(-20 °C): IR (neat) 3080, 2970, 2870, 1640, 1460, 1450, 1420, 1380, 1365, 1180, 1140, 880, 780, 680 cm^{-1}; ^1H NMR (CCl_4) δ 0.91 (s, 12 H), 1.20 (s, 6 H), 4.77 (s, 2 H), 4.82 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 24.21 (q, 1,2-CH_3), 32.94 (q, 4-CH_3), 43.80 (s, C-4), 47.66 (s, C-1,2), 102.71 (t), 169.60 (s); mass spectrum (70 eV), m/z (relative intensity) 178 (11, M^+), 163 (100), 135 (38), 122 (45), 121 (60). Anal. Calcd for $C_{13}H_{22}$ (178.3): C, 87.56; H, 12.44. Found: C, 87.36; H, 12.64.

Octamethylcyclopentanone (3). A solution of **2** (1.96 g, 10.0 mmol) in 100 mL of hexane was added dropwise (≈60 min) to a rapidly stirred mixture of 10 mL of BF_3·OEt_2 (80 mmol) in 300 mL of hexane at ambient temperature. The mixture was stirred for another 30 min and then hydrolyzed with 400 mL of aqueous $NaHCO_3$ solution (5%). The organic layer was dried with $CaCl_2$ and evaporated to give **3** contaminated by traces of **5**, which were removed by column chromatography: **5** was washed from a column of silica gel 60 (l = 15 cm, i.d. = 2.5 cm) with 100 mL of hexane/ether (v/v = 99/1). **3** (1.13 g, 58%) was then eluted with 150 mL of CH_2Cl_2. Analytical data of **3** is given in ref 2.

1,2,2,3,3,4,4-Heptamethyl-5-methylenecyclopentan-1-ol (6). Compound **2** (0.98 g, 5.0 mmol) was added to 10 mL of a 1.6 M solution of CH_3Li in ether. The ether was distilled off, and the residue was heated at 140 °C for 2 h to give a brownish mixture, which was cooled and treated with 5 mL of the CH_3Li solution as before. After the mixture was cooled, 10 mL of ether was added, and the solution was hydrolyzed with 10 mL of concentrated aqueous NH_4Cl solution. The organic layer was dried with $CaCl_2$ and evaporated to give a mixture of **6** and some nonidentified byproducts. The mixture was separated by column chromatography (silica gel 60, l = 15 cm, i.d. = 2.5 cm). After elution of the byproducts with 100 mL of hexane/ether (v/v = 99/1), pure **6** (0.86 g, 88%) was washed from the column with hexane/ether (v/v = 92/8). Colorless plates with mp 40–45 °C (from pentane) were obtained: IR (neat) 3330, 2950, 1450, 1380, 1075, 910, 735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82 (s, 3 H), 0.84 (s, 3 H), 0.93 (s, 3 H), 1.07 (s, 3 H), 1.09 (s, 3 H), 1.11 (s, 3 H), 1.17 (s, 1 H), 1.27 (s, 3 H), 4.95 (s, 1 H), 5.18 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 18.67 (q), 22.54 (q), 23.73 (q), 23.97 (q), 25.60 (q), 29.96 (q), 30.53 (q), 45.00 (s), 46.17 (s), 48.79 (s), 82.27 (s), 105.84 (t), 169.77 (s). Anal. Calcd for $C_{13}H_{24}O$ (196.3): C, 79.52; H, 12.32. Found: C, 78.77; H, 12.15.

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2-Halogenated Purine Nucleosides: Synthesis and Reactivity[1]

