

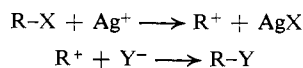
# Stereochemistry and Mechanism in Reactions of Silver Salts with Alkyl Halides. The Reaction of Silver Nitrite with Alkyl Halides<sup>1,2</sup>

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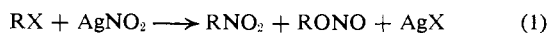
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**Abstract:** The steric course of the reaction of silver nitrite with optically active 2-iodooctane is independent of the solvent; in ethyl ether, acetonitrile, or petroleum ether the products have the inverted configuration. In contrast, the stereochemistry of the reaction employing  $\alpha$ -phenylethyl chloride is solvent dependent; in ethyl ether, and in benzene,  $\alpha$ -phenylethyl nitrite and  $\alpha$ -phenylnitroethane are produced with retention of configuration whereas in acetonitrile, cyclohexane, or petroleum ether they are formed with inversion.

The view that the reactions of silver salts with alkyl halides are "SN1-like" and routinely proceed *via* carbonium ions rests primarily on two kinds of observations.<sup>3</sup> One is that the reactivity sequence found when



alkyl halides are treated with silver salts is the same as the SN1 pattern of reaction rates (tertiary > secondary > primary). However, in 1955 it was shown that this reactivity pattern is not a valid basis for the routine assignment of a carbonium ion mechanism to the reaction of silver salts with organic halides.<sup>4</sup> Specifically, the reaction of silver nitrite with a wide variety of alkyl halides (eq 1) exhibits a number of the characteristics of



a carbonium ion process (including the SN1 rate pattern); but it also exhibits the characteristics of an SN2 process and is best regarded as proceeding *via* a transition state having both SN1 and SN2 character, the proportions varying gradually with the structure of the halide.<sup>4,5</sup> The view that reactions of silver salts with alkyl halides are ordinarily concerted processes in which the "pull" by the silver ion and the "push" by the nucleophile play a role is strongly supported by the independent studies of several other groups of investigators.<sup>6,7</sup>

(1) This research was supported, in part, by a grant from the Explosives Department of E. I. du Pont de Nemours and Co. and, in part, by the Air Force Office of Scientific Research, Office of Aerospace Research, U. S. Air Force, under AFOSR Grant No. 122-65.

(2) Paper XXIV in the series, "The Chemistry of Aliphatic and Alicyclic Nitro Compounds," presented at the 144th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1963, Abstracts, p 20M. For the preceding paper in this series see R. C. Kerber, G. W. Urry, and N. Kornblum, *J. Am. Chem. Soc.*, **87**, 4520 (1965).

(3) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp 358, 387-389. Ingold has qualified his claim that these reactions proceed by way of carbonium ions with a footnote (p 358), "Metal-ion-catalyzed SN2-like substitutions may exist, but as yet no strong evidence for them has been forthcoming." However, he cites *no* evidence in support of this possibility and from the concomitant discussion it is clear that the qualifying statement is made with little, if any, conviction.

(4) N. Kornblum, R. A. Smiley, R. K. Blackwood, and D. C. Iffland, *J. Am. Chem. Soc.*, **77**, 6269 (1955).

(5) Only in the case of  $\alpha$ -phenylethyl chloride was the reaction with silver nitrite found to proceed by way of a carbonium ion<sup>4</sup> and, as will be seen from the present study, even this halide reacts by the concerted mechanism in acetonitrile and in petroleum ether. The possibility that *t*-butyl halides also react with silver nitrite by an essentially pure SN1 mechanism was recognized but, in contrast to the  $\alpha$ -phenylethyl case, no evidence was available on this point (*cf.* ref 4, p 6272).

The second type of observation cited in support of the idea that the reactions of silver salts with alkyl halides are "SN1-like" is that the stereochemical course of these substitutions follows the rules applicable to SN1 substitutions, and not the different rules of SN2 substitutions.<sup>3</sup> In other words, in their reactions with silver salts 2-octyl (and  $\alpha$ -phenylethyl) halides undergo substitution with inversion accompanied by racemization; in contrast, substitution by the SN2 mechanism simply occurs with inversion.<sup>3</sup>

Realization that the sweeping assignment of a carbonium ion mechanism to the reactions of silver salts with alkyl halides actually has no justification on kinetic grounds prompted us to investigate the stereochemistry of these processes. In the present paper we describe a study involving silver nitrite; in the one which follows<sup>3</sup> we describe the results of an investigation of the reactions of silver nitrate and summarize the situation as regards the mechanism of silver salt reactions. It may be stated at once that our stereochemical studies confirm the earlier conclusion<sup>4</sup> that silver salt reactions ought not be regarded as routinely proceeding *via* a carbonium ion mechanism.

