

Summary

Benzylmethylacetamide has been prepared in a pure dextro and a mixed levo modification.

Evidence is submitted to show that when this compound undergoes the Hofmann rearrangement the amine hydrochloride so obtained is optically active. It is further shown that the rotatory power has the same sign as the amide from which it is produced, and that the value of the specific rotation of the *d*-amine hydrochloride produced from the *d*-acid amide is the same as the value of the amine hydrochloride obtained by Jones and Wallis from *d*-benzylmethylacetazide.

A discussion of these results is given with special reference to the Walden inversion.

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[CONTRIBUTION FROM THE WALKER CHEMICAL LABORATORY OF THE RENSSELAER POLYTECHNIC INSTITUTE]

THE PREPARATION OF CYCLOPROPYL CYANIDE AND TRIMETHYLENE CHLOROBROMIDE¹

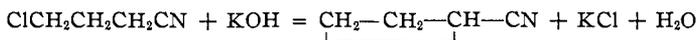
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Cyclopropyl Cyanide.—During the last few years workers in this Laboratory have found it necessary to prepare quantities of cyclopropyl cyanide as the starting material in a series of investigations on the stability of certain cyclopropane derivatives. Since the ordinary procedures for the preparation of this rather costly reagent have given unsatisfactory yields, a number of attempts have been made to devise a better process.

Cyclopropyl cyanide was first made by Henry in 1898 by the distillation of γ -chlorobutyronitrile with dry potassium hydroxide,



but its true nature was not recognized until a year later.² Although certain workers have claimed that this process gives "satisfactory" results, this has not been the general experience, since losses arise as the result of hydrolysis and polymerization. More recent descriptions of the method have been given by Haller and Benoist, Nicolet and Sattler and by one of us.³ It is

¹ The experimental data reported herein have been abstracted from theses on cyclopropane derivatives which have been presented to the Rensselaer Polytechnic Institute by Raymond J. Anderson, John Lachmann and Gustavus E. Smith in partial fulfillment of the requirements for the degree of Chemical Engineer.

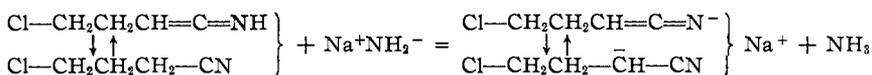
² M. L. Henry, *Bull. sci. acad. roy. belg.*, [3] 36, 34 (1898); *ibid.*, [3] 37, 17–22 (1899).

³ Haller and Benoist, *Ann. chim.*, [9] 17, 28 (1922); Nicolet and Sattler, *This Journal*, 49, 2068 (1927); Cloke, *ibid.*, 51, 1180–1181 (1929).

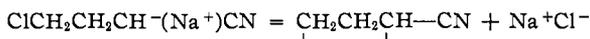
our opinion that the 40–55% yields of Nicolet and Sattler were unusually good for the potassium hydroxide method.

Other attempts to devise better methods for the preparation of cyclopropyl cyanide have been recorded. Bruylants and Stassens⁴ carried out the reaction with potassium hydroxide in alcohol, but only γ -ethoxybutyronitrile was obtained and not a trace of cyclopropyl cyanide. In another investigation in which sodium alcoholate was allowed to react with γ -chlorobutyronitrile Bruylants⁵ obtained a mixture of the cyclopropyl cyanide and γ -ethoxybutyronitrile. By the action of pyridine and quinoline at water-bath temperature on γ -chlorobutyronitrile, this investigator obtained only vinylacetonitrile and none of the cyclic compound. The present paper describes the preparation of the cyclopropyl cyanide by the action of sodamide on γ -chlorobutyronitrile in both liquid ammonia and ether solutions.

The formation of cyclopropyl cyanide by the action of sodamide on γ -chlorobutyronitrile may be explained in the same way as the alkylations of such substances as ethyl acetoacetate, diethyl malonate, phenylacetonitrile, etc. Thus, the γ -chlorobutyronitrile may be assumed to exist in two tautomeric forms, *viz.*, the nitrile, $\text{ClCH}_2\text{CH}_2\text{CH}_2\text{CN}$, and the imide, $\text{ClCH}_2\text{CH}_2\text{CH}=\text{C}=\text{NH}$, structures. In the light of the carbide ion theory of Stieglitz, which has been extended by Rising⁶ to salts of phenylacetonitrile, the action of sodamide on the γ -chlorobutyronitrile may first be assumed to give both the "nitride" ion, $\text{ClCH}_2\text{CH}_2\text{CH}=\text{C}=\text{N}^-\text{Na}^+$, and the "carbide" ion, $(\text{ClCH}_2\text{CH}_2\text{CHCN})^-\text{Na}^+$, which also are tautomeric, as follows



