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Protection of the Amino Group of Adenosine and Guanosine Derivatives by Elaboration into a 2,5-Dimethylpyrrole Moiety†

Ireneusz Nowak and Morris J. Robins*

Department of Chemistry and Biochemistry, Brigham Young University, Provo, Utah 84602-5700

morris_robins@byu.edu

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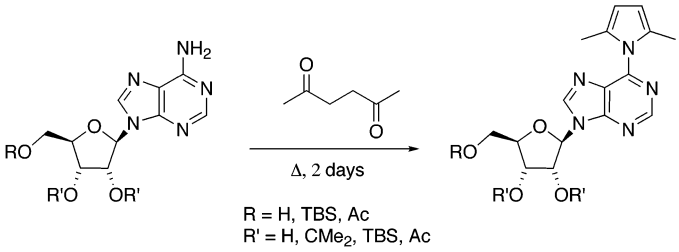
ABSTRACT



Protection of the amino group of adenine and guanine nucleosides was effected by heating the substrates in 2,5-hexanedione. The resulting 2,5-dimethylpyrrole adducts were stable toward bases but were hydrolyzed with TFA/H_2O to regenerate the amino function.

Multistep syntheses of modified nucleosides depend on the protection/deprotection of functional groups. During the course of a synthetic scheme, which required addition of a carbene to unsaturated nucleoside derivatives, the need arose to mask the 6-amino group of adenosine. Usual protecting groups that were investigated did not survive the basic conditions employed for generation of the nucleoside alkene. We previously elaborated the 6-amino group of adenine-type nucleosides into a 6-(1,2,4-triazol-1-yl) moiety,[1] and we employed a modified Appel reaction for introduction of a 6-(imidazol-1-yl) group into purine nucleosides.[2] However, these triazole and imidazole heterocycles are weakly basic enough to function as leaving groups for S_NAr reactions with nitrogen, oxygen, or sulfur nucleophiles.[1,2] Elaboration of the 6-amino function into a 2,5-dimethylpyrrole attracted our attention because this transformation has been used for protection of primary amines of aliphatic,[3,4] aromatic,[3,5] heterocyclic,[3,6] and carbohydrate[7,8] origin. Applications in medicinal chemistry have included syntheses of benzolactam,[9] amino alcohol,[4] and serotonin[6] analogues, and it was found that substitution of a pyrrole ring at C6 of a purine derivative resulted in enhancement of biological activity.[10]

† Nucleic Acid Related Compounds. 120. Paper 119: Janeba, Z.; Francom, P.; Robins, M. J. *J. Org. Chem.* **2003**, *68*, 989−992.

