It must be concluded that the oxidation with permanganate of 5-nitrouracil, as well as of uracil itself, under the conditions used does not yield fractions representing specific carbon atoms of the ring system. The conclusions of Lagerkvist,[5] therefore, concerning the role of bicarbonate as a precursor of carbon 6 of uracil must be viewed with considerable doubt.

Experimental

Uracil-4-C^{14}.—The method of Davidson and Baudisch[6] was used for the synthesis of uracil from urea and a sample of malic acid-4-C^{14} prepared in this Laboratory by methods recently described.[7] The identity and purity of the twice-recrystallized uracil-4-C^{14} were established by the determination of the ultraviolet absorption spectrum in 0.01 *N* hydrochloric acid. Both the ϵ_{max} and the ratio of optical densities at 260 and 280 mμ agreed to within 1% with published data.[8]

5-Nitrouracil-4-C^{14}.—The isotopic nitrouracil was prepared by the method of Johnson and Matsuo[9] from a portion of the uracil-4-C^{14} diluted somewhat with non-radioactive uracil. The increase in weight during this process was 94% of that required by theory. The material was recrystallized once from water.

Oxidation of Uracil-4-C^{14}.—The procedures described by Heinrich and Wilson[1] for the cleavage of the pyrimidine ring, collection of the carbon dioxide, hydrolysis of the oxaluric acid, separation of the calcium oxalate and its subsequent oxidation to carbon dioxide were followed closely, except that the *p*H was maintained between 5 and 7 with the aid of a *p*H meter.

Oxidation of 5-Nitrouracil.—The method of Behrend and Offe[4] was followed for the oxidation step, followed by procedures similar to those mentioned above for uracil.

Acknowledgment.—The authors wish to thank Professor Melvin Calvin for his interest in this work.

RADIATION LABORATORY AND DEPARTMENT OF CHEMISTRY[10]
UNIVERSITY OF CALIFORNIA
BERKELEY 4, CALIF.

(6) D. Davidson and O. Baudisch, THIS JOURNAL, **48**, 2379 (1926).
(7) E. C. Jorgensen, J. A. Bassham, M. Calvin and B. M. Tolbert, *ibid.*, **74**, 2418 (1952).
(8) J. M. Ploeser and H. S. Loring, *J. Biol. Chem.*, **178**, 431 (1949).
(9) T. B. Johnson and I. Matsuo, THIS JOURNAL, **41**, 782 (1919).
(10) The work described in this paper was sponsored by the Atomic Energy Commission.

A Convenient Preparation of Ethyl 2-Pyridylacetate

BY NEWTON N. GOLDBERG, BRUNO M. PERFETTI AND ROBERT LEVINE

RECEIVED MARCH 5, 1953

The following three methods are reported in the literature for the preparation of ethyl 2-pyridylacetate (I): (1) the alcoholysis of 2-pyridylacetanilide, which was prepared by the Beckmann rearrangement of 2-phenacylpyridine oxime,[1,2] (2) in 25% yield by the reaction of the potassium derivative of 2-picoline (prepared from the tar base and potassium amide) with diethyl carbonate[3] and (3) in 35–40% yield by the esterification of the lithium salt of 2-pyridylacetic acid, which was prepared by the carbonation of 2-lithiopyridine, which was in turn prepared from phenyllithium and 2-picoline.[4] These three methods have the common disadvantage that they are lengthy processes.

We have now found that by modifying the method developed in this Laboratory for the acylation of the lithium derivatives of methylated tar bases,[5,6] I may be prepared in 44.5% yield by the addition of a dilute ethereal solution of 2-picolyl lithium to a dilute ethereal solution of diethyl carbonate over a five-hour period. In addition to I, a small amount of di-2-picolyl ketone was isolated as its dipicrate.

Procedure.—2-Picolyllithium (0.4 mole) in 800 ml. of absolute ether was prepared as described previously[5] by the interaction of 0.4 mole of phenyllithium (prepared from 0.8 mole of lithium ribbon[7] and 0.4 mole (62.8 g.) of bromobenzene) and 0.4 mole (37.2 g.) of 2-picoline and was added over a five-hour period to a rapidly stirred cold (ice–salt-bath) solution of diethyl carbonate (0.2 mole, 23.6 g.) in 700 ml. of anhydrous ether. The ether was not allowed to reflux during the addition of the 2-picolyllithium. After the addition of the 2-picolyllithium was complete, the cooling bath was removed. The reaction mixture was heated to reflux, poured onto 200 g. of ice and extracted with several 200-ml. portions of ether. The combined ethereal phases were dried and concentrated and the residue fractionated to give 14.7 g. (44.5%) of ethyl 2-pyridylacetate, b.p. 110–113° (6 mm.); picrate, m.p. 138.8–139.2°.[5] The tarry residue was extracted for 18 hours with petroleum ether, b.p. 60–70°, in a Soxhlet extractor to give a small amount (< 0.1 g.) of a semi-solid material, which contained di-2-picolyl ketone, as indicated by the analysis of its dipicrate, m.p. 190–191° (from 95% ethanol) (undepressed by the dipicrate of the ketone obtained by the carbonation of 2-picolyllithium).

