



Fig. 1.—Fluorinating system.

dropwise from the separatory funnel until reaction begins, then cooling the flask in ice water as needed. Gas products enter the column and pass up through the fluorinating mixture composed of  $\text{SbF}_3$  and  $\text{SbCl}_5$  in the ratio of about 60 g. to 200 ml., respectively. A large excess of  $\text{SbCl}_5$  is necessary to keep the mixture fluid and may be recovered after the reaction. Transit time for a gas bubble is from 2 to 4 seconds depending on the temperature and consequent fluidity of the mixture. A freshly prepared fluorinating mixture requires a column temperature between 25 and 35° for efficient reaction; at these temperatures much solid material is present which may clog the gas inlet. After a few ml. of product have been condensed in the cold trap, the operating temperature may be raised to 45°, where no solids are present, without impairing efficiency. If the reaction is begun at the higher temperature, especially with  $\text{CH}_2\text{Cl}_2$ , much of it is decomposed. Progress of the reaction may be easily followed by bleeding off a small amount of the gas and measuring its density with a gas density balance.<sup>5</sup>

(5) J. D. Edwards, Technological Paper No. 89, U. S. Bureau of Standards.

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## Synthesis of Nitriles in Ethylene Glycol<sup>1</sup>

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Low-boiling nitriles cannot be made from alkyl halides and sodium cyanide in aqueous alcohol because of the difficulty of isolating the products from the solvent. However, other solvents which dissolve appreciable amounts of sodium cyanide can be used. Thus, ethylene glycol has been used in the preparation of 5-hexenenitrile from 5-bromo-1-pentene,<sup>2</sup> and its monoalkyl ethers, as well as tetrahydrofurfuryl alcohol, have been used in the preparation of succinonitrile and adiponitrile.<sup>3</sup>

There are relatively few examples in the literature of the formation of secondary cyanides by displacement reactions, and none at all of tertiary cyanides. Low yields in these reactions are commonly attributed to olefin formation,<sup>4</sup> but there have been no quantitative studies to bear this out.

Several of the solvents tried were found to be quite unsatisfactory. *n*-Butyl bromide was largely unchanged after a 40-hour reflux with sodium

(1) From the M.S. thesis of Peter V. Susi, September, 1951.

(2) F. B. LaForge, N. Green and W. A. Gersdorff, *THIS JOURNAL*, **70**, 3707 (1948).

(3) A. O. Rogers, U. S. Patent 2,415,261, Feb. 4, 1947.

(4) D. T. Mowry, *Chem. Revs.*, **42**, 189 (1948).

cyanide in *n*-butyl cellosolve or nitrobenzene. *t*-Butyl chloride in *t*-butyl alcohol gave a high yield of isobutylene. *t*-Butyl bromide in hydrogen cyanide gave a little olefin along with unidentifiable material, although the sodium cyanide dissolved in the hydrogen cyanide to the extent of 0.54 g. per 100 cc. *t*-Butyl bromide in cold saturated aqueous sodium cyanide gave only a black tar.

Ethylene glycol proved to be a much more suitable solvent, even though it is not miscible with the alkyl halides. Table I shows the results of experiments with several primary, secondary and tertiary halides. In all runs there is some loss in the form of undistillable black residues. Other than this, the main side-reaction is the formation of glycol monoalkyl ethers (solvolysis); olefins are a relatively minor product.

The reactions with the primary halides were particularly gratifying. Valeronitrile, for instance, was prepared in 90% yield after one hour of reflux, and was readily separated from the reaction mixture by distillation. The best yield reported in aqueous alcohol after 25–30 hours of reflux and a careful, 10-hour distillation is 80%.<sup>5</sup> Butyronitrile has been made in aqueous alcohol, but not isolated.<sup>6</sup>

TABLE I

REACTION OF ALKYL HALIDES WITH SODIUM CYANIDE

Alkyl halide	Initial temp., °C.	Reaction time, hr.	Nitrile	Yield, % Ether	Olefin
<i>n</i> -BuBr	101	1	90		
<i>n</i> -PrBr	72	1	92		
<i>i</i> -PrBr	60	24	39		
<i>i</i> -PrBr <sup>a</sup>	60	15	39	16	7
<i>s</i> -BuBr <sup>a</sup>	92	4	28	Low	
<i>s</i> -BuCl	68	22	No reaction		
<i>t</i> -BuBr <sup>a</sup>	73	3 <sup>b</sup>	Low	44	
<i>t</i> -BuCl	50	6	Low	41	
<i>t</i> -BuCl <sup>a</sup>	46	6	10 <sup>c</sup>	27	18

<sup>a</sup> Sulfuric acid added. <sup>b</sup> Reaction seemed to be complete in one hour. <sup>c</sup> Impurities may reduce this to about 5%.

