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The Rearrangement of N-Bromosuccinimide to β-Bromopropionyl Isocyanate[1]

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The proof of structure of the rearrangement product of N-bromosuccinimide is presented. A survey of the conditions for the rearrangement is included.

Recently others[2] and ourselves[3] have described the rearrangement of N-bromosuccinimide (NBS) to β-bromopropionyl isocyanate. This paper presents details of the proof of structure indicated previously, a survey of the conditions under which the rearrangement may occur and a brief discussion of the reactions of the isocyanate.

The product was formed in highest yield from the reaction of allyl chloride with NBS in the presence of trace quantities of benzoyl peroxide using chloroform as the solvent. Other conditions under which it was formed will be discussed later. The product was isolated by distillation at reduced pressure to yield β-bromopropionyl isocyanate (I). The infrared spectrum of I showed intense maxima at 2250, 1735 and 1400 cm.$^{-1}$; no bands were noted in the 3600–3000 or 1700–1500 cm.$^{-1}$ regions. The molecular weight was found to be 178 with a mass spectrometer; the partial mass spectrum is indicated in Table I.

TABLE I

MASS SPECTRUM OF β-BROMOPROPIONYL ISOCYANATE

m/e	Fragment	m/e	Fragment
178	$BrCH_2CH_2CONCO$	93	$BrCH_2$
135	$BrCH_2CH_2CO$	70	CONCO
107	$BrCH_2CH_2$	155	C_3H_2BrCl
98	CH_2CH_2CONCO		

It was apparent from the molecular weight that the product was an isomer of NBS. The infrared spectrum eliminated species having OH or NH. The 1735 cm.$^{-1}$ band in the infrared spectrum indicated the presence of carbonyl group, and the 2250 cm.$^{-1}$ band eventually was attributed to an isocyanate group[4] when the product was found to react vigorously with water to yield carbon dioxide. The mass spectrometer cracking pattern (Table I) then indicated the most probable structure for the product. Carbon and hydrogen analyses of I were in agreement with the postulated structure, but the nitrogen and halogen analyses were inconsistent with a simple molecular formula. The mass spectrograph indicated the presence of a small amount of chlorobromopropene (approximately 1%); X-ray absorption analysis indicated the product to contain 45 ± 2% bromine and 2 ± 1% chlorine. It is presumed that the discrepancy in the elemental analysis was caused by the presence of the chlorobromopropene. The isocyanate was too heat-sensitive to allow fractionation on any efficient column at hand.

The reaction of I with water led to the formation of carbon dioxide and β-bromopropionamide[2,5] which was identified by mixed melting point and comparison of its infrared spectrum with that of an authentic sample prepared from β-bromopropionyl bromide and ammonia. The reaction of I with methanol gave colorless needles, II, m.p. 137–138°; reaction of I with aniline in methylene chloride gave a product, III, m.p. 183–184°. These products were formulated as methyl β-bromopropionylcarbamate and N-phenyl-N′-β-bromopropionylurea, respectively, on the basis of elemental analyses and infrared spectra. The treatment of phenylurea with β-bromopropionyl chloride in dry tetrahydrofuran solution gave III, identified by comparison of melting points, mixed melting point, and infrared spectrum with III prepared from the product of the NBS rearrangement.

The synthesis of I was accomplished in the manner described by Belliter[6] for acetyl isocyanate, and the route was similar to that used by Martin and Bartlett[2] for I. Treatment of β-bromopropionic acid with phosphorus tribromide gave 59% of the previously unreported β-bromopropionyl bromide. The acyl bromide was allowed to react with dry, powdered silver cyanate to yield I whose infrared spectrum was superimposable upon that of I isolated from the rearrangement of NBS. Samples of II and III prepared from this sample of the isocyanate had melting points of 137–138° and 183–184°, respectively, undepressed upon admixture with the previously described samples; the infrared spectra of samples II and III from both sources were identical.