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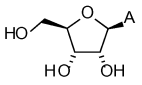
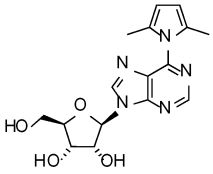
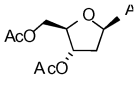
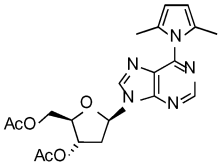
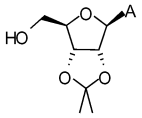
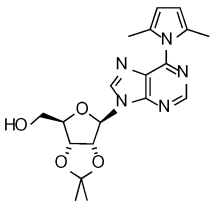
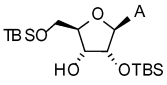
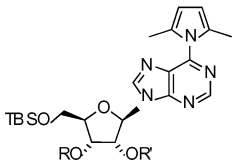
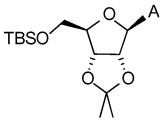
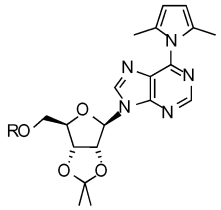
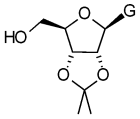
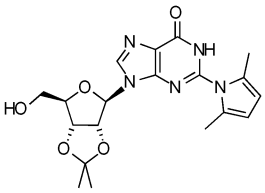
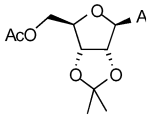
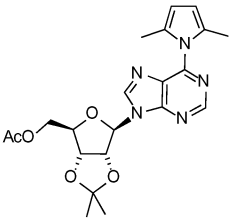
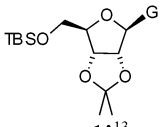
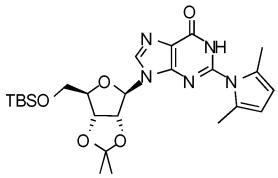
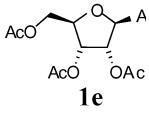
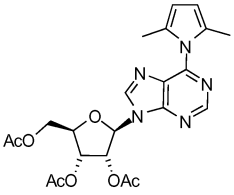
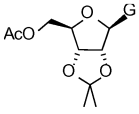
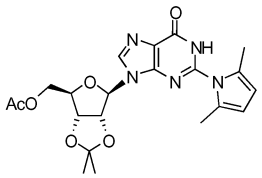
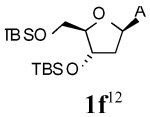
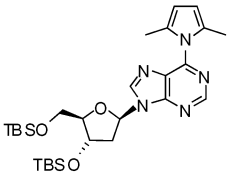
Table 1. Elaboration of the Amino Group in Nucleosides **1** into the 2,5-Dimethylpyrrole Moiety of Products 2[a,b]

entry	substrate **1**	product(s) **2** (yield %)[c]	entry	substrate **1**	product(s) **2** (yield %)[c]
1	 **1a**	 **2a** (35)	7	 **1g**	 **2g** (30)
2	 **1b**	 **2b** (56)	8	 **1h**	 **2h** R = H, R' = TBS (and) **2h'** R = TBS, R' = H (69)
3	 **1c**	 **2b** R = H (39) **2c** R = TBS (45)	9	 **1i**	 **2i** (47)
4	 **1d**[11]	 **2d** (54)	10	 **1j**[13]	 **2j** (23)
5	 **1e**	 **2e** (62)	11	 **1k**	 **2k** (56)
6[d]	 **1f**[12]	 **2f** (15)			

[a] Reactions were performed by the general procedure (ref 14) unless noted otherwise. [b] Substrates and products had clean UV and ^{1}H and ^{13}C NMR spectra and HRMS data. [c] Isolated yields. [d] Reaction performed at 130 °C.

Subsequent removal of the pyrrole ring to regenerate the amine can be effected readily by ozonolysis or by treatment with hydroxylamine hydrochloride. Electron-rich pyrrole rings do not survive in the presence of oxidizing agents or

strong electrophiles, but their usefulness has been demonstrated when a need exists to mask weakly acidic NH_2 groups for reactions that employ strongly basic (e.g., Grignard or organolithium) reagents.[3−6] An additional practical consequence for nucleoside chemistry involves the enhanced lipophilicity of 2,5-dimethylpyrrole derivatives, especially with respect to the solubility of guanine-containing nucleosides, which are notorious for self-aggregation by hydrogen bonding. We now report reactions of adenine and guanine nucleosides with 2,5-hexanedione, which give new acid-sensitive but base-stable 2,5-dimethylpyrrole adducts for further synthetic manipulations.

The nucleoside or sugar-protected derivative was heated in neat 2,5-hexanedione (∼10 equiv) for 2 days. The excess diketone was removed under oil-pump vacuum, and the product was purified by chromatography. It is noteworthy that this method was applied successfully to unprotected as well as sugar-protected nucleosides (Table 1).[14] The major limitations were solubility of the nucleoside and stability of the starting material and/or product for an extended period at elevated temperatures. The majority of adenine and guanine derivatives tested gave the elaborated pyrrole products, but cytidine and its sugar-protected derivatives failed to give the 4-(2,5-dimethylpyrrol-1-yl) adducts under the same conditions. The apparent thermal instability of the

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(14) **General Procedure.** A solution of 2′,3′-*O*-isopropylideneadenosine (**1b**) (1.0 g, 3.26 mmol) in 2,5-hexanedione (4 mL) was heated at 150−160 °C for 2 days. Volatiles were evaporated in vacuo, and the oily residue was dissolved in CH_2Cl_2 (5 mL) and deposited on silica gel. Chromatography (EtOAc/hexanes, 1:1) gave pyrrole adduct **2b** (56%) as an orange oil.

