took place until the animal became limp and coma ensued. Corneal reflux disappeared and the pupils were dilated before death, a condition obviously due to gradual asphyxia. The left ventricle was contracted, the blood was dark and of asphyxial hue. Marked depression was evident which did not appear with the oxazolidone.

Since the slight drop in temperature with small doses of oxazolidone or phenacetin might have been due to temperature depression with consequent inhibition of muscular tone, a study of the effect of the drugs on the temperature of rabbits artificially rendered febrile was undertaken. For the experimental fever, sterile horse serum was injected intravenously in the ear vein, (7.5 cc. per kg.). The dosage of drugs used was 1 g. per kg. From a comparison of several animals, the following conclusions were drawn: (1) both oxazolidone and phenacetin produced sharp drops in the fever temperature; (2) they both brought the temperature back to normal; (3) instead of holding the temperature at normal, both drugs eventually forced the temperature below the normal for 2 to 3 hours; (4) ultimately, there was not the rise above the normal which appeared in the untreated animals and fever controls at the end of the experiments. The results showed practically the same effect with both drugs except that the oxazolidone forced the temperature somewhat lower.

Summary

1. Details for a satisfactory method of formation of arylamino ethanols have been developed. The procedure consists in the condensation of an aryl amine with chloro-ethyl chloroformate, then decomposition of the resulting ester with excess of potassium or sodium hydroxide.

2. Oxazolidones can be isolated as intermediate products in the second step.

3. The 3-*p*-ethoxyphenyl-2-oxazolidone was compared with phenacetin as regards its antipyretic and analgesic properties. It was found that the new product had properties very similar to those of phenacetin.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

TETRAHYDRO-1,3,2-OXAZONES AND SUBSTITUTED GAMMA-AMINO PROPANOLS

BY J. S. PIERCE WITH ROGER ADAMS[1]

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In the preceding paper[2] it has been pointed out that the amino ethanol and amino propanol groupings occur very frequently in many of the most important alkaloids. Although the amino ethanols have been studied and used frequently in synthetic work, the γ-amino propanols have seldom been used and are less well-known. This has been due to the fact that until recently, the raw materials necessary for making these substances according to the methods applicable to the formation of amino ethanols

[1] This paper is an abstract of Part I of the material contained in a thesis by J. S. Pierce presented in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

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

were difficult to obtain and very expensive. Trimethylene-chlorohydrin has become cheap and can now be used in large amounts. It can be converted into tertiary amino propanols, $R_2NCH_2CH_2CH_2OH$, by the action of secondary amines.

When trimethylene-chlorohydrin is condensed with a primary amine, however, the reaction does not run so smoothly and a mixture always results from which the yield of pure seondary amino propanol, $RNHCH_2CH_2CH_2OH$, is always low. It has been pointed out[2] that secondary amino ethanols may be formed by the action of primary amines upon β-chloroethyl chloroformate, and subsequent treatment with sodium or potassium hydroxide. The same series of reactions may be carried out using γ-chloropropyl chloroformate, under which conditions γ-chloropropyl carbamates are the initial products, tetrahydro-1,3,2-oxazones the secondary products, and γ-amino propanols the final products.

$$RNH_2 + ClCO_2CH_2CH_2CH_2Cl \longrightarrow RNHCO_2CH_2CH_2CH_2Cl + HCl$$

$$RNHCO_2CH_2CH_2CH_2Cl + KOH \longrightarrow RNCO_2CH_2CH_2CH_2 + KCl$$

$$RNCO_2CH_2CH_2CH_2 + 2KOH \longrightarrow RNHCH_2CH_2CH_2OH + K_2CO_3$$

The reactions proceed in every case similarly to those described in the previous paper.

The γ-chloropropyl carbamates are conveniently formed in aqueous suspension and for purification are distilled under diminished pressure. They are colorless oils which solidify upon cooling to form low-melting solids. The yields are always over 80%.

The tetrahydro-1,3,2-oxazones are formed by refluxing the γ-chloropropyl carbamates with 1 mol. of sodium or potassium hydroxide in alcoholic solution and are obtained in excellent yields. The products are, in general, stable solids, readily purified by crystallization from the common solvents.

The substituted γ-amino propanols are formed in nearly quantitative yields by treating the tetrahydro-1,3,2-oxazones or the γ-chloropropyl carbamates with 4 mol. of potassium or sodium hydroxide in alcohol solution. The products are high-boiling oils, colorless when pure but in general obtained as pale yellow. Upon standing the substances gradually decompose into thick, dark-colored viscous liquids.

