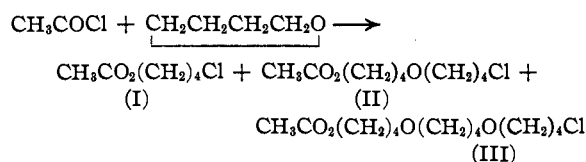


[CONTRIBUTION FROM THE WALKER LABORATORY OF THE RENSSELAER POLYTECHNIC INSTITUTE]

The Reaction of Tetrahydrofuran and 2,5-Dimethyltetrahydrofuran with Acyl Halides<sup>1</sup>

BY JOHN B. CLOKE AND FREDERICK J. PILGRIM

The need for certain  $\delta$ -halogenobutyl and similar esters led us to study the action of acyl halides on tetrahydrofuran. In the case of acetyl chloride, the reaction gave not only  $\delta$ -chlorobutyl acetate (I), as was anticipated, but also at least two other products whose properties correspond to the acetate of ditetramethylene glycol chlorohydrin, *i. e.*,  $\delta$ -( $\delta$ -chlorobutoxy)-butyl acetate (II) and to the related compound (III)



Since the yield of  $\delta$ -chlorobutyl acetate by the foregoing process was but 42% in one run and somewhat better than 50% in another, zinc chloride was added to the reaction mixture in view of its well-known action in the fission of ethers. In one run we employed an amount of anhydrous zinc chloride corresponding to that used by Underwood<sup>2</sup> for the preparation of esters from ordinary ethers, but this led to the formation of much sludge and only 10% of the desired ester. However, it was found eventually that by decreasing the amount of zinc chloride to a few milligrams, a 76% yield of (I) and some of the higher boiling products (II and III) could be obtained. Similar results were obtained in the preparation of analogous  $\delta$ -chloro esters from both tetrahydrofuran and 2,5-dimethyltetrahydrofuran. However, acetyl bromide gave bromoacetates which could not be separated easily from the accompanying dibromide. Likewise, in our work thus far on the action of acetyl fluoride on tetrahydrofuran we have not yet separated in a state of purity the several products formed.

The  $\delta$ -chlorobutyl acetate can be methyl alcoholized to give tetramethylene chlorohydrin. It also will give tetramethylene chlorobromide, although the optimum conditions for this reaction have not yet been ascertained.

(1) The data reported herein have been taken from a thesis presented to the Rensselaer Polytechnic Institute in 1939 by Frederick John Pilgrim in partial fulfillment of the requirements for the degree of Bachelor of Science in Chemistry.

(2) Underwood and Wakeman, *THIS JOURNAL*, **52**, 387 (1930); Underwood, Bari and Toone, *ibid.*, **52**, 4087 (1930).

## Experimental Part

**Furan.**—The major part of the required furan was prepared in batches by the decarboxylation of 500 g. of furoic acid in the presence of 500 cc. of refined quinoline and 3 g. of cupric oxide<sup>3</sup> contained in a 2-liter flask, which was heated in an oil-bath to 225°. The furan and carbon dioxide mixture was passed through a soda-lime tower, which was immersed in water at 75°, when the furan was liquefied by the use of a spiral condenser cooled by circulating ice water. The crude furan, obtained in yields of about 150 cc. per hour, was dried and distilled, giving approximately 85% yields.

**Tetrahydrofuran.**—The furan was hydrogenated in 200-g. lots in the presence of 20 g. of Raney nickel<sup>4</sup> at initial pressures ranging from 800–1500 pounds per sq. in. (55–100 atm.) in an American Instrument Co. high pressure hydrogenator. Yields of about 97% of tetrahydrofuran were obtained.

