if possible, these carbohydrates. Chromatographic adsorption[4] on a silicic acid[5]–Celite[6] mixture led to the isolation of 15 mg. of a compound (m.p. 97°, $[\alpha]_D$ −32.9° Me_2CO *ca.* 0.2) which analyzed for $C_{12}H_{20}O_6$; the physical constants are those of diisopropylidene-β-D-fructose.[7] The compound showed no depression of melting point when mixed with an authentic sample of diisopropylidene-D-fructose.

Although fructose has been shown to be a normal constituent of seminal plasma[8] it does not appear to have been isolated heretofore from blood.

It should be noted that the procedure used in the isolation of the fructose prevents even speculation as to the normal concentration of this sugar in blood, or to the form in which it occurs since the acid used in acetonation may have hydrolyzed a fructose derivative.

Experimental

The sirup obtained by concentrating the ether–petroleum ether soluble material (as indicated above[2]) was thoroughly extracted with petroleum ether (b.p. 30–60°) and the petroleum ether soluble material concentrated to dryness under reduced pressure at room temperature. The material was then separated into two fractions in the following manner: the sirup was dissolved in 10 ml. of benzene and filtered through a column (16 cm. × 2 cm.) packed with a mixture of silicic acid and Celite (3:1 by weight). The column was then washed with 150 ml. of benzene, extracted and the entire column eluted with acetone (250 ml.). The acetone eluate (representing the material adsorbed from benzene solution by silicic acid–Celite) was concentrated to dryness under reduced pressure at room temperature, redissolved in benzene and rechromatographed under the same conditions with the exception that in place of the benzene wash the column was developed with 100 ml. of benzene containing 1% (by volume) of *t*-butyl alcohol. The column was extruded and streaked with alkaline permanganate.[9] The zone at approximately the center of the column was cut and eluted with acetone, concentrated to dryness under reduced pressure at room temperature. The material crystallized after standing several days at 4°. After recrystallization from petroleum ether (b.p. 30–60°) the compound melted at 95–96°, $[\alpha]_D$ −32.9° (Me_2CO *ca.* 0.2).

Anal. Calcd. for $C_{12}H_{20}O_6$: C, 55.43; H, 7.74. Found: C, 55.45; H, 7.53.

The compound showed no depression of melting point when mixed with an authentic sample of diisopropylidenefructose.

---

[4] W. H. McNeely, W. W. Binkley and M. L. Wolfrom, *ibid.*, **67**, 527 (1945).

[5] Baker and Adamson, Silicic Acid Powder (Reagent) Lot No. 6123.

[6] No. 535 obtained from Johns-Manville, New York.

[7] E. Fischer, *Ber.*, **28**, 1165 (1895); H. Ohle and I. Koller, *ibid.*, **57**, 1573 (1924).

[8] J. Mann, *Biochem. J.*, **40**, 481 (1946).

[9] L. Zechmeister and W. H. McNeely, This Journal, **64**, 1919 (1942); B. W. Lew, M. L. Wolfrom and R. M. Goepp, Jr., *ibid.*, **67**, 1865 (1945); **68**, 1449 (1946).

