Articles

8-Purinyl versus 2-Benzimidazolyl Carbanions: Charge Demands of the Heterocycles and Ligand Properties of the Bis(heteroaryl)methanes[1]

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Two new purinyl derivatives, 8-benzyl-7-methylpurine (**8**) and bis(7-methylpurin-8-yl)methane (**9**), have been synthesized and their corresponding carbanions investigated in DMSO. The application of our previously proposed π-charge/shift relationships to the ^{13}C and ^{15}N shifts of the carbanions has made it possible to map π-charges and obtain the values of the charge demand of the heterocyclic rings, a resonance index of the π-electron-withdrawing power of the substituent. The charge demand of the 7-methylpurin-8-yl substituent is found to be the highest among the previously investigated azinyl and azolyl substituents and is comparable with that of the strongest classical electron-withdrawing functions. The replacement of the fused benzene ring in the benzimidazolyl substituent by a pyrimidine ring containing the nitrogen atoms in appropriate positions causes a considerable increase in the electron-withdrawing capacity of the heterocycle. Spectroscopic and reactivity data confirm the strong electron-withdrawing nature of the purinyl ring. The ^{13}C NMR spectrum shows the existence of the carbanions of both purinyl derivatives as a mixture of geometric isomers, a consequence of the high double-bond character along the bond linking the carbanionic carbon to C(8) of the purinyl ring. Bis(7-methylpurin-8-yl)methane can be easily converted to its stable NH tautomer by means of basic catalysis. It behaves as an "active methylene" compound giving high-yield condensations with electrophiles. Finally, unlike the corresponding benzimidazol-2-yl derivative, bis(7-methylpurin-8-yl)methane reacts with metal acetates to give neutral methanates [ML_2] (M = Zn, Cu, Co; LH = bis(7-methylpurin-8-yl)methane), where the ligand is present as an anionic system. On the basis of this and previous data, it is concluded that charge demand plays a strategic role in obtaining stable chelates of this sort.

In a series of papers,[2,3] we have shown that ^{13}C NMR shifts of trigonal delocalized carbanions give access to the π-electron density q_C residing on the carbanionic carbon and to the charge demands c_X of groups X attached to it by means of relationships 1−3.

$$\delta^{13}C = 122.8 + \sum A_i - 160(q_C^{\pi} - 1) \quad (1)$$

$$c_X^X = (2 - q_C^{\pi})/2 \quad (2)$$

$$c_X^{Ph} = 2 - c_{Ph} - q_C^{\pi} \quad (3)$$

Relationship 1 relates the experimental ^{13}C shift of a carbanionic carbon to its π-electron density q_C by means of an intercept correction constituted by the ^{13}C shift of ethene (122.8 ppm) and the shielding contribution A_i of the various substituents directly bonded to the anionic site. In this relationship, the carbon atom of ethylene plays the role of a neutral model of the trigonal carbon atom, and the shielding A_i accounts for all of the interactions (except for resonance effects) exerted by the substituent on the adjacent carbon atom. The A_i values can be obtained as the difference between the ^{13}C shift of the β-carbons of the β-heteroarylstyrene and styrene itself, by following a previously used procedure (we have already shown that styrene derivatives, in addition to the vinyl systems CH_2=CHX, are good models for obtaining the shielding contribution for the substituent X).[2,4]

Relationships 2 and 3 allow an empirical evaluation of the charge demands *c*, defined as the fraction of π-charge withdrawn by a group X from the carbanionic carbon bonded to it; these are available once the π-elec-

(1) Part 7 in bis(heteroaryl)methanes. For part 6, see: Abbotto, A.; Bradamante, S.; Capri, N.; Rzepa, H.; Williams, D. J.; White, A. *J. Org. Chem.* **1996**, *61*, 1770−1778. For part 5, see ref 3.

(2) (a) Bradamante, S.; Pagani, G. A. *J. Org. Chem.* **1984**, *49*, 2863−2870. (b) Bradamante, S.; Pagani, G. A. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1035−1046. (c) Bradamante, S.; Pagani, G. A. *Pure Appl. Chem.* **1989**, *61*, 709−716. (d) Barchiesi, E.; Bradamante, S.; Ferraccioli, R.; Pagani, G. A. *J. Chem. Soc., Perkin Trans. 2* **1990**, 375−383. (e) Berlin, A.; Bradamante, S.; Pagani, G. A. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1525−1530. (f) Abbotto, A.; Alanzo, V.; Bradamante, S.; Pagani, G. A. *J. Chem. Soc., Perkin Trans. 2* **1991**, 481−488. (g) Abbotto, A.; Bradamante, S.; Pagani, G. A. *J. Org. Chem.* **1993**, *58*, 444−448. (h) Abbotto, A.; Bradamante, S.; Pagani, G. A. *J. Org. Chem.* **1993**, *58*, 449−455.

(3) Abbotto, A.; Bradamante, S.; Pagani, G. A. *J. Org. Chem.* **1996**, *61*, 1761−1769.

(4) For a detailed description of the origin of relationship 1, its parameters, and assumed ^{13}C shift sensitivity (160 ppm/electron), see refs 2a,c and Bradamante, S.; Pagani, G. A. Benzyl and Heteroarylmethyl Carbanions: Structure and Substituent Effects In *Advances in Carbanion Chemistry*; Snieckus, V., Ed.; Jai Press: London, 1996; Vol. 2, pp 189−263.

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Table 1. Charge Demand of Heteroaryl Substituents in $PhCH^-X$ (c_X^{Ph}) and X_2CH^- (c_X^X)

X	c_X^{Ph}	c_X^X
2-thiazolyl[a]	0.413−0.380	0.318
2-oxazolyl[a]	0.346	
N-methylimidazol-2-yl[a]	0.283	0.254
2-benzothiazolyl[a]	0.457−0.471	0.316
2-benzoxazolyl[a]	0.424−0.436	0.288
N-methylbenzimidazol-2-yl[a]	0.382	0.276[b]
2-pyridyl[c]	0.411	0.302[d]
4-pyridyl[c]	0.408	0.299[d]
2-quinolyl[d]		0.313
3-pyridazinyl[e]	0.417	
2-pyrimidyl[e]	0.430	
4-pyrimidyl[e]	0.501	
pyrazinyl[e]	0.446	

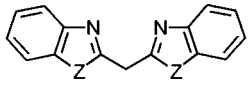
[a] Reference 3. [b] This work. [c] Reference 2b. [d] Reference 6. [e] Reference 2f.

tron density q_C residing on the carbanionic carbon (and therefore its ^{13}C chemical shift) is known. We used charge demands as a quantitative resonance index of the electron-withdrawing power of the X substituents: in particular, the $PhCH^-X$ systems originated the c_X^{Ph} values[5] and the $^-CHX_2$ carbanions originated the c_X^X values[5] (both scales are shown in Table 1). Relationships 1−3 have been validated by means of their successful application to a large number of benzyl and methylene anions stabilized by primary electron-withdrawing groups (NO_2, COR, CO_2R, SOR, SO_2R, etc.),[2b−d,h] pyridines,[2e,6] azines,[2f,6] and azoles.[3]