**$\delta$ -Chlorobutyl Acetate (1) Reaction of Acetyl Chloride with Tetrahydrofuran without a Catalyst.**—In the first run on the preparation of  $\delta$ -chlorobutyl acetate, 185 g. (2.57 moles) of tetrahydrofuran<sup>5</sup> was boiled with 435 g. (5.55 moles) of redistilled acetyl chloride for twelve hours in an all-glass apparatus. The acetyl chloride and most of the unchanged tetrahydrofuran (A) were then distilled in the water-bath, leaving 242 g. of crude residue (B). The recovered acetyl chloride-tetrahydrofuran mixture (A) was then boiled again for twelve hours, whereby 60 g. of crude product (C) and another distillate (D) were obtained. The repetition of the process on the distillate (D) gave a further 14 g. yield of crude product (E), where the process was discontinued.

Two distillations of the combined residues (B), (C), and (E) gave 164 g. of  $\delta$ -chlorobutyl acetate of b. p. 90–92° at 21 mm., 91 g. of product (F) of b. p. 157–165° at 20 mm. and a third product (G) of boiling point 165 to 200° at 23 mm. with intermediate fractions. The redistillation of (F) gave 74 g. of product of b. p. 165–167° at 24 mm., whereas (G) gave a product of b. p. 175–178° at 10 mm. (°C., uncorr.).

The foregoing process gave a 42.5% yield of  $\delta$ -chlorobutyl acetate.<sup>6</sup> Various preparations boiled as follows: 78–79° at 15 mm., 90–91° at 20 mm., and 92–93° at 22 mm. Our material possessed a density  $d^{20}_4$  of 1.0805 and a refractive index  $n^{20}_D$  of 1.43489, which correspond to a molecular refractivity,  $M_D$  of 36.29 as compared with the calculated value of 36.43.

*Anal.* Calcd. for  $\text{C}_8\text{H}_{11}\text{O}_2\text{Cl}$ : Cl, 23.56. Found: Cl, 23.47, 23.47.

(3) Gilman and Louisinian, *Rec. trav. chim.*, **52**, 156 (1933); Wagner and Simons, *J. Chem. Ed.*, **13**, 265 (1936); Starr and Hixon, *THIS JOURNAL*, **56**, 1595 (1934); Shepard, Winslow and Johnson, *ibid.*, **52**, 2083 (1930).

(4) Cloke and Ayers, *ibid.*, **56**, 2144 (1934); Heisig, *ibid.*, **61**, 525 (1939).

(5) We are indebted to H. Tennent and C. Wear for this material.

(6) Bennett and Heathcoat, *J. Chem. Soc.*, 268 (1929).

The redistilled product (F) of b. p. 165–167° at 24 mm. possessed a density,  $d^{20}_4$ , of 1.0471 and a refractive index,  $n^{20}_D$ , of 1.44474, which correspond to a molecular refractivity,  $M_D$ , of 56.85. The molecular refractivity calculated for the compound  $\text{CH}_3\text{COOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$  is 56.54.

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{18}\text{O}_2\text{Cl}$ : Cl, 15.94. Found: Cl, 16.05, 16.09, 16.27.

The redistilled product (G) of b. p. 175–178° at 10 mm., of which only a few grams were obtained, possessed a chlorine content corresponding to the formula  $\text{CH}_3\text{COO}(\text{CH}_2)_6\text{O}(\text{CH}_2)_4\text{O}(\text{CH}_2)_4\text{Cl}$ .

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{27}\text{O}_4\text{Cl}$ : Cl, 12.01. Found: Cl, 12.61, 12.58, 12.54.

### $\delta$ -Chlorobutyl Acetate. (2) Reaction of Acetyl Chloride with Tetrahydrofuran in the Presence of Zinc Chloride.

In view of the long period of heating required to bring about the interaction of acetyl chloride and tetrahydrofuran, anhydrous zinc chloride was added with the expectation that it would increase the yield. In the first run, 261 g. (3.32 moles) of acetyl chloride was added gradually to 111 g. (1.54 moles) of tetrahydrofuran and 53.2 g. (0.39 mole) of anhydrous zinc chloride in an all-glass apparatus, which was protected from the entrance of atmospheric moisture. Much heat was evolved at first and the reaction mixture turned dark. At the end of twelve hours of refluxing a considerable amount of sludge was found to have been formed in the flask. The mixture was extracted with ether, the ethereal solution was washed with water, dried over calcium chloride and distilled, giving only a 10% yield of  $\delta$ -chlorobutyl acetate and a small amount of fraction boiling from 96–160° at 25 mm.

