concentration. Ribonucleic acid isolated by our procedure was found to be similar in regard to viscosity to the high molecular weight ribonucleic acid obtained from tobacco mosaic virus.[9] The sedimentation constant for rabbit liver sodium ribonucleate, a typical example of our product, indicates that this material probably has a higher molecular weight than ribonucleic acid prepared with the use of guanidine hydrochloride according to Volkin and Carter.[17] It was found by the latter authors that the sedimentation constant of rabbit liver ribonucleate is more than doubled when the *p*H is lowered from 6.8 to 4.8. In view of the fact that the sedimentation data obtained by Cohen and Stanley[9] for the freshly prepared nucleic acid from tobacco mosaic virus were obtained from sedimentations in acid solution at *p*H 4.9, it is possible that their material if it had been studied at *p*H 6.8 would have shown a sedimentation constant comparable to that observed for our ribonucleic acid. If this assumption is correct, our ribonucleic acid appears to have an average molecular weight close to that of the ribonucleic acid of tobacco mosaic virus. Analysis of our ribonucleate by means of the ultracentrifuge also indicated that this material is probably rather polydisperse.

The mild hydrolysis by acid or alkali was found to result in rather marked changes in the ultraviolet absorption spectrum as shown in Table II. The observed increases in absorption at 260 mμ after acid and alkaline hydrolysis are both slightly less than the increases obtained by Tsuboi[26] with mouse liver ribonucleic acid, although the control value of the extinction coefficient obtained by this author for untreated ribonucleic acid was higher than that reported above for our ribonucleic acid prepared with the use of sodium dodecyl sulfate. It is likely that the nucleic acid obtained by Tsuboi had already suffered degradation during the isolation procedure. It is apparent that the extraction of ribonucleic acid from tissues by the Schmidt–Thannhauser or the Schneider procedures for the analysis of the nucleic acids will result in changes in the absorption coefficients of the nucleates.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WEST VIRGINIA UNIVERSITY]

The Preparation of Nitro Compounds from Oximes. I[1]

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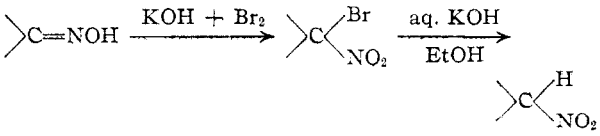
The conversion of oximes to nitro compounds by hypobromite oxidation to an α-bromonitro compound, followed by reductive debromination, has been examined. Only strictly alicyclic ketoximes give the corresponding nitro compounds and, even here, the yields are poor. With aldoximes and the oximes of aliphatic and aromatic ketones, the sequence fails completely.

In 1899 Forster[2] quantitatively prepared bromonitrocamphane from camphor oxime by treatment with potassium hydroxide and bromine. He later reduced the bromonitrocamphane with aqueous alcoholic potassium hydroxide and isolated nitrocamphane in 80% yield.[3] These reactions may be summarized as



Forster's preparation of bromonitrocamphane has been repeated by Ginnings and Noyes[4] and by Knapp and Lipp.[5] Cherkasova and Mel'nikov[6] have reported the preparation of chloronitro and bromonitro compounds from aliphatic aldoximes and ketoximes by the hypohalite oxidation[7] first described by Forster. However, their experimental procedure for the oxidation of aldoximes was not described in detail and has not been verified in this Laboratory.

This method of synthesizing aliphatic and alicyclic nitro compounds was undertaken in order to determine its generality, since it would be a very useful adjunct to the existing procedures for preparing nitro compounds.

Oximes of the 14 carbonyl compounds listed in Table I have been allowed to react with aqueous sodium hydroxide–bromine solution at 0–5° producing aliphatic and alicyclic bromonitro compounds in the indicated yields. The reaction failed with all aromatic oximes[8] and aldoximes. Pure bromonitro compounds readily purified by

(1) Presented in part before the Division of Organic Chemistry of the American Chemical Society, Atlantic City, N. J., September 17, 1952.

(2) M. O. Forster, *J. Chem. Soc.*, **75**, 1141 (1899).

(3) M. O. Forster, *ibid.*, **77**, 254 (1900).

(4) R. M. Ginnings and W. A. Noyes, THIS JOURNAL, **44**, 2567 (1923).

(5) H. Knapp and P. Lipp, *Ber.*, **73**, 915 (1940).

(6) M. Cherkasova and N. N. Mel'nikov, *J. Gen. Chem., (U.S.S.R.)*, **19**, 321 (1949).

