availability of the sulfur atom's two lone electron pairs for resonance stabilization of the aromatic system.

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Derivatives of 5-Amino-4-methylpyrimidine

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We have been interested in synthetic routes which lead to aminopyrimidines easily converted to aminovinylpyrimidines.[3] A number of workers,[4-6] particularly in the last few years, have reported the synthesisis of 5-amino-4-methylpyrimidine (I) and we wish to report some new experimental procedures for the synthesis of this compound and several new derivatives.

2,4-Dichloro-6-methyl-5-nitropyrimidine was reduced with excess Raney nickel to give 5-amino-2,4-dichloro-6-methylpyrimidine (II) in 66% yield. Reaction of II with hydrogen with palladium-on-charcoal catalyst and magnesium oxide gave I in 31% yield and 5-amino-2-chloro-4-methylpyrimidine in 34.7% yield. The latter compound was easily dechlorinated to give I in 78% yield with the above catalyst.

We investigated a second route for the preparation of I, namely, the chlorination of 5-amino-6-methyluracil to give II; however, this method is inferior due to low yields and formation of a by-product, an aminochloro-N-methylanilinomethylpyrimidine, since dimethylaniline is used along with phosphorus oxychloride in the reaction.

Reductive alkylation[7] of I with a large excess of freshly distilled acetaldehyde with palladium on charcoal gave a 78% yield of 5-N-ethylamino-4-methylpyrimidine; with Raney nickel the reaction was unsuccessful.

An attempt was made to prepare 5-bromo-4-methylpyrimidine by the catalytic dechlorination of 5-bromo-2,4-dichloro-6-methylpyrimidine. 5-Bromo-6-methyluracil was chlorinated with phosphorus oxychloride in 84.8% yield. The compound was catalytically reduced with palladium-on-charcoal and magnesium oxide until two moles of hydrogen was absorbed. However, only a 42.8% yield of 4-methylpyrimidine was isolated from the reaction mixture. Very recently Whittaker[8] attempted to prepare 5-bromopyrimidine through the same synthetic route with the reaction following a similar course as that described for the methyl derivative above.

(1) Public Health Research Fellow, 1951–1953.

(2) This note comprises portions of theses presented by Irving C. Kogon in partial fulfillment of the requirements for the Degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn and by W. J. Einstman in partial fulfillment of the requirements for the degree of Master of Science in the Graduate School of the Polytechnic Institute of Brooklyn.

(3) (a) C. G. Overberger and I. C. Kogon, THIS JOURNAL, **76**, 1065 (1954); (b) **76**, 1879 (1954).

(4) J. R. Marshall and J. Walker, *J. Chem. Soc.*, 1004 (1951).

(5) K. Yanai, *J. Pharm. Soc. Japan*, **62**, 315 (1951); *C. A.*, **45**, 5150 (1951).

(6) S. Gabriel and J. Colman, *Ber.*, **34**, 1234 (1901).

(7) W. S. Emerson, "Organic Reactions," Edited by R. Adams, Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, Chap. 3, p. 174.

(8) N. Whittaker, *J. Chem. Soc.*, 1646 (1953).

Experimental[9]

5-Amino-2,4-dichloro-6-methylpyrimidine.—2,4-Dichloro-6-methyl-5-nitropyrimidine was prepared by the chlorination of 6-methyl-5-nitrouracil following the procedure of Marshall and Walker.[4] The nitro group was then reduced as follows: a mixture of 10.3 g. (0.05 mole) of 2,4-dichloro-6-methyl-5-nitropyrimidine, 35 ml. of absolute alcohol and $^1/_2$ teaspoon of Raney nickel catalyst was hydrogenated for three hours until the theoretical amount of hydrogen was absorbed. The catalyst was removed by filtration and washed with ethanol. After the removal of the solvent a purple residue remained which was sublimed at 110° (3 mm.) to give 5.9 g. (66%), m.p. 108–110°, of a light yellow crystalline material. Two sublimations raised the melting point to 113–114°, (m.p. 115–116.5° prepared by reduction of the nitro compound with palladium-on-charcoal in ether).[5]

Preparation of this compound from 5-amino-6-methyluracil and phosphorus oxychloride gave low yields of 5-amino-2,4-dichloro-6-methylpyrimidine under a wide variety of experimental conditions with and without small additions of dimethylaniline.

