The diethyl acetals of methyl-*n*-hexyl and phenylpropyl ketones were prepared and analyzed for the first time.

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ALKYL AMINO-ETHANOL AND PROPANOLS[1]

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RECEIVED OCTOBER 24, 1927 PUBLISHED JANUARY 5, 1928

Many naturally occurring compounds of therapeutic importance contain the grouping alkyl-N-C-C-O or alkyl-N-C-C-C-O. Among these compounds are cocaine, quinine, strychnine, hydrastine, hyoscine, atropine and adrenaline. Also, many synthetic medicinals, as procaine, stovaine, alypine, apothesin, butyn and homatropine contain one of these groups.

Since the linkages referred to above are prevalent in so many compounds of marked physiological action, a good method for the preparation of simple substances containing these groupings should be of considerable value in the synthesis of more complex compounds, as those mentioned above. A large number of alkyl amino-ethanols have been prepared by Matthes[2] by the action of ethylene oxide on the monoalkyl amines, but there was usually obtained as by-product the corresponding alkyl dihydroxyethylamine. The latter compounds were difficult to separate from the desired product. A similar method was used by Knorr and Matthes[3] and Knorr and Schmidt.[4] Knorr[5] also condensed aqueous methylamine with ethylene chlorohydrin to form methylamino-ethanol.

This paper deals with the preparation of alkyl amino-ethanol and alkyl aminopropanols by the method used by Otto[6] and Adams and Segur[7] for aryl amino-ethanols and Pierce with Adams[8] for aryl-aminopropanols. By this method there are no by-products of tertiary amines and in most cases the yield of pure product is fair.

Discussion of Results

The condensation of the alkyl amines with β-chloro-ethylchloroformate and with γ-chloropropylchloroformate took place readily, as was the case

[1] The author wishes to express his thanks to Professor Roger Adams, of the University of Illinois, for his valuable suggestions at the outset of this work. Also, acknowledgment is made to the Chemical Department of the University of South Dakota, at which place part of this work was done.

[2] Matthes, *Ann.*, **315**, 104 (1901).

[3] Knorr and Matthes, *Ber.*, **31**, 1069 (1898).

[4] Knorr and Schmidt, *Ber.*, **31**, 1073 (1898).

[5] Knorr, *Ber.*, **22**, 2088 (1889).

[6] Otto, *J. prakt. Chem.*, [2] **44**, 15 (1890).

[7] Adams and Segur, THIS JOURNAL, **45**, 785 (1923).

[8] Pierce with Adams, *ibid.*, **45**, 790 (1923).

of the aryl amines.[7,8] The reaction of β-chloro-ethylallyl carbamate and γ-chloropropylalkyl carbamates with alcoholic potash was much more vigorous than that of the corresponding aromatic compounds. The addition of alcoholic potash to each of the carbamates mentioned in this paper caused the precipitation of potassium chloride and potassium carbonate, indicating the splitting out of hydrochloric acid and carbon dioxide. In all cases the reaction took place without the application of heat and with β-chloro-ethylallyl carbamate the reaction took place almost spontaneously, the heat given off being sufficient to boil the alcohol within a few seconds after the carbamate and potash were mixed.

3-Allyl-2-oxazolidone was obtained by refluxing an alcoholic solution of β-chloro-ethylallyl carbamate with 1.75 moles of potassium hydroxide and vacuum distilling the product. Attempts were made to prepare pure 3-alkyl tetrahydro-1,3,2-oxazones by ring closure of the γ-chloropropyl alkyl carbamates with alcoholic potash and vacuum distilling the products, but constant-boiling products were not obtained.

When the alkyl carbamates mentioned above were refluxed in alcohol solution with 4 moles of potassium hydroxide, no oxazolidone nor oxazones but amino alcohols were isolated. This indicates that, as in the aromatic series,[7,8] these ring nitrogen compounds are decomposed by excess of alcoholic potash. β-Chloro-ethylallyl carbamate yielded β-allylamino-ethanol and the γ-chloropropyl alkyl carbamates yielded the corresponding γ-alkyl amino-propanols.