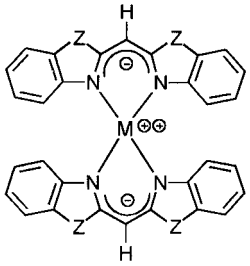
We have communicated[3] that the charge demands c_X^{Ph} and c_X^X of the heterocycles in the carbanions of 2-benzylimidazole, 2-benzylbenzimidazole, and bis(imidazol-2-yl)methane are particularly small. The insolubility of the carbanion of bis(*N*-methylbenzimidazol-2-yl)methane (**3**) prevents the c_X^X of the benzimidazol-2-yl group in this system from being obtained.[3] Charge demands c_X^X are thought to affect[7] the capacity of the bis(heteroaryl)methane systems LH to act as bidentate carbanionic ligands L^- and give neutral methanates [ML_2]. Bis(benzothiazol-2-yl)methane (**1**) and bis(benzoxazol-2-yl)methane (**2**) give the neutral methanates **4**[8,9] and **5**[9] (M = Zn, Cu, Co, Ni, Pd) with metal acetates, whereas bis(*N*-methylbenzimidazol-2-yl)methane (**3**) does not.[9] We ascribe this behavior to the fact that the heterocycle in compounds **1** and **2**, but not in compound **3**, is strongly electron-withdrawing, as is demonstrated by the charge demand c_X^{Ph} and c_X^X values of the benzothiazol-2-yl, benzoxazol-2-yl, and benzimidazol-2-yl groups (Table 1). In fact, since the ligands in chelates **4**-**6** are present as carbanionic entities, strongly electron-withdrawing heterocycles with large c_X^X values give stability to the carbanionic frame. In terms of the equilibrium (eq 4), the chelates based on strongly electron-

$$2LH + M(AcO)_2 \rightleftarrows [ML]_2 + 2AcOH \qquad (4)$$

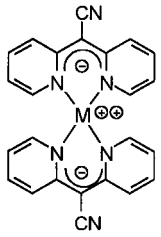
withdrawing systems (e.g., **1** and **2**) are not basic enough to be protonated by the acetic acid formed in the reaction. Further evidence that stabilization of the carbanionic structure of the ligand is a decisive factor in allowing the formation of neutral chelates is provided by two additional examples: bis(pyrid-2-yl)acetonitrile gives the neutral methanate **6**,[6] whereas bis(pyrid-2-yl)methane does not.



1: Z = S
2: Z = O
3: Z = NMe



4: Z = S
5: Z = O



6

In order to obtain definitive evidence concerning the role of the charge demand of the heterocyclic ligand in allowing the formation of neutral chelates from bis(heteroaryl)methanes, we identified our target with a heterocycle that would present a much higher charge demand with a minimum of structural and steric modification in comparison with the benzimidazolyl ring. We chose the 8-purinyl system in which the benzene ring fused to the imidazole is replaced by a pyrimidine, a heterocycle that we have shown[2f] possesses a high charge demand. We here report the synthesis of 8-benzyl-7-methylpurine (**7**) and the ^{13}C NMR study of the corresponding anion to obtain the c_X^{Ph} value. As before,[2,3] we obtained the shielding contribution A_i of the substituent as the difference in the shifts of β-carbons in styrene and 7-methyl-8-styrylpurine (**8**). Finally, we synthesized bis(7-methylpurin-8-yl)methane (**9**) (BPUMH) in order to obtain the c_X^X value from the ^{13}C shifts of the corresponding carbanion and to ascertain whether this system can provide neutral methanates upon contact with divalent transition metal acetates. The investigation into the obtaining of neutral methanates [ML_2] was completed by checking the reaction of bis(*N*-methylbenzimidazol-2-yl)methane (**3**) with transition divalent metal ions under basic conditions. In addition to its possible bioorganic significance, the interest and relevance of compound **9** is that it is a bis-*aza* analogue of (**3**); the differences between heterocycles **3** and **9** are therefore amenable to

(5) In charge demand notation, the subscript identifies the group X for which the charge demand is evaluated, and the superscript identifies the system (benzylic or symmetrically disubstituted) from which c_X is calculated and to which it refers. A detailed description of the significance of charge demands *c* can be found in refs 2b,d, 3, and 4.

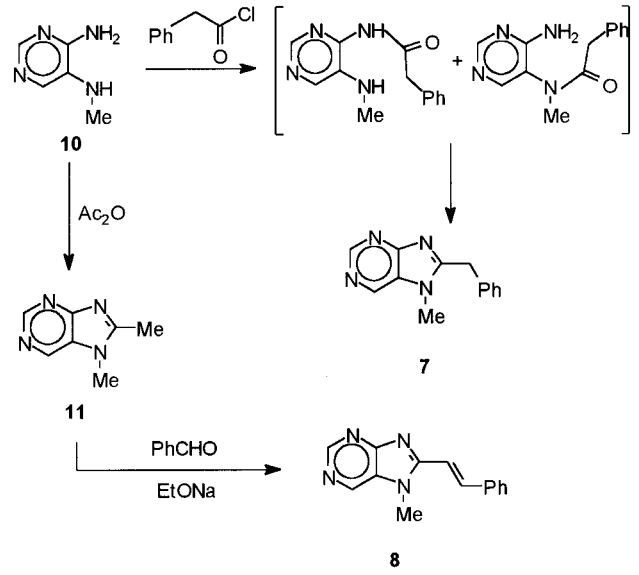
(6) Abbotto, A.; Bradamante, S.; Pagani, G. A.; Rzepa, H.; Stoppa, F. *Heterocycles* **1995**, *40*, 757−776.

(7) Another factor exerted by the heterocycle that possibly affects the stability of chelates is the ring size of the heterocycles (five- or six-membered). An account describing the results of a detailed investigation into this subject will be submitted elsewhere; Abbotto, A.; Bradamante, S.; Pagani, G. A. Manuscript in preparation.

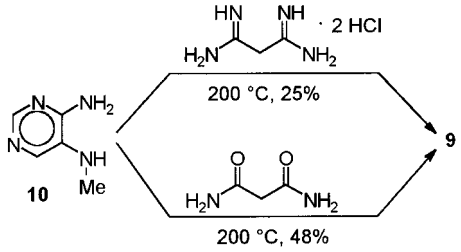
(8) Abbotto, A.; Alanzo, V.; Bradamante, S.; Pagani, G. A.; Rizzoli, C.; Calestani, G. *Gazz. Chim. Ital.* **1991**, *121*, 365−368.

(9) Abbotto, A. Ph.D. Thesis, University of Milano, Milano, Italy, 1993.

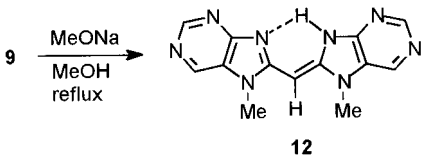
Scheme 1



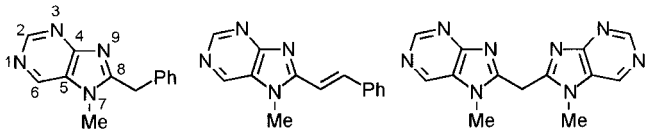
Scheme 2



Scheme 3



electronic effects only, which makes the comparison of their behavior toward metal ions particularly instructive.



Results

Synthesis. All of the synthetic strategies we have envisaged for the preparation of purine derivatives **7**−**9** involve 4-amino-5-(*N*-methylamino)pyrimidine (**10**) (AMAP) as a starting material. This compound was prepared according to Bredereck's procedure[10] by alkaline ring opening of 7-methylpurine. The treatment of AMAP (**10**) with phenylacetyl chloride gave a mixture of acylation products that underwent ring closure upon heating at 210 °C and removing of the formed water (Scheme 1). Neither phenylacetic acid at 200 °C nor phenylacetamide in ethylene glycol at 200 °C reacted with AMAP. The styryl derivative **8** was prepared by base-catalyzed condensation of benzaldehyde with 7,8-dimethylpurine (**11**), which was in turn prepared by the action of acetic anhydride on AMAP (Scheme 1).

