Experimental

Reagents.—Potassium *t*-butoxide was obtained from Mine Safety Appliances, Inc., as the sublimed powder. Analyses indicated a minimum purity of 98.5 wt. %, the major impurity being K_2CO_3. Dimethyl sulfoxide was obtained from Crown-Zellerbach. The material was freshly distilled from Linde 13X Molecular Sieves before use. The hydrocarbons were obtained from Matheson Coleman and Bell (reagent grade), as was dimethyl sulfone. Diglyme (dimethyl ether of diethylene glycol), obtained from Matheson Coleman and Bell, was distilled from Linde 13X Molecular Sieves before use.

Procedure.—The reactions were carried out by contacting 3 mmoles of the olefinic or aromatic hydrocarbon with 7.0 ml. of a 0.6 *M* solution of potassium *t*-butoxide in dimethyl sulfoxide. All reaction mixtures were prepared in a nitrogen drybox and carried out in a thermostated bath at 55 ± 0.2°. Reaction product analyses were performed by gas chromatography (comparing relative retention volumes with those of authentic samples) and mass spectrometry.

The Use of the Allyl Group as a Blocking Group for the Synthesis of N-Substituted Purines[1]

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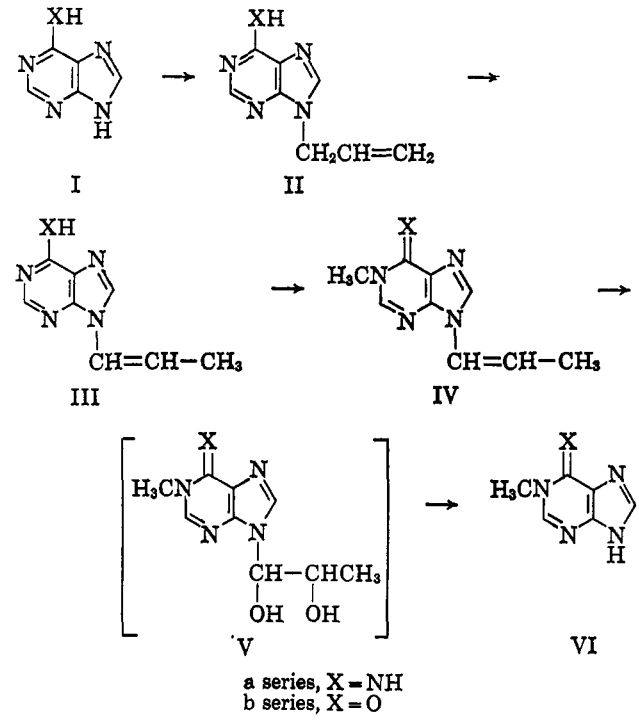
It has been amply demonstrated that the position of alkylation[2,3] or sugar coupling[2,4] of purines can be controlled by N substitution of purines by removable blocking groups. Thus the ribose moiety has been useful in the preparation of 1-substituted purines[2,5,6] and the benzyl group has been used to prepare both 1- and 7-substituted purines.[2-4] The use of the ribose blocking group is limited, practically, to cases in which one can utilize naturally occurring ribonucleosides as starting materials, and even then the method leaves something to be desired, since the acid cleavage of the ribose moiety results in sugar decomposition products that often make the isolation of the desired purine difficult and the yield low. The use of the benzyl group avoids most of these problems, but catalytic hydrogenolysis of the benzyl group is usually difficult and slow.[2] In some cases ring reduction occurs as readily as removal of the benzyl group resulting in low yields of the desired purines.[7] The benzhydryl group[8] is apparently not significantly better in this regard.[7]

In a search for a better blocking group, and one whose removal is compatible with the acidic lability of purine nucleosides, we turned to the allyl group since it has been shown that allyl ethers are facilely rearranged by means of potassium *t*-butoxide in dimethyl sulfoxide to propenyl ethers[9] that can be oxidatively cleaved under mild conditions at a basic pH.[10]

To test the potential of this procedure applied to purines, 9-allyladenine (IIa) was prepared by the alkylation of adenine (I) with allyl bromide in N,N-dimethylacetamide in the presence of potassium carbonate.[11] Treatment of 9-allyladenine (IIa) with potassium *t*-butoxide in dimethyl sulfoxide gave a good yield of 9-propenyladenine (IIIa), which was alkylated with methyl iodide to give 1-methyl-9-propenyladenine (IVa) hydriodide. Treatment of IVa with potassium permanganate under basic conditions presumably resulted in hydroxylation of the double bond, but this intermediate (Va) was not stable to the conditions of the reaction and 1-methyladenine (VIa)[14] was obtained directly in good yield. Since it is well known that 1-substituted adenines can rearrange to N^6-substituted adenines under basic conditions, the absence of N^6-methyladenine in VIa was established by means of thin layer chromatography.

The same sequence of reactions was applied to 9-allylhypoxanthine (IIb) and again a good yield of 1-methylhypoxanthine (VIb) was readily obtained. The preparation of 7-substituted purines from 3-allylpurines by this procedure is currently under investigation. Possible applications of this procedure to other nitrogen heterocycles is obvious.



