g., m. p. 190–213°, was recrystallized three times from dioxane yielding a product that melts at 248.5°.

Substituted 2-N⁴-Acetylsulfanilamidoquinoxalines

The amines were dissolved or suspended in pyridine and *p*-acetylaminobenzenesulfonyl chloride added while the mixture was stirred.

2-N⁴-Acetylsulfanilamido-5(or 8)-chloroquinoxaline.—To a mixture of 11.7 g. of the amine in 60 ml. of dry pyridine was added 16.7 g. of *p*-acetylaminobenzene sulfonyl chloride in four portions at ten-minute intervals, During the addition, the mixture warmed up to 35°. After being stirred for one hour, the resultant clear yellow solution was heated on a water-bath at 65° for one-half hour. The mixture was then poured into 800 ml. of hot water and the product, which crystallized when the mixture was stirred, was filtered and air dried. The crude product, 20.0 g., was dissolved in 250 ml. of 1.3 *N* sodium hydroxide and filtered; 4.45 g. of insoluble material, m. p. 208–210°, was obtained. The filtrate was acidified with glacial acetic acid yielding light yellow amorphous material, m. p. 245–252° (14.7 g., 62% yield). The analytical sample was crystallized from glacial acetic acid, m. p. 252–255°.

2-N⁴-Acetylsulfanilamido-6(or 7)-carboxamidoquinoxaline.—A mixture of 1.08 g. of 2-chloro-6(or 7)-carbamidoquinoxaline, 1.07 g. of acetylsulfanilamide, 0.65 g. of potassium carbonate and 50 mg. of copper powder in a Pyrex test-tube was stirred and heated at 180–190° in an oil-bath for fifteen minutes. The dark mixture was extracted with 10 cc. of 10% sodium hydroxide, filtered from the chloro compound that had not reacted and precipitated by acidification with dilute acetic acid. The oil that separated solidified on trituration with isopropyl alcohol. Recrystallization from glacial acetic acid yielded product, m. p. 277° about 500 mg.

Sulfonamides

The acetyl derivatives were hydrolyzed by boiling with aqueous sodium hydroxide or ethanolic hydrogen chloride.

2-Sulfanilamido-5(or 8)-chloroquinoxaline.—A solution of 11.95 g. of the acetyl compound in 75 ml. of 2.5 *N* sodium hydroxide was heated for one-half hour on a steam-bath. The crude product, 10.25 g., 97% yield, was precipitated by neutralization with acetic acid. The crude product, m. p. 210–213°, was purified in 87% recovery by dissolving in hot 5 *N* ammonium hydroxide, treating with charcoal and precipitating with acetic acid, m. p. 213–215°.

Acknowledgment.—The authors are indebted to Dr. R. T. Major and Dr. Max Tishler for their kind encouragement and advice.

Summary

The preparation of sixteen substituted derivatives of 2-sulfanilamidoquinoxaline is described, as well as the preparation of seventy-four other new quinoxaline compounds.

RAHWAY, NEW JERSEY RECEIVED MAY 28, 1948

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, AMERICAN HOME FOODS, INC.]

2-Acyloxyacetylthiophenes

BY FRANK KIPNIS,* HAROLD SOLOWAY AND JOHN ORNFELT

During synthetic work on substances containing the thiophene ring, it became desirable to prepare 2-hydroxyacetylthiophene (I) and a series of

I, R = OH III, R = Br
II, R = OCOR′

esters (II) derived therefrom. The intermediate which seemed to offer most promise was bromoacetylthiophene (III) which had been prepared by Brunswig[1] by the addition of bromine to a solution of 2-acetylthiophene in carbon disulfide stirred with a stream of carbon dioxide. In the present work, it was found more convenient to prepare this compound by treatment of the ketone in carbon tetrachloride with bromine in the presence of iron filings as catalyst.

