Specificity of the 1-Methyladenine Receptors in Starfish Oocytes: Synthesis and Properties of Some 1,8-Disubstituted Adenines, 1,6-Dimethyl-1*H*-purine, and of the 1-(Azidobenzyl)adenines

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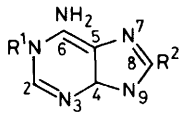
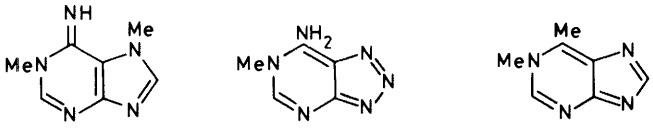
A selective synthesis of 1,6-dimethylpurine (**16**) and the preparations of the 1-(azidobenzyl)adenines (**11**)—(**13**), 8-azido-1-benzyladenine (**10**), and 1-methyladenine derivatives (**2**)—(**9**) with various 8-substituents (azido, chloro, bromo, amino, alkyl, and hydroxymethyl) are described. The syntheses were based upon the 1-alkylation of the corresponding 9-substituted purines followed by deprotection at N-9. The ability of those compounds to replace the hormone 1-methyladenine (**1**) in releasing meiosis inhibition in starfish oocytes was tested, and the earlier hypothesis about structure-activity relationships has been confirmed. The low level of activity of the 8-azido derivatives of 1-methyl- and 1-benzyl-adenines, probably due to blocking of the N-7, N-9 region and reduction of the pK_a value, precludes their use as photoaffinity labelling reagents for the receptors of 1-methyladenine. The active compounds 1-(4-azidobenzyl)adenine (**13**) and 1-(3-azidobenzyl)adenine (**12**) are possibly better candidates for this purpose.

In starfish, fully grown oocytes are arrested at the prophase stage of meiosis. Meiosis is reinitiated by the action of a relay hormone, 1-methyladenine[1] (**1**), produced by the follicle cells, under the influence of a hormonal peptide of neural origin.[2] It has been demonstrated that 1-methyladenine (**1**) controls meiosis by interacting with stereospecific receptors localized exclusively on the oocyte plasma membrane.[3] From studies of structure-activity relationships[4,5] for 1-methyladenine analogues, it has been concluded that substitution on N-1 and a cationic charge are prerequisites for inducing activity, while substitution in the 9- or 7-positions is detrimental to the interaction between the hormone and its receptors.

The isolation and characterization of 1-methyladenine receptors would benefit from the design of photoaffinity labelling reagents. In the adenine field, 8-azido derivatives have usually been the reagents of choice for this purpose.[6–8] Thus, a logical candidate for photoaffinity labelling the receptor sites of 1-methyladenine was 8-azido-1-methyladenine (**2**). No compounds with substituents in the 8-position of 1-methyladenine had been studied previously. We have synthesized and tested a series of 1-methyladenines (**2**)—(**9**) bearing 8-substituents differing in bulk, or electronic or solubility properties and thus offering the opportunity of examining the hypothesis that the hormone binds to the receptors in the N-7, N-9 region and acts through its protonated form. Because the 1-benzyl group had been found to be a better substituent for inducing activity than 1-methyl,[5] we also prepared 8-azido-1-benzyladenine (**10**). The three 1-(azidobenzyl)adenines (**11**)—(**13**) were synthesized as alternative potential photoaffinity labelling reagents. Additional information about structure-activity relationships for 1-methyladenine was gained by testing 1,7-dimethyladenine[9] (**14**), 1-methyl-8-aza-adenine[10] (**15**), and 1,6-dimethylpurine (**16**). This last compound was prepared by a separate route.



(**1**) R^1 = Me, R^2 = H
(**2**) R^1 = Me, R^2 = N_3
(**3**) R^1 = Me, R^2 = Cl
(**4**) R^1 = Me, R^2 = Br
(**5**) R^1 = Me, R^2 = NH_2
(**6**) R^1 = R^2 = Me
(**7**) R^1 = Me, R^2 = Et
(**8**) R^1 = Me, R^2 = Pr^i
(**9**) R^1 = Me, R^2 = $HOCH_2$
(**10**) R^1 = $PhCH_2$, R^2 = N_3
(**11**) R^1 = 2-$N_3C_6H_4CH_2$, R^2 = H
(**12**) R^1 = 3-$N_3C_6H_4CH_2$, R^2 = H
(**13**) R^1 = 4-$N_3C_6H_4CH_2$, R^2 = H

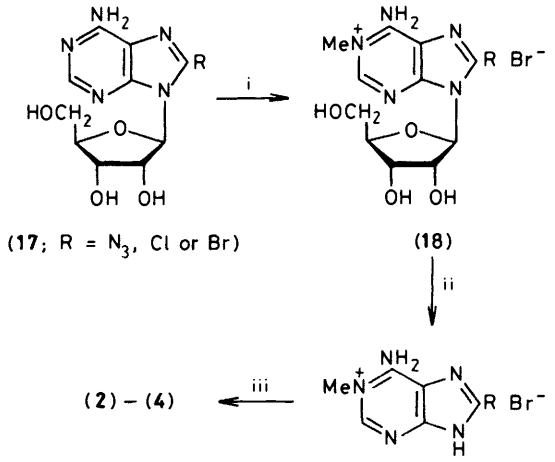


(**14**) (**15**) (**16**)

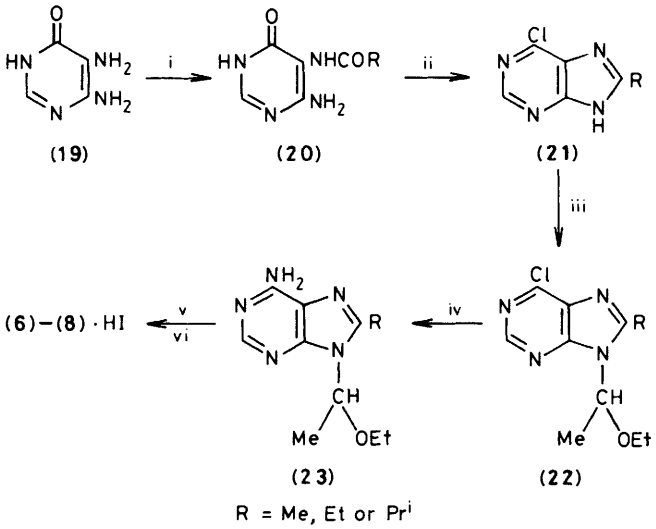
Results and Discussion

Synthesis.—Selective alkylation of adenine at N-1 had been found to be dependent on preliminary protection of N-9.[11] Since we assumed that an 8-substituent would not modify this directing effect, we selected a route for the synthesis of the 8-substituted 1-alkyladenines (**2**)—(**10**) involving alkylation of 8,9-disubstituted adenines. 8-Azido-1-methyladenine (**2**) and the 8-halogeno-1-methyladenines (**3**) and (**4**) were prepared from the corresponding 8-substituted adenosines[12,13] (**17**) and methyl bromide in dimethylacetamide (DMA) solution at 20 °C (Scheme 1). The salts (**18**) obtained as precipitates were heated in glacial acetic acid to cleave the ribosyl moiety.[14] Similarly, 8-azidoadenosine[12] reacted with benzyl bromide to give 8-azido-1-benzyladenine (**10**). 8-Amino-1-methyladenine (**5**) was isolated in good yield by catalytic hydrogenation of the azido analogue (**2**) over palladium on charcoal.

