no trace of excess C^{13} was found in the carboxyl group of the phenylacetic acid.

DEPARTMENT OF BIOCHEMISTRY
COLLEGE OF PHYSICIANS AND SURGEONS
COLUMBIA UNIVERSITY
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Thio-Michler Ketone and bis-(Dimethylaminopyridyl)-thioketone[1]

BY D. S. TARBELL AND V. P. WYSTRACH[2]

It became necessary to prepare considerable amounts of thio-Michler ketone (bis-(4-dimethylaminophenyl)-thioketone) and related compounds, having an electron-donating group in the para position to the thioketone function. The method described below, which is a modification of Graebe's synthesis,[3] was found to be by far the most convenient procedure of several that were tried for thio-Michler ketone.

The action of sulfur at 190° on bis-(2-dimethylamino-5-pyridyl)-methane has been reported[4] to yield the corresponding thioketone, bis-(2-dimethylamino-5-pyridyl)-thioketone, melting at 196° with decomposition. He obtained by the same procedure a compound melting at 166–168° without decomposition, and, since only a sulfur analysis had been reported by Tchitschibabin,[4] we had our sample analyzed for carbon and hydrogen. The result agreed with the thioketone structure for the compound; apparently the thioketone is either dimorphic or the previously[4] reported melting point is in error.[5]

Experimental

Thio-Michler Ketone.—One hundred grams (0.33 mole) of auramine (4,4′-dimethylaminobenzophenone imide hydrochloride) was dissolved in 850 cc. of alcohol on the steam-bath. The solution was cooled to room temperature, and a fairly rapid stream of ammonia gas was bubbled in until the crystals of auramine had gone into solution (ten to fifteen minutes). Hydrogen sulfide gas was bubbled in for fifteen minutes at room temperature and then for thirty minutes at the boiling point of the solution. The thioketone began to crystallize out at this point. The reaction mixture was cooled in an ice-bath, and the deep red-violet crystals collected and washed with two 150-cc. portions of methanol. The rather crude product usually amounted to 61.0–62.3 g. and melted at 193–200°.

The crude material was placed in a large Soxhlet extractor and extracted with 500 cc. of chloroform. After the extraction was complete, about half of the solvent was allowed to distill up into the extractor and the process was interrupted at this point. This procedure left the proper amount of solvent in the flask for recrystallization. Methanol (500 cc.) was then added slowly to the chloroform solution of the thioketone, and the mixture boiled for a few minutes. After standing overnight in the ice box, the deep purple crystals were collected by filtration and washed with two 150-cc. portions of cold methanol. The yield by this procedure was 41.5–44.1 g. (56–59%), m. p. 202–204°.

***bis*-(2-Dimethylamino-5-pyridyl)-thioketone.**—This product was prepared in very poor yield from the corresponding dipyridylmethane and sulfur,[4] and melted at 166–168°.

Anal.[6] Calcd. for $C_{15}H_{18}N_4S$: C, 62.91; H, 6.33. Found: C, 62.89; H, 6.31.

(1) The work done in this note was carried out under a contract, recommended by the National Defense Research Committee, between the Office of Scientific Research and Development and the University of Rochester. The National Defense Research Committee assumes no responsibility for the accuracy of statements contained in this note.

(2) Present address: American Cyanamid Company, Stamford, Connecticut.

(3) Graebe, *Ber.*, **20**, 3267 (1887); other procedures are given by Wallach, *Ann.*, **259**, 303 (1890); Fehrmann, *Ber.*, **20**, 2857 (1887); Baither, *ibid.*, **20**, 3289 (1887); Reddelien and Danilof, *ibid.*, **54**, 3132 (1921).

(4) Tchitschibabin and Knunjanz, *ibid.*, **62**, 3048 (1929).

(5) In a paper published after our work was complete, Kahn and Petrow, *J. Chem. Soc.*, 858 (1945), reported an improved method for the preparation of bis-(2-dimethylamino-5-pyridyl)-thioketone, using the dipyridylmethane and sulfur in pseudocumene solution. They did not give the melting point of the product.

(6) Analysis by Dr. Carl Tiedcke.

