Synthetic Transformations of Transient Purinyl Radicals: Formation of Mono- and Diarylated and Heteroarylated Nucleosides[1]

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Photolysis of 2,6-dihalogenated purine nucleosides produced, through cleavage of the carbon–halogen bond, both purin-2-yl and purin-6-yl radicals (or caged radical pairs) which were intercepted by aromatic solvents such as benzene to produce 2-aryl- or 2,6-diarylpurine nucleosides. Heteroarylations and their selectivities involving pyrrole, thiophene, furan, and pyridine systems were also explored. In all cases, except for the "π-deficient" pyridine, the photoinduced heteroarylations were regiospecific and the products photostable. Photoinduced hydration of 2-substituted 6-chloropurine nucleosides provides an excellent approach for the synthesis of uncommon 2-substituted inosine analogues. High-field ^{13}C NMR data suggest that the 2,6-disubstituted purine nucleosides prefer the anti conformation in solution.

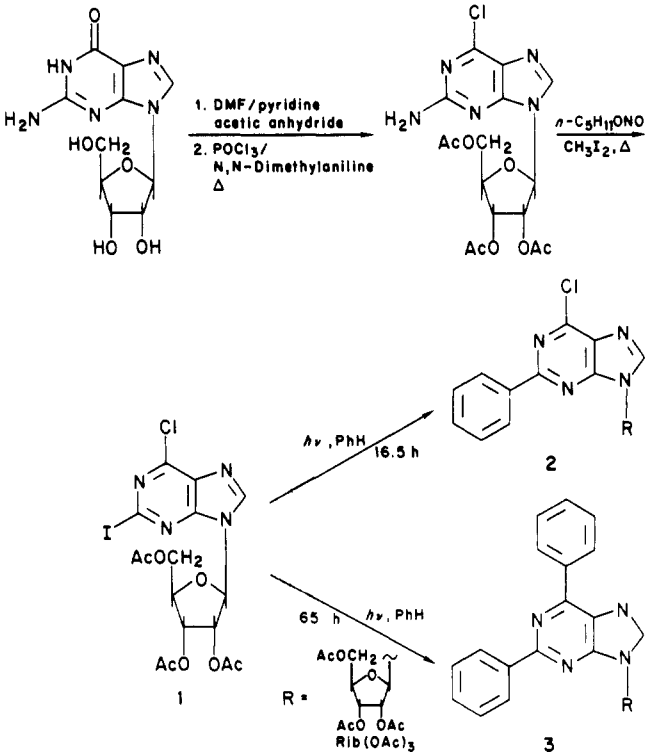
Transient purinyl radicals or the corresponding radical pairs are cleanly produced when 6-iodopurines are photolyzed with ultraviolet light.[2] The intermediacy of such radicals has also been inferred in previous studies from our laboratory on the reductive deamination and the halogenative deamination of 6-aminopurines.[3-5] Photochemically generated purinyl radicals or their equivalent provide an excellent synthetic approach to specific arylated and heteroarylated purines. This paper reports on the synthesis and the physical properties of these uncommon purine derivatives.

Few general methods for the introduction of aryl groups at carbon-6 in purine nucleosides are known. Taylor and Martin have reported that a suitable leaving group at C-6 can be displaced by an alkylidenephosphorane and the resulting ylide can be converted by hydrolysis or by reaction with a carbonyl to the 6-aralkyl or 6-aralkenyl derivative.[6] Bergstrom and Reddy recently reported[7] that the nickel-catalyzed coupling between aryl-Grignard reagents and protected 6-chloropurine nucleosides gives, in moderate yields, the corresponding 6-aryl nucleosides. A good general method for the introduction of aryl groups at the 2-position of purines is not known, although synthesis of 2-arylpurines has been accomplished by ring closure of imidazole intermediates with aldehydes.[8,9]

Results and Discussion

Homolysis of the aryl carbon–iodine bond (dissociation energy ~65 kcal/mol) to produce free or caged aryl radicals which subsequently react with aromatic or heteroaromatic substrates to produce biaryls or phenyl-substituted heterocyclic products has been investigated.[10-13] Light-induced homolysis of the carbon–halogen bond has been reported to occur for certain halopyrimidines.[14]

Scheme I. Photolytic Arylation Reactions of 2,6-Dihalogenated Purine Nucleoside



Some arylpyrimidines have been synthesized by this method.[15-18] We have reported previously that photolysis of 6-iodopurines in benzene or in heteroaromatic compounds results in the formation of 6-arylated or 6-heteroarylated purines.[2] In this paper we present examples of the selectivity that can be achieved in these reactions as well as some representative examples of 2-arylated and 2,6-diarylated and heteroarylated purine derivatives. A new approach to the synthesis of 2-substituted inosines is also mentioned.