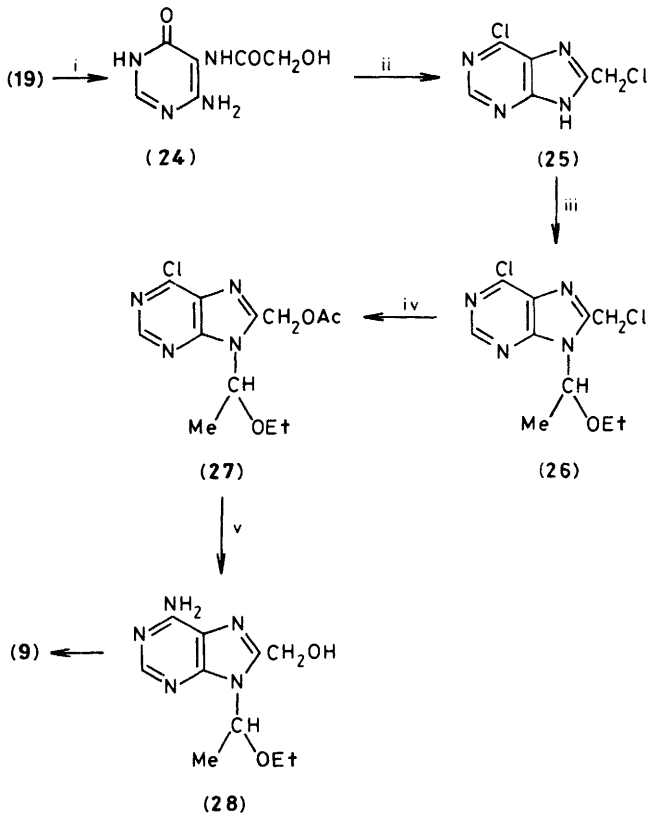
For the synthesis of the 8-alkyl-1-methyladenines (**6**)—(**8**), it was found to be necessary to introduce substituents initially into both the 8- and 9-positions of adenine by an indirect (Scheme 2) rather than a direct[15–17] route. The 5-acylamino-4-



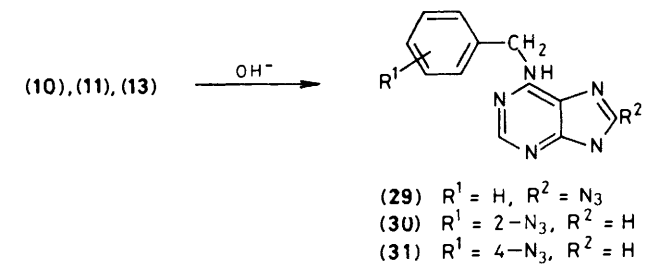
Scheme 1. *Reagents:* i, MeBr, DMA; ii, AcOH, 100 °C; iii, NH_3H_2O



Scheme 2. *Reagents:* i, RCO_2H; ii, $POCl_3$, $PhNEt_2$; iii, $MeCH(OEt)_2$ (acetal); iv, NH_3; v, MeI; vi, AcOH



Scheme 3. *Reagents;* i, $HOCH_2CO_2H$; ii, $POCl_3$, $PhNEt_2$; iii, $MeCH(OEt)_2$, heat; iv, AcONa, 20 °C; v, NH_3



Scheme 4.

amino-6-oxopyrimidines[18] (**20**), prepared by treatment of 4,5-diamino-6-oxopyrimidine (**19**) with aliphatic acids, were heated with phosphorus oxychloride and diethylaniline to effect both the cyclization of the imidazole ring and the introduction of the chloro group. Protection of N-9 in the chloropurines (**21**) by the ethoxyethyl group (EOE) was achieved by refluxing them in acetal;[17] the resulting products (**22**) were heated in ethanolic ammonia to afford the 8-alkyl-9-(1-ethoxyethyl)adenines (**23**), and these were methylated directly with methyl iodide and deprotected with glacial acetic acid at room temperature. A similar but longer route was needed for the synthesis of 8-hydroxymethyl-1-methyladenine (**9**) from 4,5-diamino-6-oxopyrimidine (**19**) and glycolic acid, as shown in Scheme 3.

The reaction of adenosine with the azidobenzyl bromides in DMA at 40 °C, followed by heating of the resulting salts in glacial acetic acid,[14] gave the corresponding 1-(azidobenzyl)-adenines (**11**)—(**13**). Protection from light is required. Care must also be exercised in the neutralization of the 1-(azidobenzyl)adenine (**11**)—(**13**) and the 1,8-disubstituted adenine (**2**)—(**10**) solutions to prevent a Dimroth rearrangement from occurring. The pH of the aqueous solutions should never exceed 8, and the free bases should be isolated immediately. This rearrangement was turned to our advantage as a confirmation of the structure of the 1-substituted[11] and 1,8-disubstituted adenines. For example, treatment of 8-azido-1-benzyladenine (**10**) with 0.1M-sodium hydroxide solution on a steam-bath for 1.5 h resulted in rearrangement to the known 8-azido-6-benzylaminopurine[7,8] (**29**). Similarly, 1-(2-azidobenzyl)adenine (**11**) gave 6-(2-azidobenzylamino)purine[8] (**30**), and 1-(4-azidobenzyl)adenine (**13**) produced 6-(4-azidobenzylamino)purine[8] (**31**) (Scheme 4).

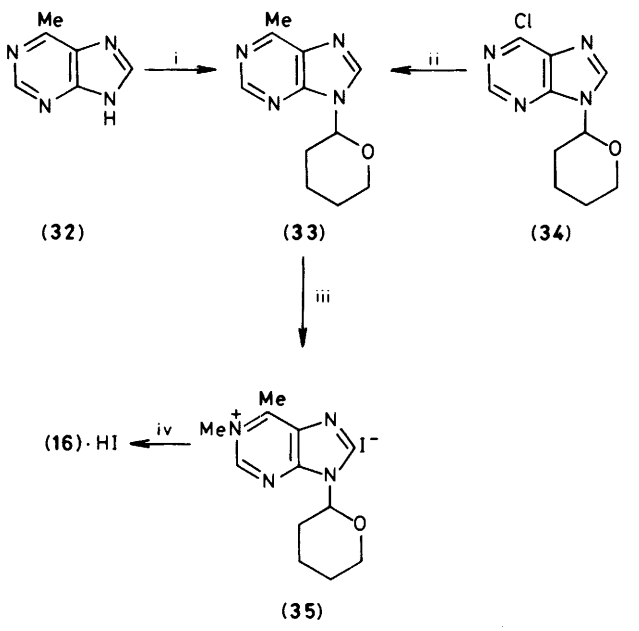
Further evidence that the 8,9-disubstituted adenines had been alkylated at N-1, as with 9-substituted adenines,[11] was gained by examination of the u.v. spectra of the 8-substituted 1-methyladenine products (Table 1). In all compounds (**2**)—(**9**), the negatively charged form (basic solution) absorbs more strongly and at longer wavelength than the protonated form (acid medium).[19] The common bathochromic and hyperchromic effects resulting from the substitution at the 8-position can also be observed.[20]