Experimental Part

β-Chloro-ethyl and γ-Chloropropyl Alkyl Carbamates.—These compounds were prepared by the method described by Pierce with Adams[8] for the preparation of γ-chloropropyl aryl carbamates, sodium carbonate being used as a condensing agent, and the reaction mixtures being kept cool by the addition of ice. As these carbamates are much more soluble in water than the aryl carbamates, the aqueous layers were extracted with ether. The crude carbamates, which were obtained in yields of 84–92%, were purified by vacuum distillation. The yield of pure product was usually about 85% of the crude product. However, for the preparation of the oxazolidone, oxazones and amino alcohols, usually the crude products were used.

All of the carbamates prepared were soluble in alcohol, ether, ethyl acetate, chloroform, carbon disulfide and benzene. In water, β-chloro-ethylallyl carbamate and γ-chloropropylmethyl carbamate were slightly soluble, and the solubility decreased with increase in molecular weight until γ-chloropropylamyl carbamate was practically insoluble.

3-Allyl-2-oxazolidone.—3-Allyl-2-oxazolidone was prepared by refluxing for two hours β-chloro-ethylallyl carbamate, in 2–3 volumes of alcohol, with 1.75 moles of potassium hydroxide. The reaction mixture was cooled, the alcoholic solution decanted from the inorganic residue, the residue extracted with alcohol and the combined alcoholic extract evaporated on a hot-plate at a temperature of 125°. The solution was cooled, filtered into a Ladenburg flask and fractionated *in vacuo*. A very poor yield of pure product was obtained as three fractionations were necessary to separate the ring compound from the amino alcohol and unchanged carbamate present.

The pure product was soluble in water, alcohol, ether, benzene, chloroform, acetone and ethyl acetate, and slightly soluble in carbon disulfide and petroleum ether.

Alkyl Tetrahydro-1,3,2-oxazones.—Several attempts were made to purify by fractional distillation the crude products obtained by refluxing the γ-chloropropyl alkyl carbamates with about 1.5 moles of potassium hydroxide in alcohol. Constant-boiling products were never obtained but the products formed usually had a boiling point, at the pressure used, about 15° above that of the corresponding carbamate. Usually the products had about 0.7% less nitrogen than the pure oxazone would have and they contained a trace of chlorine, indicating the presence of some unchanged carbamate. As it has been shown definitely, in the aromatic series, that 3-aryl tetrahydro-1,3,2-oxazones are intermediates[8] in the preparation of arylaminopropanols, from the corresponding γ-chloropropyl aryl carbamates, the high-boiling products referred to above are doubtless 3-alkyl tetrahydro-1,3,2-oxazones.

β-Allylamino-ethanol and γ-Alkyl Aminopropanols.—Allylamino-ethanol and the alkyl aminopropanols were prepared as were the corresponding aryl amino-ethanols[7] and propanols.[8] However, due to the greater solubilities of the alkyl compounds, the method of isolation and purification was modified somewhat.

Two methods were used for the isolation of allylamino-ethanol and the alkyl aminopropanols. In one method potassium carbonate was added in considerable excess to the alcoholic solution of the amino alcohol and, after the mixture had stood for two hours, the solution was filtered, the alcohol evaporated and the residual liquid vacuum distilled. The other method consisted of steam distilling the reaction mixture, acidifying the distillate, evaporating to low volume, neutralizing the acid with sodium hydroxide, salting out the amino alcohol with potassium carbonate and vacuum distilling the prod-

