[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Basis for the Reported Optical Activity of the Salts of Aliphatic Nitro Compounds: 2-Nitroöctane

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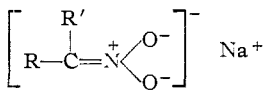
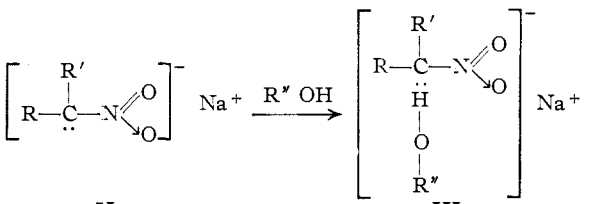
In 1927 it was reported that optically active 2-nitrobutane gives an active sodium salt when treated with sodium methoxide; by the action of bromine this salt was transformed into optically active 2-bromo-2-nitrobutane.[3] These findings were corroborated by a similar study employing optically active 2-nitroöctane.[4] Once again active salts were obtained which, upon treatment with bromine, gave optically active 2-bromo-2-nitroöctane. In addition, the active sodium salts of 2-nitroöctane were converted back to active 2-nitroöctane at −10 and at −70°. In the former instance the regenerated product had 24% of its original optical activity while the experiment conducted at −70° gave 2-nitroöctane with 71% of the original rotation. These demonstrations of asymmetry rendered the accepted structure for the salts of nitroparaffins, I, untenable and in its place structure II, in which the anion is sta-



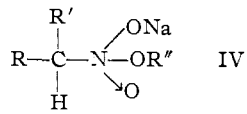
I

bilized by forming a hydrogen bond with the solvent to give III, was proposed.[3,4,5]



II III

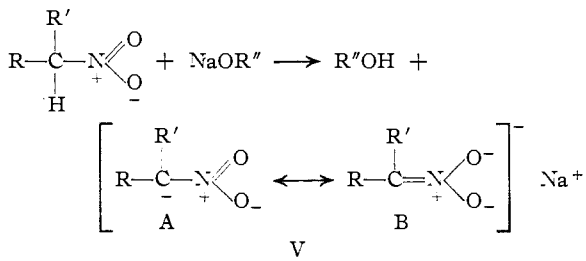
Alternatively, it has been suggested that instead of removing an *alpha* hydrogen the base, *e.g.*, R″ONa, may add to the nitro group with the formation of a salt such as IV,[6] thus leaving the



IV

asymmetric center unaffected. This proposal has, however, not met with general acceptance.[5,7]

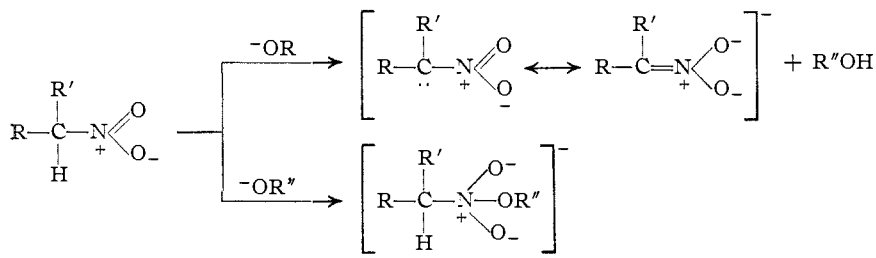
The theory of resonance leads to the view that the acidity of aliphatic nitro compounds is a consequence of resonance stabilization of the anion produced by removal of the *alpha* hydrogen; in fact, it is postulated that the contribution of form



V

VB is more important than that of structure VA.[8] From the resonance standpoint, therefore, the salts derived from optically active nitroparaffins of the type under discussion should be inactive.

It appeared that the resonance prediction and the experimental facts could be reconciled if it were assumed that the nitroparaffins are subject to two competing reactions when treated with alkali alkoxides. One reaction leads to racemization and the other to retention of configuration at the *alpha* carbon, the net result being partial retention of activity; *i.e.*



As a test of this hypothesis the preparation of optically active 2-nitroöctane having a deuterium atom in place of the *alpha* hydrogen was undertaken. This, when treated with alkoxide and then acidified, should give a regenerated 2-nitroöctane in which the percentage loss of optical activity and deuterium are identical.

However, in the orienting experiments with undeuterated, optically active 2-nitroöctane it be-

(1a) Allied Chemical and Dye Fellow 1944–1945.

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(2) X-R Fellow of the Purdue Research Foundation.

(3) Kuhn and Albrecht, *Ber.*, **60**, 1297 (1927).

(4) Shriner and Young, THIS JOURNAL, **52**, 3332 (1930).

(5) H. Gilman, ed. "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, ed. 2, Vol. I, p. 391.

(6) T. W. J. Taylor and W. Baker, "Sidgwick's Organic Chemistry of Nitrogen," new ed., Clarendon Press, Oxford, 1937, p. 239.

(7) Hass and Riley, *Chem. Rev.*, **32**, 401 (1943).

(8) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 67.

came apparent that, contrary to the accepted view,[4] the reaction of 2-bromoöctane with silver nitrite does not give a product consisting simply of 2-octyl nitrite and 2-nitroöctane. Further study revealed the presence of three additional compounds: 2-octanol, 2-octanone and 2-octyl nitrate, the last of which cannot be separated from 2-nitroöctane by the procedure used in the earlier investigation.[4,9] Thus, the 2-nitroöctane previously employed was contaminated with 2-octyl nitrate and, as will be shown below, the optical activity ascribed to the salts of 2-nitroöctane is actually due to this impurity.[10]

The 2-nitroöctane used at the beginning of this investigation was prepared according to the earlier workers[4] and had essentially the same physical constants as their material. In agreement with their observations, it was found that at room temperature the optical rotation of the nitro compound in sodium ethylate reached a constant value as soon as the solutions were mixed. The reading remained constant over a period of fifteen days and, upon acidification, the product had *ca.* 20% of the original activity. On the other hand, the report that operating at −70° yields regenerated 2-nitroöctane possessing 71% of the original rotation[4] appears to be a consequence of failure to allow salt formation to go to completion. It is clear from the data in the experimental portion of this paper that at −60 to −70° the reaction of 2-nitroöctane with sodium ethoxide is a very slow process which is still incomplete after five days. Given sufficient time, however, the reaction at −60 to −70° gives regenerated 2-nitroöctane which has undergone the same loss of activity as at room temperature.

