(American Cyanamid). The reagent dissolved in the amine with the immediate evolution of methyl mercaptan. The reaction mixture was allowed to stand at room temperature for two hours. A mixture of 100 cc. of ethanol and water (1:1) was added to the pasty mass. The precipitate (5.9 g., 80.3% yield) was recovered by filtration. The melting point of 87–90° was raised to 91.5–92.5° by one crystallization from a mixture of ethanol and water (1:1).

1-(*t*-Butyl)-3-nitroguanidine.—*t*-Butylamine (7.3 g., 0.1 mole), 10.8 g. (0.08 mole) of 2-methyl-1(or 3)-nitro-2-thiopseudourea and 25 cc. of absolute ethanol were heated on a water-bath at 45° for six minutes. The contents on standing overnight at room temperature deposited 8.9 g. (70.0%) of white crystals. The melting point of 192–196° was raised to 199–201° by one crystallization from methanol.

INDIAN HEAD, MARYLAND

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INSTITUTE OF POLYMER RESEARCH, POLYTECHNIC INSTITUTE OF BROOKLYN]

Monomer Synthesis. X.[1] The Preparation and Polymerization of 4-Vinylpyrimidine and 2-N,N-Dimethylamino-4-vinylpyrimidine

BY C. G. OVERBERGER AND IRVING C. KOGON[2]

RECEIVED OCTOBER 27, 1953

Convenient syntheses of 4-vinylpyrimidine and 2-N,N-dimethylamino-4-vinylpyrimidine are described. These are the first simple vinylpyrimidines reported in the literature. The general reaction consists of the conversion of the appropriate methylpyrimidine to the β-hydroxyethyl derivative followed by dehydration over solid potassium hydroxide. A number of derivatives of the two vinylpyrimidines are reported. Polymers have been prepared by radical catalysis and characterized. The vinylpyrimidines are inactive against sarcoma 180.

It was of interest to prepare vinylpyrimidines in order to study their polymerization and the properties of their polymers. In particular the effect of a vinyl monomer, which would give a polymer of related structure to a portion of a polynucleic acid, on abnormal cell mitosis was of interest. Many of the most promising compounds tested against sarcoma 180 with the exception of nitrogen mustards contain a pyrimidine or triazine ring. Rather few synthetic polymeric materials have been screened, this being largely due to their insolubility. It is unlikely that a polymer containing carbon–carbon chains would diffuse through the cell wall although polyesters and polyamides would probably be susceptible to enzymatic hydrolysis. It was hoped that the relatively water-soluble vinylpyrimidines would diffuse through the cell wall and polymerize within the cell due to the probable one-electron transfer, oxidation–reduction process within the cell. Association of this polymer with the chromosome would then be realized. Up to now, this type of approach has received no attention. This paper will describe the synthesis of 4-vinylpyrimidine and 2-N,N-dimethylamino-4-vinylpyrimidine and their effect on sarcoma 180. In addition, their polymerization with a radical catalyst is reported.

No simple vinylpyrimidines have previously been recorded. Price and Zomlefer[3] reported the attempted preparation of 4-hydroxy-6-methyl-2-vinylpyrimidine by reaction of β-hydroxyethylacetamidine and acetoacetic ester. When this product was heated in decalin, dehydration occurred but only polymeric material was obtained. Recently several styryl derivatives have been reported.[4] 4-(β-Phenylvinyl)-pyrimidine was prepared from 4-methylpyrimidine and benzaldehyde.[5] Ross found that 6-methyluracil would not condense to give the styryl derivative but that a 5-nitro group activated the methyl group and the styryl derivative was obtained. The *p*-dimethylamino and the *p*-nitro derivatives also have been prepared.[6]

The synthesis shown was used to prepare 2-N,N-dimethylamino-4-vinylpyrimidine.

Compound I also has been reported by Russell, Elion and Hitchings[7] by reaction of 2-ethylmercapto-4-hydroxy-6-methylpyrimidine with an ethanolic solution of dimethylamine in a sealed tube at 130°. Reduction of the chloro compound with palladium-on-charcoal and magnesium oxide was more satisfactory than chemical methods. The Mannich base VI was obtained from II as indicated. This compound is stable in refluxing 20, 40 and 65% aqueous sodium hydroxide, 15% ethanolic sodium hydroxide and 15% potassium *t*-butoxide. Graham, *et al.*,[8] have reported the only known case of formation of a Mannich base on a methylpyrimidine from 4-acetyl-5-methyl-2-phenylpyrimidine. They suggest that reaction occurs on the acetyl methyl group.

The conversion of II to give III and IV was carried out with paraformaldehyde and an excess of methylpyrimidine at 160° for 3.5 hours in a sealed tube. Compound II was always recovered and could be conveniently recycled without further purification. When the reaction tube was heated at 160° for 24 hours, a third product was isolated also, an analysis and molecular weight of which indicated a dimer. Attempts to condense II with IV with sodium ethoxide or by employing the sealed tube conditions of the condensation reaction with formaldehyde were unsuccessful. The picrate of the

(1) This is the tenth in a series of articles concerned with the synthesis of monomers and their polymerization; for the ninth paper in this series, see C. G. Overberger and Irving C. Kogon, THIS JOURNAL, **76**, 1065 (1954).