This general procedure for preparing γ-arylamino propanols has been applied to γ-alkylamino propanols. The details for the production of the alkyl compounds are somewhat different from the details for the aryl compounds and will be published in a later communication.

Experimental Part

γ-Chloropropyl Chloroformate, $ClCO_2CH_2CH_2CH_2Cl$.—This product is readily obtained in yields of over 80% by cooling trimethylene-chlorohydrin with ice and salt and passing in phosgene slowly until 1 mol. has been added. The reaction mixture

is allowed to stand for some time and is then washed with water and dil. sodium carbonate solution. It is then distilled; b. p., 177°; d_{20}^{25}, 1.2946; n_{D}^{20}, 1.4456.

Analysis. Subs., 0.2212: AgCl, 0.4005. Calc. for $C_4H_6O_2Cl$: Cl, 45.10. Found: 44.90.

There is always obtained at the same time a small amount of high boiling material which boils at 265–270° (740 mm.). This is undoubtedly the γ,γ-dichloropropyl carbonate.

γ-Chloropropyl Aryl Carbamates

Slightly more than 2 mol. of primary aromatic amine is suspended in 150 cc. of water. To this mixture 1 mol. of γ-chloropropyl chloroformate is added in small portions over about 15 minutes while the mixture is stirred with a mechanical stirrer and shaken frequently. If, during the addition, amine hydrochloride separates, more water is added in order to keep it completely in solution. The reaction mixture is now mechanically stirred for 1 to 2 hours, or allowed to stand for about 12 hours without stirring. The oily layer, which consists chiefly of γ-chloropropyl aryl carbamate, is separated from the aqueous solution of amine hydrochloride and shaken with 4 portions of 1:3 hydrochloric acid and finally with water. In cases where the carbamates are solid at room temperature, they can be kept in the liquid state by using hot water for washing; if rather high melting, the products may be filtered directly from the reaction mixture. The yield of crude ester is usually about 90%. Most of the esters may be purified by distilling under diminished pressure, preferably at 5 mm. or less.

If the aryl amines which are being used are expensive or if they form hydrochlorides sparingly soluble in water, the reaction may be run satisfactorily by using a suspension of 1 mol. of amine in an aqueous solution containing sufficient sodium carbonate to neutralize the hydrochloric acid formed during the reaction. The yields under these conditions are just as satisfactory as when excess of amine is used.

In the case of the condensation of *p*-aminobenzoic acid and γ-chloropropyl chloroformate, the *p*-aminobenzoic acid was merely dissolved in 1 mol. of aqueous alkali and this solution treated directly.

Tetrahydro-1,3,2-oxazones

γ-Chloropropyl aryl carbamate is dissolved in about 5 times its weight of alcohol which containes 1 mol. of caustic potash. This solution is heated for 2 hours on a steam cone, after which it is cooled and the potassium chloride removed with the aid of suction. The solid potassium chloride is best washed with a little alcohol to remove traces of oxazone that may be held by the inorganic salt. The combined filtrates are evaporated until no solvent remains. There is always contained in this residue a small amount of unchanged γ-chloropropyl carbamate which may be removed by treating the residue with a small amount of ether. The impurity of unchanged material is soluble and the oxazone remains undissolved. It is purified directly by crystallization from hot water, when very small amounts of amino alcohol which are also present as impurities are removed. The yields of product are in general 50–65% of recrystallized material and considerably higher of crude material.

It is possible to carry out this reaction in aqueous suspension, but the reaction takes place much more slowly and the yields are not so satisfactory as those given above.

In the case of the *p*-carboxy compound, aqueous alkali is satisfactory, since the presence of the carboxyl group in the γ-chloropropyl-*p*-carboxycarbanilate renders it soluble and gives a homogenous reaction mixture. The yield of product is not so good as in the other cases. Alcoholic solution is not satisfactory since the salt of the acid is insoluble and thus gives poor results.

