

ether. The ether extract was washed with four 10-ml. portions of 6 *N* sodium hydroxide. The ether solution was dried and evaporated to leave a yellow oil which was dissolved in 15 ml. of absolute alcohol and treated with dry hydrogen chloride gas. Addition of dry ether precipitated a colorless solid which was recrystallized from absolute alcohol and dry ether to give (VIII).

N-Benzohydril-N-methyl- β -morpholinoethylamine Dihydrochloride (IX).—A solution of 7.0 g. (0.08 mole) of morpholine and 7.41 g. (0.025 mole) of (VI) in 25 ml. of 70% ethyl alcohol was placed in a closed flask and allowed to stand at room temperature for twenty-four hours. The solvent was removed by distillation from a steam-bath under reduced pressure. The residue was extracted with dry ether and the ether solution washed with water, dried and evaporated to leave a colorless oil that could not be crystallized from petroleum ether or alcohol-water mixtures. The oily product was dissolved in 30 ml. of absolute alcohol and dry hydrogen chloride gas added. After addition of 200 ml. of dry ether a colorless crystalline precipi-

tate formed which was recrystallized from absolute alcohol and dry ether to give (IX).

Summary

1. The synthesis of certain *N*-benzohydril-ethanolamines by reaction of benzohydril bromide with ethanolamines of the type $\text{RNHCH}_2\text{CH}_2\text{OH}$ has been studied. When R was methyl or benzyl the desired *N*-benzohydrilethanolamines were obtained, but when R was phenyl only ether formation resulted.

2. The *N*-benzohydrilethanolamines were converted to *N*-benzohydril- β -chloroethylamines, one of which was condensed with dimethylamine and morpholine, respectively, to give substituted ethylenediamines.

LINCOLN, NEBRASKA

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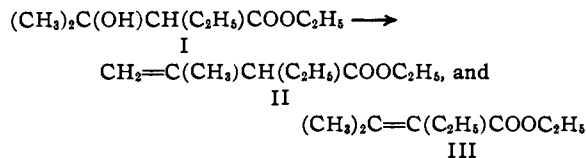
[CONTRIBUTION FROM KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE]

Isomeric Unsaturated Esters. II. The Dehydration of Ethyl 3-Hydroxy-2-ethyl-3-methylbutanoate

BY RALPH C. HUSTON, GORDON L. GOERNER AND HANS H. GYÖRGY

In a previous communication¹ the dehydration of ethyl 3-hydroxy-2,3-dimethylbutanoate was shown to yield a mixture of α,β and β,γ unsaturated esters which were readily separated because of their large difference in boiling points. The β,γ unsaturated ester, contrary to the report in the literature, was found to possess the lower boiling point. It appeared that other unsaturated esters might be recorded erroneously.

Blaise and Maire² dehydrated ethyl 3-hydroxy-2-ethyl-3-methylbutanoate (I) and obtained an unsaturated ester boiling at 167°. To this they assigned formula III. They also obtained a small quantity of an ester boiling at 175°.

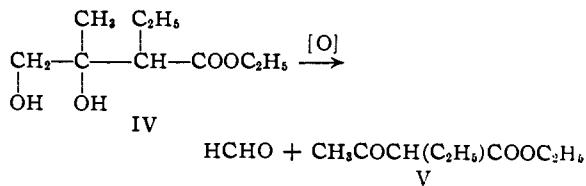


This was assumed to be an isomer of the low boiling ester. Hydrolysis of the ester boiling at 167° yielded an acid distilling at 100° (10 mm.). If esters II and III are analogous to those obtained by Huston and Goerner,¹ ester II should boil at 167° and ester III at the higher temperature. Further evidence that Blaise and Maire had probably assigned the incorrect formula to their low boiling ester was found in the fact that Crossley and LeSueur³ report a boiling point of 175–180° (748 mm.) for a mixture of ester III and ethyl 2-(1-methylethyl)-2-butenate obtained by de-

hydrobromination of ethyl 2-bromo-2-ethyl-3-methylbutanoate by diethylaniline.