**The 2-Octyl System.** A simple generalization describes the stereochemistry of the reactions of silver nitrite with 2-bromooctane<sup>9</sup> and 2-iodooctane. The products, 2-nitrooctane and 2-octyl nitrite, are always produced with inversion regardless of the solvent. Table I presents our results.<sup>10,11</sup>

**The  $\alpha$ -Phenylethyl System.** Here, in contrast to the 2-octyl system, the stereochemical course of the reac-

(6) J. A. Vona and J. Steigman, *J. Am. Chem. Soc.*, **81**, 1095 (1959); G. S. Hammond, M. F. Hawthorne, J. H. Waters, and B. M. Graybill, *ibid.*, **82**, 704 (1960).

(7) However, a discredited idea does not die easily: *cf.* S. Oae, *ibid.*, **78**, 4030 (1956); D. V. Banthorpe in "Rodd's Chemistry of Carbon Compounds," Vol. IA, 2nd ed, Elsevier Publishing Co., Amsterdam, 1964, p 278; D. J. Pasto and M. P. Serve, *J. Am. Chem. Soc.*, **87**, 1515 (1965). Incidentally, Banthorpe has a somewhat oversimplified description of the course of the reaction of silver nitrite with alkyl halides (p 274); a more precise description will be found in N. Kornblum, *Org. Reactions*, **12**, 103 (1962).

(8) N. Kornblum and D. E. Hardies, *J. Am. Chem. Soc.*, **88**, 1707 (1966).

(9) In ethyl ether (ref 4).

(10) In the 2-octyl series the iodide, nitrite and nitro compound all have the same sign of rotation when of the same configuration: N. Kornblum, L. Fishbein, and R. A. Smiley, *J. Am. Chem. Soc.*, **77**, 6261, 6266 (1955).

(11) While, as will be seen from the sequel, it is not a crucial matter for the present argument, it is of interest that little, if any, racemization occurs. See, in particular, p 6263 of ref 10.

**Table I.** Summary of the Reactions of Silver Nitrite with Optically Active 2-Iodoctane in Various Solvents<sup>a</sup>

Solvent	2-Iodo-octane, $\alpha_D$ , deg	2-Octyl nitrite, $\alpha_D$ , deg	2-Nitro-octane, $\alpha_D$ , deg
Ethyl ether <sup>b</sup>	-53.3	+3.12	+12.3
Petroleum ether	-18.9	+1.22	+5.67
Acetonitrile	-11.6	+0.71	+3.74

<sup>a</sup> All rotations are observed rotations of the pure liquid in a 1-dm tube at temperatures in the range 25–28°. <sup>b</sup> See ref 10.

tion depends on the solvent. Treatment of optically active  $\alpha$ -phenylethyl chloride in ethyl ether solution with silver nitrite gives the nitro compound and nitrite ester of the *same* configuration as the chloride.<sup>12</sup> However, when the reaction is conducted in cyclohexane the  $\alpha$ -phenylethyl nitrite and  $\alpha$ -phenylnitroethane are of the *inverted* configuration relative to the chloride. When the reaction is carried out in benzene it follows the same stereochemical course as in ethyl ether, *i.e.*, the nitrite ester and nitro compound are both formed with *retention* of configuration. Finally, in acetonitrile the nitrite ester and nitro compound have the *inverted* configuration. Table II summarizes these seemingly capricious results.

