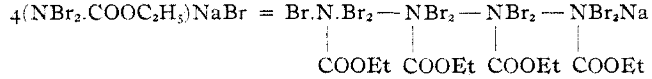
by Hantzsch,[1] and he obtained the dibromoderivative, four molecules of which are united chemically with a molecule of sodium bromide to form ethylic dibromoamidocarboxylate sodium bromide, $4NBr_2COOC_2H_5$, NaBr, as a yellow granular powder the sodium bromide of which is firmly in union and cannot be removed by washing with water. It is most likely that the constitution of this body is quite different from what has been assigned to it by Hantzsch. In all probability it has a complicated formula, as can be inferred from the unstable nature of the monochlorocarbamic ester as also from the less energy of bromine for reactions of this kind. It might be a condensed compound having the formula given below:



$$4(\mathrm{NBr_2.COOC_2H_5})\mathrm{NaBr} = \begin{array}{cccc} \mathrm{Br.N.Br_2} — & \mathrm{NBr_2} — & \mathrm{NBr_2} — & \mathrm{NBr_2Na} \\ | & | & | & | \\ \mathrm{COOEt} & \mathrm{COOEt} & \mathrm{COOEt} & \mathrm{COOEt} \end{array}$$

The formation of such a compound may be explained thus: Bromine acting on urethane in conjunction with soda forms NaBrNCOOEt, analogous to the formation of potassium acetobromoamide by the action of bromine and caustic potash on acetamide. Now this further adds two atoms of bromine to form $NBr_3NaCOOEt$, making the nitrogen pentavalent. Four molecules of this condense, with the elimination of sodium bromide, to form the above compound.

$$4NBr_3NaCOOEt = 3NaBr + 4NBr_2COOEt, NaBr.$$

We are at present engaged in preparing the chloroderivatives of other esters of chlorocarbamic acid and also of alkyl and acyl substituted carbamic esters.

We take this opportunity of expressing our best thanks to Prof. P. C. Ray for the interest he has taken in the above investigation.

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ACYL DERIVATIVES OF o-AMINOPHENOL.

BY J. H. RANSOM AND R. E. NELSON.

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In an extended piece of work published some years ago the senior author[2] found that when *o*-nitrophenylethylcarbonate is reduced with tin and hydrochloric acid a urethane is obtained soluble in bases and evidently having the carbethoxy radical attached to nitrogen. By modifying the conditions, a basic substance was isolated in which the carbethoxy radical is attached to oxygen. On standing, this rapidly changes to the urethane. The same urethane was obtained from *o*-aminophenol and chlorocarbonic-ethylether in ether solution. A similar rearrangement

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[1] *Ber.*, **27**, 1248 (1894).

[2] *Am. Chem. J.*, **23**, 1.

occurs when *o*-nitrophenylbenzoate is reduced in acid solution. In determining the constitution of the urethane, Ransom made the diacyl derivative, using benzoyl chloride in alkaline solution. He found that the same diacyl derivative is produced when benzoyl *o*-aminophenol is treated with chlorocarbonic-ethylether. In both cases saponification gives benzoic acid and hydroxyphenylurethane, indicating that in the latter case a molecular rearrangement has occurred, so as to leave the lighter acyl group attached to nitrogen. Other diacyl derivatives were made and in every case the lighter acyl group was found attached to nitrogen. But if one of the amine hydrogen atoms is first replaced by a hydrocarbon radical no rearrangement occurs, isomeric substances being formed when the acyl radicals are introduced in reverse order. The same is true when the amine and hydroxyl groups are in the meta or para position to each other.

It seemed desirable to determine if a carboxylester group would become attached to nitrogen in place of a lighter carbonyl group already there; also, if of two carboxylester groups introduced the lighter one would go to the nitrogen. Finally it seemed of interest to determine if rearrangement would occur in case the radicals introduced were of nearly the same weight. If the rearrangement did not occur, or proceeded more slowly, it was thought there would be a better chance of studying the mechanism of the rearrangement.

Hydroxyphenylisoamylurethane.—Two grams of *o*-aminophenol were suspended in ether and the calculated amount (2 mol.) of chlorocarbonic-isoamylether slowly added. The hydrochloride of one molecule of the *o*-aminophenol precipitated. After filtering, the ether solution was evaporated, leaving about two grams of a solid. It crystallized from boiling ligroin in white needles melting at 68.5–69.5°. The crystals are insoluble in cold water and dilute acids, but are sparingly soluble in hot water, and very soluble in chloroform, benzol, alcohol and ether. The compound is also quite soluble in dilute alkalies from which solution it is precipitated by acids, showing its acid character.

The same substance was also made by the reduction, with tin and hydrochloric acid, of *o*-nitro-isoamylcarbonate (made according to Ransom's method). The melting point was the same and a mixture of the two had the same melting point as either.

Another quantity of *o*-nitro-isoamylcarbonate was reduced, but as soon as the action was complete the product was thrown into a concentrated solution (1 : 1) of potassium hydroxide kept cold in a freezing mixture. This solution was quickly extracted with ether and the ether solution dried with potassium hydroxide. When dry, the ether was saturated with dry hydrochloric acid. A white precipitate separated which was filtered out and quickly dried on a porous plate in a desiccator. The melting point was 134° and the substance was quite soluble in cold water and acids;

but alkalies precipitated an oil from the solution. A small amount was dissolved in water and allowed to stand. Soon an oil separated which was extracted with ether and the ether evaporated. A solid remained which was soluble in alkalies and had all the properties of the urethane described above. Evidently the substance melting at 134° is the hydrochloride of *o*-aminophenyl-isoamylcarbonate which changes to the urethane on being warmed with water. In the dry condition it is quite stable.