TABLE I

γ-CHLOROPROPYL CARBANILATES

Name	Formula	Form	M. p. °C.	B. p. °C.	Press Mm. of Hg.	$d_{20°}^{20°}$	Index of refraction	Analysis: Wt. G.	Analysis: Obt. or req.	Analysis: Calc. %	Analysis: Found %
	$C_{10}H_{12}O_2NCl$	wh. need. fr. ether and lig.	35–36	190	3.5	...	...	0.6032	25.93 cc. of 0.1115 *N* H_2SO_4	N,	6.6	6.8
o-Methyl-	$C_{11}H_{14}O_2NCl$	wh. need. fr. ether and lig.	46–46.5	182.5	4.5	...	...	0.5442	22.87 cc. of 0.1025 *N* H_2SO_4	N,	6.2	6.1
p-Methyl	$C_{11}H_{14}O_2NCl$	straw-col. oil	.....	188	4.5	1.186	$n_D^{18°}$ 1.494	0.4707	20.68 cc. of 0.09932 *N* $AgNO_3$	Cl,	15.57	15.47
o-Chloro-	$C_{10}H_{11}O_2NCl_2$	straw-col. oil	.....	178.5	3.5	1.310	$n_D^{20°}$ 1.546	0.3413	27.71 cc. of 0.09932 *N* $AgNO_3$	Cl,	28.58	28.59
p-Chloro-	$C_{10}H_{11}O_2NCl_2$	wh. need. fr. ether and lig.	53–53.5	193	3.5	...	...	0.5064	20.25 cc. of 0.1025 *N* H_2SO_4	N,	5.7	5.8
p-Ethoxy-	$C_{12}H_{16}O_3NCl$	wh. need. fr. ether and lig.	63–63.5	198.5	4	...	...	0.3667	14.38 cc. of 0.1025 *N* H_2SO_4	N,	5.5	5.7
p-Carboxy-	$C_{11}H_{12}O_4NCl$	wh. cryst. fr. ether and lig. or hot water	191–192.5	...	...	...	...	0.3329	13.27 cc. of 0.1025 *N* H_2SO_4	N,	5.5	5.8
α-Naphthyl-carbamate	$C_{14}H_{14}O_2NCl$	wh. need. fr. ether and lig.	75.5–76.5	206.5	4	...	...	0.2939	9.50 cc. of 0.1115 *N* H_2SO_4	N,	5.4	5.1

TABLE II

TETRAHYDRO-1,3,2-OXAZONES

Name	Formula	Form from hot water	M. p. °C.	Analysis [Wt. G.]	Obt. or req.		Calc. %	Found %
3-Phenyl-1,3,2-	$C_{10}H_{11}O_2N$	wh. plates	94–94.5	0.3588	21.10 cc. of 0.09546 *N* H_2SO_4	N,	7.9	7.9
3-*o*-Tolyl-	$C_{11}H_{13}O_2N$	wh. prisms	87–87.5	0.5444	25.50 cc. of 0.1115 *N* H_2SO_4	N,	7.4	7.4
3-*p*-Tolyl-	$C_{11}H_{13}O_2N$	wh. needles	127.5–128	0.2705	14.05 cc. of 0.1025 *N* H_2SO_4	N,	7.4	7.5
3-*o*-Chlorophenyl-	$C_{10}H_{10}O_2NCl$	wh. cubes	99	0.4166	18.38 cc. of 0.1061 *N* $AgNO_3$	Cl,	16.7	16.6
3-*p*-Chlorophenyl-	$C_{10}H_{10}O_2NCl$	wh. plates	111.5–112	0.2670	13.37 cc. of 0.09546 *N* H_2SO_4	N,	6.7	6.7
3-*p*-Ethoxyphenyl-	$C_{12}H_{15}O_3N$	wh. plates	112.5–113	0.3987	17.71 cc. of 0.1025 *N* H_2SO_4	N,	6.4	6.4
3-*p*-Carboxyphenyl-	$C_{11}H_{11}O_4N$	wh. plates	231–232	0.2248	8.35 cc. of 0.1115 *N* H_2SO_4	N,	6.4	6.0
3-*α*-Naphthyl-	$C_{14}H_{13}O_2N$	wh. needles	149.5–150.5	0.4165	15.95 cc. of 0.1115 *N* H_2SO_4	N,	6.2	6.0

γ-Arylamino Propanols

γ-Chloropropyl aryl carbamates are treated with 4 mol. of caustic potash dissolved in an amount of ethyl alcohol equivalent to 5 times the weight of the carbonate. The mixture is heated on a steam-bath for 2 hours, cooled and filtered from inorganic salts. The alcoholic filtrates are evaporated and the residue treated with dil. hydrochloric acid. In this way traces of γ-chloropropyl aryl carbamates are removed, since they are insoluble in the acid, and may be extracted with ether. The acid solution is made alkaline with strong caustic soda and the oily layer of γ-ethylamino-propanol extracted with ether. Upon evaporation and fractionation, yields of amino alcohol ranging from 80% to nearly quantitative are obtained. The products may be purified by fractionation under diminished pressure at 15 mm. but preferably at 4 mm. The substances all have a tendency to decompose on standing, forming thick, dark colored oils.