(7) R. Robin, *Ann. chim.*, **16**, 77 (1921), investigated the oxidation of oximes with iodine and sodium carbonate and found that aromatic aldoximes yielded peroxides. With aliphatic aldoximes the aldehydes were reported to be reformed and ketoximes were unattacked by this reagent.

(8) The failure of this reaction with α-indanone, fluorenone and benzophenone oximes parallels the observation by I. D. DePaolini, *Gazz. chim. ital.*, **61**, 551 (1931), that ketoximes derived from phenyl ketones did not produce bromonitroso compounds when treated with bromine in pyridine solution.

vacuum distillation were obtained only from alicyclic ketoximes.

TABLE I

YIELDS OF BROMONITRO COMPOUNDS AND NITRO COMPOUNDS

Carbonyl cpd.	% Bromonitro from oxime cpd.	% Nitro cpd. from bromonitro cpd.
Cyclobutanone	74	4
Cyclopentanone	42	32
Cyclohexanone	46	28
2-Methylcyclohexanone	25	..
4-Methylcyclohexanone	22	..
Cycloheptanone	24	..
α-Indanone	0	..
Fluorenone	0[a]	..
Propanone	18[b]	0
Butanone	46	0
3-Pentanone	38	0
Benzophenone	0[c]	..
Butanal	0[d]	..
Heptanal	0	..

[a] Oxime recovery was 64–92%. [b] Bromoform and carbon tetrachloride identified in the reaction product. [c] Only benzophenone isolated. [d] Butanoic acid was isolated in 43% yield. Use of the Cherkasova and Mel'nikov proceddure described for acetaldoxime[6] led to butanoic acid as the only identifiable product.

Nitric acid was ordinarily used for this purpose in order to avoid the risk of further bromination or the very vigorous reaction resulting from the use of hydrogen peroxide–concentrated nitric acid mixtures. Distillation of the crude product without this auxiliary oxidation resulted in lower yields of bromonitro compounds and extensive decomposition in the distillation flask.

Except for fluorenone oxime no other oximes were recovered from these reaction mixtures even in those cases where no bromonitro compounds were isolated. After isolation of the bromonitro compounds, the reaction mixtures were frequently acidified with sulfur dioxide or dilute sulfuric acid. Extraction of these acidified mixtures yielded the corresponding ketone or carboxylic acid formed from the oxidation of the ketone or aldehyde. This was particularly frequent with aliphatic oximes. From methyl ketoximes identifiable amounts of bromoform and carbon tetrabromide also were obtained. In no case did the material balance approach 100% and the most favorable yields of bromonitro compounds were obtained with the lower cycloketoximes. The physical properties and halogen analyses of bromonitro compounds prepared from oximes are collected in Table II.

TABLE II

PHYSICAL CONSTANTS AND ANALYSES FOR BROMONITRO COMPOUNDS

Compound	B.p. °C.	Mm.	$n^{25}D$	d^{25}_4	Molar refraction Calcd.	Found	Br, % Calcd.	Found
1-Bromo-1-nitrocyclobutane	83	23	1.4910	1.628	32.34	32.02	44.40	44.34[a]
1-Bromo-1-nitrocyclopentane	99	20	1.4999[b]	1.573[b]	36.47	36.27	41.19	41.29
1-Bromo-1-nitrocyclohexane[c]	116	20	1.5070[b]	1.507[b]	41.09	41.08	38.41	38.38
2-Methyl-1-bromo-1-nitrocyclohexane	74	2	1.5029	1.451	45.71	45.25	35.98	35.77
4-Methyl-1-bromo-1-nitrocyclohexane	77	2	1.4945	1.421	45.71	45.55	35.98	35.95
1-Bromo-1-nitrocycloheptane	83	2	1.5095	1.456	45.71	45.65	35.98	35.90
2-Bromo-2-nitropropane[d]	71–74	50	1.5080	...				
2-Bromo-2-nitrobutane[e]	68	28	1.4676[b]	1.500[b]	34.06	33.54	43.91	43.84
3-Bromo-3-nitropentane	70	10	1.4662	1.421	38.67	38.20	40.77	40.83

[a] Ref. 12. [b] Measured at 20°. [c] S. Nametkin, *J. Russ. Phys. Chem. Soc.*, **42**, 584 (1910), reported $n^{19}D$ 1.5055, d^{19}_4 1.5148. [d] L. W. Seigle and H. B. Hass, *J. Org. Chem.*, **5**, 105 (1940), reported b.p. 73–75° at 50 mm. [e] Lit. values: $n^{18}D$ 1.4724; d^{18}_4 1.523. Ref. 7.