From u.v. and n.m.r. studies together with pK_a determinations,[21] it was concluded that in 1-alkyladenines the

Table 1. U.v. spectra of 8-substituted 1-methyladenines and *N*-methyladenines

Compound	pH	$\lambda_{max.}$(nm)	$\varepsilon \times 10^{-3}$
(2)	1.0	282	
	11.0	291	
(3)	1.0	261	14.7
	11.0	272	15.3
(4)	1.0	263	15.9
	11.0	273	16.1
(5)	1.0	271	11.8
	13.0	284	15.0
(6)	1.0	261	13.0
	13.0	273	15.4
(7)	1.0	262	13.4
	13.0	273	15.7
(8)	1.0	263	
	13.0	273	
(9)	1.0	263	13.5
	13.0	273	15.8
(1)[a]	4.0	259	11.7
	13.0	270	14.4
3-Methyladenine[a]	1.0	274	15.9
	12.0	272	12.8
7-Methyladenine[a]	1.0	272	13.8
	12.0	270	10.5

[a] Ref. 18, p. 489.



Scheme 5. *Reagents:* i, dihydropyran H^+; ii, $Ph_3\overset{+}{P}MeBr^-$, Bu^nLi; iii, MeI; iv, HCl

predominant tautomer in water was the 6-amino form, also observed in the solid state.[22] 8-Substitution does not seem to modify this characteristic, because the shape of the u.v. spectral curves of the 1,8-disubstituted adenines (**2**)—(**9**) in aqueous solution is similar to that in the spectrum of aqueous 1-methyladenine with two well-defined bands and no fine structure.[21]

1,6-Dimethylpurine (**16**) was a particularly interesting target molecule since a specific synthesis of this type of alkyl-substituted purine had not yet been reported. Unprotected 6-methylpurine (**32**) reacting with dimethyl sulphate in methanol in the presence of potassium hydroxide, gave a mixture of *x*-N,6-dimethylpurines[23,24] in which 1,6-dimethylpurine (**16**) was detected as a minor component.[24] We expected that 9-substitution on 6-methylpurine, as on adenine,[11] would direct methylation to N-1 in aprotic solvents. 6-Methylpurine (**32**), when treated with dihydropyran in ethyl acetate in the presence of toluene-*p*-sulphonic acid, yielded one new product to which we assigned the structure 6-methyl-9-tetrahydropyran-2-ylpurine (**33**) (Scheme 5). Confirmation of the structure assignment was obtained by comparison with a sample of this compound synthesized unambiguously from 6-chloro-9-tetrahydropyran-2-ylpurine (**34**) and methyltriphenylphosphonium bromide by a modified Wittig reaction.[25] The product (**33**) was treated with methyl iodide in DMA to give a precipitate, 1,6-dimethyl-9-tetrahydropyran-2-ylpurinium iodide (**35**). Deprotection was achieved by refluxing the suspended salt (**35**) in ethanol in the presence of hydrochloric acid. Assignment of the structure of (**16**) as 1,6-dimethylpurine was based upon its physical properties. The ^{1}H n.m.r. spectra of the free base (**16**), recorded from $CDCl_3$ and $(CD_3)_2SO$ solutions, were found to be different from those of the other two obtainable isomers, namely 3,6-dimethylpurine and 6,7-dimethylpurine,[23,24] resembling the spectra previously attributed to 1,6-dimethylpurine[24] (Table 2). Additional confirmation of the structure was derived from the u.v. spectrum of the 1,6-dimethylpurine (**16**) which is similar to the spectra of 1-methyl-[26] and 1-ethyl-adenine,[27] with the expected hyperchromic effect induced by the 6-methyl substituent superimposed.[20]

Table 2. ^{1}H N.m.r. chemical shifts of 1,6-dimethyl-1*H*-purine[a,b] (**16**)

Solvent	2-H	8-H	NCH_3	CCH_3	Δδ(2-H) − (8-H)
$CDCl_3$	8.65	8.44	4.02	2.95	0.21
	(8.67)	(8.51)	(4.10)	(3.01)	(0.15)
$(CD_3)_2SO$	8.83	8.35	4.02	2.87	0.58
	(8.91)	(8.30)		(2.90)	(0.61)

[a] In p.p.m. relative to Me_4Si. [b] Values in parentheses are from ref. 24.

Table 3. Biological activity of 1-methyladenine analogues[a]

Compound	pK_a (proton gain)	Activity[a]
(1)	7.2[b]	1—2 × 10^{-7}M
(2)	4.6[c]	2 × 10^{-5}M[d]
(3)	4.3[c]	Inactive[e]
(4)	4.1[c]	Inactive[e,f]
(5)	7.7[g]	8 × 10^{-8}M
(6)	7.5[g]	4 × 10^{-7}M
(7)	7.5[g]	Inactive[e]
(8)	7.5[g]	Inactive[e]
(9)	6.8[g]	5 × 10^{-6}M
(10)	*h*	10^{-4}M[d]
(11)	*i*	Inactive
(12)	*i*	10^{-6}M
(13)	*i*	10^{-8}M
(14)	*j*	Inactive[e]
(15)	3.25[k]	Inactive[e,f]
(16)	5.3[c]	Inactive[e]

[a] Expressed as the threshold concentration for inducing 100% germinal vesicle breakdown in starfish oocytes. [b] Ref. 28. [c] Determined by titration. [d] Possible contamination with the 8-NH_2 analogue due to photodecomposition (even though protected from light) may be responsible for this observed weak activity. [e] Lower concentration tested 10^{-4}M. [f] No inhibitory properties. [g] Spectroscopic determination. [h] *Ca.* 4 by comparison with (**2**). [i] *Ca.* 7 by comparison with (**1**). [j] *Ca.* 6.5 by comparison with 1,7-dibenzyladenine.[21] [k] Ref. 10.

Biological Activity.—The biological activity of analogues of 1-methyladenine (**1**) was expressed as the threshold concentration necessitated for inducing 100% of germinal vesicle breakdown in oocytes of the starfish *Asterias rubens*[5] (Table 3). The results confirmed the earlier hypothesis[5] that protonation of the hormone or its analogues (pK_a *ca.* 7) is a prerequisite for activity, and binding to the receptors take place in the imidazole region of the molecules, analogues with a pK_a close to 7 bearing bulky 8-substituents [(**7**)—(**9**)] being inactive or of low activity.

The biological activity was found to be highly dependent on the position of the azido substituent in the 1-(azidobenzyl)-adenines (**11**)—(**13**). While the *p*-azido isomer was found to be more active than the unsubstituted compound,[5] activity decreased dramatically with the *m*- and especially with the *o*-derivative. It has been shown[5] that in 1-substituted adenines, lipophilic substituents such as benzyl or long chain alkyl, exerted a favourable effect on activity. The increase in the lipophilic character when an azido substituent is introduced on the phenyl ring of 1-benzyladenine may explain the high activity of the *p*-isomer, while negative steric factors should mask this effect in the *m*- and *o*-derivatives.