DEPARTMENT OF MICROBIOLOGY
THE JOHNS HOPKINS UNIVERSITY
SCHOOL OF HYGIENE AND PUBLIC HEALTH
BALTIMORE, MARYLAND

Reactions of Toluic Acids with Sulfur. I. Stilbenedicarboxylic Acids

BY WILLIAM G. TOLAND, JR., JOHN B. WILKES AND FREDERICK J. BRUTSCHY

RECEIVED NOVEMBER 1, 1952

Previous methods for the preparation of 4,4′-stilbenedicarboxylic acid have involved a number of steps, such as conversion of stilbene to the dibromide, to the dinitrile, and finally to the diester,[1] or by the decarboxylation of more complex acids.[2] The preparation of 3,3′-stilbenedicarboxylic acid does not appear to have been reported. We have found that a shorter, more economical route to both these acids is provided by the reaction of the corresponding toluic acid with sulfur. Spectroscopic evidence indicates that the 4,4′-stilbenedicarboxylic acid thus formed is the *trans* isomer. The reaction of sulfur with amine and hydroxyl-substituted aromatic compounds leads to attachment of sulfur to the aromatic ring, but the dehydrodimerizing action of sulfur has been demonstrated in the conversion of toluene to stilbene and tetraphenylthiophene, of *m*- and *p*-xylenes to the corresponding dimethylstilbenes,[3] and in the dehydropolymerization of 4-picoline.[4] The mechanism of some of these reactions has been discussed.[5] Previously reported dehydrodimerization reactions, however, do not involve compounds containing reactive functional groups such as the carboxyl group.

With *p*-toluic acid, 50–70% yields of 4,4′-stilbenedicarboxylic acid are obtained by reaction with sulfur. Other products are hydrogen sulfide, a large amount of a sulfur-containing acid of higher molecular weight, believed to be tetra-(*p*-carboxyphenyl)-thiophene, and a small amount of an unidentified compound of lower molecular weight. Sulfur reacts with *m*-toluic acid to give lower yields of 3,3′-stilbenedicarboxylic acid, but no stilbene derivatives were obtained from the reaction of sulfur with *o*-toluic acid under the conditions studied.

Several variables of the reaction of sulfur with *p*-toluic acid to yield 4,4′-stilbenedicarboxylic acid were investigated, and the optimum reaction conditions are shown in Table I. The rate of reaction increases rapidly with temperature, but the yield decreases simultaneously. Impurities in the toluic acid prolong the reaction time, and increased reaction time decreases the yield. The higher the toluic acid:sulfur ratio, the higher is the yield, based on *p*-toluic acid reacted. More than 90% of the theoretical amount of sulfur cannot be used in the absence of solvent, or the reaction mixture solidifies before the reaction is complete.

Experimental

Materials.—The isomeric toluic acids were made by the air oxidation of the corresponding xylenes, using a soluble cobalt salt catalyst, and purified by filtering and washing the residue with xylene, followed by distillation through a 90-cm. glass helices-packed column. Isomer content was determined by ultraviolet spectrography. Sublimed flowers of sulfur, U.S.P., were used.

Reaction of *p*-Toluic Acid with Sulfur.—A mixture of *p*-toluic acid and sulfur was heated in a three-neck flask equipped with an air-cooled condenser, stirrer and thermowell. At reaction temperature, the mixture darkened and hydrogen sulfide was evolved. After partial reaction had occurred, a yellow solid, consisting largely of 4,4′-stilbenedicarboxylic acid, began to separate. The threshold tem-

---

[1] G. P. Hager, A. M. VanArendonk and H. A. Shonle, This Journal, **66**, 1982 (1944).

[2] F. Bell and D. H. Waring, *J. Chem. Soc.*, 1024 (1948).

[3] L. Aronstein and A. S. Van Nierop, *Rec. trav. chim.*, **21**, 448 (1902).

[4] H. I. Thayer and B. B. Corson, This Journal, **70**, 2330 (1948).

[5] A. W. Horton, *J. Org. Chem.*, **14**, 761 (1949).

