CONDENSATION OF CHLORAL WITH PHOSPHORAMIDIC ESTERS, AND SOME PROPERTIES OF THE COMPOUNDS OBTAINED

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Chloral condenses with various carboxamides. The adducts formed are crystalline substances which usually show physiological activity. Some of them have been approved as medicinal preparations. For example, the chloral adduct of nicotinamide has a soporific and sedative action [1]. Various compounds of this type show insecticidal, fungicidal, and herbicidal properties [2-4]. The reactions of chloral with arenesulfonamides go similarly and lead to the formation of the corresponding adducts [5]. Since most organophosphorus compounds are physiologically active, we considered that products of the reactions of amides of phosphorus acids with chloral might be of interest. The formal resemblance of such products with the extremely effective insecticide chlorophos and its analogs — products of the condensation of dialkyl hydrogen phosphites with chloral — enables us to draw certain analogies.

Aqueous solutions of dialkyl (2,2,2-trichloro-1-hydroxyethyl)phosphoramidates $(RO)_2P(O)NHCH(OH)\cdot CCl_3$ [6] are lethal to domestic flies.

The introduction of a second chloral molecule into these compounds is difficult because the second N-hydrogen atom is reluctant to enter into condensation. It is stated in a patent [7] that some amides of phosphorus acids $(RZ)_2P(Z)NHR'$ condense with chloral in presence of organic bases at elevated temperatures.

We here describe the condensation of alkylphosphoramidic esters with chloral in accordance with the scheme

$$(RO)_2P(O)NHR' + CCl_3CHO \rightarrow (RO)_2P(O)N(R')CH(OH)CCl_3$$

We prepared previously undescribed dialkyl alkylphosphoramidates by the usual method for phosphoramidic esters [8] and characterized them (Table 1). The condensation of chloral with dialkyl alkylphosphoramidates occurs only in presence of catalytic amounts of concentrated sulfuric acid. The reaction is slow and takes several days. Depending on the structure of the organophosphorus compound, the products are crystalline solids or thick liquids which decompose on distillation. The crystalline adducts were recrystallized from a suitable solvent and then had sharp melting points; liquid adducts were purified from unchanged reactants by washing with water and were then dried (Tables 2 and 3).

The IR spectra of the initial amides contain intense absorption bands in the 1000-1130 cm^{-1} region, of which one with ν_{max} 1000 cm^{-1} is associated with the vibrations of the P—(O—C) group, while two others are associated with the stretching vibrations of the C—N bond [9]. The intense band at 1230 cm^{-1} belongs to the P=O group, and in dilute solution it is displaced to 1265 cm^{-1}. The N—H bond is manifested in the spectra at about 3240 cm^{-1} as a broad absorption band which is replaced by a narrow peak at 3430 cm^{-1} only in extremely dilute solutions. Such behavior in the stretching vibrations of the P=O and N—H bonds is indicative of strong intermolecular interaction. The presence of a strong hydrogen bond may be one of the causes of the slowness of the condensation of dialkyl alkylphosphoramidates with chloral. As in the spectra of the initial amides, in the spectra of the products of the condensation of phosphorus-containing amides with chloral there is a broad absorption band at about 3205 cm^{-1}. Dissolution of the product in CCl_4, even at very high dilution, leads to only a slight shift in the band to 3270 cm^{-1}. On this basis we assign the absorption band at about 3205 cm^{-1} to the vibrations of a hydrogen-bonded hydroxyl. The frequency of the stretching vibrations of the P=O group is 1230-1240 cm^{-1} also does not change when the solu-