Effect of Conditions upon the Yield of Isocyanate.—Chloroform and bromoform are the only solvents in which the rearrangement has been found to occur with allylic halides. No rearrangement was noted when mixtures of N-bromosuccinimide, allyl chloride and benzoyl peroxide were refluxed in carbon tetrachloride, methylene chloride, *sym*-tetrachloroethane (both at reflux and at 80°), ethylene chloride, trichloroethylene, benzene, toluene, high boiling petroleum ether, nitromethane, dimethyl sulfoxide, excess allyl chloride or excess allyl bromide. Mixtures of carbon tetrachloride and chloroform have been used successfully, though both the qualitative rate of reaction and yield of rearrangement product diminished as the percentage of chloroform in the solvent was lowered. Detectable amounts of isocyanate were formed with as little of 0.5% chloroform present in

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[1] Presented at the Miami Meeting of the American Chemical Society, April, 1957.

[2] J. C. Martin and P. D. Bartlett, THIS JOURNAL, **79**, 2533 (1957); Abstracts of the Atlantic City Meeting of the American Chemical Society, September, 1956, p. 23-O.

[3] H. W. Johnson, Jr., and D. E. Bublitz, THIS JOURNAL, **79**, 753 (1957).

[4] H. Hoyer, *Ber.*, **89**, 2677 (1956), and references cited therein.

[5] C. S. Hamilton and C. L. Simpson, THIS JOURNAL, **51**, 3158 (1929).

[6] O. C. Belliter, *Ber.*, **36**, 3213 (1903).

the carbon tetrachloride. Martin and Bartlett[2] found the rearrangement to occur in carbon tetrachloride in the bromination of 1,4-endoxocyclohexane. Relatively large amounts of the ether were present in the reaction mixture.

The effect of the structure of the olefin on the yield of isocyanate is not clear as yet. The highest yields were obtained with allyl chloride (70%). The rearrangement also occurs with allyl bromide, methallyl chloride, 2,3-dibromopropene and 2-*t*-butyl-3-bromopropene.[7] On the other hand, crotyl bromide, 1-bromopropene, cinnamyl chloride, benzal chloride, benzyl chloride and benzotrichloride failed to yield the rearrangement product. Dr. J. C. Martin has noted,[8] and we have confirmed, that cyclohexene reacts with N-bromosuccinimide to give the isocyanate. Using chloroform solvent and benzoyl peroxide catalyst the rearrangement to I occurred if the ratio of NBS:cyclohexene was 2:1; if the ratio was 1:2, no isocyanate was found. We have noted that the rearrangement occurred when allylbenzene was refluxed with NBS and benzoyl peroxide in chloroform; no rearrangement was noted with styrene, propenylbenzene, isopropenylbenzene or toluene. Thus far the compounds with which the rearrangement has been noted are cyclohexene, allylbenzene, allylic halides having an open 1-position and 1,4-endoxocyclohexane.

A brief study of the effect of the concentration of allyl chloride upon the yield of isocyanate was made. With fixed concentrations of NBS (10%) and benzoyl peroxide (0.5%) in chloroform, the yield of isocyanate varied from 69 ± 5% to 65 ± 5% as the mole ratio of allyl chloride to NBS was altered from 1 to 0.1. When the ratio was dropped to 0.01, only a trace of isocyanate was noted. The rearrangement also was attempted without chloroform and without allyl chloride; no isocyanate was detected in either case. The qualitative reaction rates followed the yields. It appears that both the allyl chloride and chloroform are necessary for the rearrangement.

In one experiment it was found that the isocyanate was formed in 0.5% yield when one mole of N-bromosuccinimide was refluxed with 0.5 mole of benzoyl peroxide in carbon tetrachloride. In chloroform a solution of NBS and benzoyl peroxide could be refluxed for 24 hours without formation of the isocyanate. In benzene the reactants gave no isocyanate upon refluxing for periods of up to 24 hours. Apparently, though the chloroform and allyl chloride are not required, the presence of some solvent which can form relatively stable free radicals seems to be required.

