dried over Drierite and fractionated through a column 10 in. long, 1/4 in. in diameter and packed with a tantalum spiral. The fraction boiling at 42.2° at 38 mm. weighed 1.12 g., n^{25}_{D} 1.5774, d^{25}_{4} 2.3853; molar refractivity calcd. 29.35, found 29.31. Auger reported b.p. 131° at 760 mm., d^{0}_{4} 2.41.[14]

Kinetic Runs.—All runs were made in 100-ml. volumetric flasks in a constant temperature bath maintained at 35.0 ± 0.1°. Chloroform was introduced into the reaction vessels by the use of a 0.25-ml. "tuberculin" syringe graduated in 0.01 ml. and found to deliver 0.250 ml. with an average deviation of 0.002 ml. The runs were carried out by dissolving 0.250 ml. of chloroform (at a known temperature) in 80 ml. of the aqueous salt solution under nitrogen in each of several reaction vessels. After the material had reached thermal equilibrium in the bath, 20 ml. of similarly equilibrated standard sodium hydroxide solution was added. "Points" were taken by quantitatively transferring the contents of a reaction flask into a titration flask containing a known amount (an excess) of acid. The contents were then titrated with standard sodium hydroxide solution to the phenolphthalein end-point. In most runs, a point was taken within one or two minutes, the hydroxide ion concentration determined used as the "initial concentration" and its difference from that originally added used in correcting the original concentration of chloroform to get its "initial concentration." This procedure eliminated several possible sources of error, such as that due to phosgene present as an impurity in the chloroform, but the resultant changes in the rate constants were usually negligible.

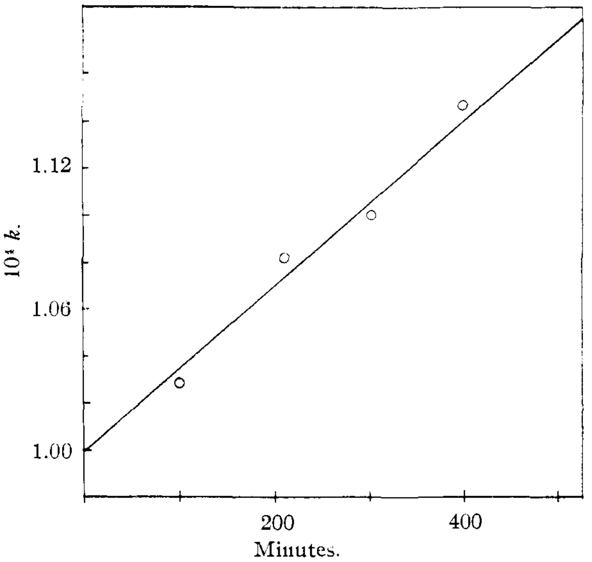

Fig. 2.—Integrated rate constants for the basic hydrolysis of chloroform in the presence of 0.160 N NaI (run 7) plotted against time.

Calculation of Rate Constants.—Rate constants were calculated from each point by use of the integrated rate equation[2]

$$k = \frac{2.303}{t(a[3+f] - b)} \log \frac{b(a-x)}{a(b-[3+f]x)}$$

where $a = [\mathrm{CHCl_3}]_0$, $b = [\mathrm{OH^-}]_0$, $x = \Delta[\mathrm{CHCl_3}]_t$, t = time (in seconds), k = rate constant (expressed in liters/mole of chloroform × seconds), and f = fraction of the chloroform hydrolyzed which gives formate. For f, a value of 0.15 was used in all cases, since the preliminary results of an investigation into the effect of reaction conditions on the value of f show that this value should not be far wrong in any of the present runs. It should also be noted that the value of k is rather insensitive to changes in f, particularly when chloroform is used in considerable excess as it was in all of the present cases. Data for a typical run are shown in Table III. A plot of the integrated rate constant *versus* time and the extrapolation to zero time for a run using sodium iodide are shown in Fig. 2.