(2) Public Health Research Fellow 1951–1953. This paper comprises a portion of a thesis presented by Mr. 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.

(3) C. C. Price and J. Zomlefer, *J. Org. Chem.*, **14**, 210 (1949).

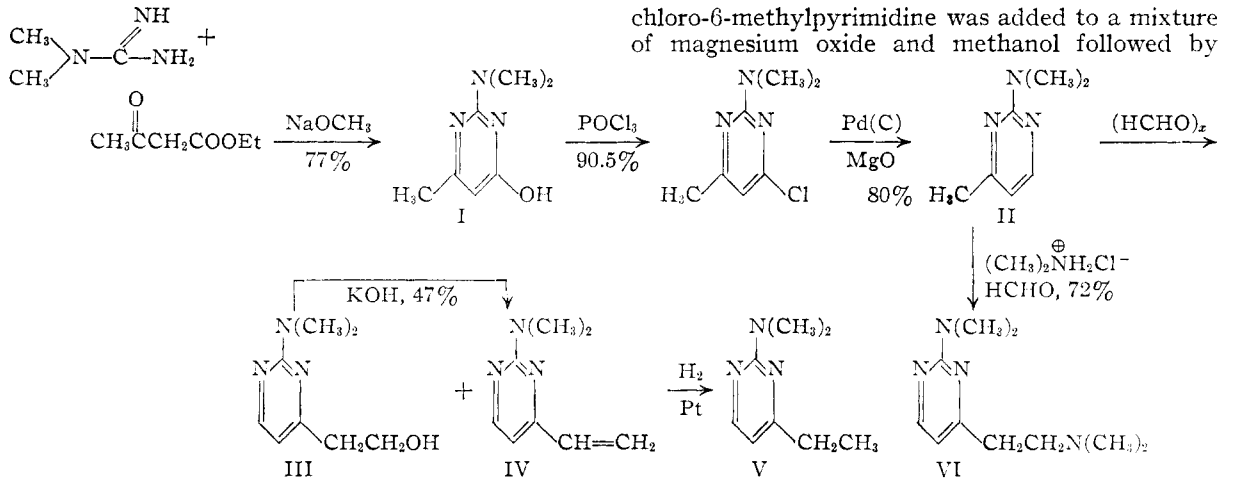
(4) D. M. Brown and G. A. R. Kon, *J. Chem. Soc.*, 2147 (1948).

(5) W. C. J. Ross, *ibid.*, 1128 (1948).

(6) D. M. Brown and W. C. J. Ross, *ibid.*, 1715 (1948).

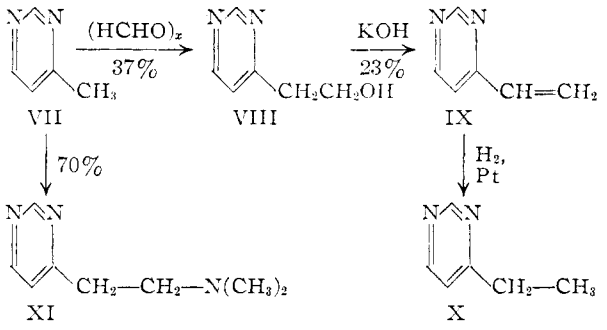
(7) P. B. Russell, G. B. Elion and G. H. Hitchings, THIS JOURNAL, **71**, 474 (1949).

(8) B. Graham, A. M. Griffith, C. S. Pease and B. E. Christensen, *ibid.*, **67**, 1294 (1945).



vinyl compound IV prepared from the potassium hydroxide dehydration was identical with the picrate of IV obtained directly in the condensation reaction. The infrared spectrum for the vinyl compound indicated ethylene peaks at 6.1 and 10.6 μ. Disappearance of these peaks occurred on hydrogenation to the ethyl compound V. Frank, *et al.*,[9] reported a mixture of 5-ethyl-(2-hydroxyethyl)-pyridine, 5-ethyl-2-vinylpyridine and the starting aldehyde collidine, from the reaction of the latter with paraformaldehyde.

The following synthesis was used to prepare 4-vinylpyrimidine. Compound VII was prepared from 6-methyluracil[10] by chlorination to give 2,4-dichloro-6-methylpyrimidine[11,12] and dechlorination. Marshall and Walker[12] have reported the catalytic reduction of 2,4-dichloro-6-methylpyrimi-



dine with palladium-on-strontium carbonate with magnesium oxide in a 1-to-1 mixture of water–ether to give 2-chloro-4-methylpyrimidine. Miyaki and Katooka[13] have catalytically dehalogenated 2,4-dichloro-6-methylpyrimidine with palladium-on-calcium carbonate to give 4-methylpyrimidine but no yield was reported. We have found that 10% palladium-on-charcoal and magnesium oxide in methanol gave 4-methylpyrimidine and that the mode of addition was important. When 2,4-dichloro-6-methylpyrimidine was added to a mixture of magnesium oxide and methanol followed by water and catalyst a spontaneous exothermic reaction took place and attempts to hydrogenate the mixture failed. The compound isolated was the 2,4-dimethoxy derivative[14] reported previously by heating the dichloro compound in sodium and methanol. However, when 2,4-dichloro-6-methylpyrimidine was added to a mixture of magnesium oxide and water followed by methanol and a catalyst, hydrogenation proceeded smoothly to give 4-methylpyrimidine (VII). Compound VII formed a Mannich base in 70% yield.

