromine Derivatives of Benzalacetophenone[1]

BY NORMAN H. CROMWELL

The only secondary amines that have been found to add to the carbon–carbon double bond of α-bromo-α,β-unsaturated ketones to form α-bromo-α-aminoketones are piperidine[2] and morpholine.[3,4] The present investigation was made in order to extend these studies to other heterocyclic amines for comparison with these previously mentioned experiments.

The strong heterocyclic base, pyrrolidine, has been found to resemble piperidine in these reactions. In cold anhydrous solutions pyrrolidine was found to add rapidly to α-bromobenzalacetophenone to give α-bromo-α-N-pyrrolidinobenzylacetophenone, I.



The α-bromo-α-aminoketone I reacted in the usual way with sodium ethoxide to give the red α-N-pyrrolidinobenzalacetophenone, II. Pyrrolidine was also found to react rapidly with benzalacetophenone dibromide to give one equivalent

(1) Presented before the Division of Organic Chemistry, American Chemical Society, Atlantic City, N. J., September, 1941. For paper IV in this series see Cromwell, THIS JOURNAL, **63**, 837 (1941).

(2) Dufraisse and Moureu, *Bull. soc. chim.*, (4) **41**, 466 (1927).

(3) Cromwell, THIS JOURNAL, **62**, 2897 (1940).

(4) Cromwell, *ibid.*, **62**, 3470 (1940).

of II and two equivalents of α,β-di-N-pyrrolidinobenzylacetophenone, III.

It was found that pyrrole would not react with α-bromobenzalacetophenone. This was to be expected because of the acidity of this heterocyclic compound. Tetrahydroquinoline was also found to be too weak a base to form appreciable amounts of an α-bromo-α-aminobenzylacetophenone with the unsaturated bromide. It was also found that this latter base would not react with the secondary bromine atoms in benzalacetophenone dibromide. However, this base was strong enough to react with the tertiary bromine in various α-amino-α-bromobenzylacetophenones.

When I, α-bromo-α-N-piperidinobenzylacetophenone and α-bromo-α-N-morpholinobenzylacetophenone were each treated with two equivalents of tetrahydroquinoline the corresponding α,β-diaminoketones, IV, V and VI, respectively, were obtained in good yields.

The structures of these diamino ketones were assigned as shown here by analogy with the proved structures of previously prepared α,β-diaminoketones.[1,3] The hydrolysis of one of these, α-N-piperidino-β-N-tetrahydroquinolinobenzylacetophenone, V, gave only the expected products, benzaldehyde and ω-piperidinoacetophenone.[1,3]

The studies of these reactions and products are being continued and extended.

Experimental

α-Bromo-α-N-pyrrolidinobenzylacetophenone, I.—α-Bromobenzalacetophenone (20.12 g.) was dissolved in a mixture of 15 ml. of low boiling petroleum ether and 25 ml. of dry ether. This solution was cooled to −10° and pyrrolidine[5] (4.95 g.) added rapidly. A white precipitate came down immediately. After standing for one-half hour at −10°, the white precipitate was filtered off and washed rapidly with cold petroleum ether. After drying in vacuum for one-half hour the white precipitate (16 g.) melted at 106–107° (instantaneous, decomposed). The analytical samples were weighed out immediately.

Anal.[6] Calcd. for $C_{19}H_{20}NOBr$: N, 3.92. Found: N, 3.80, 3.81.

This compound decomposed rapidly at room temperature to a red oil. The freshly prepared product was soluble in dilute hydrochloric acid.

This tertiary bromide gave an immediate precipitate of silver bromide with alcoholic silver nitrate, but only a very slow reaction took place with water solutions of this reagent. This was found to be a very reactive halogen when compared with that in other bromides. α-Bromobenzalacetophenone gave no appreciable reaction even when alcoholic silver nitrate solutions of it were boiled for five minutes. Benzalacetophenone dibromide gave a slow reaction with an alcoholic silver nitrate solution at room temperature but reacted rapidly when the solution was warmed.

A second experiment was carried out in the above described manner using pyrrole in place of pyrrolidine. No reaction took place with the α-bromobenzalacetophenone.