Anal. Calcd. for $C_{25}H_{18}O_{15}N_8$: N, 16.72. Found: N, 16.51.

Acknowledgment.—The authors gratefully acknowledge the support of the U. S. Atomic Energy Commission during the course of this work.

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(7) The lithium ribbon was generously supplied by the Metalloy Corporation.

CONTRIBUTION NO. 904
CHEMISTRY DEPARTMENT
THE UNIVERSITY OF PITTSBURGH
PITTSBURGH 13, PA.

Some Brominated Dibenzothiophene Derivatives

BY HENRY GILMAN AND ROBERT K. INGHAM

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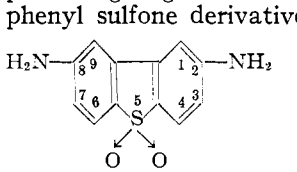
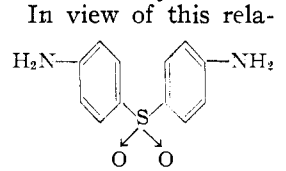
Dibenzothiophene derivatives, especially the substituted 5-dioxides, are closely related to substituted diphenyl sulfones; several compounds possessing high antituberculous activity are diphenyl sulfone derivatives. In view of this rela-



2,8-Diaminodibenzothiophene-5-dioxide



p,p'-Diaminodiphenyl sulfone

tionship and the demonstrated activity of 2-halo-7-aminodibenzofurans[1] the preparation of 2-bromo-

(1) V. C. Barry, L. O'Rourke and D. Twomey, *Nature*, **160**, 800 (1947).
(1) M. P. Oparina, *Khim Farm. Prom.*, No. 4, 15 (1934); (*C. A.*, **29**, 1820 (1935)).
(2) M. P. Oparina, *J. Gen. Chem.* (*U.S.S.R.*), **5**, 1699 (1935); (*C. A.*, **30**, 2567 (1936)).
(3) M. J. Weiss and C. R. Hauser, THIS JOURNAL, **71**, 2023 (1949).

7-aminodibenzothiophene-5-dioxide was undertaken.

The preparation of 2-bromodibenzothiophene-5-dioxide has been reported by Courtot,[2] the compound being obtained by oxidation of 2-bromodibenzothiophene with potassium dichromate; however, no experimental details were given. The only other report is that of Muth and Putzer,[3] who report the chromic acid oxidation of 2-bromodibenzothiophene. During the present investigation, the oxidation of the bromo derivative with hydrogen peroxide was found to be convenient and to give moderate yields of the desired product.

An attempted catalytic reduction of 2-bromo-7-nitrodibenzothiophene-5-dioxide was not successful. The compound was readily reduced by tin and hydrochloric acid. The results of pharmacological rests of the 2-bromo-7-aminodibenzothiophene-5-dioxide will be reported elsewhere.

Since the 2,8-substituted dibenzothiophenes may be regarded as "closed models" of the *p,p'*-substituted diphenyl sulfides, the preparation and testing of 2-bromo-8-aminodibenzothiophene appeared desirable. The 2-bromo-8-nitro- and 2-bromo-8-aminodibenzothiophenes have been reported,[4] but no experimental details were included in this report.

A procedure for the preparation of 3-bromodibenzothiophene from the 3-amino analog has been reported.[5] In addition to the repetition of this method, the 3-bromo compound was also synthesized by the reduction of 3-bromodibenzothiophene-5-dioxide with lithium aluminum hydride. It is noteworthy that reduction of the dioxide was effected without replacement of the bromine atom. The method may prove useful for the reduction of other substituted dibenzothiophene-5-dioxides either for structure proof or for the synthesis of otherwise difficultly obtainable derivatives.