The general entry we followed for the preparation of bis(7-methylpurin-8-yl)methane (BPUMH) (**9**) was the condensation of AMAP (**10**) with malonic acid derivatives. The reaction of **10** with malonammidine bis-hydrochloride at 200 °C without solvent afforded **9** in 25% yields; when malonamide was used under the same conditions, the yields could be increased to 48% (Scheme 2).

BPUMH is almost insoluble in all nonhydroxylic organic solvents but is appreciably soluble in water. Consequently, the second synthetic approach provides a crude reaction mixture from which BPUMH can be purified more easily (because no inorganic salts (NH_4Cl) are formed unlike in the reaction with malonammidine hydrochloride), and no tediously long extractions are needed to obtain the product. The reaction of AMAP with carboxamides appears to be unprecedented and should be preferred to the reaction with ammidines, which has been reported in the literature as a pathway for the production of purine derivatives.[11]

A stable enamine tautomer of BPUMH can be obtained by heating a methanolic solution of **9** at reflux in the presence of MeONa under an inert atmosphere. The NH-enamine **12** is formed almost quantitatively (Scheme 3). The two purinyl rings and the two methyl groups are isochronous at room temperature in DMSO-d_6, showing a fast intermolecular proton exchange. The 4.60 ppm peak due to the enamine proton disappears upon deuteration. Further evidence of the formation of the enamine is provided by the ^{13}C NMR (Table 2) and the MS spectrum, which shows the expected molecular peak as the parent peak.

From 8-benzyl-7-methylpurine (**7**) and bis(7-methylpurin-8-yl)methane (**9**), the corresponding conjugate carbanions $\mathbf{7}^-$ and $\mathbf{9}^-$ were prepared in DMSO using dimsylsodium as a base. The reasons for our choice of DMSO as a solvent have been documented elsewhere.[2] Under these conditions, the interaction with the gegenion—and the effect of this on the π-electronic distribution in the anions—is minimized and much smaller than in other common organic solvents, as is suggested by the fact that DMSO is known to be a highly dissociating medium and a good coordinating system for the sodium cation.[12]

NMR Shift Assignments. The ^{13}C and ^{15}N NMR shifts of compounds **7** and **9**, as well as of their conjugate carbanions $\mathbf{7}^-$ and $\mathbf{9}^-$, are shown in Table 2. We here provide a detailed interpretation of the NMR data when the assignments are not straightforward.

(a) ^{13}C Shifts. The ^{13}C shift assignments of compounds **7**, $\mathbf{7}^-$, **9**, $\mathbf{9}^-$, **12**, and **15** were based on splitting patterns and the known chemical shifts of purine.[13] Ambiguities sometimes occurred, and when possible, discrimination was based on the multiplicity of patterns and the values of the long-range coupling constants. In compound **9**, the assignments of C(4) and C(8) were as follows: 158.78 ppm, C(4), double doublet, $^3J_{C(4)-H(2)} =$

(10) Bredereck, H.; Effenberger, F.; Rainer, G. *J. Lieb. Ann. Chem.* **1964**, *673*, 82.

(11) For the synthesis of 8-alkylpurines, see: Bredereck, H.; Effenberger, F.; Österlin, H. G. *Chem. Ber.* **1967**, *100*, 2280−2291.

(12) (a) Hogen-Esch, T. E.; Smid, J. *J. Am. Chem. Soc.* **1966**, *88*, 307−324. (b) Arnett, E. M.; McKelvey, D. R. *J. Am. Chem. Soc.* **1966**, *88*, 2598−2599. (c) Gutman, V. *The Donor−Acceptor Approach to Molecular Interactions*; Plenum Press: New York, 1978; Chapters 7 and 10.

(13) Breitmaier, E.; Voelter, W. *Carbon-13 NMR Spectroscopy*; VCH: Weinheim, 1987; p 284.

Table 2. $^{13}C^{a}$ and $^{15}N^{b}$ NMR Shifts (ppm) of 8-Benzyl-7-methylpurine (7), Its Conjugate Carbanion 7^-, Bis(7-methylpurin-8-yl)Methane (9), Its Conjugate Carbanion 9^-, Its Enaminic Form 12, and Its Neutral Complex with Zn(II) 15, in DMSO^{c}

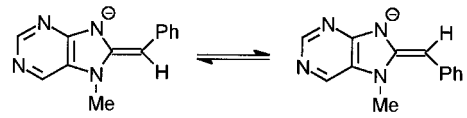
		purine ring positions									phenyl ring positions						
compd		1	2	3	4	5	6	7	8	9	ortho	meta	para	ipso	CH_2/CH^-	^1J, Hz^d	CH_3
7^e		276.6	152.05	269.3	159.83^f	127.20	139.72	139.4	159.07^f	244.0	128.89	128.63	126.82	135.67	32.90	130.5	30.47
7$^{-\,g}$	95%	244.8	150.63	237.2	165.61	130.78	121.55	98.6	158.67	200.6	123.82	128.30	117.33	144.02	73.52	149.1	29.24
	5%^{h}		143.86		156.42				157.96			129.20		144.55	71.14	150.5	27.60
9		279.7	152.15	271.5	158.78	127.26	140.09	146.2	155.90	246.0					26.88	131.8	30.75
9$^{-\,i}$	50%		150.58		162.58	127.25	129.46		160.49						60.12	153.4	29.12
	25%		149.14		164.84	130.24	121.35		156.27						60.76^j	148	28.46
	25%^{k}		155.72		147.28	101.58	l		145.13						60.84^j	148	29.62
			155.60		147.14	101.14	l		145.04								29.44
	m	262.0	151.01	255.4	163.02	128.16	129.86	110.7	160.96	202.5					60.46	153.3	29.53
12			150.48		162.54	127.71	129.96		160.46						60.07	153.7	29.09
15			151.33		158.26^n	126.34	132.80		157.44^n						60.02	168.5	29.60

^{a} Relative to Me_4Si (0.0 ppm). ^{b} Relative to liquid NH_3 (0.0 ppm), 380.23 ppm from neat nitromethane. ^{c} 0.50 M solutions at 27 °C, unless otherwise noted. ^{d} Relative to the methylene or methine bridge. ^{e} 0.10 M. ^{f} Values can be exchanged. ^{g} 0.25 M. ^{h} Only a limited number of signals of the minor isomer were detected and assigned. ^{i} 0.15 M. ^{j} Broad. ^{k} Two series of signals, each corresponding to one purine ring, were detected for this isomer. ^{l} Assignment for this position was not unequivocally performed. ^{m} 45 °C. ^{n} Values can be exchanged.

9.7 Hz, in line with $^3J_{C(4)-H(2)} = 10.9$ Hz in purine,[14] and $^3J_{C(4)-H(6)} = 3.4$ Hz, in line with $^3J_{C(4)-H(6)} = 4.8$ Hz in purine;[14] 155.90, C(8), triplet, $^2J = 9$ Hz, in line for instance with C(2) of **1**, **2**, and corresponding benzyl derivatives (triplet, $^2J = 8.5-9$ Hz).[3] In compound $\mathbf{9}^-$, the assignments of C(4) and C(8) at 45 °C were as follows: 163.02 ppm, C(4), double doublet, $^3J_{C(4)-H(2)} = 9.6$ Hz and $^3J_{C(4)-H(6)} = 3.4$ Hz; 160.96, C(8), singlet, in line for instance with C(2) of **1**, **2**, and corresponding benzyl derivatives (singlet or doublet with $^2J < 2$ Hz).[3]

(b) ^{15}N Shifts. The shift assignments of the four nitrogen atoms of the purine ring in the neutral compounds **7** and **9** were based on the reported nitrogen shieldings for 7-methylpurine.[15] In anions $\mathbf{7}^-$ and $\mathbf{9}^-$, all of the nitrogen atoms experience a high-field displacement with respect to the neutrals. This is related to an increase in π-electron density and is consistent with the observed behavior of the pyridine-like and pyrrole-like nitrogen atoms of previously investigated anions.[2e,f,3,6] On the basis of this, it is assumed that the chemical shift order of the four nitrogen atoms of the neutrals is maintained in the anions.

