[CONTRIBUTION FROM THE ROSS CHEMICAL LABORATORY, ALABAMA POLYTECHNIC INSTITUTE]

Preparation of Some Bis-(N,N-dialkyl)amides of Aliphatic Phosphonic Acids

GENNADY M. KOSOLAPOFF AND LAMAR B. PAYNE

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Eleven phosphonodiamides of the general type $RP(O)(NR'_2)_2$, in which the radicals were varied from methyl to *n*-butyl, have been prepared. A decided decline in the ease of formation of these amides was noted to occur with the increase of the size of the radicals of the amines. A tentative value for the atomic refraction of nitrogen in compounds of this class was calculated.

The general class of aliphatic phosphonodiamides is but sparingly represented in the present chemical literature. The pioneering work of Michaelis records the preparation of but two substances in the family of possible compounds having the structure $RP(O)(NR_2)_2$.[1]

Yet, compounds of this type can be expected to be of considerable interest in the light of the work of Audrieth and Toy on the solubilities of amides of phosphoric acid formed from primary and secondary amines,[2] and the previous work of one of us,[3] with hexamethylphosphoramide.

It was felt that the preparation of a series of such compounds with radicals of progressively increasing size would be of interest in the general study of properties of organophosphorus compounds. An additional point of interest in this connection was the report by Doak and Freedman concerning the difficulties encountered in the preparation of such amides from secondary amines and the dichlorides of aromatic phosphonic acids.

We set out, in the present work, to prepare twelve compounds of this general type by condensation of phosphonic dichlorides with secondary amines. It was found that, while dimethylamine and diethylamine reacted satisfactorily with the phosphonic dichlorides at moderate temperatures, the amines with larger radicals were very significantly less reactive and a satisfactory condensation with di-*n*-propylamine was attained only in a relatively high-boiling solvent. Even under rather drastic conditions this amine failed to condense with butylphosphonic dichlorides, in the sense of forming the desired amide. Preliminary trials with di-*n*-butylamine also gave discouraging results since the butyl amides could not be prepared with equipment at our disposal.

The reaction of aliphatic phosphonic dichlorides with dimethylamine and diethylamine is readily carried out in refluxing heptane. The amide, formed in the reaction, tends to increase the solubility of the amine hydrochloride in this solvent so that a complete removal of the salt cannot be accomplished by simple filtration. Since the distillation of the filtered reaction mixture, which still retains some amine hydrochloride, usually leads to more or less severe decomposition, it was found to be necessary to eliminate the dissolved amine salt by treatment of the filtered solution with concentrated sodium hydroxide, prior to distillation. With this technique it was possible to obtain consistent yields of 70–88% of the desired amides. The reaction of phosphonic dichlorides with di-*n*-propylamine could not be brought to completion in refluxing heptane even after several days; replacement of this solvent by ethylbenzene served to eliminate this difficulty and the amides of methyl-, ethyl-, and propyl-phosphonic acids were obtained in 25–30% yields. Considerable amounts of amine hydrochlorides were retained in solution by these reaction mixtures and could not be totally precipitated by dilution with heptane. Washing the reaction mixtures with sodium hydroxide was, therefore, imperative.

The eleven phosphonamides, which were prepared, were colorless liquids which were soluble in the common organic solvents and had appreciable solubility in water. This solubility presented some experimental difficulties since the amides fluidized all the commercially available stopcock lubricants and recourse was finally made to graphite powder for lubrication of the distillation apparatus.

The above-mentioned difficulty in the preparation of amides from the higher amines confirms the work of Doak and Freedman,[4] but appears to be in conflict with a report which came to our attention after the present work had been completed. In this report[5] several amides of the general type $ROCH{=}CHP(O)(NR'_2)_2$ are described, in which dimethyl-, diethyl- and di-*n*-butyl-amines are represented. Although the preparation of amides from the lower amines is described in some detail, it is unfortunate that the details of work with dibutylamine are not supplied by the authors. It is intimated that the

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(1) A. Michaelis, *Ann.*, **326**, 129 (1903).

(2) L. F. Audrieth and A. D. F. Toy, *J. Am. Chem. Soc.*, **63**, 2117 (1941); **64**, 1337 (1942); **64**, 1553 (1942).

(3) G. M. Kosolapoff, *Organophosphorus Compounds*, John Wiley & Sons, New York, 1950, pp. 299 and 313.

(4) G. O. Doak and L. D. Freedman, *Report at the National Meeting of the American Chemical Society*, September, 1954.

(5) K. N. Anisimov, N. E. Kolobova, and A. N. Nesmeyanov, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 665 (1955).

procedure used for the higher amine was the same as that employed with the lower amines and that petroleum ether was used as the solvent. Since yields of the butylamides reported in this paper were about 50%, it appears that an unexpectedly considerable difference in reactivity exists between the saturated and the unsaturated phosphonic dichlorides.