Experimental

The melting points reported were determined on a Kofler Heizbank and are corrected. The ultraviolet spectra were de-

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(11) In the absence of base the allylation takes place predominantly at N-3.[3,12] 9-Allyladenine has also been prepared from 5-amino-4,6-dichloropyrimidine.[13]

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termined in aqueous solution with a Cary Model 14 spectrophotometer; the infrared spectra were determined in pressed potassium bromide disks with a Perkin-Elmer Model 221 spectrophotometer; the proton magnetic resonance spectrum was determined as a 10% (w./v.) solution in dimethyl sulfoxide-d_6 with a Varian Associates Model A-60 spectrometer.

9-Allyladenine (IIa).—A suspension of 1.35 g. (10.0 mmoles) of adenine (Ia) and 1.52 g. (10.1 mmoles) of anhydrous potassium carbonate in 100 ml. of N,N-dimethylacetamide containing 0.88 ml. (10.0 mmoles) of allyl bromide was stirred at 130° for 18 hr. After filtration the solution was evaporated to dryness *in vacuo*. The residue was dissolved in 100 ml. of chloroform. The chloroform solution was washed with 25 ml. of water, dried over magnesium sulfate, and evaporated to dryness *in vacuo*. The residue crystallized from ethanol–acetonitrile: yield, 471 mg. (27%); m.p. 143–145°; λ_{max} in mμ ($\epsilon \times 10^{-3}$), at pH 1 260 (13.7), pH 7 261 (13.8), and pH 13 261 (13.8); $\bar{\nu}$ in cm.$^{-1}$, 3300 (NH), 3150 and 3100 (CH), 1650 (NH), and 1595 and 1570 (C=C, C=N).

This material was identical with an authentic sample of 9-allyladenine prepared in another manner.[13]

Examination of the filtrate showed that it contained about an equal mixture of 3- and 9-allyladenine.

9-Propenyladenine (IIIa).—To a solution of 184 mg. (1.00 mmole) of potassium *t*-butoxide in 3.7 ml. of dimethyl sulfoxide was added 175 mg. (1.00 mmole) of 9-allyladenine. The resulting solution was heated in a 100° oil bath for 20 min., diluted with 3.7 ml. of water, and taken to pH 8 with solid carbon dioxide. The thick sludge that resulted was evaporated to dryness *in vacuo*. A suspension of the residue in 25 ml. of water was extracted with three 50-ml. portions of chloroform. After drying over magnesium sulfate, the chloroform solution was evaporated to dryness *in vacuo*. A white solid residue remained: yield, 144 mg. (82%); m.p. 197°; λ_{max} in mμ ($\epsilon \times 10^{-3}$), at pH 1 233 (20.8) and 256 (sh) (14.4), pH 7 260 (13.1), and pH 13 260 (12.7); $\bar{\nu}$ in cm.$^{-1}$, 3370 and 3310 (NH), 3140 (CH), 1645 (NH), 1590 and 1570 (C=C, C=N), and 1470 (C—CH_3); τ in p.p.m., 8.1 and 8.2 (C=H—CH_3). This material was used in the next step without further purification.

1-Methyl-9-propenyladenine (IVa).—To a solution of 381 mg. (2.18 mmoles) of 9-propenyladenine in 30 ml. of N,N-dimethylformamide was added slowly 0.31 ml. (5.00 mmoles) of methyl iodide. The solution was sealed tightly and stirred at room temperature for 18 hr. It was then evaporated to dryness *in vacuo*. A solution of the residue in 100 ml. of water was brought to pH 10 with concentrated ammonium hydroxide. Evaporation of the solution to 20 ml. gave a white precipitate: yield, 396 mg. (57%); m.p. 298–300°; λ_{max} in mμ ($\epsilon \times 10^{-3}$), at pH 1 231 (20.6) and 256 (sh) (9.15), pH 7 227 (20.0) and 256 (sh) (8.84), and pH 13 226 (18.3) and 256 (sh) (8.30); $\bar{\nu}$ in cm.$^{-1}$, 3310 (NH), 3160 and 3040 (CH), 1690 and 1630 (NH and C=C), 1595, 1575, and 1510 (C=C, C=N), and 1470 (C—CH_3). The analytical sample was obtained by recrystallization from ethanol.

Anal. Calcd. for $C_9H_{11}N_5 \cdot HI$: C, 34.07; H, 3.81; N, 22.08. Found: C, 34.28; H, 4.08; N, 22.08.