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TABLE 1

Compound	Yield, %	bp, °C (p, mm)	n_D^{20}	d_4^{20}	MR	P, %
$(CH_3O)_2P(O)NHC_2H_5$	85.3	122—124 (10)	1.4275	1.1438	34.38* 34.86	19.53* 20.26
$(CH_3O)_2P(O)NHC_3H_7$	80.7	132—134 (11)	1.4290	1.1101	38.78 39.08	18.19 18.56
$(CH_3O)_2P(O)NHC_4H_9$	84.5	143—154 (9)	1.4326	1.0782	43.65 44.10	16.50 17.12
$(C_2H_5O)_2P(O)NHC_2H_5$†	79.5	79—81 (0.03)	1.4254	1.0583	—	—
$(C_2H_5O)_2P(O)NHC_3H_7$‡	90.0	140 (10)	1.4278	1.0338	48.51 48.72	15.94 15.90
$(C_2H_5O)_2P(O)NHC_4H_9$**	84.8	101—103 (0.035)	1.4300	1.0194	52.95 53.39	14.61 14.83
$(C_3H_7O)_2P(O)NHC_2H_5$	69.0	85—89 (0.03)	1.4295	1.0160	53.07 53.37	14.95 14.83
$(C_3H_7O)_2P(O)NHC_3H_7$	85.3	96—98 (0.03)	1.4310	1.0035	57.51 57.95	13.59 13.90
$(C_3H_7O)_2P(O)NHC_4H_9$	91.0	105—107 (0.03)	1.4330	0.9910	62.15 62.57	12.68 13.07
$(C_4H_9O)_2P(O)NHC_2H_5$	84.2	98—100 (0.03)	1.4335	0.9911	62.21 62.57	12.95 13.07
$(C_4H_9O)_2P(O)NHC_3H_7$	84.0	112—113 (0.03)	1.4360	0.9838	66.71 66.19	11.96 12.35
$(C_4H_9O)_2P(O)NHC_4H_9$	88.3	128—130 (0.03)	1.4380	0.9740	71.41 71.80	11.28 11.69
$(i\text{-}C_4H_9O)_2P(O)NHC_2H_5$	91.8	96—98 (0.025)	1.4295	0.9796	62.43 62.57	13.11 13.07

*The upper values were found, and the lower were calculated.
†[12] gives: bp 96-97° (1 mm); n_D^{20} 1.4258; d_4^{20} 1.0590.
‡[13] gives: bp 112° (8 mm).
**[14] gives: bp 107° (0.035 mm); n_D^{25} 1.4260.

TABLE 2

Compound	Yield, %	mp, °C	Solvent	Analysis, %		
				P	Cl	N
$(CH_3O)_2P(O)N(C_2H_5)CH(OH)CCl_3$	74,8	128—129	Benzene	10.01* 10.32	35.48* 35.44	4.71* 4.66
$(CH_3O)_2P(O)N(C_3H_7)CH(OH)CCl_3$	63,8	132—134	»	9.67 9.85	33.91 33.86	4.46 4.45
$(CH_3O)_2P(O)N(C_4H_9)CH(OH)CCl_3$	50,8	125—126	»	9.34 9.44	32.55 32.42	4.40 4.26
$(C_2H_5O)_2P(O)N(C_2H_5)CH(OH)CCl_3$	48,0	76—78	»	9.35 9.44	31.95 32.42	3.88 4.26
$(C_2H_5O)_2P(O)N(C_3H_7)CH(OH)CCl_3$	62,0	123—124	Water	9.06 9.05	31.06 31.09	3.87 4.08
$(C_2H_5O)_2P(O)N(C_4H_9)CH(OH)CCl_3$	44,4	88—90	Benzene	8.27 8.69	30.15 29.87	3.90 3.93

*The upper values were found, and the lower were calculated.

tion is diluted. The intense absorption bands in the region 750-850 cm^{-1} may be assigned to the asymmetric vibrations of the CCl_3 group, and the bands in the region 1100-1110 cm^{-1} to the vibrations of the alcoholic C—O bond (Fig. 1). Thus, the formation of an adduct between chloral and the amide undoubtedly occurs.

The alcoholic character of the hydroxyl is displayed in reactions with carboxylic anhydrides, which leads to acyl derivatives:

$$(RO)_2P(O)N(R')CH(OH)CCl_3 + (CH_3CO)_2O \rightarrow (RO)_2P(O)N(R')CH(CCl_3)OCOCH_3$$

The presence of an acyl group in these derivatives is confirmed by the presence in their IR spectra of intense bands due to the stretching vibrations of the C=O link at 1770 cm^{-1} and to the stretching vibrations of C—O adjacent to carbonyl in the region 1190-1220 cm^{-1}. A certain increase in the frequency of the carbonyl absorption is to be explained by the presence of chlorine atoms in the β-position relative to the phosphorus atom [10].