The starting compound for these photoinduced transformations was 2-iodo-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (1) which was prepared from guanosine as previously described by us (Scheme I).[5,19]

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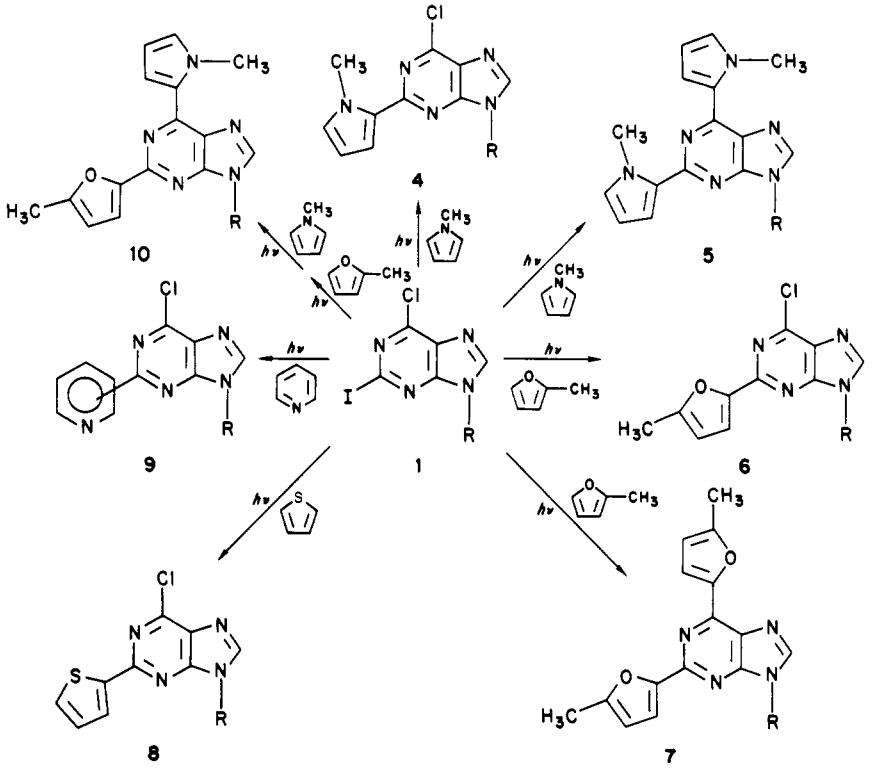
Scheme II. Photoinduced Heteroarylations Involving Purinyl Radicals[a]



[a] R = Rib(OAc)$_3$.

Photolysis of **1** in dry, nitrogen-purged benzene (Hanovia 450-W mercury lamp, Vycor filter) for 25 h gave 2-phenyl-6-chloronebularine (**2**) (59%) and 2,6-diphenylnebularine (**3**) (21%) (Scheme I). Compound **2** was characterized by its mass spectrum [m/z 488 (M^+, ^{35}Cl), 490 (M^+, ^{37}Cl)], by its high-field ^1H and ^{13}C NMR data which showed the attachment of the phenyl ring on the purine base, and by its UV spectrum which was consistent with the presence of a phenyl ring conjugated to the purine system. 2,6-Diphenylnebularine (**3**) was similarly characterized by its spectral data.

Selectivity in the formation of **2** or **3** can be achieved by controlling reaction times. Thus, when **1** was photolyzed in benzene for 16.5 h, compound **2** was the sole product and was isolated in 80% yield. Longer reaction times resulted in increased formation of **3**, until at 65 h, compound **3** was the only isolable product. These arylations could be monitored very conveniently by mass spectrometry.

Extension of these reactions to photoinduced heteroarylations involving both π-excessive and π-deficient systems was also investigated. Thus, when **1** was allowed to react with *N*-methylpyrrole under photolysis (Hanovia 450-W mercury lamp, Vycor filter) for 2 h, 2,6-bis(*N*-methylpyrr-2-yl-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)-purine (**5**) was isolated in 61.4% yield as the sole product (Scheme II). Compound **5** was found to be photostable as reaction times of up to 11 h gave similar yields and no photorearranged products. It was identified by its mass spectrum [m/z 536 (M^+)], by its ^1H and ^{13}C NMR spectra, and by its bathochromically shifted UV spectrum [λ_{max} 331.5 nm (ϵ 3.1 × 10^4) (ethanol)]. Compound **5** exhibited interesting fluorescence properties, emitting at 450 nm when excited at 330 nm. The absence of the monoheteroarylated product **4** in this reaction involving relatively short reaction times can be explained by the increased reactivity of the π-excessive pyrrole ring compared to benzene. However, formation of the monoheteroarylated product can be maximized with the use of lower intensity light. Thus, when **1** was photolyzed in *N*-methylpyrrole for 2 h (Rayonet, 2537 Å), 2-(*N*-methylpyrr-2-yl)-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (**4**) was isolated in 63% yield, along with a 24% yield of **5**. The position of substitution on the pyrrole ring in **4** (and also **5**) was deduced from the high-field ^1H NMR spectrum (in $CDCl_3$) which showed H-3 of the pyrrole moiety as a doublet of doublets at δ 8.19 with $J_{3,4}$ = 3.9 Hz and $J_{3,5}$ = 1.8 Hz. The downfield shift of this proton from 6.11 ppm in *N*-methylpyrrole is consistent with heteroarylation at the 2-position of the pyrrole ring.[2] The observed coupling constants, particularly $J_{3,4}$, are characteristic of 2-substituted pyrroles.[20]