Conclusion

In the present work, we have described an unequivocal synthesis of the last unknown *N*-methyl derivative of 6-methylpurine (**32**), namely 1,6-dimethylpurine (**16**), and of a series of 1,8-disubstituted adenines (**2**)—(**10**). We have shown that the directive effect of a substituent at N-9 in a purine ring, for a second substitution at N-1 with alkyl halides in aprotic solvents, may be extended from adenine[11] to other types of purines. Cumulative information about structure-activity relationships has been gained to confirm the earlier hypothesis[5] that the 1-methyladenine receptor for triggering meiosis appears to require, in the hormone or its analogues, an N-1 substituent of defined structure and polarity on the adenine ring, a cationic charge mainly in the pyrimidine ring, and binding potential in the region of the imidazole ring. Unfortunately, because of their weak and possibly questionable biological activity, 8-azido-1-methyladenine (**2**) and 8-azido-1-benzyladenine (**10**) cannot be expected to act efficiently as active photoaffinity labelling reagents, in contrast to other 8-azidoadenine derivatives.[6–8] 1-(4-Azidobenzyl)adenine (**13**) and 1-(3-azidobenzyl)adenine (**12**) appear to be possible, alternative candidates for this purpose because of their high level of biological activity.

Experimental

M.p.s were determined on a Büchi melting point apparatus and are uncorrected. ^1H N.m.r. spectra were recorded on Varian A-60A, T-60, or HA-100 spectrometers using Me_4Si as internal reference. U.v. absorption spectra were measured on a Beckman Acta MVI spectrophotometer. pK_a Values were calculated from curves relative to 0.05M-mixed phosphate-borate buffer solutions of the compounds. I.r. spectra were recorded with a Perkin-Elmer model 337 spectrophotometer using Nujol mulls. Low resolution mass spectra were obtained from a Varian MAT CH5 spectrometer coupled with a 620i computer and Statos recorder or from a Riber R 1010 spectrometer. High resolution mass spectra (h.r.m.s.) were obtained from a Varian MAT 311 spectrometer and field desorption mass spectra (f.d.m.s.) from a Varian MAT 731 instrument. Mass spectra of chloro compounds refer to ions containing ^{35}Cl only. Microanalyses were performed by Mr. Joseph Nemeth and his associates, University of Illinois, or by Service Central d'Analyses, France. Light petroleum refers to the fraction with b.p. 40—60 °C.

8-Azido-1-methyladenine (**2**).—To a solution of 8-azidoadenosine[12] (**17**; X = N_3) (0.750 g, 2.4 mmol) in DMA (20 ml) was added methyl bromide (2 ml). The solution was sealed tightly, protected from light, and stirred at room temperature for 5 days. The solvent was removed under reduced pressure.To the residue was added glacial acetic acid (15 ml). A precipitate formed immediately but was dissolved as the mixture was warmed. After being warmed on a steam-bath for 2.5 h, the solution was allowed to cool to room temperature, and then refrigerated. A precipitate, which formed slowly during several days, was collected by filtration, washed with acetic acid, and dried *in vacuo*. This was dissolved in warm water (10 ml), and the pH of the solution was adjusted to 8 with concentrated aqueous ammonia. The resulting precipitate was collected, washed, and dried *in vacuo* at 110 °C. The product gave the correct analysis for the quarter hydrate of *8-azido-1-methyladenine* (**2**) (240 mg, 50%). An analytically pure, dry sample, obtained by drying the hydrate at 140 °C under reduced pressure, did not melt below 200 °C, but gradually decomposed to a dark brown solid above 150 °C; δ[$(CD_3)_2SO$] 3.73 (3 H, s, NCH_3), 8.10 (2 H, br s, NH_2), and 8.17 (1 H, s, 2-H); $\nu_{max.}$ 2 130 cm^{-1} (N_3); *m/z* (f.d.m.s.) 190 (M^+) (Found: C, 37.7; H, 3.3; N, 58.7. $C_6H_6N_8$ requires C, 37.89; H, 3.16; N, 58.95%).

8-Chloro-1-methyladenine (**3**).—This was prepared by the same procedure as that for (**2**), from 8-chloroadenosine[13] (**17**; X = Cl) (0.732 g, 2.43 mmol) and methyl bromide (2 ml) in DMA (20 ml). The final solid obtained from ammonia precipitation was dried at 140 °C under reduced pressure leaving an analytically pure sample of product (**3**) (232 mg, 52%) with a high m.p. (slow darkening above 260 °C); δ[$(CD_3)_2SO$] 3.73 (3 H, s, CH_3), 8.27 (1 H, s, 2-H), and 8.42 (2 H, br s, NH_2); *m/z* 183 (M^+), 166, 155, 149, 142, 129, 121, and 102 (Found: C, 39.4; H, 3.4; Cl, 19.4; N, 38.2. $C_6H_6ClN_5$ requires C, 39.25; H, 3.29; Cl, 19.3; N, 38.14%).

8-Bromo-1-methyladenine (**4**).—This was prepared by the same procedure as that for (**2**) and (**3**), from 8-bromoadenosine (**17**; X = Br) (2.0 g, 5.8 mmol) and methyl bromide (2 ml) in DMA (35 ml). The final precipitate was collected by filtration, washed well with water, and dried *in vacuo* at 110 °C to give an analytically pure product (1.024 g, 76%) as the quarter hydrate. Pulverization and drying at 140 °C *in vacuo* gave the unhydrated *product* (**4**), which gradually decomposed above 250 °C; δ[$(CD_3)_2SO$] 3.70 (3 H, s, CH_3), 8.16 (1 H, s, 2-H), and 8.36 (2 H, br s, NH_2); *m/z* 228 (M^+), 148, 121, and 94 (Found: C, 31.7; H, 2.5; N, 30.6. $C_6H_6BrN_5$ requires C, 31.51; H, 2.63; N, 30.70%).

8-Amino-1-methyladenine (**5**).—A suspension of 8-azido-1-methyladenine (**2**) (336 mg, 1.77 mmol) and 10% Pd on charcoal (50 mg) in ethanol (50 ml) was shaken overnight under H_2 at room temperature. The organic product was dissolved by being warmed, with the addition of some drops of water. The catalyst was filtered off and the solvent was evaporated to leave a white powder (252 mg, 87%). The *product* (**5**) was recrystallized from ethanol with some drops of water added. Drying at 110 °C *in vacuo* left a product which gave variable analytical results with at least 1 H_2O retained per molecule. Prolonged heating at 140 °C *in vacuo* caused the product to turn brown without further significant drying; δ[$(CD_3)_2SO$] 3.68 (3 H, s, CH_3), 5.40 (4 H, br s, 2 NH_2), and 7.98 (1 H, s, 2-H); *m/z* 164 (M^+), 147, 136, 123; h.r.m.s. M^+ 164.0811 ($C_6H_8N_6$ requires 164.0810) (Found: C, 39.5; H, 5.6; N, 45.4; O, 9.9. $C_6H_8N_6{\cdot}H_2O$ requires C, 39.56; H, 5.53; N, 46.13; O, 8.78%).

