Some *N*-Substituted Aminodiphenylphosphines

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As part of our current research study of derivatives of monoaminophosphine (PH_2NH_2),[1] an analogue of hydrazine, we have had occasion to synthesize several new *N*-substituted aminodiphenylphosphines and their sulfur derivatives.[2,3] As we believe that our synthetic results may be of general interest, we are reporting at this time. The *N*-substituted aminodiphenylphosphines reported herein were prepared from diphenylchlorophosphine by one of two procedures: a) in the case of *N*-alkyl substituted aminophosphines and the monoaryl-substituted aminophosphines, the diphenylchlorophosphine was directly amminolyzed by the proper aliphatic or aromatic amine; b) in the case of the *N*-diphenyl compound the amine was first converted to the corresponding sodium amide and was then reacted with the diphenylchlorophosphine.

EXPERIMENTAL[4]

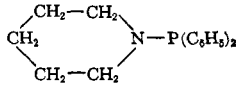
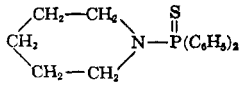
Materials. The diphenylchlorophosphine was obtained from the Victor Chemical Co. and was purified by fractionation under reduced pressure. The sources of the amines used were: *t*-butylamine from Rohm and Haas used as received; 2,6-diethylaniline from the Ethyl Corp. used as obtained; piperidine, Fisher Scientific purified grade, used as obtained; diallylamine, Union Carbide research sample used as received. Sodium hydride dispersed in Bayol-85 from Metal Hydrides, Inc., was used in the formation of the substituted sodium amides.

Procedure. As an example of the procedure used in the direct amminolysis of the diphenylchlorophosphine, the following description of the synthesis of *N*-*t*-butylaminodiphenylphosphine is presented:

A solution of 22 g. (0.1 mole) diphenylchlorophosphine in 30 ml. of dry benzene was added dropwise with stirring to a chilled solution of 18.2 g. (0.25 mole) of *t*-butylamine in 40 ml. of dry benzene. The solution was cooled and the rate of addition adjusted so as to keep the temperature in the range of 0° to 5°. Stirring was continued for 30 min. after all the diphenylchlorophosphine had been added. The reaction mixture was filtered and the amine hydrochloride precipitate was washed with small portions of dry benzene. The solvent was stripped from the combined filtrate and washings and and the liquid residue distilled; 16.7 g. (65%) of a substance

TABLE I

SOME *N*-SUBSTITUTED AMINODIPHENYLPHOSPHINES AND DERIVATIVES

Formula	Yield, %	M.P.	% C	% H	% N	% P	% S
$t\text{-}C_4H_9NHP(C_6H_5)_2$	65	38–40	74.68[a] 74.78[b]	7.83 8.03	5.44 5.66	12.03 12.19	
$t\text{-}C_4H_9NHP(S)(C_6H_5)_2$	84	120.5–121.5					11.07 11.33
$2,6\text{-}(C_2H_5)_2C_6H_3NHP(C_6H_5)_2$	46	88–89			4.20 4.49	9.29 9.11	
$2,6\text{-}(C_2H_5)_2C_6H_3NHP(S)(C_6H_5)_2$	57	135–136	72.29 72.49	6.61 7.02			8.77 8.55
	57	160–164[c] (0.5 mm.)	75.80 75.82	7.48 7.63	5.20 5.06	11.50 11.15	
	91	101–102					10.64 10.92
$(CH_2{=}CHCH_2)_2N{-}P(C_6H_5)_2$	50	141–143[c] (0.5 mm.)			4.97 4.97	11.01 11.07	
$(C_6H_5)_2NP(C_6H_5)_2$	23	130–132	81.56 81.30	5.70 5.67	3.96 4.01	8.77 9.02	
$[(t\text{-}C_4H_9)NHP(CH_3)(C_6H_5)_2]I$	—	198.5–200	51.14 51.51	5.80 5.88			

[a] Calcd. [b] Found. [c] Boiling points.

(1) H. H. Sisler, A. Sarkis, H. S. Ahuja, R. J. Drago, and N. L. Smith, *J. Am. Chem. Soc.*, 81, 2982 (1959).

