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CHLOROPHENOXYETHOXYETHANOLS FROM POLYCHLOROBENZENES

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There are numerous references in the literature to the synthesis of various halophenoxyethanols, or ethylene glycol halophenyl ethers, by the reaction of sodium halophenates with ethylene chlorohydrin (1–4). The corresponding esters have also been reported, including acetates, methacrylates, crotonates, maleates, and cinnamates (4–7).

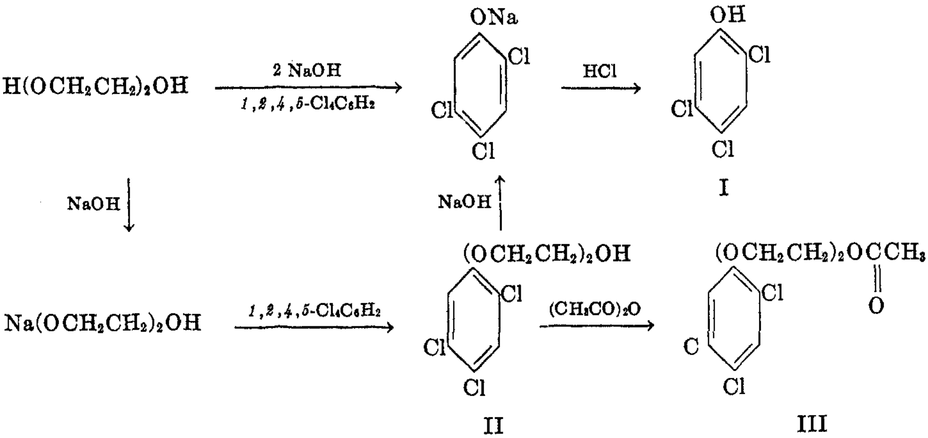
Another procedure used less frequently for the synthesis of halophenoxyethanols involves the condensation of halophenols with ethylene oxide (3, 5). By this method 2-(pentachlorophenoxyethoxy)ethanol and 2-(pentachlorophenoxyethoxyethoxy)ethanol, the analogous derivatives of diethylene glycol and triethylene glycol, respectively, were prepared. In one instance 2-(2,4-dichlorophenoxyethoxy)ethanol was made by the reaction of sodium 2,4-dichlorophenate with diethylene glycol chlorohydrin (8). The acetates of these compounds have also been reported (9).

This paper is concerned with the synthesis of chlorophenoxyethoxyethanols and chlorophenoxyethoxyethoxyethanols by the condensation of polychlorobenzenes with diethylene glycol and triethylene glycol, respectively, in the presence of sodium hydroxide and an excess of the glycol.

The hydrolysis of 1,2,4,5-tetrachlorobenzene with sodium hydroxide in solution of methanol at 160° in an autoclave (10) yields 2,4,5-trichlorophenol. This phenol is also formed from 1,2,4,5-tetrachlorobenzene when ethylene glycol and propylene glycol are used as solvents at 170–200° at atmospheric pressure (11).

Investigation of this reaction using diethylene glycol as solvent at 200° gave 2,4,5-trichlorophenol (I) as the major product, and a small amount (5%) of an oil obtained as a steam-distillation residue. Lower reaction temperatures favored the formation of an intermediate compound, 2-(2,4,5-trichlorophenoxyethoxy)ethanol (II). At 125° using 1,2,4,5-tetrachlorobenzene and sodium hydroxide in a molar ratio of 1 to 2.5, the maximum alkali consumption was 1.1 moles as determined by titration of hydroxyl ion during the course of the reaction. One-tenth mole of 2,4,5-trichlorophenol was isolated from the reaction mixture corresponding to a yield of 10%. This was subsequently confirmed in a larger scale experiment, in which an 11% yield of the phenol and 72.5% of 2-(2,4,5-trichlorophenoxyethoxy)ethanol were obtained. This compound was esterified with acetic anhydride to give 2-(2,4,5-trichlorophenoxyethoxy)ethyl acetate (III) in 91.6% yield.

EXPERIMENTAL



Purity of chlorobenzenes. The purity of the chlorobenzenes used in the synthesis of chlorophenoxyethoxyethanols was determined by infrared analysis.