(15) (a) **6-(2,5-Dimethylpyrrol-1-yl)-9-(*β*-D-ribofuranosyl)purine (2a).** UV (MeOH) max 284 nm (ϵ 12 100), min 245 nm (ϵ 4100); ^{1}H NMR ($CDCl_3$) δ 2.18 (s, 6H), 3.32 (br s, 1H), 3.78 (d, J = 12.6 Hz, 1H), 3.80 (br s, 1H), 3.98 (dd, J = 0.9, 12.6 Hz, 1H), 4.36 (s, 1H), 4.48 (d, J = 5.4 Hz, 1H), 4.98 (dd, J = 5.4, 7.3 Hz, 1H), 5.50 (br s, 1H), 5.93 (d, J = 7.3 Hz, 1H), 5.99 (s, 2H), 8.21 (s, 1H), 8.86 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.2, 62.3, 71.3, 74.1, 86.9, 90.7, 109.1, 129.4, 129.7, 145.2, 150.3, 151.6, 152.1; EI-MS *m*/*z* 345 ([M$^+$] 25%), 256, 213 (100%), 198; HRMS calcd for $C_{16}H_{19}N_5O_4$ 345.1437, found 345.1431. (b) **9-(2,3-*O*-Isopropylidene-*β*-D-ribofuranosyl)-6-(2,5-dimethylpyrrol-1-yl)purine (2b).** UV (MeOH) max 283 nm (ϵ 12 100), min 247 nm (ϵ 4200); ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 3H), 1.69 (s, 3H), 2.22 (s, 6H), 3.82−3.88 (m, 1H), 4.02 (dd, J = 12.7, 1.5 Hz, 1H), 4.60 (s, 1H), 5.17 (dd, J = 1.5, 5.8 Hz, 1H), 5.31 (dd, J = 4.4, 5.8 Hz, 1H), 5.46 (d, J = 10.7 Hz, 1H), 6.00 (s, 2H), 6.03 (d, J = 4.4 Hz, 1H), 8.22 (s, 1H), 8.93 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.0, 24.7, 26.9, 62.2, 81.2, 83.6, 86.2, 92.3, 108.6, 113.6, 128.8, 129.2, 144.2, 149.8, 151.6, 152.1; MS *m*/*z* 385 ([M$^+$] 80%), 370, 354, 296, 213 (100%), 198; HRMS calcd for $C_{19}H_{23}O_4N_5$ 385.1750, found 385.1753. (c) **9-(5-*O*-*tert*-Butyldimethylsilyl-2,3-*O*-isopropylidene-*β*-D-ribofuranosyl)-6-(2,5-dimethylpyrrol-1-yl)purine (2c).** UV (MeOH) max 283 nm (ϵ 11 700), min 245 nm (ϵ 3400); ^{1}H NMR ($CDCl_3$) δ −0.02 (s, 3H), 0.00 (s, 3H), 0.81 (s, 9H), 1.42 (s, 3H), 1.66 (s, 3H), 2.18 (s, 6H), 3.81 (dd, J = 3.7, 11.4 Hz, 1H), 3.91 (dd, J = 3.3, 11.4 Hz, 1H), 4.50 (m, 1H), 4.96 (dd, J = 2.2, 6.2 Hz, 1H), 5.28 (dd, J = 2.7, 6.1 Hz, 1H), 5.96 (s, 2H), 6.28 (d, J = 2.6 Hz, 1H), 8.34 (s, 1H), 8.94 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −6.2, −6.1, 12.9, 17.6, 24.7, 25.2, 26.6, 63.0, 80.9, 84.4, 86.9, 91.3, 108.2, 113.3, 128.5, 129.0, 143.3, 149.4, 151.6, 152.3; EI-MS *m*/*z* 499 ([M$^+$] 100%), 484, 442, 296, 212, 129; HRMS calcd for $C_{25}H_{37}N_5O_4Si$ 499.2614, found 499.2621. (d) **9-(5-*O*-Acetyl-2,3-*O*-isopropylidene-*β*-D-ribofuranosyl)-6-(2,5-dimethylpyrrol-1-yl)purine (2d).** UV (MeOH) max 283 nm (ϵ 12 100), min 247 nm (ϵ 3900); ^{1}H NMR ($CDCl_3$) δ 1.39 (s, 3H), 1.63 (s, 3H), 1.98 (s, 3H), 2.18 (s, 6H), 4.27 (dd, J = 5.9, 12.2 Hz, 1H), 4.38 (dd, J = 4.4, 12.2 Hz, 1H), 4.49−4.53 (m, 1H), 5.05 (dd, J = 3.9, 5.9 Hz, 1H), 5.47 (dd, J = 2.0, 5.9 Hz, 1H), 5.95 (s, 2H), 6.21 (d, J = 2.0 Hz, 1H), 8.18 (s, 1H), 8.92 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.4, 20.5, 25.2, 27.0, 63.8, 81.2, 84.0, 84.6, 90.9, 109.0, 114.8, 129.2, 129.6, 143.7, 150.3, 152.3, 152.5, 170.2; FAB-MS (thioglycerol) *m*/*z* 427 ([M$^+$] 100%), 411, 367; HRMS calcd for $C_{21}H_{25}N_5O_5$ 427.1855, found 427.1866. (e) **9-(2,3,5-Tri-*O*-acetyl-*β*-D-*erythro*-pentofuranosyl)-6-(2,5-dimethylpyrrol-1-yl)purine (2e).