

boiling in an equal mixture of ethanol and concentrated hydrochloric acid for eighteen hours. (The methyl and ethyl homologs required only three hours under the same conditions.) After saturation with hydrogen chloride, the crystalline platelets of amine hydrochloride were separated and converted to amine by shaking with 20% sodium hydroxide solution and ether. The ether extract on distillation gave 37% of 2-*i*-butyl-4-bromoaniline, a colorless oil, b. p. 146–147° (9 mm.), n_D^{25} 1.5811.

Anal. Calcd. for $C_{10}H_{14}BrN$: C, 52.64; H, 6.19; Br, 35.03; N, 6.14. Found: C, 53.03; H, 6.20; Br, 34.40; N, 6.23.

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Aryl Esters of Substituted Benzenesulfonic Acids

The esters of benzenesulfonic acid listed in the table were prepared by the Hinsberg¹ method with slight variations. One mole of the arylsulfonyl chloride and one mole of the phenol were heated together with stirring at 60–70°. One mole of dilute sodium hydroxide solution (0.7 *N*) was added during a half-hour period, keeping the temperature at 60–80°. The reaction mass was heated for an additional hour at 60–80°. As the reaction proceeded, the ester precipitated and crystallized. The slurry was cooled, filtered, and washed with water. The dried crystals were purified by repeated crystallizations from ethyl alcohol containing a little benzene.

chloroacetyl group acts as a neighboring group in the displacement of the *p*-toluenesulfonyl group from a position *trans* to it on the cyclohexane ring, under conditions similar to those employed by Winstein and co-workers.¹ Although a first order reaction was observed, the products were not isolated.

All melting points are corrected and the micro-analyses were performed by Mrs. C. F. Spencer.

Ethylene Glycol Bis-trichloroacetate.—Ethylene glycol (5.6 ml., 0.1 mole) and trichloroacetic acid (32.7 g., 0.2 mole, Dow Chemical Co.) were distilled slowly at atmospheric pressure until the temperature had reached 125° and about 3.5 ml. of distillate (largely water) had collected. The residue, which crystallized on cooling, was mixed with some cold water, and the solid (17.6 g., m. p. 40–41°) removed by filtration. After recrystallization from an ethanol-water mixture, 50% recovery of a product melting at 41–42° was obtained. The substance was very soluble in most organic solvents including alcohols, hydrocarbons, ethers, and chlorinated hydrocarbons. It was difficultly soluble in hot water. The compound was also prepared by the reaction of trichloroacetyl chloride and ethylene glycol in pyridine. It is probable that the ester undergoes hydrolysis with some ease.

Anal. Calcd. for $C_6H_4O_4Cl_6$: C, 20.40; H, 1.13; Cl, 60.34; sapon. equiv., 353. Found: C, 20.34; H, 1.18; Cl, 60.60; sapon. equiv., 324.

***trans*-1,2-Cyclohexanediol Bis-trichloroacetate.**—*trans*-1,2-Cyclohexanediol² (11.6 g., 0.1 mole) and pyridine (32 ml., 0.4 mole) were mixed and trichloroacetyl chloride³ (36.4 g., 0.2 mole) was slowly added with sufficient cooling to keep the temperature in the range of 60–70°. The mix-

