electron-transfer (et)/addition (ad)/elimination (el) mechanism.

4. Further Conclusions. It is interesting to compare the activation parameters for reaction of $CH_3\dot{C}HOH$ (in which radical anion and nitroxyl are *produced*, see eq 3)[9] with those[9] for heterolytic *decomposition* of the nitroxyl (rate constant k_{hs}, eq 3). For the heterolysis the activation enthalpies (average 35 kJ mol^{-1}) are higher, whereas the activation entropies [average −53 J $(mol\ K)^{-1}$] are the same as those for the production of nitroxyl (−50 units). If it is taken into account that the formation reaction is bimolecular (with an intrinsic energy loss), whereas the heterolysis reaction is unimolecular (where *one* molecule is broken up to give *three* components, thereby leading to an intrinsic entropy gain), the same number for the overall entropy loss means that there is a lot more solvent immobilization in the transition state of the heterolysis than in the formation of the nitroxyl. This is probably the consequence of deprotonation (from the hemiacetal OH) in the transition state of the heterolysis, eq 4c (as shown by the solvent kinetic isotope effect[9]).

Another relevant aspect is the thermodynamics of the reaction of α-hydroxyalkyl radicals with nitrobenzenes. For instance, in the case of $\dot{C}H_2OH$, the weakest electron donor in its class, (outer-sphere) electron transfer is thermodynamically highly favorable [on the basis of the redox potentials,[20] the driving force (ΔG) for the reaction $\dot{C}H_2OH$ + 4-NAP → CH_2O + 4-$NAP^{\bullet-}$ + H^+ is equal to 1 eV, which corresponds to 96 kJ mol^{-1}]. In spite of this, the reaction proceeds exclusively by addition.[9] For an explanation it has to be considered that an important part of the driving force results from hydration of the proton,[30] and is therefore not available unless the proton is fully hydrated in the transition state (which is not the case, see section 3b). However, even if it was taking place, this would lead to an even more drastic reorganization of the solvent shell than in the case of addition, with a correspondingly high loss[25] of entropy.

In this connection, it is interesting to compare nitroaromatics with molecular oxygen. Like nitroaromatics, oxygen reacts with α-hydroxyalkyl radicals exclusively by addition,[15a,32] and this in spite of the fact that electron transfer (to give alkanone, $O_2^{\bullet-}$, and H^+) is thermodynamically even more favorable than in the case of the nitrocompounds, which are weaker oxidants than O_2.[20] It has previously been pointed out[5e,10] that this similarity in behavior may be related to the ability of nitroaromatics to replace oxygen as a radiation sensitizer.

Note Added in Proof. The electron-transfer/addition mechanism suggested shows strong parallelisms with that[33] proposed for collapse of ion and radical pairs produced by charge-transfer photochemistry of electron donor–acceptor complexes.

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Synthesis and Properties of Purinophanes: Relationship between the Magnitude of Hypochromism and Stacking Geometry of Purine Rings†[1]

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Abstract: Twelve purinophanes **1–12**, in which two purine rings are fixed with different modes of stacking by two or three polymethylene chains, have been prepared by either stepwise introduction of the linking chains or quasi-dimerization of disubstituted purine derivatives. The five kinds of stacking geometries of the two component rings in the purinophanes were determined by X-ray analysis and/or ^1H NMR. The interplanar distances vary from 3.2 to 6.6 Å. All of the purinophanes **1–12** show large hypochromism (decrease in integrated absorption intensity compared with two molar monomeric references or one molar dimeric linear compound), and the maximum value was 47.6% for **6**. This is the largest value so far observed for dimeric nucleic acid bases. The hypochromism values of the purinophanes **1–8**, **11**, and **12** are almost identical in four different media (ethanol, water, 0.1 N HCl, 0.1 N NaOH). The bridge protons of these purinophanes show complex multiplets in their NMR spectra, in contrast to the first-order coupling patterns of acyclic reference compounds. These results indicate that the conformations of **1–8**, **11**, and **12** are almost frozen in the various media, at room temperature. On the basis of the structures determined by X-ray analysis, hypochromism values were calculated for three purinophanes by the Pariser–Parr–Pople method including configurational interactions. These, however, gave not always satisfactory agreement with observed values. By use of the simplified equation for hypochromism presented by Ts'o et al., the relationship between the hypochromism values and the geometrical parameters from the X-ray results was analyzed. Good correlations between them were found, and empirical formulas are postulated to estimate the values of hypochromism for a given geometry of two purine rings stacked in parallel.

It is well-known that nucleic acid bases are stacked with interplanar distances of about 3.4 Å in the helical structure of DNA and this stacking brings about a significant decrease in the intensity of the longest wavelength absorption band. In fact, the double helix absorbs roughly 40% less than does a mixture of the component monomers. This phenomenon, i.e., hypochromism, has been widely used as the evidence of stacked structures of various π systems, including nucleic acid bases in solution. Theoretical explanations of hypochromism were carried out independently by

† Dedicated to Professor Emanuel Vogel of Cologne University on the occasion of his 60th birthday.

‡ The Institute of Scientific and Industrial Research.

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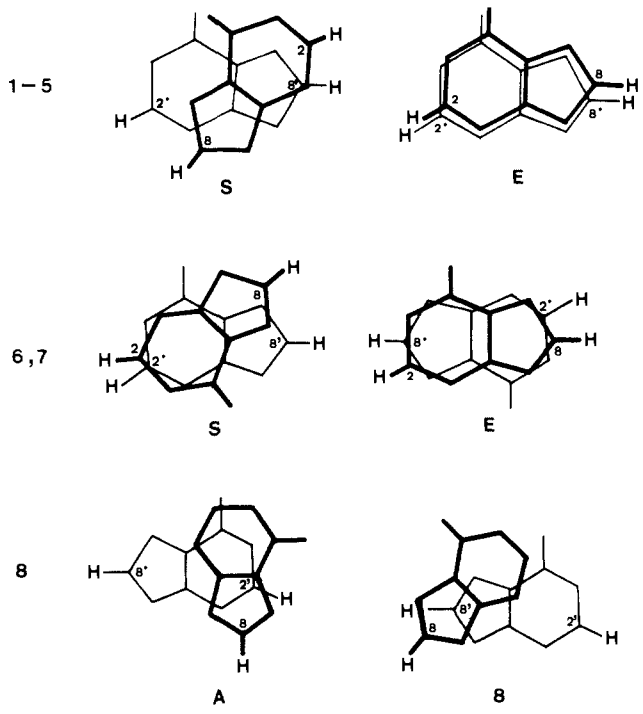


Figure 1. Two possible stacking forms of **1–8**.

