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PHENOXYMETHYL 2-CHLOROETHYL ETHERS[1]

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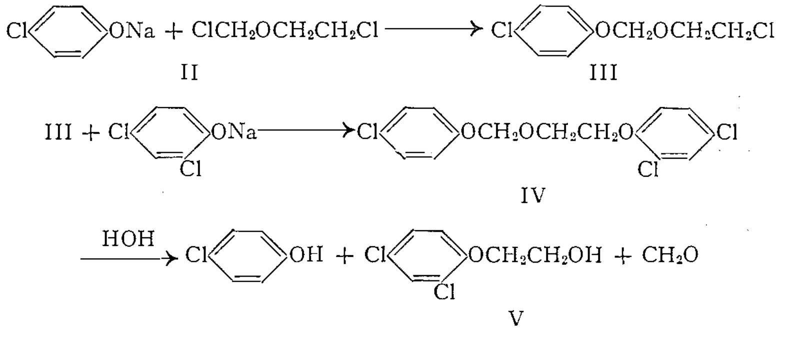
ABSTRACT

A series of phenoxymethyl 2-chloroethyl ethers has been prepared for testing as possible insecticides.

In this investigation a series of phenoxymethyl 2-chloroethyl ethers, $ArOCH_2OCHXCH_2Cl$ (I, X = H or CH_3), was prepared for testing as possible insecticides by alkylating various phenols with 2-chloroethyl (1, 2) and 1-chloro-2-propyl (5) chloromethyl ether. The toxic effects of these ethers (I) on insects is described by Musgrave and Kukovica (3).

It is well known that the halogen atom linked α to the oxygen atom of chloroethers is more reactive than the β-halogen (2). This considerable difference in the halogen reactivities was also noted in the reactions between chloromethyl chloroethyl ether (II) and sodium phenoxides.

When chloromethyl 2-chloroethyl ether (II) was treated with aqueous or alcoholic solutions of a sodium phenoxide at room temperature, only a monophenoxy derivative was formed and a higher reaction temperature was necessary in order to form the diphenoxy derivative, $ArOCH_2OCH_2CH_2OAr$. In order to establish that the α-chlorine and not the β-chlorine reacted under the milder conditions, the reaction product (III) of sodium *p*-chlorophenoxide and II was heated with sodium 2,4-dichlorophenoxide. The resulting product (IV) on mild acid hydrolysis yielded *p*-chlorophenol and 2,4-dichlorophen-



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oxyethanol (V) (4) and not 2,4-dichlorophenol and *p*-chlorophenoxyethanol, the products expected had the β-chlorine of II reacted before the α-chlorine. The wide difference in the degree of reactivity between the two chlorine atoms of II is further emphasized by the fact that III remains unaltered after boiling with diethylamine in benzene solution for several hours and requires prolonged boiling with alcoholic potassium thiocyanate in order to form 2-thiocyanatoethyl *p*-chlorophenoxymethyl ether. Phenoxymethyl 2-chloroethyl ether (I, Ar = C_6H_5, X = H) is stable in aqueous alkali but resinifies explosively when warmed with a drop of concentrated hydrochloric acid.

EXPERIMENTAL

Preparation of 2-Chloroethyl Phenoxymethyl Ethers

Method A

To a stirred solution of sodium (1 mole) in absolute ethanol (1 liter) was added the phenol (1 mole) and then dropwise chloromethyl 2-chloroethyl ether (1 mole) (1, 2) over about one-half hour, the temperature being kept at 20–25° by cooling. The reaction mixture was stirred for an additional two hours, the ethanol was distilled off *in vacuo*, and the residue treated with water. The product was extracted with benzene, washed with sodium hydroxide and with water. The solvent was then removed and the residue distilled.

Method B

To a stirred solution (or suspension) of sodium phenoxide (1 mole) in water (200 ml.) was added dropwise chloromethyl 2-chloroethyl ether (1 mole) in benzene (400 ml.) over about one-half hour, the temperature being kept at 10° by cooling. After the solution had been stirred for an additional two hours the benzene layer was separated from the reaction mixture, washed with sodium hydroxide and with water. The solvent was removed and the residue distilled.

TABLE I

PHENOXYMETHYL 2-CHLOROETHYL ETHERS ($ROCH_2OCH_2CH_2Cl$) FROM CHLOROMETHYL 2-CHLOROETHYL ETHER AND THE APPROPRIATE PHENOL

