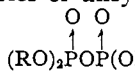
for carrying out the toxicity tests, to Dr. Howard Adler for his helpful advice, and to Dr. L. F. Audrieth for his criticisms in the preparation of the manuscript.

Summary

1. A series of unsymmetrical tetraalkyl pyrophosphates  $(RO)_2\overset{O}{\overset{\uparrow}{P}}O\overset{O}{\overset{\uparrow}{P}}(OR')_2$ were prepared, (a) by the action of dialkyl chlorophosphate on dialkyl phosphoric acid in the presence of a tertiary base and, (b) by the interaction of dialkyl chlorophosphate and trialkyl phosphate. Compounds whose preparation and properties are described are the dimethyl diethyl-, dimethyl di-*n*-propyl-, dimethyl di-isopropyl-, diethyl di-*n*-propyl-, diethyl di-isopropyl-, diethyl di-*n*-butyl-, di-*n*-propyl di-isopropyl-, and the di-isopropyl di-*n*-butyl pyrophosphates.

2. Alkaline hydrolysis of diethyl dibutyl pyrophosphate yields the diethyl and dibutyl phosphoric acids, thus establishing the structures of the unsymmetrical pyrophosphates prepared by the indicated procedures.

3. Comparative toxicity data for the unsymmetrical tetraalkyl pyrophosphates are presented. Substitution of two of the ethyl groups in tetraethyl pyrophosphate with two other alkyl groups results in only a slight decrease in toxicity.

4. Results of hydrolysis studies covering the dimethyl- and diethyl-dialkyl pyrophosphates show that the rates decrease as the size of the alkyl group becomes larger, except for compounds containing two isopropyl groups which are markedly more resistant. This decrease in reactivity is attributed to steric effects.

CHICAGO HEIGHTS, ILL. RECEIVED NOVEMBER 14, 1949

[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT DIVISION, COMMERCIAL SOLVENTS CORPORATION]

Effect of Strain on the Properties of Some 2-Nitroalkylamines

BY MURRAY SENKUS

Earlier work had shown that amines like isopropylamine, morpholine, N-methylaniline and others react with formaldehyde and nitroparaffins or with nitroalcohols derivable from formaldehyde and nitroparaffins to yield 2-nitroalkylamines in good yields; also, that hydrogenation of each of these compounds yields the corresponding polyamine.[1]

Further study of the above reaction has revealed that the yield of a 2-nitroalkylamine under a given set of conditions, for the most part, depends on the structures of the groups attached to the nitrogen in the starting amine. Thus, diisopropylamine (I), N-(1-methylpropyl)-isopropylamine (II), N-(tetrahydrofurfuryl)-isopropylamine (III) and some other amines react with formaldehyde and 2-nitropropane to give the desired 2-nitroalkylamines in much lower conversions than the amines studied earlier; also in contrast to the 2-nitroalkylamines isolated earlier,[1] the 2-nitroalkylamines derived from (I), (II), (III) and others exhibit marked instability. These properties, together with other data, are given in the experimental section of this paper.

It is believed that the low yields of some 2-nitroalkylamines reported herein, as well as the instability of some of the compounds, can be explained on the basis of steric effects. The arguments in support of this theory are advanced in the discussion section.

Experimental

The 2-nitroalkylamines were prepared according to methods described in the earlier work.[1] The yields of some 2-nitroalkylamines prepared by these methods were low, and in order to improve the yields of two of the nitro compounds, the following procedures were developed. **N-(2-Nitroisobutyl)-diisopropylamine** was prepared by distilling a mixture of 650 g. (6.4 moles) of diisopropylamine and 238 g. (2 moles) of 2-nitro-2-methyl-1-propanol through a laboratory column at a 10:1 reflux ratio. Water which formed in the reaction was removed as an azeotrope with the excess diisopropylamine, b. p. 73°. After the formation of water had ceased, the residue was rectified. This rectification gave the desired product in 87% conversion. **N-(2-Nitroisobutyl)-N-(tetrahydrofurfuryl)-isopropylamine** was prepared by refluxing a mixture of 143 g. (1 mole) of (III), 119 g. (1 mole) of 2-nitro-2-methyl-1-propanol and 200 ml. of toluene. Water which formed in the reaction was collected in a moisture trap. The conversion here was 78%.

