

## Chemotherapeutic Nitrofurans. VIII.<sup>1</sup> The Synthesis of Certain 3,4-Dichloro-5-nitrofurans

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3,4-Dichloro-5-nitrofurvaldehyde, 3,4-dichloro-5-nitrofurfuryl alcohol, 3,4-dichloro-5-nitrofuoroic acid and certain of their derivatives have been prepared and their antimicrobial activity has been measured.

The chemotherapeutic activity of numerous 5-nitrofuran derivatives has prompted the preparation of the 3,4-dichloro analogs of certain of the more active structures. The starting point for this series was 3,4-dichlorofuroic acid which was prepared by chlorination of ethyl furoate according to the method of Hill and Jackson.<sup>3</sup> By the action of thionyl chloride in benzene, an excellent yield of the acid chloride was obtained along with a small amount of the acid anhydride. 3,4-Dichlorofuraldehyde was prepared by a Rosenmund reduction of the acid chloride.<sup>4</sup> The semicarbazone, oxime and diacetate derivatives of the aldehyde also were prepared.

Reduction of 3,4-dichlorofuroic acid with lithium aluminum hydride proceeded smoothly to give 3,4-dichlorofurfuryl alcohol. This alcohol in turn was converted to its acetate with acetic anhydride and to its methyl ether with methyl iodide and alkali.

Nitrations of the dichlorofuraldehyde, dichlorofurfuryl methyl ether and dichlorofurfuryl acetate met with varying degrees of success. The most straightforward results were obtained with the methyl ether which nitrated satisfactorily to give a 43% yield of purified 3,4-dichloro-5-nitrofurfuryl methyl ether. Likewise, nitration of the dichlorofurfuryl acetate gave a 41% yield of the nitrated product. In one case, where the dichlorofurfuryl alcohol first was acetylated in acetic anhydride and the entire crude reaction mixture then nitrated, a small amount of 3,4-dichloro-5-nitrofurfuryl nitrate was isolated. Hydrolysis of 3,4-dichloro-5-nitrofurfuryl acetate to the free alcohol was accomplished with dilute sulfuric acid. This

(1) For the previous paper in this series, see F. F. Ebetino and G. Gever, *J. Org. Chem.*, **27**, 188 (1962).

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(3) H. B. Hill and L. L. Jackson, *Am. Chem. J.*, **12**, 22 (1890).

(4) T. Okuzumi, *Nippon Kagaku Zasshi*, **79**, 1366 (1958); *C.A.*, **54**, 24633 (1960).

reaction always was accompanied by some degradation, and in some cases, when the hydrolysis time was shortened to minimize this degradation, a crystalline by-product containing no nitrogen was obtained.

In contrast to the above two nitrations, the nitration of 3,4-dichlorofuraldehyde was quite unsatisfactory. The highest yield of pure 3,4-dichloro-5-nitrofuraldehyde isolated from this method was 2.5%. By treating the crude nitration mixture with semicarbazide it was possible to obtain 13% of the semicarbazone derivative. It was found that the desired dichloronitrofuraldehyde (or its derivatives) could be more advantageously prepared by nitric acid oxidation of 3,4-dichloro-5-nitrofurfuryl alcohol or its acetate. By this method were prepared the oxime, 1-aminohydantoin<sup>5</sup> and 3-amino-5-(4-morpholinyl-methyl)-2-oxazolidinone<sup>6</sup> derivatives.

The attempted nitration of ethyl 3,4-dichlorofuroate in acetic anhydride was completely unsuccessful, but the desired 3,4-dichloro-5-nitrofuroic acid was obtained by the method of Hill and his co-workers.<sup>3,7</sup> This acid was in turn converted to its butyl ester.

A comparison of the *in vitro* microbiological activity of these 3,4-dichloro-5-nitrofurans with the parent unchlorinated compounds is shown in Table I in which R represents the 5-nitro-2-furyl and R<sup>1</sup> the 3,4-dichloro-5-nitro-2-furyl group. We are indebted to the Microbiology Section of these Laboratories for the compilation of these data.