TABLE I

| Compound | Crude yield, % | Chlorine, % | | Sulfur, % | | M. p., °C. ^a |
|---|----------------|-------------|----------|-----------|--------|-------------------------|
| | | Found | Calcd. | Found | Calcd. | |
| <i>p</i> -Chlorophenyl <i>m</i> -nitrobenzenesulfonate | 87.0 | 11.24 | 11.30 | 10.27 | 10.22 | 104–105 |
| <i>p</i> -Bromophenyl <i>p</i> -bromobenzenesulfonate | 93.0 | 40.53 Br | 40.76 Br | 8.04 | 8.18 | 121–122 |
| <i>p</i> -Chlorophenyl <i>p</i> -bromobenzenesulfonate ^b | 96.5 | 10.23 Cl | 10.11 Cl | 9.47 | 9.22 | 109–110 |
| <i>p</i> -Bromophenyl <i>p</i> -chlorobenzenesulfonate ^c | 88.5 | 10.17 Cl | 10.11 Cl | 8.94 | 9.22 | 95.5–97.5 |
| 2,4-Dichlorophenyl <i>p</i> -chlorobenzenesulfonate | 94.5 | 31.79 | 31.51 | 9.58 | 9.50 | 118–119 |
| 2,4,5-Trichlorophenyl <i>p</i> -chlorobenzenesulfonate | 92.0 | 37.56 | 38.12 | 8.80 | 8.62 | 130–131 |
| 2,4,6-Trichlorophenyl <i>p</i> -chlorobenzenesulfonate | 96.4 | 38.14 | 38.12 | 8.72 | 8.62 | 97–98 |
| 2,3,4,6-Tetrachlorophenyl <i>p</i> -chlorobenzenesulfonate | 83.0 | 44.37 | 43.61 | 7.72 | 7.88 | 123–124 |
| Pentachlorophenyl <i>p</i> -chlorobenzenesulfonate | 93.0 | 48.80 | 48.25 | 7.34 | 7.27 | 146.5–147.5 |
| <i>p</i> -Tolyl <i>p</i> -chlorobenzenesulfonate | 97.5 | 12.80 | 12.54 | 11.56 | 11.34 | 76–77 |
| <i>o</i> - <i>s</i> -Butylphenyl <i>p</i> -chlorobenzenesulfonate | 88.2 | 10.87 | 10.91 | 9.79 | 9.87 | 60–61.5 |
| <i>p</i> - <i>t</i> -Butylphenyl <i>p</i> -chlorobenzenesulfonate | 93.7 | 11.04 | 10.92 | 9.82 | 9.87 | 92–93 |
| <i>o</i> -Allylphenyl <i>p</i> -chlorobenzenesulfonate | 89.0 | 11.58 | 11.48 | 10.29 | 10.38 | 53–59 |
| 2-Biphenyl <i>p</i> -chlorobenzenesulfonate | 92.5 | 10.31 | 10.28 | 9.32 | 9.30 | 85.5–86.5 |
| <i>p</i> -Methoxyphenyl <i>p</i> -chlorobenzenesulfonate | 95.3 | 12.11 | 11.87 | 10.73 | 10.73 | 90–91 |

^a Uncorrected. ^b Br calcd. 22.99; found 22.95. ^c Br calcd. 22.99; found 22.92.

(1) Hinsberg, *Ber.*, **23**, 2962 (1890).

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Some New Glycol Trichloroacetates

We have prepared several new glycol trichloroacetates which may serve as model substances for carbohydrate trichloroacetates. Two methods were used. The first method consisted of the direct reaction of the glycol with trichloroacetic acid in the absence of a catalyst and either with or without the presence of a water entrainer. The second method employed trichloroacetyl chloride in the presence of pyridine. This method was suitable for the preparation of mixed esters.

An attempt was made to determine whether the tri-

ture was then allowed to stand overnight at room temperature. It was then shaken with 200 ml. of water, and the yellow oil which separated crystallized on refrigeration, yield 37.2 g., 91%. The crude product (m. p. 59–61°) was recrystallized from an alcohol-water mixture to a constant melting point of 60–61°.

Anal. Calcd. for $C_{10}H_{10}O_4Cl_6$: C, 29.48; H, 2.46; Cl, 52.33; sapon. equiv., 407. Found: C, 29.40; H, 2.55; Cl, 52.09; sapon. equiv., 402.

***trans*-1,2-Cyclohexanediol Monotrighloroacetate.**—*trans*-1,2-Cyclohexanediol² (11.5 g., 0.1 mole) and trichloroacetic acid (16.4 g., 0.1 mole, Dow Chemical Co.) and benzene (100 ml.) were heated under reflux in an all-glass

(1) Winstein, Hanson and Grunwald, *THIS JOURNAL*, **70**, 812 (1948).

(2) "Org. Syn.," **28**, 35 (1948).

(3) Prepared from trichloroacetic acid and benzoyl chloride according to the method of Brown, *THIS JOURNAL*, **60**, 1352 (1938).

apparatus equipped with a water trap. After removal of the water which had formed, the remainder of the benzene was distilled off and the residual oil poured into 500 ml. of ice-water and stirred vigorously. The crude solid (13.9 g., 53%, m. p. 74-77°), was recrystallized from *n*-hexane and then melted at 76-77°. Criegee and Stanger,⁴ who prepared this substance from cyclohexene oxide and trichloroacetic acid, reported a melting point of 76-77°.

trans-1,2-Cyclohexanediol Trichloroacetate *p*-Toluene-sulfonate. (a) Trichloroacetylation of the Mono-*p*-toluenesulfonate.—*trans*-1,2-Cyclohexanediol *p*-toluenesulfonate (8.1 g., 0.03 mole) prepared in 84% yield (m. p. 97°) by a modification of the method of Criegee and Stanger⁴ or Winstein, Hess and Buckles⁵ and pyridine (5 ml., 0.06 mole) were mixed and the trichloroacetyl chloride³ (3.4 ml., 0.03 mole) added slowly without cooling. The reaction mixture crystallized on standing overnight, and after 200 ml. of water had been stirred in, the crystalline suspension was refrigerated. The crude solid was removed, washed with water, and dried in air (10 g., 80%, m. p. 98-102°). It was recrystallized three times from absolute alcohol and once from *n*-hexane and then melted at 104.0-104.5°.