Compound VIII was prepared from VII in a similar manner as described previously for the dimethylamino derivative. No vinyl compound was obtained in the reaction, but starting material VII and a tarry residue were always obtained. The alcohol was converted to the vinyl compound IX as described previously. The infrared spectrum of IX showed peaks at 6.1 and 10.6 μ indicative of vinyl double bonds. On hydrogenation over palladium-on-charcoal, X was obtained, the infrared spectrum of which showed the disappearance of the double bond frequencies.

2-N,N-Dimethylamino-4-vinylpyrimidine was successfully polymerized in toluene at 80° with 2,2′-azo-bis-isobutyronitrile as a catalyst. The polymer was insoluble in water and fluoresced a blue color under ultraviolet light. The polymer had an average molecular weight of 863 as indicated by nitrogen analysis and molecular weight determinations. No polymer was obtained with anionic catalysts such as *n*-butylmagnesium bromide and triphenylmethylsodium.[15] This was also the case for 4-vinylpyrimidine.

Polymerization of 4-vinylpyrimidine was effected in a similar way. Nitrogen analysis and molecular weights indicated a low molecular weight polymer.

2-N,N-Dimethylamino-4-vinylpyrimidine was copolymerized with styrene with 2,2′-azo-bis-isobutyronitrile as a catalyst. The polymer was insoluble in water and fluoresced a blue color under ultraviolet light. Neither 2-N,N-dimethylamino-4-vinylpyrimidine nor 4-vinylpyrimidine have shown any evidence of ability to retard the growth of sarcoma 180.

(9) R. L. Frank, J. R. Blegen, R. J. Dearborn, R. L. Myers and F. E. Woodward, THIS JOURNAL, **68**, 1368 (1946).

(10) J. Donleavy and M. Kise, "Organic Syntheses," 2nd edition, Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 422.

(11) S. Gabriel and J. Coleman, *Ber.*, **32**, 1533 (1951).

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

(13) T. Miyaki and E. Katooka, *J. Pharm. Soc. Japan*, **60**, 367 (1940); *C. A.*, **35**, 1408 (1941).

(14) S. Gabriel and J. Coleman, *Ber.*, **32**, 2926 (1899).

(15) R. G. Beaman, THIS JOURNAL, **70**, 3115 (1948).

Experimental[16]

2-N,N-Dimethylamino-4-hydroxy-6-methylpyrimidine.—To a cooled solution of sodium methoxide prepared from 240 ml. of methanol and 10.1 g. (0.4 g. atom) of sodium was added 54.4 g. (0.2 mole) of *asym*-dimethylguanidine sulfate. The mixture was refluxed for 30 minutes, allowed to cool and 63.2 g. (0.4 mole) of acetoacetic ester (technical) was added and the reaction mixture refluxed for 23 hours. After cooling the yellow mixture, 200 ml. of water was added and the solution carefully acidified with glacial acetic acid until neutral to litmus. The mixture was then extracted continuously with methylene chloride for 24 hours and dried over anhydrous sodium sulfate. After removal of the drying agent and the solvent, a yellow crystalline residue remained, which was recrystallized from isopropyl alcohol to give a white crystalline product, 47 g. (77%), m.p. 175–176° (m.p. 106°, prepared from 2-ethylmercapto-4-hydroxy-6-methylpyrimidine and dimethylamine).[7]

Anal.[17] Calcd. for $C_7H_{11}N_3O$: C, 54.80; H, 7.23; N, 27.45. Found: C, 54.93; H, 7.40; N, 27.25.

The picrate was prepared in ether and melted at 206–208°. The yellow precipitate was recrystallized from ethanol, needles, m.p. 207–208°.

Anal. Calcd. for $C_{13}H_{14}N_6O_7$: N, 21.9. Found: N, 21.5.

4-Chloro-2-N,N-dimethylamino-6-methylpyrimidine.—A mixture of 30.6 g. (0.2 mole) of 2-N,N-dimethylamino-4-hydroxy-6-methylpyrimidine and 80 ml. of phosphorus oxychloride (b.p. 105–107°) was refluxed for four hours. The amber colored solution was poured into approximately 400 g. of an ice–water mixture, followed by the addition of Norite. After 10 minutes, the reaction mixture was filtered and chilled to 0–5°. The solution was carefully neutralized with 27% ammonium hydroxide until neutral to litmus. The white crystalline precipitate was removed by filtration and sublimed at 30° (0.1 mm.), 34.2 g. (90.5%), m.p. 35–36°.