Geometric Isomerism in the Anions. The ^{13}C NMR spectrum of the benzyl anion $\mathbf{7}^-$ shows that two distinct isomers (*E* and *Z*) are present in DMSO solution at 27 °C, one of which is largely predominant. The presence of geometric isomers is due to the partial double-bond character of the bond linking the carbanionic carbon and the heterocycle and is in line with the isomer equilibrium observed for the anions of benzylazoles[3] and benzylazines.[2e,f,6] NOE experiments on the anions of benzylazines (e.g., 2-benzylpyridine, benzylpyrazine, etc.) allowed it to be determined that the phenyl ring in the most stable isomer prefers to stay syn to the pyridic nitrogen atom of the heterocyclic ring (the atom bearing the delocalized negative charge). Because of the lack of protons in proper positions, we could not perform the same measurement for anion $\mathbf{7}^-$. Semiempirical calculations using the AM1 and the PM3 SCF-MO Hamiltonian included in the MOPAC package[16] were performed on the geometric isomers of anion $\mathbf{7}^-$, with the keywords AM1 (or PM3), EF, PRECISE, and CHARGE=−1. The counterion was not included in the calculation in order to properly mimic the nature of anionic species in DMSO, where they exist as solvent-separated or free ions. The geometries were fully optimized without any constraint, in the gas phase.



Both the AM1 and PM3 computations predict that isomer *E* is the most stable by 0.9 and 4.1 kcal/mol, respectively; however, the small difference in relative energy and the known limited accuracy of semiempirically computed energy values does not allow any definitive conclusion to be drawn concerning the relative stability of the two isomers. Since the semiempirical approach is usually considered to be sufficiently accurate in geometry optimization, the computed planar structure of the *E* isomer (against the nonplanar geometry of the second species) suggests that its predicted higher stability is justified by a more efficient delocalization along the entire system.

Three sets of ^{13}C NMR resonances were detected for the solution of the anion ($\mathbf{9}^-$) of BPUMH at 27 °C in DMSO, with two of them having the two purine rings as isochronous and the third having two series of signals, each corresponding to a heterocyclic ring. At 45 °C all of the multiple peaks of the decoupled ^{13}C NMR spectrum collapse into a single set of resonances, thus showing that the three species undergo a fast interconversion (in the NMR time scale) under these conditions. The three anionic species slowly interconverting at room temperature were identified as the three geometric isomers (*E*,*E*)-$\mathbf{9}^-$, (*E*,*Z*)-$\mathbf{9}^-$, and (*Z*,*Z*)-$\mathbf{9}^-$.

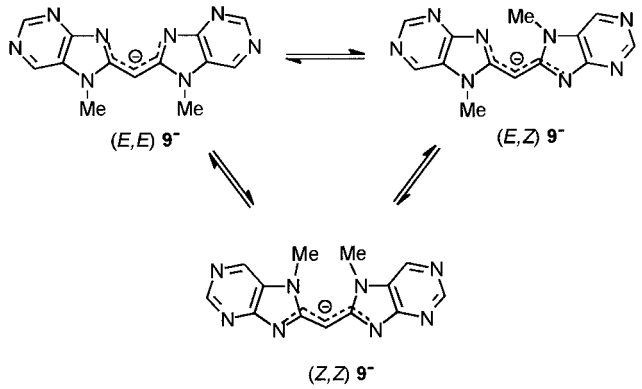
As in the case of benzyl anion $\mathbf{7}^-$, we cannot assign each set of NMR signals to a specific isomer, with the exception of the species (*E*,*Z*)-$\mathbf{9}^-$, in which the corresponding carbon sites of the two rings are chemically nonequivalent. In agreement with the simultaneous presence of the three isomers at the equilibrium, AM1 computations in the gas phase do not predict any of these species as being much more stable than the others (the

(14) See ref 13, p 290.
(15) Witanowski, M.; Stefaniak, L.; Webb, G. A. In *Annual Reports on NMR Spectroscopy*; Webb, G. A., Ed.; Academic Press: London, 1986; Vol. 18, p 483.
(16) MOPAC 6.0: Stewart, J. J. P. *QCPE* **1990**, 455.

Table 3. Variations of the Local π-Electron Densities Δq^{π} (me) for Each *i*th Position on Going from the Neutral 8-Benzyl-7-methylpurine (7) and Bis(7-methylpurin-8-yl)Methane (9) to Their Conjugate Anions 7^- and 9^-, Respectively[a,b]

		purine ring positions									phenyl ring positions			
compd		1	2	3	4	5	6	7	8	9	ortho	meta	para	ipso
7^-	*c*	87	9	88	−36	−22	114	111	3	118	32	2	59	−52
9^-	*d*	48	7	44	−27	−6	64	97	−32	119				

[a] Positive values correspond to an increment of π-electron density. [b] Obtained from $\Delta q^{\pi} = -(\Delta\delta^{13}\text{C}/160)$ and $\Delta q^{\pi} = -(\Delta\delta^{15}\text{N}/366.34)$ for carbon and nitrogen atoms, respectively. [c] 95% isomer. [d] Chemical shift values of 9^- obtained at 45 °C were used.



relative energies of the three optimized geometries fall in a range of 2.5 kcal/mol). It is worth noting that the calculated nonplanarity of the *Z*,*Z* isomer, which is probably due to the steric interaction of the methyl groups (the dihedral angle between the planes of the two rings is ca. 45°), does not seem to affect the energy dramatically. This, together with the similar result found in the case of benzyl anion **8**, suggests that the deviation from planarity of the anionic system has little effect on its stabilization.

***π*-Charge Mapping of the Anions and Charge Demands of the 8-Purinyl Substituent.** The variations in the local π-electron densities of each carbon atom of the phenyl and heterocyclic rings going from the neutral to the conjugate anion can be calculated from relationship 5, which is derived from relationship 1. Similarly, the ^{15}N-shift/π-electron density relationship (eq 6)[2f−h,3] makes it possible to calculate the variations in the local π-electron density of nitrogen atoms.

$$\Delta\delta^{13}\text{C} = -160\Delta q_{\text{C}}^{\pi} \quad (5)$$

$$\Delta\delta^{15}\text{N} = -366.34\Delta q_{\text{N}}^{\pi} \quad (6)$$

The calculated values for the systems **7**-7^- and **9**-9^- are shown in Table 3. The data for 7^- refer to the predominant (95%) species in solution, whereas the chemical shifts in anion 9^- at coalescence temperature were considered when applying the π-charge/shift relationships. Table 4 summarizes the π-electron density of the central carbanionic carbon, q_{C} (as obtained from relationship 1), and of the aromatic rings, q_{Het} and q_{Ph} (the latter values account for how many electrons have been withdrawn by these groups from the deprotonated carbanionic carbon). Table 4 also shows the total π-electron densities q_{tot} of anions 7^- and 9^- as the sum of their calculated partial π-electron densities. Finally the charge demands c_{X}^{Ph} and c_{X}^{X} of the 7-methylpurin-8-yl ring have been calculated by applying relationships 2 and 3 and from the data of Table 4 (Table 5). Details of the procedure we followed in order to obtain the above values have been previously reported.[3]