Tinoco[2] and Rhodes.[3] According to their theories, the origin of hypochromism is the interaction between one particular electronic excited state of a given chromophore and the different electronic states of the neighboring chromophores. Depending on the relative orientation of the transition moments, hypochromism (parallel stacking) or hyperchromism (linear array) is observed. Quantitative evaluations of hypochromism values based on a given geometry of the chromophores, however, have been rarely performed. This is due mainly to the difficulty in molecular orbital calculation, where a number of configurational interactions between various electronic states must be taken into account, and partly to the lack of suitable model compounds with well-defined structures. To get information about the geometrical effects upon hypochromism, a variety of model compounds have been prepared so far. The most systematic study was carried out by Leonard et al.,[4] who synthesized a number of singly linked nucleic acid bases or nucleoside analogues, by changing the length of the bridging chain, bridging positions at the base rings, and the combination of nucleic acid bases. Related studies were also done by Zemlicka et al.[5] for singly bridged dinucleosides and by Golankiewicz et al.[6] for pyrimidinophanes. In spite of the syntheses of these model compounds, a quantitative treatment of the relationship between geometrical factors and hypochromism is still lacking, due to the conformational flexibility of the compounds in solution. Therefore, a series of model compounds with two

Scheme I

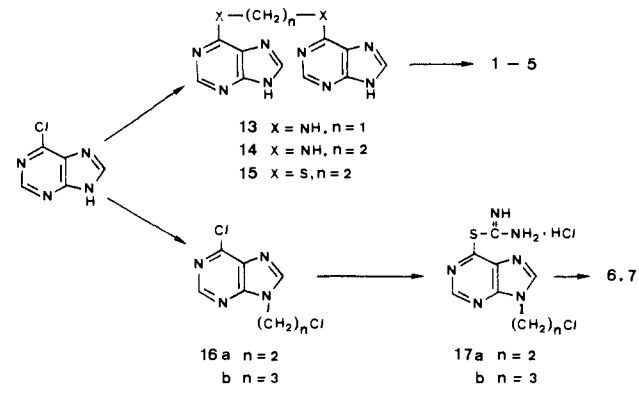
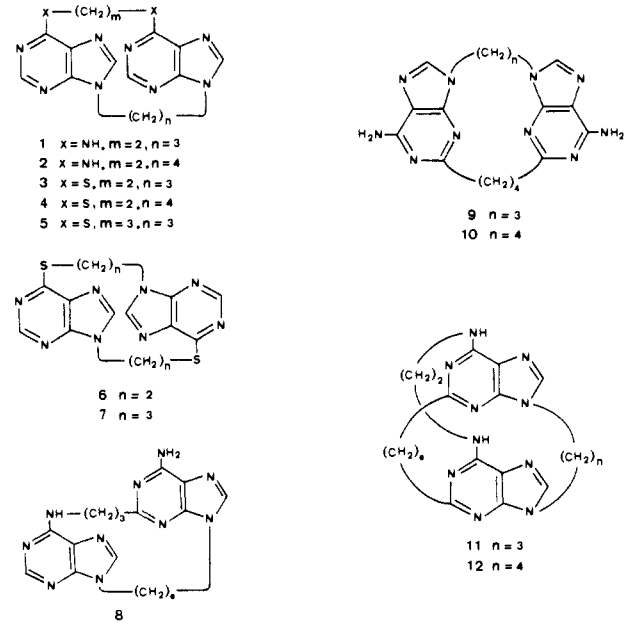


Table I. Yields (Percent) and Stacking Modes of **1–5**

	1	2	3	4	5
method A	4	12	2		6
method B			10	15	8
stacking mode[a]	*E*	*E*	*S*	*S*	*E* + *S*

[a] *E*, eclipsed form; *S*, skewed form.

nucleic acid bases fixed face-to-face with different stacking modes has been desired. Purinophanes seem to be suitable for this purpose, since the interaction between two purine rings is the greatest[4a] among all pairs of nucleic acid bases, and a purine ring has several linking positions to connect two identical rings with different stacking modes. In the present study, we designed and synthesized twelve purinophanes **1–12**. From molecular model



considerations, the interplanar distances in all of these purinophanes except for **9** and **10** are expected to be fixed around 3.4 Å. This 3.4-Å distance is the same as that between the two base planes in the DNA helix and also identical with the vertical distance between two stacked π systems with van der Waals contact. Thus, the study on the relationship between structural factors and the magnitude of hypochromism in the present rigid systems may serve as a satisfactory basis for understanding the phenomenon of hypochromism in a variety of systems.

Results

Synthesis. The low symmetry of purine rings, compared with aromatic hydrocarbons such as naphthalene, makes the usual coupling reactions[7] for the syntheses of cyclophanes inapplicable

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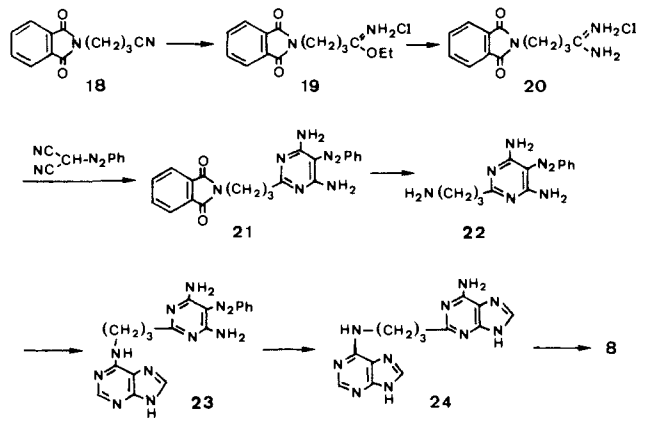
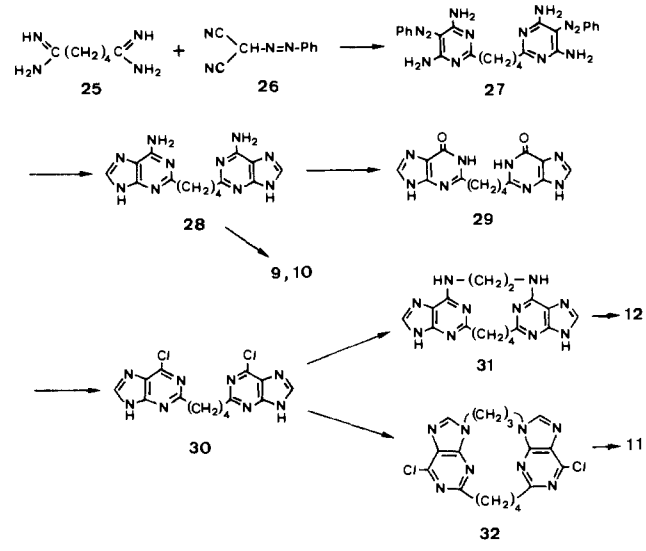
(6) (a) Golankiewicz, K.; Celewicz, L. *Pol. J. Chem.* **1978**, *52*, 1035–1038. (b) Koroniak, H.; Golankiewicz, K. *Ibid.* **1978**, *52*, 1567–1570. (c) Golankiewicz, K.; Celewicz, L. *Ibid.* **1979**, *53*, 2075–2081. (d) Kazmieczak, F.; Golankiewicz, K. *Ibid.* **1980**, *54*, 2357–2363.