Experimental[6]

2-Bromodibenzothiophene-5-dioxide.—Fifteen grams (0.058 mole) of 2-bromodibenzothiophene was suspended in 200 ml. of glacial acetic acid. To this solution was slowly added 30 ml. of 30% hydrogen peroxide, and the mixture was then slowly warmed to reflux temperature. On warming, the solid entirely dissolved, a precipitate forming shortly thereafter. The mixture was refluxed for one hour, cooled, filtered and the precipitate washed well with water. The white sulfone melted at 261–262° and weighed 16.0 g. (93.5%). Courtot[2] reports a m.p. of 266–267°; Muth and Putzer[3] report a m.p. of 256°. After digestion with absolute ethanol the 2-bromodibenzothiophene-5-dioxide melted at 261.5–262°.

2-Bromo-7-nitrodibenzothiophene-5-dioxide.—Into a three-necked, 250-ml. flask was placed 15.0 g. (0.051 mole) of 2-bromodibenzothiophene-5-dioxide. Fifty milliliters of concentrated sulfuric acid was added, forming a thick paste, and then 33 ml. of fuming nitric acid (sp. gr. 1.50) was added slowly. The stirred mixture was warmed to 80° and there maintained for two hours. Upon cooling, the reaction mixture was filtered and immediately washed well with water to stop action of the concentrated acids. The crude yield was 14.0 g. (80%) of a light yellow solid, melting over the range from 250–300°. Three recrystallizations from glacial acetic acid gave 9.0 g. (52%) of pale yellow needles, melting at 319–321°. After one recrystallization the m.p. range was 295–315°; after the second, 315–320°; and following the third, 319–321°.

Anal. Calcd. for $C_{12}H_6O_4SNBr$: S, 9.43. Found: S, 9.39, 9.39.

2-Bromo-7-aminodibenzothiophene-5-dioxide.—An attempted catalytic reduction employing Raney nickel and an ethanolic suspension of the nitro compound was unsuccessful, only starting material being obtained. Nine grams (0.0264 mole) of 2-bromo-7-nitrodibenzothiophene-5-dioxide was suspended in 175 ml. of absolute ethanol. To this mixture were added 17.0 g. of granular tin and 175 ml. of concentrated hydrochloric acid. The mixture was stirred at reflux temperature for two hours. Complete solution did not occur; however, the suspended precipitate soon changed in coloration from yellow to white. The amine hydrochloride was filtered, suspended in water and decomposed with ammonium hydroxide. There was thus obtained 7.0 g. of yellow solid, melting from 315–320°. A mixed m.p. with starting material was greatly depressed. Two recrystallizations from acetone–methanol gave 5.5 g. (67%) of a yellow solid (Norit A did not lessen the intensity of the yellow coloration), melting at 331–333°, with some decomposition.

Anal. Calcd. for $C_{12}H_8O_2SNBr$: Br, 25.77. Found: Br, 25.47, 25.54.

2-Bromo-8-nitrodibenzothiophene.—Ten grams (0.038 mole) of 2-bromodibenzothiophene was partially dissolved in 100 ml. of glacial acetic acid, and 15 ml. of fuming nitric acid (sp. gr. 1.50) was added dropwise. No noticeable change occurred; the reaction mixture was warmed to 50°, and the suspended solid slowly turned yellow. The mixture was stirred at this temperature for 1.5 hours and then filtered directly. There was thus obtained 10.0 g. of solid melting from 160–200°. Recrystallization from glacial acetic acid raised the m.p. range to 170–207°. The product was digested for two hours with refluxing ethanol and then again recrystallized from glacial acetic acid; the m.p. range was 233–242°. Two additional recrystallizations from this solvent gave 3.0 g. (25.5%) of pale yellow needles, melting at 254–256°.

2-Bromo-8-aminodibenzothiophene.—To a suspension of 2.5 g. (0.0081 mole) of 2-bromo-8-nitrodibenzothiophene in 50 ml. of absolute ethanol was added about 0.5 g. of Raney nickel catalyst. The initial reaction pressure was 40 lb./sq. in. After shaking overnight, 4 lb./sq. in. had been absorbed. The solution was filtered free from catalyst and diluted with water to give 2.0 g. of a light violet solid melting from 100–130°. Three recrystallizations from ethanol gave 1.0 g. (45%) of solid, melting at 149–150°.

3-Bromodibenzothiophene. (A) From **3-Aminodibenzothiophene.**—The previously published procedure[5] was followed, with one exception. The method called for a thorough extraction of the reaction product with ether; however, the residue was found to be quite soluble in this solvent. The ether was evaporated and the residual material dissolved in hot ethanol; filtration and dilution of the cooled filtrate with water gave light brown platelets, melting from 82–91°. Two recrystallizations from ethanol gave a 39% yield of product, melting from 93–96°.