**Table II.** Summary of the Reactions of Silver Nitrite with Optically Active  $\alpha$ -Phenylethyl Chloride in Various Solvents<sup>a</sup>

Expt no.	Solvent	$\alpha$ -Phenyl-chloride, $\alpha_D$ , deg	$\alpha$ -Phenyl-ethyl nitrite, $\alpha_D$ , deg	$\alpha$ -Phenyl-nitro ethane, $\alpha_D$ , deg
1	Ethyl ether	+35.45	+8.47	-3.14
2	Ethyl ether	-17.97	-3.55	+0.88
3 <sup>b</sup>	Ethyl ether	-20.68	-4.25	+1.28
4 <sup>b</sup>	Ethyl ether	-43.65	-8.45	+2.80
5	Acetonitrile	-24.07	+3.77	-4.95
6	Acetonitrile	-38.79	+6.93	-3.59
7	Acetonitrile	-24.33	+3.67	-4.78
8	Benzene	+33.78	+8.95	-0.57
9	Benzene	+20.59	+4.13	-1.11
10	Benzene	-26.76	-0.41	+0.12
11	Cyclohexane	-37.90	+12.94	-4.72
12 <sup>c</sup>	Cyclohexane	+9.98	-1.88	+1.03
13	Petroleum ether (bp 35–37°)	-10.62	+2.72	-1.86

<sup>a</sup> All rotations are observed rotations of the pure liquid in a 1-dm tube at temperatures in the range 25–32°. <sup>b</sup> See ref 10. <sup>c</sup> We are indebted to Dr. W. D. Gurowitz for this experiment.

Although we shall discuss these data together with the results of experiments employing silver nitrate,<sup>8</sup> it is appropriate to emphasize here that, of the solvents employed, silver nitrite is only soluble in acetonitrile. It is extremely insoluble in both ethyl ether and in cyclohexane and is almost equally insoluble in benzene (*cf.* the Experimental Section). In these last three solvents the reaction almost certainly occurs on the surface of the silver nitrite.

(12) In the  $\alpha$ -phenylethyl series the chloride and nitrite ester which have the same sign of rotation belong to the same configurational series;<sup>10</sup> however,  $\alpha$ -phenylnitroethane has the opposite sign of rotation as the chloride and nitrite ester when it has the same configuration: N. Kornblum, W. D. Gurowitz, H. O. Larson, and D. E. Hardies, *J. Am. Chem. Soc.*, **82**, 3099 (1960). Our 1955 papers<sup>10</sup> employ the wrong configurational assignment for  $\alpha$ -phenylnitroethane.

## Experimental Section

Optically active  $\alpha$ -phenylethyl chloride and 2-octyl iodide were prepared as previously.<sup>10</sup> Silver nitrite was prepared as before<sup>18</sup> except that it was partially dried by washing with distilled methanol, with anhydrous ethyl ether, and was then dried to constant weight in a vacuum desiccator over concentrated sulfuric acid. Acetonitrile was distilled three times from phosphorus pentoxide and once from anhydrous potassium carbonate. The ethyl ether was Mallinckrodt anhydrous. Petroleum ether (bp 35–37°) was redistilled and kept over Drierite. The benzene and cyclohexane (Phillips research grade) were distilled from sodium.

All experiments and distillations involving silver nitrite or nitrite esters were conducted in total darkness. Illumination, when needed, was yellow light from a 15-w lamp covered with a Wratten series OA filter. All reaction vessels were flame dried, the solvent employed was distilled directly into the reaction flask, and reaction mixtures were protected from atmospheric moisture.

**Reactions of Optically Active  $\alpha$ -Phenylethyl Chloride with Silver Nitrite.** **A. In Benzene.** A stirred slurry of silver nitrite (110 g, 0.71 mole) and 275 ml of benzene was cooled to 5° under nitrogen.  $\alpha$ -Phenylethyl chloride (55.6 g, 0.39 mole,  $\alpha^{25D} + 33.78^\circ$ ) was added dropwise in 1 hr, after which the system was allowed to come to room temperature and stirred for 14 hr. At the end of this time a negative Beilstein test was obtained. The silver salts were removed by filtration and washed with benzene; the combined filtrate and washings were concentrated *in vacuo* and then separated into a light fraction and a residual oil by flash distillation. Rectification of the light fraction gave 34.0 g (58% yield) of  $\alpha$ -phenylethyl nitrite,  $n^{20D}$  1.4925,  $\alpha^{27D} + 8.95^\circ$ , bp 50° (5 mm). *Anal.* Calcd for  $C_8H_9NO_2$ : C, 63.57; H, 6.00; N, 9.27. Found: C, 63.31; H, 5.75; N, 9.41.