### Experimental<sup>8,9</sup>

**3,4-Dichlorofuroyl Chloride.**—A mixture of 158 g. (0.873 mole) of 3,4-dichlorofuroic acid<sup>3</sup> (m.p. 170° minimum) and 800 ml. of dry benzene was heated to reflux on the steam bath. To the refluxing suspension was added dropwise during 2 hr., 200 ml. (2.7 moles) of thionyl chloride. Refluxing was continued overnight after which the benzene and excess thionyl chloride were distilled off. The residue on vacuum distillation gave 163 g. (93.7%) of the acid chloride boiling at 67–81° (1.5 mm.). On redistillation through a packed column, practically the entire product boiled at 75–76° (2.5 mm.). The acid chloride solidifies on cooling and melts at about 26°.

*Anal.* Calcd. for C<sub>6</sub>HCl<sub>2</sub>O<sub>2</sub>: total Cl, 53.3; hydrolyzable Cl, 17.8. Found: total Cl, 52.85; hydrolyzable Cl, 17.6.

The residue from the distillation of the crude acid chloride solidified on cooling. It was washed free of acid with sodium carbonate solution, then washed with

(5) W. Traube and E. Hoffa, *Ber.*, **31**, 162 (1898).

(6) G. Gever, U.S. Patent 2,802,002 (1957).

(7) H. B. Hill and W. S. Hendrixson, *Am. Chem. J.*, **15**, 145 (1893).

(8) Microanalyses by Mr. Gordon Ginther and Mr. Al Mayer of these Laboratories.

(9) All melting points were taken on a Fisher-Johns apparatus and are uncorrected.

TABLE I. *In vitro*

	Tube			
	<i>E. coli</i>	<i>S. typhosa</i>	<i>P. vulgaris</i>	<i>Ps. aeruginosa</i>
$R = \text{---} \begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{---} \end{array} \text{NO}_2$ , $R^1 = \text{---} \begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{---} \end{array} \begin{array}{c} \text{NO}_2 \\ \text{Cl} \end{array}$				
$RCH=NNHCONH_2$	0.5-1.0	1.0	2-6	>20
$R^1CH=NNHCONH_2$	>0.1	>0.1	5 <sup>a</sup>	0 <sup>a</sup>
$RCH=N-N \begin{array}{c} \diagup \text{CO} \\   \quad \diagdown \\ \text{H}_2\text{C} \quad \text{CO} \\   \quad \diagup \\ \text{NH} \end{array}$	0.3-1.3	1-2	..	>78
$R^1CH=N-N \begin{array}{c} \diagup \text{CO} \\   \quad \diagdown \\ \text{H}_2\text{C} \quad \text{CO} \\   \quad \diagup \\ \text{NH} \end{array}$	0.9	>4	..	0 <sup>a</sup>
$RCH_2OCH_3$	<1.0-1.4	1.8	1-2	27-58
$R^1CH_2OCH_3$	6	6	11	>22
$RCH_2OH$	4-20	1.43	<1-6	11-29
$R^1CH_2OH$	>25	>25	>25	>25
$RCO_2C_4H_9-n$	<0.2-3	>1.5	2.5	>2.6
$R^1CO_2C_4H_9-n$	9P <sup>a</sup>	0 <sup>a</sup>	0 <sup>a</sup>	6 <sup>a</sup>
$RCH=NOH$	<1->3	<0.2	3.1-12.5	12.3-32.3
$R^1CH=NOH$	0.2	2	6	13
$RCH=N-N \begin{array}{c} \diagup \text{CO} \\   \quad \diagdown \\ \text{H}_2\text{C} \quad \text{CH} \end{array} \begin{array}{c} \diagup \text{O} \\   \quad \diagdown \\ \text{CH} \text{---} \text{CH}_2 \text{---} \text{CH}_2 \\   \quad \diagup \\ \text{N} \end{array} \begin{array}{c} \diagup \text{CH}_2 \text{---} \text{CH}_2 \\   \quad \diagdown \\ \text{CH}_2 \text{---} \text{CH}_2 \\   \quad \diagup \\ \text{O} \end{array}$	>0.14-0.6	1.3-2.5	>9	>9
$R^1CH=N-N \begin{array}{c} \diagup \text{CO} \\   \quad \diagdown \\ \text{H}_2\text{C} \quad \text{CH} \end{array} \begin{array}{c} \diagup \text{O} \\   \quad \diagdown \\ \text{CH} \text{---} \text{CH}_2 \text{---} \text{CH}_2 \\   \quad \diagup \\ \text{N} \end{array} \begin{array}{c} \diagup \text{CH}_2 \text{---} \text{CH}_2 \\   \quad \diagdown \\ \text{CH}_2 \text{---} \text{CH}_2 \\   \quad \diagup \\ \text{O} \end{array}$	16 <sup>a</sup>	8 <sup>a</sup>	0 <sup>a</sup>	0 <sup>a</sup>