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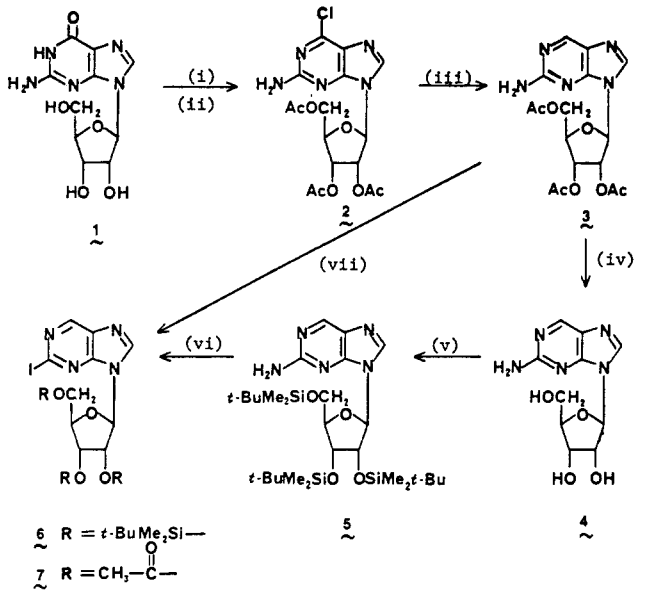
Although considerable attention has been devoted to the synthesis and reactions of 6-halogenated purine nucleosides,[3-7] the same cannot be said for the corresponding 2-halogenated compounds.[8,9] This is in part due to limitations in synthetic accessibility to this class of nucleosides. 2-Halogenated purines are potentially key synthetic intermediates to a variety of novel 2-substituted purine nucleosides. A logical approach to 2-halogenated purines may be via the corresponding 2-amino compound. 2-Amino-9-β-D-ribofuranosylpurine is an important biologically active nucleoside. It is a potent inhibitor of a number of purine metabolizing enzymes including adenosine deaminase,[10] purine nucleoside phosphorylase,[11] and adenosine kinase.[12] It is incorporated in *E. coli* and phage T4 DNA.[13,14] However, an efficient general method for the preparation of this compound is not currently available. Previous syntheses involved, as the key step, the hydrogenolysis of the corresponding 6-chloro compound (protected) using Pd/C and hydrogen, treatment of the protected 6-thio compound with Raney nickel in water, and coupling of a halogenated sugar with protected 2-aminopurine in the presence of mercuric chloride.[9,13,15,16] Photochemical methods are rarely used in nucleoside synthesis. We wish to report a high yielding and reproducible photochemical synthesis of 2-aminopurine nucleoside, its conversion to the corresponding novel 2-halogenated compound, and the synthetic utilization of the latter.

Scheme I[a]



[a] (i) Ac_2O, $(C_2H_5)_3N$, *N,N*-(dimethylamino)pyridine; (ii) $POCl_3$, *N,N*-diethylaniline, Δ; (iii) $(C_2H_5)_3N$, THF, $h\nu$; (iv) NH_3, C_2H_5OH; (v) *t*-Bu$(CH_3)_2SiCl$, imidazole, DMF, Δ; (vi) *n*-$C_5H_{11}ONO$, CH_2I_2, $(CH_3)_3SiI$, hexane, Δ; (vii) *n*-$C_5H_{11}ONO$, CH_2I_2, CH_3CN.

The starting material for the synthesis was guanosine (**1**) which was selectively acetylated in 93% yield by using acetic anhydride, triethylamine, and 4-(dimethylamino)-pyridine in acetonitrile.[17] Treatment of the triacetylated guanosine with phosphorus oxychloride and *N,N*-diethylaniline at 70 °C for 1 h gave the 6-chloro compound

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(2) Deceased, May 22, 1986.
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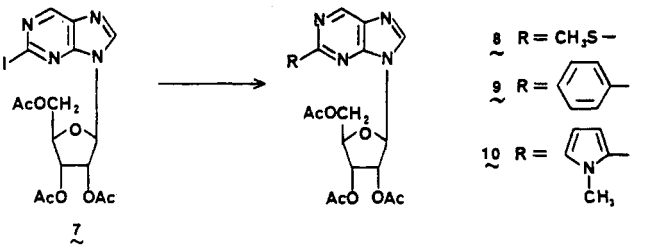
Scheme II