TABLE II

IDENTIFICATION OF PRODUCTS

Compound	Property	Observed	Reported	Reference
<i>n</i> -BuCN	B.p.	138–142°	140.75°	<i>a</i>
<i>n</i> -PrCN	B.p.	116–119°	117.28°	<i>a</i>
<i>i</i> -PrCN	B.p.	103–104°	103.7°	<i>a</i>
	<i>n</i> <sup>20</sup> D	1.3728	1.37348	<i>a</i>
<i>s</i> -BuCN	B.p.	124–126°	125.4°	<i>a</i>
	<i>n</i> <sup>20</sup> D	1.3857	1.38562	<i>a</i>
<i>t</i> -BuCN	B.p.	100–107°	103.5 <sup>ob</sup>	<i>b</i>
	<i>n</i> <sup>20</sup> D	1.3809	1.3792	<i>b</i>
<i>i</i> -PrOR <sup>c</sup>	B.p.	142.5–143°	144°	<i>d</i>
<i>t</i> -BuOR <sup>c</sup>	B.p.	153–154°	153°	<i>e</i>

<sup>a</sup> J. Timmermans, "Physico-chemical Constants of Pure Organic Compounds," Elsevier Publishing Company, Inc., New York, N. Y., 1950, pp. 531–541. <sup>b</sup> Boiling point at 738 mm., F. C. Whitmore, C. I. Noll and V. C. Meunier, *THIS JOURNAL*, **61**, 683 (1939). <sup>c</sup> R =  $-\text{CH}_2\text{CH}_2\text{OH}$ . <sup>d</sup> L. H. Cretcher and W. H. Pittenger, *THIS JOURNAL*, **46**, 1503 (1924). <sup>e</sup> T. W. Evans and K. R. Edlund, *Ind. Eng. Chem.*, **28**, 1186 (1936).

(5) R. Adams and C. S. Marvel, *THIS JOURNAL*, **42**, 310 (1920).

(6) K. W. Rosenmund, K. Luxat and W. Tiedemann, *Ber.*, **56**, 1950 (1923).

Although the yields of secondary cyanides are only fair, the fact that they can be easily obtained in a single step may make the reaction useful. Isobutyronitrile, for instance, cannot be made in aqueous alcohol, and is difficult to make by indirect methods. It is doubtful whether this method of preparing *t*-butyl cyanide (pivalonitrile) is practical.

In a few runs part of the excess sodium cyanide was neutralized with sulfuric acid in an attempt to reduce the over-all alkalinity. This reduced the proportion of glycol ether in the product; the effect was small, however, and it was concluded that the alkoxide ion,  $\text{HOCH}_2\text{CH}_2\text{O}^-$ , which might have been present in the unbuffered solution, was not directly responsible for ether formation.

#### Experimental

The alkyl halides and ethylene glycol were redistilled before use. The sodium cyanide was Baker Analyzed, 98% minimum.

The general procedure was to mix 150 cc. of ethylene glycol, 0.5 mole of the alkyl halide and 0.55 mole of sodium cyanide in a 500-cc. three-necked flask, and to heat under reflux with constant stirring until the end of the reaction. The initial temperature, measured by a thermometer in the vapor, was always close to the boiling point of the halide, and the end of the reaction was marked by a rapid rise in temperature to a constant value as the last of the halide was used up. In a few runs 0.1 mole of sulfuric acid and an additional 0.2 mole of sodium cyanide were added before heating. In the reaction with *n*-butyl bromide it was observed that the heat of reaction was sufficient to maintain spontaneous reflux at the start.

The liquid products were distilled from the reaction mixture through a three-ball Snyder column. Where further purification of the nitriles was required they were washed with 4 *N* hydrochloric acid, 10% sodium bicarbonate and water, dried and redistilled through a 9-inch or 18-inch packed column. Their properties are listed in Table II. The odor revealed that traces of isocyanide were still present in all cases.