TABLE III

KINETICS OF THE BASIC HYDROLYSIS OF CHLOROFORM IN THE PRESENCE OF 0.160 N NaCl AT 35.0°

$[\mathrm{CHCl_3}]_0 = 0.03095$, $[\mathrm{OH^-}]_0 = 0.03528$, 0.1776 N NaOH used for back titration

Time, sec.	Change in alkali titer, ml.	$k \times 10^4$, sec.$^{-1}$ mole^{-1} l.
5,940	2.10	1.95
10,800	3.56	1.93
17,040	5.37	2.02
24,600	7.18	2.02
28,320	7.93	2.00
	Av.	1.98 ± 0.04

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ATLANTA, GEORGIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE PURDUE RESEARCH FOUNDATION, PURDUE UNIVERSITY]

Vapor Phase Nitration of Aliphatic Ethers, Alcohols, Ketones and Carboxylic Acids[1,2]

BY H. B. HASS[3a] AND D. E. HUDGIN[3b]

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The vapor phase nitration technique has been extended to include aliphatic ethers, alcohols, ketones and acids. Nitration of aliphatic ethers produced nitro ethers and nitro alkanes. The alcohols gave nitro alkanes, and in one case a nitro alcohol. Ketones yielded nitro ketones and nitro alkanes. Propionic acid, on nitration, produced β-nitropropionic acid.

The vapor phase nitration of alkanes, cycloalkanes, aromatics and haloalkanes has been studied in our laboratories. We have now extended this type of nitration to include aliphatic ethers, alcohols, ketones and carboxylic acids. Many nitro derivatives of ethers,[4-6] alcohols,[7] ketones,[8-10] and

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(2) Acknowledgment is gratefully made to the Commercial Solvents Corporation for sponsoring the research fellowship on which this work was accomplished.

(3) (a) Sugar Research Foundation, 52 Wall St., New York 5, N. Y.; (b) Mallinckrodt Chemical Works, St. Louis, Missouri.

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carboxylic acids[11-15] are reported in the literature. We have successfully produced nitro derivatives of these types of compounds through direct nitration in the vapor phase.

Upon nitration of six aliphatic ethers, the nitro ethers were formed, as well as nitro alkanes produced by fission of carbon–carbon and carbon–oxygen bonds (see Table I). From preliminary evidence furnished by the vapor phase nitration of these aliphatic ethers, and based only on products formed, the following tentative generalizations have been made: 1. Simple, saturated aliphatic ethers yield products containing not more than one nitro group per molecule. 2. Any hydrogen atom in the ether, except α-hydrogens, is capable of being substituted by a nitro group. 3. No nitro ethers are formed as a result of fission of a carbon–carbon bond. 4. All possible nitro alkanes are formed by fission of a carbon–carbon or a carbon–oxygen bond. 5. Oxidation and/or hydrolysis reactions which accompany nitration yield aldehydes, ketones, alcohols, acids and nitric oxide. 6. The higher aliphatic ethers give higher yields of nitro compounds than the lower ethers probably because of the decreased probability of attack upon the alpha positions.

Vapor phase nitration of isobutyl alcohol produced small yields (less than 5%) of 2-methyl-2-nitro-1-propanol, 2-nitropropane and nitromethane. Ethanol, 1-propanol, 1-butanol and 2-methyl-1-propanol gave the expected nitro alkanes produced by fission of carbon–carbon bonds, but no nitro alcohols were found in the reaction mixture (see Table I). Rather than direct nitration of isobutyl alcohol having occurred, it is conceivable that NO_2 or N_2O_3 added to isobutylene (formed by dehydration of the alcohol), followed by the hydrolysis of the nitro nitrite or nitro nitrate formed.

TABLE I

Compound nitrated	Nitro compounds identified
Dimethyl ether	Nitromethane
Diethyl ether	Nitromethane, nitroethane, β-nitroethyl ethyl ether
Diisopropyl ether	Nitromethane, 2-nitropropane, β-nitroisopropyl isopropyl ether
Di-*n*-propyl ether	Nitromethane, nitroethane, 1-nitropropane, probably nitropropyl propyl ethers
Methyl *t*-butyl ether	Nitromethane
Di-*n*-butyl ether	Nitromethane, nitroethane, 1-nitropropane, 1-nitrobutane, probably nitrobutyl butyl ethers
Ethanol	Nitromethane
1-Propanol	Nitromethane, nitroethane
1-Butanol	Nitromethane, nitroethane, 1-nitropropane
2-Methyl-1-propanol	Nitromethane, 2-nitropropane, 2-nitro-2-methyl-1-propanol
Acetone	Nitromethane, probably nitroacetone
Diisopropyl ketone	Nitromethane, 2-nitropropane, 2,4-dimethyl-2-nitro-3-pentanone, 2,4-dimethyl-1-nitro-3-pentanone
Di-*n*-propyl ketone	Nitromethane, nitroethane, 1-nitropropane, 1-nitro-4-heptanone, 1,1-dinitropropane
Propionic acid	β-Nitropropionic acid