The amides prepared in the present work were used to establish a tentative value for the atomic refraction of nitrogen in phosphonamides derived from secondary amines. This was done by the conventional calculation of the theoretically expected molar refraction, from the density and the index of refraction of each compound, and subtraction from this magnitude of the atomic contributions of all the elements except nitrogen. Since the methyl compounds are usually somewhat anomalous in the refractivity of a homologous series, the averaging of the results over the series was done by weighting the values obtained from the higher members by a factor of two. In this manner, the best value for atomic refraction of nitrogen was found to be 2.42. Without such weighting, the average value was 2.45.

EXPERIMENTAL

The necessary phosphonic dichlorides were prepared conventionally from dialkyl alkylphosphonates, by hydrolysis of the esters to the free acids, followed by treatment of the latter with phosphorus pentachloride.[6]

The solvents and the amines used in the preparation of the amides were dried and distilled just before the reaction. Freshly distilled phosphonic dichlorides were employed. Customary precautions against the entry of atmospheric moisture into the reaction mixtures were used.

The phosphonic dichloride (1 mole) diluted with one volume of the solvent (heptane or ethylbenzene) was added dropwise into a well-stirred and cooled solution of 4.1 moles of the amine in the hydrocarbon solvent (500 ml. to 1 l.) and the resulting mixture was slowly heated to reflux. Approximately 24 hours of refluxing was necessary to complete the reaction with dimethyl- and diethyl-amines; some 48 hours were needed for the di-*n*-propylamine. The yields of the dimethyl amides were improved from 70–75% to 80–83% by slow introduction of the amine during the refluxing period to make up the small volatilization loss through the condenser. The higher amines gave satisfactory yields without such addition.

The cooled reaction mixture was filtered and the filtrate was treated with 25–50 ml. of 30% sodium hydroxide solution with cooling. After agitation for 2–3 hours, the organic layer was separated, dried, and distilled.

It was noticed that the reaction mixture residue, left after the removal of the solvent, usually had a strikingly bright red color. The origin of this color is unknown, although it had been noticed previously by one of us in reactions of compounds containing the P(O)Cl group with various amino compounds, especially sulfanilamide.

The amount of amine hydrochloride separated from the reaction mixtures, involving di-*n*-propylamine and phosphonic dichlorides, was in all cases within a few grams of the theoretically expected amount. Nevertheless, as indicated above, distillation of the washed, crude product gave disappointingly low yields of the amides, with considerable amounts of dark, undistillable residues. Since all precautions were taken against introduction of moisture, it is unlikely that these residues could have been the anhydrides of the type postulated by Doak and Freedman.[4] These residues released the amine after hydrolysis with mineral acids.

The properties of the products and the analyses are shown below.

TABLE I

PROPERTIES OF BIS-(N,N-DIALKYL)AMIDES OF ALKYL PHOSPHONIC ACIDS

Compound	d^{30}_4	n^{30}_D	B.p., °C.	MM.	Nitrogen	
					Calc'd	Found
$CH_3PO[N(CH_3)_2]_2$	1.0157	1.4539	138	32	18.65	18.45
$CH_3CH_2PO[N(CH_3)_2]_2$	0.9971	1.4550	142	31	17.06	17.13
$CH_3CH_2CH_2PO[N(CH_3)_2]_2$	.9758	1.4564	149	33	15.72	15.71
$CH_3CH_2CH_2CH_2PO[N(CH_3)_2]_2$	.9618	1.4542	157	33	14.57	14.44
$CH_3PO[N(C_2H_5)_2]_2$	.9562	1.4565	166	33	13.58	13.40
$CH_3CH_2PO[N(C_2H_5)_2]_2$	.9689	1.4591	183	26	12.71	12.51
$CH_3CH_2CH_2PO[N(C_2H_5)_2]_2$	.9542	1.4580	189	28	11.95	12.01
$CH_3CH_2CH_2CH_2PO[N(C_2H_5)_2]_2$	.9314	1.4585	137	3.5	11.28	11.39
$CH_3PO[N(CH_2CH_2CH_3)_2]_2$	.9395	1.4603	137	3.5	10.67	10.44
$CH_3CH_2PO[N(CH_2CH_2CH_3)_2]_2$	.9346	1.4600	137	1.2	10.13	10.09
$CH_3CH_2CH_2PO[N(CH_2CH_2CH_3)_2]_2$	.9289	1.4620	141	1.2	9.64	9.45

AUBURN, ALABAMA

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[6] G. M. Kosolapoff, *J. Chem. Soc.*, 3222 (1954).