** UV (MeOH) max 283 nm (ϵ 12 200), min 247 nm (ϵ 4900); ^{1}H NMR ($CDCl_3$) δ 2.129 (s, 3H), 2.131 (s, 3H), 2.17 (s, 3H), 2.22 (s, 6H), 4.41 (dd, J = 5.4, 12.2 Hz, 1H), 4.48−4.52 (m, 2H), 5.73 (t, J = 5.1 Hz, 1H), 5.99 (s, 2H), 6.01 (d, J = 5.2 Hz, 1H), 6.27 (d, J = 4.9 Hz, 1H), 8.23 (s, 1H), 8.95 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.5, 20.3, 20.4, 20.6, 62.8, 70.3, 73.1, 80.2, 86.8, 109.0, 129.1, 129.7, 143.1, 150.4, 152.5, 152.9, 169.3, 169.5, 170.2; EI-MS *m*/*z* 471 ([M$^+$] 20%), 470, 258, 226, 212, 139 (100%), 97; HRMS calcd for $C_{22}H_{25}N_5O_7$ 471.1753, found 471.1756. (f) **9-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-*β*-D-*erythro*-pentofuranosyl]-6-(2,5-dimethylpyrrol-1-yl)purine (2f).** UV (MeOH) max 283 nm (ϵ 11 900), min 245 nm (ϵ 3700); ^{1}H NMR ($CDCl_3$) δ 0.06 (s, 3H), 0.08 (s, 3H), 0.13 (s, 6H), 0.89 (s, 9H), 0.93 (s, 9H), 2.20 (s, 6H), 2.43−2.56 (ddd, J = 3.7, 6.2, 13.2 Hz, 1H), 2.66−2.81 (m, 1H), 3.80 (dd, J = 3.1, 11.0 Hz, 1H), 3.89 (dd, J = 4.0, 11.0 Hz, 1H), 4.04−4.11 (m, 1H), 4.63−4.72 (m, 1H), 5.97 (s, 2H), 6.57 (t, J = 6.6 Hz, 1H), 8.39 (s, 1H), 8.91 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −5.6, −5.5, −4.9, −4.8, 13.4, 17.9, 18.3, 25.6, 25.8, 41.0, 62.6, 71.9, 84.5, 88.0, 108.7, 129.0, 129.6, 143.3, 150.0, 152.0, 152.9; EI-MS *m*/*z* 557 ([M$^+$] 75%), 500, 368, 287, 213 (100%), 155; HRMS calcd for $C_{28}H_{47}N_5O_3Si_2$ 557.3217, found 557.3223. (g) **9-(3,5-Di-*O*-acetyl-2-deoxy-*β*-D-*erythro*-pentofuranosyl)-6-(2,5-dimethylpyrrol-1-yl)purine (2g).** UV (MeOH) max 283 nm (ϵ 12 100), min 247 nm (ϵ 4400); ^{1}H NMR ($CDCl_3$) δ 2.10 (s, 3H), 2.17 (s, 3H), 2.21 (s, 6H), 2.69 (ddd, J = 2.7, 6.1, 14.2 Hz, 1H), 3.06 (ddd, J = 6.3, 7.8, 14.2 Hz, 1H), 4.37−4.48 (m, 3H), 5.47−5.50 (m, 1H), 5.99 (s, 2H), 6.55 (dd, J = 6.3, 7.8 Hz, 1H), 8.28 (s, 1H), 8.94 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.1, 20.4, 20.5, 36.8, 63.3, 74.0, 82.3, 84.5, 108.5, 128.8, 129.3, 143.0, 149.8, 151.9, 152.6, 169.9, 170.0; FAB-MS (thioglycerol) *m*/*z* 414 ([M + H$^+$] 100%), 437 ([M + Na + H$^+$] 15%); HRMS calcd for $C_{20}H_{24}N_5O_5$ 414.1777, found 414.1785. (h) **9-[2(3),5-Bis-*O*-(*tert*-butyldimethylsilyl)-*β*-D-ribofuranosyl]-6-(2,5-dimethylpyrrol-1-yl)purine (2h).** UV (MeOH) max 283 nm (ϵ 12 200), min 244 nm (ϵ 3900); FAB-MS *m*/*z* 573 ([M$^+$] 100%), 516, 497, 423, 370, 343, 301; HRMS calcd for $C_{28}H_{47}N_5O_4Si_2$ 573.3166, found 573.3173. (i) **9-(2,3-*O*-Isopropylidene-*β*-D-ribofuranosyl)-2-(2,5-dimethylpyrrol-1-yl)purin-6-one (2i).