Photolysis of **1** in 2-methylfuran as solvent for 6 h gave the monoheteroarylated product **6** in 71% yield together with a trace amount of the 2,6-bis(5-methylfur-2-yl)purine nucleoside **7** (Scheme II). The regiochemistry of the reaction was again apparent from the high-field ^1H NMR data. Formation of the heteroarylated product **8** (75%) was achieved by photolysis of **1** in dry thiophene in the Hanovia apparatus for 7 h. Previous studies of radical attack on the thiophene ring system has shown the formation of both the α- and β-substituted thiophenes.[21] 2-Arylthiophenes have been converted photochemically to 3-arylthiophenes.[22] The "purinyl radical" reaction on thiophene appears to be regiospecific for the α-position to form a very photostable product. The use of longer reaction times in both this and the furan case resulted in

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Table I. Correlation of Conformation with Carbon Chemical Shifts (δ) of 2,6-Disubstituted Purine Nucleosides

compound	solvent	C1′	C2′	C3′	C4′	C5′	Δ(C2′–C3′)	confmtn
adenosine	Me_2SO-d_6	87.9	73.4	70.6	85.8	61.6	2.8	anti
inosine[c]	Me_2SO-d_6	87.6	74.2	70.4	85.7	61.4	3.8	anti
8-bromoinosine[c]	Me_2SO-d_6	90.5	71.2	70.5	86.3	61.9	0.7	syn
tri-*O*-acetylinosine[a]	$CDCl_3$	86.5	73.3	70.5	80.3	63.0	2.8	anti
8-bromotri-*O*-acetyladenosine[b]	$CDCl_3$	88.9	71.8	70.4	79.8	62.8	1.4	syn
1	$CDCl_3$	86.7	73.3	70.5	80.8	62.9	2.8	anti
2	$CDCl_3$	82.3	73.2	70.1	80.1	62.6	3.1	anti
3	$CDCl_3$	87.0	73.2	70.2	80.0	62.7	3.0	anti
4	$CDCl_3$	87.0	73.1	70.0	80.8	62.6	3.1	anti
5	$CDCl_3$	86.5	73.1	70.2	79.8	62.7	2.9	anti
6	$CDCl_3$	87.5	73.5	70.3	80.4	62.8	3.2	anti
8	$CDCl_3$	87.7	73.4	70.3	80.2	62.8	3.1	anti
10	$CDCl_3$	86.9	73.5	70.5	80.2	63.1	3.0	anti
11	Me_2SO-d_6	87.2	73.9	70.3	85.5	61.2	3.6	anti

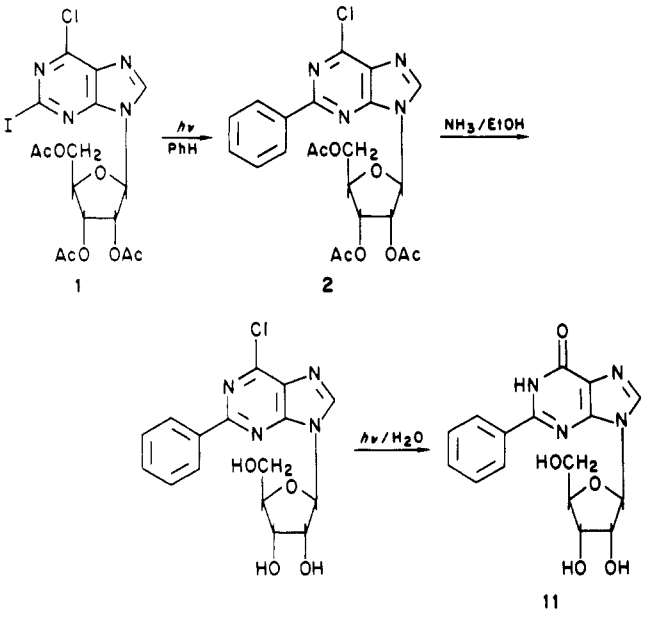
[a] Prepared from photolysis of 6-iodo-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine in wet CH_3CN. [b] Prepared by the procedure in ref 27. [c] Data from ref 26.

considerable polymerization of the photosolvents and the diheteroarylated products could not be isolated and purified from this intractable mixture. The π-deficient heterocycle, pyridine, also participated in these heteroarylations, to give albeit a 14% yield of the isomerically mixed product **9** (Scheme II).