5-Amino-4-methylpyrimidine. (A).—When 5-amino-2,4-dichloro-6-methylpyrimidine was hydrogenated over 10% palladium-on-charcoal in the presence of excess magnesium oxide a 31% yield of 5-amino-4-methylpyrimidine was obtained. References 4, 5 and 6 all prepared this compound using different reducing agents. The mother liquor was distilled off on a steam-bath and the crystalline residue was sublimed at 83° (0.01 mm.). A slightly yellowish, crystalline compound, 5-amino-2-chloro-4-methylpyrimidine, (34.7%), m.p. 91–92°, was collected (m.p. 92°, no yield reported),[5] (m.p. 87°, no yield reported),[4] (m.p. 93.5°).[5]

(B).—A mixture of 2.4 g. (0.016 mole) of 5-amino-2-chloro-4-methylpyrimidine, 0.1 g. of 10% palladium-on-charcoal catalyst, 10 ml. of absolute ethanol, 20 ml. of distilled water and 4 g. (0.1 mole) of magnesium oxide was hydrogenated for 1 hour until no more hydrogen was absorbed. The catalyst was removed by filtration and the filtrate extracted continuously with chloroform for 48 hours and the solution dried over anhydrous sodium sulfate. After the removal of the drying agent and solvent, a solid residue remained, 1.8 g. (78%), m.p. 149–150°. A mixed melting point with an authentic sample, m.p. 149–151°, gave no depression, m.p. 149–150°.

5-N-Ethylamino-4-methylpyrimidine.—A mixture of 5.2 g. (0.048 mole) of 5-amino-4-methylpyrimidine, 5.3 g. (0.120 mole) of acetaldehyde, 1 g. of 10% palladium-on-charcoal and 20 ml. of absolute ethanol was hydrogenated for 5 hours at 50°. After the theoretical quantity of hydrogen was absorbed, the mixture was filtered and the catalyst washed well with ethanol. After the removal of the solvent, the residue was distilled to give a yellow liquid, 5.6 g. (86.1%), b.p. 124–126° (7 mm.). On redistillation a pale yellow liquid, 5.1 g. (78.4%), b.p. 123–125° (7 mm.), was obtained which solidified on standing, m.p. 55–56°.

Anal.[10] Calcd. for $C_7H_{11}N_3$: C, 61.21; H, 8.09; N, 30.63. Found: C, 60.95; H, 8.32; N, 30.43.

The picrate was prepared by adding excess ethereal picric acid to an ethereal solution of the free base. The yellow crystalline precipitate was recrystallized from ethanol and had a m.p. 138–139°.

Anal. Calcd. for $C_{13}H_{14}N_6O_7$: N, 22.9. Found: N, 22.8.

5-Bromo-2,4-dichloro-6-methylpyrimidine.—5-Bromo-6-methyluracil was prepared by the procedure described by Behrend[11] (97.6%), m.p. 238° with dec. (90%, m.p. 230°, with slow dec.).[11] A mixture of 14 g. (0.0683 mole) of 5-bromo-6-methyluracil and 31.8 g. (0.2 mole) of phosphorus oxychloride (b.p. 105–107°) was refluxed for 3 hours. After cooling, the dark brown mixture was carefully poured with rapid stirring into 300 g. of an ice–water mixture. A green crystalline precipitate appeared which was removed by filtration and air dried for several hours. The compound was

(9) All melting points are corrected.

(10) Analyses by Drs. Weiler and Strauss, Oxford, England; Dr. K. Ritter, Zurich, Switzerland, Dr. F. Schwarzkopf, Long Island City, N. Y.

(11) R. Behrend, *Ann.*, **229**, 17 (1885).

then sublimed at 40° (0.1 mm.) and 14.0 g. (84.8%) of product collected, m.p. 41–42°.