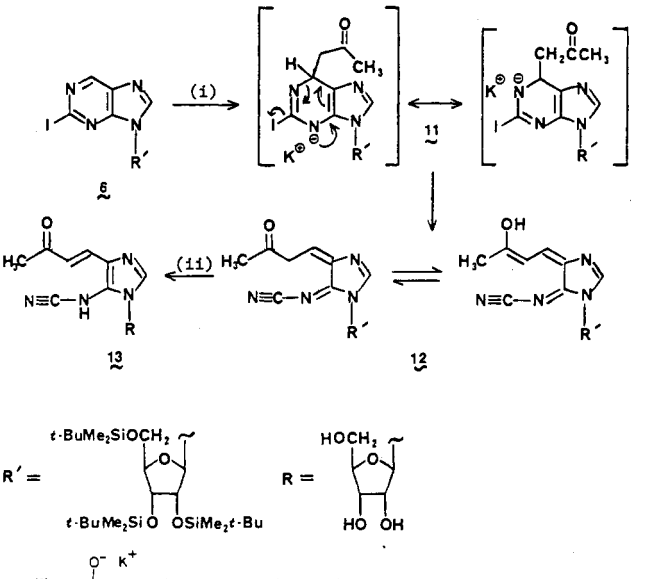


2 in about 89% yield. Photolysis of 2 in dry, nitrogen-purged THF containing 10% triethylamine in a Rayonet photochemical reactor (2537 Å) produced the 2-aminopurine nucleoside 3 in 84% isolated yield (Scheme I). This reaction is a photoinduced reductive dehalogenation and has not been reported previously in purine nucleoside chemistry. A plausible mechanistic interpretation of the conversion is that an exciplex is formed between 2 and triethylamine[18] and that this is followed by electron transfer, carbon–chlorine bond cleavage, and hydrogen atom abstraction from the amine. Support for this mechanism comes from several observations. First, in the absence of triethylamine, 2 is not converted to 3. Second, the reaction does not proceed in the absence of light and is slow at longer wavelengths (e.g., 3500 Å, compound 2 absorbs at 220, 249, and 310 nm). Third, in competition experiments with triethylamine and excess benzene, the only product isolated was 3.

2-Aminopurine nucleosides are excellent potential precursors for a variety of new 2-substituted purines via their 2-halogenated derivatives. Development of a procedure for the conversion of an amino group to a halogen in the purine system has been reported previously by us.[5,19] A modification of this procedure was used for the halogenations described here. Thus, nucleoside 5 (i.e., the silylated derivative of 4) can be converted to the new 2-iodopurine 6 in 67% yield by a deamination–halogenation reaction using *n*-pentyl nitrite, diiodomethane, and trimethylsilyl iodide in hexane. The acetylated 2-aminopurine nucleoside 3 may be converted by a similar procedure (but without trimethylsilyl iodide) to the corresponding 2-iodo compound 7 (Scheme I).

When compound 7 was photolyzed in dry nitrogen-purged dimethyl disulfide in acetonitrile, the novel 2-(methylthio)purine nucleoside 8 was isolated in 61% yield (Scheme II). Nucleoside 7 can participate in photoinduced arylation reactions. For example, photolysis in benzene results in the formation of the protected 2-phenylpurine 9 in 47% yield. Extension to photoinduced heteroarylations is also possible. Thus, photolysis of 6 in the presence of *N*-methylpyrrole for 1 h resulted in the formation of 10 in 75% yield. High-field ^{1}H NMR data (in $CDCl_3$) was used to confirm the regiochemistry of the heteroarylation reaction. The chemical shift of the H-3 proton of the pyrrole ring (δ 7.22) and the coupling constants ($J_{3,4}$ = 3.9 Hz and $J_{3,5}$ = 1.8 Hz) provide strong evidence for reaction at the α-position of the pyrrole ring.[20] The heteroarylated nucleoside 10 shows a bathochromically shifted UV spectrum compared to nebularine with absorption maxima at 332 (ϵ 10 000), 296 (ϵ 10 000), and 242 nm (ϵ 8000). It is a highly fluorescent compound with emission at 444 nm when excited at 339 nm.

Scheme III[a]



[a] (i) $CH_3C(O^-K^+)=CH_2$, THF, −48 °C, *hν*; (ii) Bu_4NF, THF.

