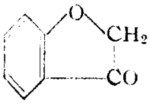
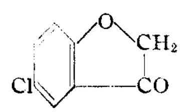
Cyclization of Phenoxyacetic Acid and Some Chlorophenoxyacetic Acids

BY M. L. KALINOWSKI AND L. W. KALINOWSKI*

In the course of our studies on the relationship between the chemical structure and the herbicidal activity of organic compounds, such as 2,4-dichlorophenoxyacetic acid, it appeared of interest to prepare coumaran-3-one (I), 5-chlorocoumaran-3-one (II), and 5,7-dichlorocoumaran-3-one (III).


I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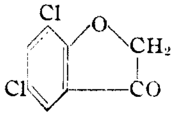
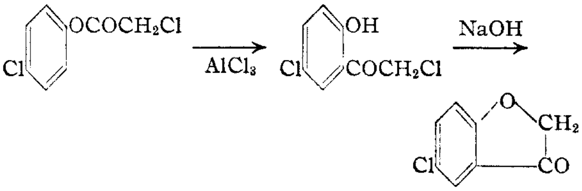

III

Three methods of preparation were considered, (1) the cyclization of the corresponding phenoxyacetyl chloride by means of aluminum chloride,[1] (2) the cyclization, by means of dilute alkali, of the corresponding 2-hydroxy-ω-chloroacetophenone,[2] and (3) the cyclodehydration of the corresponding phenoxyacetic acid in benzene solution with phosphorus pentoxide.[3]



Compound (I) was prepared by all three methods; (II) was obtained in traces by methods (1) and (3), and in fair yield by method (2). The disubstituted coumaranone (III) could not be prepared by any of these methods. It appears that the cyclization of phenoxyacetic acid is partially suppressed by chlorine substitution in the 4-position, and apparently completely suppressed by chlorine substitution in the 2,4-positions.

An attempt to effect the Fries rearrangement of 2,4-dichlorophenyl chloroacetate to 3,5-dichloro-2-hydroxy-ω-chloroacetophenone was unsuccessful. This failure of the Fries reaction to take place is not entirely unexpected in view of the work of Tarbell and Fanta.[4] These investigators point out the unreactive character of the phenolic nucleus with two chlorine atoms meta to the position where substitution is to take place, and the further decrease in reactivity by α-substitution in the acetate portion of the molecule.

When 2,4-dichlorophenoxyacetic acid was treated with phosphorus pentoxide the expected 5,7-dichlorocoumaran-3-one was not obtained. However, a good yield of material, m. p. 111.5–112.5°, was isolated which was identified as 2,4-dichlorophenyl-2′,4′-dichlorophenoxyacetate. It appears that cleavage at the ether linkage is effected by phosphorus pentoxide followed by esterification of unreacted 2,4-dichlorophenoxyacetic acid by the phenol fragment. During the reaction, the phosphorus pentoxide acquired a black color, probably due to decomposition products of glycolic acid, and a strong phenolic odor was noted in the crude reaction mixture.

In view of this unexpected reaction of 2,4-dichlorophenoxyacetic acid, the reaction products from the reaction of phenoxyacetic acid and phosphorus pentoxide, and 4-chlorophenoxyacetic acid and phosphorus pentoxide were examined carefully for ester formation. However, in neither case could any ester be found.

In order to have authentic samples of the esters for purposes of identification, phenyl phenoxyacetate, 4-chlorophenyl-4′-chlorophenoxyacetate, and 2,4-dichlorophenyl-2′,4′-dichlorophenoxyacetate were prepared from the phenoxyacetyl chlorides and the appropriate phenols.

Experimental

Cyclization of Acid Chlorides with Aluminum Chloride.—The phenoxyacetyl chlorides were prepared with thionyl chloride. Except that *s*-tetrachloroethane was employed as the solvent in the cyclization reaction, coumaran-3-one, m. p. 99–100°, and 5-chlorocoumaran-3-one, m. p. 114–116°, were prepared according to the procedure given by Stoermer and Atenstadt.[1]

The reaction with 2,4-dichlorophenoxyacetyl chloride in the common Friedel–Crafts solvents under a variety of conditions of temperature and reaction time yielded a resinous product from which no 5,7-dichlorocoumaran-3-one could be isolated.