Table 4. Experimental π-Electron Densities *q* (e) for Conjugate Anions 7^- and 9^- of 8-Benzyl-7-methylpurine (7) and Bis(7-methylpurin-8-yl)Methane (9)

compd	q_{Het}[a]	q_{Ph}[b]	q_{C}[c]	q_{tot}[d]
7^-	10.471	6.075	1.389	17.935[e]
9^-	10.315		1.390	22.020[f]

[a] π-Electron density resident on the purine ring: $q_{\text{Het}} = 10 + \sum(\Delta q^{\pi})_{\text{purine ring}}$; data are taken from Table 3. [b] π-Electron density resident on the phenyl ring: $q_{\text{Ph}} = 6 + \sum(\Delta q^{\pi})_{\text{phenyl ring}}$; data are taken from Table 3. [c] π-Electron density resident on the carbanionic carbon, calculated applying relationship 1, using $A_{\text{Ph}} = 13.00$ (ref 2b), $A_{\text{purine}} = 0.0$ (see Table 5), and chemical shift values reported in Table 2. [d] Total π-electron density of the anionic system, to be compared with the theoretical value of 18 and 22 π-electrons for 7^- and 9^-, respectively. [e] $q_{\text{tot}} = q_{\text{Het}} + q_{\text{Ph}} + q_{\text{C}}$. [f] $q_{\text{tot}} = 2q_{\text{Het}} + q_{\text{C}}$.

Table 5. Shielding Contribution A_{X} and Charge Demand of the 7-Methylpurin-8-yl Substituent (X) in $PhCH^-X$ 7^- (c_{X}^{Ph}) and X_2CH^- 9^- (c_{X}^{X})

A_{X}[a]	c_{X}^{Ph} [b]	c_{X}^{X} [c]
0.0	0.536	0.305

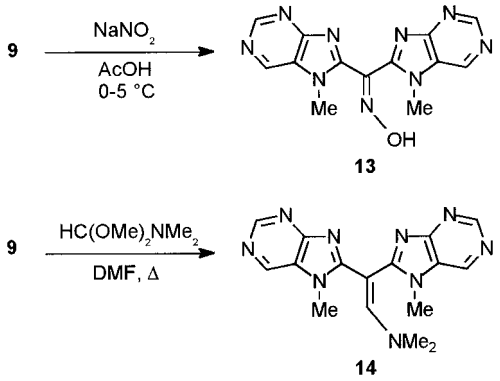
[a] Calculated from the difference between the shifts of β-carbons in 4-methyl-8-styrylpurine (**8**) (113.17 ppm) and styrene (113.2 ppm; ref 18, p 161); see text. [b] Calculated applying relationship 3, with $c_{\text{Ph}} = q_{\text{Ph}} - 6$; data are taken from Table 4. [c] Calculated applying relationship 2; data are taken from Table 4.

Reaction of BPUMH with Electrophiles and Preparation of Neutral Chelates with Divalent Transition Metals. The high charge demand c_{X}^{X} of the 7-methylpurin-8-yl substituent (0.305), which is comparable with that of the COR (0.32−0.34) and COOR (0.27) groups,[2g] suggests that BPUMH might behave as an "active methylene" compound and react with electrophiles at the central methylene. We have already shown that 2-benzothiazolyl ($c_{\text{X}}^{\text{X}} = 0.316$),[3] 2-benzoxazolyl ($c_{\text{X}}^{\text{X}} = 0.288$),[3] and 2-thiazolyl ($c_{\text{X}}^{\text{X}} = 0.318$)[3] methylene derivatives undergo azo coupling with benzendiazonium chloride, nitrosation, condensation with aliphatic and aromatic aldehydes,[17] and condensation with dimethylformamide dimethyl acetal and triethyl orthoformate to give enamine and enol ether derivatives, respectively.[1]

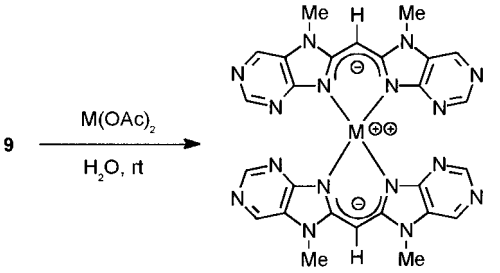
Scheme 4 summarizes the selected reactions with electrophiles investigated in this study. BPUMH (**9**) undergoes high-yield nitrosation with HNO_2 (formed in situ from sodium nitrite and acetic acid) to give the oxime **13**. Condensation of **9** with dimethylformamide dimethyl acetal furnished the enamine **14**. The reaction conditions were consistently milder than those required by the 2-benzothiazolyl and 2-benzoxazolyl derivatives **1** and **2**. The practically pure enamine **14** could be directly isolated from the reaction mixture: the absence of the need for chromatographic purification required in the previous cases led to a 2-fold increase in final yields.

Like the 2-benzothiazolyl and 2-benzoxazolyl methylene derivatives **1** and **2**, BPUMH reacts with metal

Scheme 4



Scheme 5

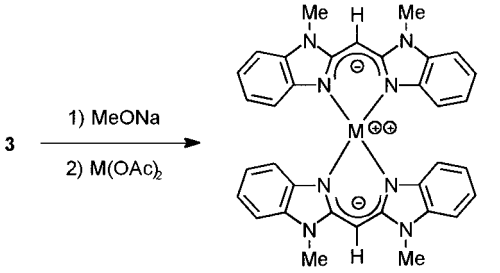


15: M = Zn (15 min, 59%)
16: M = Cu (15 min, 38%)
17: M = Co (30 h, 63%)

acetates in H_2O to furnish the corresponding neutral methanates $[ML_2]$ **15**−**17** (M = Zn, Cu, Co), in which the purinyl derivative acts as a carbanionic ligand (Scheme 5). Zn(II) and Cu(II) chelates form immediately upon the mixing of the reagents at room temperature, whereas the Co(II) chelate requires several hours of reaction under an inert atmosphere. All of the obtained chelates are stable in air and do not need any particular storage precautions. They are moderately soluble in hydroxylic solvents. The ^{13}C NMR data concerning the Zn(II) chelate **15** (Table 2) provide unequivocal evidence of the carbanionic nature of the ligand in the complex. In particular, the chemical shift of the carbanionic carbon (60.02 ppm) is almost identical with that of the corresponding site of the anion ($\mathbf{9}^-$) of BPUMH (60.46 ppm). All of the chelates have almost superimposable IR spectra. Given that the 2-benzothiazolyl derivative **1** affords a tetrahedral Zn(II) neutral chelate,[8] it is likely that all of the complexes prepared in this study have a similar arrangement around the metal.