Anal. Calcd. for $C_5H_3BrCl_2N_2$: total halogen, 62.3; N, 11.6. Found: total halogen, 62.0; N, 11.5.

Dehalogenation of 5-Bromo-2,4-dichloro-6-methylpyrimidine.—A mixture of 12.05 g. (0.05 mole) of 5-bromo-2,4-dichloro-6-methylpyrimidine, 4.0 g. (0.1 mole) of magnesium oxide, 0.1 g. of 10% palladium-on-charcoal, 50 ml. of ethanol and 100 ml. of water was hydrogenated for 48 hours until the theoretical amount of hydrogen was absorbed. The catalyst was removed by filtration and washed with methylene chloride. The filtrate was then extracted continuously with methylene chloride for 5 hours and dried over anhydrous sodium sulfate. After the drying agent and solvent were removed, the residue was distilled to give a colorless liquid, 2.0 g. (42.8%), b.p. 33–34° (11 mm.), $n^{25}D$ 1.4936; (141–142° (atm.) $d^{16}_{15.9}$ 1.031, no yield reported),[12] (b.p. 86° (114 mm.), $n^{29}D$ 1.4916, no yield reported),[4] (b.p. 141–145° (atm.) $n^{25}D$ 1.4940, (30%)).[3b] The picrate was prepared in the usual manner, m.p. 129–130°. A mixed melting point with an authentic sample, *m.p. 131–132.2°, gave no depression, m.p. 129–130°.*

(12) S. Gabriel and J. Coleman, *Ber.*, **32**, 1533 (1899).

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The Stobbe Condensation with Perinaphthanone-7 and 8-Methylperinaphthanone-7[1]

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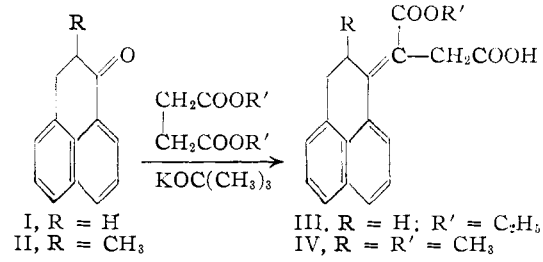
In the course of investigations being carried out in this Laboratory on the synthesis of 3,4-benzpyrenes the Stobbe condensation with perinaphthanone-7 (I) and 8-methylperinaphthanone-7 (II) was investigated. The condensation of diethyl succinate with I was carried out in like manner to the procedure described for tetralone-1 using potassium *t*-butoxide as the condensing agent.[3] From the resulting mixture of half-esters which was obtained in 43% yield, β-carbethoxy-β-(7-perinaphthylidene)-propionic acid (III) was isolated. The structure of III was proved by oxidation of the half-ester with potassium permanganate, perinaphthanone-7 being isolated in 61% yield. The use of larger amounts of potassium *t*-butoxide or sodium hydride[4] as the condensing agent gave only tarry products.

Under the above conditions 8-methylperinaphthanone-7 (II) failed to react, but the modified procedure described for hindered ketones[5] gave a 29% yield of oily half-ester from which a crystalline product, β-carbomethoxy-β-(8-methylperinaphthylidene-7)-propionic acid (IV), was isolated. The double bond in IV was shown to be exocyclic by comparison of the ultraviolet absorption spectra of III and IV.

Attempts to decarbethoxylate the half-ester III with a mixture of hydrobromic and acetic acids[6] or hydrochloric and acetic acids[3] resulted in the formation of intractable tars.



I, R = H
II, R = CH_3

III, R = H; R' = C_2H_5
IV, R = R' = CH_3

Experimental[7]

Perinaphthanone-7 (I).—The preparation of perinaphthanone-7 by the cyclization of 50 g. (0.25 mole) of β-(1-naphthyl)-propionic acid, m.p. 155.5–156°, with 160 ml. of anhydrous hydrogen fluoride was carried out according to the procedure described by Fieser and Gates[8] with some modification. The crude ketone was distilled at reduced pressure, b.p. 136–140° at 0.1 mm., and recrystallized from methanol to give a total of 37.8 g. (83% yield) of pale yellow prisms of comparable purity to that obtained by Fieser and Gates.