The residue from the flash distillation was dissolved in dry acetone and to this solution (under nitrogen) was added thiourea (20 g) and sodium iodide (40 g), with cooling. The mixture was agitated for 48 hr at room temperature and then poured into ice water overlaid with petroleum ether (bp 65–67°). The petroleum ether phase was washed with water, concentrated, and then washed repeatedly with 85% phosphoric acid. The phosphoric acid was washed with petroleum ether and discarded. The acid-washed oil was added to the petroleum ether which had been used to wash the phosphoric acid and the solution was thoroughly washed with distilled water, dried over anhydrous magnesium sulfate, and concentrated *in vacuo* to a tan oil whose infrared spectrum, taken on a film 0.025 mm thick, was free of nitrate ester, alcohol, and ketone bands.<sup>14</sup> Rectification gave 3.4 g (6% yield) of pure  $\alpha$ -phenylnitroethane,  $n^{20D}$  1.5216,  $\alpha^{25D} - 0.57^\circ$ , bp 62° (0.3 mm). *Anal.* Calcd for  $C_8H_9NO_2$ : C, 63.57; H, 6.00; N, 9.27. Found: C, 63.33; H, 6.13; N, 9.15.

**B. In Acetonitrile.** To a stirred, ice-cold solution of silver nitrite (115 g, 0.75 mole) in 300 ml of acetonitrile 60 g (0.43 mole) of  $\alpha$ -phenylethyl chloride ( $\alpha^{27D} - 38.79^\circ$ ) was added dropwise. After 100 hr at ice temperature a negative Beilstein test was obtained. On working up as in the preceding experiment there was obtained 23.1 g (36% yield) of  $\alpha$ -phenylethyl nitrite;  $n^{20D}$  1.4925,  $\alpha^{27D} + 6.93^\circ$ , bp 41° (3 mm). *Anal.* Calcd for  $C_8H_9NO_2$ : C, 63.57; H, 6.00; N, 9.27. Found: C, 63.75; H, 5.81; N, 9.19. The  $\alpha$ -phenylnitroethane (6.4 g, 9% yield) had  $n^{20D}$  1.5212,  $\alpha^{30D} - 3.59^\circ$ . *Anal.* Calcd for  $C_8H_9NO_2$ : C, 63.57; H, 6.00; N, 9.27. Found: C, 63.71; H, 6.21; N, 9.23.

**C. In Cyclohexane.** The reaction was carried out at 0–5° for 68 hr; 225 ml of cyclohexane, 45 g of  $\alpha$ -phenylethyl chloride (0.32 mole,  $\alpha^{25D} - 37.90^\circ$ ), and 75 g of silver nitrite were employed. This gave 23.1 g (48% yield) of  $\alpha$ -phenylethyl nitrite, bp 48.2° (5 mm),  $n^{20D}$  1.4923,  $\alpha^{25D} + 12.94^\circ$ . *Anal.* Calcd for  $C_8H_9NO_2$ : C, 63.57; H, 6.00; N, 9.27. Found: C, 63.85; H, 6.17; N, 9.31. The 4.5 g (9% yield) of  $\alpha$ -phenylnitroethane produced had

(13) N. Kornblum, B. Taub, and H. E. Ungnade, *ibid.*, **76**, 3209 (1954).

(14) In the 2-octyl and the  $\alpha$ -phenylethyl series the nitro compound produced by the reaction of silver nitrite with the halides is contaminated by small amounts of the corresponding nitrate ester which are not removed by distillation: N. Kornblum, N. M. Lichtin, J. T. Patton, and D. C. Iffland, *ibid.*, **69**, 307 (1947). The use of cold, concentrated sulfuric acid, developed in 1947, to remove nitrate ester works well in the 2-octyl series but results in decomposition of  $\alpha$ -phenylnitroethane. The alternate procedure described here converts the nitrate ester to the water-soluble thiuronium salt which can then be washed away from the  $\alpha$ -phenylnitroethane. Any ketones or alcohols present are removed by the phosphoric acid.

bp 57° (0.15 mm),  $n_D^{20}$  1.5212,  $\alpha_D^{20}$  -4.72°. *Anal.* Calcd for  $C_8H_9NO_2$ : C, 63.57; H, 6.00; N, 9.27. Found: C, 63.74; H, 6.25; N, 9.06.