Hydrogenation of the 2-nitroalkylamines was carried out according to the earlier methods.[1] With the exception of N-(2-nitroisobutyl)-N-(benzyl)-cyclohexylamine and of N-(2-nitroisobutyl)-N-(furfuryl)-cyclohexylamine the 2-nitroalkylamines failed to give the desired polyamines but gave, instead, complex mixtures. For example, N-(2-nitroisobutyl)-diisopropylamine gave the products set forth in Table I.

TABLE I

PRODUCTS FROM THE HYDROGENATION OF N-(2-NITROISOBUTYL)-DIISOPROPYLAMINE (160 G.)

Boiling range, °C.	Weight, g.	Neutralization equivalent	Remarks
35–39	4	60	Isopropylamine
39–50	3		
50–70	4		
70–75	4		
75–82	4		
82–84	42	99	Diisopropylamine
84–112	6		
112–113	7	114	N-(Methyl)-diisopropylamine
113–140	2		
140–200	21		

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[1] (a) Senkus, THIS JOURNAL, 68, 10 (1946); (b) Johnson, *ibid.*, 68, 12, 14 (1946).

TABLE II

SOME NEW 2-NITROALKYLAMINES AND DIAMINES

Amino	Boiling point °C.	Mm.	d^{20}_{20}	$n^{20}D$	Nitrogen, % Calcd.	Found
N-(2-Nitroisobutyl)-diisopropylamine	95–97	5	0.9547	1.4588	13.86	13.62
N-(2-Nitroisobutyl)-N-(methyl)-isopropylamine	92–93	10	0.9745	1.4288	16.09	16.00
N-(2-Nitroisobutyl)-N-(1-methylpropyl)-isopropylamine	71	0.25	0.9503	1.4532	13.01	12.78
N-(2-Nitroisobutyl)-N-(benzyl)-cyclohexylamine	M. p. 73.4				9.65	9.43
N-(2-Nitroisobutyl)-N-(tetrahydrofurfuryl)-isopropylamine	106–108	.1	1.0327	1.4684	11.47	11.94
N-(2-Nitroisobutyl)-N-(furfuryl)-cyclohexylamine	153–155	.1	1.0775	1.5010	10.00	10.08
N-(2-Nitroisobutyl)-N-(methyl)-phenylisopropylamine	135–138	.25	1.0217	1.5101	11.20	10.97
N-(2-Nitroisobutyl)-di-cyclohexylamine	M. p. 110.7				9.93	9.88
N-(2-Aminoisobutyl)-N-(benzyl)-cyclohexylamine	122	.2	0.9672	1.5247	10.61	10.83
N-(2-Aminoisobutyl)-N-(furfuryl)-cyclohexylamine	142–143	5.0	0.9892	1.4983	11.20	10.87

The 2-nitroalkylamines which were prepared during the present work, as well as the polyamines, are listed in Table II, together with some analytical data.

The reaction of **N-(2-nitroisobutyl)-isopropylamine with water** was studied in order to ascertain whether the formation of this 2-nitroalkylamine is reversible. To 100 g. of the compound was added 500 ml. of water and the mixture was distilled for nine hours through a 4-foot column packed with glass helices at a reflux ratio which was sufficiently high to maintain a vapor temperature of 33–34°. The distillation yielded 30.5 g. of isopropylamine; conversion, 83%. The residue was extracted with ethyl ether. Fifty grams of 2-nitro-2-methyl-1-propanol was isolated from this extract; conversion, 62%.

In another experiment, 100 g. of **N-(2-nitroisobutyl)-N-(isopropyl)-methylamine** was treated as above. The 2-nitroalkylamine reverted to N-(isopropyl)-methylamine and 2-nitro-2-methyl-1-propanol completely in three hours.

