SOME ESTERS OF PHOSPHORUS THIOACIDS THAT CONTAIN THE FRAGMENTS OF CYCLIC AMINO ACID DERIVATIVES

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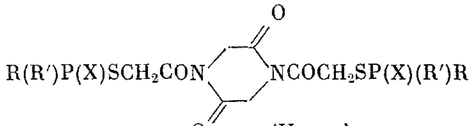
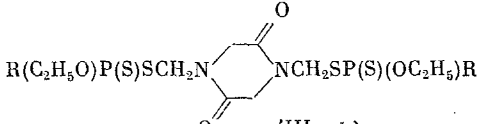
Previously we described [1, 2] a number phosphorus thioacid derivatives, which contain amino acid fragments of general formula R(R'O)P(X)SCH$_2$—CONH—A—COY (X = S, O; Y = OR", NHCH$_3$; A = amino acid fragment) (I), among which were found active insecticides and acaricides with a selective action and either a low or moderate toxicity for animals. It was shown [1-3] that both the toxicity and selectivity of action are noticeably affected by the nature of the amino acid fragment. In this connection we synthesized for biological testing a number of structurally close compounds, which contain the fragments of cyclic amino acid derivatives, and specifically of 2,5-diketopiperazine and pyroglutamic acid.



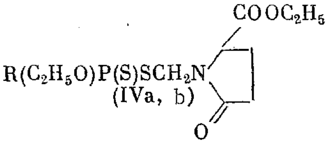
(IIa—g)

$R = R' = C_2H_5O$, $X = S(a)$; $R = CH_3$, $R' = CH_3O$, $X = S(b)$; $R = CH_3$, $R' = C_2H_5O$, $X = S(c)$; $R = R' = C_6H_5$, $X = S(d)$; $R = R' = C_2H_5O$, $X = O(e)$; $R = CH_3$, $R' = C_2H_5O$, $X = O(f)$; $R = R' = C_6H_5$, $X = O(g)$.



(IIIa, b)

$R = C_2H_5O(a)$, $CH_3(b)$.



(IVa, b)

$R = C_2H_5O(a)$, $CH_3(b)$.

Compounds (II)-(IV) were obtained by reacting either the Na or the K salts of phosphorus thio- and dithioacids with 1,4-di(chloroacetyl)-2,5-diketopiperazine (V) [4], 1,4-di(chloromethyl)-2,5-diketopiperazine (VI), or 1-chloromethyl-5-carbethoxy-2-pyrrolidinone (VII). The purity of (II)-(IV) was confirmed by the elemental analysis and TLC data, and the structure was confirmed by the NMR and IR spectroscopy methods (Table 1).

For (IVb), which contains two chiral centers in the molecule, the phenomenon of anisochronicity is observed in the PMR spectrum, taken in CCl$_4$ or benzene, which is especially noticeable on the signals of the protons of the Me group attached to the P atom: two close doublets [δ 2.40 ppm, $\Delta\delta$ 1.33 Hz (CCl$_4$); δ 1.90 m ppm, $\Delta\delta$ 2.70 Hz (C$_6$H$_6$)]. For compounds (IIc) and (IIIb), which also represent a mixture of diastereomeric racemates, the diastereomeric anisochronicity is observed only in the ^{31}P—{^{1}H} NMR spectra, taken in benzene: two close signals (δ 103.47 ppm, $\Delta\delta$ 1.83 Hz) for (IIb) and (δ 110.11 ppm, $\Delta\delta$ 1.1 Hz) for (IIIb).

The contact insecticidal activity was tested on houseflies (*Musca domestica* L.), rice weevil (*Calendra orizae* L.), and black beet aphis (*Aphis fabe* L.); the contact acaricidal activity was tested on the spider mite (*Tetranychus urticae* K.); the toxicity of (IIIa, b) and (IVa, b) was determined on white mice (orally) (Table 2). Compounds (IIa-g) displayed a

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TABLE 1. Constants, Yields, and Elemental Analysis Data for Esters of Phosphorus Thioacids, Containing the Fragments of Cyclic Amino Acid Derivatives (II)-(IV)