The realization that the 2-nitroöctane contained an optically active impurity resulted from two observations:

(1) As shown below despite the fact that the *d*-2-nitroöctane originally possessed a lower rotation than the levo isomer, formation of the salt of *d*-2-nitroöctane followed by regeneration with acid gave a product with the same residual activity as the regenerated levo enantiomorph.[11]

l-2-Nitroöctane $[\alpha]^{24}D$ −13.9° —(excess NaOEt, room temp.)→ Sodium salt $[\alpha]^{25}D$ −2.5° —(excess alcoholic HCl)→ *l*-2-Nitroöctane $[\alpha]^{26}D$ −2.5°

d-2-Nitroöctane $[\alpha]^{25}D$ +4.5° —(excess NaOEt, room temp.)→ Sodium salt $[\alpha]^{25}D$ +2.7° —(excess alcoholic HCl)→ *d*-2-Nitroöctane $[\alpha]^{25}D$ +2.6°

Fig. 1.

(2) When the regenerated *d*-2-nitroöctane was subjected to the sodium ethoxide–hydrogen chloride cycle a second time it underwent no further loss of activity.

The "2-nitroöctane" was then split into two fractions by shaking with aqueous sodium hydroxide. About two-thirds went into solution, racemizing completely in the process. The insoluble portion was optically active and remained so even upon being dissolved in ethanolic sodium ethoxide. Since the "2-nitroöctane" was "analytically pure" it was anticipated that the contaminant would have the same or almost the same composition as 2-nitroöctane. However, the aqueous alkali insoluble fractions from three runs gave erratic analyses which did not bear out this expectation. Nor did acidification of the aqueous alkaline solution give a product which analyzed for 2-nitroöctane. These results, which are now understandable in light of subsequent findings, will be discussed in a forthcoming paper dealing with the action of alkali on the nitroparaffins.

Removal of 2-octyl nitrate, as well as any other impurities present in the "2-nitroöctane,"[10] was achieved by treatment with cold 96% sulfuric acid. The 2-nitroöctane then has the correct elementary composition, is optically active; $[\alpha]^{27}D$ +15.8 and −16.5°, and gives a negative test for nitrate esters.

Thus purified, 2-nitroöctane is completely soluble in aqueous sodium hydroxide and the resulting solution is devoid of optical activity; the 2-bromo-2-nitroöctane obtained upon bromination is also completely inactive. When ethanolic sodium ethoxide is employed as the base the sodium salt is again totally inactive and the 2-bromo-2-nitroöctane produced by brominating the salt is also racemic. Finally, the 2-nitroöctane regenerated upon acidification of the sodium salt is completely racemic.

These results bear out the prediction made from resonance considerations that the salts of optically active nitroparaffins should be inactive.[8] The conclusion that structure V is the correct one for the salts of aliphatic nitro compounds is also consonant with the various other properties of these substances. There remains, of course, the problem of explaining the optical activity reported for the salts of 2-nitrobutane.[3] It seems quite likely that these data are in error and this possibility is now being investigated in this Laboratory.

As noted earlier, 2-octyl nitrate is one of the products resulting from the interaction of silver nitrite and 2-bromoöctane; in a given run it has the same sign of rotation as the 2-nitroöctane.

(9) Although the reaction of alkyl halides with silver nitrite (the Victor Meyer reaction) has been known for some time the formation of nitrate esters has not been reported. Nor has the production of the corresponding alcohol and ketone (or aldehyde) been noted. This reaction is being investigated by Mr. E. P. Oliveto of this Laboratory.

(10) This may be an oversimplification since there is evidence (*cf.* Experimental Portion) that the 2-nitroöctane fraction contains material (in addition to 2-octyl nitrate) which has a higher b. p. and n_D than 2-nitroöctane. Whether this provides part of the activity attributed to the salts of 2-nitroöctane cannot be stated at present.

(11) These nitro compounds were prepared from samples of 2-bromoöctane which had identical optical purity. The reason for the rather extensive racemization which occurred in one case is not known.

The nitrate ester can be isolated from the "2-nitroöctane" cut (and also from lower boiling fractions) by taking out the 2-nitroöctane with aqueous alkali and then treating the residue with 85% phosphoric acid to remove the various other impurities.

The formation of 2-octyl nitrate apparently is a consequence of the thermal instability of silver nitrite which decomposes according to the equation[12,13]: $2\ AgNO_2 \rightarrow AgNO_3 + Ag + NO$.

When silver nitrite is subjected to the conditions employed in the preparation of 2-nitroöctane 40 to 60% is decomposed and silver nitrate, metallic silver and nitric oxide are formed.[14] This, coupled with the fact that silver nitrate readily reacts with 2-bromoöctane to give 2-octyl nitrate affords an explanation of the presence of the nitrate in the reaction product.

The 2-octanone and 2-octanol produced in the reaction between silver nitrite and 2-bromoöctane presumably are derived from 2-octyl nitrite which decomposes rapidly at 90 to 100° to give 2-octanone and 2-octanol,[15] a finding in accord with the thermal instability of other aliphatic nitrites.[16]

$$2RCH_2ONO \longrightarrow RCH_2OH + RCHO + 2NO$$

This instability clarifies the surprising finding that in only one preparation of 2-nitroöctane was a fraction isolated whose chemical and physical properties corresponded to those of 2-octyl nitrite, and even here, the material was not quite pure as demonstrated by its refractive index. That 2-octyl nitrite was also produced in the various other runs was demonstrated by the sulfanilic acid–α-naphthylamine color test.[17]

Acknowledgment.—It is a pleasure to record our indebtedness to Mr. M. Cenker, Miss S. Heller and Mr. E. P. Oliveto of this Department for their assistance in various phases of this work. Our thanks are also due the Allied Chemical and Dye Corporation and the Purdue Research Foundation for fellowships which expedited this investigation.

Experimental

2-Octanol.—(A) Eastman Kodak Co. White Label 2-octanol was purified *via* the acid phthalate ester according to Kao and Yen,[18] b. p. 77° at 15 mm.; $n^{20}D$ 1.4264; $n^{25}D$ 1.4244; d^{20}_4 0.8202. Literature value: $n^{20}D$ 1.4264[19,20]; $n^{20}D$ 1.4265[18]; $n^{25}D$ 1.4244[21]; d^{20}_4 0.8205[18]; d^{25}_4 0.8201–0.8202[19]; d^{20}_4 0.82008.[20] While other values for the density and refractive index of 2-octanol are recorded,[22,23,24,25] it seemed likely, from a study of these papers, that the determinations were carried out with incompletely purified 2-octanol.