Anal. Calcd. for $C_7H_{10}ClN_3$: C, 48.86; H, 5.87; N, 24.49. Found: C, 48.56; H, 5.87; N, 24.37.

The picrate was prepared in ether and recrystallized from ethanol and melted at 128–129°.

Anal. Calcd. for $C_{13}H_{13}ClN_6O_7$: N, 20.9. Found: N, 20.5.

2-N,N-Dimethylamino-4-methylpyrimidine.—A solution of 2.5 g. (0.05 mole) of 4-chloro-2-N,N-dimethylamino-6-methylpyrimidine, 6.0 g. (0.15 mole) of magnesium oxide, 45 ml. of ethanol, 90 ml. of water and 0.1 g. of 10% palladium-on-charcoal was hydrogenated for 45 minutes at room temperature and at 1.5 atmospheres hydrogen pressure until the theoretical amount of hydrogen was absorbed. The mixture was filtered, washed with ethanol and extracted continuously with methylene chloride for 20 hours, followed by drying over anhydrous sodium sulfate for 24 hours. After removal of the drying agent and solvent, the product was distilled to give a colorless liquid, 5.6 g. (82.4%), b.p. 85–88° (20 mm.). The product was redistilled through a modified Claisen flask, b.p. 103–106° (40 mm.), to give a colorless liquid, 5.4 g. (79.5%), $n^{25}D$ 1.5323, d^{25}_4 1.0195.

Anal. Calcd. for $C_7H_{11}N_3$: C, 61.31; H, 8.02; N, 30.6. Found: C, 61.60; H, 8.04; N, 30.4.

The picrate was prepared in ether, m.p. 146–148°, recrystallized from ethanol, and melted at 147–148°.

Anal. Calcd. for $C_{13}H_{14}N_6O_7$: N, 22.9. Found: N, 22.7.

Sealed Tube Reaction between 2-N,N-Dimethylamino-4-methylpyrimidine and Paraformaldehyde. (A).—The general procedure was similar to that described in reference 18 for the preparation of 2-vinylpyrazine. Into 3 Carius tubes (1″ diameter by 2 ft. length) there was placed a combined total of 69.5 g. (1.2 moles) of 2-N,N-dimethylamino-4-methylpyrimidine and 11.25 g. (0.375 mole) of paraformaldehyde. The tubes were heated at 162° for 24 hours. The contents were rinsed from the tubes with the aid of chloroform and the solution dried over anhydrous sodium sulfate. After the removal of the drying agent and solvent, the residue was distilled *in vacuo*. Four main fractions were collected: (I) b.p. 84–85° (15 mm.) containing 30 g. (43%) of 2-N,N-dimethylamino-4-methylpyrimidine, $n^{25}D$ 1.5323. A mixed melting point of its picrate, m.p. 146–148°, with an authentic sample m.p. 147–148° gave no depression, m.p. 146–148°; (II) b.p. 93–95° (6.0 mm.), slightly yellow limpid liquid, 7.0 g.; (III) b.p. 123–133° (0.4 mm.), slightly viscous liquid, 4.0 g.; (IV) b.p. 165–170° (0.5 mm.), a viscous liquid which solidified on standing, 4.0 g. A large tarry non-distillable residue of approximately 25 g. remained. Fraction II was redistilled to give 4 g. of starting material and a slightly yellow colored liquid, b.p. 95–98° (10 mm.), 2.0 g., $n^{25}D$ 1.5604, d^{25}_4 1.0853. The compound turned yellow on standing at room temperature but remained almost colorless after standing in the refrigerator for several months. Analysis indicated a vinylpyrimidine structure.

Anal. Calcd. for $C_8H_{11}N_3$: C, 64.47; H, 7.43; N, 28.17. Found: C, 64.34; H, 7.54; N, 28.05.

The picrate was prepared by adding excess ethereal picric acid to an ethereal solution of the vinylpyrimidine and recrystallized from ethanol to give a melting point 128.5–131.5°.

Anal. Calcd. for $C_{14}H_{14}N_6O_7$: N, 22.2. Found: N, 22.2.

Fraction III was redistilled to give a light yellow carbinol, b.p. 123–125° (1.5 mm.), 3.0 g., $n^{25}D$ 1.5539, d^{25}_4 1.1150.

Anal. Calcd. for $C_8H_{13}N_3O$: C, 57.45; H, 7.83; N, 25.1. Found: C, 57.72; H, 7.55; N, 25.4.

Fraction IV was recrystallized twice from isopropyl alcohol. A white crystalline product (2.0 g.) was collected, m.p. 109–110°. Analysis and molecular weight indicated a dimeric structure.

Anal. Calcd. for $C_{15}H_{22}N_6$: C, 62.91; H, 7.74; N, 29.3; mol. wt., 286. Found: C, 62.98; H, 7.86; N, 29.3; mol. wt., 284 (Rast).