Subsequent runs, summarized in Table I, led to the use of a 10–20 mg. portion of zinc chloride, a period of refluxing of about an hour and the direct distillation of the mixture without the hydrolysis procedure mentioned above. Run 10, made in this way, gave 72 g., a 76% yield, of  $\delta$ -chlorobutyl acetate and 9 g. of the higher boiling products, which account for most of the tetrahydrofuran.

TABLE I

Run	$\text{CH}_3\text{-COCl}$	Tetrahydrofuran	$\text{ZnCl}_2$	Yield, G.	%	Time re-flux, hr.	Remarks
1	261 g.	111 g.	53.2 g.	20	10	12	Heavy sludge
2	135	66	10	30	20	1.5	Heavy sludge
3	212	90	2	36	14	2	Light sludge
4	94	48	7.3	30	27	No	Heavy sludge
5	94	48	0.5	40	38	1	Light sludge
6	94	48	0.3	54	52	1	Light sludge
7	94	48	0.1	54	52	2.5	Light sludge
8	94	48	10 mg.	71	70	0.5	No sludge. no discoloring
9	65	50	10 mg.	72	71	0.5	No discoloring
10	65	50	10 mg.	79	76	1.5	Direct distn.

### (3) Reaction of Acetyl Chloride with Tetrahydrofuran in the Presence of Anhydrous Aluminum Chloride.

—A weight of 48 g. (0.67 mole) of tetrahydrofuran and 94 g. (1.12 moles) of acetyl chloride was allowed to react in the presence of 1 g. of anhydrous aluminum chloride. The reaction, which was very violent, gave much sludge and a poor yield of  $\delta$ -chlorobutyl acetate. No attempts were made to find the optimum amount of catalyst.

**$\delta$ -Chlorobutyl Propionate.**—When 93 g. (1.01 moles) of propionyl chloride, 70 g. (0.98 mole) of tetrahydrofuran and 15 mg. of zinc chloride were allowed to react for one hour, hydrolyzed and distilled,  $\delta$ -chlorobutyl propionate was obtained in a 73% yield together with some higher boiling products. The propionate had a b. p. of 93.5–94.5° at 15 mm. and 101.5–102.5° at 20 mm.;  $d^{20}_4$  1.0537;  $n^{20}_D$  1.43640;  $M_D$  (calcd.) 40.99;  $M_D$  (found), 40.84.

*Anal.* Calcd. for  $\text{C}_7\text{H}_{13}\text{O}_2\text{Cl}$ : Cl, 21.56. Found: Cl, 21.38, 21.63.

**$\delta$ -Chlorobutyl *n*-Butyrate.**—A one and one-half hour period of heating 50 g. (0.69 mole) of tetrahydrofuran, 90 g. (0.85 mole) of *n*-butyryl chloride and 10 mg. of zinc chloride gave a 62% yield of the chlorobutyl butyrate and a small amount of higher fractions. It is probable that a longer period of refluxing would improve the yield. The ester had a b. p. of 105.5–106.5° at 15 mm., and 112.5–113.5° at 20 mm.;  $d^{20}_4$  1.0302;  $n^{20}_D$  1.43791;  $M_D$  (calcd.), 45.61;  $M_D$  (found), 45.54.

*Anal.* Calcd. for  $\text{C}_8\text{H}_{15}\text{O}_2\text{Cl}$ : Cl, 19.87. Found: Cl, 20.21, 20.08.