We have been able to nitrate acetone, diisopropyl ketone and di-*n*-propyl ketone in the vapor phase to form the expected mononitro ketones and nitro alkanes. Cyclohexanone produced only adipic acid and tar. The nitration of propionic acid produced β-nitropropionic acid.

The above listed generalizations and experimental results agree with the vapor phase nitration mechanism proposed by Bachman and coworkers.[26]

Experimental

Nitration Apparatus and Technique of Operation.—The nitration of the ethers, alcohols, ketones and acids required apparatus of design slightly modified from that previously employed in this Laboratory.[16]

The compound to be nitrated was passed through a calibrated jet into a preheater which was maintained at a temperature of 300°. The preheater consisted of a coil of eight turns (12 cm. in diameter) of 10-mm. Pyrex tubing immersed in a molten bath of potassium nitrate and sodium nitrite. The preheated vapor was then met by a fine stream of nitric acid (not preheated) immediately prior to entering the nitration coil. The mixed materials passed through the nitration coil, maintained at 400°, made of ten turns (12 cm. in diameter) of 10-mm. Pyrex tubing. The emerging vapor was condensed by passing through two condensers in a series, then into a flask surrounded by ice, and finally into a Dry Ice trap.

Due to the relatively low boiling points of acetone, dimethyl ether and diethyl ether, the apparatus was modified by removing the calibrated jet and allowing the vapors of these compounds to enter the preheater coil directly.

The reaction products separated into two layers, the lower aqueous layer containing recovered nitric acid plus a small amount of lower molecular weight nitro alkanes and oxidized products; the upper organic layer containing the unreacted compound, nitro derivatives of the compound and nitro alkanes. The organic layer from the reaction mixture was washed with a saturated sodium bicarbonate solution followed by a sodium bisulfite solution. The reaction mixture from the nitration of acetone did not receive the sodium bisulfite wash. The resulting mixture was then dried and distilled to remove the lower-boiling components. The distillate was extracted with 10% sodium hydroxide to remove the nitro alkanes; the resulting alkaline solution was separated, extracted with ether to remove the insoluble organic materials, and neutralized with glacial acetic acid. This neutralized solution was extracted with ether, the extracts dried and rectified to yield the nitro alkanes.

The high-boiling material left in the distillate flask after removing the low-boiling components, was rectified through the 15-plate modified Podbielniak column to yield the desired nitro derivatives. Yields for the most part were low, but no attempts were made to vary conditions to improve them. Yields of nitro compounds were about 20% in the case of ethers and ketones (except acetone) when calculated upon the compound being nitrated. Acetone, the alcohols and propionic acid gave yields of nitro compounds of 5% or less. In the case of ethers and ketones, roughly half of the nitro compounds formed were nitro derivatives of the starting compound.

Identification of Nitro Compounds. Nitromethane.—This compound was identified by its boiling point of 100–101° and by the formation of methazonic acid (reddish-brown color) when treated with NaOH. Further evidence was obtained by treating nitromethane with nitrous acid to form a nitrolic acid (red Na salt). This reaction is characteristic of primary nitro compounds.

Nitroethane.—This compound was identified by its b.p. of 112–114° (750 mm.), and the nitrolic acid reaction.

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Hydrolysis of the sodium salt gave an aldehyde which formed a 2,4-dinitrophenylhydrazone of acetaldehyde, m.p. 145°.