<sup>a</sup> Tablet method; zone in mm. (3 mm. tablet).

water and dried. Vacuum sublimation and recrystallization from carbon tetrachloride gave pure 3,4-dichlorofuroic anhydride, m.p. 128.5-129.5°.

*Anal.* Calcd. for  $C_{10}H_2Cl_4O_5$ : C, 34.9; H, 0.59; Cl, 41.2. Found: C, 35.0; H, 0.70; Cl, 41.3.

**3,4-Dichlorofuraldehyde.**—A mixture of 168 g. (0.84 mole) of 3,4-dichlorofuroyl chloride, 650 ml. of dry benzene, 42 g. of Pd-BaSO<sub>4</sub> catalyst and 300 mg. of finely powdered thiourea was stirred and heated at a gentle reflux while a stream of hydrogen was passed through as rapidly as foaming would permit. The progress of the reaction was followed by titrating the liberated hydrogen chloride with 1 N NaOH. About 90% of the hydrogen chloride was liberated in 7 hr., after which the rate of evolution fell off rapidly. The catalyst was filtered off and washed with fresh solvent. The clear benzene solution was stirred with 250 ml. of saturated sodium bisulfite solution overnight. The solids that had formed were filtered, washed with benzene and dried. The free aldehyde was obtained by dissolving this bisulfite addition compound in water, making alkaline with sodium carbonate solution and warming. After chilling, the product was filtered, washed with water and air dried. Extraction of the aqueous filtrate and washings with ether gave some additional product. The total yield of the dichlorofuraldehyde was 93.5 g (67.5%), m.p. 47-48°. This product is very volatile and will sublime slowly even at room temperature. By sublimation or recrystallization from dilute

## MICROBIOLOGICAL TEST RESULTS.

dilution technique— (mg./100 ml.; 24 hr.)					Cup plate technique— Concn. (mg./100 ml.)/diameter of zone of inhibition (mm.)		
<i>Strep.</i> <i>pyogenes</i>	<i>Strep.</i> <i>agalactiae</i>	<i>S.</i> <i>aureus</i>	<i>S.</i> <i>Choler-</i> <i>aesuis</i>	<i>B.</i> <i>abortus</i>	<i>C.</i> <i>albicans</i>	<i>M.</i> <i>canis</i>	<i>N.</i> <i>asteroides</i>
0.5-1.7	0.5-12	<0.5-1	0.5	..	109/11	109/17	..
>0.1	>0.3	>0.1	>0.1	..	4.6/0	4.6/15	..
0.47-0.8	2.5-3.0	0.62-1.33	0.5	0.5	46.8/0	46.8/0	..
>4	3	0.2-0.6	>4	>4	40.8/0	40.8/0	..
>7	<14-58	<7-14	0.8-2	0.8-2	254/37	254/41	254/0
5	1	1	22	22	223/58	20/70	11/15
20-32	10-26	<3-20	1-2	1-2	151/13	151/50	180/16
>25	>25	>25	>25	>25	191/16	191/65	200/37
>0.2-1.6	>4	>3	>4	<0.3	50/13	26/20	182/10P
26 <sup>a</sup>	21 <sup>a</sup>	19 <sup>a</sup>	0 <sup>a</sup>	22 <sup>a</sup>	9.8/20	9.8/60	8.2/72
0.5-3.4	<14.8-63.5	<1.5-6.3	<0.2-3	<0.2-1	20/30	20/55	186/27
0.2	2	0.2	2	0.1	17.4/32	17.4/C	19.4/25
2.5-4.5	10	0.3	2	0.8-3	292/0	292/0	..
17 <sup>a</sup>	16 <sup>a</sup>	16 <sup>a</sup>	5 <sup>a</sup>	16 <sup>a</sup>	6.4/0	6.4/0	..

alcohol, the melting point may be raised to 50-50.5° (literature<sup>4</sup> m.p. 52-53°);  $\lambda_{\text{max.}}^{5\% \text{ alc.}}$  283.5 m $\mu$  ( $\epsilon$  11,930).