** Mp 184−186 °C; UV (MeOH) max 254 nm (ϵ 11 800), 276 nm (ϵ 8600), min 232 nm (ϵ 6200), 267 nm (ϵ 8300); ^{1}H NMR ($CDCl_3$) δ 1.38 (s, 3H), 1.63 (s, 3H), 2.27 (s, 6H), 3.73 (d, J = 12.2 Hz, 1H), 3.92 (d, J = 12.2 Hz, 1H), 4.46 (s, 1H), 5.02 (d, J = 5.9 Hz, 1H), 5.09 (dd, J = 3.9, 5.9 Hz, 1H), 5.82 (s, 1H), 5.86 (s, 2H), 6.03 (d, J = 3.9 Hz, 1H), 8.26 (br s, 1H), 11.30 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 12.7, 25.1, 27.0, 61.5, 81.2, 84.1, 86.8, 89.9, 108.1, 113.1, 123.0, 129.0, 139.2, 145.4, 147.5, 157.0; EI-MS *m*/*z* 401 ([M$^+$] 75%), 386, 268, 229 (100%), 212; HRMS calcd for $C_{19}H_{23}O_5N_5$ 401.1699, found 401.1707. (j) **9-(5-*O*-*tert*-Butyldimethylsilyl-2,3-*O*-isopropylidene-*β*-D-ribofuranosyl)-2-(2,5-dimethylpyrrol-1-yl)purin-6-one (2j).** UV (MeOH) max 254 nm (ϵ 12 800), 277 nm (ϵ 11 000), min 231 nm (ϵ 8800), 267 nm (ϵ 10 300); ^{1}H NMR ($CDCl_3$) δ 0.057 (s, 3H), 0.063 (s, 3H), 0.87 (s, 9H), 1.37 (s, 3H), 1.61 (s, 3H), 2.31 (s, 6H), 3.80 (dd, J = 3.4, 11.4 Hz, 1H), 3.88 (dd, J = 2.9, 11.2 Hz, 1H), 4.40−4.43 (m, 1H), 4.86 (dd, J = 2.4, 5.9 Hz, 1H), 5.03 (dd, J = 2.9, 5.9 Hz, 1H), 5.91 (s, 2H), 6.12 (d, J = 2.9 Hz, 1H), 8.08 (s, 1H), 11.90 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ −6.0, −5.9, 12.7, 17.9, 24.9, 25.5, 26.8, 63.2, 80.8, 84.8, 86.3, 90.6, 108.8, 113.7, 122.4, 128.8, 138.3, 145.2, 147.7, 158.1; EI-MS *m*/*z* 515 ([M$^+$] 65%), 500, 458, 440, 400, 312 (100%), 83; HRMS calcd for $C_{25}H_{37}O_5N_5Si$: 515.2564, found: 515.2569. (k) **5′-*O*-Acetyl-2′,3′-*O*-isopropylideneguanosine (1k).** Ac_2O (7 mL) was added to a suspension of 2′,3′-*O*-isopropylideneguanosine (3.0 g, 9.3 mmol) in dried pyridine (20 mL). The mixture was stirred at ambient temperature overnight and then concentrated in vacuo. The residue was suspended in MeOH and deposited on a silica gel column. Elution (EtOAc/MeOH, 10:1 → 1:1) gave material that was recrystallized (MeOH) to give **1k** (1.46 g, 43%) as a white powder: mp > 250 °C; UV (MeOH) max 255 nm (ϵ 14 500), min 222 nm (ϵ 2800); ^{1}H NMR (DMSO-d_6) δ 1.33 (s, 3H), 1.53 (s, 3H), 2.02 (s, 3H), 4.04−4.32 (m, 3H), 5.17 (dd, J = 3.4, 6.3 Hz, 1H), 5.30 (dd, J = 1.7, 6.1 Hz, 1H), 6.06 (d, J = 1.8 Hz, 1H), 6.34 (br s, 2H), 7.91 (s, 1H), 10.87 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 20.6, 25.3, 27.0, 64.2, 81.2, 83.7, 84.3, 88.4, 113.4, 117.0, 136.4, 150.6, 153.8, 156.9, 170.2; FAB-MS (glycerol) *m*/*z* 366 ([M + H$^+$] 100%); HRMS calcd for $C_{15}H_{20}O_6N_5$ 366.1413, found 366.1408. (l) **9-(5-*O*-Acetyl-2,3-*O*-isopropylidene-*β*-D-ribofuranosyl)-2-(2,5-dimethylpyrrol-1-yl)purin-6-one (2k).** UV (MeOH) max 254 nm (ϵ 11 700), 277 nm (ϵ 9900), min 232 nm (ϵ 8600), 267 nm (ϵ 9400); ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 3H), 1.61 (s, 3H), 2.00 (s, 3H), 2.30 (s, 6H), 4.22 (dd, J = 5.4, 12.1 Hz, 1H), 4.27 (dd, J = 3.7, 11.9 Hz, 1H), 4.87 (dd, J = 3.4, 6.3 Hz, 1H), 5.23 (dd, J = 2.9, 6.3 Hz, 1H), 5.90 (s, 2H), 6.09 (d, J = 2.9 Hz, 1H), 7.92 (s, 1H), 11.87 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.9, 20.4, 25.9, 26.9, 63.5, 80.7, 83.8, 84.2, 90.0, 109.0, 114.8, 123.1, 129.0, 138.8, 145.5, 147.9, 158.1, 170.2; FAB-MS (glycerol) *m*/*z* 444 ([M + H$^+$] 100%), 443 ([M$^+$] 50%); HRMS calcd for $C_{21}H_{26}O_6N_5$ 444.1882, found 444.1886.