2-Nitropropane.—2-Nitropropane was identified by its b.p. of 118–118.5°, and by a pseudonitrole reaction,[17] which is characteristic of secondary nitro compounds. Further identification consisted in condensing 2-nitropropane with 2-bromo-2-nitropropane to form 2,3-dinitro-2,3-dimethylbutane, m.p. 210°.[18]

The 2-nitropropane was converted to acetone by dissolving in base and treating with mineral acid. The 2,4-diphenylhydrazone of acetone was then prepared and identified by its m.p. of 127°, which, in turn, showed no m.p. depression with an authentic sample.

1-Nitropropane.—1-Nitropropane was identified by its b.p. of 130–131°, and refractive index of 1.4016 at 20°, which checked the literature values.[19] It gave a nitrolic acid reaction. Acidification of the sodium salt gave an aldehyde that formed a 2,4-dinitrophenylhydrazone, m.p. 153°, which showed no m.p. depression with an authentic sample of the 2,4-dinitrophenylhydrazone of propanal.

1-Nitrobutane.—1-Nitrobutane was identified by its b.p. of 149–150°, n^{20}_D 1.4108, and density of 0.972 which checked the literature values.[7] It gave the nitrolic acid reaction.

β-Nitroethyl Ethyl Ether.—This compound gave the nitrolic acid reaction and had the following constants: b.p. 58–59° (5.5 mm.) (calcd. to 180° at 760 mm. pressure), n^{25}_D 1.4160, d^{25}_4 1.079, MR^{25} 27.63 (calcd. value 27.94). The b.p. as reported by Henry[4] was 178°, at 760 mm. The nitro ether was reduced to the corresponding amine with hydrogen at 1500 lb. pressure per sq. in. in the presence of Raney nickel catalyst. The amino ether, when purified by rectification, had the following constants: b.p. 108° (750 mm.), d^{25}_4 0.8410, n^{20}_D 1.4108. These values agree with those given in the literature for β-aminoethyl ethyl ether.[20] The neutral equivalent for the amino ether was 88 ± 2 (calcd. value is 89). The melting point of its picrate, 122°, agreed with that reported in the literature.[4]

β-Nitroisopropyl Isopropyl Ether.—The high-boiling fraction of the reaction mixture from the vapor phase nitration of diisopropyl ether was rectified to give a 20-ml. fraction, b.p. 47–49° (2 mm.), n^{25}_D 1.4218, d^{25}_4 0.995. This fraction gave a nitrolic acid reaction.

Anal. Calcd. for $C_6H_{13}NO_3$: N, 9.52. Found: N, 9.42, 9.55.

β-Nitroisopropyl isopropyl ether was reduced to β-aminoisopropyl isopropyl ether by the same method used above for β-nitroethyl ethyl ether. The amino ether, after being rectified, gave the following constants: b.p. 127° (750 mm.), n^{25}_D 1.4143, d^{25}_4 0.8400. The neutral equivalent was 116 ± 1 (calcd. 117). The amine formed a picrate, m.p. 158–159°.

Anal. Calcd. for $C_6H_{15}NO$: N, 11.97. Found: N, 11.82, 11.90.

Nitrobutyl Butyl Ethers.—On rectification of the high-boiling portion of the reaction mixture from the vapor phase nitration of di-*n*-butyl ether, a fraction of 83 ml., b.p. 102–105° (9 mm.), d^{25}_4 0.973, n^{25}_D 1.4280, resulted. This fraction gave a strong pseudonitrole reaction and a negative nitrolic acid reaction.

Anal. Calcd. for $C_8H_{17}NO_3$: N, 8.00. Found: N, 7.90, 7.95.

Reduction of this material with hydrogen and Raney nickel catalyst at 1600 lb. pressure per sq. in. gave an amine b.p. 55–56° (13 mm.) (calcd. to 178°, at 750 mm.), n^{23}_D 1.4250, d^{23}_4 0.8343. The neutral equivalent was 147 ± 2 (calcd. value was 145).

Anal. Calcd. for $C_8H_{19}NO$: N, 9.66. Found: N, 9.55, 9.61.

2-Methyl-2-nitro-1-propanol.—This nitro alcohol was identified by its m.p. of 87–88°. It showed no m.p. depression when mixed with an authentic sample of 2-methyl-2-nitro-1-propanol.