**$\delta$ -Chlorobutyl Benzoate.**—A mixture of 110 g. (0.52 mole) of benzoyl chloride, 50 g. (0.69 mole) of tetrahydrofuran and 10 mg. of zinc chloride, when refluxed for an hour, gave a 54.5% yield of  $\delta$ -chlorobutyl benzoate and considerable higher boiling material. In this case the tetrahydrofuran was used in excess in order to see what effect this would have on the yield of chlorobutyl benzoate, which in this single run was less than in the case of the aliphatic esters. The product was an oily liquid of b. p. 140–142.5° at 4 mm.;  $d^{20}_4$  1.1429;  $n^{20}_D$  1.52028;  $M_D$  (calcd.), 55.92;  $M_D$  (found), 56.54.

*Anal.* Calcd. for  $\text{C}_{11}\text{H}_{13}\text{O}_2\text{Cl}$ : Cl, 16.69. Found: Cl, 16.61, 16.58.

**$\delta$ -Bromobutyl Acetate.**—The reaction of 50 g. (0.69 mole) of tetrahydrofuran and 90 g. (0.73 mole) of acetyl bromide in the presence of 5 mg. of zinc chloride took place with the evolution of much heat. At the end of one hour of refluxing, 109 g. of a fraction of b. p. 87–93° at 15 mm. was obtained. The redistillation of this gave a product of b. p. 89.5–92° at 15 mm., which, however, gave consistently high values for bromine. The same discrepancy was also noted after five further distillations. The values for the density ( $d^{20}_4$  1.4921) and refractive index ( $n^{20}_D$  1.46799), likewise, gave a molecular refractivity ( $M_D$  37.91) which did not correspond with that computed for the ester ( $M_D$  39.33) from the atomic refractivities of Auwers and Eisenlohr, assuming molecular weights. The impurity responsible for these discrepancies is doubtless tetramethylene dibromide.

*Anal.* Calcd. for  $\text{C}_8\text{H}_{11}\text{O}_2\text{Br}$ : Br, 41.00. Found: Br 46.63.

**$\delta$ -Bromobutyl Benzoate.**—A mixture of 100 g. (0.54 mole) of benzoyl bromide and 35 g. (0.49 mole) of tetrahydrofuran was allowed to react in the presence of 10 mg. of zinc chloride. After the vigor of the reaction had subsided, the mixture was refluxed for one-half hour and then distilled at 9 mm., giving 94 g. of  $\delta$ -bromobutyl benzoate

(7) Grishkevich-Trokhimovskii, *J. Russ. Phys.-Chem. Soc.*, **48**, 901 (1916); *C. A.*, **11**, 785 (1917).

(8) V. Braun, *Ber.*, **46**, 1782 (1913).

(76%) of b. p. 155–157°;  $d^{20}$ , 1.3539, and  $n^{20D}$  of 1.53694, together with some high boiling fractions;  $M_D$  (calcd.), 58.92;  $M_D$  (found), 59.26.

*Anal.* Calcd. for  $C_{11}H_{18}O_2Br$ : Br, 31.11. Found: Br, 31.16, 31.25, 31.09.

**2,5 - Dimethyltetrahydrofuran.**—Redistilled Eastman Kodak Co. 2,5-dimethylfuran of b. p. 91–94° (10 parts) was reduced in the presence of Raney nickel (1 part) in a high pressure hydrogenator as in the case of the furan itself. However, high temperatures must be avoided during the hydrogenation. The reduced product boiled from 89–91° (uncorr.), which is somewhat less than the boiling points reported for the compound prepared by other methods.

**$\alpha$ -Methyl- $\delta$ -chloroamyl Acetate.**—A mixture of 106 g. (1.06 mole) of 2,5-dimethyltetrahydrofuran and 204 g. (2.83 mole) of acetyl chloride was allowed to react in the presence of 10 mg. of zinc chloride. The mixture was then refluxed for one-half hour, carefully hydrolyzed and then worked up in the usual way, giving 145 g. of the chloro ester, a yield of 77%. The product had a b. p. of 85.5–87° at 15 mm. or 94–95° at 20 mm.;  $d^{20}$ , 1.0132;  $n^{20D}$  1.43288;  $M_D$  (calcd.), 45.74;  $M_D$  (found), 45.67.