Cyclization of 2-Hydroxy-ω-chloroacetophenones.—Although this method is indirect, it was found to be the most satisfactory one for the preparation of coumaran-3-one,[5] and 5-chlorocoumaran-3-one.[2]

However, 5,7-dichlorocoumaran-3-one could not be prepared by this procedure. The desired 3,5-dichloro-2-hydroxy-ω-chloroacetophenone was not obtained by heating 2,4-dichlorophenyl chloroacetate with aluminum chloride. Instead a light tan, non-lachrymatory compound, m. p. 135–135.5°, was obtained in 53% yield. This compound was not identified.

Anal. Calcd. for $C_8H_5Cl_3O_2$: Cl, 44.3. Found: Cl, 29.0, 29.7.

The compound 2,4-dichlorophenyl chloroacetate, b. p. 125–130° (1 mm.), has not been reported. The compound was prepared by heating 2,4-dichlorophenol with an excess of chloroacetyl chloride.

Anal. Calcd. for $C_8H_5Cl_3O_2$: Cl, 44.3. Found: Cl, 44.4.

Reaction of the Phenoxyacetic Acids with Phosphorus Pentoxide.—Coumaran-3-one and 5-chlorocoumaran-3-one were prepared by this method according to the procedure given by Stoermer and Bartsch.[3] A reaction time of eight to ten minutes seems to give a maximum yield of coumaranone. For both phenoxyacetic acid and 4-chlorophenoxyacetic acid a longer reaction time of forty-five minutes gave a heavy oil from which no coumaranone or ester could be isolated.

To a solution of 15 g. of 2,4-dichlorophenoxyacetic acid in 125 cc. of anhydrous benzene, 20 g. of phosphorus pentoxide was added. The reaction mixture was stirred and refluxed for forty-five minutes. The phosphorus pentoxide was removed by filtration, the filtrate was washed several times with water, dried over sodium sulfate, and the benzene removed by distillation. A residue of 12 g. of pasty,

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[1] Stoermer and Atenstadt, *Ber.*, **35**, 3562 (1902).

[2] Fries, Hasselbach and Schroder, *Ann.*, **405**, 370 (1914).

[3] Stoermer and Bartsch, *Ber.*, **33**, 3177 (1900).

[4] Tarbell and Fanta, THIS JOURNAL, **65**, 2170 (1943).

[5] Fries and Pfaffendorf, *Ber.*, **43**, 215 (1910).

brown solid was obtained which had a strong phenolic odor, and from which no 5,7-dichlorocoumaran-3-one could be isolated by steam distillation. The residue was triturated with a small amount of cold methanol, and the solid was recrystallized from Skelly C, m. p. 111.5–112.5° (yield 8.0 g.) A mixed m. p. with an authentic sample of 2,4-dichlorophenyl-2′,4′-dichlorophenoxyacetate showed no depression.

Anal. Calcd. for $C_{14}H_8Cl_4O_3$: C, 45.9; H, 2.18; Cl, 38.8. Found: C, 46.0; H, 2.18; Cl, 40.1.

A shorter reaction time of ten minutes afforded a lower yield of ester, and none of the 5,7-dichlorocoumaran-3-one.

Preparation of the Phenyl Esters of the Phenoxyacetic Acids.—The ester 2,4-dichlorophenyl 2′,4′-dichlorophenoxyacetate was prepared by heating equivalent amounts of 2,4-dichlorophenol and 2,4-dichlorophenoxyacetyl chloride at 130–140° for three hours. The reaction product was recrystallized from Skelly C, m. p. 112–113°.

Anal. Calcd. for $C_{14}H_8Cl_4O_3$: Cl, 38.8. Found: Cl, 38.0.

In a similar manner, 4-chlorophenyl 4′-chlorophenoxyacetate was prepared, m. p. 118–119°.

Anal. Calcd. for $C_{14}H_{10}Cl_2O_3$: Cl, 23.9. Found: Cl, 24.0.

Phenyl phenoxyacetate was prepared in a similar manner, m. p. 54–57° (reported[6] m.p. 58°).

Herbicidal Activity Tests

The various phenoxyacetic acids, cyclized derivatives, and phenyl esters were tested for plant growth regulating activity. Snap beans, grown under field conditions, were used as the test plant. Approximately 40 mg. of a solution of 1% of the compound in lanolin was applied to the pulvinus of the primary leaves when the first trifoliate leaves were expanding. Each of the compounds was applied to two plants, and the treated plants were observed over a period of eight weeks.

