SYNTHESIS AND SOME PROPERTIES OF ACRYLIC AND METHACRYLIC DERIVATIVES OF CHLOROPHOS AND ITS ANALOGS

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The preparation and possible physiological activity of the acrylic derivatives of chlorophos and a number of its analogs were reported previously [1, 2]. In particular, the methacrylic derivative of chlorophos exhibits fungicidal properties [3]. In order to ascertain the relation between the structure and physiological activity of the studied type of compounds we obtained some new acrylic, methacrylic and α-fluoroacrylic compounds based on chlorophos and its analogs, in particular, the butyl and phenyl analogs.

The products were synthesized by the reaction of chlorophos and its analogs with the appropriate acid chlorides of the acrylic series in the presence of Na_2CO_3 as the HCl acceptor using the procedure described in [1]. The obtained compounds (Table 1) are either crystalline substances or viscous colorless liquids that are not amenable to vacuum-distillation. They are insoluble in water and hydrocarbons, but are soluble in benzene, acetone, chloroform, dimethylformamide or dioxane. When heated or allowed to stand at room temperature for a long time the compounds polymerize with the formation of self-extinguishing polymers. The structure of the compounds is confirmed by their IR spectra, where absorption bands appear in the 1635-1655 cm^{-1} region, which testify to the presence of the C=C bond, while the band of the stretching vibrations of the trichloromethyl group is present in the 800 cm^{-1} region.

We ran some comparative toxicological tests on both the previously described [1] and some of the freshly obtained acrylic derivatives of chlorophos and its analogs with respect to warm-blooded animals, pathogenic fungi and harmful insects. The toxicity for warm-blooded animals was determined on white mice by the Miller–Teinter method, with a calculation of the LD_{50} and its confidence limits, employing the

TABLE 1. Some Unsaturated Derivatives of Chlorphos and Its Analogs

Compound	Yield, %	Mp., °C	n_D^{20}	d_4^{20}	MR found	MR calculated	Found/calculated, % C	H	Cl	P
$(C_6H_5O)_2P(O)-CH(CCl_3)-O-C(=O)-C(H)=CH_2$	42	55—56	—	—	—	—	46,90 / 46,87	3,50 / 3,23	25,40 / 24,41	7,28 / 7,11
$(C_6H_5O)_2P(O)-CH(CCl_3)-O-C(=O)-C(H)=CH_2$	88	*	1,4752	1,2419	89,72	89,40	39,63 / 39,46	5,93 / 5,70	27,71 / 26,88	7,88 / 7,74
$(C_6H_5O)_2P(O)-CH(CCl_3)-O-C(=O)-C(CH_3)=CH_2$	30	*	1,4740	1,2216	94,24	94,01	40,93 / 41,04	6,18 / 5,90	26,50 / 25,96	7,43 / 7,56
$(C_6H_5O)_2P(O)-CH(CCl_3)-O-C(=O)-C(F)=CH_2$	74	*	1,4693	1,2584	90,92	89,29	38,88 / 37,74	6,17 / 5,11	23,50 / 25,71	8,21 / 7,48
$(CH_3O)_2P(O)-CH(CCl_3)-O-C(=O)-C(H)=CH_2$	54	38—39	—	—	—	—	27,16 / 26,99	3,22 / 3,23	34,40 / 34,14	9,81 / 9,94

*The compounds decompose when vacuum-distilled at 0.05 mm; they were purified by repeated washing.

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TABLE 2. Toxicity for Warm-Blooded Animals and Fungicidal Action of Some Unsaturated Derivatives of Chlorophos and Its Analogs