Carbon–carbon bond-forming reactions of 2-iodinated purines are also potentially feasible through the $S_{RN}1$ reaction.[21,22] However, when the 2-iodinated purine 6 was photolyzed in the presence of the potassium enolate of acetone in anhydrous THF at −48 °C for 20 min, the expected 2-acetonylpurine derivative was not isolated. Instead, a highly functionalized imidazole 13 was obtained after deprotection (Scheme III). Any plausible mechanism for this transformation would require, as the initial step, the addition of potassium acetone enolate to the 1,6-π-bond of 6 in a reaction related (but not mechanistically similar) to the photoinduced addition of methanol to nebularine.[23] Ring opening[24] and concomitant ejection of iodide in 11 would give 12, which can be isolated and characterized. However, during further manipulations (e.g., deprotection and purification), the latter apparently undergoes a 1,5-sigmatropic hydrogen shift to give the thermodynamically more stable 13. The structure of 13 was deduced from its mass spectrum (M^+ = 308), UV data (309 nm), FTIR spectrum (2125, 1675, 1625 cm^{-1}) and high-field NMR data including delayed decoupling. In the 90.6-MHz ^{13}C NMR spectrum, the C=O (197.1 ppm), C=C (123.1, 137.7 ppm), C≡N (129.8 ppm), and CH_3 (27.3 ppm) groups could be easily discerned. The remaining carbon resonances were those expected for the imidazole and ribose portions of the molecule. The 360-MHz ^{1}H NMR data complimented the ^{13}C NMR information and also established the trans stereochemistry about the C=C bond (J = 15.6 Hz).

In summary, a highly efficient methodology to the 2-aminopurine nucleoside 4 is described. This compound can be easily transformed into the corresponding 2-halogenated purine system which can be converted to thioalkylated, arylated, and heteroarylated purines and to a highly functionalized imidazole nucleoside.

Experimental Section

Irradiations were accomplished in a Hanovia 450-W mercury photolysis apparatus or in a Rayonet photochemical reactor. The melting points provided are uncorrected and were taken on a Thomas-Hoover melting point apparatus fitted with a microscope. Nuclear magnetic resonance spectra using tetramethylsilane as

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an internal standard were recorded on JEOL Model FX90Q and Bruker Model WM360 pulse Fourier transform spectrometers. A Hewlett-Packard 5985 GC/MS system was used for the mass spectra. The ultraviolet spectra were recorded on a Varian Cary Model 219 spectrophotometer. Infrared spectra were recorded on an IBM Model 98 Fourier transform instrument. Satisfactory elemental analyses could not be obtained for the new compounds described because of their instability.

2-Amino-6-chloro-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)purine (2)[25] was prepared from guanosine in 83% overall yield by selective acetylation with acetic anhydride, triethylamine, and 4-(dimethylamino)pyridine in acetonitrile,[17] followed by reactio of the product with $POCl_3$ and *N,N*-diethylaniline at 70 °C for 1 h.

2-Amino-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)purine (3). A solution of **2** (0.760 g, 1.78 mmol) in triethylamine (60 mL) and tetrahydrofuran (240 mL) was purged with nitrogen and photolyzed in a Rayonet photochemical reactor (2537 Å) for 17 h. The solvent was then removed, and the residue was chromatographed on preparative silica gel plates with ethyl acetate/methanol (19:1) as the eluting solvent. 2-Amino-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)purine (**3**) (0.586 g, 1.5 mmol, 84%) was obtained as tan crystals: mp 142 °C (lit.[16] mp 142–143 °C).

2-Amino-9-β-D-ribofuranosylpurine (4). To 220 mL of dry ethanol saturated with ammonia gas at ice–salt bath temperatures was added 1.817 g (4.62 mmol) of **3**. The solution was stirred at this temperature for 1 h and then at 25 °C for 23 h. The solvent was removed under reduced pressure, and the residue was purified by crystallization from H_2O/ethanol to give 1.184 g (4.43 mmol, 96%) of **4**: mp 164–166 °C (lit.[15] mp ~165 °C); ^{13}C NMR (Me_2SO-d_6) δ 61.7, 70.7, 73.7, 85.6, 86.6, 127.3, 141.1, 149.6, 153.2, 160.6; ^1H NMR (Me_2SO-d_6) δ 3.59 (m, 2 H), 3.91 (m, 1 H), 4.13 (m, 1 H), 4.51 (m, 1 H), 4.99 (d, 1 H), 5.12 (d, 1 H), 5.41 (d, 1 H), 5.85 (d, 1 H), 6.51 (s, 2 H), 8.29 (s, 1 H), 8.60 (s, 1 H); UV (EtOH) λ_{max} 244 nm (ε 6.6 × 10^3), 308 (ε 7.7 × 10^3).