DEPARTMENT OF CHEMISTRY
THE UNIVERSITY OF ROCHESTER
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Acetylation of D-Mannose Phenylhydrazone

BY M. L. WOLFROM AND MARY GRACE BLAIR[1]

Crystalline pentaacetates of D-glucose phenylhydrazone[2] and D-galactose phenylhydrazone[3,4] are known; tetraacetates of D-glucose phenylosazone[5,6,7] and D-galactose phenylosazone[7] have been synthesized; and the pentaacetates of the enantiomorphous and racemic forms of galaheptose phenylosazone[8] have been reported. On extending the mild acetylation conditions employed by Wolfrom, Konigsberg, Soltzberg and Georges[7] to D-mannose phenylhydrazone, a crystalline product was obtained that was characterized by analysis as the O-tetraacetate of an anhydride of a hexose phenylhydrazone. It is thus established that the phenylhydrazone of D-mannose undergoes anhydride formation with great ease. Such a reaction has hitherto been obtained with sugar osazones and then only by acetylation followed by alkaline deacetylation[9] or by acid treatment.[10] Percival[11] has presented evidence against the pyrazoline structure suggested for these substances by Diels and co-workers.[12] While no definitive structure for the presently described product may be established on the evidence now available, the apparent presence of four O-acetyl groups would favor a pyrazoline structure (I).

(1) Sugar Research Foundation Fellow of The Ohio State University Research Foundation (Project 190).

(2) A. Hofmann, *Ann.*, **366**, 277 (1909).

(3) M. L. Wolfrom and C. C. Christman, THIS JOURNAL, **53**, 3413 (1931).

(4) J. Compton and M. L. Wolfrom, *ibid.*, **56**, 1157 (1934).

(5) L. L. Engel, *ibid.*, **57**, 2419 (1935).

(6) K. Maurer and B. Schiedt, *Ber.*, **68B**, 2187 (1935).

(7) M. L. Wolfrom, M. Konigsberg, S. Soltzberg (and L. W. Georges), THIS JOURNAL, **58**, 490 (1936).

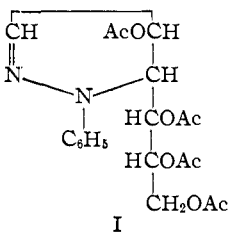
(8) R. M. Hann and C. S. Hudson, *ibid.*, **61**, 336 (1939).

(9) E. G. V. Percival, *J. Chem. Soc.*, 1770 (1936); E. E. Percival and E. G. V. Percival, *ibid.*, 1320 (1937).

(10) E. Fischer, *Ber.*, **20**, 821 (1887); O. Diels and R. Meyer, *Ann.*, **519**, 157 (1935).

(11) E. G. V. Percival, *J. Chem. Soc.*, 783 (1945).

(12) O. Diels, R. Meyer and O. Onnen, *Ann.*, **525**, 94 (1936).



I

Experimental

To a suspension of 10 g. of D-mannose phenylhydrazone in 175 cc. of dry pyridine was added slowly 65 cc. of acetic anhydride and the resultant mixture was kept at room temperature for two days, whereupon it was poured with stirring into 7 volumes of ice and water. The resultant precipitated sirup was washed several times with water by decantation and crystallized from ethanol by the addition of water; yield 14.3 g. (92%) of crude product, 9.0 g. (58%) after one recrystallization from absolute ethanol, m. p. 123° (no dec.) unchanged on further crystallization from absolute ethanol or from acetone–water, $[\alpha]^{26}D$ + 12° (*c* 4, pyridine).

Anal. Calcd. for $C_{12}H_{12}O_4N_2(COCH_3)_4$: C, 57.13; H, 5.75; N, 6.67; CH_3CO, 9.5 cc. 0.1 *N* NaOH per 100 mg. Found: C, 57.32; H, 5.86; N, 6.77; O-acetyl as CH_3CO, 9.6 cc. (method of Kunz and Hudson[13]), 9.6 cc. (method of Freudenberg and Harder[13]).

(13) A. Kunz and C. S. Hudson, THIS JOURNAL, **48**, 1982 (1926); K. Freudenberg and M. Harder, *Ann.*, **433**, 230 (1923); *cf.* ref. 7.

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5-Hydroxypentanal and Some of its Reactions

BY G. FORREST WOODS AND HERMAN SANDERS

R. Paul[1] has reported the preparation of 5-hydroxypentanal in 35–39% yield by the hydrolysis of 2,3-dihydropyrane in a dilute acid medium, and the preparation of pentamethylene glycol, in 50% yield starting from dihydropyrane, by the reduction of 5-hydroxypentanal with aluminum amalgam.

In exploring the chemistry of pyrane compounds we have repeated this work and found that, with changes and modifications of procedures, 2,3-dihydropyrane is an excellent starting material for the preparation of both 5-hydroxypentanal and pentamethylene glycol of excellent quality and in high yields.

5-Aminopentanol-1 has been obtained by several different procedures.[2,3,4,5] However, reductive amination of 5-hydroxypentanal is a more convenient and satisfactory method of preparing this otherwise difficultly obtainable compound. The product obtained from this procedure was contaminated with small amounts of pentamethylene glycol. It was found that purification was readily accomplished by the formation of the bisulfate salt. This substance has the advantage of being a stable, white crystalline solid with a sharp melting point, and capable of recrystallization from alcohol–ether. This salt can be titrated for one or two hydrogen ions upon choice of appropriate indicators and conditions.