The rearrangement appears to require a free radical type catalyst. The reaction occurred with benzoyl peroxide as a catalyst or upon illumination of the reaction system with a mercury arc lamp. Using carefully purified materials and a nitrogen atmosphere, allyl chloride, chloroform and NBS did not react upon refluxing for 24 hours (94% of the NBS was recovered unchanged). Likewise the addition of free radical inhibitors such as picric acid or trinitrobenzene precluded reaction, though the addition of an excess of peroxide (and consequent swamping of the inhibitor) caused the rearrangement to occur. When using low concentrations of reactants (0.05 molar), the reaction was inhibited by oxygen.

No rearrangement was noted when N-chlorosuccinimide or N-iodosuccinimide was allowed to reflux with allyl chloride and chloroform in the presence of benzoyl peroxide or upon irradiation of the mixtures with an unfiltered mercury arc using Vycor apparatus. Studies of other N-bromoimides are being carried out, and the results will be published at a later date.

The present rearrangement bears some resemblence to the Hofmann hypohalite reaction of amides since in both cases a N-haloamide rearranges to an isocyanate.[9] The conventional Hofmann reaction involves ionic species while the present rearrangement appears to involve free radical intermediates.

Experimental[10]

Reaction of N-Bromosuccinimide with Allyl Chloride.—A mixture of 500 ml. of dry chloroform,[11] 53.4 g. of NBS (0.30 mole), 2.3 g. of allyl chloride (0.03 mole), and 10 mg. of benzoyl peroxide was refluxed for 4 hours until no iodine was liberated from aqueous potassium iodide. Most of the chloroform was removed by distillation; the residue was distilled at reduced pressure to yield 32.0 g. (64%) of β-bromopropionyl isocyanate (I), b.p. 68–69° (10 mm.), $n^{27}\text{D}$ 1.4915. The analytical sample was distilled using a 15-cm. helices packed column, to give a product having identical physical constants. The product was unstable toward light, and a sample sealed off under 0.07 mm. pressure turned first orange and then red after standing exposed to ordinary room light for a period of 3 weeks. A similarly prepared sample kept at −78° protected from light remained colorless for 4 weeks; infrared spectrum (10% in carbon tetrachloride): 2980(vw), 2250(s), 1735(s), 1430(m, shoulder), 1400(s), 1340(w), 1275(doublet, w), 1220(w), 1200(w), 1180(w), 1170(w), 1155(w), 1075(s), 1030(m), 1015(m), 925(w), 900(w), 870(w).

Anal. Calcd. for $C_4H_4NO_2Br$: C, 26.99; H, 2.26; N, 7.87; Br, 44.90. Found: C, 26.8; H, 2.5; N, 7.2; Br, 49.0.

The mass spectrum values were: 178, 135, 107, 70, 98, 93. A small amount of mass 155 containing 1 Br and 1 Cl is also present in the sample. X-Ray absorption analysis for halogen indicated the sample to contain 45 ± 2% Br and 2 ± 1% Cl. A small sample of I was treated with water, the colorless solution was evaporated, and the residue recrystallized from chloroform to yield colorless needles of β-bromopropionamide,[5] m.p. 115–116°, not depressed by admixture with an authentic sample prepared from β-bromopropionyl bromide and ammonium hydroxide.

Olefins.—Reactions with allyl bromide, methallyl chloride, 2,3-dibromopropene, β-*t*-butylallyl bromide and allyl-

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(7) That all the compounds listed in this paragraph give β-bromopropionyl isocyanate has been confirmed through preparation of samples of II or III from each reaction mixture followed by comparison of melting points, mixed melting points and infrared spectra with authentic samples.

(8) J. C. Martin, Department of Chemistry, University of Illinois, Urbana, Ill., private communication.

(9) E. S. Wallis and J. F. Lane, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 267.

