

colorless crystals, m.p. 150.2–152.1°. *Anal.* Calcd. for $C_6H_5N_4$: C, 62.78; H, 4.68; N, 32.54. Found: C, 62.82; H, 4.68; N, 32.47.

2-Pyrimidyl-2'-thiazolylamine.—The sodium salt of 2-aminopyrimidine (22.18 g., 0.189 mole) and 2-chlorothiazole (22.58 g., 0.189 mole) were heated in an oil-bath at 95° for 2.75 hours when it became necessary to cool the reaction mixture in order to moderate an exothermic reaction which had developed; the reaction mixture was then heated for an additional 6 hours at 95°, cooled, suspended in 50 ml. of water and steam distilled (6 g. of 2-chlorothiazole was recovered). The residue from the steam distillation was filtered, washed with cold water and dried at 100°; yield 3.1 g. (9.5%), m.p. 209–211.8°. Cream colored crystals were obtained upon recrystallization from ethanol, m.p. 211–212.1°. Vacuum sublimation under 6 mm. pressure and recrystallization from ethanol gave colorless crystals, m.p. 212.1–212.6°. *Anal.* Calcd. for $C_7H_5N_4S$: C, 47.18; H, 3.39; N, 31.44; S, 17.99. Found: C, 47.22; H, 3.44; N, 31.44; S, 17.89.

2-Anilinoypyrimidine.¹⁰—A mixture of aniline (3.26 g., 0.035 mole) and sodium amide (1.37 g., 0.035 mole) in 35 ml. of dry benzene was heated and stirred for 3.25 hours in an oil-bath at 92° under an atmosphere of nitrogen. 2-Chloropyrimidine (4 g., 0.035 mole) in 20 ml. of anhydrous benzene was added to the cooled reaction mixture. After the addition, this mixture was heated and stirred at gentle reflux for 4.5 hours, cooled and then steam distilled. The distillate was acidified with concentrated hydrochloric acid and shaken to extract the amine from the benzene portion of the distillate. A brown colored solid was precipitated from the acidic solution upon adjusting it to a pH 10; yield 2.7 g. Solution of this substance in boiling water and filtration from insoluble impurities produce 1.3 g. (22%) of colorless needles, m.p. 114.3–115.2°.

Acknowledgment—We are grateful to the Wm. S. Merrell Company for the funds that made this research possible and for many helpful discussions in connection with this investigation.

(10) T. B. Johnson and F. W. Heyl, *Am. Chem. J.*, **33**, 244 (1907), prepared this compound by the reduction of 4-chloro-2-anilinoypyrimidine, m.p. 116°.

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The Hydrolysis of Glucose-4-phosphate¹

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The mechanism by which galactose may be derived from glucose in biological systems is one which holds considerable interest. Robinson³ suggested that D-glucose-4-phosphate, if present in nature, might be hydrolyzed at the C–O– bond at carbon number four with a resultant Walden inversion. This mechanism is referred to repeatedly, but it has never been tested directly. Cohn⁴ has shown, using O¹⁸, that hydrolysis of glucose-1-phosphate may occur at the C–O– bond or the –O–P bond depending on the catalyst used.

Experimental

The disodium and barium salts of D-glucose-4-phosphoric acid were prepared in this Laboratory.⁵

Acid Hydrolysis.—To 28 mg. of barium D-glucose-4-phosphate was added excess (2 ml. of 0.1 N) sulfuric acid. After barium sulfate was removed by centrifugation, the solution was maintained at 100° for 30 hours. The hy-

(1) Work performed under Contract N6onr-218, Office of Naval Research.

(2) To whom inquiries concerning this article should be addressed.

(3) R. Robinson, *Nature*, **120**, 44 (1927).

(4) M. Cohn, *J. Biol. Chem.*, **180**, 771 (1949).

(5) F. J. Reithel and C. K. Claycomb, *THIS JOURNAL*, **71**, 3669 (1949).

drolysis mixture was concentrated, extracted with pyridine⁶ and chromatographed⁷ (descending) on Whatman No. 1 paper, using *s*-collidine–water as a solvent. The spray used was that recommended by Trevelyan.⁸ Well defined glucose spots were obtained, but no galactose spot was discernible. There was no difficulty in differentiating the spots due to the glucose and galactose standards.

Hydrolysis at pH 7.—A solution of 21.4 mg. of the disodium salt of glucose-4-phosphoric acid in 2.0 ml. of water was found to be at pH 7.2. After 42 hours heating at 100° in a stoppered tube 50% of the compound was hydrolyzed as evidenced by analysis for inorganic phosphate.⁹ The solution was chromatographed as above and identical results were obtained.