1-Methyladenine (VIa).—A solution of 200 mg. (0.628 mmole) of 1-methyl-9-propenyladenine hydroiodide in 15 ml. of 0.5 *N* methanolic sodium hydroxide was treated with a 4% aqueous potassium permanganate solution. After the dark brown precipitate that formed became very thick, it was removed by filtration and the addition of permanganate resumed. This process was continued until a brown color no longer developed, and an aliquot of the reaction mixture showed no starting compound when examined by thin layer chromatography. Evaporation of the methanol in a nitrogen stream left an aqueous solution that produced a crystalline precipitate: yield, 60 mg. (64%); m.p. 310–312° dec.; λ_{max} in mμ ($\epsilon \times 10^{-3}$), at pH 1 257 (11.7), pH 7 264 (10.8), and pH 13 269 (14.1); $\bar{\nu}$ in cm.$^{-1}$, 3400 (NH), 3240 and 2950 (CH), 2900–2600 (acidic NH), and 1690, 1645, and 1555 (NH, C=C, C=N). The ultraviolet spectra agree with the literature values.[14] A thin layer chromatogram run on 60 μl. of this material on silica gel H using 1:1 chloroform–methanol as solvent showed only one ultraviolet absorbing spot when sprayed with Ultraphor. N^6-Methyladenine, run as a standard on the same plate, traveled much further than 1-methyladenine.

9-Propenylhypoxanthine (IIIb).—To a solution of 552 mg. (3.00 mmoles) of potassium *t*-butoxide in 11 ml. of dimethyl sulfoxide (dried with molecular sieve) was added 528 mg. (3.00 mmoles) of 9-allylhypoxanthine.[15] The resulting solution, protected by a calcium chloride tube, was heated in a 95° oil bath for 20 min., then cooled to room temperature, diluted with 30 ml. of water, and taken to pH 7 with solid carbon dioxide. After the mixture was cooled, the precipitate that had formed was collected by filtration: yield, 440 mg. (83%); m.p. 301–303° dec.; λ_{max} in mμ ($\epsilon \times 10^{-3}$), at pH 1 227 (16.8) and 248 (sh) (10.5), pH 7 226 (21.8) and 250 (sh) (10.8), and pH 13 220 (20.7), 254 (9.90), and 267 (sh) (6.98); $\bar{\nu}$ in cm.$^{-1}$, 3045 and 2850 (CH), 2800–2600 (acidic H), 1685 (C=O), 1585, 1570, and 1510 (C=C, C=N), and 1470 (C—CH_3). This material was used in the next step without further purification.

1-Methyl-9-propenylhypoxanthine (IVb).—A solution of 352 mg. (2.00 mmoles) of 9-propenylhypoxanthine and 372 mg. (2.00 mmoles) of methyl *p*-toluenesulfonate in 30 ml. of N,N-dimethylacetamide containing a suspension of 324 mg. (2.35 mmoles) of anhydrous potassium carbonate was stirred and heated at 100° for 2 hr. The inorganics were removed by filtration and the solution evaporated to dryness *in vacuo*. The residue was partitioned between chloroform and water. The chloroform layer, after drying over magnesium sulfate, was evaporated to dryness *in vacuo*. A white crystalline residue was obtained: yield, 357 mg. (94%); m.p. 220°; λ_{max} in mμ ($\epsilon \times 10^{-3}$), at pH 1 220 and 253 (sh) (9.06), pH 7 225, 254 (sh) (8.38), and 270 (sh) (5.00), and pH 13 225, 254 (sh) (8.74), and 270 (sh) (5.15); $\bar{\nu}$ in cm.$^{-1}$, 3090, 3040, 2960, 2920, 2860 (CH), 1665 (C=O), 1570, 1535 and 1510 (C=C, C=N), and 1450 (C—CH_3). The analytical sample was obtained by recrystallization from ethanol: m.p. 220°.

Anal. Calcd. for $C_9H_{10}N_4O$: C, 56.84; H, 5.30; N, 29.44. Found: C, 57.08; H, 5.50; N, 29.50.

1-Methylhypoxanthine (VIb).—To a solution of 357 mg. (1.88 mmoles) of 1-methyl-9-propenylhypoxanthine in 15 ml. of 0.5 *N* methanolic sodium hydroxide there was added dropwise a 4% aqueous potassium permanganate solution. After the dark brown precipitate that formed became very thick, it was removed by filtration and the addition of permanganate resumed; the process was repeated. The addition of permanganate was continued until there was no longer a brown color. The colorless reaction solution was taken to pH 5 with dilute hydrochloric acid and evaporated to dryness *in vacuo*. The residue crystallized from water: yield, 164 mg. (58%); m.p. above 260°; λ_{max} in mμ ($\epsilon \times 10^{-3}$), at pH 1 249 (9.40), pH 7 250 (9.00), and pH 13 260 (9.60); $\bar{\nu}$ in cm.$^{-1}$, 3080, 3040, 2920, 2860 (CH), 2800–2500 (acidic NH), 1690 (C=O), and 1585 and 1530 (C=C, C=N). The ultraviolet spectra agree with the literature values[17] and with those of a sample of 1-methylhypoxanthine prepared by the method of Shaw.

(15) This compound was prepared from 5-amino-4,6-dichloropyrimidine[18] by the procedure developed in these laboratories.[16]

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The Monomolecular and Bimolecular Reduction of Aryl Olefins

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Recent studies have confirmed the similarity of the mechanisms of the disilylation reaction[1-4] and of the

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