(10) Microanalyses were by Dr. Adelbert Elek, 4763 W. Adams, Los Angeles, Calif.; Fred Geiger, 312 Yale St., Ontario, Calif.; and by the analytical laboratories of the Dow Chemical Co., Midland, Mich. The mass spectra and X-ray absorption data were furnished by the Spectroscopy Laboratory of the Dow Chemical Co. Melting points are not corrected.

(11) In some experiments reagent grade chloroform purified by extraction with concentrated sulfuric acid, water and sodium hydroxide with subsequent drying over phosphorus pentoxide and distillation was used. No difference in product or yield was noted. The NBS was recrystallized from water and vacuum-dried in some cases. No differences in reaction between this material and the commercially available product (Matheson, Coleman, and Bell) were noted. The allyl chloride was dried over calcium chloride and distilled.

benzene were carried out as indicated for allyl chloride above. A peak was present at 2250 cm.$^{-1}$ in the infrared spectrum of the crude reaction mixture of each. No isocyanate was observed under the same conditions with 1-bromopropene, 1,3-dichloropropene or crotyl bromide. Increase of the mole ratio of allylic halide:NBS from 0.1 to 1.0 made no difference in the course of the reaction.

Reactions of NBS with cyclohexene were carried out as specified above for allyl chloride. When the mole ratio of cyclohexene:NBS was 2:1, no maximum was noted at 2250 cm.$^{-1}$ in the infrared spectrum of the crude reaction mixture. If the mole ratio was 1:2, the yield of isocyanate was estimated to be 20–30% on the basis of the infrared spectrum using the 2250 cm.$^{-1}$ maximum. Replacing the allyl chloride with allylbenzene also resulted in the formation of the isocyanate. No isocyanate was noted using styrene, isopropenylbenzene or propenylbenzene.

Solvents.—Replacement of the chloroform by bromoform in the reaction of allyl chloride with NBS resulted in the formation of the isocyanate, as judged from the appearance of the 2250 cm.$^{-1}$ peak in the infrared spectrum of the crude reaction mixture. Other solvents which were tried in the reaction of NBS with allyl chloride and benzoyl peroxide were low boiling petroleum ether, benzene, carbon tetrachloride, methylene chloride, trichloroethylene, *sym*-tetrachloroethane, ethylene chloride, toluene, nitromethane, dimethyl sulfoxide, excess allyl chloride and excess allyl bromide. No isocyanate was formed in these reactions as judged by the absence of the 2250 cm.$^{-1}$ maximum in the spectrum of the crude mixtures.

A series of experiments was carried out in which carbon tetrachloride–chloroform mixtures were used as solvents. The conditions were as shown in the first paragraph of the section.

$CHCl_3$, %	100	98	10	1	0.2
Yield, %	65	60–65	*ca.* 10	*ca.* 0.2	Trace

A reaction in which the solvent was 1:1 chloroform–benzene, other conditions as indicated in the first paragraph, gave no isocyanate.

Inhibition.—A reaction mixture in which the benzoyl peroxide was omitted, other conditions being as stated in the first paragraph, gave no isocyanate after 24 hours if the reactants were purified carefully and the reaction run under nitrogen. Addition of benzoyl peroxide to this mixture caused the rearrangement to occur normally. Substitution of picric acid or trinitrobenzene for the benzoyl peroxide inhibited the rearrangement. Addition of 1 mole/mole benzoyl peroxide/inhibitor caused the rearrangement to occur normally.

Other N-Haloimides.—The reaction of 0.0028 mole of allyl chloride with 0.0028 mole of N-chlorosuccinimide or N-iodosuccinimide in 5 ml. of chloroform with 10 mg. of benzoyl peroxide gave no isocyanate in 24 hours as judged from the absence of an infrared maximum at 2250 cm.$^{-1}$ in the infrared spectrum.