**D. In Ethyl Ether.** The reaction was conducted at 0–5° for 24 hr; 40 g of  $\alpha$ -phenylethyl chloride,  $\alpha_D^{20}$  +35.45°, 75 g of silver nitrite, and 200 ml of ethyl ether were used. This gave 25.59 g (60% yield) of  $\alpha$ -phenylethyl nitrite,  $n_D^{20}$  1.4925, bp 53° (5 mm),  $\alpha_D^{20}$  +8.47°, infrared spectrum identical with that of an authentic sample. The 3.92 g (9% yield) of  $\alpha$ -phenylnitroethane, bp 78° (0.6 mm),  $n_D^{20}$  1.5216,  $\alpha_D^{20}$  -3.14°, exhibited no nitrate ester, hydroxyl, or carbonyl absorption in the infrared. *Anal.* Calcd for  $C_8H_9NO_2$ : C, 63.57; H, 6.00; N, 9.27. Found: C, 63.38; H, 5.97; N, 9.21.

**E. In Petroleum Ether.** This reaction was conducted at 0–5° for 92 hr using 200 ml of petroleum ether (bp 35–37°), 75 g of silver nitrite, and 42 g of  $\alpha$ -phenylethyl chloride,  $\alpha_D^{20}$  -10.62°. The  $\alpha$ -phenylethyl nitrite obtained had bp 44° (3 mm),  $n_D^{20}$  1.4920, and  $\alpha_D^{20}$  +2.72°, 28.6 g (63% yield). The  $\alpha$ -phenylnitroethane, 4.9 g (10% yield), had  $\alpha_D^{20}$  -1.86°,  $n_D^{20}$  1.5214, and bp 71° (1 mm). Here, the sodium iodide–thiourea treatment for removing  $\alpha$ -phenylethyl nitrite<sup>14</sup> was not employed so that the  $\alpha$ -phenylnitroethane probably contained a few per cent of nitrate ester.

**Reactions of Optically Active 2-Iodoctane with Silver Nitrite.**  
**A. In Petroleum Ether.** To a stirred slurry of 200 ml of petroleum ether (bp 35–37°) and 75 g (0.48 mole) of silver nitrite was added 72 g (0.3 mole) of levorotatory 2-iodooctane ( $n_D^{20}$  1.4881,  $\alpha_D^{20}$  -18.86°) over a period of 30 min. After an additional 24 hr at room temperature (negative halide test) silver salts were removed by filtration and the product was rectified. Dextrorotatory 2-octyl nitrite (light yellow),  $\alpha_D^{20}$  +1.22°,  $n_D^{20}$  1.4087, bp 40° (4 mm), was obtained (21.2 g). *Anal.* Calcd for  $C_8H_{17}NO_2$ : C, 60.34; H, 10.76; N, 8.80. Found: C, 60.60; H, 11.01; N, 9.02. A liquid had collected in the cold trap during the rectification; when it was rectified a total of 1.98 g of colorless liquid,  $n_D^{20}$  1.4125–1.4127, bp 38–42° (38 mm), which analyzed for octenes was obtained. *Anal.* Calcd for  $C_8H_{16}$ : C, 85.63; H, 14.37. Found: C, 85.72; H, 14.36.

In addition 6.60 g of a higher boiling colorless liquid was obtained by rectification of the reaction product, bp 58–60° (1 mm),  $n_D^{20}$  1.4275–1.4276. This showed absorption peaks at 6.15 and at 7.84  $\mu$  and was, therefore, contaminated with 2-octyl nitrate.<sup>15</sup> Since repeated rectification did not remove the nitrate ester recourse was had to the sulfuric acid method.<sup>14</sup> In this way 3.91 g (8% yield) of pure 2-nitrooctane,  $\alpha_D^{20}$  +5.67°,  $n_D^{20}$  1.4277, bp 54° (1 mm), was obtained; it did not show absorption peaks at 6.15 or 7.84  $\mu$ . *Anal.* Calcd for  $C_8H_{17}NO_2$ : C, 60.34; H, 10.76; N, 8.80. Found: C, 60.20; H, 10.72; N, 8.73.