Nitroacetone.—The high-boiling fraction from the vapor phase nitration of acetone gave an odor of acetic acid, an acidic reaction in aqueous solution, a red color with ferric chloride, a yellow salt with an aqueous silver nitrate solution, was water-soluble and partially decomposed on distillation. These physical and chemical characteristics have been described in the literature[8,21–24] as typical of nitroacetone.

From the above evidence, presence of nitroacetone in the reaction mixture was indicated. Attempts at further purification and preparation of derivatives were unsuccessful primarily due to instability of the compound.

2,4-Dimethyl-2-nitro-3-pentanone.—In rectifying the high-boiling portions from the reaction product of the vapor phase nitration of diisopropyl ketone, a solid product was obtained. This material, after being crystallized twice from absolute alcohol, had a m.p. of 56–57°. It was insoluble in water and in a 10% NaOH solution, and gave a positive nitrogen test.

Anal. Calcd. for $C_7H_{13}NO_3$: C, 52.80; H, 8.23; N, 8.81. Found: C, 52.80, 52.90; H, 8.33, 8.26; N, 8.99, 8.87.

This nitro ketone was reduced to the corresponding amino alcohol with hydrogen at 1600 lb. pressure per sq. in. in the presence of Raney nickel catalyst. The following constants were obtained for the amino alcohol; n^{25}_D 1.4520, d^{25}_4 0.9046, neutral equivalent 132. These values check closely the values obtained on an authentic sample of 2,4-dimethyl-2-amino-3-pentanol.

An amine hydrochloride was prepared from the amino alcohol.

Anal. Calcd. for $C_7H_{16}NOCl$: Cl, 21.2. Found: Cl, 21.2.

2,4-Dimethyl-1-nitro-3-pentanone.—A liquid fraction, b.p. 81° (4 mm.), n^{24}_D 1.4492, d^{24}_4 1.058 and *MR* 40.25 (*MR* for a nitroheptanone is 40.18), was obtained from nitration of diisopropyl ketone. This liquid fraction, as distinguished from the solid fraction obtained from the nitration of diisopropyl ketone, gave the nitrolic acid reaction and was soluble in base. Attempts to prepare an oxime and a 2,4-dinitrophenylhydrazone failed. When reduced with hydrogen under pressure in the presence of Raney nickel catalyst, a black tar formed.

Anal. Calcd. for $C_7H_{13}NO_3$: C, 52.80; H, 8.23; N, 8.81. Found: C, 52.45, 52.33; H, 7.37, 7.44; N, 8.96, 8.90.

This nitro ketone was then dissolved in base, and treated with mineral acid to form 2,4-dimethyl-3-oxopentanal, which gave a bis-2,4-dinitrophenylhydrazone, m.p. 165–166°.

Anal. Calcd. for $C_{19}H_{19}N_8O_8$: C, 46.80; H, 4.57; N, 23.00. Found: C, 47.17; H, 4.23; N, 23.12.

1,1-Dinitropropane.—This compound, from the nitration of di-*n*-propyl ketone, had a b.p. of 40–42° (1.5 mm.) and gave a positive pseudonitrole reaction. On treatment with potassium hydroxide, a potassium salt was formed.

Anal. Calcd. for $C_3H_5N_2O_4K$: N, 16.27; mol. wt., 172. Found: N, 16.06, 16.15; mol. wt., 173.5, 174.0.

1-Nitro-4-heptanone.—This compound, produced by nitrating di-*n*-propyl ketone, gave a positive nitrolic acid reaction.

Anal. Calcd. for $C_7H_{13}NO_3$: C, 52.83; H, 8.17; N, 8.74. Found: C, 53.00, 53.00; H, 8.10, 8.20; N, 8.3, 8.4.

The semicarbazone was formed.

Anal. Calcd. for $C_8H_{16}N_4O_3$: C, 44.44; H, 7.41; N, 25.93. Found: C, 44.68; H, 7.78, 7.90; N, 26.12.

β-Nitropropionic Acid.—This compound, obtained from the vapor phase nitration of propionic acid, m.p. 65.6°, gave the nitrolic acid reaction, was soluble in water, alcohol and ethanol, and insoluble in ligroin. A m.p. of 66–67° is reported in the literature.[25,26]

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