$ROCH_2OCH_2CH_2Cl$ R =	Method of prep.	% Yield	M.p. or b.p.	n_D^{20}	Formula	Analyses			
						Calc.		Found	
						C	H	C	H
Phenyl	A	68	$b_{12}=123$	1.5170	$C_9H_{11}O_2Cl$	57.91	5.94	58.05	6.01
α-Naphthyl	A	88	$b_{12}=200$	1.5912	$C_{13}H_{13}O_2Cl$	65.97	5.50	66.12	5.51
p-t-Butylphenyl	A	64	$b_{12}=163$	1.5072	$C_{13}H_{19}O_2Cl$	64.33	7.84	64.41	7.87
p-Chlorophenyl	A	76	$b_{12}=150$	1.5300	$C_9H_{10}O_2Cl$	48.87	4.52	49.22	4.65
	B	64							
2,4-Dichlorophenyl	A	50	$b_{12}=167$	1.5465	$C_9H_9O_2Cl_3$	42.27	3.52	42.62	3.58
2,3,4,5,6-Pentachlorophenyl	A	60	m.p. = 90		$C_9H_6O_2Cl_6$	30.08	1.67	30.30	2.11
p-Nitrophenyl	A	28	m.p. = 70		$C_9H_{10}NO_4Cl$	46.65	4.32	46.89	4.50
	B	4							
	C	90							
2-Methoxy-4-formylphenyl	A	30	m.p. = 59		$C_{11}H_{13}O_4Cl$	53.99	5.32	53.99	5.52
2,4-Dinitrophenyl	C	6	m.p. = 80		$C_9H_9N_2O_6Cl$	39.06	3.26	39.32	3.08

Method C

A reaction mixture of chloromethyl 2-chloroethyl ether (1 mole), dry benzene (350 ml.), and the dry sodium phenoxide (1 mole) was heated under reflux for four hours. Water was added to the cooled reaction mixture, the benzene layer was separated, washed with sodium hydroxide and with water. The solvent was removed and the residue distilled.

p-Chlorophenoxymethyl 2-(2,4-Dichlorophenoxy)ethyl Ether (IV)

To a solution of sodium (5 gm.) in absolute ethanol (250 ml.) was added 2,4-dichlorophenol (34 gm.) and 2-chloroethyl *p*-chlorophenoxymethyl ether (45 gm.) and the resulting solution heated under reflux for 40 hr. About half of the ethanol was distilled off from the reaction mixture and the residue was treated with water and extracted with benzene.

The benzene extract was washed with water and the solvent was removed. Fractional distillation of the residue yielded unchanged *p*-chlorophenoxymethyl 2-chloroethyl ether (21 gm.) and a higher-boiling fraction, b.p. (0.2 mm.) = 170–172° (27 gm.). The latter was a viscous colorless liquid, $n_D^{20} = 1.5752$. Anal. calc. for $C_{15}H_{13}O_3Cl_3$: C, 51.81; H, 3.74. Found: C, 52.11; H, 3.60.

p-t-Butylphenoxymethyl 2-p-t-Butylphenoxyethyl Ether

This was prepared in 70% yield as above from *p-t*-butylphenoxymethyl 2-chloroethyl ether. It is a colorless viscous liquid, b.p. (12 mm.) = 245–250°, $n_D^{20} = 1.5270$. Anal. calc. for $C_{23}H_{32}O_3$: C, 77.54; H, 8.98. Found: C, 77.43; H, 9.06.

Hydrolysis of p-Chlorophenoxymethyl 2-(2,4-Dichlorophenoxy)ethyl Ether (IV)

A solution of *p*-chlorophenoxymethyl 2-(2,4-dichlorophenoxy)ethyl ether (15 gm.), water (150 ml.), ethanol (150 ml.), and concentrated hydrochloric acid (25 ml.) was heated under reflux for eight hours. Most of the ethanol was distilled and the cooled residue was extracted with ether. The ether was removed from the extract and the residue was fractionally distilled. Two main fractions were collected, fraction 1 boiling at 98–105° (12 mm.) (4 gm.) and fraction 2 boiling at 160–165° (12 mm.) (7 gm.). Fraction 1 solidified on cooling and melted at 35° alone or in admixture with *p*-chlorophenol. It depressed the melting point of 2,4-dichlorophenol. Fraction 2 after crystallization from benzene melted at 58–59° alone or in admixture with authentic 2,4-dichlorophenoxyethanol (4).

1,3-bis(2-Chloroethoxymethoxy)benzene

This was prepared in 20% yield by method A using two moles of sodium and two moles of chloromethyl 2-chloroethyl ether (II) per mole of resorcinol. It is a colorless liquid boiling at 150–154° (0.3 mm.), $n_D^{20} = 1.5212$. Anal. calc. for $C_{12}H_{16}O_4Cl_2$: C, 48.83; H, 5.41. Found: C, 48.80; H, 5.39.

1,4-bis(2-Chloroethoxymethoxy)benzene

This was prepared in 52% yield by method A as above from II and hydroquinone, b.p. (0.3 mm.) = 149–150°, $n_D^{20} = 1.5197$. Anal. calc. for $C_{12}H_{16}O_4Cl_2$: C, 48.83; H, 5.41. Found: C, 48.67; H, 5.31.

