ACYL DERIVATIVES OF O-AMINOPHENOL.


In an extended piece of work published some years ago the senior author (Amer. Chem. Journ., 23, 1) found that when o-nitro phenylethylcarbonate was reduced with tin and hydrochloric acid a urethane was obtained, soluble in alkalis and evidently having the carbethoxy group attached to nitrogen. By modifying the conditions he was able to isolate an isomeric basic material in which the carbethoxy group was attached to oxygen. On standing this rapidly changed to the urethane. The same urethane was obtained on treating o-aminophenol, in ether solution, with chlorcarbonic ethylether. A similar rearrangement occurs when o-nitro phenylbenzoate is reduced in acid solution (Böttcher, Ann. Chem. Pharm., 210, 384). In determining the constitution of the oxyphenyl urethane Ransom made the diacyl derivative by using benzoyl chloride in alkaline solution. He also found that the same substance was produced when Böttcher’s benzoyl o-aminophenol was treated with chlorcarbonic ethylether in alkaline solution. In both cases saponification gave benzoic acid and oxyphenylurethane, indicating that in the latter case a molecular rearrangement of the diacyl derivative had occurred, so as to leave the lighter group attached to nitrogen. Other diacil derivatives of o-aminophenol were made and in every case the lighter group was found attached to the amide nitrogen. If one of the amide hydrogens is first replaced by a hydrocarbon radical no rearrangement occurs, but isomeric substances are formed when the acyl groups are introduced in reverse order. The same is true when the amide and hydroxyl groups are in the meta or para position to each other.

It seemed desirable to determine whether the carboxylester group would become attached to nitrogen in the presence of a carbonyl group already attached to the same nitrogen; also whether of two carboxyl 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 nearly of the same weight. If the rearrangement did not occur or proceeded more slowly than the others it was thought there would be a chance of studying more thoroughly the mechanism of the rearrangement.

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O-aminophenol was prepared by the reduction of the nitrophenol. Two grams of this were suspended in ether and the calculated amount (2 mol.) of chloroformic isoamylether slowly added. The hydrochloride of one molecule of the aminophenol precipitated. After filtering, the ether solution was evaporated, leaving about two grams of a solid. It crystallized from ligroin in white needles melting at 68.5°-69.5°. It is insoluble in cold water and acids, but is sparingly soluble in hot water and very soluble in chloroform, benzol, alcohol and ether. It is also quite soluble in dilute alkalis and from this solution is precipitated by acids thus showing its acid character.

The same substance was also produced by the reduction, with tin and acids, of o-nitrophenyl isoamylcarbonate made by Ransom's method (loc. cit.). The melting point was the same, and a mixture of the two had the same melting point as either.

Another sample of the nitroisoamylcarbonate was reduced, but as soon as the action was complete the product was thrown into a concentrated (1:1) solution of potassium hydroxide kept cold in a freezing mixture. This solution was quickly extracted with ether and the ether solution dried with solid potassium hydroxide. When dry the ether solution was saturated with dry hydrochloric acid gas. A voluminous white precipitate separated which was filtered out and quickly dried on a porous plate in a desiccator. The melting point was 133°-134° and the substance was quite soluble in cold water and acids, but alkalis precipitated an oil from the mixture. A small amount of this was dissolved in warm water and allowed to stand. Soon an oil separated which was extracted with ether. On evaporating the ether a solid remained which was soluble in alkalis and had all the properties of the urethane described above. Evidently the substance melting at 133° was the hydrochloride of o-aminophenyl isoamylcarbonate which changed to the urethane on being warmed with water. In the dry condition the hydrochloride is moderately stable.

BENZOYL O-OXYPHENYLISOAMYLURETHANE.

One and five-tenths grams of the oxyphenylisoamylurethane were dissolved in a slight excess of a 10 per cent. solution of potassium hydroxide, and to this was added 0.8 grams (one mol.) of benzoyl chloride. Slowly a brown oil separated which solidified in an ice box. After extracting with ether and recrystallizing several times from dilute alcohol white needle shaped
crystals were obtained which melted at 64°-65.5°. It is insoluble in water, dilute acids and alkalis, but soluble in ether, chloroform, benzol, and alcohol. 0.2591 grams gave 10 c. c. of nitrogen at 22.5° and 748 mm. pressure. This is equivalent to 4.39 per cent nitrogen. Calculated for C₁₉H₂₁NO₄ equals 4.28 per cent.