The 2-substituted 6-chloropurine nucleosides synthesized in this work are interesting synthetic intermediates as they can be modified further to produce some uncommon nucleosides. For example, photolysis in the same solvent produces the aforementioned symmetrical 2,6-disubstituted nucleosides. In the presence of a different solvent, unsymmetrical 2,6-substituted nucleosides are formed (e.g., Scheme II, compound **10**). Photolysis in the presence of water results in the formation of inosine analogues in excellent yields (e.g., Scheme III, compound **11**). This approach provides a direct method for the synthesis of a wide variety of 2-substituted inosine derivatives.

Finally, it should be mentioned that determination of the glycosidic bond conformation of purine nucleosides in solution is of considerable importance in the correlation of their stereochemistry with biological activity. The syn and anti conformations of natural nucleosides in solution have been determined by potential energy calculations,[23] circular dichroism,[24] and ^1H and ^{13}C NMR spectroscopy.[25,26] The data from these studies have shown that adenosine, guanosine, and inosine all prefer the anti conformation in solution. Most purine nucleoside analogues that have been studied are 8-substituted adenosines which have been shown to prefer the syn conformation in solution. Few examples of 2,6-disubstituted purine nucleoside analogues have been investigated. The purpose of this study was to provide such conformational information and also to emphasize that high-field ^{13}C NMR data can be used very effectively to determine the glycosidic conformation in solution. In the syn conformation, the proximity of the lone pair of electrons on N-3 to C-2′ results in an upfield shift of this carbon in syn compared to the anti conformation. The only other carbon resonance that changes significantly in the carbohydrate portion of the molecule is the anomeric carbon (C-1′), and its chemical shift is largely dependent on the structure of the base and not its conformation. When differences between the chemical shifts of C-2′ and C-3′ are examined, it is clear that in the syn conformation Δ(C2′–C3′) is <1.4 ppm whereas in the anti conformation this difference is ≳3.0 ppm. The results are shown in Table I and suggests that the 2,6-disubstituted purine nucleosides prefer the anti conformation in solution.

Scheme III. Synthesis of 2-Substituted Inosine Analogues



In summary, facile arylations and heteroarylations at the 2- and 2,6-positions of purine nucleosides can be achieved through the intermediacy of reactive transient purinyl radicals. The reactivities of the aromatic or heteroaromatic solvents used follow the order π-excessive (pyrrole, furan, thiophene) > benzene > π-deficient (pyridine). Except in the case of pyridine, the conversions were regiospecific. Although the genesis of the purinyl radicals (or caged radical pairs) is not fully understood, a plausible mechanism in the case of arylations and heteroarylations may involve initial formation of an exciplex followed by electron transfer and cleavage of the C–I bond of the resulting radical anion. This type of mechanism may not be operating in the hydration reaction.

Experimental Section

Irradiation was accomplished in a Hanovia 450-W mercury photolysis apparatus or in a Rayonent photochemical reactor.

Melting points are uncorrected and were determined on a Thomas-Hoover melting point apparatus fitted with a microscope. Nuclearmagnetic resonance spectra employing tetramethylsilane as the internal standard were recorded on JEOL Model FX90Q

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and Bruker Model WM360 pulse fourier transform spectrometers. Mass spectra at 30 eV were obtained on a Hewlett-Packard 5985 GC–mass spectrometer. The ultraviolet spectra were recorded on a Varian-Cary Model 219 spectrophotometer. Fluorescence spectra are uncorrected and were performed on an Aminco-Bowman Spectrophotofluorimeter using a xenon lamp. *N*-Methylpyrrole, 2-methylfuran (Aldrich), benzene (MCB Omnisolv), and pyridine (MCB) were distilled prior to use; thiophene (Aldrich) was used without further purification. Preparative-layer chromatography employed EM silica gel PF_{254} plates, activated for 3 h at 135 °C.

2-Iodo-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (1) was prepared by using literature procedures.[5,19] Guanosine was transformed by initial treatment with pyridine, acetic anhydride, and dimethylformamide to 2′,3′,5′-tri-*O*-acetylguanosine.[19] The protected guanosine was allowed to react with phosphoryl chloride, *N*,*N*-dimethylaniline, acetonitrile, and tetraethylammonium chloride to provide 2-amino-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine.[19] Treatment of the 2-amino-6-chloropurine nucleoside with *n*-pentyl nitrite and diiodomethane[5] gave **1** (83% yield, 66% overall yield from guanosine) as white cyrstals: mp 181–183 °C (lit.[5] mp 181–183 °C); ^{13}C NMR ($CDCl_3$) δ 20.4, 20.5, 20.8, 62.9, 70.5, 73.3, 80.8, 86.7, 116.9, 132.2, 143.4, 150.7, 151.9, 169.4, 169.5, 170.2; ^{1}H NMR ($CDCl_3$) δ 2.11 (s, 3 H), 2.13 (s, 3H), 2.18 (s, 3 H), 4.43 (m, 3 H), 5.65 (t, 1 H), 5.81 (t, 1 H), 6.23 (d, 1 H), 8.27 (s, 1 H); UV (MeOH) λ_{max} 222.5 nm (ε 2.1 × 10^4), 258 (ε 6.6 × 10^3), 281 (ε 9.3 × 10^3); mass spectrum, *m*/*z* (relative intensity) 540 (M$^+$, 1.0), 538 (M$^+$, 2.1), 283 (6.6), 282 (2.3), 281 (15.3), 280 (2.3), 259 (68.7), 139 (100.0).