Finally the latter carbide salt may be supposed to undergo almost instantaneous internal condensation to give the cyclopropyl cyanide and sodium chloride



Dry sodamide was first employed in place of the potassium hydroxide of Henry in order to eliminate the hydrolysis of the nitriles, since it was first supposed that the hydrolyses were chiefly responsible for the losses in the Henry reaction. Next, after the foregoing work had demonstrated that a large amount of polymerization also occurred, the reaction was carried out in liquid ammonia with the expectation that the low temperature would minimize the polymerization. The first results, however, were disappoint-

⁴ Bruylants and Stassens, *Bull. sci. acad. roy. belg.*, [5] 7, 702–719 (1921).

⁵ Bruylants, *ibid.*, [5] 6, 479–486 (1920).

⁶ Rising and Zee, *THIS JOURNAL*, 49, 541–545 (1927); 50, 1699–1707 (1928); Rising, Muskat and Lowe, *ibid.*, 51, 262–265 (1929).

ing, since only 40–50% yields of the monomeric cyclic nitrile were obtained, polymerization accounting for most of the loss. Finally, these polymerization losses were largely eliminated: first, by the neutralization of the excess sodamide in the liquid ammonia–ether solution by the use of ammonium chloride; and, second, and more important, by the carrying out of all distillation work under diminished pressure with the aid of a very efficient condensing system. In this way, the later runs, starting with 21 g. of the γ -chlorobutyronitrile and 10 g. of sodamide, have consistently given from 75–90% of the cyclopropyl cyanide. With ether as the solvent and a comparatively long period of stirring and gentle simmering, the same quantities of reagents have given yields which have been about 10–20% lower, due to larger polymerization losses. Similar results have been obtained by E. C. Knowles⁷ in the preparation of 1-phenyl-1-cyanocyclopropane from α -phenyl- γ -chlorobutyronitrile.

Trimethylene Chlorobromide.—Trimethylene chlorobromide was required for the preparation of the γ -chlorobutyronitrile, $\text{ClCH}_2\text{CH}_2\text{CH}_2\text{Br} + \text{KCN} = \text{ClCH}_2\text{CH}_2\text{CH}_2\text{CN} + \text{KBr}$,⁸ which was employed in the synthesis of the cyclopropyl cyanide. The trimethylene chlorobromide has been prepared by the addition of hydrogen bromide to allyl chloride,⁹ by the action of mercuric chloride on trimethylene dibromide,¹⁰ and by the addition of sulfuric acid to a mixture of trimethylene chlorohydrin and hydrobromic acid solution.¹¹ Although the last process is definitely superior to those which precede, it has never given entirely satisfactory results in this Laboratory, since the product contains considerable quantities of trimethylene dibromide. The formation of the latter compound, which has always occurred with us, not only leads to diminished yields of the trimethylene chlorobromide, but it also entails a time-consuming fractionation. This difficulty is eliminated by the method which is described in this paper by means of which 90–94% yields of practically pure chlorobromide have been obtained by the addition of trimethylene chlorohydrin to phosphorus tribromide. The addition of the tribromide to the chlorohydrin has been found by Van Wyck¹² to be much less advantageous. Furthermore, the interaction of phosphorus trichloride and trimethylene bromohydrin gave poor yields, as would be expected.

Experimental Part

Trimethylene Chlorohydrin, $\text{ClCH}_2\text{CH}_2\text{CH}_2\text{OH}$.—The trimethylene chlorohydrin which was used for the preparation of the trimethylene chlorobromide was prepared

⁷ Doctorate Dissertation, Rensselaer Polytechnic Institute.

⁸ "Organic Syntheses," John Wiley and Sons, Inc., New York, 1928, Vol. VIII, p. 52.

⁹ Reboul, *Ann. chim. phys.*, [5] **14**, 487 (1878); Bruylants, *Bull. sci. acad. roy. belg.*, **12**, 1085–1094 (1908).

¹⁰ Friedel and Silva, *Jahresb.*, 498 (1874).

¹¹ Kamm and Marvel, *THIS JOURNAL*, **42**, 307 (1920).

¹² Van Wyck, "Thesis," Rensselaer Polytechnic Institute.

according to the directions of Marvel and Calvery.¹³ The process of Hultman, Davis and Clarke¹⁴ gives less trouble.