(B) From **3-Bromodibenzothiophene-5-dioxide.**—3-Bromodibenzothiophene-5-dioxide (0.5 g., 0.0017 mole) and 0.2 g. (0.005 mole) of lithium aluminum hydride were placed in a 250-ml., three-necked flask, and 100 ml. of anhydrous ether was added. The reaction mixture was refluxed for 1.5 hours, with stirring. The cooled mixture was then hydrolyzed by the dropwise addition of water. Dilute hydrochloric acid was added to dissolve the resulting precipitate; the layers were separated and the aqueous layer was extracted twice with ether. The combined ether solutions were evaporated, leaving a light yellow gum. The residue was extracted with hot ethanol; dilution of the ethanolic extract with water gave a white solid melting from 40–63°. Three recrystallizations from absolute ethanol gave 0.2 g. (44.5%) of white needles melting at 98–99°. A mixed m.p. with the 3-bromodibenzothiophene prepared from 3-aminodibenzothiophene showed no depression.

The reduction of dibenzothiophene-5-dioxide with lithium aluminum hydride has been reported.[7] The 3-bromodiben-

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(3) F. Muth and B. Putzer, PBL 63936. (Enlargement Print of Frames 1004-10.0 of FIAT microfilm Reel C 60, PB 17657.) March 1933. 7 pp. *Photo Ger.*, **5**, 568a, No. 7 (May 16, 1947).

(4) C. Courtot, L. Nicolas and T. H. Liang, *Compt. rend.*, **186**, 1624 (1928).

(5) G. Illuminati, J. F. Nobis and H. Gilman, THIS JOURNAL, **73**, 5887 (1951).

(6) All melting points are uncorrected.

(7) F. G. Bordwell and W. H. McKellin, THIS JOURNAL, **73**, 2251 (1951).

zothiophene-5-dioxide sample was prepared by H. A. Pacevitz.[8]

(8) H. Gilman, A. L. Jacoby and H. A. Pacevitz, *J. Org. Chem.*, **3**, 120 (1938).

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA

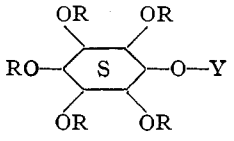
Pentamethyl and Triacetyl Derivatives of *myo*-Inositol[1]

BY G. E. MCCASLAND AND STEPHEN BOUTSICARIS

RECEIVED FEBRUARY 5, 1953

To facilitate another investigation which is still in progress we have prepared the partially alkylated or acylated inositols described below.

In 1947 McGowan[2] reported the preparation of the first pentamethyl ether of *myo*-inositol (I, R = CH_3, Y = H). His product was a sirup but did



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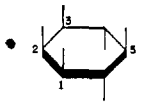

II

yield a crystalline monoacetate of m.p. 101°. By saponification of this monoacetate we have now obtained the pentamethyl ether itself in crystalline form, m.p. 51°. We have further characterized the ether by converting it to its monobenzoate, m.p. 133°.

Such a pentaalkyl ether (or its monoester) can have only a single structure I, but twenty diastereomers are possible. However, the configuration II of the starting material here used limits the possible diastereomers to four, since no inversions of configuration would be expected.

In 1915 Griffin and Nelson[3] reported a procedure for conversion of *myo*-inositol to acetylated mono- and dimethyl ethers. While repeating this procedure we isolated a previously unreported by-product of m.p. 71°. This compound is apparently the first crystalline triacetate[4] of *myo*-inositol, as indicated by its analysis, and its transformation into the known hexaacetate on further acetylation.

Three structures are possible for an inositol triacetate, and ten diastereometric configurations are probable when the starting material II is used.

Each product here reported appears to consist of a single pure isomer, but the configurations (and structure for the triacetate) remain undetermined.

Experimental

M.p.'s (corrected) were taken on Köfler micro-block; microanalyses by Mr. R. S. Pyke.

***myo*-Inositol Pentamethyl Ether Monoacetate of M.P. 101°.**—Fifty grams of anhydrous *myo*-inositol when methylated by the procedure of West and Holden,[5] as modified by McGowan,[2] gave 10 g. of crude pentamethyl ether (colorless sirup, b.p. 123–145° (150 μ)), which on acetylation as described[2] gave 7.0 g. (22%) of the pentamethyl monoacetate, m.p. 100–101° (reported[2] 101°).