(7) Higuchi, H.; Tani, K.; Otsubo, T.; Sakata, Y.; Misumi, S. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 4027–4036 and references cited therein.

Scheme II



Scheme III



for purinophanes. Therefore, the two bridges in the purinophanes **1–5** were introduced stepwise. Thus, singly bridged dimers **13–15** were first prepared starting from 6-chloropurine as shown in Scheme I. These were subjected to ring-closure reactions at the 9- and 9′-positions with α,ω-dibromoalkanes under high-dilution conditions. The cyclization reaction was carried out by the following two methods: (A) in the presence of sodium hydride in DMF and (B) in the presence of potassium carbonate in DMSO. Yields by the two methods are summarized in Table I. From the table it is obvious that the latter method is superior to the former one, although method B could not be applied to the synthesis of **1** and **2** because of the low solubility of the starting acyclic compounds in DMSO. The coupling reaction of **13** and 1,3-dibromopropane to obtain a homologue of **1** failed using the above two methods, presumably due to ring strain.

In principle, two isomers, eclipsed (fully overlapped) and skewed forms (*E* and *S* forms in Figure 1, respectively), are possible for the compounds **1–5**, but only one isomer was obtained, except for **5**, as shown in Table I. The structures were determined by NMR and X-ray analyses. In the case of **5**, a mixture of both isomers was obtained, and in spite of various attempts to separate these, we were unable to isolate the pure isomers.

The synthesis of **6** and **7** was successfully achieved by a dimeric cyclocondensation reaction of **17a** and **17b** in the presence of potassium carbonate in DMSO under high-dilution conditions. Both purinophanes were obtained only in the skewed form (*S* form in Figure 1). Although the yields from these reactions were poor (**6**, 10%; **7**, 19%), it is noteworthy that the fairly strained compound **6** with an interplanar distance of 3.2 Å was obtained.

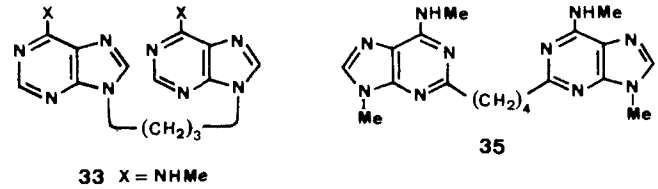
Purinophane **8**, in which one of the two bridges is linked at the unsymmetrical positions (2, $N^{6'}$) of the heterorings, was prepared starting from **18** through a synthetic sequence as shown in Scheme II. The final coupling reaction of **24** and 1,3-dibromopropane was carried out by method B. In this case only one isomer (A form) of the two possible forms (A and B forms in Figure 1) was obtained.

It is somewhat curious that only one isomer of the two possible forms (*E* and *S* or A and B in Figure 1) was obtained for the purinophanes **1–8** (except **5**). Presumably, the steric factor is responsible for the phenomenon, considering the fact that **1–8** have relatively short interplanar distances (except **5**) and the isomer obtained has less overlapped structure than the other possible isomer (except **1** and **2**).

For the synthesis of triply bridged purinophanes **11** and **12** three linking chains were introduced stepwise between two purine rings in the decreasing order of difficulty (Scheme III). The most difficult bridging is a connection between the 2- and 2′-positions. Since direct alkylation at this position of a purine ring is not accessible, we employed procedures that give the formation of the heteroring after introduction of a tetramethylene chain.[8] The reaction of diamidine **25** with phenylazomalononitrile **26** in the presence of sodium butoxide in butanol gave **27**, which was converted to **28** by a procedure similar to the synthesis of 2-methyladenine.[10] Two adenine moieties of **28** were transformed to 6-chloropurines **30** via **29** as usual.[11,12] By treatment of **30** with ethylenediamine in DMSO–H_2O, the doubly bridged compound **31** was obtained. For the final bridging, method B was applied to **31** to give the desired compounds **11** and **12**. Since the yield of **11** by this reaction was extremely low (less than 1%), an alternative synthetic route was investigated. After several attempts, **11** was successfully synthesized in a yield of 8% by treatment of **32** with ethylenediamine.

Purinophanes **9** and **10** were prepared by applying method B to **28**.

Monomeric and dimeric references **33–37**, **38**,[11] and **39**[11] were also prepared.



35

33 X = NHMe
34 X = SMe

36 X = NHMe
37 X = SMe

38 X = NH_2
39 X = NHMe

NMR Spectra. ^1H NMR spectra (100 MHz) of the purinophanes were measured in deuteriochloroform. Bridge protons of the compounds **1–6**, **8**, **11**, and **12** show complex multiplets in the region of 3–5 ppm, while the corresponding protons of acyclic dimers **33–35** appear with the first-order splitting. The result indicates that these purinophanes have more or less rigid structure in solution. On the other hand, bridge protons of **7**, **9**, and **10** show more simple and broad signals, which changed to well-resolved, complex signals at lower temperature, suggesting somewhat

(8) Although compound **27** is already known,[9] we modified the reaction sequence.
(9) Taylor, E. C.; Vogl, O.; Cheng, C. C. *J. Am. Chem. Soc.* **1959**, *81*, 2442–2448.
(10) Robins, R. K.; Dille, K. J.; Willits, C. H.; Cristensen, B. E. *J. Am. Chem. Soc.* **1953**, *75*, 263–266.
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Table II. ^{1}H NMR Chemical Shifts (δ) of H2 and H8 of Purinophanes in $CDCl_3$, Their Differences from Monomeric References, and Stacking Modes