General Preparation of 5-Acylamino-4-amino-6-oxo-1,6-dihydropyrimidines (**20**).—4,5-Diamino-6-oxopyrimidine (**19**)

(3.78 g, 30 mmol) was added to the organic acid (100 ml) and the mixture was refluxed for 1.5 h, and then cooled in ice–water. The precipitate was filtered off and dried at 100 °C, and the product was recrystallized from water with decolourization on charcoal. After being filtered, it was dried under reduced pressure at 110 °C overnight. The following compounds were thus obtained.

5-Acetylamino-4-amino-6-oxo-1,6-dihydropyrimidine (**20**; R = Me), obtained from acetic acid, as a hemihydrate, even after prolonged heating at 140 °C. White needles (4.07 g, 81%), m.p. > 300 °C; δ[$(CD_3)_2SO$] 2.08 (3 H, s, CH_3), 6.28 (2 H, br s, NH_2), 7.83 (1 H, s, 2-H), and 8.65 (1 H, br s, NH); $\lambda_{max.}(H_2O)$ (pH 1) 260 nm (ε 8 500); $\lambda_{max.}(H_2O)$ (pH 13) 255 nm (4 900); *m/z* 168 (M^+), 126, and 98 (Found: C, 40.75; H, 5.15; N, 31.5. $C_6H_8N_4O_2 \cdot 0.5H_2O$ requires C, 40.68; H, 5.12; N, 31.62%).

4-Amino-6-oxo-5-propanoylamino-1,6-dihydropyrimidine (**20**; R = Et), obtained from propanoic acid, as white needles (3.70 g, 68%), m.p. > 300 °C; δ[$(CD_3)_2SO$] 1.18 (3 H, t, CH_3), 2.40 (2 H, q, CH_2), 6.20 (2 H, br s, NH_2), 7.87 (1 H, s, 2-H), and 8.57 (1 H, s, NH); $\lambda_{max.}(H_2O)$ (pH 1) 260 nm (ε 8 600); $\lambda_{max.}(H_2O)$ (pH 13) 255 nm (5 100); *m/z* 182 (M^+), 126, and 98 (Found: C, 45.9; H, 5.5; N, 30.5. $C_7H_{10}N_4O_2$ requires C, 46.15; H, 5.53; N, 30.75%).

4-Amino-5-(2-methylpropanoyl)amino-6-oxo-1,6-dihydropyrimidine (**20**; R = Pr^i (4.35 g, 74%), obtained from 2-methylpropanoic acid, m.p. 269 °C (decomp.); δ[$(CD_3)_2SO$] 1.18 (6 H, d, 2 CH_3), 2.67 (1 H, m, CH), 6.08 (2 H, br s, NH_2), 7.87 (1 H, s, 2-H), and 8.58 (1 H, br s, NH); $\lambda_{max.}(H_2O)$ (pH 1) 260 nm (ε 8 400); $\lambda_{max.}(H_2O)$ (pH 13) 255 nm (4 900); *m/z* 196 (M^+), 153, 126, and 98 (Found: C, 48.8; H, 6.3; N, 28.25. $C_8H_{12}N_4O_2$ requires C, 48.97; H, 6.16; N, 28.55%).

4-Amino-5-hydroxyacetylamino-6-oxo-1,6-dihydropyrimidine (**24**) (3.18 g, 58%), obtained from glycolic acid (15.2 g, 100 mmol) in water solution (80 ml). Preparation similar to that for compounds (**20**); m.p. > 300 °C; δ[$(CD_3)_2SO$] 4.07 (2 H, s, CH_2), 6.38 (2 H, br s, NH_2), 7.85 (1 H, s, 2-H), and 8.50 (1 H, br s, NH); $\lambda_{max.}(H_2O)$ (pH 1) 259 nm (ε 8 300); $\lambda_{max.}(H_2O)$ (pH 13) 256 nm (5 100); *m/z* 184 (M^+), 167, 153, 137, 126, and 98 (Found: C, 38.9; H, 4.4; N, 30.25. $C_6H_8N_4O_3$ requires C, 39.13; H, 4.38; N, 30.42%).

General Preparation of 8-Alkyl-6-chloro-9H-purines (**21**).—To phosphorus oxychloride (40 ml) containing *N,N*-diethylaniline (4 ml) was added the 5-acylamino-4-amino-6-oxopyrimidine (**20**) (15 mmol), and the mixture was refluxed for 6 h. The excess of phosphorus oxychloride was then distilled off under reduced pressure and the residue poured onto cracked ice. The cooled solution was made strongly basic with 10M-KOH and extracted with diethyl ether (2 × 100 ml). The cooled aqueous solution was then cautiously acidified to pH 1 with concentrated HCl and continuously extracted with diethyl ether for 48 h. The ether was evaporated and the residue recrystallized from toluene leaving yellow crystals. White crystals were obtained by decolourization of the crude product on charcoal in refluxing ethanol. The following compounds were thus obtained.

6-Chloro-8-methyl-9*H*-purine (**21**; R = Me) (1.04 g, 41%); an analytical sample was obtained by recrystallization from toluene, m.p. 212 °C (decomp.); $\lambda_{max.}(H_2O)$ (pH 1) 265 nm; $\lambda_{max.}(H_2O)$ (pH 11) 277 nm [lit.,[29] m.p. 212—213 °C; $\lambda_{max.}(H_2O)$ (pH 1) 265 nm; $\lambda_{max.}(H_2O)$ (pH 11) 277 nm]; δ($CDCl_3$) 2.75 (3 H, s, CH_3) and 8.68 (1 H, s, 2-H).

6-Chloro-8-ethyl-9*H*-purine (**21**; R = Et) (1.42 g, 52%). An analytical sample was obtained by recrystallization from benzene–toluene, m.p. 166 °C (decomp.); $\lambda_{max.}(H_2O)$ (pH 1) 265 nm; $\lambda_{max.}(H_2O)$ (pH 13) 277 nm [lit.,[30] m.p. 170—172 °C; $\lambda_{max.}(H_2O)$ (pH 1) 265 nm; $\lambda_{max.}(H_2O)$ (pH 13) 277 nm]; δ($CDCl_3$) 1.53 (3 H, t, CH_3), 3.12 (2 H, q, CH_2), and 8.72 (1 H, s, 2-H).

6-Chloro-8-isopropyl-9H-purine (**21**; R = Pr^i) (1.59 g, 54%). An analytical sample was obtained by recrystallization from toluene, m.p. 164 °C (decomp.); δ($CDCl_3$) 1.60 (6 H, d, 2 CH_3), 3.40 (1 H, m, CH), and 8.73 (1 H, s, 2-H); $\lambda_{max.}(H_2O)$ (pH 1) 266 nm (ε 12 000); $\lambda_{max.}(H_2O)$ (pH 13) 278 nm (11 300); *m/z* 196 (M^+), 181 and 145 (Found: C, 48.6; H, 4.6; Cl, 18.3; N, 28.1. $C_8H_9ClN_4$ requires C, 48.87; H, 4.61; Cl, 18.0; N, 28.49%).