Anal. Calcd. for C_3H_7OCl : Cl, 37.51. Found: Cl, 37.40.

Trimethylene Chlorobromide, $ClCH_2CH_2CH_2Br$.—Two methods were studied for the preparation of the trimethylene chlorobromide. In the first process one mole of trimethylene chlorohydrin was distilled with two moles of 48% hydrobromic acid in a continuous separation apparatus similar to that of Hultman, Davis and Clarke. Three variations of the method gave only 40% yields of the pure chlorobromide.

In the optimum variation of the second process, the phosphorus tribromide method, a two-liter, three-necked, round-bottomed flask was provided with a dropping funnel, a motor stirrer and a small reflux condenser to which was attached a calcium chloride tube. One mole (271 g.) of phosphorus tribromide was then run into the flask, which was immersed to the neck in an ice-bath; the stirrer was started and, as soon as the tribromide was cold, a two-mole quantity (189 g.) of trimethylene chlorohydrin was allowed to drop slowly into the cold tribromide over a period of two hours. The solution was then heated with stirring on a water-bath for about ten hours. At this point the mixture was allowed to cool, when it was poured into a liter of cold water and then washed with several portions of 10% sodium carbonate solution until all acid had been removed. Finally the chlorobromide was dried over calcium chloride and distilled, which gave 296 g. of chlorobromide, b. p. 140–143°. This corresponds to a 94% yield.

In several earlier runs in which 1.75 moles of chlorohydrin and 1 mole of phosphorus tribromide were used, but without the stirring during the heating on the boiling water-bath, 90% yields of the trimethylene chlorobromide were obtained.

γ -Chlorobutyronitrile.—The γ -chlorobutyronitrile was made by the action of potassium cyanide on the trimethylene chlorobromide.⁸

Cyclopropyl Cyanide, $\overline{CH_2CH_2}CHCN$.—Three different procedures were employed for the preparation of the cyclopropyl cyanide. Although the first method has been found to be inferior to the other two, it has been included for the sake of completeness.

Procedure 1. The Preparation of Cyclopropyl Cyanide in Liquid Ammonia.—About 250 cc. of liquid ammonia was run out of a cylinder into a 500-cc. Dewar flask. A quantity of sodamide (Kahlbaum's) was then ground up in a mortar under ether in order to exclude direct contact with moist air. At this point the γ -chlorobutyronitrile was added to the ammonia, and this was followed by the moist sodamide, which was added in small portions with a spoon. After standing for five hours, during which the flask was connected with a calcium oxide tower, about 200–300 cc. of anhydrous ether was added to the ammonia solution; next the ether–ammonia solution was separated from the solid by filtration through a Büchner funnel under a hood and the residue was washed with a little ether. The solution was then distilled on the water-bath with the aid of a Vigreux column until most of the ether had been removed; finally, the residue was transferred to a 50-cc. round-bottomed flask and distilled through a 1 × 60 cm. Vigreux column. The results of the first four of several such runs are given in Table I.

In another run in which the liquid ammonia was allowed to evaporate completely before the ether was added, only polymers of the cyclopropyl cyanide were obtained; several of these were formed.

Procedure 2. Optimum Procedure for the Preparation of the Cyclopropyl Cyanide.—As before, the sodamide (Kahlbaum's) was ground up in a mortar under about 150 cc. of dry ether, but to a greater degree of subdivision. About half of the ether was

¹³ Marvel and Calvery, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1928, Vol. VIII, p. 112.

¹⁴ Hultman, Davis and Clarke, *THIS JOURNAL*, 43, 369 (1921).

TABLE I
 RESULTS OF RUNS

Run	γ -Nitrile, g.	NaNH_2 , g.	Time in hrs. of standing	Yield, %
1	50	25	5	44.7
2	50	30	5	51.5
3	25	16	5	43
4	50	30	5	35.4

then carefully decanted from the sodamide into a dry flask, when the sodamide was transferred a little at a time to a solution of 21 g. of γ -chlorobutyronitrile in 250 cc. of liquid ammonia in a Dewar flask, which was well shaken after each addition of the sodamide. Except when it was necessary to add or remove material, the flask was connected to a 152-cm. lime tower. The addition of the sodamide was made by means of a medicine dropper, which readily sucked up the fine sodamide together with the ether. From time to time some of the previously decanted ether was returned to the mortar in order to keep the sodamide completely covered by a layer of ether. After all of the sodamide had been transferred to the ammonia-ether solution, the mixture was shaken more or less steadily during the periods recorded in Table II.