Trichloro- and tetrachloro-benzenes. To obtain the individual isomers, a mixture of the chlorobenzenes was dissolved in hot acetic acid, cooled to 40°, and filtered to remove most of the 1,2,4,5-tetrachlorobenzene. The filtrate was distilled to remove the acetic acid and then fractionated to separate 1,2,4-trichloro-, 1,2,3-trichloro-, and 1,2,3,4-tetrachloro-benzene. For 1,2,4,5-tetrachlorobenzene, a technical grade was recrystallized from benzene.

The composition of chlorobenzenes was as follows:

	Infrared Analysis, Chlorobenzenes, %			
	1,2,3-tri-	1,2,4-tri-	1,2,3,4-tetra-	1,2,4,5-tetra-
1,2,4-Trichlorobenzene, Sample No. 1	11	87		
1,2,4-Trichlorobenzene, Sample No. 2	5	95		
1,2,3-Trichlorobenzene	96	4		
1,2,3,4-Tetrachlorobenzene			85	15
1,2,4,5-Tetrachlorobenzene				99.5

Pentachlorobenzene. Chlorination of a mixture of trichlorobenzene, and fractionation of the product gave pentachlorobenzene in 100% purity.

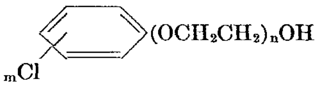
Hexachlorobenzene. This was Distillation Products Industries white label material.

Preparation of chlorophenoxyethoxyethanols. The chlorophenoxyethoxyethanols were prepared by the condensation of chlorobenzenes with either diethylene glycol or triethylene glycol using an excess of sodium hydroxide. The glycol was used in proportions of 500–1000 g. per mole of chlorobenzene, its function being that of diluent as well as reactant. The molar ratio of chlorobenzene to sodium hydroxide varied between 1 to 1 and 1 to 1.5 for most of the condensations; two experiments were effected at a ratio of 1 to 2.5 involving the use of a large excess of sodium hydroxide which was not required generally. No attempt was made to study temperature and time of reaction for optimum yields.

Two different techniques were employed in the recovery of the chlorophenoxyethoxyethanols. For compounds No. 1, 2, 3, 9, and 10, Table I, the reaction mixture was diluted with water and the oil which separated was distilled under reduced pressure to obtain the

TABLE I

CHLOROPHENOXYETHOXYETHANOLS

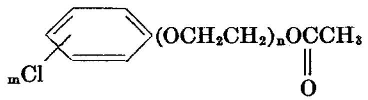


m = 2 to 5 inclusive
n = 2, 3

No.	Compound	Yield, %	b.p., °C.	Mm.	n_D^{25}	Empirical Formula	Analyses							
							C		H		Cl		OH	
							Calc'd	Found	Calc'd	Found	Calc'd	Found	Calc'd	Found
1	2-(3,6-Dichlorophenoxyethoxy)-ethanol	29.9	167–170	2	1.5470	$C_{10}H_{12}Cl_2O_3$	47.82	47.48	4.82	4.78	28.25	27.37	6.78	7.22
2	2-(3,6-Dichlorophenoxyethoxyethoxy)ethanol	60.9	198–201	2.5	1.5330	$C_{12}H_{16}Cl_2O_4$	48.81	48.81	5.44	5.76	24.05	23.80	5.76	4.57
3	2-(2,3-Dichlorophenoxyethoxyethoxy)ethanol	41.0	187–190	1.5	1.5335	$C_{12}H_{16}Cl_2O_4$	48.81	48.51	5.44	6.06	24.05	21.94	5.76	4.88
4	2-(2,3,6-Trichlorophenoxyethoxy)-ethanol	63.7	190–193	4.5	1.5550	$C_{10}H_{11}Cl_3O_3$	42.06	42.19	3.86	4.09	37.29	37.09	5.95	5.80
5	2-(2,3,6-Trichlorophenoxyethoxyethoxy)ethanol	82.1	212–216	2.5	1.5375	$C_{12}H_{15}Cl_3O_4$	43.73	43.87	4.56	4.67	32.27	30.21	5.16	5.17
6	2-(2,4,5-Trichlorophenoxyethoxy)-ethanol	72.5	197–198	6	1.5610	$C_{10}H_{11}Cl_3O_3$					37.29	35.84	5.95	5.91
7	2-(2,4,5-Trichlorophenoxyethoxyethoxy)ethanol	68.5	199–200	1.6	1.5460	$C_{12}H_{15}Cl_3O_4$					32.27	30.86	5.16	5.66
8	2-(2,3,4,5-Tetrachlorophenoxyethoxy)ethanol	41.8	195–198	2.6	1.5655	$C_{10}H_{10}Cl_4O_3$	37.53	37.35	3.20	3.45	44.32	43.38	5.62	5.66
9	2-(2,3,4,5-Tetrachlorophenoxyethoxyethoxy)ethanol	33.7	214–217	2.4	1.5450	$C_{12}H_{14}Cl_4O_4$	39.80	39.88	4.85	4.71	38.96	35.69	4.69	5.69
10	2-(Pentachlorophenoxyethoxyethoxy)ethanol	58.5	222–224	1.1	1.5585	$C_{12}H_{13}Cl_5O_4$	36.16	36.25	3.28	3.81	44.49	43.60	4.26	3.89