***myo*-Inositol Pentamethyl Ether of M.P. 51°.**—A solution of the pentamethyl ether monoacetate (7.0 g.) in 140 ml. of 1 *N* sodium hydroxide was kept at 25° for one hour, then neutralized with 12 *M* hydrochloric acid. The solution was saturated with potassium carbonate and extracted repeatedly with chloroform. The dried extract on evaporation left 6.0 g. of brown sirupy residue, which on vacuum-distillation gave 3.0 g. of a colorless viscous sirup, b.p. 127° (150 μ). The sirup solidified on standing overnight at 5°. The solid product was recrystallized twice from ligroin (b.p. 80–100°) giving 2.5 g. (42%) of ***myo*-inositol pentamethyl ether**, colorless crystals, m.p. 50–51°. The crystals are soluble in water, alcohol, or benzene.

Anal. Calcd. for $C_{11}H_{22}O_6$: C, 52.78; H, 8.86. Found: C, 52.38; H, 8.49.

On reacetylation of the crystalline pentamethyl ether, the monoacetate of m.p. 101° was again obtained.

***myo*-Inositol Pentamethyl Ether Monobenzoate of M.P. 133°.**—To the pentamethyl ether (0.60 g.) in 3.0 ml. of dry pyridine was added with stirring 0.50 ml. of benzoyl chloride. After five minutes the crystals which had separated were collected, washed with water, with 0.5 *M* sodium carbonate, and again with water, and dried. By recrystallization from ligroin, 0.65 g. (76%) of ***myo*-inositol pentamethyl ether monobenzoate**, colorless crystals, m.p. 132–133°, were obtained. The crystals are soluble in alcohol or benzene.

Anal. Calcd. for $C_{18}H_{26}O_7$: C, 61.00; H, 7.40. Found: C, 60.99; H, 7.31.

***myo*-Inositol Triacetate of M.P. 71°.**—*myo*-Inositol (20 g.) was treated by the methylation and acetylation procedure[3] of Griffin and Nelson. The filtered ethereal mother liquors, from which the acetylated mono- and dimethyl ethers had already crystallized, on long standing formed a third crop of crystals. This third crop was recrystallized from ethanol, giving 0.30 g. (0.8%) of colorless crystals, m.p. 70–71°. The crystals are soluble in chloroform but not in water. Analysis indicates that the new compound is a triacetate of (unmethylated) *myo*-inositol.

Anal. Calcd. for $C_{12}H_{18}O_9$: C, 47.06; H, 5.92. Found: C, 47.49; H, 5.89.

The triacetate (0.27 g.) on further acetylation with 5 ml. of hot acetic anhydride containing 0.1 g. of zinc chloride gave the expected *myo*-inositol hexaacetate (0.30 g., 79%) of m.p. 212–213° (reported[6] 211–212°).

Although the use of methylating agents in the procedure may seem superfluous, no more direct method for preparing this triacetate has yet been found.

(6) L. Maquenne, *Ann. Chim.*, [6] **12**, 100 (1887).

CHEMISTRY DEPARTMENT
UNIVERSITY OF TORONTO
TORONTO, CANADA

Antimony(III) Fluoride–Dioxane Addition Compound[1]

BY H. M. HAENDLER, R. H. GLAZIER AND D. W. BRECK

RECEIVED APRIL 8, 1953

Antimony(III) fluoride, which is reported to occur as a molecular crystal,[2] does not show the tendency to form addition compounds with many organic compounds that is so characteristic of the other halides of antimony(III). Solubility measurements in various organic solvents,[3] such as benzene or chlorobenzene, gave no indication of reaction. There was, however, some evidence of reac-

(1) Aided by a grant from the Research Council of Ontario.

(2) J. C. McGowan, *J. Soc. Chem. Ind.*, **66**, 446 (1947).

(3) E. Griffin and G. Nelson, THIS JOURNAL, **37**, 1566 (1915).

(4) The only previously reported triacetate of *myo*-inositol was an amorphous, gummy, hygroscopic substance of unstated m.p. and uncertain purity. See H. Müller, *J. Chem. Soc.*, **101**, 1781 (1912).

(5) E. S. West and R. F. Holden, *Org. Syntheses*, **20**, 97 (1940).

(1) This research was supported by the Research Corporation and is taken in part from the M.S. thesis of R. H. Glazier.

(2) A. Byström and A. Westgren, *Arkiv. Kemi, Mineral Geol.*, **17B**, No. 2, 1 (1943); R. W. G. Wyckoff, "Crystal Structures," Interscience Publishers, Inc., New York, N. Y., 1951, Chap. V, table p. 17b.

(3) D. W. Breck, J. L. Harvey and H. M. Haendler, *J. Phys. Colloid Chem.*, **53**, 906 (1949).