6-Chloro-8-chloromethyl-9H-purine (**25**). Preparation similar to that for compounds (**21**), from 4-amino-5-hydroxyacetylamino-6-oxopyrimidine (**24**) (15 mmol), to give *compound* (**25**) (1.22 g, 31%). Recrystallization from CCl_4 gave an analytical sample, m.p. 226 °C (decomp.); δ[$(CD_3)_2SO$] 5.10 (2 H, s, CH_2) and 8.90 (1 H, s, 2-H); $\lambda_{max.}(H_2O)$ (pH 1) 270 nm (ε 11 400); $\lambda_{max.}(H_2O)$ (pH 13) 280 nm (11 700); *m/z* 202 (M^+) and 167 (Found: C, 35.7; H, 1.95; Cl, 35.0; N, 27.2. $C_6H_4Cl_2N_4$ requires C, 35.50; H, 1.99; Cl, 34.92; N, 27.60%).

1,8-Dimethyladenine (**6**).—A suspension of 6-chloro-8-methylpurine (**21**; R = Me) (1.685 g, 10 mmol) in acetaldehyde diethyl acetal was refluxed overnight. The resulting solution was cooled, filtered through Celite, and the solvent was evaporated, leaving a yellow solid that was used without further purification: 6-chloro-9-(1-ethoxyethyl)-8-methylpurine (**22**; R = Me); δ(CCl_4) 1.18 (3 H, t, CH_3CH_2), 1.77 (3 H, d, CH_3CH), 2.75 (3 H, s, 8-CH_3), 3.37 (2 H, m, CH_2O), 6.15 (1 H, q, CH), and 8.67 (1 H, s, 2-H); *m/z* 240 (M^+), 195, 168. The crude product was dissolved in ethanol (100 ml) and the solution was saturated with ammonia at 0 °C, and then heated at 100 °C in a sealed tube for 4 h. The solvent was evaporated at room temperature and the solid residue was dissolved in ethyl acetate. This solution was washed with 1M-NaOH solution (50 ml) and water (2 × 50 ml). The organic layer was dried (Na_2SO_4) and the solvent was removed under reduced pressure to leave crude 9-(1-ethoxyethyl)-8-methyladenine (**23**; R = Me); δ($CDCl_3$) 1.17 (3 H, t, CH_3CH_2), 1.73 (3 H, d, CH_3CH), 2.53 (3 H, s, 8-CH_3), 3.33 (2 H, m, CH_2), 5.92 (br s, NH_2), 6.08 (q, CH) (last two signals superimposed = 3 H), and 8.32 (1 H, s, 2-H); *m/z* 221 (M^+), 176, 149, and 122. This compound was dissolved in DMA (20 ml) and methyl iodide (1 ml) was added. The solution was stirred overnight at room temperature, and the solvent was removed under reduced pressure. At this stage, h.p.l.c. control (Lichrosorb RP 8 column, mobile phase: H_2O, 60; MeOH, 35; AcOH, 5%) revealed some deprotection of N-9 in the expected product. The residue was triturated with glacial acetic acid (10 ml) which caused the precipitation of fine yellow crystals. These were filtered off and dried at 100 °C *in vacuo*, then dissolved in water (20 ml). This solution was stirred with an anion-exchange resin (20 mmol equiv.; weakly basic, OH^- form) for 2 h. The resin was filtered off and the water was evaporated from the filtrate to give *1,8-dimethyladenine* (**6**) (603 mg, 37%). An analytical sample was obtained by recrystallization from a small volume of water and drying at 140 °C, m.p. > 300 °C (decomposed slowly above 250 °C); δ[$(CD_3)_2SO$] 2.42 (3 H, s, 8-CH_3), 3.72 (3 H, s, 1-CH_3), and 8.10 (1 H, s, 2-H); *m/z* 163 (M^+), 146, 135, 122, 121, and 108 (Found: C, 51.7; H, 5.6; N, 42.7. $C_7H_9N_5$ requires C, 51.52; H, 5.56; N, 42.92%).

8-Ethyl-1-methyladenine (**7**). This was prepared similarly to (**6**), from 6-chloro-8-ethylpurine (**21**; R = Et) (10 mmol); compound (**7**) (832 mg, 47%), m.p. > 300 °C (slow decomposition above 250 °C); δ[$(CD_3)_2SO$] 1.25 (3 H, t, CH_3CH_2), 2.72 (2 H, q, CH_2), 3.67 (3 H, s, 1-CH_3), and 8.07 (1 H, s, 2-H); *m/z* 177 (M^+), 162, 160, 149, 135, 122, and 121 (Found: C, 54.4; H, 6.2; N, 39.3. $C_8H_{11}N_5$ requires C, 54.22; H, 6.26; N, 39.52%).

6-Chloro-9-(1-ethoxyethyl)-8-ethyl-9H-purine (**22**; R = Et), δ(CCl_4) 1.20 (3 H, t, CH_3CH_2O), 1.53 (3 H, t, 8-CH_2CH_3), 1.80 (3 H, d, CH_3CH), 3.10 (q, 8-CH_2CH_3), 3.38 (m, CH_2O) (last two signals superimposed = 4 H), 6.17 (1 H, q, CHO), and 8.53 (1 H, s, 2-H); *m/z* 254 (M^+), 209, 182.

9-(1-Ethoxyethyl)-8-ethyladenine (**23**; R = Et), δ($CDCl_3$) 1.25

(3 H, t, CH_3CH_2O), 1.52 (3 H, t, 8-CH_2CH_3), 1.83 (3 H, d, CH_3CH), 3.10 (q, 8-CH_2CH_3), 3.38 (m, CH_2O) (last two signals superimposed = 4 H), 5.9—6.3 (3 H, two superimposed signals, CH + NH_2), and 8.30 (1 H, s, 2-H); *m/z* 235 (M^+), 190, and 163.

8-*Isopropyl*-1-*methyladenine* (**8**). In a preparation similar to that for (**6**) and (**7**), from 6-chloro-8-isopropylpurine (**21**; R = Pr^i) (10 mmol) was obtained a hydrated product (886 mg) that contained at least 2 H_2O per molecule after drying overnight at 140 °C, and gave variable analytical results. *Compound* (**8**), m.p. > 200 °C (darkened above this temperature); δ[$(CD_3)_2SO$] 1.40 (6 H, d, 2 CH_3), 3.20 (1 H, m, CH), 3.83 (3 H, s, 1-CH_3), and 8.37 (1 H, s, 2-H); *m/z* 191 (M^+), 176, 174, 163, 159, 149, 135, 122, and 121; h.r.m.s. M^+, 191.1172 ($C_9H_{13}N_5$ requires 191.1171).

6-Chloro-9-(1-ethoxyethyl)-8-isopropyl-9*H*-purine (**22**; R = Pr^i), δ($CDCl_3$) 1.22 (3 H, t, CH_3CH_2), 1.48, 1.53 [6 H, 2d, $(CH_3)_2CH$], 1.85 (3 H, d, CH_3CH), 3.1—3.8 [3 H, br m, CH_2 + $CH(CH_3)_2$], 6.17 (1 H, q, CHO), and 8.67 (1 H, s, 2-H); *m/z* 268 (M^+), 223, and 196.

9-(1-Ethoxyethyl)-8-isopropyladenine (**23**; R = Pr^i), δ($CDCl_3$) 1.20 (3 H, t, CH_3CH_2), 1.42, 1.47 [6 H, 2d, $(CH_3)_2CH$], 1.82 (3 H, d, CH_3CH), 3.1—3.7 (3 H, br m, CH + CH_2CH_3), 5.92, 6.12 (3 H, br s + q, NH_2 + CHO), and 8.28 (1 H, s, 2 H); *m/z* 249 (M^+), 205, 190, 177, and 162.