TABLE III

ANILINO-PROPANOLS

Name	Formula	Form	B. p. °C	$d_{20°}^{20°}$	Index of refraction	Analysis Wt. G.	Product	N Calc. %	N Found %
γ-	$C_9H_{13}ON$	straw-col. oil	180.5 (20.5 mm.) 154 (5 mm.)	1.073	$n_D^{18°}$ 1.568	0.5603	38.24 cc. of 0.09546 *N* H_2SO_4	9.3	9.2
γ-*o*-Methyl-	$C_{10}H_{15}ON$	straw-col. oil	164 (3 mm.)	1.055	$n_D^{20°}$ 1.560	0.5612	34.79 cc. of 0.09546 *N* H_2SO_4	8.5	8.3
γ-*p*-Methyl-	$C_{11}H_{15}ON$	straw-col. oil	163.5 (3.5 mm.)	1.045	$n_D^{20°}$ 1.558	0.4730	30.03 cc. of 0.09546 *N* H_2SO_4	8.5	8.5

γ-*o*-Chloro-	$C_9H_{12}ONCl$	straw-col. oil	151.5 (3.5 mm.)	1.200	$n_D^{20°}$ 1.574	0.6038	28.73 cc. of 0.1115 *N* H_2SO_4	7.6	7.5
γ-*p*-Chloro-	$C_9H_{12}ONCl$	straw-col. oil	167 (3.5 mm.)	1.205	$n_D^{19°}$ 1.580	0.5849	27.14 cc. of 0.1115 *N* H_2SO_4	7.6	7.3
γ-*p*-Ethoxy-	$C_{10}H_{13}O_2N$	straw-col. oil and wh. plates from ether and lig.	M. p., 42–42.5 B. p., 177 (3.5 mm.)	...	...	0.4964	23.24 cc. of 0.1115 *N* H_2SO_4	7.2	7.4
γ-*p*-Carboxy-	$C_{11}H_{13}O_3N$	wh. needles from hot water	M.p., 151–152	...	...	0.4825	22.73 cc. of 0.1115 *N* H_2SO_4	7.2	7.4
γ,α-Naphthyl-amino-propanol	$C_{13}H_{15}ON$	yellowish oil	B. p., 201.5 (3.5 mm.)	1.137	...	0.4978	19.70 cc. of 0.1115 *N* H_2SO_4	7.0	6.2

In the case of the γ-*p*-carboxyanilino-propanol, the product remains dissolved in the excess alkali and is obtained by careful acidification with hydrochloric acid.

Summary

1. γ-Chloropropyl aryl carbamates were formed from aromatic amines and γ-chloropropyl chloroformate.

2. γ-Chloropropyl aryl carbamates and potassium hydroxide in alcohol solution are converted into tetrahydro-1,3,2-oxazones when 1 mol. of alkali is used, into γ-arylamino propanols when 4 mol. of alkali are used.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NOTRE DAME UNIVERSITY]

THE PREPARATION OF OXALIC ACID FROM ACETYLENE

BY M. LUCRETIA KEARNS, L. HEISER AND J. A. NIEUWLAND

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In 1919, it was found by the authors that oxalic acid could be prepared on a practical scale, in almost pure condition, from acetylene and nitric acid, with mercuric nitrate as a catalyst. It was desired to discover, if possible, the course of the reaction which afforded the oxalic acid, and the role played by the mercuric nitrate in the reaction. Not much work has been published on the reactions of acetylene with nitric acid or with mercuric nitrate.

Baschieri[1] used fuming nitric acid with acetylene, and obtained nitroform and carbon dioxide, together with a mixture of acids, crystallizing in part from benzene in pale yellow needles, and two neutral substances: (1) a small quantity of a yellow oil, and (2) a solid, $C_6H_4O_8N_4$, separating from ether, alcohol, light petroleum or water in yellowish-white needles. When strongly heated, this latter substance gave hydrocyanic acid.

Giuseppe Testoni and L. Mascarelli[2] repeated Baschieri's experiment with some modifications, and found in addition to Baschieri's nitroform and neutral substances: (1) a straw-yellow "explosive substance," which when crystallized from benzene or

[1] Baschieri, *Atti. accad. Lincei*, **9**, 391 (1900).

[2] Testoni and Mascarelli, *ibid.*, **10**, 442 (1901).