*Anal.* Calcd. for C<sub>5</sub>H<sub>2</sub>Cl<sub>2</sub>O<sub>2</sub>: C, 36.4; H, 1.22; Cl, 43.0. Found: C, 36.1; H, 1.21; Cl, 42.6.

The semicarbazone, m.p. 241-245° dec. (66% alcohol), was prepared in the usual manner;  $\lambda_{\text{max.}}^{2\% \text{ DMF}}$  300 m $\mu$  ( $\epsilon$  27,800).

*Anal.* Calcd. for C<sub>5</sub>H<sub>5</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>2</sub>: Cl, 31.9; N, 18.9. Found: Cl, 31.35; N, 19.0.

The oxime, m.p. 172-172.5° (alcohol), was prepared in the usual manner.  $\lambda_{\text{max.}}^{5\% \text{ alc.}}$  267.5 m $\mu$  ( $\epsilon$  16,860).

*Anal.* Calcd. for C<sub>5</sub>H<sub>3</sub>Cl<sub>2</sub>NO<sub>2</sub>: C, 33.3; H, 1.68; Cl, 39.4. Found: C, 33.3; H, 1.55; Cl, 39.45.

The diacetate, m.p. 70-71° (alcohol), was prepared in the usual manner.

*Anal.* Calcd. for C<sub>9</sub>H<sub>3</sub>Cl<sub>2</sub>O<sub>5</sub>: Cl, 26.6. Found: Cl, 26.05.

**3,4-Dichloro-5-nitrofurraldehyde. A. From Dichlorofuraldehyde.**—A nitrating mixture was prepared by adding 18.5 g. of 70% nitric acid (0.21 mole) containing 2 drops of concd. sulfuric acid to 75 ml. acetic anhydride during 5 min. at 25-30°. Then, 16.5 g (0.1 mole) of dichlorofuraldehyde was added during 6 min. at 40-45°. The cooling bath was removed and the reaction stirred for 0.5 hr. At the end of this time, 110 ml. of water and 35 g. of trisodium phosphate were added and the mixture warmed at 55-60° for 1 hr. It then was cooled, neutralized with

sodium carbonate solution and extracted with ether. Evaporation of the ether left a dark oil which was refluxed under nitrogen for 0.5 hr. with a mixture of 16 ml. of concd. sulfuric acid and 50 ml. of water. The resulting mixture was steam distilled. Some unreacted starting material distilled first, then an intermediate mixture of starting material and product and lastly the dichloronitrofulaldehyde as a yellowish solid. The last fraction along with the pot residue was extracted with ether, dried and the ether removed. Vacuum sublimation removed some additional starting aldehyde from the residue which on cooling gave 0.5 g. (2.5%) yellow crystals melting at 83-87°. Recrystallization from benzene-petroleum ether raised the melting point to 87.5-88.5°;  $\lambda_{\text{max}}^{5\% \text{ alc.}}$  316 m $\mu$  ( $\epsilon$  9800); 243.5 m $\mu$  ( $\epsilon$  5840).

*Anal.* Calcd. for  $\text{C}_5\text{HCl}_2\text{NO}_4$ : C, 28.6; H, 0.48; Cl, 33.8; N, 6.67. Found: C, 28.95; H, 0.50; Cl, 33.65; N, 6.56.

In some runs, the pot residue after the steam distillation of the starting aldehyde was diluted with alcohol to dissolve the remaining oil, then treated with a solution of semicarbazide hydrochloride. There was obtained 3.4 g. (13%) of the *semicarbazone*. After recrystallization from acetic acid, the product decomposed gradually above 225°;  $\lambda_{\text{max}}^{2\% \text{ DMF}}$  267.5 m $\mu$  ( $\epsilon$  21,500); 377.5 m $\mu$  ( $\epsilon$  14,200).

*Anal.* Calcd. for  $\text{C}_6\text{H}_4\text{Cl}_2\text{N}_4\text{O}_4$ : C, 27.0; H, 1.51; Cl, 26.6; N, 21.0. Found: C, 26.9; H, 1.49; Cl, 26.1; N, 21.3.

