THE REACTION OF CYANOGEN BROMIDE WITH THE SODIUM SALTS OF CARBOXYLIC ACIDS

II. THE REACTION OF CYANOGEN BROMIDE WITH THE SODIUM SALTS OF ALIPHATIC ACIDS[1]

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ABSTRACT

Cyanogen bromide reacts with the sodium salts of lower aliphatic acids at 250–300° C to form an α-keto isocyanate as the primary product. The latter undergoes subsequent pyrolytic decomposition to a nitrile and carbon dioxide. A mechanism is proposed to account for the observed interchange of labelled carbon atoms between the CN group of the cyanogen bromide and the carboxyl group of the salt in the over-all reaction.

INTRODUCTION

In the heterogeneous reaction between cyanogen bromide and sodium benzoate at 250–300° C, it was shown, by the use of carbon-14-labelled reactants, that an interchange of carbon atoms between the CN group of the cyanogen bromide and the carboxyl group of the benzoate occurs according to the following over-all reaction (1):

$$CNBr + RC^{*}OONa \rightarrow RC^{*}N + CO_2 + NaBr. \quad [1]$$

Preliminary experiments with sodium salts of several aliphatic acids and cyanogen bromide under similar conditions (2) seemed to indicate that a different mechanism was in operation, since a significant portion of carbon dioxide carbon originated in the aliphatic carboxyl group. In a more detailed investigation, however, which is described in this communication, it was established that the interchange of carbon atoms in accordance with reaction [1] occurs also when R is aliphatic ($R = CH_3, C_2H_5$—), although other simultaneously occurring pyrolytic reactions tend to obscure this reaction.

Although the sodium salts of several aliphatic acids were employed in this study, the most significant observations were made with sodium propionate as a reactant. Upon reaction with cyanogen bromide at 250–300° C under the conditions described previously, the latter salt yielded, in addition to the expected propionitrile, carbon dioxide and sodium bromide, two other compounds. Dipropionamide collected as a sublimate in the cooler part of the apparatus.[4] The other product was collected along with propionitrile in the cold trap attached to the pyrolysis tube. Unlike a nitrile, this compound reacted readily with ammonia under anhydrous conditions. The latter material possessed the properties of propionylurea, forming carbon dioxide and acid upon alkaline hydrolysis. In an experiment in which sodium acetate was the starting material, the nitrile fraction was passed through a mixture of glass and fuller's earth at 300° C. The formation of some carbon dioxide afforded additional evidence that the primary product of the reaction of cyanogen bromide with the sodium salt of an aliphatic acid is a compound yielding nitrile and carbon dioxide on pyrolysis, and forming monoacylurea with anhydrous ammonia. This primary product is an α-keto isocyanate, on the basis of the foregoing evidence.

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[4] *Zappi and Bouso (3) have reported the formation of monoamides in the reaction of sodium acetate and sodium propionate with cyanogen chloride.*

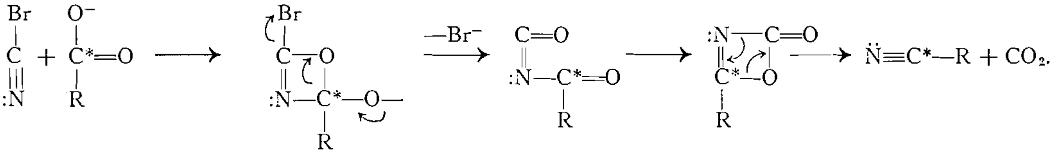
The reaction of cyanogen bromide with the sodium salt of an aliphatic acid may therefore be summarized as follows:

$$\mathrm{CNBr + RCOONa \rightarrow RCONCO + NaBr}$$

$$\mathrm{RCONCO \rightarrow RCN + CO_2.}$$

Only with lower aliphatic acids and under high vacuum is it possible for some of the α-keto isocyanate to escape complete pyrolysis. In the previously investigated reaction of sodium benzoate with cyanogen bromide, benzoyl isocyanate is undoubtedly formed initially, but it immediately pyrolyzes because of its low volatility.