perature for the reaction is about 245°, but it was found advantageous to work close to a reflux temperature (270–275°). When evolution of hydrogen sulfide ceased, the mixture was cooled to 140°, and about 5 ml. of hot xylene was added for each gram of *p*-toluic acid. The solution was refluxed 30 minutes, filtered hot, and the cake washed with hot xylene. Evaporation of the xylene yielded any unreacted *p*-toluic acid and sulfur and some of the acids of higher molecular weight. The toluic acid could be distilled off and reused. The filter cake was extracted with hot dioxane, which dissolves more than 20 g. of higher polymer acids per 100 ml. The remaining cake consisted largely of 4,4′-stilbenedicarboxylic acid, with a small amount of an unidentified, yellow polymeric acid. The stilbenedicarboxylic acid was dissolved in a slight excess of boiling aqueous KOH, allowing about 4 g. of stilbenedicarboxylic acid per 100 ml. of solution, and the potassium salt of the stilbenedicarboxylic acid crystallized from the solution. The free acid was precipitated from the hot salt solution by addition of an excess of HCl and digestion of the hot solution to ensure the absence of the insoluble half-acid salt and to coagulate the otherwise colloidal precipitate. Purification of 4,4′-stilbenedicarboxylic acid can also be effected through the ammonium or guanidine salts.

TABLE I

REACTION OF *p*-TOLUIC ACID WITH SULFUR

Run	Reactants, mole Toluic	S	*p*-Toluic acid purity, %	*T*, °C.	Hr.	*p*-Toluic acid reacted, %	SDCA[a] Yield, %
1	1.0	0.5	97.8	260	4.5	51.7	60.6
2	1.0	0.05	92.6	260	4.0	5.7	70.6
3	1.0	1.0	Pure	271	2.0	79.5	57.3
4	1.0	0.5	97.8	275–280	3.0	55.0	53.6

[a] SDCA = 4,4′-stilbenedicarboxylic acid, yield based on *p*-toluic acid reacted.

4,4′-Stilbenedicarboxylic Acid.—Repeated recrystallization of the potassium salt of stilbenedicarboxylic acid gives a white, sulfur-free product. The free acid, m.p. 460° (sealed tube), has a neutral equivalent of 134.1. Permanganate oxidation gave terephthalic acid almost quantitatively. The acid chloride was prepared by reaction of thionyl chloride in the presence of pyridine, m.p. 228–232°. The diethyl ester, b.p. 195–203° (0.1–0.09 mm.), m.p. 129.9–130.0°, was prepared from the acid chloride. Previous workers report for the acid chloride, m.p. 223–224°[2] and 227–228°.[6] For the diethyl ester, a m.p. of 130–131° is reported.[1] The absorption spectrum of an aqueous solution of the potassium salt shows broad peaks at 3425, 3275 3150 and approximately 2300 Å. The configuration of the spectrum closely resembles the spectra of *p*-toluic acid and dimethyl terephthalate, but is displaced to longer wave lengths. It closely resembles published spectra[7,8] of *trans*-*p,p*′-stilbene derivatives but not those of *cis*-stilbene derivatives. The acid and its solution show intense blue fluorescence when irradiated with ultraviolet light of the appropriate wave length, which is not a characteristic of *cis*-stilbene.[7] Irradiation of stilbenedicarboxylic acid with 2537 Å. light causes a change in the spectrum similar to *trans* to *cis* isomerization of stilbene. Hence, the available evidence points to the conclusion that the product is the *trans* isomer of 4,4′-stilbenedicarboxylic acid.

The solubility of 4,4′-stilbenedicarboxylic acid in most neutral solvents is less than 20 mg./100 ml. It is moderately soluble in dimethyl formamide, acetic anhydride and molten toluic acid, and somewhat soluble in ethylene glycol and diethylene glycol. Solubility in boiling sulfolane is about 2.5 g./100 ml., and the acid can be recrystallized from this solvent.

Tetra-(*p*-carboxyphenyl)-thiophene.—The dioxane-soluble, xylene-insoluble products could not be crystallized from dioxane. A brown to orange, finely divided solid was obtained by pouring the solution slowly into a large excess of xylene or water. Sulfur analyses of this crude material gave values varying from 5.10 to 5.41%, compared to 5.67% for tetra-(*p*-carboxyphenyl)-thiophene. Oxidation of the compound with permanganate gave terephthalic acid. The molecular weight of the crude compound, determined ebulliometrically in acetone, was 520 ± 30 (theoretical for tetra-(*p*-carboxyphenyl)-thiophene, 564.62). As sulfur reacts with stilbene and its analogs to form thiophene derivatives[3–5] it seems probable that the main by-product is impure tetra-(*p*-carboxyphenyl)-thiophene, which has not yet been isolated in pure form due to contamination with low polymers of the type reported by Thayer and Corson.[4]

