

Action of Alkylolamines.⁴—Fifteen grams of α -chlorostearate (from α -hydroxystearic acid) was heated to refluxing with 20 g. of monoethanolamine until all chlorine had reacted. The reaction mixture was dissolved in water and extracted with ether. Upon removal of ether and recrystallization from methanol, white flake-like crystals were obtained (yield 10 g.), melting at 85°. Calcd. for $C_{22}H_{44}O_2N$; N, 7.2. Found: N, 6.9. Mixed with the product obtained from bromostearic acid by similar treatment, there was no lowering of the melting point.

The amide was hydrolyzed with mineral acid and the product was crystallized from alcohol m. p. 220° (dec.). It had the composition of α -(N- β -hydroxyethyl)-amino-stearic acid.

Anal. Calcd. for $C_{20}H_{41}O_3N$: C, 70.0; H, 12.0; N, 4.1. Found: C, 69.5; H, 12.6; N, 4.8.

The same reaction carried out on the methyl chlorostearate, made by the direct chlorination of methyl stearate, led to the formation of a crystalline solid melting at 94° on repeated recrystallization from methanol. This solid when mixed with that obtained from bromostearic acid, lowered the melting point of the latter and was not identical with the amide described above. It contained only 4.6% N. When chlorinated methyl laurate was treated with ethanolamine, a thick sirup was obtained from which no definite solid would crystallize.

(4) Guest, U. S. Patent 2,277,015 (1943).

Preparation of Butoxymyristic Acid.—30 g. of α -bromomyristic acid was treated with slight excess of 2 moles of sodium butoxide in excess *n*-butanol. On acidification, an oil, b. p. (4 mm.) 200–208°, was formed.

Anal. Calcd. for $C_{13}H_{26}O_2$: neut. equiv., 300. Found: neut. equiv., 293; iodine value, 4.

The mixed acids obtained from a highly purified fraction of methyl chloromyristate were not identical as shown by distillation and analysis: oil, b. p. (6 mm.) 183–212°.

Anal. Found: neut. equiv., 258; iodine value, 88.

Summary

The chlorination of methyl caprylate, laurate, myristate and stearate by dry chlorine was studied. Various catalysts were used in the unsuccessful endeavor to change the type of reaction, for example to produce α -chloro esters exclusively.

It was found that a large proportion of polychloro ester was formed even in the presence of a large proportion of unaltered ester.

An attempt was made to find a general method of determining the position in the ester of the substituent chlorine.

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[CONTRIBUTION FROM THE LABORATORIES OF WALLACE & TIERNAN COMPANY, INC.]

A Carbonyl Reduction by Potassium Hydroxide in Ethanol

BY MARTIN RUBIN

The system ROH-ROM, particularly in the case where M is aluminum, is an efficient reagent, under suitable experimental conditions, for the reduction of carbonyl compounds to the carbinols.¹ Magnesium,² tin,³ zirconium,³ sodium,⁴ zinc and calcium⁵ have been used in place of aluminum in this system. Potassium hydroxide in benzyl alcohol has been used to reduce some aldehydes⁶ and potassium hydroxide in ethanol under reflux has been utilized for the reduction of substituted benzophenones⁷ and at 200–300° for high molecular weight aliphatic ketones.⁸ Under these conditions the potassium is predominantly in the form of the alkoxide.^{9,10}

In the course of an investigation leading to a synthesis of diethylstilbestrol¹¹ and various of its functional variants,¹² we had occasion to subject the ketone, anisyl-3-hexanone-4, to the action of potassium hydroxide in ethanol at 200–220°.

(1) A. L. Wilds, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 178.

(2) Meerwein and Schmidt, *Ann.*, **444**, 221 (1925).

(3) Young, Hartung and Crossley, *THIS JOURNAL*, **58**, 100 (1936).

(4) Verley, *Bull. soc. chim.*, [4] **37**, 871 (1925).

(5) Meerwein, Bock, Kirschnick, Lenz and Migge, *J. prakt. Chem.*, **147**, 211 (1936).

(6) Palfray, Sabetay and Mastagli, *Compt. rend.*, **203**, 1523 (1936).

(7) Montagne, *Rec. trav. chim.*, **41**, 703 (1922).