	H2		H8		$\Delta\delta$(H2) −	stacking
compd	δ	$\Delta\delta$	δ	$\Delta\delta$	$\Delta\delta$(H8)	mode
36	8.43		7.71			
38			7.70			
33	8.40	−0.03	7.92	+0.21		
1	8.10	−0.33	7.47	−0.24	−0.09	*E*
2	8.18	−0.25	7.37	−0.34	+0.09	*E*
8	8.04	−0.39	7.52	−0.19	−0.20	A
			7.21	−0.49	+0.10	
37	8.74		7.93			
34	8.73	−0.01	8.12	+0.19		
3	8.60	−0.14	7.52	−0.41	+0.28	*S*
4	8.56	−0.18	7.54	−0.39	+0.21	*S*
5	8.48	−0.26	7.73	−0.20	−0.06	?
	8.21	−0.53	7.52	−0.41	−0.12	?
6	8.37	−0.37	7.91	−0.02	−0.35	*S*
7	8.34	−0.40	7.95	+0.02	−0.42	*S*

Table III. Evaluated Ring Current Effects (δ)[a] of Faced Purine Rings Assuming a Vertical Distance of 3.4 Å in the Two Stacking Forms of **1–8** Shown in Figure 1

		H2(H2′)	H8(H8′)	H2(H2′) − H8(H8′)
1–5	*S* from	−0.10	−0.60	+0.50
	E from	−0.50	−0.35	−0.15
6, 7	*S* from	−0.60	−0.20	−0.40
	E from	−0.30	−0.50	+0.20
8	A from	−0.40	−0.20	−0.20
			−0.40	0.00
	B from	0.00	−0.80	+0.80
			−0.20	+0.20

[a] Negative sign represents upfield shift.

flexible structures in solution at room temperature.

The chemical shifts of the ring protons (H2, H8) of the purinophanes and reference compounds are summarized in Table II. The signals were assigned by a comparison of the chemical shifts with those of monomeric references and by considering that H8 protons have weaker intensity compared with H2 protons. Almost all protons of the purinophanes shifted to higher field compared with acyclic or monomeric references owing to the ring current effect of an opposed purine ring. The ring current magnetic anisotropy of an adenine ring was studied by Pullman et al.[13] On the basis of their results the values of the ring current effect for some possible stacking modes of purinophanes, which are shown in Figure 1, were evaluated assuming a vertical distance of 3.4 Å. The choice of 3.4 Å as the distance between the two base planes is very reasonable from molecular model considerations and from the X-ray results for most of the present purinophanes. The results are summarized in Table III. By comparing the calculated values with the observed ones, especially the difference of the anisotropy between at H2 and H8, i.e., $\Delta\delta$(H2) − $\Delta\delta$(H8), we determined the stacking modes as shown in Table II. In the case of **5**, unequivocal structural assignments were not possible, since the two purine rings in **5** are expected to be not in parallel. The validity of the assignments in Table II are supported by X-ray analysis for **3**, **4**, **6**, and **8**, as described below.

Structure. In order to confirm the assignments of the stacking modes of the purinophanes in Table II and to obtain exact structural parameters for a quantitative treatment of the geometrical effects upon hypochromism, X-ray analysis[14] was carried out for six typical purinophanes **3**, **4**, **6**, **8**, **9**, and **12**. The final *R* values for all the compounds are low except for **8**, where the disorder of solvent chloroform molecules prevents the lowering

(13) (a) Giessner-Prettre, C.; Pullman, B. *J. Theor. Biol.* **1970**, *27*, 87–95; (b) *Biochem. Biophys. Res. Commun.* **1976**, *70*, 578–581; (c) *Biopolymers* **1976**, *15*, 2277–2286.

(14) Seyama, F.; Sakata, Y.; Kasai, N.; Misumi, S., submitted for publication in *Bull. Chem. Soc. Jpn.*

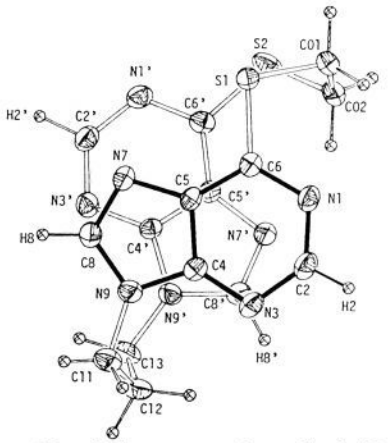

Figure 2. View of **3** on the least-squares plane defined with a purine ring.

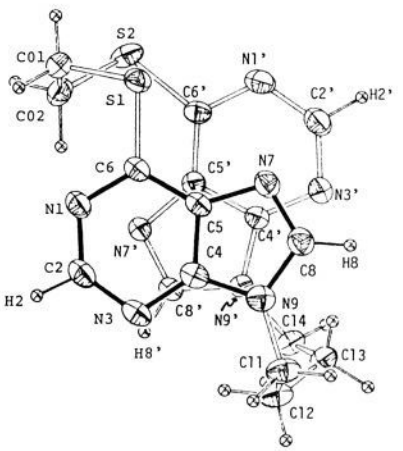

Figure 3. View of **4** on the least-squares plane defined with a purine ring.

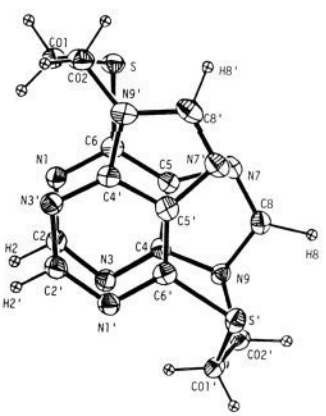

Figure 4. View of **6** on the least-squares plane defined with a purine ring.

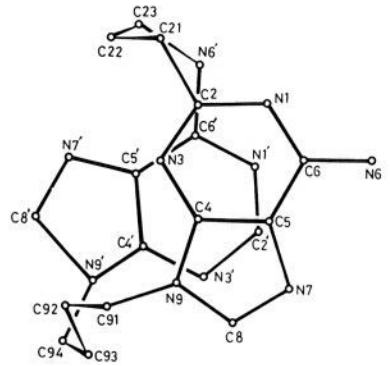

Figure 5. View of **8** on the least-squares plane defined with a purine ring.