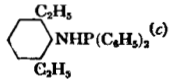
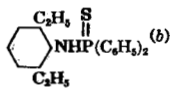
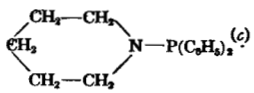
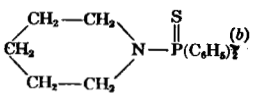
(2) Recent studies have resulted in the isolation of a variety of substituted phosphine derivatives containing P—N bonds. See (a) A. B. Burg and P. J. Slota, *J. Am. Chem. Soc.* 80, 1107 (1958), (b) K. Issleib and W. Seidel, *Ber.* 92, 268 (1959), (c) G. S. Harris, *Proc. Chem. Soc.* 1959, 119, (d) E. J. Reist, I. G. Junga, and B. R. Baker, *J. Org. Chem.* 25, 666 (1960).

(3) J. R. Van Wazer, *Phosphorus and Its Compounds* Vol. 1, Interscience Publisher, Inc., New York, 1958. Chapt. 6, pp. 307–308.

(4) The boiling and melting points are uncorrected. The analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

TABLE II

PRINCIPAL INFRARED ABSORPTION BANDS[a] FOR SOME *N*-SUBSTITUTED AMINODIPHENYLPHOSPHINES AND THEIR SULFIDES

Formula															
t-$C_4H_9NHP(C_6H_5)_2$[c]	3400w	3100m	3000s	1500s	1450s	1370s		1220s	1100s	980s		840m	740s			700s
t-$C_4H_9NHP(S)(C_6H_5)_2$[b]	3400w		3000s	1460s	1450s	1390s		1215s	1100s	1000s		850m	755m		715s	700m
 [c]		3115w	3000s	1460s				1180m	1125m	1000w		805w	750s			700s
 [b]	3350w		3000s	1460s		1400s		1180m	1105m		920m	805m	750s		715s	700s
 [c]			3000s		1450s		1330w	1225m	1060s	950s			750s			700s
 [b]			3000s	1475s		1400s		1205w	1100s	1070m	940s	845w	750w	740s	715s	700m
$(CH_2{=}CH{-}CH_2)_2N{-}P(C_6H_5)_2$[c]		3150w	2950w		1435s			1160w	1100m	1000m	930s		750s			700s
$(C_6H_5)N{-}P(C_6H_5)_2$[d]		3100s			1435m			1175w	1130m	960m			750w	735s		680s

[a] s = strong, m = medium, w = weak. [b] Nujol mulls on sodium chloride plates. [c] Liquid on sodium chloride plates. [d] Liquid on potassium bromide plates.

melting at 38–40° was obtained. Analytical data (Table I) confirmed the formula $C_4H_9NHP(C_6H_5)_2$.

The identity of the product was further established by splitting to *t*-butylamine hydrochloride and diphenylchlorophosphine by means of an ethereal solution of hydrogen chloride. The identity of these two substances was established by physical constants (melting point and mixed melting point, boiling point, and infrared spectra).

The NMR spectrum of the protons in the product agrees precisely with that expected for the structure $(CH_3)_3CNHP(C_6H_5)_2$.

This *N*-substituted aminodiphenylphosphine as well as several others prepared in this study was converted to the corresponding aminophosphine sulfide by reaction with an excess of sulfur in carbon disulfide in accordance with the following procedure:

To a continuously stirred solution of 1.3 g. (0.005 mole) of *N*-*t*-butylaminodiphenylphosphine in 25 ml. of dry carbon disulfide was added 0.3 g. (0.009 mole) of sulfur. The solution was warmed to about 35° and allowed to react for 10 hr., during which time the color changed from light brown to yellow and finally became almost colorless. On reduction of the volume of the reaction mixture through vacuum evaporation of most of the solvent, 1.2 g. (84%) of white prismatic crystals was obtained; m.p. 120.5–121.5°. Analytical data (Table I) confirmed the formula

$$C_4H_9NHP(S)(C_6H_5)_2.$$

The aminophosphine was further characterized by conversion to the methyl iodide adduct $[(t\text{-}C_4H_9)NHP(CH_3)(C_6H_5)_2]I$ by reaction with a benzene solution of methyl iodide. The adduct was obtained as white needles melting at 198.5–200°. Analytical data are given in Table I.