8-*Hydroxymethyl*-1-*methyladenine* (**9**). 6-Chloro-8-chloromethylpurine (**25**) (2.03 g, 10 mmol) was used to prepare crude 6-chloro-8-chloromethyl-9-(1-ethoxyethyl)purine (**26**), by refluxing in acetaldehyde diethyl acetal; δ($CDCl_3$) 1.23 (3 H, t, CH_3CH_2), 1.93 (2 H, d, CH_3CH), 3.52 (2 H, br m, CH_2CH_3), 5.05 (2 H, s, CH_2Cl), 6.20 (1 H, q, CH), and 8.82 (1 H, s, 2-H). This compound was stirred overnight at room temperature in DMA (30 ml) in the presence of sodium acetate (1.64 g, 20 mmol). The solvent was evaporated under reduced pressure, and the solid residue was extracted with CCl_4. Evaporation of the solvent left a yellow oil, 8-acetoxymethyl-6-chloro-9-(1-ethoxyethyl)-9*H*-purine (**27**); δ(CCl_4) 1.28 (3 H, t, CH_3CH_2), 1.58 (3 H, s, d, CH_3CH), 2.25 (3 H, s, CH_3CO), 3.42 (2 H, br m, CH_2CH_3), 5.42 (2 H, s, 8-CH_2O), 6.17 (1 H, q, CH), and 8.64 (1 H, s, 2-H). This crude product, when caused to react as usual with ammonia, gave 9-(1-ethoxyethyl)-8-hydroxymethyladenine (**28**); δ($CDCl_3$) 1.17 (3 H, t, CH_3CH_2), 1.75 (3 H, d, CH_3CH), 3.43 (2 H, m, CH_2CH_3), 5.03 (2 H, s, 8-CH_2O), 6.13—6.27 (3 H, q + br s, CHO + NH_2), and 8.30 (1 H, s, 2-H). The usual treatment of this compound with methyl iodide, followed by acetic acid, and neutralization of the salt with ammonia gave the expected *compound* (**9**) (0.63 g, 35%), m.p. > 300 °C (slow decomposition above 250 °C) δ[$(CD_3)_2SO$] 2.05 (3 H, s, CH_3), 4.62 (2 H, s, CH_2), and 8.13 (1 H, s, 2-H); *m/z* 179 (M^+), 161, 150, 134, 121, and 105 (Found: C, 46.7; H, 5.1; N, 38.8. $C_7H_9N_5O$ requires C, 46.92; H, 5.06; N, 39.09%).

8-*Azido*-1-*benzyladenine* (**10**).—The preparation of this compound was essentially the same as for compounds (**2**)—(**4**), from 8-azidoadenosine[12] (**17**; X = N_3) (0.75 g, 2.4 mmol) and benzyl bromide (2 ml) in DMA (20 ml). The crude product was suspended in warm water and dissolved by addition of 6M-HCl. The solution was filtered, and the product was reprecipitated by addition of aqueous ammonia until the solution reached pH 7.5. The dried *product* (**10**) (0.235 g, 37%) gradually decomposed above 140 °C; δ[$(CD_3)_2SO$] 5.48 (2 H, br s, CH_2N), 7.13—7.40 (5 H, m, Ph), 8.15 (2 H, br s, NH_2), and 8.37 (1 H, s, 2-H); $\nu_{max.}$ 2 130 cm^{-1} (N_3); $\lambda_{max.}$ (95% EtOH) 294 and 237 nm; $\lambda_{max.}$ (95% EtOH) (pH 2) 285 nm; $\lambda_{max.}$ (95% EtOH) (pH 10) 291 nm; *m/z* 266 (M^+) (f.d.m.s.) (Found: C, 53.95; H, 3.9; N, 42.0. $C_{12}H_{10}N_8$ requires C, 54.14; H, 3.76; N, 42.11%).

General Preparation of the Azidobenzyl Bromides.—The azidotoluene (6.65 g, 50 mmol), *N*-bromosuccinimide (9.8 g, 55 mmol), and 2,2′-azo(2-methylpropionitrile) (0.8 g) were heated in the dark under nitrogen in refluxing dry benzene. The reaction was generally complete after 5 h. The mixture was poured into water and diethyl ether, and the ether layer was dried (Na_2SO_4). After evaporation of the solvent, the residue was dissolved in a small volume of light petroluem and chromatographed through silica gel (Lichroprep Si 60; 100 g) with light petroluem as eluant. The fractions containing the bromide were pooled and the solvent was evaporated, leaving a crude product which was used without further purification. 2-Azidobenzyl bromide (6.9 g, 67%); $\nu_{max.}$ 2 120 cm^{-1}; δ(CCl_4) 4.35 (2 H, s, CH_2) and 6.9—7.5 (4 H, m, ring H) [lit.,[31] $\nu_{max.}$ 2 150 cm^{-1}; δ(CCl_4) 4.37, 6.9—7.4]. 3-Azidobenzyl bromide (7.85 g, 74%); $\nu_{max.}$ 2 120 cm^{-1}; δ(CCl_4) 3.47 (2 H, s, CH_2) and 6.7—7.4 (4 H, m, ring H). 4-Azidobenzyl bromide (7.4 g, 70%); $\nu_{max.}$ 2 120 cm^{-1}; δ(CCl_4) 4.40 (2 H, s, CH_2) and 6.7—7.4 (4 H, m, ring H).

General Preparation of the 1-(*Azidobenzyl*)*adenines* (**11**)—(**13**).—All preparations were carried out in the dark or under red light. A solution of adenosine (1.34 g, 5 mmol) and the azidobenzyl bromide (3.2 g, 15 mmol) in DMA (20 ml) was heated at 40 °C for 3 days. The solvent was evaporated under reduced pressure and the residue was triturated with diethyl ether (3 × 20 ml) and then heated at 100 °C for 4 h in glacial acetic acid. After the solution had been cooled to room temperature, the white crystalline precipitate that was formed was filtered off and washed with acetic acid. After being dried it was dissolved in hot water and decolourized with charcoal. A white product was recovered by neutralization with ammonia, cooling to room temperature, and filtration. Drying *in vacuo* at 100 °C gave an analytical sample.

The following were obtained. 1-(2-*Azidobenzyl*)*adenine* (**11**) (0.69 g, 52%) from 2-azidobenzyl bromide; m.p. > 180 °C (quickly darkened above this temperature); δ[$(CD_3)_2SO$] 5.37 (2 H, s, CH_2), 6.7—7.6 (4 H, m, phenyl H), 7.97, 8.23 (1 H + 1 H, 2s, 2-H + 8-H); $\nu_{max.}$ 2 120 cm^{-1} (N_3); $\lambda_{max.}$(H_2O) (pH 1) 256 nm; $\lambda_{max.}$(H_2O) (pH 13) 263, 258sh, and 271sh nm; *m/z* 238 ($M^+ - N_2$), 211, 135, 119, and 108 (Found: C, 54.0; H, 3.65; N, 42.0. $C_{12}H_{10}N_8$ requires C, 54.13; H, 3.79; N, 42.08%).