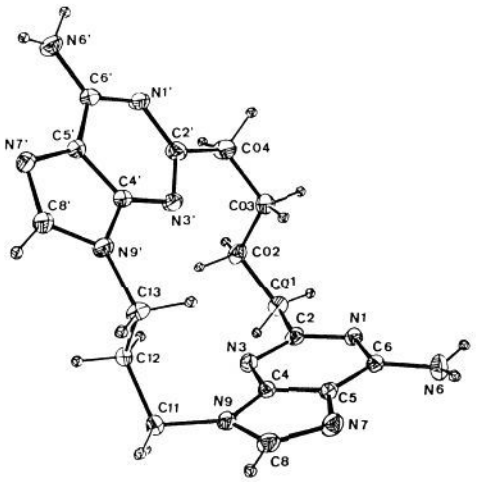

Figure 6. ORTEP drawing of **9**.

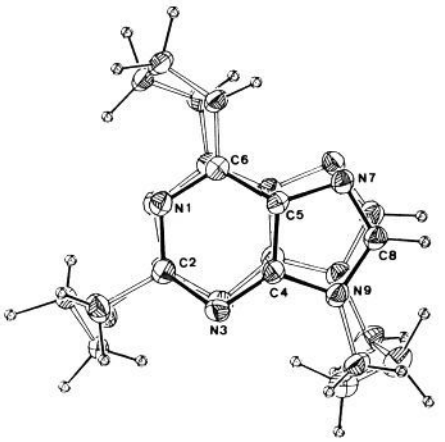

Figure 7. View of **12** on the least-squares plane defined with a purine ring.

(final R values: **3**, 0.048; **4**, 0.052; **6**, 0.059; **8**, 0.101; **9**, 0.045; **12**, 0.058). The resulting ORTEP drawings[14] are shown in Figures 2–7. The base planes are almost parallel to each other in these purinophanes, except for **9** (dihedral angle: **3**, 5.5°; **4**, 6.6°; **6**, 1.6°; **8**, 11.6°; **9**, 121.8°; **12**, 13.9°). The observed interplanar distances (D_v) are listed in Table VII. In agreement with the results in Table II, the stacking modes of **3**, **4**, and **6** have turned out to be in the skewed form and the geometry of **8** is in the A form. As seen in Figures 2 and 3, the stacking modes of the two base rings in the homologues **3** and **4** are quite similar. Figure 4 shows that the two component rings of **6** are stacked in such a way that one of the rings rotates 60° around an axis at the center of the six-membered rings. As a result, the six-membered rings in **6** are entirely overlapped. Figure 7 shows that the two purine rings in **11** are fully overlapped, as expected from molecular model examinations.

Hypochromism. The electronic spectra of the purinophanes and related references were measured in an organic solvent (ethanol) and aqueous solutions (neutral, 0.1 N hydrochloric acid, 0.1 N sodium hydroxide). Typical spectra are shown in Figures 8–11. Difference spectra, obtained by substracting the intensity of a given purinophane from that of the corresponding monomeric reference, are also shown in the figures. It is clear from the figures that large hypochromism is observed for the purinophanes in the longest wavelength absorption band. For a quantitative treatment, values of hypochromism (% H) were evaluated according to eq 1, where

$$\% H = [(1 - (f_D/2f_M)]100 \quad (1)$$

$$f = 4.32 \times 10^{-9} \int \epsilon(\lambda)/\lambda^2 \, d\lambda \quad (2)$$

f_M and f_D are oscillator strengths (eq 2) of monomer and dimer,

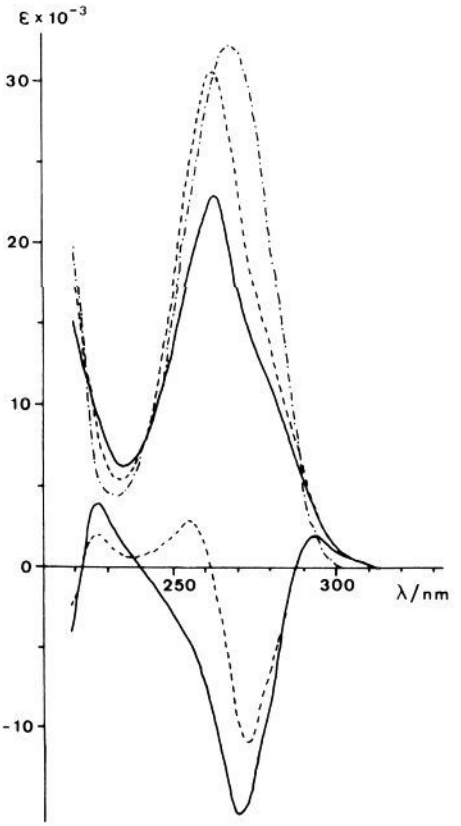

Figure 8. Electronic spectra of **1** (—), **33** (---), and **36** (×2) (-·-) in water and difference spectra of **1** and **33** vs **36** (×2).

Table IV. Hypochromism Values (Percent) of Purinophanes and Related Compounds in Four Media

	H_2O	0.1 N HCl	0.1 N NaOH	EtOH
1	28.6	33.1	28.0	27.8
3	26.3	25.5	31.6	32.4
4	26.6	25.1	25.9	24.1
6	47.6			47.3
7	23.0	28.6	29.5	22.4
8	15.7	15.7		13.9
9	8.5	−2.8		2.8
10	8.3	3.9		3.8
11		30.1		29.9
12		30.6		26.1
33	7.9	0.0	9.4	−0.6
34	12.2	10.6	12.3	−0.6
35	12.9	0.9		

respectively. The results are summarized in Table IV. Blank spaces in the table are due to the low solubility of the compounds in the media. As seen from Table IV, all purinophanes show quite large hypochromism values in contrast to the small values of linear dimers. The largest value (47.6% in water) was observed for **6**, where the interplanar distance is quite short (around 3.20 Å) and the two component purine rings are considerably overlapped. To our knowledge, this is the largest value, caused by two nucleic acid bases, so far reported. Even compound **8**, where the two purine rings are not stacked in parallel, but inclined as shown in Figure 6, shows a relatively large value. This clearly suggests the importance of the fixation of two nucleic acid bases at a short distance. Otherwise, small values will be obtained as a result of averaging values of several potential conformations, including nonstacked ones, with opposite signs due to hyperchromic effects. Another characteristic point seen in Table IV is that the hypochromism values of the purinophanes, except for **9** and **10**, remain almost unchanged in the four different media. On the other hand, linear dimers **33**–**35** show media-dependent behavior, which is quite similar to that reported by Leonard et al.[4a] for related