Phenoxyacetic acid, coumaran-3-one, and phenyl phenoxyacetate were without action.

The 4-chlorophenoxyacetic acid was very active, as was the 4-chlorophenyl ester. A slight effect was noted within two days after application, and within ten days the stems were badly swollen and the trifoliate leaves were dwarfed. After eight weeks the plants were alive but were very stunted. When 4-chlorophenoxyacetic acid was cyclicized to 5-chlorocoumaran-3-one all herbicidal activity was lost.

As was expected, 2,4-dichlorophenoxyacetic acid was very active. The 2,4-dichlorophenyl ester possessed the same order of activity, but seemed to act somewhat more slowly.

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[6] Morel, *Bull. soc. chim.*, [3] **21**, 967 (1899).

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RECEIVED DECEMBER 31, 1947

Difluoroboron-acetoacetanilide

BY JOSEPH R. KILLELEA

A recent application of the Knorr reaction in this laboratory[1] prompted a study of the use of boron fluoride as the acid catalyst for the cyclization. Small quantities of the expected 4-methylcarbostyril (I) were obtained in some cases. In every case the principal product was difluoroboron-acetoacetanilide (II).[2]

Experimental

Difluoroboron-acetoacetanilide.—To 20 ml. of a 40% solution of boron fluoride in absolute ethanol[3] is added 5.0 g. of acetoacetanilide. The solution is allowed to stand for fifteen minutes and then poured cautiously into an excess of dilute sodium carbonate. The filtered solid is stirred with normal hydrochloric acid to remove inorganic matter and dried over sodium hydroxide. It is dissolved in the minimum volume of dry dioxane, the solution filtered, and the product precipitated by the addition of petroleum ether. The product (5.0 g., 79%) forms fine needles and melts at 154–155°.

Anal. Calcd. for $C_{10}H_{10}O_2NBF_2$: B, 4.8; F, 16.9; N, 6.23. Found: B, 5.2; F, 16.7; N, 6.22.

Properties.—(a) **Hydrolysis.**—One gram of (II) is stirred with 50 ml. of a very dilute ferric chloride solution at room temperature. No color is observed until considerable time (one-half to one hour) has elapsed. The color gradually deepens as hydrolysis proceeds and reaches its maximum after six to eight hours. The solution gives positive qualitative tests for boric acid and fluorides. Nearly the theoretical quantity of acetoacetanilide may be recovered by extraction.

(b) **Cyclization.**—One gram of (II) is stirred with 3 ml. of concentrated sulfuric acid and the solution warmed to 80–90°. Reaction sets in with the evolution of acidic gases (wet litmus) containing boron (green flame). Nearly the theoretical quantity of (I) may be isolated by the usual method.[1]

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[1] Searles and Lindwall, THIS JOURNAL, **68**, 988 (1946).

[2] Similar compounds from β-diketones have been reported by Morgan, *J. Chem. Soc.*, **125**, 1963 (1924).

[3] The Knorr cyclization was attempted in other solvents and under various conditions. These directions represent a convenient method of preparation of (II).

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RECEIVED NOVEMBER 20, 1947

Isomerization of Alkyl Phosphites. VII. Some Derivatives of 2-Bromoethane Phosphonic Acid

BY GENNADY M. KOSOLAPOFF

The reaction of triethyl phosphite with ethylene bromide readily leads to a very reactive diethyl 2-bromoethane phosphonate. It was felt to be of interest to prepare a number of derivatives of this substance through the reactive halogen atom.

The action of alcoholic potassium hydroxide on this ester was found to give good yields of diethyl vinyl phosphonate, which had been earlier reported by Kabachnik,[1] who used a rather involved reaction sequence for his synthesis.

Dialkylamines react with the bromo compound in aqueous solution to give good yields of the corresponding diethyl 2-dialkylaminoethane phosphonates. As might be expected, the use of a nonpolar solvent leads to dehydrohalogenation and the formation of the above-mentioned vinyl derivative.

Experimental Part

Triethyl phosphite (33.2 g., 0.2 m.) and ethylene bromide (150 g., 0.8 m.) were heated for three hours to 160°

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[1] Kabachnik, *Izvest. Akad. Nauk. S. S. S. R.*, No. 2, 233 (1947).