2-Phenyl-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (2). To 300 mL of dry benzene was added 0.284 g (0.527 mmol) of 2-iodo-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (**1**). The solution was transferred to a Hanovia photochemical reactor, purged with nitrogen, and photolyzed for 16.5 h by employing a 450-W mercury UV source with a Vycor glass sleeve filter. The solvent was then removed (40 °C, reduced pressure) and the residue chromatographed on silica gel plates. After elution with 7:3 ethyl acetate:hexane, the band at R_f 0.63 afforded 0.207 g (0.423 mmol, 80.3%) of **2** as a light yellow low melting solid: ^{13}C NMR ($CDCl_3$) δ 20.4, 20.5, 20.6, 62.6, 70.1, 73.2, 80.1, 82.3, 128.6, 128.7, 131.1, 136.3, 143.7, 151.5, 151.9, 159.9, 169.3, 169.4; ^{1}H NMR ($CDCl_3$) δ 1.96 (s, 3 H), 2.11 (s, 3 H), 2.18 (s, 3 H), 4.40 (m, 3 H), 5.85 (t, 1 H), 6.12 (t, 1 H), 6.24 (d, 1 H), 7.49–7.46 (m, 3 H), 8.25 (s, 1 H), 8.53–8.46 (m, 2 H); UV (EtOH) λ_{max} 236 nm (ε 1.7 × 10^4), 286 (ε 1.6 × 10^4), 274 (ε 1.5 × 10^4); fluorescence (EtOH) excitation 325 nm and emission 382 nm; mass spectrum, *m*/*z* (relative intensity) 490 (M$^+$, 1.1), 488 (M$^+$, 2.8), 259 (sugar$^+$, 37.8), 233 (5.4), 232 (3.4), 231 (17.1), 230 (3.8), 229 (Pur$^+$, 1.0), 199 (1.3), 196 (1.8), 195 (7.5), 194 (Pur$^+$ – Cl, 0.9), 157 (12.6), 139 (100).

2,6-Diphenyl-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (3). A solution consisting of 0.072 g (0.134 mmol) of **1** in 90 mL of dry benzene was photolyzed as described for **2** for 65 h. Separation on silica gel plates with 7:3 ethyl acetate:hexane as the developing solvent gave 0.042 g (0.078 mmol, 58.2%) of **3** as a light yellow low melting solid: ^{13}C NMR ($CDCl_3$) δ 20.4, 20.5, 20.6, 62.7, 70.2, 73.2, 80.0, 87.0, 128.5, 128.6, 130.0, 130.3, 131.1, 135.8, 138.0, 142.9, 152.8, 154.9, 159.2, 169.4, 169.5, 170.4; ^{1}H NMR ($CDCl_3$) δ 1.97 (s, 3 H), 2.11 (s, 3 H), 2.19 (s, 3 H), 4.41 (m, 3 H), 5.93 (t, 1 H), 6.20 (t, 1 H), 6.29 (d, 1 H), 7.59–7.48 (m, 6 H), 8.23 (s, 1 H), 8.66 (m, 2 H), 8.86 (m, 2 H); UV (EtOH) λ_{max} 266 nm (ε 2.7 × 10^4), 310 (ε 1.0 × 10^4); fluorescence (EtOH) excitation 322 nm and emission 375 nm; mass spectrum, *m*/*z* (relative intensity) 530 (M$^+$, 4.2), 471 (M$^+$ – $C_2H_3O_2$, 2.2), 301 (Pur$^+$ + CH_2O, 10.6), 274 (9.6), 273 (48.9), 272 (13.1), 271 (Pur$^+$, 2.0), 259 (sugar$^+$, 11.7), 199 (1.3), 157 (12.3), 139 (100).

2-(*N*-Methylpyrr-2-yl)-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (4). A N_2-purged solution of 0.103 g (0.192 mmol) of **1** in 65 mL of dry *N*-methylpyrrole was photolyzed in a quartz reaction vessel for 2 h by using a Rayonet photochemical reactor (2537-Å lamps). The solvent was removed (40 °C, reduced pressure) and the residue was chromatographed on silica gel plates (3:2 ethyl acetate:hexane).