TABLE 3.

Compound	Yield, %	n_D^{20}	d_4^{20}	MR	P, %
$(C_3H_7O)_2P(O)N(C_2H_5)CH(OH)CCl_3$	73.1	1.4620	1.2523	78.26* 78.80	8.88* 8.70
$(C_3H_7O)_2P(O)N(C_3H_7)CH(OH)CCl_3$	66.2	1.4620	1.2162	83.74 83.32	8.46 8.37
$(C_3H_7O)_2P(O)N(C_4H_9)CH(OH)CCl_3$	75.2	1.4625	1.2046	87.83 87.93	8.31 8.06
$(C_4H_9O)_2P(O)N(C_2H_5)CH(OH)CCl_3$	72.3	1.4647	1.2172	87.26 87.93	8.43 8.06
$(C_4H_9O)_2P(O)N(C_3H_7)CH(OH)CCl_3$	71.4	1.4584	1.1713	92.91 92.55	8.30 7.78
$(C_4H_9O)_2P(O)N(C_4H_9)CH(OH)CCl_3$	75.8	1.4600	1.1534	97.96 97.17	7.80 7.52
$(i\text{-}C_4H_9O)_2P(O)N(C_2H_5)CH(OH)CCl_3$	76.0	1.4578	1.2075	86.87 87.93	8.43 8.06

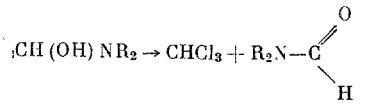
*The upper values were found, and the lower were calculated.

TABLE 4

Compound	Yield, %	bp, °C (p, mm)	n_D^{20}	d_4^{20}	MR	Analysis, % C	H	P	N
$(C_2H_5O)_2P(O)N(C_2H_5)CHO$	80.5	59.5—61 (0.025)	1.4319	1.1017	48.96* 48.73	40.19* 40.19	7.92* 7.61	14.53* 14.83	6.78* 6.70
$(C_2H_5O)_2P(O)N(C_3H_7)CHO$	86.8	64.5—65.5 (0.025)	1.4330	1.0776	53.78 53.35	42.34 43.05	8.53 8.07	13.72 13.90	5.98 6.29
$(C_2H_5O)_2P(O)N(C_4H_9)CHO$	51.9	72—73 (0.025)	1.4338	1.0459	58.98 57.97	45.90 45.57	8.92 8.44	13.34 13.08	6.20 5.91
$(C_3H_7O)_2P(O)N(C_2H_5)CHO$	36.3	76—77 (0.025)	1.4320	1.0455	58.80 57.97	— —	— —	13.37 13.08	5.66 5.91
$(C_3H_7O)_2P(O)N(C_3H_7)CHO$	76.3	84—85 (0.025)	1.4335	1.0305	63.49 62.58	— —	— —	12.22 12.35	5.75 5.58
$(C_3H_7O)_2P(O)N(C_4H_9)CHO$	74.7	89—91 (0.025)	1.4360	1.0173	63.12 67.20	— —	— —	11.68 11.70	— —
$(C_4H_9O)_2P(O)N(C_2H_5)CHO$	48.2	87.5—88 (0.025)	1.4371	1.0211	63.00 67.20	— —	— —	11.72 11.70	5.43 5.28
$(C_4H_9O)_2P(O)N(C_3H_7)CHO$	40.0	92—93 (0.025)	1.4370	1.0018	72.96 71.82	— —	— —	11.12 11.11	5.02 5.02
$(C_4H_9O)_2P(O)N(C_4H_9)CHO$	37.1	102—103 (0.025)	1.4350	0.9924	77.03 75.44	— —	— —	10.48 10.58	4.30 4.78
$(i\text{-}C_4H_9O)_2P(O)N(C_2H_5)CHO$	44.2	78—79.5 (0.025)	1.4355	1.0226	67.65 67.20	50.27 49.81	9.21 9.06	11.85 11.70	5.31 5.28

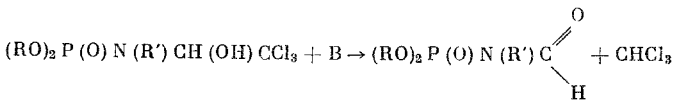
*The upper values were found, and the lower were calculated.