Analytical data, yield data, and melting points for aminodiphenylphosphines and their sulfides prepared by procedures analogous to the above are summarized in Table I.

The preparation of *N*-diphenylaminodiphenylphosphine was carried out according to the following procedure: A solution of 1.7 g. (0.01 mole) diphenylamine in 10 ml. of dry (over calcium hydride) diethylene glycol dimethyl ether was added to a suspension of 0.8 g. of sodium hydride (54% dispersion in oil) in 25 ml. of the diglyme. After the theoretical amount of hydrogen (0.2 l.) had been evolved, 2.2 g. (0.01 mole) of diphenylchlorophosphine was added with stirring to the mixture. The temperature was raised to and held at 110° for 1.5 hr. The solid reaction product was filtered hot, washed with dry ethyl ether and weighed 0.6 g. (calculated weight of sodium chloride, 0.6 g.). The filtrate and ether washings were combined and the solvents removed under reduced pressure. The residue was recrystallized from ethanol. The resulting crystals weighed 0.8 g. (23%) and melted at 130–132°. The product was further characterized by alkaline hydrolysis to diphenylamine and diphenylphosphinic acid. Both of these substances were isolated and identified by melting point (including mixed melting point with known samples) and infrared spectra.

Infrared spectra. The infrared spectrum of each of the phosphorus-nitrogen derivatives obtained in this study was examined using a Perkin Elmer Model 21 spectrograph. The principal bands in each spectrum are listed in Table II.

DISCUSSION

As indicated in Table II the infrared spectra of all the new compounds show the P—N bands in the 870–750 cm.$^{-1}$ region. This agrees well with the findings of Reist, Junga, and Baker with respect to diaminophosphine sulfides.[2d] The sulfides all showed an extra absorption band at approximately 715 cm^{-1}.

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Some Halogenated 1,2,3-Benzotriazin-4(3H)ones

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In the course of routine screening, 1,2,3-benzotriazin-4(3H)one was found[1] to have sedative activity. In an attempt to prepare compounds exhibiting an enhancement of this activity, a number of benz-halogenated and 3-dialkylaminoalkyl analogs of the parent compound were prepared for pharmacological evaluation, not only as sedatives, but also for other types of activity as well.[2]

In line with this approach, since the completion of this work a note describing 4-substituted 1,2,3-benzotriazines as having "apresoline-like" adrenergic blocking activity has also appeared.[3]

Of the several methods referred to in the literature,[4] three seemed best suited for this work. The first of these (method A), involved cyclization *via* diazotization of an anthranilamide to the desired 1,2,3-benzotriazin-4(3H)one and was of the most general application.

The second procedure (method B) utilized the reaction of a dialkylaminoalkyl chloride with a benz-halogenated-1,2,3-benzotriazin-4(3H)one. The yields by this method, however, were generally lower than those obtained by method A.

A third, but even less successful approach (method C), involved the reaction of a dialkylaminoalkylamine with the diazotized methyl ester of an anthranilic acid.

The substituted anthranilamides were obtained by the action of ammonia, or dialkylaminoalkylamines, on the corresponding isatoic anhydrides, which in turn were prepared by reaction of the

(1) We are indebted for this and for all other activity data to Dr. A. C. Osterberg and his associates, Experimental Therapeutics Research Section, Pearl River Laboratories.

(2) For example, 7-chloro-3-amino-1,2,4-benzotriazine and its 1-oxide have been reported to have a high order of antiprotozoan activity against avian malaria by F. J. Wolf, K. Pfister, R. M. Wilson, Jr., and C. A. Robinson, *J. Am. Chem. Soc.*, **76**, 3551 (1954) and by F. J. Wolf, R. M. Wilson, Jr., K. Pfister, and M. Tishler, *J. Am. Chem. Soc.*, **76**, 4611 (1954).

(3) C. Grundmann and H. Ulrich, *J. Org. Chem.*, **24**, 272 (1959).

(4) E. Van Heyningen, *J. Am. Chem. Soc.*, **77**, 6562 (1955) and Refs. 1, 2, and 3 in that paper.