To one gram of this diacyl derivative 2 c. c. of a 10 per cent. solution of alcoholic potash were added. Saponification began at once and when all had passed into solution it was acidified and extracted with ether. The ether solution was washed with a solution of sodium bicarbonate and the ether evaporated. The residue after recrystallization from ligroin melted at 68.5°-69.5°, and when mixed with the urethane having the same melting point no depression of melting point was observed. From the sodium bicarbonate solution, on acidifying, benzoic acid separated and was identified in the usual way. The result indicates that the benzoyl group was attached to oxygen.

ACTION OF CHLORCARBONICISOAMYLEETHER ON BENZOYL O-AMINOPHENOL.

Benzoyl o-aminophenol was prepared following the method of Ransom. Two grams of this were dissolved in excess of a 10 per cent. solution of potassium hydroxide and 1.6 grams of chlorcarbonicisoamyl ether slowly added. On shaking, an oil slowly separated and this was extracted with ether. From the ether an oily residue was obtained which after several recrystallizations from alcohol formed a white solid melting at 64°-65.5°. A mixture with the supposed isomer had the same melting point. Saponification resulted in the production of benzoic acid and the urethane (m. p. 64°-65.5°). 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 CHLORCARBONICETHYLEETHER ON OXYPHENYLISOAMYLURETHANE.

One and one-fourth grams of oxyphenylisoamylurethane were dissolved in 4 c. c. of a 10 per cent. solution of potassium hydroxide and to this was added 0.7 grams of chlorcarbonicethylether. A heavy red oil separated. This was extracted with ether and the ether solution washed successively with dilute alkali, dilute acid and water. It was then dried with calcium chloride and the ether allowed to evaporate. The oil did not solidify. It was distilled under a pressure of 16 mm. at 185°-200°, the distillate soon solidifying to a yellow crystalline mass. After several recrystallizations
from dilute alcohol the crystals became white and melted at 65°-66°. It is insoluble in water, acids and alkalis, but soluble in alcohol, ether, chloroform, and benzol.

**ACTION OF CHLORCARBONIC ISOAMYLETHYL ON OXYPHENYLETHYLURETHANE.**

The ethylurethane was prepared according to Ransom's method and two grams of it were dissolved in a slight excess of potassium hydroxide. To this was added the calculated amount (1 mol.) of chlorcarbonicisoamylether. After shaking, a light yellow oil separated which became darker on standing. This was extracted with ether and the ether allowed to evaporate. An oil remained which refused to solidify even in a freezing mixture. It was distilled under a pressure of 15 mm. at 184°-190°, the distillate solidifying to a crystalline mass. After several recrystallizations it became white and melted at 65°-66°. It has all the properties of its supposed isomer above described. On saponifying some of the impure material two substances were obtained. A part melted at 133°-134° and is probably carbamylaminophenol produced from the urethane by loss of alcohol. The other part after purification melted at 84°-85° and on mixing with oxyphenylethylurethane (m.p. 86-87) the melting point was raised slightly. Evidently the carboethoxy group remains attached to nitrogen and no rearrangement occurs in preparing the diacyl derivative by this method. Since the supposed isomer is identical with this, there must have been a rearrangement during its preparation in the sense that the two carboxyl radicals exchanged places, the lighter changing from oxygen to nitrogen. The following equations express the reactions involved and the rearrangement that must have occurred in one case.  

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\begin{align*}
KOC_6H_4NHCOOC_6H_4Cl & \rightarrow C_2H_5OCOC_6H_4XHCOOC_6H_4NHCOOC\_4H_4 > C_6H_4OCOC_6H_4XHCOOC_6H_4
\end{align*}
\]

The final product is o-oxyphenylethylurethaneisoamylecarbonate.

**SUMMARY.**

The work here outlined, together with that previously reported, shows that when two carboxyl radicals (COOR and COOR') are introduced into the molecule of ortho aminophenol the lighter one becomes attached to the amide 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 radicals are carbonyls (COR and COR'). 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 ($C_4H_5CO - 105$, $C_5H_9COO - 115$) would result in the formation of isomeric substances was not realized, the velocity of the rearrangement being almost instantaneous in every case. Consequently the mechanism of the rearrangement cannot be explained. It is possible that there is an equilibrium of the two isomeric forms and that one of them is in large excess, but there is little evidence to support this view. Work already begun with the orthoaminomercaptans may throw light upon the problem.