With cyclohexanone oxime it was found that the optimum formula ratio of oxime to total sodium hydroxide to bromine was about 1:24:8—essentially as indicated by Forster for camphor oxime—and this ratio of reagents was used with all other oximes. The preferred reaction temperature was 0–5° and the mixing time of the reagents had little effect on the yield of product as long as the moderately exothermic reaction was kept within the indicated temperature range with an ice–salt-bath. An intense blue or blue-green color developed immediately upon mixing the oxime with the hypobromite solution in every case that a bromonitro compound was formed. This color is attributed to the corresponding bromonitroso compound and it is inferred that the reaction mixture consists of a mixture of bromonitroso and nitro compounds. Rather than exposing the mixture to air—as reported by Forster—to complete the oxidation of the nitroso intermediate, the crude product was oxidized by shaking with aqueous bromine or nitric acid or a hydrogen peroxide–nitric acid mixture.

The aqueous potassium hydroxide–ethanol reduction of bromonitro compound reported by Forster to be nearly quantitative for the preparation of nitrocamphane was unsuccessful with aliphatic bromonitro compounds and only at best moderately satisfactory with alicyclic bromonitro compounds.

The properties and nitrogen analyses for alicyclic nitro compounds are summarized in Table III. For completeness the values for other nitrocycloalkanes obtained as described in the following paper are included. All nitro compounds gave a blue color indicating secondary structure when subject to the red-white-blue test.[9]

As displacement reactions in the cyclobutane series have been reported to be accompanied by rearrangement[10] the structure of the nitrocyclobutane by this synthesis was established by catalytic hydrogenation to cyclobutylamine. Cyclo

(9) H. B. Hass and E. F. Riley, *Chem. Revs.*, **32**, 373 (1943).

(10) J. D. Roberts and V. C. Chambers, THIS JOURNAL, **73**, 5034 (1951).

TABLE III

PHYSICAL CONSTANTS AND ANALYSES FOR NITROCYCLOALKANES

Compound	B.p. °C.	B.p. Mm.	$n^{25}D$	d^{25}_4	Molar refraction Calcd.	Molar refraction Found	N, % Calcd.	N, % Found[a]
Nitrocyclobutane	77	40	1.4432[c]	1.096[c]	24.47	24.47	13.85	13.62
Nitrocyclopentane[b]	90	40	1.4518	1.086	28.71	28.76	...	...
Nitrocyclohexane[d]	109	40	1.4620[c]	1.061	33.33	33.30	..	...
2-Nitro-1-methylcyclohexane[e]	100	20	1.4608	1.046	37.95	37.75	9.78	9.61
4-Nitro-1-methylcyclohexane[e]	102	20	1.4567	1.037	37.95	38.13	9.78	9.70
Nitrocycloheptane[e,f]	114	20	1.4710[c]	1.063[c]	37.95	37.64	...	...

[a] Ref. 12. [b] S. Nametkin, *J. Russ. Phys. Chem. Soc.*, **43**, 1605 (1911), reported $n^{23}D$ 1.4518, d^{23}_4 1.0776. [c] Measured at 20°. [d] S. Nametkin, *J. Russ. Phys. Chem. Soc.*, **40**, 1573 (1908), reported $n^{19}D$ 1.4612, d^{19}_4 1.068. [e] For preparation see following paper. [f] H. Stone, Ph.D. Thesis, The Ohio State University, 1950, reported $n^{20}D$ 1.4722; d^{20}_4 1.063.

butylamine thus obtained was identical with authentic cyclobutylamine prepared from cyclobutanecarboxylic acid *via* the Schmidt reaction. Furthermore, both samples of cyclobutylamine yielded identical benzenesulfonamide derivatives.

Infrared spectra of the alicyclic bromonitro compounds and nitro compounds listed in Tables II and III will be reported elsewhere.

Acknowledgment.—The authors are indebted to Dr. N. Kornblum for many helpful suggestions during the course of this work.

Experimental

The oximes were prepared from the corresponding ketones by reaction with hydroxylamine in the usual manner.[11] The yield of oximes was in each case 70–90%. All 14 oximes except cyclobutanone oxime have been previously described and the physical properties of the oximes prepared compared satisfactorily with literature values. Cyclobutanone oxime recrystallized from 30–60° petroleum ether melted 84–85°. *Anal.*[12] Calcd. for C_4H_7NO: C, 56.44; H, 8.29. Found: C, 56.31; H, 8.33.

Preparation of Bromonitro Compounds from Oximes.—The following procedure for the preparation of 1-bromo-1-nitrocyclohexane is representative of the generalized procedure applied to the oximes indicated in Table I.