(B) Part of the octanol employed was prepared by the action of methylmagnesium iodide on *n*-heptanal[21]; yield 60–90%, b. p. 76° (15 mm.); $n^{20}D$ 1.4264; d^{20}_4 0.8201.

***d* and *l*-2-Octanol.**—Racemic 2-octanol[26] was resolved according to Ingersoll.[27] The *d*-2-octanol distilled at 87° (20 mm.); $n^{20}D$ 1.4264; d^{20}_4 0.8202; $[\alpha]^{25}D$ +10.2° (no solvent); the *l*-2-octanol had a b. p. of 87° (20 mm.); $n^{20}D$ 1.4264; d^{20}_4 0.8201; $[\alpha]^{25}D$ −10.6° (no solvent).

***d*-2-Bromoöctane.**—The directions of the previous workers[4] were followed up to the point where the reaction mixture is decomposed with ice water. Following this the octyl bromide was separated from the aqueous layer and washed with three 10-ml. portions of cold concentrated sulfuric acid. The bromide was then successively washed with ice water, aqueous sodium bicarbonate and water. It was then dried over "Drierite," and rectified through a 12-inch modified Widmer column[28] fitted with a variable take-off head; yield 80–88%, b. p. 70° (10 mm.), $n^{20}D$ 1.4500, d^{20}_4 1.090, $[\alpha]^{25}D$ +31.0° (no solvent).

Anal. Calcd. for $C_8H_{17}Br$: Br, 41.44. Found: Br, 41.35.

***l*-2-Bromoöctane.**—This compound was prepared in the same manner as the dextro enantiomorph; yield 83–88%, b. p. 70° (10 mm.), $n^{20}D$ 1.4500; d^{20}_4 1.092; $[\alpha]^{25}D$ −30.5° (no solvent).

"*d* and *l*-2-Nitroöctane."—Using 61 g. of *d*-2-bromooctane, and following as closely as possible[29] the procedure of the previous investigators[4] 6.6 g. (11% yield) of "*l*-2-nitroöctane" was obtained; b. p. 96–97° (23 mm.), $n^{20}D$ 1.4284, d^{20}_4 0.921, $[\alpha]^{25}D$ −14.3 (c = 6, abs. ethanol).

Anal. Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 59.35; H, 10.66; N, 9.16.[30] The following constants are reported[4] for "2-nitroöctane": b. p. 100–103° (18 mm.), $n^{20}D$ 1.4292, d^{20}_{20} 0.9165, $[\alpha]^{25}D$ −10.8° (abs. ethanol).

That the "2-nitroöctane" thus prepared is a mixture was demonstrated by shaking it with 10% aqueous sodium hydroxide; about 25–30% of the "2-nitroöctane" failed to dissolve despite repeated treatment with 10% aqueous alkali for periods ranging up to seventy-two hours. The insoluble material was further processed as described under 2-octyl nitrate.

In several other preparations the reaction was run in a slightly modified manner. Thus 48 g. (0.3 mole) of silver nitrite was introduced into the reaction flask along with an equal weight of quartz sand which had been digested with hydrochloric acid and ignited. The flask was cooled to 0° and 50 g. (0.26 mole) of *l*-2-bromoöctane was added dropwise in the course of two hours, with stirring. Following this, the stirring at 0° was continued for four hours. The mixture was then heated at 120° for two hours with stirring. After coming to room tem-

(12) Centnerzwer and Checinski, *Bull. intern. acad. polonaise sci., Classe sci. mat. nat.* **A**, 156 (1935).

(13) Blumenthal and Checinski, *ibid.*, **A**, 166 (1935).

(14) This experiment was carried out by Miss Sabine Heller of this Department.

(15) Unpublished work by E. P. Oliveto of this Laboratory.

(16) E. W. R. Steacie, "Atomic and Free Radical Reactions," Reinhold Publishing Corp., New York, N. Y., 1946, p. 142.

(17) Bose, *Analyst*, **56**, 504 (1931).

(18) Kao and Yen, *J. Chinese Chem. Soc.*, **2**, 21 (1934).

(19) Coppock and Goss, *J. Chem. Soc.*, 1789 (1939).

(20) Svetlov and Vul'fson, *J. Applied Chem.*, (U. S. S. R.), **9**, 1613 (1936).

(21) Ellis and Reid, THIS JOURNAL, **54**, 1674 (1932).

(22) Naogi and Jatker, *Indian J. Physics*, **8**, 397 (1934).

(23) Whitmore and Herndon, THIS JOURNAL, **65**, 3428 (1933).

(24) Bruhl, *Ann.*, **203**, 29 (1880).

(25) Waterman and Neuyl, *Rec. trav. chim.*, **57**, 533 (1932).

(26) After it had once been demonstrated that pure 2-octanol could be obtained by the method of Kao and Yen[18] the pure 2-octyl hydrogen phthalate which is an intermediate was resolved before saponification.

(27) A. W. Ingersoll, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1944, Vol. II, p. 400.

(28) Smith and Adkins, THIS JOURNAL, **60**, 657 (1937).

(29) No mention is made of the quality of the silver nitrite used. Our silver nitrite was recrystallized by dissolving the Mallinckrodt product in water (preheated to 65°), filtering and cooling the filtrate to 0°. The resulting crystals were collected and washed with cold acetone. The yellow-green needles thus obtained were air dried to constant weight. All work was done with minimum exposure to light.

(30) Microanalyses by Miss Theta Spoor of the University of Illinois.

perature, the product was extracted with 30–60° petroleum ether, the solvent was removed by distillation, and the residue rectified through a 13-inch Stedmann column. There was obtained 10 g. of a fraction which had properties corresponding to those of "2-nitroöctane" (b. p. 92–97° at 12 mm., $n^{20}D$ 1.4284). This was chromatographed over an aluminum oxide–Celite column using low boiling petroleum ether as the eluent. After removing the petroleum ether the residue had $n^{20}D$ 1.4277; yield 7.3 g. (18%), $[\alpha]^{25}D$ + 4.5° (c = 10, abs. ethanol).

Anal. Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.30; H, 10.55; N, 8.82, 8.83. Lit. values,[4] b. p. 102–105° (23 mm.), $n^{20}D$ 1.4324, $[\alpha]^{25}D$ +15.84° (abs. ethanol).