cytidine adducts was suggested by darkening of the color of the reaction mixtures and formation of insoluble resins on the surface of the flask. Analogous darkening and resin formation was observed with reactions of 3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyadenosine (**1f**) (entry 6), as was anticipated for a more thermally labile deoxynucleoside. However, in this case the pyrrole adduct **2f** was obtained in 15% yield (along with 28% of recovered starting material) when the reaction was conducted at 130 °C for 2 days.

Protection of the sugar hydroxyl groups as acetyl esters rather than as silyl ethers resulted in slightly higher yields when the temperature was controlled at ≤150 °C (entry 7). Although the TBS protecting group improves solubility, its hydrolytic stability under prolonged heating is limited. This condensation of a diketone with the amino function results in release of two molecules of superheated water into the reaction medium. Sublimation of TBSOH (entries 3, 6, 8, and 10) and formation of deprotected nucleoside **2b** (entry 3) was observed in some cases. In addition to its hydrolytic lability, migration of the TBS protecting group between O2′ and O3′ on the sugar moiety complicates some reactions, as observed with **1h** (entry 8). The combined yield (69%) of the 2′,5′- (**2h**) and 3′,5′-bis-*O*-TBS (**2h′**) isomers (1:1 ratio) is quite good, even though migration and hydrolysis of the silyl groups occurred.