**B. From Dichloronitrofurfuryl Acetate.**—A solution of 0.52 g. (0.00223 mole) of the ester in 2 ml. of 70% nitric acid was heated on the steam bath at an internal temperature of 80-85° for 40 min. The solution then was diluted with 3 ml. of water and 5 ml. of 2-propanol. The aldehyde present was isolated as the semicarbazone by the addition of an aqueous semicarbazide hydrochloride solution. There was obtained 0.25 g. (44%) of the semicarbazone. Approximately the same yield may be obtained by using the alcohol instead of the acetate in this oxidation. The *oxime*, prepared in the usual manner, decomposed at 148-149° (benzene-petroleum ether);  $\lambda_{\text{max}}^{5\% \text{ alc.}}$  245 m $\mu$  ( $\epsilon$  16,100); 350 m $\mu$  ( $\epsilon$  10,250).

*Anal.* Calcd. for  $\text{C}_5\text{H}_3\text{Cl}_2\text{N}_2\text{O}_4$ : C, 26.7; H, 0.89; Cl, 31.5. Found: C, 26.8; H, 1.11; Cl, 31.35.

**1-(3,4-Dichloro-5-nitrofurylideneamino)-hydantoin**, decomposing at 246-247° (acetic acid), was prepared from the aldehyde and 1-aminohydantoin hydrochloride<sup>6</sup> in aqueous alcoholic solution;  $\lambda_{\text{max}}^{5\% \text{ alc.}}$  271 m $\mu$  ( $\epsilon$  22,600); 372.5 m $\mu$  ( $\epsilon$  15,000).

*Anal.* Calcd. for  $\text{C}_7\text{H}_7\text{Cl}_2\text{N}_4\text{O}_6$ : C, 31.3; H, 1.31; Cl, 23.1; N, 18.25. Found: C, 31.1; H, 1.31; Cl, 22.8; N, 18.2.

**3-(3,4-Dichloro-5-nitrofurylideneamino)-5-(4-morpholinylmethyl)-2-oxazolidinone**, decomposing at 178-179° (benzene), was prepared from the aldehyde and 3-amino-5-(4-morpholinylmethyl)-2-oxazolidinone<sup>6</sup> in acidic aqueous alcoholic solution;  $\lambda_{\text{max}}^{10\% \text{ alc.}}$  227.5 m $\mu$  ( $\epsilon$  21,500); 365 m $\mu$  ( $\epsilon$  14,000).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{14}\text{Cl}_2\text{N}_4\text{O}_6$ : C, 39.7; H, 3.59; Cl, 18.0; N, 14.25. Found: C, 39.4; H, 3.35; Cl, 17.95; N, 14.3.

**Butyl 3,4-Dichloro-5-nitrofuoroate.**—A mixture of 22.5 g. (0.1 mole) of 3,4-dichloro-5-nitrofuoric acid,<sup>3</sup> and 75 ml. of thionyl chloride was refluxed overnight after which the excess thionyl chloride was removed as completely as possible by vacuum distillation. To the crude acid chloride remaining was added 75 ml. of dry butyl alcohol and the mixture warmed on the steam bath until the reaction was over. Excess butyl alcohol was removed under vacuum and the crude ester remaining was dissolved in ether. The ethereal solution was washed with

sodium carbonate solution, then with water and dried. From the sodium carbonate solution by acidification was recovered 1.75 g of the starting acid. The ester was recovered from the ethereal solution by removal of the ether. The ester remaining was heated on the steam bath under high vacuum to remove as much butyl alcohol as possible. The semisolid ester was purified by recrystallization from alcohol to m.p. 49–50°. The yield was 24.5 g (94%). The analytical sample melted at 51–52°;  $\lambda_{\text{max}}^{\text{alc.}}$  228 m $\mu$  ( $\epsilon$  14,000); 306.5 m $\mu$  ( $\epsilon$  10,500).

*Anal.* Calcd. for  $\text{C}_9\text{H}_9\text{Cl}_2\text{NO}_5$ : Cl, 25.1; N, 4.97. Found: Cl, 25.1; N, 4.86.