By following this last procedure 40 g. of *d*-2-bromoöctane was converted to 7.4 g. (23% yield) of "*l*-2-nitroöctane," b. p. 84–87° (12 mm.), $n^{20}D$ 1.4277, $[\alpha]^{25}D$ −13.9° (c = 10.4, abs. ethanol).

Anal. Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.19; H, 10.70; N, 8.71, 8.55. Lit. values,[4] b. p. 100–103° (18 mm.), $n^{20}D$ 1.4292; $[\alpha]^{20}D$ −10.8° (abs. ethanol).

Despite the excellent analyses, these last two preparations of "2-nitroöctane" were found to be contaminated with 25–30% of aqueous alkali insoluble material. These samples of "2-nitroöctane" were used in the experiments described in Fig. 1 and also in the isolation of the non-racemizing, aqueous alkali insoluble component (see below).

Pure *d*- and *l*-2-Nitroöctane.—After attempts to isolate pure 2-nitroöctane by rectification had failed the following procedure was devised. Ninety grams (0.46 mole) of *l*-2-bromoöctane was treated with 120 g. (0.78 mole) of silver nitrite according to the earlier investigators.[4] After one distillation from a modified Claisen flask, the fractions having $n^{20}D$ 1.4275–1.4320 were combined and added to 96% sulfuric acid (precooled to 0°). Five ml. of acid was used for each ml. of material. The mixture was stirred by hand at 0° for five minutes. The resulting deeply colored solution was poured onto 150 g. of crushed ice covered with 50 ml. of 30–60° petroleum ether. The ether layer was separated and the aqueous phase extracted with more petroleum ether. The ether solutions were combined and most of the solvent removed by warming on the steam-bath in a current of air. The residue was extracted with four 50-ml. portions of 85% phosphoric acid. The organic layer, which separates completely only after some hours, was isolated, washed with water and then dried over anhydrous sodium sulfate. After removal of the petroleum ether the residual liquid was rectified through the 12-in. modified Widmer column.[23] There was obtained 4.2 g. (11% yield) of *d*-2-nitroöctane; b. p. 102–104° (20 mm.); $n^{20}D$ 1.4280; d^{20}_4 0.9166; m_D (calcd.) 44.76[31]; m_D (found) 44.69; $[\alpha]^{27}D$ +15.8° (c = 5, abs. ethanol).

Anal.[32] Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.23, 60.20; H, 10.91; 10.67; N, 8.80, 8.59.

The identical procedure was followed for the synthesis of the levorotatory isomer; from 135 g. of *d*-2-bromooctane 7.6 g. (12% yield) of *l*-2-nitroöctane was obtained; b. p. 103–105° (20 mm.), $n^{20}D$ 1.4281, d^{20}_4 0.9149, m_D (calcd.[31]) 44.76, m_D (found) 44.77, $[\alpha]^{25}D$ −16.5° (c = 17.5, abs. ethanol).

Anal.[32] Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.03; H, 10.44; N, 9.01.

These samples of 2-nitroöctane, unlike the earlier preparations, are completely soluble in 10% aqueous sodium hydroxide. Furthermore, in contrast to the earlier preparations, they give no color when treated with sulfuric acid containing diphenylamine.

(31) H. Gilman, ed. "Organic Chemistry," Vol. 2, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1751.

(32) Our thanks are due Messrs. W. L. Brown and H. L. Hunter of the Eli Lilly Research Laboratory for these analyses.

Experiments with "*d*- and *l*-2-Nitroöctane"

(a) Action of Ethanolic Sodium Ethoxide at 24 to 25° Followed by Acidification (Fig. 1).—To 1.05 g. of "*l*-2-nitroöctane" ($[\alpha]^{26}D$ −13.9) in 40 ml. of absolute ethanol was added 12 ml. of 0.72 *N* ethanolic sodium ethoxide. The resulting yellow solution was optically active, $[\alpha]^{25}D$ −2.5°, and still showed this rotation after fifteen days at room temperature.

After thirty hours at room temperature 15 ml. of the above solution was acidified at 22° with 5 ml. of 0.743 *N* alcoholic hydrochloric acid following which 3 ml. of water was added to dissolve the precipitated sodium chloride, $[\alpha]^{25}D$ −2.5°.

Following this same procedure a solution of 0.3 g. of "*d*-2-nitroöctane" ($[\alpha]^{25}D$ +4.5°) in 3 ml. of absolute ethanol was treated with 1.2 ml. of 1.89 *N* alcoholic sodium ethoxide: $[\alpha]^{25}D$ +2.7°, which value did not change in the course of twenty-five hours at room temperature. At the end of this time the solution was acidified at room temperature with 1.0 ml. of 2.432 *N* alcoholic hydrogen chloride. After centrifuging to remove sodium chloride, the acidified solution had $[\alpha]^{25}D$ +2.6°.

(b) Action of Ethanolic Sodium Ethoxide at −60 to −70° Followed by Acidification.—A solution of 1.38 g. of "*l*-2-nitroöctane" ($[\alpha]^{25}D$ −13.9°) in 50 ml. of absolute ethanol (precooled to −60°), was added to 15 ml. of 0.72 *N* alcoholic sodium ethoxide (precooled to −60°). A sample was withdrawn after three hours at −60° and allowed to come to room temperature, $[\alpha]^{24}D$ −2.3°. This rotation did not change after fifteen days at room temperature.

The main portion of the ethanolic ethoxide solution was kept at −60° for ten days. From time to time 5-ml. aliquots were withdrawn and ethanolic hydrogen chloride was added; the temperature of the reaction mixture was maintained at −60° throughout the acidification process and for twenty minutes thereafter. Following this, the solutions were brought to room temperature, one ml. of water was added to dissolve the sodium chloride, and rotations were taken. Table I summarizes the results of these experiments.