Compound	Yield, %	mp, °C	Found, %			Empirical formula	Calculated, %		
			C	H	P		C	H	P
(IIa)	62,5	Viscous oil *	33,86	5,00	10,85	$C_{16}H_{28}N_2O_8P_2S_4$	33,91	4,98	10,93
(IIb)	55,9	124–126	–	–	12,72	$C_{12}H_{20}N_2O_6P_2S_4$	–	–	12,95
(IIc)	41,5	Viscous oil *	32,71	4,62	12,26	$C_{14}H_{24}N_2O_6P_2S_4$	33,19	4,77	12,22
(IId)	88,3	210–211	–	–	8,62	$C_{32}H_{28}N_2O_4P_2S_4$	–	–	8,92
(IIe)	87,9	98–100	36,26	4,78	11,84	$C_{16}H_{28}N_2O_{10}P_2S_2$	35,95	5,28	11,59
(IIf)	47,3	101–103	35,17	5,13	12,82	$C_{14}H_{24}N_2O_8P_2S_2$	35,44	5,09	13,05
(IIg)	73,2	218–219	–	–	9,10	$C_{32}H_{28}N_2O_6P_2S_2$	–	–	9,35
(IIIa)	85,5	34–34,5	33,00	5,42	12,24	$C_{14}H_{28}N_2O_6P_2S_4$	32,93	5,53	12,13
(IIIb)	90,0	98–107	32,11	5,25	13,63	$C_{12}H_{24}N_2O_4P_2S_4$	31,99	5,37	13,75
(IVa)	71,7	– †	–	–	8,98	$C_{12}H_{22}NO_5PS_2$	–	–	8,71
(IVb)	94,4	– ‡	–	–	9,61	$C_{11}H_{20}NO_4PS_2$	–	–	9,52

*Purified by chromatography.

†n_D^{20} 1.5215, d_4^{20} 1.2258. Found: MR 88.22. Calculated: MR 87.56.

‡n_D^{20} 1.5405, d_4^{20} 1.2368. Found: MR 82.61. Calculated: MR 81.88.

TABLE 2. Physiological Activity of Esters of Phosphorus Thioacids, Containing the Fragments of Cyclic Amino Acid Derivatives (II)-(IV)

Compound	Death at given concentration, %				LD_{50}, mg/kg (mice orally)
	houseflies (0.15)	rice weevil (0.15)	black beet aphis (0.01)	spider mite (0.05)	
(IIa)	0	0	3	7	–
(IIb)	0	0	–	9	–
(IId)	0	0	10	9	–
(IIe)	0	2	7	0	–
(IIf)	12	84	3	13	–
(IIIa)	–	–	–	46	25
(IIIb)	–	–	–	71	<25
(IVa)	53	6	97	54	300
(IVb)	90	70	33	92	75
Metaphos	95 (0,015)	95 (0,015)		97 (0,005)	
Carbophos			100		

weak effect, while compounds (IIIa, b) and (IVa, b) displayed a moderate activity, which was substantially inferior to the standards, in which connection (IIIa, b) and (IVa, b) are toxic for animals.

EXPERIMENTAL

The PMR spectra were obtained on a Perkin-Elmer R-12 instrument (60 MHz), and the $^{19}P-\{^1H\}$ NMR spectra were obtained on a Bruker HX-90 instrument (36.43 MHz), using 85% H_3PO_4 as the external standard.

1,4-Di(chloroacetyl)-2,5-diketopiperazine (V). Obtained as described in [4]. It was purified by recrystallization from MeCN using activated C, and then from MeCN (instead of $PhNO_2$ [4]), mp 171.5-172°C. Literature data: mp 168.5 [4].

1,4-Di(chloromethyl)-2,5-diketopiperazine (VI). With stirring, to 9.84 g (0.056 mole) of 1,4-di(hydroxymethyl)-2,5-diketopiperazine [5] in 30 ml of $CHCl_3$ was added 13.80 g (0.116 mole) of $SOCl_2$, the mixture was refluxed for 3.5 h, 20 ml of $CHCl_3$ was added, the precipitate was filtered, and the filtrate was evaporated to give a small amount of crystals. After recrystallization from $CHCl_3$ and benzene we isolated 10.20 g (85.6%) of product with mp 173-175°. Literature data: mp 162° [5]. PMR spectrum (in $CDCl_3$, δ, ppm): 4.38 s (CH_2CO, 4H), 5.49 s (CH_2Cl, 4H).

1-Chloromethyl-5-carbethoxy-2-pyrrolidinone (VII). A mixture of 5.71 g (0.036 mole) of ethyl pyroglutamate [6], 3.64 g (0.048 mole) of 40% formalin, and 0.06 g of K_2CO_3 was heated for 4 h at 100°, extracted with $CHCl_3$, and the extracts were washed with cold water, dried over Na_2SO_3, and evaporated in vacuo. The residue was dissolved in 15 ml of dry $CHCl_3$ and then 5.54 g (0.046 mole) of $SOCl_2$ was added dropwise. The mixture was refluxed for 4 h, and the $CHCl_3$ was removed in vacuo to give 6.17 g (82.7%) of (VII) with bp 111-112° (0.5 mm), n_D^{20} 1.4672, d_4^{20} 1.2458. Found: C 46.80; H 5.87; N 6.90%. MR 47.41. $C_8H_{12}ClNO_3$. Calculated: C 46.72; H 5.88; N 6.81%. MR 47.09.