α-N-Pyrrolidinobenzalacetophenone, II.—Freshly prepared I (1.4 g.) was dropped into a cool sodium ethoxide solution (0.14 g. of sodium, 4 ml. of ethanol). This mixture was then warmed on a steam-bath for five minutes and allowed to stand at room temperature for fifteen minutes more. On adding water the precipitated sodium bromide dissolved and a red oil precipitated from the solution. This oil was dissolved in hot 95% ethyl alcohol and then cooled slowly to give orange-red plates (0.8 g.), m. p. 96–98°.

Anal. Calcd. for $C_{19}H_{19}NO$: C, 82.28; H, 6.90; N, 5.05. Found: C, 82.11; H, 6.98; N, 5.05.

This unsaturated aminoketone was soluble in dilute mineral acids. These acid solutions on standing precipitated benzyl phenyl diketone.[3]

Reaction of Pyrrolidine with Benzalacetophenone Dibromide.—Benzalacetophenone dibromide (5.0 g., one equiv.) was suspended in 75 ml. of moist ether and the solution cooled in ice water. Pyrrolidine (5 g., four equiv.) was added rapidly. A rapid reaction set in and the oily pyrrolidine hydrobromide precipitated from the red solution. After the mixture had stood in the ice chest for twenty hours it was washed several times with water to remove the pyrrolidine hydrobromide and dried. On evaporation 3.89 g. of a red semi-solid was obtained. This on extraction with 10 ml. of warm petroleum ether left a light yellow residue (1.12 g.), m. p. 119–120°. Recrystallization from hot petroleum ether gave pale yellow crystals (product III), m. p. 122–123°.

Anal. Calcd. for $C_{28}H_{28}N_2O$: C, 79.27; H, 8.10. Found: C, 79.33; H, 8.23.

This α,β-diaminoketone decomposed on standing in 95% alcohol solutions to give benzaldehyde and traces of benzyl phenyl diketone. Compound III was soluble in cold dilute mineral acids.

Concentration of the petroleum ether filtrate from product III gave 0.41 g. of α-N-pyrrolidinobenzalacetophenone, II.

α-N-Pyrrolidino-β-N-tetrahydroquinolinobenzylacetophenone, IV.—Freshly prepared I (3.1 g.) was suspended in 6 ml. of ethanol and 2.31 g. (2 equiv.) of tetrahydroquinoline added. After standing for two hours the bromide had all dissolved. The mixture was allowed to stand at room temperature for forty-eight hours and then cooled to give a yellow precipitate which was washed several times with water and dried. The residue was a yellow crystalline compound (1.2 g.), m. p. 144–146°. This was recrystallized from benzene and petroleum ether to give light yellow needles, m. p. 148–149°, dec.

Anal. Calcd. for $C_{28}H_{30}N_2O$: C, 81.91; H, 7.36. Found: C, 81.83; H, 7.62.

(5) The pyrrolidine for these experiments was prepared by the reduction of pyrrole in about 50% yields according to the method of Craig and Hixon, THIS JOURNAL, **52**, 804 (1930).

(6) The weighed samples were immediately dropped into the Kjeldahl flask containing the concd. sulfuric acid for the nitrogen determinations.

This α,β-diaminoketone was not soluble in 1–2 *N* hydrochloric acid but dissolved only in more concd. acids. Heating the acid solution in a water-bath gave benzaldehyde (60% yield) but no benzyl phenyl diketone was noted.

α-N-Piperidino-β-N-tetrahydroquinolinobenzylacetophenone, V.—α-Bromo-α-N-piperidinobenzylacetophenone (10.0 g.) prepared according to the method of Dufraisse[2] was suspended in 18 ml. of ethanol and mixed with 7.15 g. (two equiv.) of tetrahydroquinoline. A very slow reaction set in and six hours had passed before all of the bromide dissolved. After standing for two days the mixture was cooled to give 8.2 g. of a yellow crystalline precipitate, m. p. 164–166°. Recrystallization from benzene and petroleum ether gave 7.2 g. of pale yellow needles, m. p. 166–167°.

Anal. Calcd. for $C_{29}H_{32}N_2O$: C, 82.03; H, 7.60. Found: C, 81.84; H, 7.81.

This diaminoketone was only slowly soluble in warm dilute mineral acids.

Hydrolysis of V.—The diamino ketone V (3.0 g.) was heated on the steam-bath with 30 ml. of 15% sulfuric acid for one and one-half hours. The precipitated oil (0.38 g.) was shown to be only benzaldehyde.