TABLE I

SALT FORMATION AND REGENERATION EXPERIMENTS WITH "*l*-2-NITROÖCTANE"

Temp. of salt formation, °C.	Temp. history of salt soln., °C.	Temp. of acidification, °C.	$[\alpha]^{25}D$	Activity retained, %
−60	30 hr., −60	22	−2.9	21
−60	30 hr., −60	−60	−8.3	60
−60	5 days, −60	−60	−4.7	34
−60	10 days, −60	−60	−4.3	31
−60	5 days, −60 then 15 min. at 25	−60	−2.9	21
24	30 hr., 24	22	−2.5	18

A similar set of experiments was carried out with "*d*-2-nitroöctane" ($[\alpha]D^{25}$ +4.5°). Here, 3-ml. samples con-

TABLE II

SALT FORMATION AND REGENERATION EXPERIMENTS WITH "*d*-2-NITROÖCTANE"

Temp. of salt formation, °C.	Temp. history of salt soln., °C.	Temp. of acidification, °C.	$[\alpha]^{25}D$	Activity retained, %
−70	1 hr., −70	−70	+4.5	100
−68	43 hr., −68	−68	+3.6	80
−69	5.5 days, −69	−68	+3.5	78
−69	16.5 days, −69	−67	+2.4	55
−68	42 hr., −68 and 20 min., 24	−68	+2.3	50
24	3 min., 24	24	+2.2	50
24	25 hr., 24	24	+2.5	55

taining 0.304 g. of the nitro compound in absolute ethanol were treated with 1.25 ml. of 2.27 *N* ethanolic sodium ethoxide and then acidified with 1.2 ml. of 2.43 *N* ethanolic hydrogen chloride. Table II records the conditions and results of these experiments.

(c) **Repetition of Sodium Ethoxide–Hydrogen Chloride Cycle.**—The fractions of "*l*-2-nitroöctane" whose rotation had reached $+2.4 \pm 0.2°$ (Table II) after the salt formation and acidification experiments were combined. The excess acid was neutralized with barium carbonate, the mixture was centrifuged and the supernatant liquid transferred to a distillation flask where the solvent was removed. The residue, when distilled at 1 mm. pressure, gave a light yellow liquid; $n^{20}D$ 1.4279; $[\alpha]^{24}D$ +2.8 (c = 5.2, abs. ethanol). A solution of 0.156 g. of this material in 3 ml. of absolute ethanol was added to 1.5 ml. of 0.846 *N* ethanolic sodium ethoxide. After nineteen hours at room temperature the solution was cooled to −69° and acidified to litmus with alcoholic hydrogen chloride. After ten hours the mixture was brought to room temperature, the precipitated sodium chloride was removed and the rotation of the solution measured: $[\alpha]^{24}D$ +2.8 (c = 3, abs. ethanol). This value remained constant even after thirty-six hours at room temperature.

(d) **Action of Aqueous Sodium Hydroxide.**—A 1.514-g. sample of "*d*-2-nitroöctane" ($[\alpha]^{25}D$ +4.5°) was shaken with 5 equivalents of 2.68 *N* aqueous sodium hydroxide for sixty-two hours at which time *ca.* 30% remained undissolved. The resultant mixture was extracted with 60–70° petroleum ether and the rotation of the ether solution was measured; $\alpha^{20}D$ +0.22. The aqueous layer was inactive.

After removing the petroleum ether, the aqueous alkali insoluble material was distilled; yield 0.25 g. boiling at 45–46° (0.5 mm.); $n^{20}D$ 1.4255; $[\alpha]^{24}D$ +11.3 (c = 2.4, abs. ethanol).

Anal.[30] Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 57.26, 57.17; H, 10.21, 10.28; N, 7.47, 7.55.

The inactive aqueous alkaline solution was acidified at 25° with 1.1 equivalents of glacial acetic acid whereupon an oily layer formed. This was separated and upon distillation gave 0.667 g. of product; b. p. 57–61° (0.5 mm.); $n^{20}D$ 1.4287. A solution of this substance in absolute ethanol was inactive.

Anal.[30] Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 61.68, 61.63; H, 11.13, 11.04; N, 8.78, 8.76.

In precisely the same way 0.895 g. of "*l*-2-nitroöctane" ($[\alpha]^{25}D$ −13.9°) was shaken with 2.68 *N* aqueous sodium hydroxide for forty-eight hours. At the end of this time an appreciable amount of material had not dissolved. The mixture was extracted with petroleum ether and the rotation of the extract measured; $\alpha^{25}D$ −0.18. The solvent was removed and 0.16 g. of a pale yellow liquid was obtained on distillation at 0.5 mm. This material was again shaken with 5.4 equivalents of 0.9 *N* aqueous alkali for sixty-six hours; apparently nothing went into solution. The insoluble material was taken up in petroleum ether and its rotation measured; $\alpha^{25}D$ −0.20°.

That portion of the "*l*-2-nitroöctane" which dissolved in the 2.68 *N* aqueous sodium hydroxide gave a solution which was completely inactive.

(e) **Racemic 2-Bromo-2-nitroöctane from the Sodium Salt of "*l*-2-Nitroöctane."**—A 5-g. portion of "*l*-2-nitroöctane" ($[\alpha]^{25}D$ −10.8) was shaken with five equivalents of 10% aqueous sodium hydroxide for twelve hours and the undissolved material taken up in 30–60° petroleum ether. The petroleum ether solution had $\alpha^{27}D$ −0.61. One gram of material remained upon removal of the petroleum ether and from it 2-octyl nitrate was isolated (see below under 2-octyl nitrate.)

The aqueous layer was devoid of optical activity. It was cooled in an ice-salt-bath and brominated according to the previous investigators.[4] The 3.5 g. of yellow oil thus obtained had $n^{20}D$ 1.4666, d^{20}_4 1.256, $[\alpha]^{27}D$ 0.00 (no solvent, 1-dm. tube). It was then chromatographed by pouring onto an aluminum oxide–Celite column and developing with low boiling petroleum ether. Most of the solvent was removed by blowing a stream of dry air over the solution at room temperature and the remainder by shaking at 30° in a vessel evacuated to 3 mm. The colorless residue had $n^{20}D$ 1.4668, d^{20}_4 1.258, m_D (calcd.), 52.55; m_D (found), 52.51. Thus purified, the 2-bromo-2-nitroöctane was still optically inactive.

Anal.[30,33] Calcd. for $C_8H_{16}NO_2Br$: C, 40.37; H, 6.75; N, 5.88; Br, 33.58. Found: C, 40.10, 40.20; H, 6.83, 7.31; N, 5.96; Br, 33.85.

The constants reported[4] for 2-bromo-2-nitroöctane are at variance with those of our material: $[\alpha]^{25}D$ −2.22°, $n^{20}D$ 1.4499, d^{20}_{20} 1.113; when 2-bromo-2-nitroöctane is prepared from pure *d*- and *l*-2-nitroöctane (see below) it has the same constants as the sample prepared from "*l*-2-nitroöctane" and is also optically inactive.