The reaction of bis(*N*-methylbenzimidazol-2-yl)methane (**3**) with metal acetates does not lead to the formation of chelates, although chelates can be obtained provided that the weak base AcO^- is replaced by the stronger base MeO^- (Scheme 6). In this manner the Zn(II), Cu(II), and Co(II) neutral methanates can be isolated. The stability of these complexes is much less than that of the analogous derivatives of the purinyl-based ligand. However, the Zn(II) chelate is strategic for the evaluation of the charge demand of the heterocycle. In fact, the c_X^X value for the *N*-methylbenzimidazol-2-yl substituent is not available because of the solubility problems of the anion of **3**,[3] and no direct comparison can be made between the benzimidazolyl and purinyl groups. A reliable estimate of this value can be obtained by exploiting the chemical shift of 53.53 ppm for the central carbanionic carbon of

Scheme 6

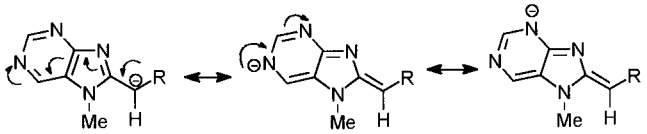


18: M = Zn (30 min, 93%)
19: M = Cu (1 h, 69%)
20: M = Co (30 min, 76%)

the neutral chelate of **3** with Zn(II). The application of relationships 1 and 2, together with the use of the already determined shielding contribution A_i,[3] gives a value of 0.276 for the c_X^X of the *N*-methylbenzimidazol-2-yl substituent. This procedure is legitimate because the chemical shifts of the carbanionic carbon in the sodium salts and neutral chelates with Zn(II) are practically identical for both the benzothiazol-2-yl (81.4[3] vs 80.6[8] ppm) and purinyl (60.5 vs 60.0 ppm (Table 2)) derivatives.

Discussion

The use of new or improved synthetic schemes has made it possible to obtain some attractive new purinyl derivatives. Our multinuclear NMR and charge demand approaches have provided interesting insights into the electronic nature of this heteroaromatic substituent. First of all, the existence of anions $\mathbf{7}^-$ and $\mathbf{9}^-$ as mixtures of geometric isomers is a consequence of the high double-bond character of the bond linking the carbanionic carbon and C(8) of the purine ring, thus demonstrating the considerable delocalizing capacity of the heterocycle. In particular, the c_X^{Ph} value (0.536) for the 7-methylpurin-8-yl substituent is not only higher than that of the azinyl and azolyl substituents investigated in our previous studies (Table 1) but also very close to that of COPh (0.56), one of the stronger classical electron-withdrawing groups.[2g] It is worth noting that both the imidazolyl and benzimidazolyl rings rank low among the electron-withdrawing heterocyclic groups shown in Table 1. Thus, the main reason of the high charge demand of the purinyl substituent is the fusion of the imidazolyl fragment to a pyrimidine ring. The properly designed position of the nitrogen atoms in the six-membered ring fused to the imidazolyl ring in this isomer of the purinyl substituent (7-methylpurin-8-yl rather than 9-methylpurin-8-yl) allows highly effective resonance delocalization of the negative charge resident on an adjacent carbanionic site, as can be seen from resonance structures A−C.



In the benzyl anion $\mathbf{7}^-$, almost 50% of the negative charge resides on the heterocyclic ring and *only* 7% is delocalized into the phenyl ring. The four nitrogen atoms host 85% of the total negative charge of the purinyl ring, a value which becomes almost 100% in the case of the

Table 6. Calculated Semiempirical (AM1) π-Charges (me) for Each *i*th Position of the Purine Ring of 8-Benzyl-7-methylpurine (7) and Its Conjugate Anion 7^-

compd	1	2	3	4	5	6	7	8	9
7	−147	+76	−135	+28	−103	+64	+338	+52	−224
$\mathbf{7}^-$ [a]	−237	+61	−239	+106	−101	−14	+287	+118	−406

[a] Calculated $q_C^\pi = 1.384$.

symmetrically disubstituted carbanion $\mathbf{9}^-$. The low π-charge resident on the aromatic carbon atoms of anions $\mathbf{7}^-$ and $\mathbf{9}^-$ is actually the average result of increases and decreases in π-electron density in comparison with the neutral precursors. The quaternary carbons at positions 4, 5, and 8 experience a decrease in π-electron density when going from the neutral to the anion, whereas a considerable increase in the negative π-charge is measured for position 6. Although the former result can be rationalized in terms of the usual π-electron density decrease in C_i of the phenyl ring (polarization effects or an increase in the σ-charge),[2d,18] the latter is clearly unexpected since no resonance structures of the type A−C can be written with the negative charge delocalized into this position. In an attempt to rationalize this unexpected NMR result, we calculated the π-charges for the benzyl derivative **7** and its conjugate anion $\mathbf{7}^-$ at the AM1 semiempirical level. Table 6 shows that the carbon atoms 2 and 6 are positively charged in the neutral system as a result of the electron-withdrawing mesomeric effect of the aza groups in the ortho and para positions. After deprotonation, the nitrogen atoms receive a considerable amount of negative charge, which leads to a decrease (or saturation) in their mesomeric effects toward the adjacent carbon atoms: as a consequence, there is a decrease in the positive charge on these carbon atoms that leads to an increase in π-electron density when going from the neutral to the anion.

The already established validity of the applied shift/charge relationships 1, 5, and 6 and the charge demand approach is further confirmed by the reactivity of BPUMH (**9**). Particularly important experimental evidence is provided by the stability of the BPUMH NH-tautomer. We have previously shown that, although enamine forms of bis(benzothiazol-2-yl)methane (**1**) and bis(benzoxazol-2-yl)methane (**2**) have never been isolated, substitution with a third strong electron-withdrawing group at the central carbon atom stabilizes the corresponding enamine tautomers.[1] Similarly, bis(pyrid-2-yl)acetonitrile exists as the corresponding NH tautomer, but bis(pyrid-2-yl)methane does not.[6] Given that the charge demand of 2-benzothiazolyl, 2-benzoxazolyl, and 2-pyridyl is already highly ranked among the π-deficient heterocycles, the stability of the BPUMH NH-enamine tautomer alone (that is, without any need for further substitution by activating groups) provides unequivocal evidence of the exceptionally high electron-withdrawing capacity of the purinyl ring. It is interesting to note that the ^{13}C NMR of the enamine **12** is almost identical with that of the carbanion $\mathbf{9}^-$, which suggests that both species have a similar π-electronic distribution despite the fact that the former is neutral and the latter is anionic.

In line with these considerations, it has been shown that BPUMH undergoes easy, clean, and high-yield condensation with electrophiles behaving as an "active methylene" compound. With the exception of our own previous studies, electrophilic reactions of the methylene of bis(heteroaryl)methanes have rarely been reported in the literature.[19]

A further manifestation of the overall electron deficiency of the purine system provided by the fused pyrimidine ring can be identified in the hydroxyl ion attack at position 8 of 7-methylpurine (as correctly reported by Bredereck),[10] which leads to the opening of the imidazole ring and affords 4-amino-5-(*N*-methylamino)pyrimidine. No similar reaction in benzimidazole derivatives appears to be known insofar as their ring opening requires *N*-quaternarization.

Finally, the high charge demand of the purine ring and the consequent relative stability of the carbanion of BPUMH clearly provide the basis for the easy formation of the neutral chelates $[ML_2]$, in which the heterocyclic derivative is present as an anionic ligand. The estimated c_X^X value of the *N*-benzimidazol-2-yl groups is smaller than that of any of the benzofused heterocycles so far investigated by our group (see Table 1). This result rationalizes the unique behavior of the benzimidazolyl derivative toward coordination with divalent metals in comparison with the other bis(heteroaryl)methanes. To obtain the corresponding neutral chelate, a stronger base than AcO^- must be used. In other words, the acetic acid in eq 4 must be replaced by a weaker acid (such as methanol), which is no longer capable of reacting with the carbanionic site of the ligand in the complex in order to shift the equilibrium toward the uncomplexed neutral heterocycle.