No.	Compound	Species of fungus*	B†	LD_{50}, mg /kg (C)	Selectivity index (C/B)
(I)	$(CH_3O)_2P(O)-CH(CCl_3)-O-C(=O)-CH_3$	a	0,15	800	5333
		b	0,15	(700--900)	
(II)	$(CH_3O)_2P(O)-CH(CCl_3)-O-C(=O)-C(H)=CH_2$	a	0,10	110	1100
		b	0,10	(101--119)	
(III)	$(CH_3O)_2P(O)-CH(CCl_3)-O-C(=O)-C(CH_3)=CH_2$	a	0,05	455	8100
		b	0,05	(376--534)	
(IV)	$(C_4H_9O)_2P(O)-CH(CCl_3)-O-C(=O)-C(H)=CH_2$	a	0,05	600	12000
		b	0,05	(537--663)	
(V)	$(C_4H_9O)_2P(O)-CH(CCl_3)-O-C(=O)-C(CH_3)=CH_2$	a	‡	1160	—
		b	‡	(1148--1160)	
(VI)	$(C_4H_9O)_2P(O)-CH(CCl_3)-O-C(=O)-C(F)=CH_2$	a	0,25	670	2680
		b	0,25	(554--786)	
(VII)	$(ClC_2H_4O)_2P(O)-CH(CCl_3)-O-C(=O)-C(F)=CH_2$	a	0,25	265	1060
		b	0,25	(273--257)	
(VIII)	$(C_2H_5)_2P(O)-CH(CCl_3)-O-C(=O)-C(H)=CH_2$	a	—	435	—
		b	—	(341--529)	
(IX)	$(C_6H_5O)_2P(O)-CH(CCl_3)-O-C(=O)-C(CH_3)=CH_2$	a	—	Over 800	—
		b	—		

*a) Trichophyton gypseum; b) Epidermophyton Kaufmann–Wolf.

†The lowest concentration in % that causes a complete suppression of fungal growth.

‡The fungicidal properties were not tested due to the poor solubility; a minus sign means that the compound fails to act on the fungus culture at a concentration of 0.25%.

subscutaneous injection of aqueous emulsions of the test compounds [4]. Here OP-7 served as the emulsifier, which was taken on the basis of 1 : 0.5.

As test objects to study the fungicidal action we took Trichophyton gypseum and Epidermophyton Kaufmann–Wolf, which are fungi that damage the skin and its appendages for man and animals. The cultures of the fungi were sown on solid Saburo medium, which contained increasing doses of the test compounds. The criterion of fungicidal action was considered to be the absence of fungal growth for a month, with luxuriant growth in the control. The contact insecticidal action was determined on the housefly (Musca domestica L) and the granary weevil (Calandra granaria L), while the systemic action was determined on the aphid (Aphis fabae Scop.) and the spider mite (Tetranychus urticae Koch).

The results of the tests are summarized in Table 2, where compound (I), namely the O, O-dimethyl ester of 1-acetoxy-2,2,2-trichloroethylphosphonic acid (chloracetophos), is given for comparison. This compound has found use in medicine for the treatment of fungal diseases in man [5,6]. As can be seen from Table 2, replacing the acetyl radical in the chloracetophos molecule by either the acryloyl or methacryloyl radical increases the toxicity of the compound and enhances the fungicidal properties, which leads to an increase in the selectivity index of compound (III). A lengthening of the alkoxyl radical attached to the phosphorus atom decreases the toxicity with respect to warm-blooded animals [compounds (II) and (IV), and (III) and (V)] and increase the selectivity index of (IV). The insertion of a chlorine atom in the alkoxyl group attached to the phosphorus leads to an increase in the toxicity of (VII).

Chloracetophos, which is a weak insecticide, causes the death of houseflies and the granary weevil when deposited as 0.5% solutions. We were unable to detect its systemic action with respect to sucking insects. The acrylic, methacrylic and α-fluoroacrylic derivatives of chlorophos and its analogs (compounds (II) and (IX), see Table 2), even at a concentration of 2-5% , fail to exhibit an expressed toxic effect on insects when applied topically. A systemic action is not exhibited when the plants are treated with 1% solutions of the test compounds, while a further increase in the concentration leads to plant blight.

EXPERIMENTAL METHOD

O, O-Diphenyl (1-acryloyloxy-2, 2, 2-trichloroethyl)phosphonate. To a suspension of 49 g of O,O-diphenyl (1-hydroxy-2, 2, 2-trichloroethyl)phosphonate and 106 g of Na_2CO_3 in 250 ml of absolute $CHCl_3$, containing 0.1 g of hydroquinone, at 15-16°C, with vigorous stirring, was added in drops a solution of 46.6 g of acryloyl chloride in 150 ml of absolute $CHCl_3$. Then the mixture was stirred at ~20° for 12 h. The

precipitate was filtered, and the filtrate was evaporated in vacuo. After evaporation, the residue was dissolved in 100 ml of benzene and washed 3-4 times with aqueous Na_2CO_3 and NaCl solutions. The solution was then dried over $CaSO_4$ and evaporated in vacuo. A double recrystallization of the residue from acetone gave 23.5 g (42%) of a white crystalline compound with mp 55-56°.