2-Iodo-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)purine (7). To a solution consisting of 15 mL of acetonitrile, 2 mL of diiodomethane, and 4 mL of *n*-pentyl nitrite was added 0.300 g (0.76 mmol) of **3**. The solution was protected from moisture and heated under nitrogen at 50 °C for 7 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel plates (4:1 ethyl acetate/hexane). The only major band (R_f 0.68) gave 0.133 g (0.26 mmol, 35%) of **7** as a low-melting solid: ^{13}C NMR ($CDCl_3$) δ 20.4, 20.7, 20.8, 63.0, 70.6, 73.3, 80.7, 86.2, 119.5, 134.4, 150.0, 152.0, 169.4, 169.5, 170.2; ^1H NMR ($CDCl_3$) δ 2.10 (s, 3 H), 2.13 (s, 3 H), 2.17 (s, 3 H), 4.43 (m, 3 H), 5.64 (t, 1 H), 5.83 (t, 1 H), 6.24 (d, 1 H), 8.22 (s, 1 H), 8.90 (s, 1 H); ^{15}N NMR (Me_2SO-d_6) δ 177.8 (d, J = 8.2 Hz, N-9), 256.0 (d, J = 12.8 Hz, N-7), 284.3 (s, N-3), 313.5 (d, J = 11.6 Hz, N-1); UV (EtOH) λ_{max} 219 nm (ε 2.0 × 10^4), 247 (ε 7.6 × 10^3), 278 (ε 9.2 × 10^3); mass spectrum, m/z (relative intensity) 504 (M^+, 4.0), 259 (sugar$^+$, 52.9), 247 (base + 2 H, 71.9), 246 (Base + H, 6.4).

2-(Methylthio)-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-purine (8). To 10 mL of dry dimethyl disulfide in 40 mL of acetonitrile was added 1.32 g (2.62 mmol) of **7**. The solution was purged with nitrogen and photolyzed for 27 h in a quartz Hanovia reactor with a Vycor filter. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel plates (ethyl acetate). The band at R_f 0.5 gave 0.68 g (1.60 mmol, 61%) of **8** as a yellow oil: ^{13}C NMR ($CDCl_3$) δ 14.7, 20.4, 20.5, 20.7, 62.8, 70.2, 72.9, 79.9, 86.8, 131.6, 142.5, 149.2, 151.7, 167.2, 169.3, 169.4, 170.3; ^1H NMR ($CDCl_3$) δ 2.08 (s, 3 H), 2.10 (s, 3 H), 2.15 (s, 3 H), 2.65 (s, 3 H), 4.39 (m, 3 H), 5.70 (t, 1 H), 6.05 (t, 1 H), 6.16 (d, 1 H), 8.09 (s, 1 H), 8.94 (s, 1 H); UV (EtOH) λ_{max} 231 nm (ε 1.1 × 10^4), 261 (ε 8.6 × 10^3), 305 (ε 5.5 × 10^3); mass spectrum, m/z (relative intensity) 424 (M^+, 17.7), 259 (sugar$^+$, 49.1), 167 (base + 2H, 32.6), 166 (base + H, 28.1), 165 (base, 8.5), 139 (100.0).