Benzoylhydroxyphenylisoamylurethane.—1.5 grams of the hydroxyphenylisoamylurethane were dissolved in potassium hydroxide solution and to this was added 0.8 gram of benzoyl chloride. Slowly a brown oil separated which solidified with difficulty in the cold. After recrystallizing several times from dilute alcohol white needle-shaped crystals were obtained, melting at 65.5°. The substance is insoluble in water, dilute acids and alkalies; but soluble in ether, chloroform, benzol and alcohol. 0.2591 g. gave 10 cc. of nitrogen at 22.5° and 748 mm. pressure. This is equivalent to 4.39% of nitrogen. Calculated for $C_{19}H_{21}NO_4$ the nitrogen equals 4.28%. Saponification of the substance with alcoholic potash produced benzoic acid and the urethane melting at 68.5–69.5°. A mixture of the two had the same melting point.

Action of Chlorocarbonic-isoamylether on Benzoylaminophenol.—Benzoyl *o*-aminophenol was prepared by Ransom's method and 2 grams of it, in alkaline solution, were treated with 1.6 grams of chlorocarbonic-isoamylether. An oil separated which was extracted with ether and the ether evaporated. Recrystallized from dilute alcohol the substance formed white crystals melting at 65.5° and its mixture with the supposed isomer had the same melting point. Saponification, as above, gave the same substances. Evidently the benzoyl group, in this as in the former case, is attached to oxygen and must have shifted from its original attachment to nitrogen.

Action of Chlorocarbonic-isoamylether on Hydroxyphenylethylurethane.—The ethyl urethane was prepared as stated and 2 grams of it, in alkaline solution were treated with the calculated amount of chlorocarbonic-isoamylether. A light yellow oil separated which was extracted with ether. On evaporating the ether an oil was left which did not solidify until it was distilled *in vacuo*. After several recrystallizations of the distillate from alcohol the white crystals melted at 65–66°. On saponifying some of the impure material two substances were obtained. A small part melted at 133–134° and is probably carbonylaminophenol, produced from the urethane by loss of alcohol. The other part melted at 84–85° and on being mixed with hydroxyphenylurethane (m. p. 86–87°) the melting point was raised slightly.

Action of Chlorocarbonic Ethylether on Hydroxyphenylisoamylurethane.—1.4

grams of the isoamylurethane were treated, in alkaline solution, with 0.7 gram of chlorocarbonic ethyl ether. A heavy red oil separated which would not solidify until it was distilled *in vacuo* (185–200° at 15 mm. pressure). After several recrystallizations of the distillate the crystals became white and melted at 65–66°. They are insoluble in acids and alkalies, but quite soluble in alcohol, ether, chloroform and benzol. Mixed with the possible isomer, described above, the melting point was not depressed. Evidently in this case a molecular rearrangement occurs as expressed in the following equation:

$$KOC_6H_4NHCOOC_5H_{11} + ClCOOC_2H_5 \longrightarrow KCl + C_2H_5OOCOC_6H_4NHCOOC_5H_{11} \longrightarrow C_5H_{11}OOCOC_6H_4NHCOOC_2H_5.$$

The final product is carbamyl *o*-hydroxyphenylethylurethane.

Summary.—The work here outlined, together with that previously reported, shows that when two carboxyl radicals (COOR and $COOR_1$) are introduced into the molecule of *o*-aminophenol the lighter one becomes attached to nitrogen, the position not being influenced by the order in which the groups are introduced; and that to accomplish this, a molecular rearrangement occurs in one case. This is also true when both of the radicals are carbonyls (COR and COR_1). In case one radical is carbonyl and the other carboxyl the latter becomes attached to nitrogen without being influenced by the relative weights of the entering groups. The hope that the introduction of radicals of nearly the same weight (C_6H_5CO and $C_5H_{11}COO$) would result in the formation of isomeric substances was not realized, the velocity of the rearrangement being, apparently, almost instantaneous in every case. Consequently the mechanism of the rearrangement is still in doubt. It is possible that there is equilibrium of the two isomeric forms, one always being in too small amounts to be isolated, but there is little evidence to support this view. Work already begun with the orthoaminomercaptans may still throw light upon the problem.

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[CONTRIBUTIONS FROM THE CHEMICAL LABORATORY OF COLUMBIA UNIVERSITY AND THE HARRIMAN RESEARCH LABORATORIES. NO. 227.]

A STUDY OF THE CHEMICAL CONSTITUTION OF INVERTASE.

[FIRST PAPER.]

BY J. M. NELSON AND SIDNEY BORN.

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Since enzymes play such important roles in most chemical reactions occurring in plants and animals, any knowledge as to their true chemical constitution is of obvious importance. In a study of this kind it is desirable to select an enzyme which can be had in comparatively large amounts and can be easily purified. Such an enzyme is yeast invertase. Pressed