(8) Schiebt, German Patent 327,510 (1920).

(9) Engel, *Compt. rend.*, **103**, 156 (1886).

(10) Lescoeur, *ibid.*, **121**, 692 (1895).

(11) Rubin, Salmon and Kozlowski, *THIS JOURNAL*, to be published.

(12) Rubin and Wishinsky, *ibid.*, **66**, 1948 (1944).

The major reaction products were the corresponding carbinol and phenol produced by scission of the anisyl ether. The structures of the products were proved by synthesis and the preparation of derived compounds, as described in the experimental section.

Experimental

Melting and boiling points are uncorrected.

***p*-Hydroxyphenyl-3-hexanol-4.**—A mixture of 60 g. of anisyl-3-hexanone-4,¹¹ 75 g. of potassium hydroxide and 240 cc. of ethanol was heated in a rocking autoclave at 200–220° for six hours. The reaction mixture was poured into 500 cc. of water, the alcohol removed by distillation and the aqueous residue extracted with ether. The ether extracts were washed with 10% potassium hydroxide solution until free of acidic material. The combined alkaline solutions were acidified, extracted with ether and the ether extracts concentrated. On distillation *in vacuo* 30 g. (54%) of colorless, viscous oil, b. p. 145–155° at 1 mm. was obtained. The product crystallized on standing and melted at 82–83° after two recrystallizations from petroleum ether.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.32; H, 9.35.

The diacetate was prepared by refluxing with acetic anhydride for one hour. It was obtained as a colorless oil, b. p. 125–127° at 0.4 mm.

Anal. Calcd. for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.02; H, 7.89.

The mono benzyl ether was prepared by refluxing equimolar quantities of the phenol and benzyl bromide in ethanol with excess alkali. It was a white solid which melted at 75–76° on recrystallization from dilute ethanol.

Anal. Calcd. for $C_{18}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.07; H, 8.21.

p-Benzoyloxyphenyl-3-hexanone-4.—Oxidation of the corresponding carbinol to the ketone was effected by stirring with a sulfuric acid solution of chromic acid for two hours at 40–50° and one hour at 60–80°. The product which crystallized on cooling the acid solution was removed by filtration and melted 80–80.5° on recrystallization from dilute ethanol.

Anal. Calcd. for $C_{19}H_{22}O_2$: C, 80.81; H, 7.85. Found: C, 80.75; H, 7.76.

Anisyl-3-hexanol-4.—The ether extract of the neutral reaction product of anisyl-3-hexanone-4 and potassium hydroxide in ethanol described above was concentrated and distilled *in vacuo*. The product, 15 g. (25%) of a clear, colorless, viscous oil, b. p. 100–105° at 0.2 mm., crystallized on cooling. After recrystallization from dilute ethanol and petroleum ether it melted at 75–76°.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.22; H, 9.84.

A. From Anisyl-3-hexanone-4 by Reduction with Sodium.—To a refluxing mixture of 206 g. of anisyl-3-hexanone-4 and 1 liter of dry isoamyl alcohol was added 100 g. of sodium in small portions. When the evolution of hydrogen was complete the mixture was poured into ice and water, the alcohol layer separated, washed with cold water until free of alkali and finally concentrated and distilled *in vacuo*. The fraction of b. p. 115–125° at 0.5 mm. weighed 180 g. (87.4%). It crystallized on standing and on recrystallization from petroleum ether melted at 75–76°. There was no mixed melting point depression with the anisyl-3-hexanol-4 described above.

B. From α -Anisylbutanal.—To the Grignard reagent from 2.5 g. of magnesium and 16 g. of ethyl iodide was added 18 g. of α -anisylbutanal. After a half hour of refluxing, the reaction mixture was worked up in the usual manner. The product, 16 g. (77%), obtained as a colorless oil, b. p. 90–95° at 0.1 mm., crystallized on cooling and melted at 75–76°. There was no depression on mixed m. p. with either of the samples prepared as described above.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.05; H, 9.54.