*Anal.* Calcd. for  $C_8H_{16}O_2Cl$ : Cl, 19.87. Found: Cl, 20.16, 20.30.

**$\alpha$ -Methyl- $\delta$ -bromoamyl Acetate.**—The reaction of 50 g. (0.5 mole) of 2,5-dimethyltetrahydrofuran, 70 g. (0.57 mole) of acetyl bromide and 5 mg. of zinc chloride took place with considerable violence. From the mixture 75 g. of product of b. p. 105–107° at 20 mm. was obtained. Although several redistillations were made, no ester could

be obtained whose analysis corresponded to pure  $\alpha$ -methyl- $\delta$ -bromoamyl acetate, as in the case of the  $\delta$ -bromobutyl acetate, probably on account of the presence of dibromide.

*Anal.* Calcd. for  $C_8H_{16}O_2Br$ : Br, 35.85. Found: Br, 38.44, 38.37, 38.60.

**Tetramethylene Chlorohydrin.**—A mixture of 60 g. of  $\delta$ -chlorobutyl acetate, 120 cc. of methanol and 0.7 cc. of concd. hydrochloric acid was warmed at 40° for three and a half days. At the end of this period most of the methyl acetate and methanol was removed by distillation under diminished pressure, being careful not to overheat the residue, since the tetramethylene chlorohydrin gives hydrogen chloride and tetrahydrofuran when heated.<sup>9</sup> A further quantity of 60 cc. of methanol was then added to the residue, and this mixture was again heated at 50° for six hours and then at 30° for seventeen, when the mixture was distilled, giving 36.5 g. of the  $\delta$ -chlorobutanol of b. p. 64–65° at 3 mm., an 80% yield.

### Summary

Acetyl chloride will react with tetrahydrofuran to give  $\delta$ -chlorobutyl acetate with certain other products. The yield of  $\delta$ -chloro ester is improved by the addition of a trace of zinc chloride. Other acyl halides react similarly both with the tetrahydrofuran and 2,5-dimethyltetrahydrofuran.

The work is being continued and extended.

(9) Kirner and Richter, *THIS JOURNAL*, **51**, 2505 (1929).

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## Studies in the Ketone Sugar Series. IX. The Validity of Hudson's Rules of Isorotation in the *l*-Sorbose Series. $\beta$ -Ethylsorbose and its Tetraacetate

BY EUGENE PACSU

By the discovery<sup>1</sup> of the true  $\alpha$ -pentaacetylfructose <2,6> and by the subsequent<sup>2</sup> interconversion of this substance and the  $\beta$ -pentaacetate, there has become known for the first time in the ketose group an  $\alpha,\beta$ -pair, the mutual relationship of the members of which has been definitely proved. According to Hudson's rules of isorotation, the different  $a_x$  constants that may be calculated from this true  $\alpha,\beta$ -pair and the  $\beta$ -derivatives of *d*-fructose should be of general applicability for all the ketoses and their derivatives. These  $a_x$  constants, with the exception of  $a_{OH}$  for chloroform solution, have been found to be throughout larger than the corresponding  $A_x$  constants in the aldose series. Difference between the values of

$a_x$  and  $A_x$  is, of course, to be expected, since the constants represent, in the latter series, the molecular rotations of carbon atom 1, H-C-X, whereas in the ketose series they express the rotational values of carbon atom 2, ROH<sub>2</sub>C-C-X, where R designates a hydrogen atom in the free ketoses and their glycosides, and an acetyl group in the acetylated products. According to the rules of isorotation, the difference in structure or configuration of the basal chain,  $b_x$ , of the ketoses should not alter to any large extent the values of the  $a_x$  constants. If large deviations be found, it would not necessarily follow that the principle of optical superposition as applied by Hudson is of no general validity, because it is possible that the deviating "constants" have been calculated from the molecular rotations of com-

(1) Pacsu and Cramer, *THIS JOURNAL*, **57**, 1944 (1935).

(2) Cramer and Pacsu, *ibid.*, **59**, 711 (1937).