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

I. THE REACTION OF CYANOGEN BROMIDE WITH SODIUM BENZOATE¹

By D. E. DOUGLAS, JEAN ECCLES,² AND ANNE E. ALMOND³

ABSTRACT

The main products of the reaction of cyanogen bromide with sodium benzoate at 250° to 300°C. are carbon dioxide, benzonitrile, and sodium bromide. Tracer studies have shown that the carbon of the carbon dioxide is derived almost entirely from the cyanogen bromide.

Zappi and Bouso (3) have investigated the reaction of cyanogen chloride with the sodium salts of several carboxylic acids, both aliphatic and aromatic, at 200 to 300°C. to form the corresponding nitriles:

$RCOONa + CICN \rightarrow NaCl + CO_2 + RCN.$

Since good yields of nitriles were obtained they proposed this reaction as a method of synthesis of these compounds.

The corresponding reaction of cyanogen bromide with the sodium salts of various carboxylic acids is being investigated because of its potential application in the synthesis of labelled molecules. By the use of carbon-14labelled reactants, it has been found that, depending on the carboxylic acid employed, the carbon of the product carbon dioxide may be derived from the carboxyl group or the cyanogen bromide. With sodium acetate and propionate the carbon dioxide carbon originates in the carboxyl group (1).

In this paper, the reaction of cyanogen bromide with sodium benzoate is described. Data are presented to show that in this case the carbon dioxide is derived almost entirely from the cyanogen bromide. Observations on the reaction of cyanogen bromide with the sodium salts of homologous fatty acids will be published later.

EXPERIMENTAL

Cyanogen bromide- C^{14} was prepared from aqueous sodium cyanide- C^{14} and bromine by a vacuum-line modification of the method Graf *et al.* (2). Benzoic acid-carboxyl- C^{14} was prepared by carbonation of phenylmagnesium bromide by standard vacuum-line procedure.

Reaction of Cyanogen Bromide with Sodium Benzoate

The apparatus (Fig. 1) consisted of a tube for the cyanogen bromide connected by a ground joint and stopcock to a U tube with a by-pass between its arms. The U tube was joined through a glass spiral to a vacuum manifold with an attached mercury manometer. A weighed sample (one to two millimoles)

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Contribution from the Division of Atomic Chemistry, Montreal General Hospital Research Institute, Montreal, Quebec. ² Technical Assistant.

 Present Address: Department of Biochemistry, Medical College St. Bartholomew's Hospital, London, England.

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A—Tube to contain cyanogen bromide. B—U tube.

E—Carbon dioxide absorption trap. F—Graduated tube for estimating yield of

C-Electrically heated Wood's metal bath. D-Spiral trap.

nitrile. M—Mercury manometer. G-—Vacuum manifold.

of sodium benzoate was suspended on a mixture of 0.5 gm. each of powdered glass and ignited fuller's earth by evaporating an aqueous slurry of the three materials with stirring. The dried powder was confined to the bottom of the U tube with two plugs of glass wool. The bottom of the U tube was immersed in an electrically heated Wood's metal bath controlled by a Powerstat transformer.

An excess of cyanogen bromide was weighed into the glass stoppered tube, which was then connected to the apparatus, and surrounded by a bath of liquid nitrogen. The whole train was evacuated by means of a fore-pump and mercury diffusion pump. The glass spiral was cooled with liquid nitrogen, and the cyanogen bromide was allowed to volatilize and pass slowly through the contents of the U tube. The process took between 10 and 20 min. No significant pressure change occurred during reaction. The contents of the spiral were later fractionated. Carbon dioxide and unreacted cyanogen bromide were frozen into a trap containing excess 0.5 N sodium hydroxide (or, 0.2 N sodium sulphide saturated with barium hydroxide when active cyanogen bromide was reactant). The nitrile was condensed with a liquid nitrogen bath into a graduated tube. A varying amount of white or brownish crystalline material condensed in the cooler part of the exit of the U tube during the reaction.

Treatment of the Reaction Products

Barium hydroxide solution in a slight excess was added to the heated solution of carbonate in sodium hydroxide from the carbon dioxide trap, and the precipitate of barium carbonate was filtered, dried, weighed, and counted.

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For final activity determination, a sample of the carbonate was decomposed with lactic acid in a vacuum transfer apparatus, and the carbon dioxide reconverted to barium carbonate. A small amount of activity was usually found in the filtrate from the first precipitation.

When the carbon dioxide was absorbed in 0.2 M sodium sulphide saturated with barium hydroxide, the barium carbonate was filtered off, weighed, and counted and a sample was decomposed with lactic acid and reconverted to barium carbonate as described above. An aliquot of the original filtrate, which contained the excess cyanogen bromide-C¹⁴ from the reaction as thiocyanate, was counted.