Ester I was prepared from propanone and ethyl 2-bromobutanoate by the Reformatsky reaction. It proved to be more stable than expected. An attempt to dehydrate it with dry hydrogen chloride⁴ was unsuccessful. Phosphorus pentoxide⁵ in benzene gave the unsaturated esters in good yield. Esters II and III could be separated readily in approximately equal quantities by fractionation under diminished pressure.

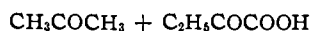
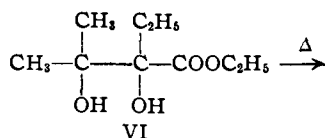
The proof of structure consisted of hydroxylating the esters to the glycols⁶ IV and VI and splitting these into aldehydes and ketones by means



of "ceric perchlorate"⁷ or by thermal decomposition. The low boiling ester gave glycol IV. This was split into methanal (which is oxidized to carbon dioxide and water) and ethyl 3-keto-2-ethylbutanoate (V). The solution containing compound V gave 2-pentanone upon alkaline hydrolysis. The high boiling ester gave glycol VI. On distillation this decomposed into propanone and 2-ketobutanoic acid.

- (1) Huston and Goerner, *THIS JOURNAL*, **68**, 2504 (1946).
 (2) Blaise and Maire, *Ann. chim.*, [8] **15**, 573 (1908).
 (3) Crossley and LeSueur, *J. Chem. Soc.*, **77**, 95 (1900).

- (4) Natelson and Gottfried, *THIS JOURNAL*, **61**, 970 (1939).
 (5) Kon and Nargund, *J. Chem. Soc.*, 2461 (1932).
 (6) Milas and Sussman, *THIS JOURNAL*, **68**, 1302 (1936).
 (7) Smith and Duke, *Ind. Eng. Chem., Anal. Ed.*, **13**, 558 (1941); **18**, 120 (1943).



The ketones were identified through the 2,4-dinitrophenylhydrazones. Catalytic hydrogenation of both unsaturated esters yielded ethyl 2-ethyl-3-methylbutanoate.⁸ Here again¹ the reduction of the β,γ ester was found to proceed much more easily than the reduction of the α,β isomer.

Hydrolysis of the esters yielded the corresponding unsaturated acids. The acid obtained from the high boiling ester III appears to be identical with the β,β -dimethyl- α -ethylacrylic acid of Kon, Smith and Thorpe⁹ which melted at 49.5°. The acid obtained from the low boiling ester appears to be identical with the acid obtained by Blaise and Maire.²

Experimental

All melting points and micro boiling points are corrected. Ethyl 3-Hydroxy-2-ethyl-3-methylbutanoate (I) was prepared by the Reformatsky reaction, using 1.5 moles of propanone per mole of ethyl 2-bromobutanoate and excess zinc, as suggested by Perkin and Thorpe.¹⁰ The propanone was dried over anhydrous potassium carbonate and the benzene over sodium. Ethyl 2-bromobutanoate was prepared by the bromination of butanoic acid¹¹ followed by its subsequent esterification.¹² Ten-mesh zinc was cleaned and dried by the method of Fieser and Johnson.¹³

A solution of 15 g. of acetone and 15 g. of ethyl 2-bromobutanoate in 75 ml. of benzene was added to 245 g. (3.75 moles) of zinc. The reaction was initiated by the addition of a small crystal of iodine and slight heating. When vigorous reflux had begun, a solution of the rest of the reactants was added at a rate rapid enough to maintain reflux. Using 585 g. (3 moles) of ethyl 2-bromobutanoate and 261 g. (4.5 moles) of propanone in 750 ml. of benzene, a reaction time of one hour was required with a maximum reaction temperature of 75°.

After refluxing for one and one-half hours the reaction mixture was cooled and poured into 1800 ml. of cold 10% (volume) sulfuric acid. After forty-five minutes the clear benzene layer was removed and the acid layer washed with benzene. The combined benzene extracts were washed with 250 ml. of 5% (volume) sulfuric acid, 250 ml. of 10% (weight) sodium carbonate, and 400 ml. of water. These were then dried over anhydrous sodium sulfate.