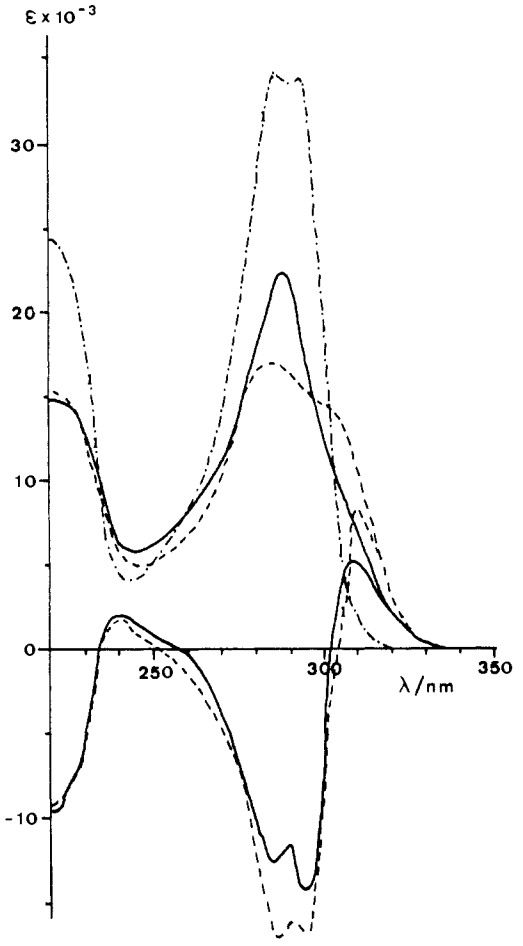

Figure 9. Electronic spectra of **3** (—), **4** (---), and **37** (×2) (-·-) in water and difference spectra of **3** and **4** vs **37** (×2).

compounds. They found that linear dimers change their structure from stacked conformation in neutral, aqueous solution to unstacked ones in both ethanol, an effective denaturing agent for DNA, and acidic media where the repulsive interaction between the positively charged residues prevents stacking. The marked media-independent behavior of the purinophanes suggests that their structure in solution is almost the same as in the crystalline state.

The effect of the separation between the rings on the magnitude of hypochromism is obvious when the values of homologues **6** and **7** or **11** and **12** are compared; i.e., the smaller the interplanar distance, the large the value of hypochromism.

The hypochromism values of **6** in 0.1 N HCl and 0.1 N NaOH could not be determined, because of the time dependency of the spectra. Thus, the initial spectra completely changed in 5–20 h (5–6 h in 0.1 N NaOH; 18–20 h in 0.1 N HCl) to other spectra, which could be interpreted as a sum of 6-thio- and 6-hydroxypurine chromophores. Therefore, we presume that the nucleophilic substitution of a sulfur atom at the 6-position of the purine ring by H_2O or OH^- occurred at room temperature owing to a stereoelectronic effect[15] found in pyrimidino-[16] and polymethylene-bridged[17] purinophanes.

In order to determine the agreement between the theoretical and observed values of hypochromism, the calculation was carried out for **3**, **4**, and **6** by the ASMO SCF CI (antisymmetrized molecular orbital self-consistent field configurational interaction) method, i.e., PPP (Pariser–Parr–Pople) method,[18] by using the

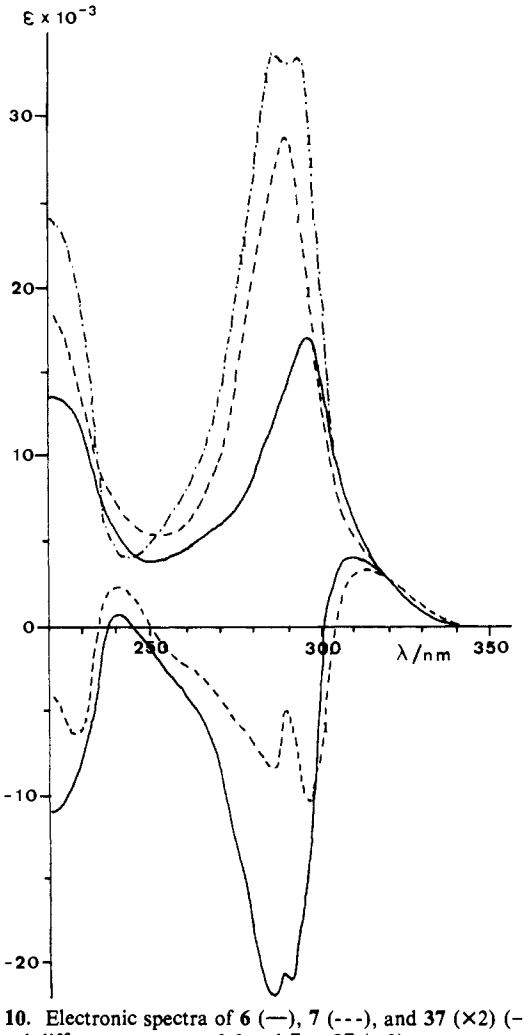

Figure 10. Electronic spectra of **6** (—), **7** (---), and **37** (×2) (-·-) in water and difference spectra of **6** and **7** vs **37** (×2).

Table V. Semiempirically Evaluated Values of the Effective Nuclear Charge (Z), Ionization Potential (I_r), and One-Center Coulomb Repulsion Integral ($rr|rr$)

r	Z	I_r, eV	$rr\|rr$, eV
C	3.25	−11.16	11.13
S	5.80	−21.15	12.46
N (azo)[a]	3.90	−14.12	12.34
N (amino)[a]	4.25	−28.53	16.57
H_3[b]	2.83	−10.256	9.326

[a] Azo nitrogen donates a π electron to the system, and amino nitrogen donates two π electrons. [b] Hyperconjugation in the methyl group is taken into account, and the group orbital of H_3 is assumed to overlap with the π orbitals.