**3,4-Dichlorofurfuryl Alcohol.**—To a refluxing mixture of 47 g. (1.23 moles) of lithium aluminum hydride in 1500 ml. of dry ether was added during 50 min. a solution of 111.5 g. (0.616 mole) of 3,4-dichlorofuroic acid in 1100 ml. of dry ether. Refluxing was continued for 1.25 hr., after which the excess hydride was decomposed with 500 ml. of wet ether and 270 ml. of water. The inorganic solids were filtered off and washed well with ether. The ethereal solution and washings were dried over sodium sulfate and the ether distilled off at atmospheric pressure. The residual crude alcohol was distilled under vacuum with the main body boiling at 80–88° (2.7 mm.). The yield was 89.2 g (86%). An analytical sample boiled at 82–82.5° (2.4 mm.) and melted at 39.5–40° after recrystallization from petroleum ether;  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  221.5 m $\mu$  ( $\epsilon$  5900).

*Anal.* Calcd. for  $\text{C}_5\text{H}_4\text{Cl}_2\text{O}_2$ : C, 36.0; H, 2.41; Cl, 42.5. Found: C, 35.8; H, 2.39; Cl, 42.0.

**3,4-Dichlorofurfuryl Methyl Ether.**—To a cooled mixture of 28.1 g. (0.168 mole) of 3,4-dichlorofurfuryl alcohol and 41.3 g. (0.291 mole) of methyl iodide, was added during 18 min. 26.0 g. (0.463 mole) of powdered potassium hydroxide at 8–14°. The cooling bath was removed and the temperature allowed to rise gradually to reflux. When the period of self-heating was over, the mixture was heated on the steam bath for 0.75 hr. After cooling, 50 ml. of water was added to dissolve the salts and the organic layer was separated. The aqueous layer was extracted with ether and the combined extracts and organic layer were dried over sodium sulfate. The ether was distilled at atmospheric pressure and the residue distilled in vacuum. There was collected 29.2 g. (96%) of the ether boiling at 73–76° (8.5–8.8 mm.). On redistillation, the product boiled at 64–65° (4.8 mm.),  $n_D^{25}$  1.49241. In common with the other furfuryl ethers,<sup>10</sup> this compound decomposed rapidly and satisfactory analytical results could not be obtained.

**3,4-Dichloro-5-nitrofurfuryl Methyl Ether.**—A nitrating mixture was prepared by adding 52.5 g. of 70% nitric acid (0.58 mole) containing 0.75 ml. of concd. sulfuric acid to 132 g. of acetic anhydride during 35 min. at 20–25°. To this mixture was added a solution of 38.1 g. (0.211 mole) of dichlorofurfuryl methyl ether in 40 g. of acetic anhydride during 17 min. at 18–21°. The reaction mixture was stirred at 10–15° for 1.5 hr., after which 250 ml. of water and 144 g. of trisodium phosphate were added. The mixture was heated at 55–60° for 1.5 hr. then cooled and the oily layer separated. The aqueous solution was extracted with chloroform and the extracts and oily layer were combined. After washing with trisodium phosphate solution and water, the chloroform was distilled off at atmospheric pressure. The residue on vacuum distillation under nitrogen gave 32.4 g. (68%) of crude nitro ether boiling at 108–117° (2.1 mm.). This crude product partially crystallized on cooling. By recrystallization from 2:1 petroleum ether:ethyl acetate, 20.5 g. (63% recovery, 43% yield on nitration) of

purified nitro ether melting at 40–43° was obtained. An analytical sample melted at 48–48.5°;  $\lambda_{\text{max.}}^{4\% \text{ alc.}}$  320  $\mu$  ( $\epsilon$  9970).

*Anal.* Calcd. for  $\text{C}_6\text{H}_5\text{Cl}_2\text{NO}_4$ : C, 31.9; H, 2.23; Cl, 31.4; N, 6.20. Found: C, 32.05; H, 2.03; Cl, 31.5; N, 6.10.

**3,4-Dichlorofurfuryl Acetate.**—To a mixture of 100.2 g. (0.6 mole) of dichlorofurfuryl alcohol and 132 g. of acetic anhydride was added 0.6 ml. of boron trifluoride etherate. The temperature rose rapidly to 90°. The mixture was heated at 100–105° for 1.5 hr., after which the excess acetic anhydride was distilled off at 30–37° (12 mm.). The residue on distillation under nitrogen gave 117 g. (93.6%) of the ester boiling at 70–74° (1.2 mm.). An analytical sample boiled at 77–78° (2.0 mm.);  $\lambda_{\text{max.}}^{4\% \text{ alc.}}$  222  $\mu$  ( $\epsilon$  6500).