Experiments with Pure *d*- and *l*-2-Nitroöctane

(a) **Racemization of Pure *d*-2-Nitroöctane by the Action of Ethanolic Sodium Ethoxide.**—To a solution of 0.5 g. of *d*-2-nitroöctane ($[\alpha]^{27}D$ +15.8) in 10 ml. of absolute ethanol was added 10 ml. (2 equivalents) of 0.63 *N* ethanolic sodium ethoxide. The resulting solution had $[\alpha]^{27}D$ 0.00° (c = 2.5, abs. ethanol).

(b) **Racemic 2-Bromo-2-nitroöctane from the Sodium Salt of Pure *d*-2-Nitroöctane.**—The optically inactive ethoxide solution obtained from *d*-2-nitroöctane (see preceding paragraph) was cooled to 0° and treated with bromine as directed by the earlier workers.[4] The crude 2-bromo-2-nitroöctane thus obtained was dissolved in 20 ml. of diethyl ether; $[\alpha]^{24}D$ 0.00° (l = 2 dm.). It was then purified as described in an earlier section of this paper. The 0.5-g. of colorless product is slightly lachrymatory; $n^{20}D$ 1.4666, d^{20}_4 1.2553, m_D (calcd.) 52.55, m_D (found) 52.57. This sample of 2-bromo-2-nitroöctane is optically inactive (petroleum ether, c = 4). As pointed out in an earlier section, these constants are at variance with those reported by the earlier workers.[4]

Anal.[33] Calcd. for $C_8H_{16}NO_2Br$: C, 40.37; H, 6.75; N, 5.88; Br, 33.58. Found: C, 40.50, 40.63; H, 7.20, 7.11; N, 6.08, 5.97; Br, 33.73, 34.00.

(c) **Racemization of Pure *l*-2-Nitroöctane by the Action of Aqueous Sodium Hydroxide.**—One and three-fourths gram of *l*-2-nitroöctane ($[\alpha]^{25}D$ −16.5°) was shaken for twenty minutes with 8 ml. of 20% aqueous sodium hydroxide. The mixture was then diluted with 8 ml. of distilled water and shaken for an additional fifteen minutes. The *l*-2-nitroöctane had now dissolved completely and the resulting solution was devoid of optical activity (l = 2 dm.).

(d) **Racemic 2-Bromo-2-nitroöctane from the Sodium Salt of Pure *l*-2-Nitroöctane.**—The optically inactive aqueous alkaline solution obtained from *l*-2-nitroöctane (see preceding paragraph) was cooled to 0° and treated with bromine in the usual manner.[4] The crude 2-bromo-2-nitroöctane is optically inactive (diethyl ether, c = 10 at a very minimum; see below). It was purified as described in an earlier section; yield 2.0 g. (80%) of a colorless, slightly lachrymatory liquid, $n^{20}D$ 1.4666, d^{20}_4 1.2544, m_D (calcd.) 52.55, m_D (found) 52.61. This sample of 2-bromo-2-nitroöctane was optically inactive (low boiling petroleum ether, c = 10).

Anal.[33] Calcd. for $C_8H_{16}NO_2Br$: C, 40.37; H, 6.75; N, 5.88; Br, 33.58. Found: C, 40.74, 40.51; H, 6.70, 6.52; N, 5.81, 5.96; Br, 33.86, 34.11.

(e) **Action of Ethanolic Sodium Ethoxide at 25° Followed by Acidification.**—To 1.93 g. of *d*-2-nitroöctane ($[\alpha]^{27}D$ +15.8) in 10 ml. of absolute ethanol was added 10 ml. of 2.4 *N* ethanolic sodium ethoxide. The resulting solution, which was optically inactive (l = 2 dm.), was cooled at 0° and to it was added 10 ml. of 4 *N* alcoholic hydrogen chloride which had also been precooled to 0°. *Ca.* 10 ml. of solvent was removed at room tempera-

(33) Microanalyses by Dr. Carl Tiedcke, New York, N. Y.

ture in an air stream and the precipitated sodium chloride separated by centrifuging. The clear alcohol solution ($\alpha^{28}D$ 0.00°, l = 2 dm.) was poured into 200 ml. of water and the excess hydrochloric acid neutralized with sodium bicarbonate. Following this, the organic layer was subjected to the 96% sulfuric acid–85% phosphoric acid treatment used in the preparation of pure 2-nitroöctane. However, no 2-nitroöctane was isolated. Instead, 2-octanone (characterized as the *p*-nitrophenylhydrazone, m. p. and mixed m. p. 92–93°) was obtained. Apparently, the Nef reaction[34] is substantially complete under the conditions used to acidify the sodium ethoxide solution.

(f) **Action of Aqueous Sodium Hydroxide Followed by Acidification.**—To 1.47 g. of *l*-2-nitroöctane $[\alpha]^{29}D$ −16.5 was added 4.5 ml. of 6 *N* aqueous sodium hydroxide. The mixture was shaken for thirty minutes, diluted with 4 ml. of water, and then shaken for an additional two hours by which time solution was complete; $[\alpha]^{28}D$ 0.00 (l = 1, c = 14.7). The inactive solution was cooled to 0° and acidified with 15 ml. of 20% acetic acid (precooled to 0°). After two hours at room temperature the oil which had separated (*ca.* one ml.) was removed and then subjected twice to the 96% sulfuric acid–85% phosphoric acid treatment used for the isolation of pure 2-nitroöctane. After distillation at 20 mm., 0.15 g. of a colorless oil was obtained; $n^{20}D$ 1.4306, $[\alpha]^{28}D$ 0.00° (c = 25, abs. ethanol).

Anal. Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.25, 60.41; H, 10.63, 10.79; N, 9.07, 8.82.

By-products of the Reaction between 2-Bromoöctane and Silver Nitrite

As noted earlier, the reaction between 2-bromoöctane and silver nitrite gives not only 2-nitroöctane and 2-octyl nitrite but also 2-octyl nitrate, 2-octanol, 2-octanone and perhaps other compounds. The complexity of the mixture obtained is demonstrated by a typical run in which 90 g. of *l*-2-bromoöctane was treated with 120 g. of silver nitrite according to the earlier investigators.[4] However, contrary to the prescribed procedure, the reaction product was distilled from a modified Claisen flask but a single time. The results of this distillation are summarized in Table III and the isolation of pure components is discussed in the following paragraphs.