Discussion

It is believed that the variations in the yields of 2-nitroalkylamines reported herein, as well as the marked instability of some of these compounds, can be explained on the basis of the F-strain theory advanced by H. C. Brown.[2] The experimental evidence, which has been obtained in support of this theory, is now voluminous, but the data on diisopropylamine-trimethylboron and dipropylamine-trimethylboron are particularly suitable for the purpose at hand.[3] Brown and Pearsall reported that the former addition compound is appreciably dissociated at −28° and entirely dissociated at room temperature. In contrast, the dipropylamine-trimethylboron compound is only slightly dissociated at room temperature. Their examination of molecular models of the two complexes revealed that the bulkier isopropyl groups require considerably more space around the nitrogen atom than do the normal propyl groups, and, therefore, set up a face-to-face strain between the amine and the reference acid. This strain has been designated as F-strain. Brown and his collaborators have examined the properties of other addition compounds and their data show clearly that large F-strain is always associated with marked instability.

According to Cerf[4] the following reactions lead to the formation of 2-nitroalkylamines.

$$(2)\quad (R')(R'')NH + HCHO \longrightarrow (R')(R'')NCH_2OH$$

$$(3)\quad (R')(R'')NCH_2OH + HC(CH_3)_2NO_2 \longrightarrow (R')(R'')NCH_2C(CH_3)_2NO_2 + H_2O$$

In practice, it is more convenient to allow the amine to react with the nitro alcohol derived from formaldehyde and, when that procedure is used, the above reactions are preceded by the dissociation of the nitro alcohol into formaldehyde and nitroparaffin

$$(1)\quad HOCH_2\text{–}C(CH_3)_2NO_2 \longrightarrow HC(CH_3)_2NO_2 + HCHO$$

When the combined steric requirements of groups R′ and R″ are small, the conversions to 2-nitroalkylamines are high. The products from these reactions show marked stability. Hydrogenations of these 2-nitroalkylamines give the expected polyamines in high yields. Examples of such pairs are isopropyl and hydrogen, butyl and butyl, cyclohexyl and furfuryl, and other pairs with similar space requirements. However, as described in the Experimental part, even the stable nitro amines react with water under appropriate conditions to yield the starting materials. Thus N-(2-nitroisobutyl)-isopropylamine (R′ = H, R″ = isopropyl) reacts slowly with excess water at 100° to yield isopropylamine, formaldehyde and 2-nitropropane. This experiment establishes that reactions (2) and (3) are reversible even when the combined space requirements of groups R′ and R″ are small. It is logical to conclude, however, that the stability of the product derives from the fact that the equilibrium constants are very high.

An examination of molecular models reveals that strain is present in N-(hydroxymethyl)-dialkylamines and in 2-nitroalkylamines when R′ is isopropyl and R″ is tetrahydrofurfuryl, 1-methylpropyl, isopropyl or methyl. The strain in these compounds like the F-strain in Brown's addition compounds would be expected to make them unstable. In other words, when R′ and R″ have the structures specified above, the equilibrium constants in reactions (2) and (3) are much lower, and in some experiments are actually less than unity. For example, it is estimated on the basis of yields, that when R′ and R″ are isopropyl groups the equilibrium constant for equation (3) is approximately 0.4. Consequently, N-(2-nitroisobutyl)-

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(2) Brown, Taylor and Gerstein, THIS JOURNAL, **66**, 435 (1944).

(3) Brown and Pearsall, *ibid.*, **67**, 1765 (1945).

(4) Cerf, *Bull. soc. chim.*, [5] **4**, 1451 (1937).

diisopropylamine is highly dissociated in the presence of water. When R′ is methyl and R″ is isopropyl (N-(2-nitroisobutyl)-N-(isopropyl)-methylamine), the equilibrium constant is approximately 300. The stability in the presence of water is much better, although it can be seen from the results in the Experimental section that the 2-nitroalkylamine dissociates readily in the presence of water. In contrast, N-(2-nitroisobutyl)-isopropylamine, in which the combined steric requirements of the groups R′ and R″ are much smaller, dissociates to a much lesser extent under the same conditions.