TABLE II

CHLOROPHENOXYETHOXYETHYL ACETATES



m = 2 to 5 inclusive
n = 2, 3

No.	Compound	Yield, %	b.p., °C.	Mm.	n_D^{25}	Empirical Formula	Analyses C Calc'd	Analyses C Found	Analyses H Calc'd	Analyses H Found	Analyses Cl Calc'd	Analyses Cl Found
1	2-(3,6-Dichlorophenoxyethoxy)ethyl acetate	90.4	169–172	2.2	1.5228	$C_{12}H_{14}Cl_2O_4$	49.18	47.09	4.78	4.92	24.20	24.05
2	2-(2,3-Dichlorophenoxyethoxyethoxy)-ethyl acetate	37.4	190–195	1.6	1.5145	$C_{14}H_{18}Cl_2O_5$	49.87	48.98	5.37	5.62	21.03	20.95
3	2-(2,3,6-Trichlorophenoxyethoxy)ethyl acetate	96.8	195–201	4.4	1.5317	$C_{12}H_{13}Cl_3O_4$	43.95	43.71	3.97	4.14	32.47	32.08
4	2-(2,3,6-Trichlorophenoxyethoxyethoxy)-ethyl acetate	79.0	207–210	4.00	1.5225	$C_{14}H_{17}Cl_3O_5$	45.24	44.37	4.32	4.86	28.75	27.99
5	2-(2,4,5-Trichlorophenoxyethoxy)ethyl acetate	91.6	200–201	4.8	1.5355	$C_{12}H_{13}Cl_3O_4$	43.95	43.50	3.97	4.13	32.47	32.31
6	2-(2,3,4,5-Tetrachlorophenoxyethoxy)-ethyl acetate	96.0	185–188	1.0	1.5435	$C_{12}H_{12}Cl_4O_4$	39.81	39.09	3.31	3.38	39.17	39.43
7	2-(Pentachlorophenoxyethoxyethoxy)-ethyl acetate	58.0	222–228	1.2	1.5448	$C_{14}H_{15}Cl_5O_5$	38.17	37.85	3.41	3.78	40.24	39.00

pure ethanol. The remaining compounds were isolated after first steam-distilling the basic reaction mixture to recover unreacted chlorobenzene, followed by acidification and steam-distillation to isolate chlorophenol formed as a by-product of the reaction. The following procedures illustrate the various modifications which were employed in the preparation of the chlorophenoxyethanols.

2-(3,6-Dichlorophenoxyethoxyethoxy)ethanol. A mixture comprising 2.5 moles (455 g.) of trichlorobenzene (95% 1,2,4-trichlorobenzene and 5% 1,2,3-trichlorobenzene), 3.125 moles (125 g.) of sodium hydroxide, and 1500 g. of triethylene glycol was heated at 155–158° for 6 hours. The reaction mixture was cooled and poured into 2 liters of water whereupon an oil separated which was distilled under reduced pressure to recover the product, b.p. 198–201° (2.5 mm.); n_D^{25} 1.5330; weight 410 g. (55.5%).