β-Carbethoxy-β-(7-perinaphthylidene)-propionic Acid (III).—A solution of 2.00 g. (0.110 mole) of perinaphthanone-7, m.p. 78–80°, in 3.00 g. (0.0172 mole) of diethyl succinate, b.p. 109–112° at 23 mm., was added to a solution of 0.48 g. (0.0123 g.-atom) of potassium in 20 ml. of anhydrous *t*-butyl alcohol with stirring in a nitrogen atmosphere. The solution was stirred at reflux for one hour. The solution was cooled, acidified with 2 ml. of concentrated hydrochloric acid in 50 ml. of water and most of the *t*-butyl alcohol removed at reduced pressure. The product was taken up in ether and the ether solution was extracted several times with a saturated sodium bicarbonate solution. The extracts were washed with ether and acidified giving a dark yellow oil which turned to a tan solid, m.p. 120–155°, 1.45 g. (43% yield). Several recrystallizations from ethyl acetate afforded **β-carbethoxy-β-(7-perinaphthylidene)-propionic acid** as almost colorless prisms, m.p. 172–173°.

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.54; H, 5.85; neut. equiv., 310.3. Found: C, 73.61; H, 5.65; neut. equiv., 311.1.

Oxidation of β-Carbethoxy-β-(7-perinaphthylidene)-propionic Acid (III).—A solution of 1.00 g. of β-carbethoxy-β-(7-perinaphthylidene)-propionic acid and 5 ml. of 1 *N* sodium hydroxide in 100 ml. of water was covered with 30 ml. of benzene. A few drops of 0.66% aqueous potassium permanganate solution was added and when the color had disappeared the solution was chilled in an ice-bath and the rest (150 ml.) of the permanganate was added dropwise over a period of two hours with stirring. The solution was then made acid to congo red and 30 ml. of additional benzene was added. The benzene layer was filtered and extracted with 10% sodium bicarbonate. The benzene solution was separated and dried over anhydrous sodium sulfate. The benzene was evaporated under dry nitrogen to give 0.36 g. of ketone, m.p. 81–82°, 61% yield. A mixed melting point with perinaphthanone-7 showed no depression.

β-Carbomethoxy-β-(8-methylperinaphthylidene-7)-propionic Acid (IV).—A solution of 1.62 g. (0.0414 g.-atom) of potassium in 44 ml. of anhydrous *t*-butyl alcohol was mixed with 6.80 g. (0.0465 mole) of dimethyl succinate, b.p. 92–94° at 20 mm., and 10 ml. of this solution was added to 1.96 g. (0.0100 mole) of 8-methylperinaphthanone-7,[9] b.p. 135–136° at 0.1 mm., under dry nitrogen. This mixture was kept at 50° in an oil-bath while the remaining ester solution was added through a Hershberg addition funnel over a period of three hours while the solution was stirred mechanically. The solution was heated an additional two hours, cooled and acidified with 6 ml. of concentrated hydrochloric acid in 50 ml. of water, and most of the *t*-butyl alcohol was removed under reduced pressure. The product was taken up in ether and extracted with 1 *N* ammonium hydroxide. The ammonia extractions were washed with

(1) This work was supported in part by a grant from the Research Corporation.

(2) Graduate Research Assistant, February, 1951, to February, 1952.

(3) W. S. Johnson, H. C. E. Johnson and J. Petersen, THIS JOURNAL, **67**, 1360 (1945).

(4) G. H. Daub and W. S. Johnson, *ibid.*, **72**, 501 (1950).

(5) W. S. Johnson, V. L. Stromberg and J. Petersen, *ibid.*, **71**, 1385 (1949).

(6) B. Riegel and J. G. Burr, *ibid.*, **70**, 1070 (1948).

(7) All melting points are uncorrected.

(8) L. F. Fieser and M. D. Gates, THIS JOURNAL, **62**, 2335 (1940).

(9) L. F. Fieser and F. C. Novello, *ibid.*, **62**, 1855 (1940).