(B).—Into each of four 12″ heavy-walled vinyl polymerization tubes of 3/4″ diameter was placed 13.7 g. (0.1 mole) of 2-N,N-dimethylamino-4-methylpyrimidine and 25 g. of paraformaldehyde, respectively. The sealed tubes were heated at 150° for 3.5 hours. The contents were rinsed from the tubes with chloroform and dried over anhydrous sodium sulfate. After the removal of solvent and drying agent, the residue was distilled *in vacuo* using a modified Podbielniak column with three main fractions being collected: (I) b.p. 84–86° (15 mm.), contained 35 g. (64%) of 2-N,N-dimethylamino-4-methylpyrimidine, $n^{25}D$ 1.5321; (II) a light yellow liquid, b.p. 98–105° (15 mm.), 4.0 g.; (III), a yellow viscous liquid, b.p. 130–140° (4 mm.), 10 g. Fraction II was redistilled to give a colorless liquid, the vinyl compound, 2.2 g., b.p. 103–105° (15 mm.), $n^{25}D$ 1.5605. Upon redistillation of fraction III, 8 g. of carbinol was recovered, $n^{25}D$ 1.5536.

Dehydration of 2-N,N-Dimethylamino-4-(2-hydroxyethyl)-pyrimidine with Potassium Hydroxide.—The procedure was similar to that described by Frank, *et al.*,[19] for the preparation of *p*-methoxystyrene. Into a 250-ml. copper distilling vessel was placed 80 g. of potassium hydroxide pellets. The vessel was then fitted with a 20-ml. dropping funnel and after the system was placed under a vacuum of 10 mm. pressure, the potassium hydroxide was heated to a temperature of 160° and the alcohol, 6 g. (0.0359 mole), was then added dropwise over a period of 2 minutes. A mixture of water and product was collected in a receiver cooled by a Dry Ice mixture. The mixture was extracted 3 times with 15-ml. portions of ether and the combined extracts were dried over anhydrous sodium sulfate. After the removal of the drying agent and solvent, the residue was distilled to give a light yellow liquid, b.p. 95–98° (14 mm.), 2.5 g. (46.7%), $n^{20}D$ 1.5608. The picrate was prepared in ether and recrystallized from ethanol, m.p. 130–133°. A mixed melting point with a picrate of the vinyl compound obtained from the sealed tube reaction, m.p. 128.5–131.5° gave no depression, m.p. 128.5–132°.

2-N,N-Dimethylamino-4-ethylpyrimidine.—A mixture of 1.49 g. (0.01 mole) of 2-N,N-dimethylamino-4-vinylpyrimidine, 0.1 g. of 10% palladium-on-charcoal catalyst and 20 ml. of absolute ethanol was hydrogenated for 1 hour at 1.5 atmospheres, until the theoretical amount of hydrogen was absorbed. The catalyst was filtered and washed with ethanol. After the removal of the solvent, the residue was

(16) All melting points are corrected.

(17) Analyses by Drs. Weiler and Straus, Oxford, England; Dr. K. Ritter, Zurich, Switzerland; Dr. F. Schwartzkopf, Queens, N. Y.

(18) L. J. Kitchen and E. S. Hanson, THIS JOURNAL, **73**, 1838 (1951).

(19) R. L. Frank, C. E. Adams, R. E. Allen, R. Gander and P. V. Smith, *ibid.*, **68**, 1365 (1946).

distilled to give a fraction, b.p. 91–92° (15 mm.), 0.75 g. (50%), $n^{25}D$ 1.5274, d^{25}_4 1.0037.

Anal. Calcd. for $C_8H_{13}N_3$: C, 63.51; H, 8.66; N, 27.7. Found: C, 63.33; H, 8.43; N, 27.9.

The picrate was prepared in ether, m.p. 109–111°, and was recrystallized from ethanol to give a melting point 110–111°.

Anal. Calcd. for $C_{14}H_{16}N_6O_7$: N, 22.1. Found: N, 21.8.

2-N,N-Dimethylamino-4-(β-dimethylaminoethyl)-pyrimidine.—The procedure was similar to that described by Heou-Feo[20] for the preparation of the Mannich base from 2-picoline. A mixture of 13.7 g. (0.1 mole) of 2-N,N-dimethylamino-4-methylpyrimidine, 8.0 g. (0.1 mole) of 37% formalin, 7.8 g. (0.1 mole) of dimethylamine hydrochloride and 10 ml. of absolute alcohol was refluxed for one hour. The yellow solution was then cooled and made basic to litmus with 30% sodium hydroxide. The mixture was then extracted with 25 ml. of chloroform and dried for 20 hours over anhydrous potassium carbonate. After the removal of the drying agent and solvent the residue was distilled to give 6.8 g. (50%) of 2-N,N-dimethylamino-4-methylpyrimidine and 7.0 g. (72.2% based on recovered 2-N,N-dimethylamino-4-methylpyrimidine), b.p. 134–135° (5 mm.), of a yellow liquid. The latter compound was redistilled to give a pale yellow liquid, 6.4 g. (66%), b.p. 135–136° (6 mm.), $n^{25}D$ 1.5368, d^{25}_4 1.0299.

