fully used for the purification of hesperidin obtained from citrus fruit:

A 10% solution of hesperidin in formamide prepared by warming to about 60° is treated for thirty minutes with activated charcoal previously boiled with dilute hydrochloric acid. The formamide when tested in a 50% aqueous solution should be slightly acid. If it is not, a little glacial acetic acid or formic acid should be added. The solution is then filtered through diatomaceous earth, diluted with an equal volume of water and allowed to stand a few hours for crystallization of the precipitated hesperidin. The crystals are then filtered off, washed with hot water and then with isopropanol. Two such crystallizations give a white crystalline product melting at 261–263° with some decomposition which compares favorably with the highest melting point previously recorded,[6] namely, 261–262°.

A test devised by C. W. Wilson and Laverra Hill (as yet unpublished) based on the color reaction of boric acid with flavone derivatives[7] gives only very slightly positive results with hesperidin thus purified. Its color density, by this test, as determined with a Beckman spectrophotometer was only 0.008 at 402 millimicrons as compared with a color density of 0.088 and 0.072 for samples purified by means of methanol and pyridine, respectively. Crude hesperidin gives a color density of 0.8 or more at this same wave length.

The formamide may be recovered by fractional distillation under vacuum, although slight decomposition into ammonia and carbon monoxide occurs during this step. According to literature[8] formamide may be stabilized by the addition of small amounts (0.001–1.0%) of a purine ring compound such as caffeine, xanthine, theobromine, uric acid, guanine, etc. However, formamide recovered without a stabilizer has been found to be still acceptable as a solvent for hesperidin.

(6) Kwang Fong Tseng and Ren Dzin Yu, J. Chinese Pharm. Assoc., I, 14–23 (English) (1936).

(7) Clarence W. Wilson, Leroy S. Weatherby and William Z. Bock, Ind. Eng. Chem., 14, 425 (1942).

(8) Edward C. Kirkpatrick (to E. I. du Pont de Nemours and Co.), U. S. Patent 2,346,425, April 11, 1944; C. A., 38, 4962 (1944).

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## Retention of the Carbon Skeleton in the Kindler–Willgerodt Reaction

BY EDGAR M. SHANTZ[1] AND D. RITTENBERG

It was assumed by Willgerodt[2] that the course of the reaction bearing his name involved no rearrangement of the alkyl chain when aralkyl ketones were converted to carboxylic acids or amides by heating with ammonium polysulfide, and it seems reasonable to assume that the Kindler[3] modification, employing anhydrous amines in place of ammonia, follows the same mechanism. However, substantial proof of this has been lack-

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(2) Willgerodt, Ber., 20, 2467 (1887); 21, 534 (1888).

(3) Kindler, Ann., 431, 187 (1923).

ing until the appearance of recent papers by Cavalieri, et al.,[4] and King and McMillan.[5,6] At the time of the appearance of this latter paper, which demonstrates by the use of branched chain ketones that the carbon skeleton is unchanged, we had just completed an experiment which offers further direct evidence of non-rearrangement of the carbon chain during the course of the reaction.

Acetophenone containing $C^{13}$ in the carbonyl group was transformed to phenylacetic acid by a modified Willgerodt reaction. The carbon dioxide obtained upon decarboxylation of this phenylacetic acid was analyzed and no excess of $C^{13}$ over normal could be detected. Subsequent oxidation of the residual dibenzyl ketone from the above experiment gave benzoic acid which was found to contain the isotopic carbon in the carboxyl group. It is thus evident that the carbon atom originally attached to the benzene ring in the acetophenone has remained there throughout the above series of reactions.

### Experimental

Barium carbonate (4.8 g.) containing an 0.34% excess of $C^{13}$ was acidified and the carbon dioxide evolved was passed into an ethereal solution of methyl magnesium iodide at $-30°$. After acidification the resulting acetic acid was distilled with water and isolated from the distillate as the silver salt (yield, 3.7 g.). This was converted to sodium acetate, which was dried and heated with 4.25 g. of p-toluenesulfonyl chloride. The resulting acetic anhydride (0.95 ml.) was refluxed for half an hour with 15 ml. of dry benzene and 6 g. of anhydrous aluminum chloride, yielding 1.14 g. of crude acetophenone.

A modified Willgerodt reaction was performed according to Schwenk and Bloch[7] by refluxing the acetophenone for three hours with 0.84 g. of morpholine and 0.30 g. of sulfur. The thiomorpholide thus obtained was refluxed for eight hours with 10 ml. of 10% aqueous potassium hydroxide, yielding 0.62 g. of crude phenylacetic acid. Distillation at 15 mm. pressure gave 0.40 g. of a pale yellow solid which was recrystallized twice from 5-ml. portions of hot water. The product was dried, yielding 167 mg. of phenylacetic acid melting at 74–75°.

The phenylacetic acid was mixed thoroughly with 2 g. of 40-mesh iron filings and decarboxylated by heating to 250°. The carbon dioxide evolved was examined in a mass spectrometer. No excess $C^{13}$ over normal could be detected, showing definitely that no rearrangement had occurred.

The residue from the decarboxylation of the phenylacetic acid (probably mostly dibenzyl ketone) was oxidized to benzoic acid by refluxing for twelve hours with 6 N sulfuric acid containing 20% sodium dichromate. The benzoic acid obtained was converted to the silver salt and this was decarboxylated by heating. The carbon dioxide evolved, when examined in the mass spectrometer, was found to contain 0.27% excess isotopic carbon. The 20% lowering of the excess isotopic carbon content found here is far outside the limits of error of the mass spectrometer and most be attributed mainly to introduction of extraneous carbon dioxide during the various reactions and is partly due to the use of normal phenylacetic and benzoic acids used for seeding in the crystallization steps. However, this in no way invalidates the results, since absolutely

(4) Cavalieri, Pattison and Carmack, THIS JOURNAL, 67, 1783 (1945).

(5) King and McMillan, ibid., 68, 525 (1946).

(6) King and McMillan, ibid., 68, 632 (1946).

(7) Schwenk and Bloch, ibid., 64, 3051 (1942).

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

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## Thio-Michler Ketone and bis-(Dimethylamino-pyridyl)-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.

(6) Analysis by Dr. Carl Tiedcke.

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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) 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.

(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).