coordinates of the constituent atoms obtained by the X-ray diffraction. The one-center Coulomb repulsion integrals were evaluated by using the Pariser–Parr approximation[18a] and are listed in Table V. The two-center Coulomb repulsion integrals were estimated by using the Mataga–Nishimoto approximation.[19] The core resonance integral was represented by the Wolfsberg–Helmholtz approximate equation,[20] and the differential overlap integral and penetration integral were neglected as usual. The oscillator strength (f) of the transition from the ground state to the excited state was calculated by eq 3, where σ_{ob} is the wave

$$f = 1.085 \times 10^{-5}\ \sigma_{ob} M_{ob}^2 \qquad (3)$$

number of the transition and M_{ob} is the corresponding transition moment. Calculated hypochromism values (% H) of the lowest

(15) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon: New York, 1983.
(16) (a) Doyama, K.; Hama, F.; Sakata, Y.; Misumi, S. *Tetrahedron Lett.* **1983**, *24*, 5253–5256. (b) Higashii, T.; Sakata, Y.; Misumi, S. *Nucleic Acids Symp. Ser.* **1985**, *16*, 125–128.
(17) Higuchi, H.; Mitsuoka, M.; Sakata, Y.; Misumi, S. *Tetrahedron Lett.* **1985**, *26*, 3849–3852.

(18) (a) Pariser, R.; Parr, R. G. *J. Chem. Phys.* **1953**, *21*, 466–471, 767–776. (b) Pople, J. A. *Trans. Faraday Soc.* **1953**, *49*, 1375–1385.
(19) Mataga, N.; Nishimoto, K. *Z. Phys. Chem.* **1957**, *13*, 140–157.
(20) Wolfsberg, M.; Helmholz, L. *J. Chem. Phys.* **1952**, *20*, 837–843.

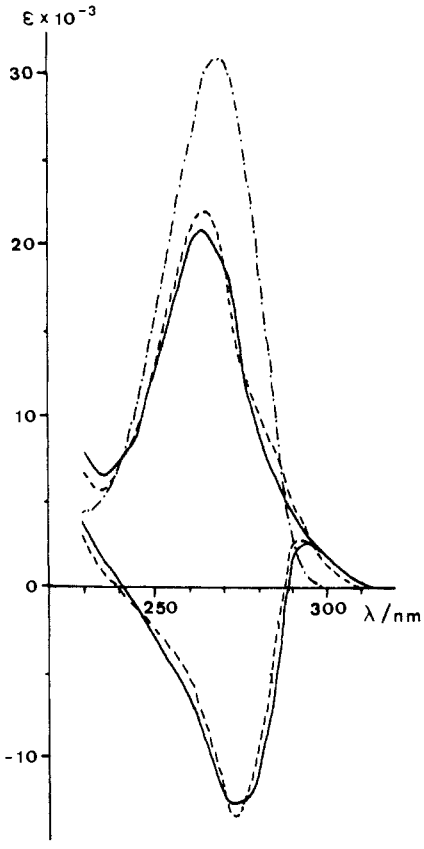

Figure 11. Electronic spectra of **11** (—), **12** (---), and **39** (×2) (-·-) in water and difference spectra of **11** and **12** vs **39** (×2).

Table VI. Calculated Hypochromism Values (Percent) of **3**, **4**, and **6** and Interplanar Distances (Å) Used for the Calculation

purinophanes	calculated values			interplanar distance
	type I	type II	type III	
3	19.0	28.9	28.5	3.18
4	11.0	23.1	20.8	3.57
6	21.0	32.6	33.8	3.20
6		36.4	38.3	3.00

energy transition were calculated by eq 1. Stacking orientations were based on the results of X-ray analysis, and the electronic effects of the polymethylene chains were neglected in the calculations of the dimers (purinophanes **3**, **4**, and **6**). The two purine rings of the dimers were assumed to be parallel. The interplanar distances between the two averaged ring planes were taken from the results of the X-ray analysis. The numbers of π orbitals and π electrons of each monomer are 14 and 16, and those of each dimer are 20 and 24, respectively. Three types of CI calculations were performed. Type I contains the ground and 48 singly excited configurations both for monomer and dimer. Type II contains the ground and all singly excited (48 for monomer; 96 for dimer) configurations. Type III contains the ground, all singly excited, and all doubly excited (48 for monomer; 96 for dimer) configurations (A double excited configuration corresponds to the concomitant excitation of two electrons in an occupied orbital to an unoccupied orbital.). Calculated hypochromism values are listed in Table VI.

As seen in the table, fairly good agreement between the theoretical and experimental values was obtained in type II and III calculations. On the other hand, the agreement was unsatisfactory in type I calculation. This indicates clearly the importance of the number of singly excited configurational interactions involved in the calculation. Doubly excited configurations may be not important, because the values by type II and III calculations are similar. Although type II and III calculations for **3** and **4** reproduced experimental values, calculated values for **6** were not satisfactory. Additional calculations were carried out for **6** assuming the interplanar distance of 3.00 Å. This treatment gave, however, no significant improvement.

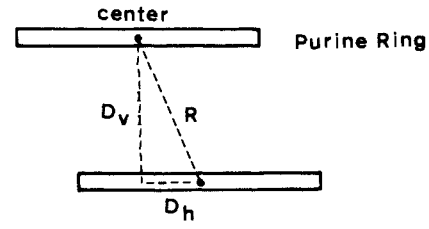

Figure 12. Definitions of D_v, D_h, and R.

Table VII. Geometrical Values of Purinophanes[a]

	D_v	D_h	R	θ
1			3.4–3.6[b]	76.5[b]
3	3.26	0.83	3.36	72.7
	3.19	1.06	3.36	80.2
4	3.59	1.01	3.73	73.8
	3.36	1.01	3.73	75.1
6	3.19	0.80	3.29	90.4
	3.27	0.36	3.29	94.9
7			3.7–3.9[b]	92.7[b]
8	3.63	1.51	3.93	116.0
	3.52	1.75	3.93	99.9
9	0.28	6.63	6.64	99.9
	1.25	6.52	6.64	71.1
10			6.7–6.9[b]	85.5[b]
11			3.4–3.6[b]	90.6[b]
12	3.58	0.54	3.62	89.7
	3.60	0.38	3.62	91.4

[a] D_v, vertical distance (Å) between the center of a purine ring and the faced ring; D_h, horizontal shift (Å) of two purine rings; R, distance (Å) between the centers of two purine rings; θ, angle between R and transition moment. [b] Evaluated on the basis of molecular model considerations.