It is noteworthy that 2′,3′-*O*-isopropylideneguanosine (**1i**) afforded the soluble 2,5-dimethylpyrrole adduct **2i** in 47% yield (entry 9). Addition of a 5′-*O*-TBS group did not improve the yield of condensation product (entry 10) and instead resulted in formation of a complex reaction mixture from which **2j** was isolated in 23% yield. The acetyl-protected derivatives **1d**,**g**,**k** (entries 4, 7, and 11) were more stable than the corresponding TBS ethers **1c**,**f**,**j** (entries 3, 6, and 10) under the reaction conditions, which resulted in higher condensation yields with the acetate esters. As expected, nucleosides with lower thermal stability such as analogues with double bonds, oxirane rings, or carbonyl substituents in the sugar moiety underwent decomposition and failed to give pyrrole-adduct products. No improvements in yields or reaction times were observed upon addition of molecular sieves to certain reaction mixtures, but no serious attempt has been made to optimize the procedure or yields.

^{1}H and ^{13}C NMR spectra of our adducts have only one set of pyrrole methyl signals.[15] This suggests that either the barrier to rotation around the C−N bond in these 2- or 6-purinyl derivatives of 2,5-dimethylpyrrole is too low to give rise to rotational isomers[16] with significant lifetimes or anisotropic effects of the sugar moiety are similar on the opposite faces of the purine ring (see ref 15 for selected data for **1k** and **2a**−**k**).

Cleavage of the pyrrole ring (deprotection of the amino function) was complete within 3 h at ambient temperature with TFA/H_2O (9:1). Acetyl esters were stable under these conditions, but TBS and isopropylidene groups were removed concomitantly.

In summary, condensation of adenine and guanine nucleosides with 2,5-hexanedione provides convenient protection of the heterocyclic amino group. This represents valuable methodology for generation of the more soluble 2,5-dimethylpyrrole derivatives of these purine compounds, which are stable in the presence of basic reagents but are cleaved readily with TFA/H_2O. Addition of carbene species to unsaturated-sugar nucleoside analogues protected as 2,5-dimethylpyrrole adducts and chemistry of the resulting spirocyclopropane compounds will be reported.

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