Anal. Calcd. for $C_9H_{10}O_2NSCl$: Cl, 15.32; neut. equiv., 115.7. Found: Cl, 15.39; neut. equiv., 115.9.

No depression in the decomposition point occurred when this product was mixed with the compound obtained by the addition of mercaptoacetic acid to benzonitrile in the presence of hydrogen chloride.

Summary

A series of α-iminoalkylmercaptoacetic acid hydrochlorides have been prepared by the addition of mercaptoacetic acid (thioglycolic acid) to nitriles in the presence of hydrogen chloride. These addition products are stable, possess characteristic decomposition points, and may be titrated as dibasic acids by the use of thymol blue as the indicator.

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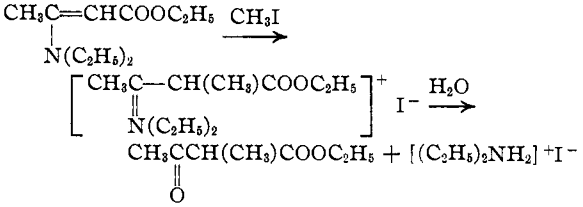
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Alkylation of Beta-Aminocrotonic Esters

BY WALTER M. LAUER AND GEORGE W. LONES

An important study of the alkylation of ethyl β-diethylaminocrotonate with methyl iodide has led Robinson[1] to formulate the reaction as follows

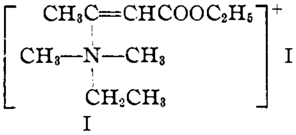


$$\mathrm{CH_3\underset{\displaystyle N(C_2H_5)_2}{\underset{|}{C}}{=}CHCOOC_2H_5} \xrightarrow{\mathrm{CH_3I}} \left[\mathrm{CH_3\underset{\displaystyle N(C_2H_5)_2}{\underset{\|}{C}}{-}CH(CH_3)COOC_2H_5}\right]^+ \mathrm{I^-} \xrightarrow{\mathrm{H_2O}} \mathrm{CH_3\underset{\displaystyle O}{\underset{\|}{C}}CH(CH_3)COOC_2H_5} + [\mathrm{(C_2H_5)_2NH_2}]^+\mathrm{I^-}$$

since diethylammonium iodide and ethyl α-methylacetoacetate were obtained after the reaction mixture was treated with water. An alternative view that the methyl group first attached itself to the nitrogen and subsequently rearranged from the nitrogen to carbon atom is still possible provided the methyl group is assigned a greater migratory aptitude than the ethyl group.

The present work was carried out in order to distinguish between these two mechanisms. The results definitely eliminate the second view and bring additional support to the formulation of Robinson.

Alkylation of ethyl β-dimethylaminocrotonate with ethyl iodide formed a product which on hydrolysis yielded ethyl α-*ethyl*acetoacetate. Now, if the initial step in the process involves the formation of a compound of structure (I)



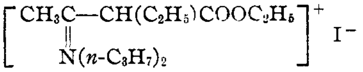
$$\left[\begin{array}{c}\mathrm{CH_3C{=}CHCOOC_2H_5}\\ |\\ \mathrm{CH_3{-}N{-}CH_3}\\ |\\ \mathrm{CH_2CH_3}\end{array}\right]^+\mathrm{I^-}$$

I

and we assign a greater migratory aptitude to the methyl group than to the ethyl group in order to account for the fact that alkylation of ethyl β-diethylaminocrotonate with methyl iodide yields ethyl α-methylacetoacetate, then the expected rearrangement product of I upon hydrolysis would give ethyl α-*methyl*acetoacetate. Instead ethyl α-*ethyl*acetoacetate was obtained.

Likewise, ethyl β-methylaminocrotonate and ethyl β-di-*n*-propylaminocrotonate upon treatment with ethyl iodide followed by hydrolysis yielded ethyl α-ethylacetoacetate. Thus, the substituent which is introduced in the α-position is determined by the alkyl halide used and is independent of the alkyl group or groups already joined to the nitrogen atom.

In the case of ethyl β-di-*n*-propylaminocrotonate it was possible to isolate the ethyl iodide addition product (II)



$$\left[\mathrm{CH_3\underset{\displaystyle N(\mathit{n}\text{-}C_3H_7)_2}{\underset{\|}{C}}{-}CH(C_2H_5)COOC_2H_5}\right]^+\mathrm{I^-}$$

II

which upon hydrolysis gave ethyl α-ethylacetoacetate and di-*n*-propylammonium iodide.

Experimental

Ethyl β-aminocrotonate was prepared according to the method of Michaelis,[2] and alkylated with ethyl iodide following the procedure of Collie.[3] After refluxing for twenty hours, a solid which was identified by means of a Volhard titration as ammonium iodide had separated out even though attempts were made to exclude moisture. The reaction mixture, after filtration, was then allowed to stand overnight with 5% sodium hydroxide. After acidification with dilute sulfuric acid, hydrolysis was completed by refluxing. Methyl propyl ketone (identified as the 2,4-dinitrophenylhydrazone, m. p. 141–142°) was obtained upon distillation.