3-Anisyl-4-bromohexane.—To a solution of 21 g. of anisyl-3-hexanol-4 in 100 cc. of dry benzene at 10° was added 10 g. of hydrogen bromide. The solution was allowed to warm up to room temperature overnight and was then refluxed for five minutes. After washing with two 25-cc. portions of sulfuric acid, followed by sodium carbonate solution and water, the benzene was distilled and the residue fractionated. The product, 19 g. (70%), was a colorless oil, b. p. 90–95° at 0.1 mm.

Anal. Calcd. for $C_{18}H_{21}OBr$: C, 57.57; H, 7.06. Found: C, 57.77; H, 7.13.

2-Ethyl-3-anisylvaleric Acid.—The Grignard reagent prepared by the entrainment procedure from 13 g. of 3-anisyl-4-bromohexane, 7 g. of ethyl iodide and 2.5 g. of magnesium was carbonated by pouring onto Dry Ice. After decomposition of the addition compound with dilute sulfuric acid the ethereal layer was extracted with 10% sodium hydroxide solution until free of acidic material. Acidification of the alkaline extracts gave an oil which crystallized on standing overnight in the icebox. After 3 recrystallizations from dilute ethanol and 2 from petroleum ether the acid, 1.5 g. (12%) melted at 133.5–134.5°.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.21; H, 8.51.

Concentration and fractionation of the neutral ether solution gave 5 g. (52%) 3-anisylhexane, b. p. 78–80° at 0.5 mm.

Anal. Calcd. for $C_{13}H_{20}O$: C, 81.19; H, 10.48. Found: C, 81.46; H, 10.00.

Three grams of a fraction b. p. 155–160° at 0.2 mm. was also obtained. The material analyzed for the dimer of 3-anisylhexane.

Anal. Calcd. for $(C_{13}H_{20}O)_2$: C, 81.63; H, 10.01. Found: C, 81.06; H, 9.76.

Ethylmethoxymethylanisylcarbinol.—The reaction between 103 g. of *p*- α -dimethoxyacetophenone¹⁸ and the Grignard reagent from 15 g. of magnesium and 110 g. of ethyl iodide gave 96 g. (77%) of carbinol, b. p. 112–113° at 0.5 mm.

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 69.07; H, 8.53.

α -Anisylbutanal.—A mixture of 80 g. of ethylmethoxymethylanisylcarbinol and 15 g. of fused potassium bisulfate was heated at 150–170° for one hour, the low boiling reaction products being allowed to distill off during the heating. Fractionation of the residue gave 55 g. (82%) of product, b. p. 95–105° at 0.7 mm.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.14; H, 8.03.

Summary

Potassium hydroxide in ethanol at 200–220° reduces anisyl-3-hexanone-4 to the corresponding carbinol and its demethylation product.

(13) Pratt and Robinson, *J. Chem. Soc.*, 123, 748 (1923).

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF WINTHROP CHEMICAL COMPANY, INC.]

Diaryloxyalkane Derivatives. Diphenoxyethanesulfonamides^{1a}

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In view of the high trypanocidal activity observed^{1b} in 4,4'-diamidinostilbene, 4,4'-diamidino- α,γ -diphenoxypropane and 4,4'-diamidino- α,ϵ -diphenoxypentane, which were prepared by Ashley, Barber, Ewins, Newberry and Self,² it seemed desirable to prepare some substances of a similar nature but in which the amidino group was replaced by some other polar functional group. The present paper reports the prepara-

(1a) Presented before the Division of Organic Chemistry at the American Chemical Society meeting in New York, September 14, 1944.

(1b) Laurie and Yorke, *Ann. Trop. Med.*, 33, 289 (1939).

(2) Ashley, Barber, Ewins, Newberry and Self, *J. Chem. Soc.*, 103 (1942).

tion of a series of α,β -diphenoxyethane-4,4'-disulfonamide derivatives, together with some other closely related substances.

α,β -Diphenoxyethane (I) was found by Huntress and Carten³ to be converted by chlorosulfonic acid to a disulfonyl chloride (II) (not isolated), from which they prepared the corresponding disulfonamide. It has been found that this disulfonyl chloride can be easily isolated and obtained pure in as high as 97% yield. By reaction of this disulfonyl chloride with the appropriate amines the disulfonamides listed in Table I were prepared.

Because of the low water-solubility of most of

(3) Huntress and Carten, *THIS JOURNAL*, 62, 603 (1940).