Separation of I was attained by the removal of the benzene under reduced pressure and the fractionation of the ester through a 60-cm. Fenske-type column packed with 3/32-inch glass helices. (This column was used for all subsequent fractionations.) The yield of ethyl 3-hydroxy-2-ethyl-3-methylbutanoate was 163 g. (31%) distilling at 76 to 77° (3 mm.), n_D^{20} 1.4310, d_4^{20} 0.9668, γ_{20} 27.8 (du Noüy, cor.¹⁴).

Dehydration of Ethyl 3-Hydroxy-2-ethyl-3-methylbutanoate.—One hundred seventy-four grams (1 mole) of ester

(8) (a) Ref. 3, p. 93; (b) Roland and McElvain, *THIS JOURNAL*, **59**, 134 (1937); (c) Hudson and Hauser, *ibid.*, **62**, 2459 (1940); **63**, 3161 (1941).

(9) Kon, Smith and Thorpe, *J. Chem. Soc.*, **127**, 572 (1925).

(10) Perkin and Thorpe, *ibid.*, **60**, 1482 (1896).

(11) "Organic Syntheses," Vol. 20, John Wiley and Sons, Inc., New York, N. Y., 1940, p. 106.

(12) *ibid.*, Vol. 23, 1943, p. 38.

(13) Fieser and Johnson, *THIS JOURNAL*, **62**, 576 (1940).

(14) Harkins and Jordan, *ibid.*, **52**, 1751 (1930).

I was refluxed for two hours with 177 g. of phosphorus pentoxide in three volumes (555 ml.) of benzene.^{4,5} The supernatant liquid was decanted and fractionated under reduced pressure. The yield of ethyl 2-ethyl-3-methyl-3-butenate (II) boiling at 57° (13 mm.) was 49 g., (31%, based on hydroxy ester); micro b.p. 167° (741 mm.), n_D^{20} 1.4250, d_4^{20} 0.9005, γ_{20} 20.61 (drop-weight, cor.¹⁵).

Anal. Calcd. for $\text{C}_8\text{H}_{16}\text{O}_2$: C, 69.19; H, 10.32. Found: C, 69.25; H, 10.30.

Fifty-one grams (33%, based on hydroxy ester) of III was obtained boiling at 67° (13 mm.); micro b.p. 180° (741 mm.), n_D^{20} 1.4430, d_4^{20} 0.9492, γ_{20} 24.05 (drop-weight, cor.¹⁵).

Anal. Calcd. for $\text{C}_8\text{H}_{16}\text{O}_3$: C, 69.19; H, 10.32. Found: C, 69.27; H, 10.25.

The total yield of the unsaturated esters was 20%, based on the bromo ester. By dehydrating the crude reaction mixture without isolating the hydroxy ester, a yield of 25% was obtained.

Reduction of the Unsaturated Esters.—One-tenth mole of the ester, 150 ml. of ethanol, 0.1 g. of the platinum oxide catalyst,¹⁶ and 50 lb. of hydrogen pressure were used. The low boiling ester (II) was completely reduced in thirty minutes. In the case of the high-boiling ester (III), four hours were necessary for complete reduction. Ethyl 2-ethyl-3-methylbutanoate, micro b.p. 167° (744 mm.), was recovered upon fractionation,⁸ n_D^{20} 1.4100, d_4^{20} 0.8686; γ_{20} 22.30 (drop-weight, cor.¹⁵).

Degradation of Ethyl 2-Ethyl-3-methyl-3-butenate (II).—Seven and eight-tenths grams (0.05 mole) of the ester was dissolved in a 7% solution of hydrogen peroxide (0.05 mole) in 2-methyl-2-propanol. Two milliliters of osmium tetroxide solution was added according to the procedure of Milas and Sussman.⁴ After fifteen-minutes the 2-methyl-2-propanol was removed under reduced pressure and the glycol treated with "ceric perchlorate."¹⁷ When the "ceric perchlorate" no longer gave a red color, the solution was made alkaline with potassium hydroxide and was refluxed for four hours. Air was bubbled through the warmed reaction mixture and then into a 5% solution of 2,4-dinitrophenylhydrazine in 20% perchloric acid. The precipitate obtained was crystallized twice from ethanol, m.p. 142–144°. A mixed melting point with a known sample of 2-pentanone-2,4-dinitrophenylhydrazone (m.p. 143–144°) gave no depression.