2-(2,3,6-Trichlorophenoxyethoxy)ethanol. This compound was prepared from 2 moles (432 g.) of 1,2,3,4-tetrachlorobenzene (85% 1,2,3,4-tetrachloro- and 15% 1,2,4,5-tetrachloro-benzene), 2 moles (80 g.) of sodium hydroxide, and 1000 g. of diethylene glycol. The reaction mixture was heated at 200° for 1 hour, and then steam-distilled, recovering 0.625 mole (135 g.) of unreacted tetrachlorobenzene. Upon acidification of the mixture to *p*H 2 with concentrated sulfuric acid and further steam-distillation, there was obtained 0.45 mole of trichlorophenol which was subsequently identified as the 2,3,6-trichloro isomer by infrared analysis. The main product was distilled under reduced pressure, b.p. 190–193° (4.5 mm.); n_D^{25} 1.5550; weight 191 g. (63.7%).

2-(2,4,5-Trichlorophenoxyethoxyethoxy)ethanol. Two moles (432 g.) of 1,2,4,5-tetrachlorobenzene, 5 moles (200 g.) of sodium hydroxide, and 1400 g. of triethylene glycol were heated at 125° for 4 hours. Basic and acidic steam distillations did not yield any tetrachlorobenzene or trichlorophenol, respectively. The product was isolated by the procedure described for 2-(2,3,6-trichlorophenoxyethoxy)ethanol; b.p. 199–200° (1.6 mm.); n_D^{25} 1.5460; weight 451 g. (86.5%).

2-(2,3,4,5-Tetrachlorophenoxyethoxy)ethanol. This compound was prepared by a modification of the general procedure. The diethylene glycol monosodium alkoxide was made by heating 3 moles of sodium hydroxide in 1800 g. of diethylene glycol at 160°. This was added dropwise with stirring to 3 moles (752 g.) of pentachlorobenzene over a period 1.5 hours. The temperature was maintained at 160° for an additional half hour, after which unreacted pentachlorobenzene and tetrachlorophenol were removed, respectively, by basic and acidic steam-distillation. There was obtained 340 g. (41.8%) of 2,3,4,5-tetrachlorophenoxyethoxyethanol, b.p. 195–198° (2.6 mm.); n_D^{25} 1.5655.

Preparation of chlorophenoxyethoxyethyl acetates. The chlorophenoxyethoxyethyl acetates were synthesized from the ethanols using acetic anhydride and sodium acetate in the proportions of 2.7 moles of acetic anhydride and 0.45 mole of sodium acetate per mole of chlorophenoxyethoxyethanol. They were all prepared from the corresponding fractionated ethanols with the exception of 2,3-dichlorophenoxyethoxyethoxyethyl acetate, which was made directly from crude material. In this case the yield of the acetate was 37.4% based on 1,2,3-trichlorobenzene. The other esters listed in Table II were obtained in very good yields without any modification of the general procedure, which is described in detail for the preparation of 3,6-dichlorophenoxyethoxyethyl acetate.

2-(3,6-Dichlorophenoxyethoxy)ethyl acetate. A mixture of 0.7 mole (174 g.) of 3,6-dichlorophenoxyethoxyethanol, 2.1 mole (215 g.) of acetic anhydride, and 0.35 mole (52 g.) of sodium acetate was heated at the reflux temperature (139°) for 1.5 hours. The reaction mixture was then cooled, poured into 500 ml. of distilled water, and the oil layer which separated was taken up in ethyl ether. The ethereal solution was neutralized with 20% sodium bicarbonate and dried with sodium sulfate. There was obtained 185 g. (90.4%) of the ester, b.p. 169–172 (2 mm.); n_D^{25} 1.5228.

SUMMARY

A general procedure is described for the synthesis of chlorophenoxyethoxyethanols by the condensation of various polychlorobenzenes with diethylene

glycol and triethylene glycol in the presence of sodium hydroxide. The method was first applied to the reaction of 1,2,4,5-tetrachlorobenzene with sodium hydroxide in 1 to 2.5 molar ratio and an excess of diethylene glycol, to give the condensation product, 2-(2,4,5-trichlorophenoxyethoxy)ethanol, in 72.5% yield.

This synthesis was extended to the preparation of nine additional chlorophenoxyethoxyethanols using 1,2,4-trichloro-, 1,2,3-trichloro-, 1,2,3,4-tetrachloro-, 1,2,4,5-tetrachloro-, pentachloro-, and hexachloro-benzene with diethylene glycol and triethylene glycol. The chlorophenoxyethoxyethanols were esterified with acetic anhydride to the corresponding chlorophenoxyethoxyethyl acetates. Fifteen new compounds are described.

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