Anal. Calcd. for $C_{10}H_{18}N_4$: C, 61.82; H, 9.33; N, 28.8. Found: C, 62.08; H, 9.06; N, 28.6.

The picrate was prepared by adding excess picric acid to an ethereal solution of free base. A yellow crystalline compound was obtained which after recrystallization from ethanol had a m.p. 152.2–153.2°.

Anal. Calcd. for $C_{16}H_{21}N_7O_7$: N, 23.1. Found: N, 22.8.

Poly-2-N,N-dimethylamino-4-vinylpyrimidine.—A mixture of 1 g. of 2-N,N-dimethylamino-4-vinylpyrimidine, 0.05 g. of 2,2′-azo-bis-isobutyronitrile and 10 ml. of dry toluene was heated at 100° in a sealed tube (previously evacuated 5 times at 10^{-5} mm.) for 5 hours. The solvent was then removed and the residue was dissolved in methanol. Water was then added and a tan crystalline product precipitated. The precipitate was removed by filtration and dried for 24 hours over concentrated sulfuric acid in a vacuum desiccator, 0.4 g. The polymer softens at 85° and melts with decomposition at 95° (capillary). Analysis and molecular weight indicate that catalyst fragments are incorporated in the polymer.

Anal. Calcd. for $(C_8H_{11}N_3)_4(C_8H_{12}N_2)_2$: N, 27.0; mol. wt., 868. Found: N, 26.6; mol. wt., 863 (Rast).

Copolymerization of 2-N,N-Dimethylamino-4-vinylpyrimidine with Styrene.—A mixture of 0.5 g. of 2-N,N-dimethylamino-4-vinylpyrimidine, 0.5 g. of styrene and 25 mg. of 2,2′-azo-bis-isobutyronitrile was heated in a vinyl polymerization tube (previously sealed under a nitrogen atmosphere) at 100° for 6 hours. The yellow viscous mixture was then dissolved in 2 ml. of methyl ethyl ketone. The solution was then added dropwise into 200 ml. of methanol, and the copolymer thus precipitated purified by two reprecipitations by methanol from methyl ethyl ketone.

Anal. N, 13.14.

4-Methylpyrimidine.—6-Methyluracil was prepared according to the procedure of Donleavy and Kise[10] and 2,4-dichloro-6-methylpyrimidine was prepared according to the procedure of Marshall and Walker.[12] 4-Methylpyrimidine has previously been prepared by reduction of the dichloro compound with zinc dust and water.[11] The following reduction scheme was employed. A solution of 20.4 g. (0.125 mole) of 2,4-dichloro-6-methylpyrimidine, 18 g. (0.045 mole) of magnesium oxide, 90 ml. of absolute alcohol and 180 ml. of water was shaken in a low pressure hydrogenation apparatus at 1–2 atmospheres of hydrogen pressure with 1.2 g. of 10% palladium-on-charcoal catalyst at room temperature. After one hour the theoretical amount of hydrogen was absorbed and the mixture was filtered and thoroughly washed with water and methylene chloride. The filtrate was extracted continuously with methylene chloride for 48 hours and then dried over anhydrous potassium carbonate for 48 hours. After the removal of the drying agent and solvent the product was fractionally distilled to give a colorless liquid, 3.5 g. (30%), b.p. 141–145° (760 mm.), $n^{25}D$ 1.4940. A tarry residue of 6 g. remained in the distilling flask (b.p. 86° (114 mm.), $n^{29}D$ 1.4916, no yield reported)[12] (b.p. 141–142° atm., $d^{16}_{15.9}$ 1.031, no yield reported[11]).

Anal. Calcd. for $C_5H_6N_2$: C, 63.89; H, 6.42; N, 29.7. Found: C, 63.62; H, 6.68; N, 29.4.

The picrate was prepared by adding excess ethereal picric acid to an ethereal solution of 4-methylpyrimidine to give a yellow crystalline product, m.p. 132–132.2° (m.p. 131–134°[11]). The mercury II chloride was obtained by adding aqueous mercury II chloride to 4-methylpyrimidine, m.p. 198–199° (m.p. 198°).[11] When methanol was used instead of ethanol, 2,4-dimethoxy-6-methylpyrimidine was obtained which is a white crystalline solid, m.p. 69–70° (Marshall and Walker obtained the compound using methanolic potassium hydroxide, m.p. 69–70°[12]); (m.p. 69–70°, with sodium methoxide[11]).

In an experiment using 27% ammonium hydroxide and methanol, a 30% yield of 4-methylpyrimidine was obtained. Similarly with ammoniacal methanol, a 28.3% yield of product was obtained.