To explain the observed interchange of carbon atoms between the CN group of the cyanogen bromide and the carboxyl group, the following mechanism is postulated:



An investigation of the pyrolysis of pure propionyl (isocyanate-C^{14}) should confirm this mechanism.

EXPERIMENTAL

The apparatus and procedure have already been described in detail (1). Approximately one millimole of the aliphatic acid sodium salt was weighed out and was suspended on a mixture of 0.5 g each of ignited fuller's earth and pulverized glass (40 mesh) by evaporation of a slurry of these materials in water. When a C^{14}-labelled sodium salt was employed, a known amount of activity was added to the weighed sample of inactive sodium salt in solution, before the latter was mixed with the fuller's earth and glass. After evaporation of the slurry, the mixture was transferred to the U-tube of the pyrolysis apparatus, and was heated in a Wood's metal bath to the appropriate temperature. The pyrolysis tube was connected, through a spiral trap cooled in liquid nitrogen, to a high-vacuum line. Slightly more than the equivalent quantity of cyanogen bromide was allowed to diffuse through the contents of the U-tube, while the latter was evacuated continuously. The carbon dioxide which collected in the spiral was converted to barium carbonate after fractionation with dry ice – acetone. The nitrile fraction was partially separated from unreacted cyanogen bromide by distillation on the vacuum line, and was reduced in ethereal solution with lithium aluminum hydride for characterization and radioassay. After decomposition of the lithium aluminum complex with dilute sulphuric acid, the amine was distilled from the mixture, after the latter had been rendered alkaline with sodium hydroxide, in a semimicro-Kjeldahl apparatus. The distillate was collected in excess dilute hydrochloric acid. The amine hydrochloride remaining after evaporation of this solution was recrystallized from an appropriate solvent. Ethanol was employed for ethylamine hydrochloride, and chloroform for propylamine and higher amine hydrochlorides. Known amounts of the hydrochlorides were plated on stainless-steel planchets for radioassay. Stearonitrile was plated directly, after purification by high-vacuum sublimation. Barium carbonate was plated on aluminum disks from a slurry. Appropriate self-absorption corrections were applied where necessary (4). Counting was performed with a helium and alcohol flow-type geiger counter with an approximately 2π geometry.

Pyrolysis of Nitrile Fraction from an Experiment with Sodium Acetate

Sodium acetate (4 millimoles) was suspended on powdered glass (40 mesh), and this mixture was placed in the U-tube of the apparatus previously described. Cyanogen bromide in slight excess was passed through the U-tube while the latter was evacuated continuously. Carbon dioxide was fractionated with dry ice – acetone and converted to barium carbonate. Yield of $BaCO_3$ 0.2227 g (28% based on acetate). The liquid remaining in the spiral trap was recycled through a mixture of fuller's earth and powdered glass at 304° C under high vacuum. An additional quantity of carbon dioxide was formed during pyrolysis, yielding 0.0945 g of barium carbonate.

Alkaline Hydrolysis of Propionylurea

The liquid reaction product from two experiments in which sodium propionate-1-C^{14} was allowed to react with cyanogen bromide under the conditions previously described was treated with ammonia in ether under anhydrous conditions. To the solid obtained from this reaction was added carrier propionylurea (5), the mixture was homogenized by crystallization, and the solid was sublimed under high vacuum. To a solution of the sublimate (5.15 mg) was added carrier propionylurea (25.9 mg) and the whole was evaporated to dryness in a bomb tube. The residue was hydrolyzed with saturated barium hydroxide solution (4 ml) at 100° C in the sealed tube overnight. A quantitative yield (52.7 mg) of barium carbonate was obtained, of specific activity 22,850 counts/minute millimole. The specific activity of the material before hydrolysis was 32,800 counts/minute millimole. A small portion of the initial activity was present in the acid recovered from the hydrolysis.