**B. In Acetonitrile.** Levorotatory 2-iodooctane (24 g, 0.3 mole,  $n_D^{20}$  1.4883,  $\alpha_D^{20}$  -11.59°), diluted with three volumes of acetonitrile, was added in 30 min to an ice-cold solution of 25 g (0.16 mole) of silver nitrite in 200 ml of acetonitrile. After stirring for 13 hr at 0–5° the product was worked up as in A. A 5.0-g yield (32%) of dextrorotatory 2-octyl nitrite, pale yellow,  $n_D^{20}$  1.4089,  $\alpha_D^{20}$  +0.71°, bp 31° (3 mm), was isolated. The dextrorotatory 2-

nitrooctane (2.30 g) had bp 62° (2 mm),  $n_D^{20}$  1.4279,  $\alpha_D^{20}$  +3.74°. Its infrared spectrum showed no peaks at 6.15 or 7.84  $\mu$ . *Anal.* Calcd for  $C_8H_{17}NO_2$ : C, 60.34; H, 10.75; N, 8.80. Found: C, 60.24; H, 10.88; N, 8.99.

**The Solubility of Silver Nitrite in Organic Solvents.**<sup>16</sup> A static experiment employing ethyl ether has already established that the solubility of silver nitrite in this solvent is undetectably small.<sup>4</sup> A dynamic solubility test in ethyl ether, cyclohexane, and benzene was carried out; the following is a typical experiment. Silver nitrite (15.4 g) was placed in an alundum thimble and this in turn was put into a Soxhlet extractor. Because silver nitrite is heat labile,<sup>14</sup> the apparatus was provided with extra cooling for the circulating solvent; by means of a thermometer placed in the thimble it was established that the temperature of the circulating solvent was always close to 20°. The entire system was protected from atmospheric moisture by a drying tube. The silver nitrite was extracted for 13 days; during this time it was exposed to ca. 40 ml of fresh cyclohexane every 10 min. At the end of this time the thimble showed no loss in weight. The cyclohexane was removed by vacuum evaporation and 10 ml of 10% nitric acid was added to the flask which was then placed on a steam cone for 3 hr. The cooled solution was made up to 15 ml with water and 1.0 ml of 0.224 *N* sodium bromide was added whereby a slight haze was formed. Potentiometric titration of the excess sodium bromide required 8.12 ml of 0.0271 *N* silver nitrate. Thus 0.6 mg of silver nitrite had dissolved.

In a similar experiment 18.4 g of silver nitrite was extracted with ethyl ether for 11 days (ca. 80 ml of fresh solvent every 10 min). Again there was no weight loss for the thimble and, on adding 10% nitric acid and aqueous sodium bromide to the flask after the ethyl ether had been removed by evaporation, no precipitate was formed. A control test showed that 1 mg of silver nitrite would have given a readily discerned precipitate.

When 13.4 g of silver nitrite was extracted with benzene for 18 days (ca. 60 ml of fresh solvent every 10 min) the thimble lost 120 mg and the residue remaining after removal of the benzene gave an immediate precipitate when treated with 10% nitric acid and 5 ml of 0.224 *N* sodium bromide. Back titration with 0.0271 *N* silver nitrate required 13.10 ml. Thus, 0.76 mmole, 118 mg, of silver nitrite had dissolved in 18 days. A second experiment employing 17.8 g of silver nitrite and extracting for 5 days (ca. 80 ml of fresh benzene every 10 min) again gave a positive test for silver ion with sodium bromide (2.0 ml of 0.224 *N* NaBr) and the back titration required 12.50 ml of 0.0273 *N* AgNO<sub>3</sub>. Thus 0.106 mmole, 16 mg, of silver nitrite was extracted by the benzene in 5 days.

**Acknowledgment.** The senior author wishes to express his appreciation to the National Science Foundation for the award of a Senior Postdoctoral Fellowship for the academic year 1964–1965 during which time this paper was written. He is also indebted to the Eidgenössische Technische Hochschule, Zürich, where this year was spent in the Laboratorium für organische Chemie, for kind hospitality.

(15) N. Kornblum, H. E. Ungnade, and R. A. Smiley, *J. Org. Chem.*, **21**, 377 (1956).

(16) We are indebted to Dr. P. J. Berrigan for these experiments.