Dialkyl alkyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidates are insoluble in water and extremely stable in it; they are also stable in acid media, but in alkaline solutions they are broken down fairly rapidly. The chloral derivatives $CCl_3CH(OH)NR_2$ decompose under the action of alkali or thermal treatment with formation of chloroform and a formamide:



$$CH(OH)NR_2 \rightarrow CHCl_3 + R_2N{-}C(=O){-}H$$

For dialkyl alkyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidates it could also be expected that breakdown in an alkaline medium would go in accordance with this scheme, though the possibility of the elimination of hydrogen chloride with formation of the epoxide $(RO)_2P(O)N(R')CH(O)CCl_2$ or of breakdown into the starting substances is not ruled out. However, when we treated our phosphorus derivatives of chloral with an organic base (triethylamine) at the boiling point of the latter we isolated only formylphosphoramidates (phosphinylformamides) (Table 4) in accordance with the scheme



$$(RO)_2P(O)N(R')CH(OH)CCl_3 + B \rightarrow (RO)_2P(O)N(R')C(=O)H + CHCl_3$$

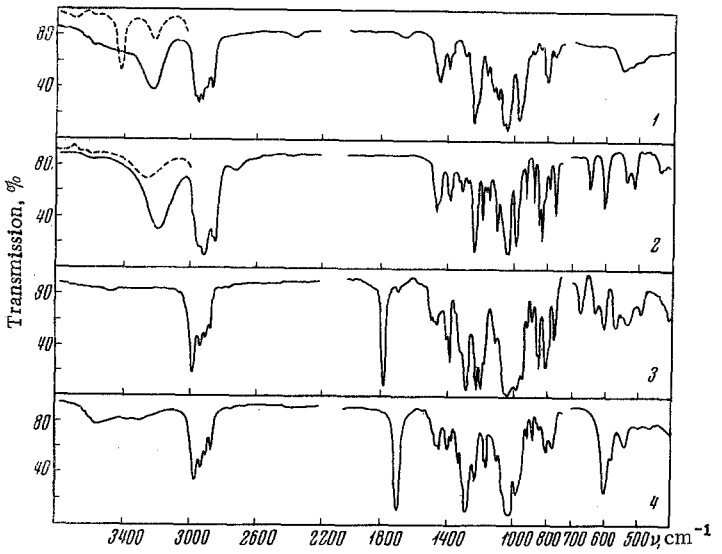
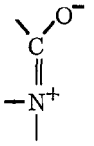


Fig. 1. IR spectra: 1) diethyl butylphosphoramidate (----- CCl_4 solution, d = 20 mm); 2) diethyl propyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidate, mineral oil mull (----- CCl_4 solution, d = 40 mm); 3) diethyl (1-acetoxy-2,2,2-trichloroethyl)propylphosphoramidate; 4) diethyl formylpropylphosphoramidate.

The nature of these products is confirmed by the results of elemental analysis and of spectral investigations. The IR spectra contain bands due to the stretching vibrations of P=O and C=O bonds at 1290-1300 and 1707 cm^{-1} respectively. Since hydrogen chloride was not liberated in the reaction and the IR spectra contain no absorption bands characteristic for an epoxide ring, the epoxide structure is excluded. Breakdown of the condensation product into the starting compounds is also ruled out because there is no N—H band in the IR spectra. Hence, as a result of the treatment of dialkyl alkyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidates with triethylamine mixed amides of phosphoric acids and formic acid are formed.

It is interesting that, unlike tertiary amides, for which the amide I band is usually observed in the region 1630-1670 cm^{-1}, in the spectra of these amides the carbonyl frequency is 1710 cm^{-1}, intermediate between $\nu_{C=O}$ for a tertiary amide and $\nu_{C=O}$ for an aldehyde. This may be attributed to the competition of the d-orbitals of the phosphorus atom for the unshared electron pair of the nitrogen, as a result of which the contribution of the ionic form of the amide  diminishes and the frequency of the carbonyl absorption increases [11].