5-Aminopentanol-1 bisulfate was refluxed with aqueous hydrogen bromide, the reaction mixture made alkaline, and subjected to steam distillation, whereupon piperidine was obtained in good yield.

(1) R. Paul, *Bull. Soc. Chim.*, [5] **1**, 971 (1934).
(2) v. Braun and Sobecki, *Ber.*, **44**, 2531 (1911).
(3) Putochin, *ibid.*, **59**, 630 (1926).
(4) Williams, *ibid.*, **60**, 2511 (1927).
(5) Keimatsu and Takamota, *J. Pharm. Soc. Japan*, 506 (1927).

Experimental

5-Hydroxypentanal.—A mixture of 300 ml. of water, 25 ml. of concentrated hydrochloric acid, and 100 g. of 2,3-dihydropyrane[6] was stirred vigorously until the mixture became homogeneous and then for an additional twenty minutes. The solution was neutralized with 20% sodium hydroxide using phenolphthalein as the indicator. The solution was extracted with ether for twelve hours using a continuous extraction apparatus. After removal of ether under reduced pressure the residue was distilled. There was obtained 95 g. (79%) of 5-hydroxypentanal, b. p. 62–66° (6–8 mm.), $n^{18}D$ 1.4534.

2,4-Dinitrophenylhydrazone of 5-Hydroxypentanal.—The yellow product melted at 109°. *Anal.*[7] Calcd. for $C_{11}H_{14}O_5N_4$: C, 46.81; H, 5.00. Found: C, 46.66; H, 4.67.

Pentamethylene Glycol.—Catalytic reduction of 63 g. of 5-hydroxypentanal with Raney nickel at 3000 p. s. i. g. at 90° required approximately one hour. Pentamethylene glycol, after removal of the catalyst, was distilled, b. p. 103–105° (3–4 mm.), $n^{20}D$ 1.4498, yield 61 g. (96%) (identified as the diphenylurethan, mixed m. p. 173–174°).

5-Aminopentanol-1.—Reductive amination of 80 g. of 5-hydroxypentanal with Raney nickel, 100 g. of liquid ammonia, and hydrogen at 3000 p. s. i. g. at 90° required approximately five hours. After removal of the catalyst, the product distilled at 85–95° (1–2 mm.); yield 70 g. (87%). This product had a neutral equivalent of 118 which corresponded to an 87% purity.

To a solution of 50 g. of crude 5-aminopentanol-1 in 200 ml. of anhydrous alcohol was added 50 g. of sulfuric acid in 200 ml. of anhydrous alcohol; the solution was cooled during the addition of the acid. After addition of 200 ml. of anhydrous ether and thorough chilling, the white crystalline product was filtered and washed with ether. Recrystallization of the crude 5-aminopentanol-1 bisulfate from alcohol–ether yielded white crystals stable in air, m. p. 102–103°; yield 85 g. (99%) based on the 5-aminopentanol-1 present in the crude product as indicated by its neutral equivalent. The neutral equivalent of the first hydrogen ion of 5-aminopentanol-1 bisulfate was determined by titration with sodium hydroxide using methyl red as the indicator. The second hydrogen ion titration was made in the presence of formaldehyde with phenolphthalein as the indicator. *Anal.* Neut. equiv. calcd. for $C_5H_{13}ON.H_2SO_4$: 201; 100.5. Found: 203, 203; 103, 101.

A concentrated aqueous solution of 28 g. of 5-aminopentanol-1 bisulfate and excess sodium hydroxide was subjected to continuous extraction with ether. After removal of the solvent under reduced pressure, the residue was distilled; yield 11 g. (77%) of pure 5-aminopentanol-1, b. p. 79–81° (1 mm.); m. p. 38–39°. This value is considerably higher than that (27–28°) recorded in the literature.[3] *Anal.* Calcd. for $C_5H_{13}ON$: C, 58.25; H, 12.70, neut. equiv., 103. Found: C, 58.48; H, 12.98, neut. equiv., 103, 103.

Conversion of 5-Aminopentanol-1 Bisulfate to Piperidine.—5-Aminopentanol-1 bisulfate (50 g.) was refluxed with a 75% excess of 48% aqueous hydrogen bromide for three hours. This solution was neutralized with 20% sodium hydroxide and an additional 20 g. of sodium hydroxide was added. The solution was subjected to steam

(6) "Organic Syntheses," **23**, 25 (1943).
(7) Microanalyses by Miss Eleanor Werble.