O,O-Dimethyl (1-acryloyloxy-2,2,2-trichloroethyl)phosphonate. The synthesis was run in the same manner as the preceding. The reaction of 85.5 g of O,O-dimethyl (1-hydroxy-2,2,2-trichloroethyl)phosphonate (chlorophos) with 30 g of acryloyl chloride in 600 ml of absolute benzene, in the presence of 106 g of Na_2CO_3 and 0.15 g of hydroquinone, gave 56.2 g (54%) of O,O-dimethyl (1-acryloyloxy-2,2,2-trichloroethyl)-phosphonate with mp 38-39° (from acetone).

O,O-Di-n-butyl (1-acryloyloxy-2,2,2-trichloroethyl)phosphonate. In a similar manner, the reaction of 56.5 g of O,O-di-n-butyl (1-hydroxy-2,2,2-trichloroethyl)phosphonate with 16.5 g of acryloyl chloride in 500 ml of absolute benzene, in the presence of 53 g of Na_2CO_3 and 0.1 g of hydroquinone, gave 57 g (88%) of O,O-di-n-butyl (1-acryloyloxy-2,2,2-trichloroethyl)phosphonate as a viscous colorless oil that decomposed when subjected to vacuum-distillation at 0.05 mm.

The product was characterized in the crude form, after its benzene solution was treated repeatedly with aqueous Na_2CO_3 and NaCl solutions, followed by drying over $CaSO_4$ and then evaporation for 6 h in vacuo (0.05 mm) at ~ 20° until the n_D^{20} had a constant value.

Di-n-butyl (1-methacryloyloxy-2,2,2-trichloroethyl)phosphonate. From 68.4 g of O,O-di-n-butyl-(1-hydroxy-2,2,2-trichlorobutyl)phosphonate and 22.2 g of methacryloyl chloride in 400 ml of absolute benzene, in the presence of 70 g of Na_2CO_3 and 0.2 g of hydroquinone, after purification by the above described method, we obtained 64.9 g (79%) of crude O,O-di-n-butyl (1-methacryloyloxy-2,2,2-trichloroethyl)phosphonate as a thick colorless liquid.

O,O-Di-n-butyl (1-α-fluoroacryloyloxy-2,2,2-trichloroethyl)phosphonate. From 13.2 g of O,O-di-n-butyl (1-hydroxy-2,2,2-trichloroethyl)phosphonate and 5.6 g of α-fluoroacryloyl chloride in 250 ml of absolute benzene, in the presence of 13 g of Na_2CO_3 and 0.05 g of hydroquinone, we obtained 11.8 g (74%) of O,O-di-n-butyl (1-α-fluoroacryloyloxy-2,2,2-trichloroethyl)phosphonate, which was purified as described above. The product is a viscous colorless liquid that is insoluble in water, but is soluble in acetone, chloroform or benzene. The attempted vacuum-distillation (0.05 mm) of the product resulted in polymerization, even in the presence of inhibitors (hydroquinone, CuCl).

CONCLUSIONS

The reaction of chlorophos and its analogs with the acid chlorides of the acrylic, methacrylic and α-fluoroacrylic acids gave some new unsaturated compounds that possess fungicidal action.

LITERATURE CITED

1. A. A Muslinkin and V. B. Loginov, Izv. Akad. Nauk SSSR, Ser. Khim., 1968, 2616.
2. B. Yasuo and K. Hiroshi, Japan Patent 6811209 (1968); C. A., 70, 37918b (1969).
3. I. D. Neklesova, M. A. Kudrina, and N. V. Egorova, in monograph: "Problems in Organic and Physical Chemistry" [in Russian], A. E. Arbuzov Institute of Organic and Physical Chemistry, Academy of Sciences of the USSR, Kazan (1971), p. 142.
4. M. L. Belen'kii, Elements in the Quantitative Estimate of the Pharmacological Effect [in Russian], Medgiz, Leningrad (1963), p. 72.
5. N. V. Egorova, M. A. Kudrina, Z. Sh. Minyusheva, I. D. Neklesova, B. A. Nikonenko, and K. V. Nikonorov, USSR Patent 280768 (1961); Byull. Izobr., No. 28 (1970).
6. I. D. Neklesova, Z. Sh. Minyusheva, M. A. Kudrina, Ya. G. Akchurina, and N. V. Egorova, Vestn. Dermatologii i Venerologii, 1972 No. 2, 58.