PAPER CHROMATOGRAPHY OF AMINE HYDROCHLORIDES AND OTHER COMPOUNDS

The amine hydrochlorides obtained from the lithium aluminum hydride reduction of the product nitriles were chromatographed on Whatman No. 1 filter paper by the ascending technique. For comparison, authentic samples of amine hydrochlorides were run in adjacent positions. Butanol saturated with 25% aqueous acetic acid was the developing solvent. The amines were detected with ninhydrin (6).

Propionylurea could not be distinguished from propionamide when these substances were chromatographed with the butanol – acetic acid – water medium as both had R_f values of 0.74. To facilitate detection on paper, these compounds were labelled with carbon-14 by synthesis from propionic acid-1-C^{14}. The developed chromatograms were placed in contact with Eastman No-Screen X-Ray film.

Dipropionamide-1-C^{14} with butanol–water as the developing solvent had an R_f of 0.91. Several unidentified spots with R_f values less than 0.74 appeared faintly on radioautographs of chromatograms of the nitrile fraction from the sodium propionate – cyanogen bromide reaction after this fraction had been treated with anhydrous ammonia. α-Cyanopropionic acid and α-isocyanopropionic acid were shown to be absent by chromatography of these substances for comparison.

RESULTS AND DISCUSSION

Data for typical experiments are presented in Tables I and II. It is evident that a significant portion of the carbon dioxide carbon is derived from the cyanogen bromide molecule. Simultaneously occurring pyrolytic reactions, other than the formation of an α-keto isocyanate and its decomposition to a nitrile and carbon dioxide, may explain in part the distribution of radioactivity among the products. Moreover, the formation and pyrolysis of a part of the α-keto isocyanate by a route other than the postulated one, could also account for this distribution of activity. Such reactions as decarboxylation and dehydration as well as the formation of free aliphatic acid in the presence of traces of hydrogen bromide are all possible under the experimental conditions employed, and one or more of these is probably responsible for the observed formation of a diamide. Variation in reaction conditions from one aliphatic acid to another is in part the result of the decreasing volatility of the intermediate α-keto isocyanate with increasing molecular weight. Thus, this intermediate was present in the nitrile fractions from the sodium acetate and propionate reactions, but with higher acids, and especially with benzoic acid, the α-keto isocyanate could have only a momentary existence in the hot zone of the pyrolysis apparatus. The postulated formation of an α-keto isocyanate in the reactions investigated offers a logical explanation of the observed interchange of carbon atoms between cyanogen bromide and the carboxyl group through the mechanism described earlier in this communication.

TABLE I

DATA FOR THE REACTION OF CNBr WITH SODIUM SALTS OF C^{14}-CARBOXYL ACIDS

Salt	Temperature, ° C	Specific activities counts/minute millimole			Amine from reduction of nitrile
		Na salt	$BaCO_3$	Amine salt	
Sodium acetate	274–277	21,000	4,740	15,200	Ethylamine
		17,650	8,120	—	
		17,650	1,675	—	
Sodium propionate	267–273	48,100	6,440	47,700	Propylamine
Sodium butyrate	300–303	453,300	44,400	321,500	Butylamine
Sodium valerate	300–303	64,400	10,230	64,000	*n*-Amylamine
Sodium stearate	274–277	79,500	38,300	53,000*	

*Stearonitrile was counted directly, after purification by distillation from a Späth bulb *in vacuo*.

TABLE II

DATA FOR THE REACTION OF C^{14}-NBr WITH SODIUM SALTS OF CARBOXYLIC ACIDS

Salt	Temperature, ° C	Specific activities counts/minute millimole		
		CNBr	$BaCO_3$	Amine salt
Sodium acetate	270–271	163,000	72,300	73,300
Sodium propionate	271–272	163,000	69,900	13,800
Sodium butyrate	267–274	163,000	53,100	6,060
Sodium trimethylacetate	294–297	883,000	576,000	231 counts/minute mg (Unidentified reduced product)
Sodium α-bromopropionate	287–291	318,200	29,080	—

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