The band at R_f 0.55 gave 0.058 g (0.118 mmol, 61.5%) of **4** as a light brown glass: ^{13}C NMR ($CDCl_3$) δ 20.4, 20.5, 20.6, 38.1, 62.6, 70.0, 73.1, 80.8, 87.0, 108.4, 116.5, 128.8, 129.1, 129,8, 142.6, 150.5, 151.7, 155.2, 169.2, 169.4, 170.3; ^{1}H NMR ($CDCl_3$) δ 2.05 (s, 3H), 2.10 (s, 3 H), 2.15 (s, 3 H), 4.10 (m, 3 H), 4.42 (s, 3 H), 5.69 (t, 1 H), 6.23–5.90 (m, 3 H), 6.79 (dd, 1 H), 8.17 (s, 1 H), 8.19 (dd, 1 H); UV (EtOH) λ_{max} 337 nm (ε 1.1 × 10^4), 298 (ε 1.0 × 10^4), 245 (ε 8.9 × 10^3); fluorescence (EtOH) excitation 355 nm and emission 440 nm; mass spectrum, *m*/*z* (relative intensity) 493 (M$^+$, 5.8), 491 (M$^+$, 15.9), 259 (sugar$^+$, 8.5), 235 (19.6), 234 (23.2), 233 (55.7), 232 (Pur$^+$, 32.9), 199 (2.9), 157 (14.1), 139 (100).

The band with R_f 0.72 gave 0.025 g (0.046 mmol, 24.0%) of **5**.

2,6-Bis(*N*-methylpyrr-2-yl)-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (5). A solution consisting of 0.187 g (0.347 mmol) of **1** and 75 mL of dry *N*-methylpyrrole was made and photolyzed for 2 h as described for **2**. Separation on silica gel plates with 7:3 ethyl acetate:hexane afforded 0.114 g (0.213 mmol, 61.4%) of **5** as a beige low melting solid: ^{13}C NMR ($CDCl_3$) δ 20.3, 20.5, 20.6, 37.7, 38.3, 62.7, 70.2, 73.1, 79.8, 86.5, 107.9, 108.9, 114.9, 119.5, 127.0, 127.3, 127.5, 129.2, 132.0, 140.6, 150.0, 151.0, 154.7, 169.1, 169.4, 170.3; ^{1}H NMR ($CDCl_3$) δ 2.07 (s, 3 H), 2.08 (s, 3 H), 2.13 (s, 3 H), 4.12 (s, 3 H), 4.23 (s, 3 H), 4.39 (m, 3 H), 5.61 (t, 1 H), 6.33–6.04 (m, 4 H), 6.76 (dd, 1 H), 6.86 (dd, 1 H), 7.12 (dd, 1 H), 7.80 (dd, 1 H), 8.11 (s, 1 H); UV (EtOH) λ_{max} 331.5 nm (ε 3.1 × 10^4); fluorescence (EtOH) excitation 330 nm and emission 450 nm; mass spectrum, *m*/*z* (relative intensity) 538 (1.1), 537 (5.5), 536 (M$^+$, 15.8), 279 (12.8), 278 (38.9), 277 (Pur$^+$, 100.0), 259 (sugar$^+$, 1.4), 199 (1.3), 197 (Pur$^+$ – C_5H_6N, 1.1), 157 (9.0), 139 (67.7).

2-(5-Methylfur-2-yl)-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (6). A solution consisting of 0.113 g (0.210 mmol) of **1** and 60 mL of dry 2-methylfuran was photolyzed for 6 h as described for **4**. Silica gel chromatography with 7:3 ethyl acetate:hexane as the developer provided two bands.

The band at R_f 0.47 gave 0.073 g (0.148 mmol, 70.5%) of **6** as a golden low melting solid: ^{13}C NMR ($CDCl_3$) δ 14.1, 20.4, 20.5, 20.6, 62.8, 70.3, 73.5, 80.4, 87.5, 109.1, 116.2, 130.0, 143.4, 149.5, 151.6 151.6, 152.5, 156.3, 169.3, 169.4, 170.3; ^{1}H NMR ($CDCl_3$) δ 2.02 (s, 3 H), 2.12 (s, 3 H), 2.17 (s, 3 H), 2.46 (s, 3 H), 4.46 (m, 3 H), 6.20–5.70 (m, 4 H), 7.37 (d, 1 H, *J* = 3.0 Hz), 8.18 (s, 1 H); UV (EtOH) λ_{max} 324 nm (ε 1.5 × 10^4), 302 (ε 1.3 × 10^4), 245 (ε 7.8 × 10^3); fluorescence (EtOH) excitation 340 nm and emission 410 nm; mass spectrum, *m*/*z* (relative intensity) 494 (M$^+$, 0.7), 492 (M$^+$, 1.8), 259 (sugar$^+$, 7.0), 237 (4.7), 236 (12.5), 235 (14.1), 234 (33.7), 233 (Pur$^+$, 2.9), 199 (4.2), 157 (12.4), 139 (100.0).