We therefore conclude that the charge demand of the heterocycles plays a primary and strategic role in the formation of this type of chelates and provides clear and definitive insights into this novel and interesting class of coordination compounds.

Experimental Section

^{13}C and ^{15}N NMR spectra were recorded using a Bruker AMX-500 spectrometer operating at 125.78 and 50.75 MHz, respectively. The spectral parameters and calibrations have been previously reported.[2f] Anhydrous *N*,*N*-dimethylformamide (DMF) was supplied by Fluka and stored over molecular sieves. Extracts were dried over Na_2SO_4. Melting points are uncorrected. Anions were prepared following the procedure already described.[2a]

4-Amino-5-(methylamino)pyrimidine (10). A mixture of 7-methylpurine[10,20] (1.82 g, 13.6 mmol) and 1 M NaOH (10 mL) was refluxed for 2 h. The yellow solution was acidified with diluted HCl, and Na_2CO_3 was added in order to adjust the pH to about 9. The solution was then evaporated to dryness. The solid residue was continuously extracted (5 h) in a Kumagawa apparatus with THF (100 mL). The yellow solution was evaporated to dryness to leave the compound (1.23 g, 9.90 mmol, 73%): mp 190−195 °C (lit.[10] mp 191−192 °C); ^1H NMR ($CDCl_3$) δ 8.25 (s, 1 H), 7.77 (s, 1 H), 4.8 (broad, 3 H), 2.88 (s, 3 H); ^1H NMR (DMSO-d_6) δ 7.84 (s, 1 H), 7.40 (s, 1 H), 6.33 (s, 2 H), 4.90 (bq, 1 H), 2.73 (d, 3 H).

Bis(7-methylpurin-8-yl)methane (9). Method A. An intimate mixture of 4-amino-5-(methylamino)pyrimidine (**10**) (1.00 g, 8.05 mmol) and malonamide (0.822 g, 8.05 mmol) was heated under nitrogen at 180 °C for 1 h. The reaction took

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place in the melt. After all **10** had reacted, another aliquot of **10** (1.00 g, 8.05 mmol) was added and the mixture was heated for another 3 h at 180 °C. The solid, red mass was treated at reflux with acetonitrile (12 mL) for 15 min. The cool mixture was then filtered, and the solid was thoroughly washed with acetonitrile (6 mL) to give the compound as a red solid (1.08 g, 3.85 mmol, 48%): mp >300 °C; ^{1}H NMR (DMSO-d_6) δ 9.17 (s, 2 H), 8.91 (s, 2 H), 4.93 (s, 2 H), 3.96 (s, 6 H). Anal. Calcd for $C_{13}H_{12}N_8$: C, 55.70; H, 4.32; N, 39.98. Found: C, 55.22; H, 4.31; N, 39.62.

Method B. An intimate mixture of 4-amino-5-(methylamino)pyrimidine (**10**) (2.83 g, 22.8 mmol) and malonoammidine dihydrochloride[21] (1.97 g, 11.4 mmol) was heated under nitrogen at 200 °C for 8 h. The reaction took place in the melt. The solid mass was then submitted to continuous extraction with THF (250 mL) in a Kumagawa apparatus. The solvent was removed from the obtained yellow solution to leave a residue which was taken up with MeOH (3 mL). The solid was separated by filtration and dried under reduced pressure to give the compound as a red solid (0.750 g, 2.67 mmol, 23%): mp >300 °C.

7,8-Dimethylpurine (11). A solution of 4-amino-5-(methylamino)pyrimidine (**10**) (0.400 g, 3.22 mmol) in acetic anhydride (20 mL) was refluxed for 10 h. The yellow solution turned to brown during the reaction. The mixture was allowed to cool, and the excess acetic anhydride was removed by distillation under reduced pressure. The brown residue was taken up with EtOH (2 mL), and the mixture refluxed for 30 min. Upon cooling a precipitate was formed which was separated by filtration to afford the compound (0.123 g, 0.830 mmol, 26%): mp 193−194 °C (lit.[11] mp 196−197 °C); ^{1}H NMR (DMSO-d_6) δ 9.04 (s, 1 H), 8.85 (s, 1 H), 3.85 (s, 3 H), 2.62 (s, 3 H).

7-Methyl-8-(*β*-styryl)purine (8). A 1 M solution of MeONa in MeOH (6 mL) was added to a mixture of 7,8-dimethylpurine (0.100 g, 0.675 mmol) and freshly distilled benzaldehyde (0.079 g, 0.74 mmol). After stirring for 3 days at room temperature, the red solution was concentrated to 2 mL and the solid was filtered to give the compound (0.089 g, 0.38 mmol, 56%): mp 244−246 °C. A white sample was obtained by recrystallization from EtOH: mp 245−247 °C; ^{1}H NMR (DMSO-d_6) δ 9.07 (s, 1 H), 8.90 (s, 1 H), 8.05 (d, 1 H, J = 16 Hz), 7.95−7.40 (m, 6 H), 4.03 (s, 3 H); ^{13}C NMR (DMSO-d_6) δ 159.17, 156.00, 152.62, 140.78, 139.74, 135.26, 129.89, 128.92, 128.10, 127.50, 113.17 (C_β with respect to phenyl ring), 29.09. Anal. Calcd for $C_{14}H_{12}N_4$: C, 71.16; H, 5.13; N, 23.72. Found: C, 71.29; H, 4.76; N, 23.96.

8-Benzyl-7-methylpurine (7). A solution of phenylacetyl chloride (2.23 g, 14.4 mmol) in anhydrous DMF (20 mL) was added dropwise to a mixture of 4-amino-5-(methylamino)pyrimidine (1.79 g, 14.4 mmol) and Et_3N (1.46 g, 14.4 mmol) in anhydrous DMF (30 mL) at room temperature. A white precipitate was formed. After stirring for 2 h, the solid was filtered off and the obtained solution was evaporated to dryness at reduced pressure. The resulting reddish oil was heated in a Kugelrohr apparatus at 220 °C under reduced pressure, and water was distilled off to leave a reddish glassy mass which was treated with a solution of $HgCl_2$ (3.00 g, 11.0 mmol) in EtOH (20 mL). The resulting yellow precipitate (the adduct of 7-methyl-8-benzylpurine with $HgCl_2$) (1.21 g) was treated for 1 h with a 0.1 M aqueous solution of $Na_2S{\cdot}9H_2O$ (25 mL). The black precipitate (HgS) was filtered off, and the obtained yellow solution was evaporated to dryness. The residue was then taken up with water and extracted with ethyl acetate (3 × 25 mL). The solvent was removed from the dried combined organic extracts to leave the product as a yellow solid (0.358 g, 1.60 mmol, 11.1%): mp 118−120 °C. An analytical sample was purified to give a pale-yellow solid: mp 122−123 °C (MeOH); ^{1}H NMR (DMSO-d_6) δ 9.08 (s, 1 H), 8.91 (s, 1 H), 7.33 (s, 5 H), 4.41 (s, 2 H), 3.85 (s, 3 H). Anal. Calcd for $C_{13}H_{12}N_4$: C, 69.62; H, 5.39; N, 24.98. Found: C, 69.90; H, 5.42; N, 24.76.