3,3′-Stilbenedicarboxylic Acid.—Refluxing 104 g. (0.765 mole) of *m*-toluic acid with 12.2 g. (0.383 mole) of sulfur at 262–267° until evolution of hydrogen sulfide ceased (5 hours), followed by extraction with two 150-ml. portions of hot xylene and washing with acetone gave 5.0 g. of dimer acid cake. Evaporation of the xylene, and extraction of the solid with 250 ml. of acetone containing 25 ml. of water, followed by xylene extraction to remove sulfur, gave an additional gram of dimer acid. Crystallization of the ammonium salt, acidification and digestion with hydrochloric acid gave 4.5 g. of acid, neutral equivalent 135.6 (theory 134.1). Oxidation with permanganate gave isophthalic acid.

The dimethyl ester was formed by refluxing 2 g. of acid with 50 ml. of methanol and 5 ml. of concentrated sulfuric acid. The ester was dissolved by addition of chloroform, the solution washed with water and sodium carbonate solution, and the ester crystallized twice from mixed chloroform and methanol to give 1.0 g. of ester, m.p. 145.5–146°.

Anal. Calcd. for $C_{18}H_{16}O_4$: C, 72.95; H, 5.44; sapn. equiv., 148.15. Found: C, 72.65; H, 5.35; sapn. equiv., 147.7.

Purified 3,3′-stilbenedicarboxylic acid, prepared by saponifying the dimethyl ester and precipitating the free acid, melted at 352–354°. Titration with 0.1 N permanganate solution in boiling 0.05 N sodium hydroxide solution to give an end-point stable for more than 30 seconds took 95% of the theoretical permanganate.

Anal. Calcd. for $C_{16}H_{12}O_4$: C, 71.63; H, 4.51. Found: C, 71.53; H, 4.60.

Acknowledgments.—We wish to thank Mr. R. D. Clark for spectroscopic analysis and interpretation, Dr. B. J. Fontana for molecular weight determinations, and Dr. J. A. Spence for preparation of the acid chloride and diethyl ester.

CALIFORNIA RESEARCH CORPORATION
RICHMOND, CALIFORNIA

---

[6] G. P. Hager and H. A. Shonle, THIS JOURNAL, **68**, 2167 (1946).

[7] G. N. Lewis, T. T. Magel and D. Lipkin, *ibid.*, **62**, 2973 (1940).

[8] M. Calvin and R. E. Buckles, *ibid.*, **62**, 3324 (1940).

The Dielectric Properties of Supercooled Liquids[1]

BY G. N. ROBERTS[2]

RECEIVED JANUARY 15, 1953

Viscosity measurements on phenyl ether[3] indicate the existence of a structural change occurring in the supercooled liquid at the melting point; the points obtained by plotting log η against $1/T$, where η is the viscosity at absolute temperature T, fall into two groups corresponding to measurements made above and below the melting point, the points of each group lying on a straight line but the line for the supercooled liquid being steeper than that for the liquid above the melting point. A similar effect has been observed for *m*-chloronitrobenzene, menthol and salol[4] and Greenwood and Martin[5] have observed corresponding discontinuities at the

---

[1] This note represents part of the work submitted by Dr. G. N. Roberts to the University of London in fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] Frick Chemical Laboratory, Princeton University, Princeton, N. J.

[3] C. Dodd and Hu Pak Mi, *Proc. Phys. Soc.* (*London*), **B62**, 454 (1949).

[4] Hu Pak Mi, Thesis, University of London, 1950.

[5] N. N. Greenwood and R. L. Martin, *J. Chem. Soc.*, 1795 (1951).