The band with R_f 0.66 afforded 0.004 g of 2,6-bis(5-methylfur-2-yl)-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (**7**). Compound **7** was only characterized by its mass spectrum, *m*/*z* (relative intensity) 538 (M$^+$, 15.9), 282 (5.6), 281 (30.1), 280 (91.2), 279 (Pur$^+$, 4.7), 259 (sugar$^+$, 7.8), 199 (3.0), 157 (14.7), 139 (100.0).

2-(Thien-2-yl)-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (8). To 60 mL of dry thiophene was added 0.235 g (0.436 mmol) of **1**. The solution was photolyzed as for **2** for 7 h. Separation gave 0.162 g (0.327 mmol, 75.0%) of **8** as a low melting light yellow glass: ^{13}C NMR ($CDCl_3$) δ 20.4, 20.5, 20.6, 62.8, 70.3, 73.4, 80.2, 87.7, 128.4, 130.0, 130.4, 141.9, 143.8, 151.3, 151.7, 156.3, 169.3, 169.4, 170.2; ^{1}H NMR ($CDCl_3$) δ 2.01 (s, 3 H), 2.12 (s, 3 H), 2.18 (s, 3 H), 4.43 (m, 3 H), 6.20–5.86 (m, 3 H), 7.14 (dd, 1 H, *J* = 3.0, 3.9 Hz), 7.40 (d, 1 H, *J* = 3.9 Hz), 8.10 (d, 1 H, *J* = 3.0 Hz), 8.23 (s, 1 H); UV (EtOH) λ_{max} 316 nm (ε 1.4 × 10^4), 270 (ε 6.5 × 10^3), 245 (ε 9.2 × 10^3); fluorescence (EtOH) excitation 331 nm and emission 378 nm; mass spectrum, *m*/*z* (relative intensity) 496 (M$^+$, 1.4), 494 (M$^+$, 3.5), 259 (sugar$^+$, 22.6), 239 (3.0), 238 (3.8), 237 (7.5), 236 (Pur$^+$, 8.4), 203 (2.0), 202 (1.7), 201 (Pur$^+$ – Cl, 8.9), 199 (1.3), 157 (14.3), 139 (100.0).

2-Pyridyl-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (9). A solution consisting of 0.127 g (0.236 mmol) of **1** and 50 mL of dry pyridine was photolyzed for 24 h as described for **4** to give 0.016 g (0.033 mmol, 14.0%) of the mixture **9** as a brown oil: UV (EtOH) λ_{max} 232 nm, 288, 321; mass spectrum, *m*/*z* (relative intensity) 491 (M$^+$, 0.9), 489 (M$^+$, 2.1), 259 (46.8), 234 (14.0), 233 (8.2), 232 (44.0), 231 (8.7), 230 (Pur$^+$, 0.7), 199 (1.3), 157 (14.1), 139 (100.0).

2-(5-Methylfur-2-yl)-6-(*N*-methylpyrr-2-yl)-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine (10). A solution consisting of 0.087 g (0.177 mmol) of **6** and 50 mL of dry *N*-methylpyrrole was photolyzed for 3 h as described for **2**. Separation afforded 0.052 g (0.097 mmol, 54.8%) of **10** as a light brown low melting glassy solid: ^{13}C NMR (CDCl3) δ 14.0, 20.4, 20.5, 20.7, 38.4, 63.1,

70.5, 73.5, 80.2, 86.9, 108.4, 109.0, 113.8, 119.6, 127.0, 127.6, 130.0, 141.4, 150.0, 151.2, 151.3, 151.8, 154.7, 169.4, 170.4; ^{1}H NMR ($CDCl_3$) δ 2.03 (s, 3 H), 2.10 (s, 3 H), 2.15 (s, 3 H), 2.44 (s, 3 H), 4.27 (s, 3 H), 4.48 (m, 3 H), 6.33-6.01 (m, 5 H), 6.88 (dd, 1 H), 7.22 (d, 1 H, J = 2.9 Hz), 7.82 (dd, 1 H, J = 3.9, 1.8 Hz), 8.08 (s, 1 H); UV (EtOH) λ_{max} 310 nm (ϵ 3.0 × 10^4), 326 (ϵ 2.8 × 10^4), 336 (2.7 × 10^4), 352 (ϵ 2.4 × 10^4), 250 (ϵ 8.3 × 10^3); fluorescence (EtOH) excitation 350 nm and emission 400 nm; mass spectrum, m/z (relative intensity) 537 (M^+, 1.7), 308 ($Pur^+ + CH_2O$, 3.4), 280 (14.1), 279 (39.9), 278 (Pur^+, 100.0), 259 ($sugar^+$, 1.5), 199 (1.7), 157 (9.1), 139 (68.3).