4-(β-Hydroxyethyl)-pyrimidine.—The procedure was similar to that described by Kitchen and Hanson[19] for the preparation of 2-(β-hydroxyethyl)-pyrazine. A sealed tube containing 10 g. (0.106 mole) of 4-methylpyrimidine and 3.0 g. (0.1 mole) of paraformaldehyde was heated at 165° for 3.5 hours. The contents of the tube were then transferred with the aid of ether to a 10-ml. distilling flask. After the removal of the solvent, the residue was distilled to give 6 g. (60%) of 4-methylpyrimidine, b.p. 140–141° (760 mm.), and 4.0 g. of product (87% based on recovered 4-methylpyrimidine), b.p. 132–139° (10 mm.). 4-(β-Hydroxyethyl)-pyrimidine, purified by distillation, had a b.p. 125–127° (9 mm.), 3.5 g. (76%), $n^{25}D$ 1.5323, d^{25}_4 1.3620. The product was a viscous liquid with a yellow tinge and a rancid odor.

Anal. Calcd. for $C_6H_8N_2O$: C, 58.16; H, 6.47; N, 22.6. Found: C, 58.21; H, 6.31; N, 22.3.

4-Vinylpyrimidine.—The procedure was similar to that described by Frank, *et al.*,[19] for the preparation of 2-vinylpyridine. After the system was evacuated to 10 mm. pressure, the potassium hydroxide was heated until molten and 10 g. (0.085 mole) of 4-(β-hydroxyethyl)-pyrimidine (to which had been added 0.1 g. of *p-t*-butylcatechol) was added dropwise over a period of 3 minutes. The mixture of water and 4-vinylpyrimidine was collected in a Dry Ice receiver and extracted 3 times with 15-ml. portions of ether. The combined extracts were dried over anhydrous sodium sulfate for 24 hours. After the removal of the drying agent and solvent the product was distilled to give a colorless liquid, b.p. 56–58° (10 mm.), 2 g. (23.4%), $n^{25}D$ 1.5405, d^{25}_4 1.0598. On standing the liquid slowly turns red.

Anal. Calcd. for $C_6H_6N_2$: C, 67.90: H, 5.70; N, 26.40. Found: C, 67.65; H, 5.77; N, 26.20.

The picrate of 4-vinylpyrimidine prepared in ether could not be recrystallized successfully but was washed several times with dry ether, m.p. 125–130°.

Anal. Calcd. for $C_{12}H_9N_5O_7$: N, 20.9. Found: N, 20.7.

4-Ethylpyrimidine.—A mixture of 1.2 g. (0.0113 mole) of 4-vinylpyrimidine, 50 mg. of 10% palladium-on-charcoal catalyst and 35 ml. of absolute ethanol was shaken in a Parr low pressure hydrogenation apparatus for one hour. The mixture was then filtered and washed carefully with ethanol. The ethanol was distilled through a modified Podbielniak column at atmospheric pressure and the product was then distilled under vacuum to give a colorless material weighing 0.8 g. (66%), b.p. 65–67° (10 mm.), $n^{25}D$ 1.4817, d^{25}_4 0.9981.

Anal. Calcd. for $C_6H_8N_2$: C, 66.66; H, 7.45; N, 25.8. Found: C, 66.40; H, 7.63; N, 25.7.

The picrate was prepared by adding excess picric acid to an ethereal solution of 4-ethylpyrimidine, m.p. 85–86°. The picrate was recrystallized from ethanol and melted at 85.5–86°.

Anal. Calcd. for $C_{12}H_{11}N_5O_7$: N, 20.7. Found: N, 20.4.

4-(β-Dimethylaminoethyl)-pyrimidine.—A mixture of 4.7 g. (0.05 mole) of 4-methylpyrimidine, 9 g. (0.05 mole) of 25% aqueous dimethylamine, 4.5 ml. of concentrated hydrochloric acid and 4.0 g. (0.05 mole) of 37% formalin was refluxed for one hour. The yellow solution was cooled and

(20) T. Heou-Feo, *Compt. rend.*, **192**, 1242 (1931).

neutralized with 20% aqueous sodium hydroxide until neutral to litmus. The mixture was then extracted with 20 ml. of chloroform and dried over anhydrous potassium carbonate. After the removal of the drying agent and solvent the residue was distilled. After collecting 2 g. of 4-methylpyrimidine there was obtained 3 g. (70%, based on recovered 4-methylpyrimidine) of a pale yellow liquid, b.p. 120–122° (30 mm.), $n^{25}D$ 1.5145, d^{25}_4 1.0205.

Anal. Calcd. for $C_8H_{13}N_3$: C, 63.54; H, 8.66: N, 27.7. Found: C, 63.79; H, 8.46; N, 27.6.

Poly-4-vinylpyrimidine.—A sealed tube, previously evacuated at 10^{-5} mm., containing a mixture of 0.7 g. of 4-vinylpyrimidine, 0.0375 g. of 2,2′-azo-bis-isobutyronitrile and 7.5 ml. of dry toluene was heated on a steam-bath for four hours. A heavy viscous oil precipitated. After decanting the solvent, the oil was washed with 1 ml. of toluene and dissolved in 3 ml. of methanol and Norite was added. Upon removal of the Norite and addition of ether, a tan amorphous precipitate appeared, 0.3 g., m.p. 127–142° dec. A molecular weight determination by the Rast method gave a value of 873. Analysis and molecular weight again indicated that catalyst fragments were present although less nitrogen was found in the polymer than was anticipated.