Hydrogenation of the above 2-nitroalkylamines provides additional evidence of their instability. Each was degraded to a mixture of amines of lower molecular weights. For example, hydrogenation of N-(2-nitroisobutyl)-diisopropylamine yielded among other amines isopropylamine, diisopropylamine and N-(methyl)-diisopropylamine. The mechanism of the formation of these compounds is obscure but it seems reasonable to attribute at least some of the degradation to reaction of the 2-nitroalkylamines with water which forms as soon as some of the nitro groups are hydrogenated. Other reactions which may contribute to the degradation are hydrogenolyses of either one or both of the methylene bonds. There is considerable strain at this location in the molecule, thus weakening the bonds and making them susceptible to cleavage by catalytic hydrogenation.

It should be noted that steric strain in the 2-nitroalkylamines does not lead to thermal instability. For example the highly hindered N-(2-nitroisobutyl)-diisopropylamine distilled at 95-97° at 5 mm. without any decomposition. Additional evidence of excellent thermal stability of 2-nitroalkylamines with bulky groups on the nitrogen can be obtained by an examination of the boiling points that are listed in Table II.

Summary

Some new 2-nitroalkylamines have been prepared from formaldehyde, 2-nitropropane and dialkylamines.

In contrast to earlier data, some of the new compounds exhibit marked instability in the presence of water, and on hydrogenation are degraded completely to amines of lower molecular weights.

The steric requirements of the alkyl groups in the dialkylamines have been considered and it is suggested that the instabilities of the 2-nitroalkylamines are attributable to steric strain.

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Dielectric Constants, Viscosities, Densities, Refractive Indices and Dipole Moment Calculations for Some Organic Halides[1]

BY WILLIAM M. HESTON, JR., EDWARD J. HENNELLY AND CHARLES P. SMYTH

In connection with the interpretation of data on the microwave absorption of liquids,[2,3,4] it was necessary to measure the dielectric constants, refractive indices, densities and viscosities of a large number of organic halides. This paper presents the results of these measurements for an homologous series and related compounds, and makes use of this large body of information on closely related liquids to examine the relations between dielectric constant and dipole moment.

Purification of Materials.—The separate purification methods used are given below. In the first two columns of Table I are listed the compounds, their sources, purification procedures, and boiling points. The superscripts refer to the manufacturer and the numbers in parentheses refer to the purification procedure used. (1) The sample was shaken with three separate portions of sodium carbonate solution, washed with distilled water until free from alkali and then placed over calcium chloride to dry. When dry, the sample was decanted and distilled. (2) The sample was shaken with three separate portions of concentrated sulfuric acid, followed by three portions of sodium carbonate solution. It was then washed with distilled water until free from alkali, dried with calcium chloride, and distilled. (3) This procedure was the same as (1), but, in addition, the distillate was placed over feathered zinc to remove the discoloration. It was then decanted and redistilled. (4) The sample was fractionally distilled as received from the manufacturer. (5) The sample was used as received from the manufacturer: (a) Columbia Organic Chemicals Company; (b) Eastman Kodak Company; (c) General Chemical Company; (d) Halogen Chemical Company; (e) Paragon Testing Laboratories.

Experimental Results

Values of the static dielectric constant, ϵ_0, in Table I were measured at a frequency of 520 kilocycles by means of a previously described heterodyne-beat apparatus,[5] modified by the introduction of an oscilloscope as a null point instrument. Refractive indices for the sodium D line, $n^{25}D$, measured with a Pulfrich refractometer at 25° are given in the third column. The densities reported in

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[1] This research was carried out with the support of the Office of Naval Research.

[2] Heston, Hennelly and Smyth, THIS JOURNAL, **70**, 4093 (1948).

[3] Laquer and Smyth, *ibid.*, **70**, 4097 (1948).

[4] Hennelly, Heston and Smyth, *ibid.*, **70**, 4102 (1948).

[5] Lewis and Smyth, *J. Chem. Phys.*, **7**, 1085 (1939).