Degradation of Ethyl 2-Ethyl-3-methyl-2-butenate (III).—The glycol of this ester was synthesized as described above. It proved to be thermally unstable, yielding propanone and 2-ketobutanoic acid. On distillation from a Claisen flask at 15 mm. pressure, the 2-ketobutanoic acid was collected as distillate. The 2,4-dinitrophenylhydrazone of propanone was recovered by placing a trap containing a 5% solution of 2,4-dinitrophenylhydrazine in 20% perchloric acid in the vacuum line. The formation of propanal by decarboxylation of the keto acid caused some difficulty in the isolation of the propanone-2,4-dinitrophenylhydrazone.

The 2,4-dinitrophenylhydrazone of the propanone obtained by the degradation melted at 124–126°; a mixed melting point with an authentic sample of propanone-2,4-dinitrophenylhydrazone (m.p. 126°) gave no depression.

The 2,4-dinitrophenylhydrazone of the 2-ketobutanoic acid melted at 139–141°. The method described by Tschelinzeff and Schmidt¹⁷ was used for the preparation of 2-ketobutanoic acid. Its 2,4-dinitrophenylhydrazone was prepared in perchloric acid solution and melted at 139–141°. A mixed melting point with the above degradation product gave no depression. No melting point is recorded in the literature for this derivative. *Anal.* Calcd. for $\text{C}_{10}\text{H}_{16}\text{N}_4\text{O}_6$: N, 19.86. Found: N, 19.65.

Hydrolysis of the Unsaturated Esters.—Both esters proved difficult to hydrolyze. Hydrolysis was carried out

(15) (a) Harkins and Brown, *ibid.*, **41**, 499 (1919); (b) "I. C. T.," Vol. IV, 1928, p. 435.

(16) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 463.

(17) Tschelinzeff and Schmidt, *Ber.*, **62**, 2210 (1929).

by refluxing in alcoholic potassium hydroxide solution and subsequently neutralizing with hydrochloric acid.

Ethyl 2-ethyl-3-methyl-3-butenolate (II) yielded an acid, b.p. 85° at 4 mm.; n_D^{20} 1.4400; neutralization equivalent calcd. 128, found 130. This acid was isolated with difficulty due to the general tendency of β,γ -unsaturated acids to rearrange to the conjugated α,β -acids in the presence of base.¹⁸ Hydrolysis of (III) yielded a white solid which, on recrystallization from water-ethanol, gave plates melting at 47–48°; b.p. 85° (2 mm.); micro b.p. 218° (741 mm.) with decomposition; neutralization equivalent calcd. 128, found 129.

(18) Gilman, "Organic Chemistry, An Advanced Treatise," second edition, Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 684.

Summary

Ethyl 3-hydroxy-2-ethyl-3-methylbutanoate has been dehydrated to ethyl 2-ethyl-3-methyl-2-butenolate and ethyl 2-ethyl-3-methyl-3-butenolate. These have been isolated and their physical constants determined.

The structure of these unsaturated esters has been assigned on the basis of the ketones to which they have been degraded.

These unsaturated esters have been hydrolyzed and the corresponding acids isolated.

EAST LANSING, MICHIGAN RECEIVED SEPTEMBER 12, 1947

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF INDIANA UNIVERSITY]

Some Derivatives of 2-Acylthiophenes¹

BY E. CAMPAIGNE AND JAMES LOREN DIEDRICH²

Several acylthiophenes ranging in side-chain length from two to eighteen carbon atoms³ have been prepared, usually by some modification of the procedure described by Johnson and May⁴ for the preparation of 2-acetylthiophene. The capric acid derivative was prepared by Schleicher,⁵ but the homologous 2-hexanoyl, 2-octanoyl, and 2-nonanoylthiophenes have not been synthesized previously.^{6a}

The acylthiophenes provide convenient intermediates for the preparation of the corresponding alcohols and alkylthiophenes. The thienyl ketones were readily reduced to the corresponding secondary alcohols by using aluminum isopropoxide in isopropyl alcohol as described by Mowry, Renoll and Huber⁶ for 2-acetylthiophene; however, the yields were somewhat lower with the higher molecular weight ketones. The alkylthiophenes were prepared from the ketones by a slight modification of the Clemmensen method described by Fieser and Kennelly.⁷

In addition to the ketones, alcohols and alkylthiophenes, the characteristics of which are summarized in Table I, the oximes, semicarbazones and 2,4-dinitrophenylhydrazones of the ketones, and the 5-chloromercuri derivatives of the alkylthiophenes were prepared and characterized.