TABLE I

COMPOUNDS PREPARED, YIELDS, CONSTANTS AND ANALYSES

Compound	Formula	Yield, % crude	B. p.	d_4^{20}	Index of ref.	Analysis Wt., g.	Analysis N_2, cc.	Analysis % Calcd.,	Analysis % Found,
β-Chloro-ethyl allyl carbamate	$C_6H_{10}O_2NCl$	92	103.5–104.5° (1.3 mm.)	1.1811	N_D^{27} 1.4668	0.2018	16.2, 29°, 740 mm.	8.6	8.5
γ-Chloropropyl allyl carbamate	$C_7H_{12}O_2NCl$	91	110–111° (1 mm.)	1.1390	N_D^{26} 1.4681	.1762	13.2, 26°, 738 mm.	7.9	8.0
γ-Chloropropyl methyl carbamate	$C_5H_{10}O_2NCl$	84	104.5–106° (1 mm.)	1.1821	N_D^{27} 1.4548	.1886	16.7, 28°, 742 mm.	9.2	9.4
γ-Chloropropyl *n*-amyl carbamate	$C_9H_{18}O_2NCl$	88	135–137° (2 mm.)	1.0629	N_D^{21} 1.4560	.2070	13.2, 27°, 735 mm.	6.7	6.8
		(Purified)							
3-Allyl-2-oxazolidone	$C_6H_9O_2N$	21	123–125° (0.7 mm.)	1.113	N_D^{27} 1.4691	.1335	14.1, 30°, 738 mm.	11.0	11.1
β-Allylamino ethanol	$C_5H_{11}ON$	48	77–80° (1.5 mm.)	0.9398	N_D^{27} 1.4602	.1584	20.5, 24°, 736 mm.	13.9	14.0
γ-Allylamino propanol	$C_6H_{13}ON$	48	88–90° (0.8 mm.)	.9319	N_D^{27} 1.4629	.1280	14.6, 23°, 738 mm.	12.2	12.4
γ-Methylamino propanol	$C_4H_{11}ON$	31	74–77° (2.5 mm.)	.9315	N_D^{27} 1.4418	.1308	19.1, 22°, 731 mm.	15.7	15.8
γ-*n*-Amylamino propanol	$C_8H_{19}ON$	47	103–105° (1.8 mm.)	.8858	N_D^{21} 1.4493	.1628	14.8, 30°, 739 mm.	9.6	9.5

uct. The latter method worked very well with γ-allylaminopropanol and γ-amylaminopropanol but was not very good for γ-methylaminopropanol and β-allylamino-ethanol, due to their great solubility in water. In all cases better yields would be obtained by working with larger amounts.

All of the amino alcohols were colorless liquids when freshly prepared but darkened on standing. All had a characteristic odor. All were soluble in water, alcohol, ether, chloroform, ethyl acetate and acetone. The solubility in water decreased with increase in molecular weight, for, although all dissolved readily, amylaminopropanol was salted out readily with potassium carbonate, allylaminopropanol was salted out a little less readily and methylaminopropanol and allylamino-ethanol could scarcely be salted out. In carbon disulfide and petroleum ether amylaminopropanol was readily soluble, while the lower molecular weight amino alcohols went into solution with difficulty.

Summary

1. Allylamine was condensed with β-chloro-ethylchloroformate to yield β-chloro-ethylallyl carbamate. The latter compound, refluxed with 1.5 moles of alcoholic potash, yielded 3-allyl-2-oxazolidone, and with 4 moles of alcoholic potash, yielded β-allylamino-ethanol.

2. Allyl-, methyl-, and *n*-amylamines condensed with γ-chloropropylchloroformate to yield the corresponding γ-chloropropyl alkyl carbamates. These carbamates, refluxed with 4 moles of alcoholic potash, yielded the corresponding γ-alkyl aminopropanols.

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[CONTRIBUTION FROM THE GATES CHEMICAL LABORATORY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 156]

THE PREPARATION OF 2-BROMO-*p*-CRESOL FROM *p*-NITROTOLUENE

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RECEIVED OCTOBER 26, 1927 PUBLISHED JANUARY 5, 1928

The usefulness of 2-bromo-*p*-cresol in standardizing bromide-bromate solutions[1] makes desirable a convenient method of preparation. It has been obtained from 2-amino-*p*-cresol through the diazo reaction[2] and its use as a dye intermediate has been suggested.[3]

In this work it has been found that the desired compound may be conveniently obtained in satisfactory yield from *p*-nitrotoluene by the following operations.

[1] Buxton and Lucas, THIS JOURNAL, **50**, 249 (1928).

[2] Plummer, Melamed and Puttfarchen, *Ber.*, **55B**, 3116 (1922).

[3] D. R. P. 156,333; *Chem. Cent.*, 1904, II, 1673.