On neutralization of the residual acid solution an oily precipitate was obtained. This was treated with benzene sulfonyl chloride in alkaline solution to remove the tetrahydroquinoline as the benzene sulfonamide. The oily product from this reaction was dissolved in ether and the unchanged amines present extracted with dilute hydrochloric acid. This acid solution on neutralization gave an oily precipitate which was taken up in ether. On passing dry hydrogen chloride into this latter solution, a white precipitate (0.50 g.) was obtained which was shown to be identical with the hydrochloride of ω-piperidinoacetophenone.[1]

α-N-Morpholino-β-N-tetrahydroquinolinobenzylacetophenone, VI.—α-Bromo-α-N-morpholinobenzylacetophenone[3] (3.5 g.) was mixed with 2.5 g. (2 equiv.) of tetrahydroquinoline in 8 ml. of ethanol. After standing for twenty-four hours only a small amount of the bromide had reacted. The mixture was heated at 50° for two hours and then cooled in the ice chest for twenty hours. A pale green precipitate, 2.18 g., was filtered off, m. p. 151–153°. This product on recrystallization from benzene and petroleum ether gave pale, yellow-green needles (1.5 g.), m. p. 153–154°.

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09. Found: C, 78.61; H, 7.33.

This product was not soluble in cold dilute mineral acids but dissolved slowly in warm solutions.

Summary

1. Pyrrolidine has been found to resemble piperidine in its reactions with α-bromobenzalacetophenone and benzalacetophenone dibromide. Tetrahydroquinoline did not react with these bromides.

2. A new α-bromo-α-aminoketone, one new α-amino-α,β-unsaturated ketone, and four new α,β-diaminoketones have been prepared.

LINCOLN, NEBRASKA RECEIVED JULY 31, 1941

[CONTRIBUTION FROM THE ANIMAL CHEMISTRY AND NUTRITION SUBSECTION OF IOWA STATE COLLEGE]

The Preparation of Δ^8-, $\Delta^{8(14)}$- and Δ^{14}-Cholestenes[1]

BY J. C. ECK AND E. W. HOLLINGSWORTH[2]

The preparation of Δ^8-, $\Delta^{8(14)}$- and Δ^{14}-cholestenes was conducted in order to make a comparison of certain properties of various mono-unsaturated derivatives of cholestane. These cholestenes are desirable as convenient cholestane derivatives for investigations of rings C and D. The double bonds are located in ring A or B in the hitherto known cholestenes which are Δ^2-cholestene (neocholestene), Δ^4-cholestene (pseudo-cholestene or coprostene) and Δ^5-cholestene (cholestene). The methods of preparation and the specific rotations of the Δ^8-, $\Delta^{8(14)}$- and Δ^{14}-cholestenes were compared also with those of the analogous Δ^8-, $\Delta^{8(14)}$- and Δ^{14}-unsaturated steroid derivatives.

Δ^8-Cholestene was prepared by the dehydration of cholestan-7-ol with anhydrous copper sulfate in xylene in the presence of propionic acid. This method of preparation of a Δ^8-unsaturated derivative is different from the method used in the preparation of previously known Δ^8-unsaturated sterol derivatives. Thus, the Δ^8-unsaturated derivatives of cholestan-3-ol[3] and coprostan-3-ol[4] were obtained by the sodium–propyl alcohol reduction of the corresponding $\Delta^{6,8}$-unsaturated derivatives in a manner similar to the preparation of the Δ^7-unsaturated derivatives of cholestan-3-ol[5] and ergostan-3-ol[6] by the sodium–ethyl alcohol reduction of the corresponding $\Delta^{5,7}$-unsaturated derivatives.

(1) Journal Paper No. J897 of the Iowa Agricultural Experiment Station, Project No. 506.

(2) Submitted from unpublished research conducted by E. W. Hollingsworth in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) Windaus, Linsert and Eckhardt, *Ann.*, **534**, 22 (1938).

(4) Windaus and Zühlsdorff, *ibid.*, **536**, 204 (1938).

(5) Schenck, Buchholz and Wiese, *Ber.*, **69B**, 2696 (1936).

(6) Windaus and Langer, *Ann.*, **508**, 105 (1933).