The nitrile was washed from the graduated tube with ethanol into a bomb tube and hydrolyzed by heating with an excess of 2 N sodium hydroxide. Benzoic acid was recovered by acidification of an aqueous solution of the sodium salt with hydrochloric acid, and recrystallized from hot water. M.p. $121.5^{\circ}-122^{\circ}C$; mixed m.p. with authentic benzoic acid $121-122^{\circ}C$.

To confirm the identification of the reaction product as benzonitrile. in experiment No. 5 the nitrile was divided into two portions one of which was hydrolyzed as described above. The other portion in dry ether was added to an excess of lithium aluminum hydride in the same solvent. After a few hours, the mixture was decomposed with water, and a few drops of saturated sodium hydroxide added. The solution was extracted continuously with ether. A crystalline hydrochloride formed on passing hydrogen chloride into the dried ether extract. The chloride content of this compound, determined by titration with mercuric nitrate was in good agreement with the theoretical value for benzylamine hydrochloride. Calc. for $C_7H_{10}N$: Cl. 24.7; found: Cl. 24.55.

A sample of the crystalline material from the exit side of the U tube of the train (experiment No. 5) was recrystallized from toluene-cyclohexane. After sublimation, it melted at 100–104°C. By hydrolysis with concentrated hydro-chloric acid at 220°–230°C., benzoic acid was obtained, with a specific activity of 249 counts/min./mgm. as compared with 253 counts/min./mgm. for the starting material. This material probably consisted of benzamide and kyaphenin, the trimer of benzonitrile, both of which yield benzoic acid under the hydrolytic conditions employed. Kyaphenin has been identified among the products of the reaction of cyanogen chloride with sodium benzoate (3).

Sodium bromide was identified in the nonvolatile residue remaining in the bottom of the U tube by extracting the fuller's earth and glass with water and precipitating bromide as the silver salt with silver nitrate.

Counting was carried out with a helium flow-type windowless counter and an Atomic Instrument Model 101-A scaler. Corrections were applied for selfabsorption in the various substances counted.

RESULTS AND DISCUSSION

Data for several typical experiments are given in Tables I and II. Owing to the difficulty of obtaining reproducible conditions in heterogeneous pyrolytic reactions of this type, there is considerable variation in the experimental results. Specific activity data show conclusively that the carbon of the product

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DATA FOR THE REACTION OF SODIUM BENZOATE-CARBOXYL-C14 WITH CYANOGEN BROMIDE

Expt. no.	Temp., °C.	Specific activity of original C ₆ H₅COOH, counts/min./mmole	Specific activity C₀H₅COOH from hydrolyzate, counts/min./mmole	Specific activity of BaCO ₃ , counts/min./mmole	Per cent yield of BaCO3	Per cent yield of C6H5
$egin{array}{c} 2 \\ 4 \\ 5 \end{array}$	280–285 296–297 284–288	160,600 39,500 30,450	139,900 28,500 32,170*	4240 356 197	$72.2 \\ 68.1 \\ 77.8$	$47 \\ 35 \\ 34$

*Benzylamine hydrochloride obtained by reduction of the benzonitrile had a specific activity of 25,400 counts/min./mmole.

TABLE II					
DATA FOR THE	REACTION OF	SODIUM BE	NZOATE WITH	CYANOGEN	BROMIDE-C ¹⁴

Expt. no.	Temp., °C.	Specific activity of CNBr, counts/min./mmole	Specific activity of BaCO3, counts/min./mmole	Per cent yield of BaCO3	Specific activity of C6H3-COOH from hydrolyzate, counts/min./mmole	Per cent activity recovered as BaCO3 and thiocynate	Per cent yield of C6H5CN
6. 7	289 296–302	$314,600 \\ 314,600$	$267,900 \\ 272,800$	86.7 49.5	9,060 490	$\begin{array}{c} 74.5 \\ 50.1 \end{array}$	$\begin{array}{c} 20\\ 46 \end{array}$

carbon dioxide is derived almost entirely from the cyanogen bromide. The presence of low activity in the barium carbonate when carboxyl-labelled sodium benzoate is a reactant (Table I) and in the recovered benzoic acid when cyanogen bromide alone is labelled (Table II) reveals that a small fraction of the carbon dioxide has its origin in the carboxyl group, probably through a simultaneously occurring alternate reaction yielding the same end products. The occurrence of a side reaction of this type also could explain the trend towards lower activity per millimole of the active product as compared with the active reactant, but this difference may include errors in correcting for self-absorption in the different materials counted.

In the absence of sufficient data on the reaction of cyanogen bromide with sodium salts of other carboxylic acids, a mechanism explaining the derivation of the carbon dioxide from cyanogen bromide is difficult to postulate. At the temperatures employed (250-300°C.), cyanogen bromide should be largely dissociated into CN radicals and bromine atoms, and it is almost certain that a free radical heterogeneous reaction takes place.

Further work should make possible a correlation of the genesis of the carbon dioxide with the general behavior of the carboxyl group of various acids, and thus suggest a mechanism for this reaction.

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