A sodium hypobromite solution was prepared by slowly adding 192 g. (1.2 moles) of bromine to a cold solution of 176 g. (4.4 moles) of sodium hydroxide dissolved in 500 ml. of water. A second solution was prepared by adding 22.6 g. (0.2 mole) of cyclohexanone oxime to a solution of 16 g. (0.4 mole) of sodium hydroxide dissolved in 200 ml. of water. The hypobromite solution was cooled to 3–5° in an ice–salt-bath and with vigorous stirring the oxime solution was slowly added at such a rate that the reaction temperature remained below 5°. This required about one-half hour. After stirring an additional 15 minutes the blue-green reaction product was extracted from the reaction mixture with 35–37° petroleum ether. The blue extract[13] was washed with water concentrated to *ca.* 50 ml. by distillation on a steam-bath and the blue liquid remaining was shaken at room temperature with *ca.* 100 ml. of concentrated nitric acid until the blue color was removed. The oxidation mixture was diluted with *ca.* 100 ml. of water and extracted with 35–37° petroleum ether. The petroleum ether extract was washed with water, 5% aqueous sodium hydroxide and again with water. After drying over anhydrous sodium sulfate, the extract was concentrated and the residual liquid distilled under reduced pressure to yield 19.0 g. (0.092 mole) of 1-bromo-1-nitrocyclohexane having the properties indicated in Table I.

With solid high melting oximes, *i.e.*, fluorenone oxime, methanol was added to the initial alkaline oxime mixture to increase the oxime solubility.[14]

Potassium Hydroxide–Ethanol Reduction of Bromonitro Compounds.—The following preparation of nitrocyclohexane is typical of the reduction of bromonitro compounds shown in Table I.

Thirteen grams (0.063 mole) of 1-bromo-1-nitrocyclohexane was dissolved in 40 ml. of 95% ethanol and to this solution 3.9 g. (0.070 mole) of potassium hydroxide dissolved in the minimum amount of water was added. The reaction mixture was refluxed for two hours. After cooling to room temperature 10% aqueous potassium hydroxide was added to make the mixture distinctly alkaline. Any unreacted 1-bromo-1-nitrocyclohexane (usually negligible) was removed by extraction with 35–37° petroleum ether. The alkaline solution was cooled to 5° and acidified with 15% aqueous hydroxylamine hydrochloride.[15] After standing overnight the nitrocyclohexane was extracted with 35–37° petroleum ether. The extract was dried over anhydrous sodium sulfate, concentrated and vacuum distilled to yield 2.30 g. of pure nitrocyclohexane having the properties indicated in Table III.

Preparation of Cyclobutylamine. A. From Cyclobutanecarboxylic Acid.—Cyclobutanecarboxylic acid was converted to cyclobutylamine in 45% yield *via* the Schmidt reaction,[16] b.p. 82–83°. The N-cyclobutylbenzenesulfonamide was obtained by treating the amine with benzenesulfonyl chloride in the usual manner[17] and was recrystallized from aqueous methanol, m.p. 85–86°.

Anal.[12] Calcd. for $C_{10}H_{13}NSO_2$: N, 6.63. Found: N, 6.68.

B. From Nitrocyclobutane.—Adapting the procedure for low pressure catalytic hydrogenation of nitroparaffins recently described by Iffland and Cassis,[18] 0.65 g. (0.064 mole) of nitrocyclobutane was converted to cyclobutylamine in 85% yield, b.p. 83–84°. The benzenesulfonamide derivative was obtained as described above, m.p. 85–86°. No depression in melting point was observed when mixed with N-cyclobutylbenzenesulfonamide obtained in Part A.

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(11) E. W. Bousquet, "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., John Wiley and Sons, New York, N. Y., 1946, p. 313; D. D. Coffman, *et al.*, *J. Polym. Sci.*, **3**, 88 (1948); E. H. Huntress and F. J. Moore, THIS JOURNAL, **49**, 2621 (1927).

(12) Microanalysis by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

(13) This extract and the bromonitro compound obtained are potent lachrymators. Bromonitrocyclopentane was the most effective in this respect.

(14) When aqueous methanolic sodium hypobromite was used with butanal oxime, a neutral saturated product containing neither nitrogen or halogen was isolated in low yield. The nature of this material is being investigated.

(15) N. Kornblum and G. E. Graham, THIS JOURNAL, **73**, 4041 (1951).

(16) H. Wolff, "Organic Reactions," Vol. III, R. Adams, Ed., John Wiley and Sons, New York, N. Y., p. 327.

(17) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd Ed., John Wiley and Sons, New York, N. Y., 1948, p. 178.

(18) D. C. Iffland and F. A. Cassis, THIS JOURNAL, **74**, 6284 (1952).