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Enamine Tautomer of Bis(7-methylpurin-8-yl)methane (12). Bis(7-methylpurin-8-yl)methane (**9**) (0.200 g, 0.713 mmol) was added portionwise to a 1 M solution of MeONa in MeOH (20 mL) under nitrogen. The reaction mixture was refluxed for 1 h. The formation of a precipitate was observed. After cooling, the solid was separated by filtration to give the raw product **12** as a brownish solid (0.188 g, 0.671 mmol, 94.1%): mp >250 °C. An analytical sample was recrystallized from water and washed with MeOH to give yellow needles: ^{1}H NMR (DMSO-d_6) δ 8.38 (s, 2 H), 8.15 (s, 2 H), 4.60 (s, 1 H), 3.97 (s, 1 H), 3.55 (s, 6 H) (peak at 4.60 ppm disappears upon deuteration); MS (EI) m/z 280 ($M^{\bullet+}$, 100), 265 (10), 248 (45), 134 (25). Anal. Calcd for $C_{13}H_{12}N_8$: C, 55.70; H, 4.32; N, 39.98. Found: C, 55.21; H, 4.12; N, 40.32.

Nitrosation of Bis(7-methylpurin-8-yl)methane. Finely divided $NaNO_2$ (0.110 g, 1.59 mmol) was added portionwise to a stirred solution of bis(7-methylpurin-8-yl)methane (**9**) (0.230 g, 0.821 mmol) in AcOH (10 mL) and water (2 mL), maintaining the temperature between 0 and 5 °C. After stirring for 20 min the solution was evaporated to dryness to leave a yellow residue which was taken up with water (3 mL). The pH of the suspension was adjusted to neutral with $NaHCO_3$, and the solid was separated by filtration and washed with water (2 mL) to give the product **13** as a light-brown solid (0.204 g, 0.659 mmol, 80.3%): mp >250 °C. An analytical sample was purified to give a whitish solid (water): ^{1}H NMR (DMSO-d_6) δ 9.29 (s, 1 H), 9.24 (s, 1 H), 9.02 (s, 1 H), 8.93 (s, 1 H), 4.23 (s, 3 H), 3.83 (s, 3 H). Anal. Calcd for $C_{13}H_{11}N_9O$: C, 50.48; H, 3.59; N, 40.76. Found: C, 50.33; H, 3.62; N, 40.61.

Condensation of Bis(7-methylpurin-8-yl)methane with *N*,*N*-Dimethylformamide Dimethyl Acetal: α,α-Bis(7-methylpurin-8-yl)-*β*-(dimethylamino)ethene (14). Bis(7-methylpurin-8-yl)methane (**9**) (0.040 g, 0.14 mmol) was added portionwise under nitrogen to a stirred solution of *N*,*N*-dimethylformamide dimethyl acetal (0.050 g, 0.42 mmol) in anhydrous DMF (4 mL). After stirring for 5 h at 50 °C, the resulting red solution was evaporated to dryness to leave an orange oil. This residue was taken up with Et_2O to give the product as a dark-orange solid (0.040 g, 0.12 mmol, 86%): mp >240 °C; ^{1}H NMR (DMSO-d_6) δ 9.09 (s, 1 H), 8.94 (s, 1 H), 8.79 (s, 1 H), 8.77 (s, 1 H), 7.87 (s, 1 H), 3.58 (s, 3 H), 3.24 (s, 3 H), 2.9 (broad, 6 H); HRMS m/z calcd for $C_{16}H_{17}N_9$ 335.1607, found 335.1612.

Metal Chelates of Bis(7-methylpurin-8-yl)methane (15−17). A solution of $Zn(OAc)_2{\cdot}2H_2O$ (0.059 g, 0.27 mmol) in water (2 mL) was added to a solution of bis(7-methylpurin-8-yl)methane (**9**) (0.150 g, 0.54 mmol) in water (15 mL). After the mixture stirred for 15 min at room temperature, the green crystalline precipitate was filtered, washed with water, and dried under reduced pressure to afford **15** as a green solid (0.098 g, 0.16 mmol, 59%): mp >250 °C; ^{1}H NMR (DMSO-d_6) δ 8.49 (s, 4 H), 8.32 (s, 4 H), 5.28 (s, 2 H), 3.77 (s, 12 H). Anal. Calcd for $C_{26}H_{22}N_{16}Zn$: C, 50.04; H, 3.56; N, 35.92. Found: C, 49.97; H, 3.79; N, 36.06.

In the same manner from $Cu(OAc)_2{\cdot}H_2O$ (0.054 g, 0.27 mmol) and bis(7-methylpurin-8-yl)methane (**9**) (0.150 g, 0.54 mmol) was obtained chelate **16** as a green solid (0.064 g, 0.10 mmol, 38%): mp >250 °C. Anal. Calcd for $C_{26}H_{22}N_{16}Cu$: C, 50.19; H, 3.57; N, 36.03. Found: C, 50.40; H, 3.68; N, 36.49.

Similarly, from $Co(OAc)_2{\cdot}4H_2O$ (0.067 g, 0.27 mmol) and bis(7-methylpurin-8-yl)methane (**9**) (0.150 g, 0.54 mmol) was obtained chelate **17**, after stirring for 30 h at room temperature under nitrogen, as an orange solid (0.105 g, 0.17 mmol, 63%): mp >250 °C. Anal. Calcd for $C_{26}H_{22}N_{16}Co$: C, 50.56; H, 3.60; N, 36.30. Found: C, 50.36; H, 3.58; N, 36.47.

Metal Chelates of Bis(*N*-benzimidazol-2-yl)methane (18−20). A 1 M methanolic solution of MeONa (1 mL) was added to a solution of bis(*N*-benzimidazol-2-yl)methane (**3**) (0.276 g, 1.00 mmol) in MeOH (8 mL) under nitrogen. After a few minutes a solution of $Zn(OAc)_2{\cdot}2H_2O$ (0.109 g, 0.50 mmol) in MeOH (2 mL) was added to the reaction mixture. After the mixture was stirred for 30 min at room temperature, the yellow crystalline precipitate was filtered, washed with MeOH, and dried under reduced pressure to afford **18** as a light-yellow solid (0.287 g, 0.47 mmol, 93%): mp >250 °C; ^{1}H

NMR (DMSO-d_6) δ 6.95 (d, 4 H), 6.86 (t, 4 H), 6.80 (d, 4 H), 6.72 (t, 4 H), 4.60 (s, 2 H), 3.63 (s, 12 H); ^{13}C NMR ($CDCl_3$) δ 157.07, 141.34, 134.76, 120.78, 118.94, 112.57, 106.00, 53.53 (central CH^-), 29.14. Anal. Calcd for $C_{34}H_{30}N_8Zn$: C, 66.29; H, 4.91; N, 18.19. Found: C, 66.51; H, 4.62; N, 18.18.

In the same manner from $Cu(OAc)_2 \cdot H_2O$ (0.050 g, 0.25 mmol) and **3** (0.138 g, 0.50 mmol), after stirring for 1 h under nitrogen, was obtained chelate **19** as a green solid (0.105 g, 0.17 mmol, 69%): mp >250 °C. Anal. Calcd for $C_{34}H_{30}N_8Cu$: C, 66.49; H, 4.92; N, 18.24. Found: C, 66.11; H, 4.18; N, 18.69.

Similarly, from $Co(OAc)_2 \cdot 4H_2O$ (0.062 g, 0.25 mmol) and **3** (0.138 g, 0.50 mmol) was obtained chelate **20**, after stirring for 30 h at room temperature under nitrogen, as an orange solid (0.116 g, 0.19 mmol, 76%): mp >250 °C. Anal. Calcd for $C_{34}H_{30}N_8Co$: C, 66.99; H, 4.96; N, 18.38. Found: C, 66.53; H, 5.07; N, 18.47.

Supporting Information Available: Copies of the ^{1}H NMR (DMSO-d_6) spectrum (full and aromatic region) of compound **14** (with DMF) (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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