1,4-bis(2-Chloroethoxymethoxy)-2,3,5,6-tetrachlorobenzene

This was prepared in 12% yield by method A from tetrachlorohydroquinone and II. The white needles melted at 117–118° after crystallization from ethanol. Anal. calc. for $C_{12}H_{12}O_4Cl_6$: C, 33.26; H, 2.77. Found: C, 33.24; H, 2.82.

1,2-bis(2-Chloroethoxymethoxy)benzene

This was prepared in 41% yield by method A from II and catechol, b.p. (0.2 mm.) = 146–148°, $n_D^{20} = 1.5222$. Anal. calc. for $C_{12}H_{16}O_4Cl_2$: C, 48.83; H, 5.41. Found: C, 48.72; H, 5.18.

1,2,3-tris(2-Chloroethoxymethoxy)benzene

This was prepared in 15% yield by method A from II and pyrogallol, b.p. (0.2 mm.) = 212–215°. Anal. calc. for $C_{15}H_{21}O_6Cl_3$: C, 44.62; H, 5.25. Found: C, 44.91; H, 5.24.

p-Chlorophenoxymethyl 2,N-Morpholinoethyl Ether

A solution of *p*-chlorophenoxymethyl 2-chloroethyl ether (III) (16 gm.), morpholine (16 gm.), and toluene (100 ml.) was heated under reflux for 24 hr. The morpholine hydrochloride was filtered and the filtrate was extracted with dilute hydrochloric acid. The acid solution was basified with sodium hydroxide and extracted with benzene. Removal of the benzene and distillation of the residue yielded 14 gm. (or 68%) of a colorless liquid b.p. (12 mm.) = 196–198°, $n_D^{20} = 1.5278$. Anal. calc. for $C_{13}H_{18}NO_3Cl$: C, 57.45; H, 6.63. Found: C, 57.27; H, 6.54.

p-Chlorophenoxymethyl 2-Dimethylaminoethyl Ether

This was prepared as above from dimethylamine and *p*-chlorophenoxymethyl 2-chloroethyl ether (III), the reaction being carried out in a sealed bomb at 120–130°. It distilled as a colorless liquid boiling at 149–150° (12 mm.), $n_D^{20} = 1.5100$. Anal. calc. for $C_{11}H_{16}NO_2Cl$: C, 57.51; H, 6.97. Found: C, 57.24; H, 6.93. The *ethiodide* melted at 106–107° after crystallization from ethyl acetate. Anal. calc. for $C_{13}H_{21}NO_2ClI$: C, 40.46; H, 5.45. Found: C, 40.41; H, 5.59. The *butiodide* melted at 86–87° after crystallization from methanol. Anal. calc. for $C_{15}H_{25}NO_2ClI$: C, 43.53; H, 6.04. Found: C, 43.55; H, 6.13.

p-Chlorophenoxymethyl 2-Diethylaminoethyl Ether

This was prepared as above from diethylamine and III. It distilled as a colorless liquid boiling at 165–167° (12 mm.), $n_D^{20} = 1.5032$. Anal. calc. for $C_{13}H_{20}NO_2Cl$: C, 60.57; H, 7.77. Found: C, 60.68; H, 7.82.

p-Chlorophenoxymethyl 1-Chloro-2-propyl Ether

This was prepared in 63% yield by method A from chloromethyl 1-chloro-2-propyl ether (5) ($ClCH_2OCH(CH_3)CH_2Cl$) and *p*-chlorophenol. It distilled as a colorless liquid boiling at 155–157° (13 mm.), $n_D^{20} = 1.5210$. Anal. calc. for $C_{10}H_{12}O_2Cl_2$: Cl, 30.2. Found: Cl, 30.5.

p-Nitrophenoxymethyl 1-Chloro-2-propyl Ether

This was prepared in 63% yield by method C from chloromethyl 1-chloro-2-propyl ether and *p*-nitrophenol. It crystallized from methanol as white prisms melting at 43–44°. Anal. calc. for $C_{10}H_{12}NO_4Cl$: C, 48.88; H, 4.89. Found: C, 49.00; H, 4.84.

p-Nitrophenoxymethyl 2-Thiocyanatoethyl Ether

A solution of *p*-nitrophenoxymethyl 2-chloroethyl ether (12 gm.) and potassium thiocyanate (6 gm.) in 95% ethanol (100 ml.) was heated under reflux for 24 hr. Most of the ethanol was distilled off and the residue treated with cold water. The white solid was filtered, washed, dried, and crystallized from benzene – petroleum ether. The white prisms melted at 58–59°. Anal. calc. for $C_{10}H_{10}N_2O_4S$: C, 47.26; H, 3.94. Found: C, 46.88; H, 4.05.

p-Nitrophenoxymethyl 1-Thiocyanato-2-propyl Ether

This was prepared as above from *p*-nitrophenoxymethyl 1-chloro-2-propyl ether. The white prisms melted at 42–43°. Anal. calc. for $C_{11}H_{12}O_4N_2S$: C, 49.25; H, 4.48. Found: C, 49.30; H, 4.78.

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