EXPERIMENTAL

IR spectra were determined with a UR-10 spectrophotometer. Solid samples were prepared as mineral oil mulls.

Dimethyl Ethylphosphoramidate. A mixture of 9 g of ethylamine, 20.2 g of triethylamine, and 150 ml of ether was prepared in a four-necked flask fitted with stirrer, reflux condenser, thermometer, and dropping funnel. The mixture was cooled, and with vigorous stirring 28.9 g of dimethyl phosphorochloridate was added from a dropping funnel. To complete the reaction the mixture was heated in a water bath for 30 min. The precipitate formed was filtered off and washed with solvent. Ether was vacuum-evaporated, and the residue was fractionated twice. All the other phosphoramidates were prepared analogously. The results are given in Table 1.

Dimethyl Ethyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidate. A mixture of 16 g of dimethyl ethylphosphoramidate, 15.6 g of chloral, and 0.3 ml of conc. H_2SO_4 was prepared in a

flat-bottomed flask. A little heat was liberated. The liquid thickened slowly, and after a few hours it crystallized. The product was recrystallized from benzene. Physicochemical data are given in Table 2. The other dialkyl alkyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidates listed in this table were prepared analogously.

Dipropyl Ethyl(2,2,2,-trichloro-1-hydroxyethyl)phosphoramidate. A mixture of 7 g of dipropyl ethylphosphoramidate, 5 g of chloral, and ten drops of conc. H_2SO_4 was prepared in a flat-bottomed flask. A little heat was liberated. The liquid thickened slowly, and after a few days the product was washed three times with water and dissolved in ether. The ethereal solution was dried over anhydrous Na_2SO_4, and ether was removed in a vacuum. The residue was a clear thick liquid. Physicochemical data for the product are given in Table 3. The other dialkyl alkyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidates listed in Table 3 were prepared similarly.

Diethyl (1-Acetoxy-2,2,2-trichloroethyl)propylphosphoramidate. A four-necked flask fitted with stirrer, reflux condenser, thermometer, and dropping funnel was charged with 7 g of diethyl propyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidate. Acetic anhydride (4.2 g, 100% excess) containing two drops of conc. H_2SO_4 as catalyst was added dropwise with stirring. The temperature of the mixture rose from that of the room to 40°, and the crystalline mass turned completely liquid. The mixture was then heated for 15-20 min in a water bath to complete the reaction. After excess of acetic anhydride and the acetic acid formed had been removed in a vacuum, the product was vacuum-distilled three times. We obtained 5 g (64%) of product, bp 120-121.5° (0.015); n_D^{20} 1.4625; d_4^{20} 1.2740. Found%: C 34.18, 34.13; H 6.16, 6.45; P 8.17, 8.28; Cl 26.89, 26.95; N 3.58, 3.78. MR 83.04. $C_{11}H_{21}Cl_3PO_5N$. Calculated%: C 34.33; H 5.46; P 8.05; Cl 27.69; N 3.64. MR 83.44.

Diethyl Ethylformylphosphoramidate [N-(Diethoxyphosphinyl)-N-ethylformamide]. A mixture of 11.4 g of diethyl ethyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidate and 25 ml of triethylamine was prepared in a flask with a reflux condenser. The mixture was boiled for 1-2 h, in the course of which the liquid became dark red. The readily volatile part was removed in a vacuum, a small amount of sediment (0.2 g) was filtered off, and the liquid was vacuum-distilled twice. Physicochemical data on the product are given in Table 4. All the other mixed amides were prepared analogously.

We thank R. R. Shagidullin for valuable advice and help in the interpretation and discussion of the IR spectra.

CONCLUSIONS

1. Some dialkyl phosphoramidates were prepared and characterized.
2. Chloral adducts of dialkyl alkylphosphoramidates were prepared and characterized.
3. Under the action of triethylamine dialkyl alkyl(2,2,2-trichloro-1-hydroxyethyl)phosphoramidates break down with formation of dialkyl alkylformylphosphoramidates.

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