2-Phenyl-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)purine (9). To 70 mL of dry benzene was added 0.081 g (0.16 mmol) of **7**. The solution was photolyzed for 6 h as described for **8**. Chromatography on silica gel plates (ethyl acetate) afforded (R_f 0.48) 0.034 g (0.077 mmol, 47%) of **9** as a pale yellow oil: ^{13}C NMR ($CDCl_3$) δ 20.4, 20.5, 20.7, 62.6, 70.1, 73.1, 79.9, 86.9, 128.4, 128.6, 128.7, 130.4, 133.1, 137.5, 144.0, 149.1, 151.6, 159.9, 169.3, 169.4, 170.3; ^1H NMR ($CDCl_3$) δ 1.96 (s, 3 H), 2.11 (s, 3 H), 2.19 (s, 3 H), 4.43 (m, 3 H), 5.91 (t, 1 H), 6.17 (t, 1 H), 6.25 (d, 1 H), 7.54–7.47 (m, 3 H), 8.22 (s, 1 H), 8.59–8.48 (m, 2 H), 9.23 (s, 1 H); UV (EtOH) λ_{max} 233 nm (ε 1.2 × 10^4), 272 (ε 1.0 × 10^4), 282 (ε 1.2 × 10^4); mass spectrum, m/z (relative intensity) 454 (M^+, 0.8), 259 (sugar$^+$, 19.5), 198 (4.0), 197 (base + 2H, 8.3), 196 (base + 1H, 1.6), 195 (base, 0.4), 139 (100.0).

2-(*N*-Methylpyrr-2-yl)-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)purine (10). A solution consisting of 0.078 g (0.16 mmol) of **7** and 70 mL of dry *N*-methylpyrrole was photolyzed for 1 h as described for **8**. Chromatography (silica gel plates, ethyl acetate) afforded (R_f 0.70) 0.056 g (0.12 mmol, 75%) of **10** as a light brown low-melting solid: ^{13}C NMR ($CDCl_3$) δ 20.4, 20.5, 20.6, 38.0, 62.7, 70.1, 73.0, 79.9, 86.6, 108.2, 115.3, 128.2, 131.2, 131.5, 142.8, 148.7, 151.2, 155.7, 169.3, 169.4, 170.3; ^1H NMR ($CDCl_3$) δ 2.03 (s, 3 H), 2.10 (s, 3 H), 2.15 (s, 3 H), 4.11 (s, 3 H), 4.40 (m, 3 H), 5.72 (t, 1 H), 6.21–6.04 (m, 3 H), 6.77 (dd, 1 H), 7.21 (dd, 1 H), 8.14 (s, 1 H), 9.07 (s, 1 H); UV (EtOH) λ_{max} 242 nm (ε 8.0 × 10^3), 296 (ε 1.0 × 10^4), 332 (ε 1.1 × 10^4); fluorescence (EtOH) excitation 339 nm and emission 444 nm; mass spectrum, m/z (relative intensity) 457 (M^+, 3.6), 259 (sugar$^+$, 2.9), 200 (base + 2H 18.8), 199 (base + H 84.9), 198 (base, 45.5), 45.5), 139 (100.0).

2-Iodo-9-(2,3,5-tris-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl)purine (6). A solution consisting of 2.047 g (7.66 mmol) of **4**, 3.843 g (25.50 mmol) *tert*-butyldimethylsilyl chloride, 2.967 g (43.59 mmol) imidazole, and 4 mL of dry DMF was stirred under N_5 at 60 °C for 11 h. The solvent was removed (1 torr), and the residue was dissolved in 75 mL of chloroform and washed with 5 × 100 mL of H_2O. The organic layer was dried (Na_2SO_4), concentrated, and purified by flash chromatography (1:1 ether/hexane) to give 2.911 g (4.77 mmol, 62%) of **5** as a tan oil: mass spectrum, m/z (relative intensity) 610 (M^+, 14.6) 580 (96.5), 553 (M^+ – *t*-Bu, 43.4), 552 (100.0).