At the cessation of the shaking the excess sodamide was neutralized by the addition of ammonium chloride (usually 2 g.), using solid phenolphthalein as indicator, when the solution was filtered through a Büchner funnel into a suction flask with the usual precautions. The suction flask was then provided with a stopper carrying a bubbling tube, which was connected through a stopcock to a source of dry air, and an exit tube, which was connected to the receiver. The latter was made by the sealing of a 76-cm. length of 8-mm. tubing 7.6 cm. from the bottom of a 2.5×25 cm. Pyrex test-tube, followed by the winding of the long tube around the test-tube and the sealing of an adapter to the end. This condenser was cooled in an ice-ammonium chloride mixture, which was contained in a liter vacuum flask. Suction was then carefully applied to the receiver, but with the stopcock practically closed, until the ammonia and some of the ether had been removed. At this point the receiver was connected with a 50-cc. modified Claisen-Vigreux distilling flask, wherein the ether solution of the nitrile was fractionally distilled under diminished pressure. Care was taken to recover any nitrile which was carried over into the receiver with the ether. The yields of cyclopropyl cyanide from the γ -chlorobutyronitrile with the other pertinent facts follow in Table II.

 TABLE II
 YIELDS OF CYCLOPROPYL CYANIDE

Run	γ -Nitrile, g.	NaNH_2 , g.	Time of addn., minutes	Reaction time, minutes	Yield, %	Yield (corr.), %
1	21	9	30	30	78.5	
2	21	10	40	20	74.7	81.3
3	21	10	30	60	89.7	
4	45	21.5	55	90	77.5	

The corrected yield in Run 2 takes into account the amount of γ -chlorobutyronitrile which was recovered. The combined runs, which boiled from about 35–38° at 16–19 mm., distilled completely from 133–135° at ordinary pressures.

Procedure 3. The Preparation of Cyclopropyl Cyanide in Ether.—A weight of 10 g. of finely ground sodamide, about 200 cc. of ether and 21 g. of γ -chlorobutyronitrile were transferred to a 500-cc. flask which was provided with a reflux condenser and a

stirrer. The temperatures and the durations of the reaction for three experiments will be found in Table III. The distillation process was the same as that described for Procedure 2. For the first two runs, in which chloronitrile was recovered, corrected yields have been given. In this procedure, however, more polymerization occurred than in Procedure 2, but less than in Procedure 1.

TABLE III
DATA FOR EXPERIMENTS

Run	Approx. temp., °C.	Reaction time, hrs.	Yield, %	Yield (corr.), %
1	30	7-8	41	64.7
2	Refluxing	16	69.4	80.2
3	Refluxing	25	74.7	..

Summary

1. Cyclopropyl cyanide may be obtained in 75-90% yields by the action of sodamide on γ -chlorobutyronitrile in a liquid ammonia-ether solution. The reaction in ether solution appears to be less efficient.

2. Trimethylene chlorobromide may be prepared in 90-94% yields by the action of phosphorus tribromide on trimethylene chlorohydrin.

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NOTES

The Cholesterol Content of Shrimp Waste.—The ethyl ether extraction of the dried shrimp and shrimp waste prepared by Vilbrandt and Abernethy¹ produced a viscous oil, dark red by transmitted light and soluble in the common organic solvents. According to elemental analysis the oil contains no sulfur, halogens, nitrogen or heavy metals.

Treatment of the oil with alcohol at 60° precipitated an insoluble brown resinous material and subsequent cooling of the alcoholic solution to 0° effected a fairly rapid separation of monoclinic crystals from the viscous, red oily residue.

Purification of Crystals.—Decolorization of the hot alcoholic solution of the crystals thus obtained with animal charcoal and subsequent crystallizations from hot alcohol produced a material which melted at 146.5°. Measurements under the microscope showed monoclinic plates with angles of 79.5 and 100.5°. The average yield of these crystals from three separate crystallizations and purifications is 19.08% on the basis of the original oil. The total quantity of sterols in the shrimp waste was not determined.

Identification.—The purified crystals were then treated with digitonin by the method of Windaus² and further identified by the Liebermann³

¹ F. C. Vilbrandt and R. F. Abernethy, "Utilization of Shrimp Waste," United States Fisheries Document No. 1079 (1930).

² A. Windaus, *Chem.-Ztg.*, **37**, 1001 (1913).

³ Oliver Kamm, "Qualitative Organic Analysis," John Wiley and Sons, Inc., New York, 1924, p. 123.