TABLE III

DISTILLATION OF *l*-2-BROMOÖCTANE–SILVER NITRITE REACTION MIXTURE

Fract.	B. p., °C., 22 mm.	Wt., g.	$n^{20}D$
1	Up to 55	1.2	1.4061
2	55–66	1.3	1.4076
3	66–70	2.2	1.4114
4	70–74	2.9	1.4122
5	74–78	3.8	1.4140
6	78–79	4.5	1.4159
7	79–83	3.1	1.4174
8	83–90	2.1	1.4220
9	90–93	1.9	1.4243
10	93–95	5.8	1.4250
11	95–99	5.8	1.4260
12	99–103	4.3	1.4275
13	103–106	3.5	1.4287
14	106–107	3.1	1.4300
15	107[a] up	2.2	1.4320

[a] Distilled at 15 mm.

(a) **2-Octanol.**—To 5 g. of material from the Victor Meyer reaction having a refractive index corresponding to 2-octanol (Fraction 11, Table III) was added 5.8 g. of phthalic anhydride and 6.3 g. of dry pyridine. The mixture was heated on a steam-bath for two hours, and was then poured into an excess of a mixture of 37% hydrochloric acid and ice. The oil which separated was taken up in benzene, the solvent was removed, and the residue rendered alkaline with aqueous sodium carbonate. The insoluble material was taken up in 30–60° petroleum ether and from this was isolated 2-octyl nitrate (see below). The aqueous layer was acidified and the 2-octyl hydrogen phthalate which crystallized was isolated by filtration and purified by two recrystallizations from 90% acetic acid; yield 2 g., m. p. 74.5–75°, a mixed m. p. with pure *d*-2-octyl hydrogen phthalate (m. p. 74.5–75°) gave no depression, $[\alpha]^{28}D$ +48.5 (c = 2, abs. ethanol), neut. eq. calcd. for $C_{16}H_{22}O_4$: 278, found 277; lit. values[27] $[\alpha]^{25}D$ +48°, m. p. (active) 75°, (racemic) 55°.

By this same procedure, 1 g. of the corresponding fraction from an *l*-2-nitroöctane preparation yielded 1.3 g. of *l*-2-octyl hydrogen phthalate; m. p. 73.5–74°, $[\alpha]^{29}D$ −44.3° (c = 2, abs. ethanol), neut. eq. calcd. 278, found 279.

Since 2-octyl nitrate is present in the fractions from which 2-octyl hydrogen phthalate was isolated, an experiment was carried out to ascertain whether or not the nitrate would undergo conversion to the phthalate. When 2 g. of pure 2-octyl nitrate was subjected to the above treatment no 2-octyl hydrogen phthalate was formed.

(b) **2-Octyl Nitrate: (1) From the Residue Remaining After Removal of 2-Octanol with Phthalic Anhydride.**—The petroleum ether solution set aside during the isolation of *d*-2-octyl hydrogen phthalate (preceding section) upon removal of the solvent left an oily residue which was shaken three hours with 5 ml. of 20% aqueous sodium hydroxide. To the resulting mixture was added 5 ml. of water and the shaking continued until the sodium salt of 2-nitroöctane had dissolved (*ca.* five minutes). The insoluble material was separated and washed with two 5-ml. portions of 85% phosphoric acid. The organic layer was taken up in 30–60° petroleum ether, washed with water and dried over anhydrous magnesium sulfate. After removal of solvent the residue was distilled at 20 mm. yielding 0.4 g. of *d*-2-octyl nitrate; $n^{20}D$ 1.4252, d^{20}_4 0.954, $[\alpha]^{27}D$ +10.2° (c = 3, absolute ethanol). After saponification with aqueous-ethanolic sodium hydroxide a sample of this material gave a positive Nitron test for nitrate ion.[35] The possibility of interference by nitrite ion was eliminated by the addition of hydrazine sulfate.[35] With ferrous sulfate, this nitrite free solution also gave a positive "brown ring" test for nitrate ion.

Pure, racemic 2-octyl nitrate (see below for preparation) has $n^{20}D$ 1.4250, d^{20}_4 0.951. The literature records the following constants for *d*-2-octyl nitrate[36] $n^{20}D$ 1.4301, d^{20}_{20} 0.954, $[\alpha]^{25}D$ +14.6°.

Anal.[30] Calcd. for $C_8H_{17}NO_3$: C, 54.85; H, 9.71; N, 8.00. Found: C, 55.09, 55.02; H, 9.68, 9.86; N, 8.03, 8.27.

It is noteworthy that the 2-octyl nitrate and the 2-nitroöctane isolated from this run are both dextrorotatory.

(2) **From the Aqueous Alkali Insoluble Component of "*l*-2-Nitroöctane."**—About 0.4 g. of the 1 g. of aqueous alkali insoluble material set aside in the earlier experiment entitled "Racemic 2-Bromo-2-Nitroöctane from the Sodium Salt of "*l*-2-Nitroöctane" was shaken for one hour with 10 ml. of 10% aqueous sodium hydroxide. The insoluble layer was separated and extracted twice with 5 ml. of 85% phosphoric acid. The undissolved material was taken up in petroleum ether, washed with water, and dried over magnesium sulfate. The solvent was removed and 0.2 g. of a colorless liquid was obtained on distillation at 2 mm.; $n^{20}D$ 1.4252, d^{20}_4 0.946, $[\alpha]^{24}D$ −10.7° (c = 2, abs. ethanol); lit. values,[36] d^{20}_{20} 0.951, $[\alpha]^{25}D$ −14.6°, $n^{20}D$ 1.4302. Racemic 2-octyl nitrate has $n^{20}D$ 1.4250 (see below for preparation).

Anal.[30] Calcd. for $C_8H_{17}NO_3$: N, 8.00. Found: N, 8.08, 8.10.

(34) Nef, *Ann.*, **280**, 263 (1894).

(35) W. W. Scott, "Standard Methods of Chemical Analysis," 5th ed., Vol. I, D. Van Nostrand Co., New York, N. Y., 1938, p. 635.

(36) Shriner and Parker, THIS JOURNAL, **55**, 766 (1933).

It should be noted that levorotatory 2-octyl nitrate was solated from a run in which *l*-2-nitroöctane was being prepared.