Anal. Calcd. for C₁₅H₁₇O₃Cl₃S: C, 43.27; H, 4.09;

(4) Criegee and Stanger, *Ber.*, **69B**, 2753 (1936).

(5) Winstein, Hess and Buckles, *This Journal*, **64**, 2798 (1942).

Cl, 25.70; S, 7.69. Found: C, 43.29; H, 4.08; Cl, 25.60; S, 7.79.

(b) Tosylation of the Mono-trichloroacetate.—*trans*-1,2-Cyclohexanediol trichloroacetate (15.7 g., 0.06 mole) and *p*-toluenesulfonyl chloride (11.4 g., 0.06 mole) were dissolved by warming with pyridine (19.3 ml., 0.24 mole) to 55°. After maintaining the mixture at this temperature for a few minutes, it was allowed to cool to room temperature and remain overnight. The solidified mixture was then stirred with cold water (500 ml.) and the residual solid removed, washed with water and dried in air (23.9 g., 96%, m. p. 103-104°). It was recrystallized from *n*-hexane (22.1 g., yield 89%) and then melted at 105°. The melting point of a mixture of the products from part (a) and part (b) was not lower than that of either product melted separately.

The reaction of this compound (0.1 *M*) with sodium acetate (0.1 *M*) in glacial acetic acid at 91° was followed by the method of Winstein and co-workers¹ and gave a first order reaction rate constant of approximately 6.7 ($k \times 10^4$ in hour⁻¹). The reaction products were not isolated.

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RECEIVED DECEMBER 28, 1949

COMMUNICATIONS TO THE EDITOR

ACTIVATION OF THIONASE BY FOLIC ACID¹

Sir:

It has been found that preparations of thionase (the enzyme responsible for the cleavage of cystathionine and cysteine²) may be inactivated by dialysis against dilute acetate buffer (0.01 *M*, *pH* 4.0). The activity of the enzyme was restored by the addition of folic acid. Adenylic acid, adenosinetriphosphate, diphosphopyridine nucleotide, vitamin B₁₂ or aureomycin did not reactivate the inactive material.

A solution of enzyme in saline had an activity toward L-allo-cystathionine such that 1.2 mg. of homocysteine was produced from 4.4 mg. of substrate in 30 min. by 1 ml. of enzyme. This solution was dialyzed for 48 hr. against the acetate buffer. The material that precipitated was redissolved in the original volume of saline and was found to be without activity. Fifty γ folic acid per ml. of digest (total volume 10 ml., 0.02 *M* histidine buffer, *pH* 7.3) was added and the activity was found to be restored to the extent that 0.7 mg. of homocysteine was produced. The relationship of activity to concentration of folic acid was reasonably linear up to concentrations of folic acid of the order of 150 γ per ml.; at this level an activity of 1.0 mg. of homocysteine was found. Similar activa-

tions with other substrates and other methods of analyses were observed.

These results are difficult to interpret since the levels of folic acid required for reactivation are of a different order of magnitude than any possible concentration in the enzyme. The purified enzyme was found to have, aside from the protein component, peaks of absorption near 245, 285 and 350 μ . These peaks disappeared during the dialysis. However, if it were assumed that certain of these peaks were due to a derivative of folic acid, less than 0.5 γ per ml. of digest was present in the fully-active preparation. Studies as to the nature of the activation by folic acid and the possibility of more active derivatives of folic acid are in progress.

LABORATORY FOR THE STUDY OF
HEREDITARY AND METABOLIC DISORDERS
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SALT LAKE CITY, UTAH FRANCIS BINKLEY

RECEIVED MAY 12, 1950

THE ISOLATION OF A NEW THYMINE PENTOSIDE FROM SPONGES¹

Sir:

When certain air-dried sponges, particularly those of the genus *Cryptotethia*, are extracted in a Soxhlet apparatus with acetone, a nicely crystal-

(1) These studies were supported by grants from the U. S. Public Health Service.

(2) F. Binkley and D. Okeson, *J. Biol. Chem.*, **182**, 273 (1950).

(1) Contributions to the Study of Marine Products. XXVIIII.