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(1) Robinson, *J. Chem. Soc.*, **109**, 1083 (1916).

(2) Michaelis, *Ann.*, **366**, 337 (1909).

(3) Collie, *ibid.*, **226**, 316 (1884).

Ethyl β-methylaminocrotonate, prepared according to the directions of Kuckert,[4] was heated (100° for twelve hours) with ethyl iodide in a sealed tube. A crystalline solid appeared in the reaction mixture in small amounts. Part of this solid proved to be methylammonium iodide (Volhard titration and preparation of picrate, m. p. 208°). The main portion of the reaction mixture was refluxed with water for fifteen minutes and then allowed to stand overnight. Extraction with ether, after acidification, gave ethyl α-ethylacetoacetate (b. p. 195–198°), which was hydrolyzed to methyl propyl ketone (identified as the 2,4-dinitrophenylhydrazone).

Ethyl β-dimethylaminocrotonate (b. p. 120–121° at 10–11 mm.) was prepared in 66% yield by the action of dimethylamine on freshly distilled ethyl acetoacetate and *alkylated with ethyl iodide* in the following manner.

Ethyl β-dimethylaminocrotonate (15 g.) and ethyl iodide (50 g.) were heated on the steam-bath for forty-five hours. As the reaction proceeded a dark red oily supernatant layer formed. After removal of the excess ethyl iodide by heating on the steam-bath, water (50 ml.) was added and heating was continued for fifteen minutes. The reaction mixture was then cooled, acidified with dilute hydrochloric acid and extracted with ether. Distillation yielded ethyl α-ethylacetoacetate (10.3 g.); b. p. 82–84° at 14 mm.

The ethyl α-ethylacetoacetate was added to 75 ml. to aqueous sodium hydroxide (5%) and allowed to stand for three hours. Dilute sulfuric acid (1:2; 10 ml.) was then added and the mixture was refluxed. A 10-ml. distillate was collected. The upper layer (6.8 ml.), which consisted of methyl propyl ketone, was dried over sodium sulfate and redistilled (b. p. 99–100°). The methyl propyl ketone was characterized by means of its 2,4-dinitrophenylhydrazone (m. p. 140°).

Ethyl β-diethylaminocrotonate prepared in accordance with the directions of Kuckert[4] was alkylated with ethyl iodide. Ethyl α-ethylacetoacetate was obtained in agreement with the results reported by Robinson.[1]

Ethyl β-Di-*n*-propylaminocrotonate.—Di-*n*-propylamine (39 g.) and freshly distilled ethyl acetoacetate (50 g.) were mixed and allowed to stand at room temperature for six weeks. The mixture was then vacuum distilled, collecting the fraction (48 g.) boiling between 149 and 151° at 9 mm.

Anal. Calcd. for $C_{12}H_{23}O_2N$: C, 67.55; H, 10.87. Found: C, 67.65; H, 10.87.

Ethyl β-di-*n*-propylaminocrotonate (25 g.) and ethyl iodide (50 g.) were refluxed on the steam-bath for twenty-four hours. After cooling, the reaction mixture solidified. The solid mass was partially freed of oil by pressing on a porous plate and placing in a vacuum desiccator for one-half hour. The weight of the impure solid was 30 g. One gram of this solid was crystallized by dissolving in absolute alcohol (5 ml.) and adding anhydrous ether until a precipitate just began to form. Cooling in an ice–salt bath caused the separation of fine white crystals (0.56 g.; m. p. 114–116°), which rapidly became yellow on standing in the air.

Anal. Calcd. for $C_{14}H_{28}O_2NI$: C, 45.5; H, 7.6; I, 34.3. Found: C, 45.2; H, 8.0; I, 33.9.

The main portion of the impure solid (25 g.) was then purified in the above described manner and 18.5 g. of crystalline product was obtained.

The salt was then added to water (50 ml.) and boiled for one-half hour. After cooling, acidification with dilute hydrochloric acid, extraction with ether and drying over anhydrous calcium sulfate, a 70% yield of ethyl α-ethylacetoacetate (5.5 g.) was obtained. This ester was again converted to methyl propyl ketone which was identified as the 2,4-dinitrophenylhydrazone; m. p. 141–142°.

The aqueous acid solution from which the ethyl α-ethylacetoacetate had been extracted was concentrated to about one-fourth of its original volume. After cooling in an ice-bath, the solution was made strongly alkaline and extracted with ether. The ether extract, dried over solid potassium hydroxide and distilled, yielded 4 ml. of di-*n*-propylamine (b. p. 108°). The amine was identified as dipropylamine di-propyldithiocarbamate (m. p. 116–117°).[5]

Summary

Several substituted β-aminocrotonic esters were alkylated with ethyl iodide. The results obtained bring additional support for Robinson's views concerning the mechanism of this process.

MINNEAPOLIS, MINN. RECEIVED NOVEMBER 27, 1936

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[4] Kuckert, *Ber.*, **18**, 618 (1885).

[5] Mulliken, "Identification of Pure Organic Compounds," Vol. II, John Wiley & Sons, Inc., New York, 1916, pp. 135–136.