Infrared Absorption Spectra.—Infrared absorption spectra were determined with a Perkin–Elmer infrared spectrophotometer with no solvent. They were determined as liquids in a demountable cell using sodium chloride windows and no spacers.

Acknowledgment.—We wish to thank the National Institutes of Health for support of this work. We are also grateful to Dr. Chester Stock of the Sloan–Kettering Institute for Cancer Research for his coöperation in the screening of these compounds.

BROOKLYN, NEW YORK

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

The Reaction of o-Phenylenediamines with Carbonyl Compounds. III. Benzophenones and Dibenzyl Ketones[1]

BY ROBERT C. ELDERFIELD[2] AND VICTOR B. MEYER

RECEIVED OCTOBER 17, 1953

The reaction of *o*-phenylenediamine with benzophenone and with dibenzyl, 4-methoxy- and 4-chloro-dibenzyl ketones has been studied. The presence of the substituents in the two latter ketones exerts a marked effect on the elimination of hydrocarbon in the reaction. Syntheses for unsymmetrically substituted dibenzyl ketones are described.

o-Phenylenediamine (I) and its mono-N-substituted derivatives have been shown to react with ketones, with the elimination of water, to give intermediate compounds which on heating split out hydrocarbons to yield benzimidazoles.[3,4] The structure of the intermediate, which is discussed in greater detail in the following paper, may be either that of a 2,2-disubstituted benzimidazoline or of a Schiff base.

The previous detailed investigation of the reaction[3] was limited almost exclusively to a study of the reaction between I and aliphatic ketones. The elimination reaction was shown to be catalyzed by strong bases and followed first-order kinetics either in the presence or absence of base. A mechanism based on elimination of the hydrocarbon as an anion was offered as providing a reasonable explanation for the observed facts.

Such a proposal, however, involves some inconsistencies. In the cases in which the alkyl groups in the ketone were unlike it was found that the group preferentially eliminated from the intermediate was the one more highly branched at the α carbon atom, *e.g.*, isopropyl was eliminated in preference to *n*-propyl. If the departing group does indeed leave as a carbanion, then the observed order of ease of elimination is the reverse of what has been considered to be the order of stability of carbanions. Experimental proof for this order of stability has been provided recently.[5]

(1) The material here presented is taken from a dissertation submitted by Victor B. Meyer in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Columbia University.

(2) University of Michigan, Ann Arbor, Michigan.

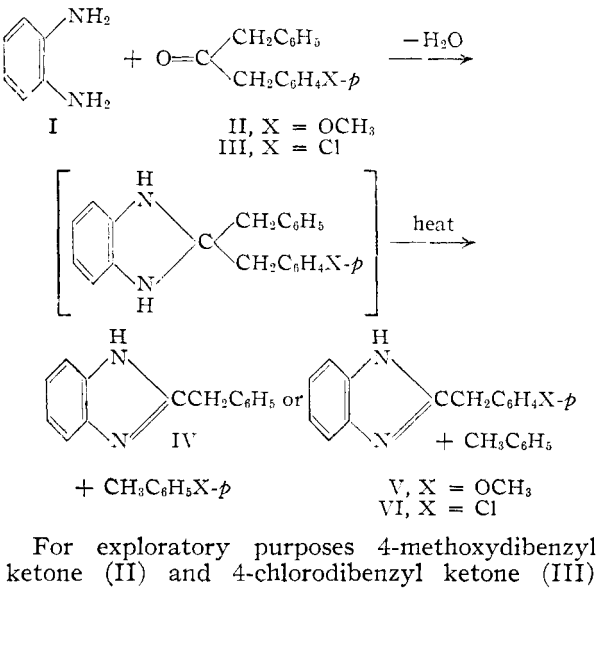
(3) R. C. Elderfield and J. R. McCarthy, THIS JOURNAL, **73**, 975 (1951).

(4) R. C. Elderfield and F. J. Kreysa, *ibid.*, **70**, 44 (1948).

(5) P. D. Bartlett, S. Friedman and M. Stiles, *ibid.*, **75**, 1771 (1953).

In order to secure additional information regarding the mechanistic details of the reaction and to extend its scope to include benzophenone and dibenzyl ketone derivatives the present investigation was undertaken.

If the suggested mechanism for the elimination is correct, then it would be anticipated that when the reaction of I is carried out with appropriately substituted dibenzyl ketones an effect on the course of the elimination reaction due to the presence of electron attracting or electron donating substituents in the ketones should be apparent. This has been found to be so with two unsymmetrically substituted dibenzyl ketones.



For exploratory purposes 4-methoxydibenzyl ketone (II) and 4-chlorodibenzyl ketone (III)