S-Phosphorylated Derivatives of 1,4-Di(mercaptoacetyl)-2,5-diketopiperazine (IIa-g). To 0.015 mole of (V) in 20 ml of dry acetone was added dropwise a solution of 0.033 mole of the salt of either the phosphorus thio- or dithioacid in 20 ml of acetone, and the stirred mixture was refluxed for 3 h and the precipitate was filtered. The filtrate was evaporated in vacuo, and the residue was dissolved in $CHCl_3$, washed in succession with water, satd. $NaHCO_3$ solution, and water, dried over Na_2SO_4, and evaporated in vacuo. The residue was dissolved in acetone, filtered, the filtrate was evaporated in vacuo, and the product was either recrystallized or purified by chromatography on a column packed with SiO_2 L 100/160 μ (the eluant was a hexane–acetone mixture in ratios that smoothly changed from 99:1 to 3:2, with checking of the fractions by TLC on the same support, using 4:1 and 3:2 hexane–acetone mixtures as the eluant) (see Table 1).

S-Phosphorylated Derivatives of 1,4-Di(mercaptomethyl)-2,5-diketopiperazine (IIIa, b). To a solution of 0.045 mole of either diethyl dithiophosphate or O-ethyl methyldithiophosphonate in 20 ml of acetone was added in drops a solution of 4.22 g (0.020 mole) of (VI), the mixture was kept at 20° for 3-4 h, filtered, the filtrate was evaporated in vacuo, and the residue was dissolved in benzene, washed in succession with water, satd. $NaHCO_3$ solution, and water, dried over Na_2SO_4, and evaporated in vacuo. The residue was crystallized by rubbing with hexane. The compounds were purified by recrystallization from either an ether–hexane (IIIa) or benzene–hexane (IIIb) mixture (see Table 1).

S-Phosphorylated Derivatives of N-Mercaptomethyl-5-carbethoxy-2-pyrrolidinone (IVa, b). Obtained in a similar manner from 0.017 mole of the salt of the phosphorus dithioacid and 3.08 g (0.015 mole) of (VII) in 20 ml of acetone. The products were kept for 1 h at 80° (1 mm) to give the pure (IVa, b) (see Table 1).

CONCLUSIONS

The reaction of the salts of phosphorus thio- and dithioacids with the 1,4-di(chloroacetyl)- and 1,4-di(chloromethyl)-2,5-diketopiperazines, and also with 1-chloromethyl-5-carbethoxy-2-pyrrolidinone, gave new thio- and dithiophosphorus compounds, which display either a moderate or weak insecticidal and acaricidal activity and a substantial toxicity for animals in a number of cases.

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REACTION OF B-HALONIUM DERIVATIVES OF CARBORANES-12 WITH TRIPHENYLPHOSPHINE

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Recently we reported the synthesis of the phenyl-9-o- and phenyl-9-m-carboranyliodonium salts [1] and their reactions with nucleophiles [2]. In the present paper we describe the reaction of the phenyl-9-o- (I) and phenyl-9-m-carboranyliodonium (II) fluoborates with triphenylphosphine (TPP), and also the "carboranylation" of PPh_3 with bis(9-m-carboranyl)bromonium fluoborate (III).

It is known that diphenylhalonium fluoborates react with TPP to give tetraphenylphosphonium fluoborate (IV). As was shown in [3, 4], these reactions proceed by the radical mechanism via the intermediate formation of the complex of the Ph_2Hal^+ cation with one PPh_3 molecule and are initiated by light.

We found that the radical reaction also proceeds easily when acetone solutions of mixtures of either (I) or (II) with TPP are illuminated with an incandescent lamp, resulting in the formation of two main products: (IV) and the corresponding 9-iodocarborane, and also ~1% of benzene and traces of diphenyl.

$$\text{(I) or (II)} + PPh_3 \rightarrow \underset{\text{(IV)}}{Ph_4\overset{+}{P}BF_4^-} + 9\text{-}o\,(m)\text{-}C_2H_2B_{10}H_9I + PhH + Ph_2$$

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