(c) **2-Octyl Nitrite.**—Fractions 1, 2 and 3 (Table III) were combined and rectified through the modified Widmer column.[28] There was obtained 2.8 g. of a pale yellow liquid, b. p. 51° (10 mm.), $n^{20}D$ 1.4092, d^{20}_4 0.861, $[\alpha]^{27}D$ +5° (*c* = 5, abs. ethanol). Pure, synthetic 2-octyl nitrite prepared in this Laboratory by two different procedures[37] has b. p. 50–51° (9 mm.), $n^{20}D$ 1.4082, d^{20}_4 0.8644; lit. values,[4] b. p. 86–90° (18 mm.), $n^{20}D$ 1.4279, d^{20}_{20} 0.852, $[\alpha]^{25}D$ +8.17° (abs. ethanol).

In common with the synthetic 2-octyl nitrite,[37] the product isolated from fractions 1–3 dissolves in 85% phosphoric acid with the liberation of brown fumes. It also gives a positive nitrite test with the Greiss-Ilosvay reagent[17]; with a solution of diphenylamine in 50% sulfuric acid the blue color characteristic of nitrites was obtained.

The 2-octyl nitrite isolated from fractions 1–3 was added to an ice-cold solution of *p*-toluidine in excess 4 *N* hydrochloric acid. The mixture was shaken for ten minutes at 0° and then treated with a solution of β-naphthol in 10% aqueous sodium hydroxide. After five minutes the solution was acidified with dilute hydrochloric acid and the red precipitate isolated by filtration. After recrystallization from glacial acetic acid the red azo compound melted 132–133° and a mixed m. p. showed no depression. Under the same conditions 2-octyl nitrate did not diazotize *p*-toluidine.

(d) **2-Octanone.**—Before derivatives of 2-octanone could be obtained it was necessary to destroy the 2-octyl nitrite which is present in the fractions containing 2-octanone. Thus, 2 g. of fraction 6 (Table III) was shaken with 5 g. of urea and 20 ml. of 85% phosphoric acid at 0° until solution was complete (*ca.* one hour). The product was then allowed to stand at 0° for ten hours and finally at 28° for two hours. The resulting solution was poured onto 20 g. of ice and the layer which separated was washed with water, dilute aqueous sodium hydroxide, and again with water. From half of the residual oil 2-octanone was isolated as the semicarbazone, m. p. 120–121°; mixed m. p. undepressed. The remainder of the oil was shaken for three hours with 10 ml. of saturated aqueous sodium bisulfite. The precipitate which formed was separated, washed three times with diethyl ether and then decomposed with dilute sulfuric acid. The resulting 2-octanone was characterized as the *p*-nitrophenylhydrazone; m. p. 90–91°, mixed m. p. undepressed. The presence of 2-octanone in fractions 5 and 7 (Table III) was also demonstrated by isolation of the semicarbazone as described above.

Under these conditions pure 2-octyl nitrite does not give the semicarbazone of 2-octanone. In contrast, if urea is not present the semicarbazone of 2-octanone is obtained.

Furthermore, 2-octyl nitrate also fails to give the semicarbazone of 2-octanone after being subjected to the urea-phosphoric acid treatment.

Decomposition of Silver Nitrite under the Conditions of the Victor Meyer Reaction[14]

Duplicating as closely as possible the conditions of the Victor Meyer reaction,[4] 6 g. of silver nitrite was heated with 60 ml. of benzene, 2-bromoöctane being omitted. The residue obtained was removed by filtration and analyzed as described below.

A weighed sample of the residue was extracted repeatedly with water (preheated to 70°); this dissolves any silver nitrite and nitrate. The nitrite content of the aqueous extract was found by titration with standard potassium permanganate. The total silver content of the extract was found by precipitating silver as the chloride. The silver nitrate present can then be calculated by difference.

The residue was next extracted with 6 *N* acetic acid (preheated to 50°) which dissolves any silver oxide present. Silver chloride corresponding to the silver oxide can be precipitated from the acetic acid solution by the addition of dilute hydrochloric acid. In no instance was any silver oxide found. The residue of metallic silver was dissolved in concentrated nitric acid and precipitated, after dilution, as silver chloride by the addition of dilute hydrochloric acid.

The results of this work are summarized in Table IV.

TABLE IV

	MOLES PER 100 G. OF RESIDUE		
Run	$AgNO_2$	$AgNO_3$	Ag
1	0.417	0.089	0.055
2	.260	.131	.132
3[a]	.256	.195	.222
4[a]	.324	.154	.196

[a] These decompositions were conducted in total darkness.

Racemic 2-Octyl Nitrate

(a) The nitrate ester was prepared by the customary procedure[36] in 69% yield, b. p. 76° (10 mm.), $n^{20}D$ 1.4250, d^{20}_4 0.951. The lit. values are b. p. 92.5–94.5° (18 mm.), $n^{20}D$ 1.4299, d^{20}_{20} 0.951.

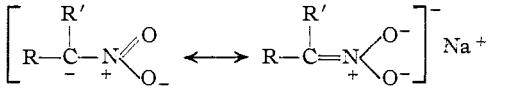
Anal.[30] Calcd. for $C_8H_{17}NO_3$: C, 54.85; H, 9.71; N, 8.00. Found: C, 55.08, 54.93; H, 9.82, 9.95; N, 7.99, 8.04.

(b) A mixture of 68 g. of silver nitrate, 47 g. of 2-bromoöctane and 80 ml. of benzene was subjected to the conditions of the Victor Meyer reaction.[4] After removal of the benzene by distillation under reduced pressure at *ca.* 30° the residue was rectified through the modified Widmer column[28]; yield 24 g. (59%), b. p. 76° (10 mm.), $n^{20}D$ 1.4250, d^{20}_4 0.953.

Summary

Contrary to earlier reports, optically active 2-nitroöctane does not give active salts when treated with sodium ethoxide or with sodium hydroxide: 2-bromo-2-nitroöctane prepared from these salts is also devoid of activity. Furthermore, 2-nitrooctane regenerated from salts by acidification is completely racemic.

It is concluded that the correct structure for the salts of aliphatic nitro compounds is



The reaction of 2-bromoöctane with silver nitrite does not give a product consisting solely of 2-octyl nitrite and 2-nitroöctane; in addition, 2-octanol, 2-octanone and 2-octyl nitrate are formed.

(37) Kornblum and Oliveto, THIS JOURNAL, **69**, 465 (1947).

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