An attempt was made to prepare suitable urethans or esters of the secondary alcohols as solid derivatives but the hydroxy group is relatively in-

active, apparently due to hindrance of the α -carbon in 2-substituted thiophenes,⁸ and no derivatives were isolated.

Experimental

Acylthiophenes.—The procedure used for the ketone preparations was essentially that of Johnson and May⁴ for the preparation of acetylthiophene. The thiophene, obtained from the Socony-Vacuum Oil Company, was distilled through a column and the fraction boiling from 82–84° was collected and stored in brown bottles until used. In each acylation freshly distilled stannic chloride was distilled through a column and the fraction boiling from 82–84° was collected and stored in brown bottles until used. In each acylation freshly distilled stannic chloride was employed. The best yields of the ketones were obtained under the following conditions: 0.5 mole of thiophene and 0.5 mole of the required acid chloride were dissolved in 500 ml. of benzene in a 3-necked flask equipped with a mechanical stirrer, thermometer and dropping funnel, and the mixture was cooled to 0° with stirring. Stannic chloride (0.5 mole) was then added dropwise over a period of one and one-half hours, maintaining the temperature at 0°. When all of the stannic chloride had been added, the cooling bath was removed and stirring was continued for one hour longer. Dilute hydrochloric acid was then added and the benzene layer was separated, washed and dried. The ketone was isolated and purified by distillation.

2-Alkylthiophenes.—The preparation of 2-octylthiophene is typical. A mixture of 125 g. of amalgamated zinc, 225 ml. of 1:1 hydrochloric acid and 26.2 g. (0.125 mole) of 2-octanoylthiophene was allowed to stand in a water-bath at 22° for three and one-half days. To complete the reaction the mixture was refluxed gently for twenty minutes. It was then cooled, extracted several times with ether and the combined ether extracts dried. The ether was removed and the residue distilled at reduced pressure. The yield of colorless oil, b.p. 106–108° at 1 mm., was 13.5 g. (55%).

1-(2-Thienyl)-alkanols.—The preparation of 1-(2-thienyl)-nonanol is typical. In a 125-ml. three-necked flask equipped with stirrer, distilling column and nitrogen-inlet tube was mixed 5.6 g. (0.025 mole) of 2-nonanoylthiophene and three times the calculated quantity of pure freshly distilled aluminum isopropoxide (5 g., 0.025 mole) in 30 ml. of dry isopropyl alcohol. The mixture was heated under an atmosphere of nitrogen to 100–110°, and acetone and isopropyl alcohol were allowed to distill from the mixture. When 12–13 ml. of distillate had been collected an additional 10 ml. of dry isopropyl alcohol was

(1) Taken from a thesis submitted by James Loren Diedrich to the Faculty of the Graduate School in partial fulfillment of the requirements for the degree, Master of Arts, in the Department of Chemistry, Indiana University, June, 1947.

(2) The Ohio Oil Company Fellow in Chemistry.

(3) Ralston and Christensen, *Ind. Eng. Chem.*, **29**, 194 (1937).

(4) Johnson and May, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 8.

(5) Schleicher, *Ber.*, **19**, 680 (1886).

(6a) Since this paper was accepted, Cagniant and Deluzarche (*Compt. rend.*, **235**, 455 (1947)) report the preparation of a series of acylthiophenes, including those described here.

(6) Mowry, Renoll and Huber, *This Journal*, **68**, 1105 (1946).

(7) Fieser and Kennelly, *ibid.*, **57**, 1615 (1935).

(8) Chabrier and Tchoubar, *Compt. rend.*, **230**, 284 (1945).