2-Phenylinosine (11). To 50 mL of dry ethanol saturated with ammonia gas at ice-salt bath temperatures was added 0.267 g (0.546 mmol) of **2**. The solution was stirred at ice-salt bath temperatures for 1 h and at 25 °C for 23 h. The solvent was removed under reduced pressure and the residue was lyophilized. The deprotected nucleoside (0.186 g) in 400 mL of water was photolyzed as described for **2** for 34 h. The solvent was removed under reduced pressure and the residue chromatographed on silica gel plates that were developed in 4:1 ethyl acetate:methanol. The band at R_f 0.22 gave 0.157 g (0.455 mmol, overall yield = 83.4%) of **11** as a light yellow crystalline compound: mp 98-101 °C; ^{13}C NMR ($CDCl_3$) δ 61.2, 70.3, 73.9, 85.5, 87.2, 122.8, 127.8, 128.5, 131.2, 132.0, 139.2, 148.5, 153.3, 157.2; ^{1}H NMR ($CDCl_3$) δ 3.72-3.54 (m, 2 H), 4.20 (m, 1 H), 4.58 (m, 1 H), 5.14 (m, 1 H), 5.97 (d, 1 H, J = 5.9 Hz), 7.60 (m, 3 H), 8.12 (m, 2 H), 8.37 (s, 1 H), 11.2 (s, 1 H); UV (EtOH) λ_{max} 290 nm (ϵ 5.8 × 10^3), 260 (4.9 × 10^3); fluorescence (EtOH) excitation 366 nm and emission 456 nm; mass spectrum, m/z (relative intensity) 254 ($Pur^+ + C_3H_2O$, 10.9), 240 ($Pur^+ + CHO$, 20.0), 225 ($Pur^+ + CH_2$, 22.7), 213 (20.0), 212 (96.4), 211 (Pur^+, 42.7).

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Registry No. **1**, 5987-76-8; **2**, 71122-76-4; **3**, 92220-51-4; **4**, 90596-68-2; **5**, 92220-52-5; **6**, 92220-53-6; **7**, 92220-54-7; **8**, 90596-69-3; **9**, 92220-56-9; **10**, 92220-55-8; **11**, 32447-14-6; guanosine, 118-00-3; 2,3,5-tri-*O*-acetylguanosine, 6979-94-8; 2-amino-6-chloro-9β-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)purine, 16321-99-6; benzene, 71-43-2; *N*-methylpyrrole, 6973-60-0; 2-methylfuran, 534-22-5; thiophene, 110-02-1; pyridine, 110-86-1; 2-phenyl-6-chloro-9β-(ribofuranosyl)purine, 56489-65-7.

Cycloaddition Reactions of Strained Ring Systems. Photochemistry of 1-Phenyl-2-carbomethoxy-3,3-dimethylcyclopropene[1]

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The sensitized irradiation of 1-phenyl-2-carbomethoxy-3,3-dimethylcyclopropene produced two novel photodimers. The minor product can be explained in terms of an initial bond formation to give a diradical intermediate. Collapse of the diradical furnishes a tricyclohexane which undergoes a subsequent cycloreversion to give a 1,4-cyclohexadiene derivative. The major photodimer is derived by cyclopropyl ring opening of the initially produced diradical followed by cyclization to give a bicyclo[1.1.0]butane derivative. Direct irradiation of 1-phenyl-2-carbomethoxy-3,3-dimethylcyclopropene afforded a mixture of 1-carbomethoxy-3,3-dimethyl-1-phenylallene, 1-carbomethoxy-3-methyl-2-phenylbutadiene, and 2-carbomethoxy-3-methyl-1-phenylbutadiene. The formation of the three products can be rationalized in terms of a vinylcarbene intermediate which inserts into the adjacent methyl group. The product distribution favors cleavage of the carbomethoxy substituted σ-bond of the cyclopropene ring. This regioselectivity can be attributed to a funneling of the excited singlet state of the cyclopropene to the energy surface of the higher lying carbene state. The photochemical and thermal behavior of several hydroxyalkyl substituted cyclopropenes derived from 1-phenyl-2-carbomethoxy-3,3-dimethylcyclopropene was also studied and the results obtained were compared to the reactions in the carbomethoxy series.

Cyclopropene[2] was first prepared some 60 years ago but, despite its unusual structure exhibiting high Baeyer strain, the molecule received minimum attention until the late 1950s. Since that time chemical and theoretical interest has been considerable and a number of reviews have appeared describing the thermal[3] and photochemical behavior[4] of this highly strained class of hydrocarbons. Suitably substituted cyclopropenes suffer the ene reaction[5,6] and also readily undergo dimerization,[7-12] cycloaddition,[13,14] and complexation with transition metals[15] as a means of releasing strain. Our research group has been involved over the past few years in a program of synthesizing unusual polycyclic ring systems which makes use of the cycloaddition behavior of cyclopropenes as the primary strategy.[13] [4 + 2] cycloaddition across the double bond in cyclopropene proceeds quite readily since it reduces ring strain by 26 kcal/mol.[16,17] The transition-state energy for this reaction, however, is very sensitive to steric

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