By hydrolysis of the bromine compound with sodium formate in methanol,[2] 2-hydroxyacetylthiophene was prepared in fair yield. The esters, which are related to the phenacyl compounds, were prepared by several methods which gave acceptable yields. In view of the ready availability of 2-acetylthiophene[3] and 2-bromoacetylthiophene, it may be indicated that the esters would probably serve as suitable derivatives for carboxylic acids, supplementing those derived from the phenacyl halides.

* Present address: Oxford Products, Inc. Cleveland, Ohio.

(1) Brunswig, *Ber.*, **19**, 2891 (1886).

(2) Levene and Walti, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 5.

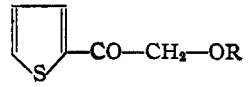
(3) Supplied by the Socony-Vacuum Oil Co. Paulsboro, N. J.

Experimental

2-Bromoacetylthiophene (III).—To a 1000-ml. interjoint flask fitted with a sealed stirrer, reflux condenser with drying tube, dropping funnel and thermometer, was added 42 g. (0.33 mole) of 2-acetylthiophene, 300 ml. of dry carbon tetrachloride and a few iron filings. The mixture was stirred and heated on the water-bath to 60° (internal) and then the bath was removed. A solution of 53.5 g. (0.67 atom) of bromine in 100 ml. of carbon tetrachloride was then added at such a rate that gentle refluxing occurred (about twenty minutes). The solution was refluxed for an additional thirty minutes, at the end of which time evolution of hydrogen bromide had ceased and the bromine coloration was absent. The volatiles were removed by distillation under slightly reduced pressure, and the residue was fractionated through a 30-cm. Vigreux column at 95–98° (1.5 mm.) to give 55 g. (80% yield) of a slightly yellow, extremely lachrymatory oil (n^{20}D 1.6258) which solidified below room temperature. The product was rather unstable at room temperature, but could be stored without decomposition at −10°. In agreement with Brunswig,[1] bromoacetylthiophene on treatment with alcoholic ammonia gave a carmine coloration, followed by a deep red-blue color on standing.

2-Hydroxyacetylthiophene (I).—In a 500-ml. 3-neck flask fitted with a sealed stirrer, reflux condenser and drying tube was placed 20.5 g. (0.1 mole) of 2-bromoacetylthiophene, 13.6 g. (0.2 mole) of anhydrous sodium formate and 180 ml. of absolute methanol. The stirrer was started and the solution was refluxed for ten hours. The volatiles were distilled at slightly reduced pressure, acetone

TABLE I

2-ACYLOXYACETYLTHIOPHENES 

R	Yield, %	M. p., °C.	Recrystallizing solvent	Formula	Analyses,[a] % C	H	S	Found C	H	S
H	38	73–74	Hexane	$C_6H_6O_2S$	50.69	4.26	22.55	50.84	4.40	22.82
$COCH_3$	58	[b]	....	$C_8H_8O_3S$	52.16	4.38	17.40	52.07	5.05	17.64
COC_6H_5	80	95–96	Carbon	$C_{13}H_{10}O_3S$	63.40	4.09	13.02	63.37	4.33	13.30
$COCH{=}CHC_6H_5$	68	118–120	tetrachloride	$C_{15}H_{12}O_3S$	66.16	4.44		65.85	4.72	
COC_4H_3O (furoyl)	43	93.5	Hexane	$C_{11}H_8O_4S$	55.92	3.41	13.57	56.07	3.54	13.04

[a] Analyses by Oakwold Laboratories, Alexandria, Virginia. [b] B. p. 113–114° (3 mm.).

was added to the residue to complete the precipitation of inorganic salts, the mixture was filtered, the filtrate stripped and the residue fractionated at 93–95° (3 mm.) to give 5.4 g. (38% yield) of an oil which solidified on standing. The crystalline material was twice recrystallized from hexane to give colorless plates melting at 73–74°.[4]

2-Acetoxyacetylthiophene (II, R′ = CH_3).—A mixture of 16.4 g. (0.08 mole) of 2-bromoacetylthiophene, 13 g. (0.16 mole) of anhydrous sodium acetate and 200 ml. of glacial acetic acid was refluxed with stirring for ten hours. At the end of that time, the mixture was cooled, diluted to 1500 ml. with ice water and extracted three times with 150 ml. of ether. The solvent layer was washed with 10% sodium carbonate solution until neutral and then with 50 ml. of saturated sodium chloride solution, dried with calcium sulfate and filtered from the desiccant. The ether was stripped and the residue distilled at 113–114° (3 mm.) to give 8 g. (55% yield) of a light yellow oil.