1-(3-*Azidobenzyl*)*adenine* (**12**) (0.95 g, 71%) from 3-azidobenzyl bromide; m.p. > 190 °C (quickly darkened above this temperature); δ[$(CD_3)_2SO$] 5.47 (2 H, s, CH_2), 6.9—7.6 (4 H, m, phenyl H), 7.97 and 8.40 (1 H + 1 H, 2s, 2 H + 8 H); $\nu_{max.}$ 2 120 cm^{-1} (N_3); $\lambda_{max.}$(H_2O) (pH 1) 257 nm; $\lambda_{max.}$(H_2O) (pH 13) 263, 258sh, and 271sh nm; *m/z* 238 ($M^+ - N_2$), 135 (Found: C, 54.4; H, 3.7; N, 42.1. $C_{12}H_{10}N_8$ requires C, 54.13; H, 3.79; N, 42.08%).

1-(4-*Azidobenzyl*)*adenine* (**13**) (0.87 g, 65%) from 4-azidobenzyl bromide; m.p. > 190 °C (quickly darkened above this temperature); δ[$(CD_3)_2SO$] 5.43 (2 H, s, CH_2), 7.0—7.5 (4 H, m, phenyl H), 7.97 and 8.40 (1 H + 1 H, 2s, 2-H + 8-H); $\nu_{max.}$ 2 120 cm^{-1} (N_3); $\lambda_{max.}$(H_2O) (pH 1) 257 nm; $\lambda_{max.}$(H_2O) (pH 13) 257, 261sh, and 272 sh nm; *m/z* 238 ($M^+ - N_2$), 211, 135, and 108 (Found: C, 54.1; H, 3.9; N, 42.2. $C_{12}H_{10}N_8$ requires C, 54.13; H, 3.79; N, 42.08%).

Dimroth Rearrangement of Compounds (**10**), (**11**), *and* (**13**).—A mixture of 8-azido-1-benzyladenine (**10**) (65 mg, 0.24 mmol) and 0.1M-NaOH (15 ml) was warmed gently in the dark to dissolve the purine. The solution was heated on a steam-bath for 1.5 h and then allowed to cool. The solution was stirred vigorously as 1M-HCl was added to neutralize it to pH 7, and then left overnight. The precipitated product was collected by filtration, washed well with water, and dried to give a sample identical with 8-azido-6-benzylaminopurine[7,8] (**29**) by n.m.r., u.v., and mass spectra and t.l.c. Analogously, 1-(2-azidobenzyl)-adenine (**11**) gave 6-(2-azidobenzyl)aminopurine[8] (**30**), and 1-(4-azidobenzyl)adenine (**13**) produced 6-(4-azidobenzyl)-aminopurine[8] (**31**).

6-*Methyl*-9-*tetrahydropyran*-2-*yl*-9H-*purine* (**33**).—A mixture of 6-methylpurine (**32**) (1.0 g, 7.5 mmol), toluene-*p*-sulphonic acid (16 mg), and dihydropyran (1.5 ml) in ethyl acetate (20 ml) was stirred at 55 °C for 48 h. The yellow solution was extracted with saturated aqueous Na_2CO_3 (10 ml), and washed with water (2 × 10 ml). The organic layer was dried ($MgSO_4$) and the solvent was removed under reduced pressure to yield a viscous yellow oil which was used without further purification; δ($CDCl_3$) 1.42—2.32 (6 H, br m, THP-H), 2.85 (3 H, s, CH_3), 3.65—3.95 (1 H, br m, THP-H), 4.11—4.29 (1 H, br m, THP-H), 5.72—5.85 (1 H, br m, THP-H), and 8.24, 8.84 (1 H + 1 H, 2s, 2-H + 8-H); $\lambda_{max.}$ (95% EtOH) 260 and 247sh nm; $\lambda_{max.}$ (95% EtOH) (pH 11) 261 and 247sh nm; *m/z* 218 (M^+), 190, 135, and 85. Alternatively, this compound was synthesized by modifying Taylor's preparation of 6-methylpurine.[25] To a stirred suspension of triphenylmethylphosphonium bromide (3.28 g) in anhydrous dimethoxyethane (50 ml) under dry nitrogen at −30 to −35 °C was added 2.4M-n-butyl-lithium (3.85 ml) in hexane. The reaction was stirred for 1 h and 6-chloro-9-tetrahydropyran-2-yl-9*H*-purine[32] (**34**) (1.0 g, 4.2 mmol) in anhydrous dimethoxyethane (10 ml) was added. The reaction mixture was allowed to come slowly to room temperature (*ca.* 1 h) and was then stirred for 4 h. Sodium carbonate (440 mg, 4.2 mmol) in water (10 ml) was added, and the resulting mixture was heated at reflux for 3 h. The mixture was taken to dryness under reduced pressure and the residue was taken up in water and extracted with chloroform. The chloroform solution was washed twice with water, dried ($MgSO_4$), and taken to dryness under reduced pressure. Repeated chromatography on silica gel was necessary to obtain a product identical by n.m.r. and mass spectra and t.l.c. with that produced by the first method.

1,6-*Dimethyl*-9-*tetrahydropyran*-2-*ylpurinium Iodide* (**35**).—To 6-methyl-9-tetrahydropyran-2-ylpurine (**33**), prepared from 6-methylpurine (1.0 g) by the first method above, was added methyl iodide (1.5 ml) and DMA (10 ml). The mixture was capped tightly and stirred at room temperature for 36 h. The resulting precipitate was collected by filtration, washed well with DMA, and dried *in vacuo* to yield an impure product (1.035 g, 39% from 6-methylpurine) that was used without further purification.

1,6-*Dimethyl*-1H-*purine* (**16**).—To a mixture of 1,6-dimethyl-9-tetrahydropyran-2-ylpurinium iodide (600 mg, 1.67 mmol) in absolute ethanol (10 ml), was added 6M-HCl to adjust the pH to 1. The solution was heated on a steam-bath for 15 min; ethanol was added periodically to maintain a constant volume. The yellow solution was refrigerated overnight. The resulting crystalline precipitate was collected by filtration, washed well with cold ethanol, and dried *in vacuo* to yield an analytically pure, white *compound* (350 mg, 76%), m.p. 239—241 °C (decomp.); δ[$(CD_3)_2SO$] 3.03 (3 H, s, CH_3C), 4.21 (3 H, s, CH_3N), and 9.04, 9.42 (1 H + 1 H, 2s, 2-H + 8-H); $\lambda_{max.}$(H_2O) (pH 1) 268 nm (ε 7 730); $\lambda_{max.}$(H_2O) (pH 13) 273 nm (7 800); *m/z* 148 (M^+ − HI), 128, 127, and 120 (Found: C, 30.4; H, 3.3; N, 20.3. $C_7H_9IN_4$ requires C, 30.47; H, 3.45; N, 20.45%). To record its ^1H n.m.r. spectra (Table 2), the free base was obtained by dissolving the hydriodide in water and stirring the solution with a weakly basic anion-exchange resin (OH^- form) for 2 h, followed by filtration of the resin and evaporation of water.

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