Acid Phosphatase Action.—The enzyme used was obtained by ammonium sulfate precipitation of potato press juice.¹⁰ A sample of 20.6 mg. of disodium glucose-4-phosphate was dissolved in 2.0 ml. of water. To each volume of this solution used was added an equal volume of molar acetate buffer, pH 5.2, and an equal volume of purified phosphatase solution. Liberation of inorganic phosphate indicated 90% hydrolysis after 12 hours incubation at 37°. A chromatogram of the solution showed only a glucose spot.

Alkaline Phosphatase Action.—Essentially identical experiments were performed using Armour intestinal phosphatase as a catalyst at a pH of 8.0. Neither chromatography nor the colorimetric method of Dische,¹¹ *et al.*, indicated the presence of galactose in the hydrolysis mixtures.

Conclusion.—The above results do not suggest the idea that Walden inversion occurs during the hydrolysis of sugar phosphates and in this they agree with the work of Cohn.⁴ The mechanism of cleavage will be further investigated with O¹⁸.

(6) F. H. Malpress and A. B. Morrison, *Nature*, **164**, 963 (1949).

(7) S. M. Partridge and R. G. Westall, *Biochem. J.*, **42**, 238 (1948).

(8) W. E. Trevelyan, D. P. Proctor and J. S. Harrison, *Nature*, **166**, 444 (1950).

(9) C. H. Fiske and Y. SubbaRow, *J. Biol. Chem.*, **61**, 63 (1924).

(10) G. Schramm and H. Flammersfeld, *Naturwissenschaften*, **34**, 216 (1947).

(11) Z. Dische, L. B. Shettles and M. Osnos, *Arch. Biochem.*, **22**, 169 (1949).

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The Reaction between Diazonium Fluoroborates and Antimony Trichloride in Organic Solvents

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The present paper describes the reaction between antimony trichloride and diazonium fluoroborates and is a continuation of our study of the reaction between the halides of certain elements and diazonium fluoroborates in organic solvents. Under conditions similar to those employed with arsenic trichloride,¹ a mixture of arylstibonic and diarylstibinic acids was obtained. A number of attempts were made to separate the mixture of primary and secondary acids. Fractional crystallization of various derivatives of these acids was used, and it was found possible to obtain the pure secondary acids in low yields. However, analyses of the primary acids and m.p.s. of the corresponding pyridinium chloroantimonates² indicated that the primary acids were invariably contaminated with small amounts of secondary acids.

The total yield as well as the ratio between the yields of the two acids varied with both the solvent

(1) G. O. Doak and L. D. Freedman, *THIS JOURNAL*, **73**, 5658 (1951).

(2) *Cf.* G. O. Doak and H. G. Steinman, *ibid.*, **68** 1987 (1946).

TABLE I
 DIARYLSTIBINIC ACIDS AND PYRIDINIUM DIARYLCHLOROANTIMONATES

R ₁ SbO ₂ H	Yield, %	Formula	Sb analyses, %		Pyridinium diaryl- chloroantimonate formula	Sb analyses, %	
			Calcd.	Found		Calcd.	Found
C ₆ H ₅ - ^a	5	C ₁₃ H ₁₁ O ₂ Sb	39.41	39.45	C ₁₇ H ₁₆ Cl ₄ NSb	24.46	24.24
<i>p</i> -CH ₃ C ₆ H ₄ - ^b	8	C ₁₄ H ₁₃ O ₂ Sb	36.13	35.93	C ₁₉ H ₂₀ Cl ₄ NSb	23.15	22.88
<i>m</i> -ClC ₆ H ₄ -	6	C ₁₂ H ₉ Cl ₂ O ₂ Sb	32.22	32.19	C ₁₇ H ₁₄ Cl ₆ NSb	21.48	20.78
<i>p</i> -ClC ₆ H ₄	12	C ₁₂ H ₉ Cl ₂ O ₂ Sb	32.22	32.30	C ₁₇ H ₁₄ Cl ₆ NSb	21.48	21.48
<i>p</i> -O ₂ NC ₆ H ₄ - ^c	20	C ₁₂ H ₉ N ₂ O ₆ Sb	30.52	30.40	C ₁₇ H ₁₄ Cl ₄ N ₂ O ₄ Sb	20.71	20.60

^a Previously prepared by A. Michaelis and A. Reese, *Ann.*, **233**, 39 (1886), and other workers. ^b Previously prepared by A. E. Goddard and V. E. Yarsley, *J. Chem. Soc.*, 719 (1928). ^c Calcd.: N, 7.02. Found: N, 6.99.

and catalyst used. The results were generally comparable to those obtained with arsenic trichloride, except that the presence of water in the solvent did not materially increase the yields of stibinic acids. The best yield of arylstibonic acid was obtained by the use of absolute alcohol as the solvent and cuprous chloride as the catalyst; the yield of *p*-nitrobenzenestibonic acid was 65% under these conditions.³ The best yield of diarylstibinic acid was obtained by the use of isopropyl or *t*-butyl alcohol and copper bronze.