*Anal.* Calcd. for  $\text{C}_7\text{H}_5\text{Cl}_2\text{O}_3$ : C, 40.2; H, 2.89; Cl, 33.9. Found: C, 39.9; H, 3.22; Cl, 33.5.

**3,4-Dichloro-5-nitrofurfuryl Acetate.**—A nitrating mixture was prepared by adding 90 g. of 70% nitric acid (1.0 mole) containing 1.3 ml. of concd. sulfuric acid to 300 g. of acetic anhydride during 20 min. at 15–20°. Then 85.4 g. (0.408 mole) of dichlorofurfuryl acetate was added during 17 min. at 15–20°. The reaction mixture was stirred after the cooling bath was removed for 0.75 hr. and at 40–45° for 1.5 hr. After cooling, 400 ml. of water and 140 g. of trisodium phosphate were added and the mixture was heated at 60–65° for 1.5 hr. It was extracted with chloroform and the combined extracts washed thoroughly with sodium carbonate solution and water. The chloroform was distilled off at atmospheric pressure and the residue vacuum distilled. There was obtained 65 g. of crude nitro ester boiling at 126–134° (1.8 mm.). Redistillation gave 42.8 g. (41%) boiling at 129–130° (1.7 mm.). For analysis, a center cut boiling at 129° (1.0 mm.) was taken,  $n_D^{25}$  1.54210;  $\lambda_{\text{max.}}^{5\% \text{ alc.}}$  317.5  $\mu$  ( $\epsilon$  8890); 230  $\mu$  ( $\epsilon$  2800).

*Anal.* Calcd. for  $\text{C}_7\text{H}_5\text{Cl}_2\text{N}_2\text{O}_6$ : C, 33.1; H, 1.98; Cl, 27.9; N, 5.51. Found: C, 33.6; H, 1.98; Cl, 27.7; N, 5.44.

The acetylation and nitration of dichlorofurfuryl alcohol may be combined into one step by nitrating the acetic anhydride solution obtained from the acetylation of the alcohol. From one such nitration, there was obtained a small amount of yellow crystalline material melting at 43–44° (cyclohexane). Analysis indicates that it is probably **3,4-dichloro-5-nitrofurfuryl nitrate**.

*Anal.* Calcd. for  $\text{C}_6\text{H}_2\text{Cl}_2\text{N}_2\text{O}_6$ : C, 23.3; H, 0.78; Cl, 27.6; N, 10.9. Found: C, 23.55; H, 0.81; Cl, 27.2; N, 10.8.

**3,4-Dichloro-5-nitrofurfuryl Alcohol**—A mixture of 12.25 g. (0.0482 mole) of the nitro acetate with 40 ml. of 5% sulfuric acid was refluxed under nitrogen for 7 hr. In some cases, with shorter hydrolysis time, when this mixture was cooled, a small amount of crystals separated. These, after recrystallization from dilute alcohol, melted at 171.5–173.5°. This material contained no nitrogen, gave no reaction with bicarbonate solution, dinitrophenylhydrazine reagent or bromine in carbon tetrachloride.

*Anal.* Calcd. for  $\text{C}_6\text{H}_4\text{Cl}_2\text{O}_3$ : C, 32.8; H, 2.18; Cl, 38.8. Found: C, 33.0; H, 2.09; Cl, 38.45.

The hydrolysis mixture, after cooling, was extracted with ether, the ether dried and removed by distillation. The dark gummy residue was extracted with hot cyclohexane. After treatment with charcoal, the extracts were cooled to give 4.07 g. (40%) of white crystals, melting at 60–65°. An analytical sample melted at 66–66.5°;  $\lambda_{\text{max.}}^{5\% \text{ alc.}}$  321.5  $\mu$  ( $\epsilon$  10,000).

*Anal.* Calcd. for  $\text{C}_6\text{H}_5\text{Cl}_2\text{NO}_4$ : C, 28.3; H, 1.43; Cl, 33.45; N, 6.61. Found: C, 28.7; H, 1.51; Cl, 33.5; N, 6.30.