A solution consisting of 0.274 g (0.45 mmol) of **5**, 2.0 mL of diiodomethane, 20 mL of nitrogen-purged hexane, 0.4 mL of trimethylsilyl iodide, and 1.0 mL of *n*-pentyl nitrite was heated under nitrogen at 60 °C for 4 h. The solution was cooled to ambient temperature, diluted with hexane (25 mL), and washed with saturated aqueous sodium sulfite (5 mL). The aqueous layer was extracted with hexane (2 × 20 mL), and the organic layers were combined and evaporated under reduced pressure. Purification by flash chromatography on silica gel (1:3 ether/hexane) gave 0.214 g (0.30 mmol, 67%) of **6** as a yellow oil: ^{13}C NMR ($CDCl_3$) δ –5.7, –5.6, –5.3, –5.1, –5.0, –4.6, 17.5, 17.7, 18.1, 25.4, 25.5, 25.7, 61.6, 70.9, 75.2, 84.8, 88.7, 118.6, 134.3, 144.0, 149.3, 151.5; ^1H NMR ($CDCl_3$) δ 0.17 to –0.13 (m, 18 H), 0.92 (m, 27 H), 4.04–3.80 (m, 2 H), 4.16 (m, 1 H), 4.32 (m, 1 H), 4.61 (m, 1 H), 6.03 (d, 1 H), 8.47 (s, 1 H), 8.87 (s, 1 H); UV (EtOH) λ_{max} 222 nm (ε 2.2 × 10^4), 247 (ε 8.2 × 10^3), 278 (ε 1.0 × 10^4); mass spectrum, m/z (relative intensity) 664 (20.1), 663 (M^+ – *t*-Bu, 47.9).

Photoinduced Reaction of 6 with Potassium Acetone Enolate. Nucleoside **6** (0.140 g, 0.19 mmol) was dissolved in dry nitrogen-purged THF and transferred via double-tipped needle to a low-temperature Hanovia photochemical apparatus with Pyrex filter. The solution was cooled to –48 °C. The potassium enolate (1.70 mmol) in THF (15 mL) was transferred via double-tipped needle to the photochemical reactor. The cooled solution was immediately photolyzed with a 450-W mercury lamp for 0.5 h. Excess NH_4Cl in methanol (5 mL) was added to quench the reaction. The mixture was filtered, and the solvent was removed under reduced pressure. Purification on silica gel plates (19:1 $CHCl_3/CH_3OH$) gave 0.09 g (0.14 mmol, 74%) of **12**, which was deprotected with tetrabutylammonium fluoride in THF. Compound **13** was obtained as a low-melting solid (0.032 g, 76%) after HPLC on Amberlite XAD-4 resin (4:1 H_2O/C_2H_5OH) and ion-exchange chromatography on Dowex 50-W resin: ^{13}C NMR (Me_2SO-d_6) δ 27.2, 60.7, 69.6, 74.7, 84.6, 87.5, 123.1, 129.8, 129.9, 133.7, 134.5, 156.2, 197.1; ^1H NMR (Me_2SO-d_6) δ 2.21 (s, 3 H), 3.50–4.20 (m, 5 H), 5.42 (d, 1 H), 6.16 (s, 1 H, D_2O exchangeable) 6.59 (d, 1 H, J = 15.6 Hz), 7.29 (d, 1 H, J = 15.6 Hz), 7.96 (s, 1 H); UV (H_2O) λ_{max} 309 nm (ε 8250); FTIR (KBr) 2125, 1675, 1625 cm^{-1}; mass spectrum, m/z (relative intensity) 308 (M^+, 3.0), 177 (base$^+$ + 2H, 18.1), 176 (base$^+$ + H, 10.0), 175 (base$^+$, 8.5), 149 (base$^+$ – CN, 100), 133 (sugar$^+$, 21.5).

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A New Regiospecific Synthesis of Enol Boranes of Methyl Ketones

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1,2-Migrations of organoborates are a cornerstone of numerous organoborane-based syntheses,[1] and a knowledge of relative "migratory aptitudes" for intermediates containing mixed groups should significantly enhance their synthetic utility. Among such "mixed" derivatives containing alkyl groups, the ease of transfer has been established as normal > secondary > tertiary for both the cyanoborate process[2] and the iodination of ethynyltrialkylborates,[3] whereas for rearrangements of α-halo boronates[4] as well as intermediates obtained from reaction of mixed boranes with α-diazo carbonyls,[5] the order is Ar > R > Cl. The latter process provides a route to regio- and stereodefined *internal* enol boranes[6] A (Scheme I, path a), but to date no method exists for the regiospecific construction of *terminal* enol derivatives B from nonketonic precursors (Scheme I, path b, G = H).

Accordingly, we have investigated the efficiency of several boranes for this purpose, including H_3B·THF, dichloroborane, 9-borabicyclo[3.3.1]nonane (9-BBN),[7] thexylborane, dicyclohexylborane, and disiamylborane—using as criteria a combination of nitrogen evolution and, after protolysis, methyl ketone formation. The former represents a rough measure of overall enol borinate formation,[5,8] and the latter indicates regiochemistry (i.e., relative migratory aptitude), as depicted in Scheme I (path b, G = H, $E^+ = H^+$).