Methyl β-Bromopropionylcarbamate (II).—To 5 ml. of methanol in a test-tube was added dropwise 2.0 g. of β-bromopropionyl isocyanate; sufficient heat was generated to cause the solvent to boil. After standing 1.5 hours, the suspension was filtered and air-dried to yield 1.9 g. of colorless needles, m.p. 138.5–139.5°. The analytical sample was recrystallized from methanol, m.p. 138–139°.

Anal. Calcd. for $C_5H_8O_3NBr$: C, 28.60; H, 3.84; N, 6.67; Br, 38.05. Found: C, 28.7; H, 3.8; N, 6.5; Br, 38.0.

N-Phenyl-N′-β-bromopropionylurea (III).—To 3 ml. of aniline in 10 ml. of methylene chloride was added dropwise 2.0 g. of I; a vigorous reaction ensued, and a precipitate formed in the test-tube. The reaction mixture was allowed to stand for 1.5 hours, and then filtered to yield 3.0 g. of yellowish powder. Recrystallization from methanol gave 2.7 g. of colorless needles, m.p. 181–183°. The analytical sample was recrystallized from methanol, m.p. 183–184°.

Anal. Calcd. for $C_{10}H_{11}N_2O_2Br$: C, 44.30; H, 4.09; N, 10.33; Br, 29.47. Found: C, 44.7; H, 4.3; N, 10.3; Br, 29.3.

β-Bromopropionyl Bromide.—A mixture of 200 g. (1.31 moles) of β-bromopropionic acid, 127 g. (0.470 mole) of phosphorus tribromide and 400 ml. of benzene was heated under reflux for 6 hours, allowed to cool, and the organic layer was separated from a small viscous layer at the bottom of the flask. The solvent was removed and the residue was distilled through a Claisen head to yield 167 g. (59%) of the acyl bromide, b.p. 50–52° (4 mm.). The analytical sample was redistilled to yield product, b.p. 50–52° (4 mm.), $n^{27}\mathrm{D}$ 1.5320.

Anal. Calcd. for $C_3H_4OBr_2$: C, 16.67; H, 1.87; Br, 74.03. Found: C, 16.4; H, 1.7; Br, 74.4.

A small amount of the acyl bromide was added to 5 ml. of concentrated ammonium hydroxide and the solution evaporated to dryness. The residue was recrystallized from chloroform to yield colorless needles of β-bromopropionamide, m.p. 114–115°.[6]

β-Bromopropionyl Isocyanate (I).—β-Bromopropionyl bromide (10.0 g.) was treated portionwise with 5 g. of dry powdered silver cyanate[6] (from potassium cyanate and silver nitrate). An ice-bath was used to keep the temperature of the reactants at room temperature or below. The suspension was distilled through a 30-cm. Holtzmann column to yield 7 g. of material, b.p. 60–70° (10 mm.). The product was treated with 3 g. of silver cyanate in a similar manner, distilled and the treatment repeated (2 more times) until there was obtained 3.3 g. (50%) of material, b.p. 68–70° (10 mm.), $n^{29}\mathrm{D}$ 1.4910, whose infrared spectrum was identical with that of the previously described sample of I.

Anal. Calcd. for $C_4H_4NO_2Br$: C, 26.99; H, 2.26; N, 7.87; Br, 44.90. Found: C, 26.9; H, 2.3; N, 7.8; Br, 44.9.

N-Phenyl-N′-β-bromopropionylurea (III).—To 1.00 g. of phenylurea in 20 ml. of dry tetrahydrofuran was added 1.97 g. of β-bromopropionyl bromide at 0°. After 1 hour, 30 ml. of methanol was added and the mixture was evaporated on a steam-bath until crystals appeared. The mixture was then cooled on an ice-bath, and the solid was collected by filtration and recrystallized from methanol to yield 0.45 g. of colorless needles, m.p. 182–184°. The mixed m.p. with the sample of III prepared from β-bromopropionyl isocyanate was 181–183°.

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