Since it has been shown that the crystalline pyridinium arylchloroantimonates serve as useful derivatives for the characterization of primary stibonic acids,² the corresponding derivatives of the secondary acids were prepared and recrystallized. However, these compounds did not give sharp, reproducible m.ps.

Experimental

Antimony trichloride (0.1 mole) was dissolved in 100 ml. of the solvent and the solution added to 0.1 mole of the diazonium fluoride in a 2-necked flask. The subsequent procedure to the end of the steam distillation was similar to that used with arsenic trichloride.¹ After steam distillation the residual liquid in the flask was treated with 150 ml. of concentrated hydrochloric acid. A crystalline precipitate of the diarylstibine trichloride separated after several hours. This was removed by filtration and dissolved in 100 ml. of ethanol and 10 ml. of concentrated hydrochloric acid. The solution was treated with Darco and filtered. Ten ml. of pyridine reagent (*cf.* ref. 2) was added to the clear filtrate to precipitate the pyridinium chloroantimonate. The latter was then recrystallized from ethanol acidified with hydrochloric acid. The purified pyridinium salt was dissolved in 2% sodium hydroxide solution, and the clear solution acidified to congo red. The diarylstibinic acid which separated was thoroughly washed with water on a buchner funnel and air dried.

The filtrate, after removal of the diarylstibine trichloride, was treated with pyridine reagent in order to precipitate the pyridinium salt of the primary acid. This salt was then recrystallized and hydrolyzed by the procedure described in a previous paper.³ Regardless of the solvent or catalyst used, the resulting arylstibonic acid was not analytically pure. Similar results were obtained when the ammonium chloroantimonate was used.

Table I lists the diarylstibinic acids and the corresponding pyridinium chloroantimonates prepared in this study. These results were obtained by the use of anhydrous isopropanol as the solvent and copper bronze as the catalyst. Although previous workers have reported m.ps. for some diarylstibinic acids, the compounds listed in the present paper softened on heating but in no case was a sharp m.p. observed.

Acknowledgment.—The authors wish to thank Miss Sadie Herndon for performing the analyses incident to this research.

(3) The ratio between nitrogen and antimony in this sample was 1.11 after attempted purification.

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The Synthesis of Ketones from Di-*t*-butyl Malonates

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Attempts to prepare ketones of the type RCO-CH₂R' by the acylation of diethyl alkylmalonates with acid chlorides, followed by hydrolysis and decarboxylation with acidic or alkaline reagents, have been almost uniformly unsuccessful, because the intermediary acylalkylmalonates preferentially undergo hydrolysis of the acyl-carbon bond to, in effect, reverse the process.² Bowman³ has utilized the benzyl esters of alkylated malonic acids to circumvent this difficulty elegantly. The acylmalonic esters formed from these compounds were cleaved to ketones by catalytic hydrogenolysis followed by thermal decarboxylation.

In the present note we wish to report the use of *t*-butyl esters of malonic acids for the preparation of ketones.⁴ Di-*t*-butyl malonate, prepared in 60% yield by the acid-catalyzed reaction between malonic acid and isobutylene, was alkylated with benzyl chloride, cyclohexyl bromide and *n*-octyl bromide to give the corresponding di-*t*-butyl alkylmalonates. Conversion of these compounds to the sodio derivatives by treatment with sodium hydride in an inert solvent, followed by reaction of the sodio compound with an acid chloride, gave oily di-*t*-butyl acylalkylmalonates which were not purified, but treated directly with *p*-toluenesulfonic acid in refluxing toluene or anhydrous acetic acid to effect cleavage of the carbo-*t*-butoxy groups to give isobutylene, carbon dioxide and the ketone. The following ketones have been prepared in this manner: phenyl β-phenylethyl ketone (70–85% yield from benzoyl chloride), *p*-nitrophenyl β-phenylethyl ketone (81% from *p*-nitrobenzoyl chloride), *o*-nitrophenyl β-phenylethyl ketone (71%

(1) Allied Chemical and Dye Corp. Fellow, 1950; Sterling-Winthrop Research Institute Fellow, 1950–1951. The Upjohn Co., Kalamazoo, Mich.

(2) See R. E. Bowman, *J. Chem. Soc.*, 322 (1950), for discussion and leading references. An exception is the case where R' = H; *i.e.*, the use of unsubstituted malonic esters gives good yields of methyl ketones. H. G. Walker and C. R. Hauser, *THIS JOURNAL*, **68**, 1386 (1946).

(3) R. E. Bowman, *J. Chem. Soc.*, 325 (1950).

(4) *Cf.* the preparation of keto esters by the use of *t*-butyl ethyl malonates, D. S. Breslow, E. Baumgarten and C. R. Hauser, *THIS JOURNAL*, **66**, 1286 (1944).