In the event, dicyclohexylborane proved most efficient,[9] and the derived enol borinate **3** reacted with various electrophiles (Eschenmoser's reagent,[12] aldehydes, and ketones) to provide good yields of the corresponding Mannich bases and crossed-aldol products, respectively. It should be emphasized that in all cases examined there was no evidence (GLPC, NMR) of product formation derived from either cyclohexyl group migration or the regioisomer due to proton scrambling.

Table I. Formation of Mannich Bases from Reaction of Enol Borinates with Dimethylmethyleneammonium Iodide

$R_2BOC(R^1)=CH_2 + Me_2N^+=CH_2I^- \rightarrow R^1COCH_2CH_2NMe_2$[a]

R	R^1	product yield,[b] %	bp, °C (torr)	picrate mp, °C
C_6H_{11}	$CH_3(CH_2)_4$	80	74–75 (1.5)	87–88
C_6H_{11}	$(CH_3)_2CH(CH_2)_2$	73	57–58 (0.70)	97–98
C_6H_{11}	C_6H_{11}	68	83–84 (0.60)	119–120

[a] All structures were confirmed by IR, ^1H NMR, mass spectral data and satisfactory (±0.3%) elemental analyses. [b] Yields of pure products isolated by distillation.

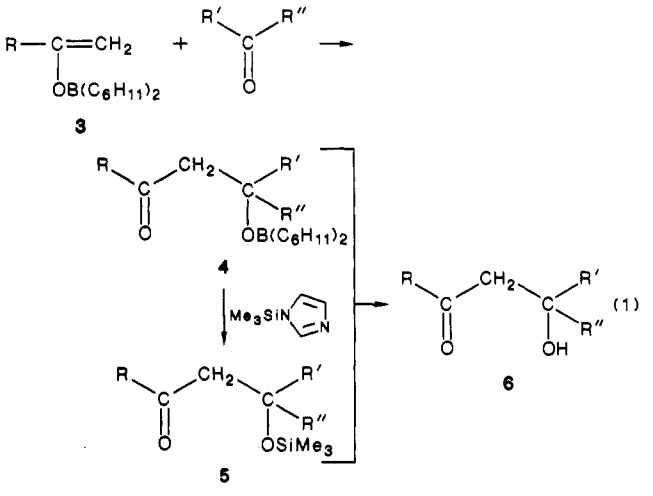
Table II. Cross-Aldol Products from Reaction of Enol Borinates with Aldehydes and Ketones

$R_2BOC(R')=CH_2 + R''COR''' \rightarrow R'COCH_2C(OSiMe_3)R''R'''$

R	R′	R″	R‴	product yield,[a,b] %
C_6H_{11}	n-C_5H_{11}	CH_3	CH_3	74
C_6H_{11}	n-C_5H_{11}	CH_3	H	70
C_6H_{11}	n-C_5H_{11}	CH_3	C_2H_5	72
C_6H_{11}	n-C_5H_{11}	C_6H_{11}	H	(60)
C_6H_{11}	n-C_5H_{11}	C_6H_5	H	70[c]

[a] All structures were verified by compatible IR, ^1H NMR, and mass spectral data. [b] Yield of isolated product. Value in parentheses indicates yield determined by GC analyses. [c] Isolated as 1-phenyl-1-octen-3-one, mp 48–49 °C.

Yields of several Mannich bases prepared in this manner are presented in Table I. Similarly, crossed-aldol products could be readily assembled (eq 1), but isolation of product



6 in pure form from boryloxy derivative **4** was often complicated by the formation of byproducts. This obstacle was circumvented by the discovery of a mild boryloxy → silyloxy exchange (**4** → **5**) upon treating derivative **4** with *N*-trimethylsilylimidazole.[13] The resulting trimethylsilyl aldol-protected derivative **5** could be easily isolated by distillation[14] or hydrolyzed to **6** without complication. Table II summarizes the results. Importantly, the entire

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