In the runs in which olefin was determined the evolved gases were passed through soda-lime to remove hydrogen cyanide, and condensed in a trap at  $-80^\circ$ . The olefins were then converted to the dibromides by passing them into a sodium tribromide solution, prepared from 70 g. of sodium bromide, 112 g. of bromine and 300 cc. of water. The dibromides were washed with sodium carbonate and sodium thiosulfate solutions, dried and weighed.

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### X-Ray Measurements of Terramycin Salts

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The hydrochloride of terramycin crystallizes from aqueous solution in the form of yellow elongated plates. These are biaxial negative with parallel extinction, and have the refractive indices  $\mu_g = 1.639$ ,  $\mu_m = 1.686$ ,  $\mu_p = 1.721 \pm 0.003$ . The highest refractive index is shown when the electric vector vibrates parallel to the direction of elongation (the *a* axis). The crystals are orthorhombic, with space group  $P2_12_12_1$ , unit cell dimensions  $a = 11.19 \text{ \AA.}$ ,  $b = 12.49 \text{ \AA.}$ ,  $c = 15.68 \text{ \AA.}$ , and four molecules per cell. The density, found from experiment to be 1.51, gives the value  $499 \pm 5$  for the molecular weight of the asymmetric unit. As it is probable that this unit consists of one molecule of the antibiotic, without water of crystallization, the molecular weight of the free

antibiotic, as given by the X-ray data, is  $462.5 \pm 5$ . This is in agreement with the molecular weight found approximately by titration methods,<sup>1</sup> and with the formula  $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_9 \cdot \text{HCl}$ , which corresponds to the analysis reported by P. P. Regna and I. A. Solomons.<sup>1</sup>

Terramycin hydrobromide crystallizes as a dihydrate, in space-group  $P2_1$ . The unit cell dimensions are  $a = 12.2 \text{ \AA.}$ ,  $b = 11.4 \text{ \AA.}$ ,  $c = 18.0 \text{ \AA.}$ , with  $\beta$  very nearly  $90^\circ$ . There are four molecules per cell, and thus two molecules of  $\text{T} \cdot \text{HBr} \cdot 2\text{H}_2\text{O}$  in each asymmetric unit.

Since the molecular structure of terramycin is not known, efforts have been exerted toward a complete X-ray analysis. The hydrobromide dihydrate was not suitable for this analysis because of the existence of two molecules in the asymmetric unit, doubling the number of atomic parameters to be determined. The hydrochloride was selected for further study, and a full three-dimensional Patterson synthesis was carried out on X-RAC, the electronic computer for crystal analysis,<sup>2</sup> using data obtained with  $\text{CuK}\alpha$  radiation. The chloride ion parameters were found to be (0.075, 0.08, 0.00). These ions form nets at  $z = 0$  and  $z = 1/2$ , with the ions 7.0 and 9.9  $\text{\AA.}$  distant from one another, in sheets which are 15.7  $\text{\AA.}$  apart.

Attempts at interpretation of the three-dimensional Patterson were made by means of the Vector Convergence Density method, utilizing photographic super-position of displaced Patterson sections.<sup>3</sup> This technique strongly indicated positions of eleven carbon, oxygen or nitrogen atoms in the molecule, and suggested six additional positions of atoms of similar weight. These peaks were all concomitant with acceptable interatomic distances, but their number and distribution were insufficient to suggest a molecular configuration. Atomic coordinates found by the Vector Convergence Density method are now being used to compute structure factor phases for a three-dimensional density map.

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(1) P. P. Regna and I. A. Solomons, *Ann. N. Y. Acad. Sci.*, **53**, 229 (1950).

(2) R. Pepinsky, *J. Appl. Phys.*, **18**, 604 (1947).

(3) C. A. Beevers and J. H. Robertson, *Acta Cryst.*, **3**, 164 (1950).

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### *o*-Nitrobenzoates

By J. U. Lowe

During an investigation of aryl nitro compounds, it became necessary to prepare several *o*-nitrobenzoates; these were prepared in satisfactory yields by the interaction of pure *o*-nitrobenzoyl chloride and the monohydric alcohols.

*o*-Nitrobenzoates.—*o*-Nitrobenzoyl chloride<sup>1</sup> (0.2 mole) and the monohydric alcohol (0.4 mole) were refluxed for 3–7

(1) K. Auwers and M. Duesberg, *Ber.*, **53**, 1207 (1920).