2-Benzoyloxyacetylthiophene (II, R′ = C_6H_5).—Directions are given for the benzoyl compound, but the furoyl and the cinnamoyl derivatives have been prepared in the same way, and other esters could undoubtedly be synthesized in a similar manner. It may be noted that ethanol may replace ethylene glycol as a solvent, but consistently higher yields have been achieved with the latter.

(4) All melting points were taken with a Fisher–Johns apparatus.

A mixture of 16 g. (0.11 mole) of sodium benzoate in 40 ml. of water was made slightly acid to litmus with 10% hydrochloric acid and then 200 ml. of ethylene glycol was added, together with 20.5 g. (0.1 mole) of 2-bromoacetylthiophene. After refluxing for twelve hours, the cooled mixture was poured into an excess of 4% sodium bicarbonate solution with stirring, causing the separation of a solid which was removed by filtration. The precipitate was washed thoroughly with bicarbonate solution, air-dried and recrystallized, first from heptane and then from carbon tetrachloride (Norite) to give 19.7 g. (80% yield) of white crystals melting at 95–96°.

The properties and analyses of the compounds prepared are noted in Table I.

Summary

2-Bromoacetylthiophene has been prepared in 80% yield by treatment of 2-acetylthiophene with bromine in the presence of catalytic quantities of iron filings.

From this bromoketone, it was possible to synthesize the α-ketol and a series of α-ketol esters.

MORRIS PLAINS, N. J. RECEIVED AUGUST 9, 1948

[CONTRIBUTION NO. 54 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TENNESSEE]

4-Hydroxybenzene-1,2,3-tricarboxylic Acid, 5-Hydroxybenzene-1,2,4-tricarboxylic Acid and their Derivatives

BY C. A. BUEHLER, R. BEECHER SPEES[1] AND PHILLIP A. SANGUINETTI[2]

In the identification of the degradation products of 6-hydroxymethyl-1,3-benzodioxan-5-carboxylic acid lactone,[3] it was necessary to synthesize 4-hydroxybenzene-1,2,3-tricarboxylic acid, 5-hydroxybenzene-1,2,4-tricarboxylic acid, the two methoxy trimethyl esters and the two methoxy tricarboxylic acids as possible reference compounds. The syntheses of the 5-hydroxy acid and its derivatives were accomplished by the scheme

$C_6H_3(CH_3)_3(1,2,4) \longrightarrow C_6H_2SO_2OH(CH_3)_3(1,2,4,5) \longrightarrow$
I II

$C_6H_2(COOH)_3OH(1,2,4,5) \longrightarrow$
III

$C_6H_2(COOCH_3)_3OCH_3(1,2,4,5) \longrightarrow$
IV

$C_6H_2(COOH)_3OCH_3(1,2,4,5)$
V

Pseudocumene, I, gave the 5-sulfonic acid, II, in good yield by treatment with concentrated sulfuric acid. This sulfonic acid on oxidation with potassium permanganate followed by alkaline fusion produced the hydroxytricarboxylic acid, III, in 55% yield. Treatment with diazomethane gave the methoxytrimethyl ester, IV, which on saponification yielded the methoxy acid, V.

The 4-hydroxy acid was synthesized in a similar manner from hemimellitene (1,2,3-trimethylbenzene). Sulfonation gave the 4-sulfonic acid

(1) Present address: Northern Illinois College of Optometry, Chicago, Illinois.

(2) Present address: Monsanto Chemical Company, Anniston, Alabama.

(3) Buehler, Harris, Shacklett and Block, THIS JOURNAL, 68, 574 (1946).