The disagreement of the experimental and calculated hypochromism values for **6** with well-defined, rigid structure prompted us to find some empirical equation to estimate the reliable values of hypochromism from a given orientation of two purine rings. Fortunately, Ts'o et al.[21] have already made a very helpful contribution in this direction. They presented a simplified equation (4) for hypochromism assuming parallel stacking of the two

$$\% H = A(1 - 3\cos^2\theta)/R^3 \quad (4)$$

identical base planes of the homodimers, where R is the distance between the transition moments located at the center of the two bases, θ is the angle between R and the transition moment, and A is a constant. In the present study, the geometrical parameters R and θ were determined from the X-ray results or from molecular model considerations. As the transition moment in a purine ring chromophore has not so far been experimentally determined, it was assumed for the evaluation of θ that it lies along the long axis of a purine ring. The observed geometrical values such as the vertical distances between two purine rings (D_v), the horizontal shift of the two rings (D_h), R (see Figure 12), and θ are all summarized in Table VII. The two rings of the purinophanes in a crystal are not equivalent, as shown by the X-ray results; thus, two different geometrical values are presented in Table VII. The values $(1 - 3\cos^2\theta)/R^3$, calculated from the values in Table VII, were plotted against % H (except for **9** and **10**, where the two purine rings are not stacked in parallel). The results are shown in Figure 13. As seen from the figure, it was found that good correlations exist between hypochromism and the geometric parameters. By analyzing the two lines the following two empirical formulas for 6-thio- (eq 5) and 6-aminopurine chromophores (eq

$$\% H = 1.30 \times 10^3(1 - 3\cos^2\theta)/R^3 \quad (5)$$

$$\% H = 1.65 \times 10^3(1 - 3\cos^2\theta)/R^3 \quad (6)$$

(21) Kondo, N. S.; Holmes, H. M.; Stempel, L. M.; Ts'o, P. O. P. *Biochemistry* **1970**, *9*, 3479–3498.

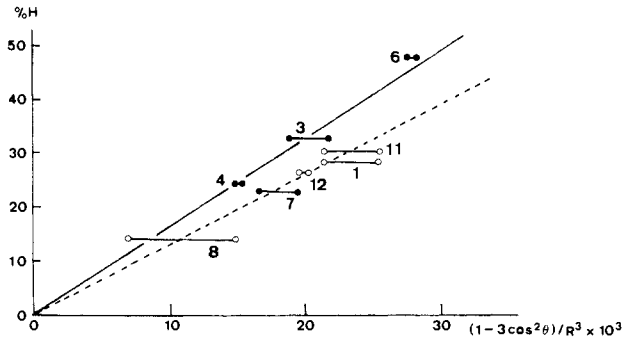

Figure 13. Relationship between % H and $(1 - 3\cos^2\theta)/R^3$ for purinophanes having 6-thiopurine (●) and 6-aminopurine (○) chromophores.

6) were obtained. Since two bases usually interact with each other in parallel fashion, these equations are useful ones for the reliable estimation of hypochromism values, without tedious calculations like types II and III in Table IV, in various systems including naturally occurring nucleotide arrays. Furthermore, the utilization of the experimental data of hypochromism for the determination of the mutual orientation of the associated molecules stacked in parallel would be greatly helped by eq 5 and 6.

Experimental Section

All melting points are uncorrected. ^{1}H NMR spectra were recorded on a JEOL FX-100 (100-MHz) or JEOL PMX-60SI (60-MHz) spectrometer with tetramethylsilane as an internal standard. Mass spectra were taken on a Hitachi RMU-7 (70 eV) by using the direct-injection technique. UV and IR spectra were measured on a Hitachi EPS-3T and a Hitachi EPI-G2, respectively. Liquid chromatography was performed on a Nihon Bunsekikogyo LC-09.

N^6,$N^{6'}$-Ethylenebis(adenine) (14). A mixture of 5.0 g (32 mmol) of 6-chloropurine, 1.1 mL (16 mmol) of ethylenediamine, and 4.6 mL of triethylamine in butanol (60 mL) was refluxed for 3 h. Precipitates were collected and washed with water. Reprecipitation by treatment successively with 2 N NaOH aqueous solution and acetic acid, and then recrystallization from ethanol–acetic acid yielded 2.7 g (57%) of **14** as a colorless powder: mp >350 °C; ^{1}H NMR (60 MHz, CF_3CO_2H) δ 4.37 (br s, 4, CH_2), 8.92 (s, 2, H2 or H8), 9.03 (s, 2, H2 or H8).

Synthesis of 1 and 2 (Coupling Reaction by Method A). To a stirred suspension of **14** (1.0 g, 3.4 mmol) in dry DMF (100 mL) was added 0.33 g (6.9 mmol) of 50% sodium hydride under a nitrogen atmosphere. After being stirred for 1 h, it became to a clear solution. This solution and a solution of 1,3-dibromopropane (0.35 mL, 3.5 mmol) in dry DMF (100 mL) were simultaneously added dropwise into dry DMF (300 mL) in a period of 4.5 h with stirring, and stirring was continued for 3 days. Removal of the solvent, chromatography on silica gel with methanol, and recrystallization from benzene yielded 46 mg (4%) of **1** as colorless plates: dec pt >325 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 2.76 (q, J = 8.5 Hz, 2, $CH_2CH_2CH_2$), 3.2–4.6 (m, 4, N^6CH_2), 4.0–4.6 (m, 4, N^9CH_2), 5.2 (br s, 2, NH), 7.47 (s, 2, H8), 8.10 (s, 2, H2); MS, 336 (M^+). Anal. Calcd for $C_{15}H_{16}N_{10}$: C, 53.56; H, 4.80; N, 41.64. Found: C, 53.36; H, 5.10; N, 41.17.

The synthesis of **2** was carried out in a manner similar to the above. Purification of the crude product by column chromatography (silica gel, 19:1 chloroform–methanol), followed by recrystallization from ethanol gave pure **2** as colorless plates (12% yield): mp 325.5–326.5 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.7–2.2 (m, 4, $CH_2CH_2CH_2CH_2$), 3.2–3.8 (m, 4, N^6CH_2), 4.25–4.9 (m, 4, N^9CH_2), 5.4 (br s, 2, NH), 7.39 (s, 2, H8), 8.20 (s, 2, H2); MS, 350 (M^+). Anal. Calcd for $C_{16}H_{18}N_{10}$: C, 54.84; H, 5.19; N, 39.97. Found: C, 54.01; H, 5.23; N, 39.52.

6,6'-(Ethylenedithio)bis(purine) (15). A mixture of 6-chloropurine (5 g, 32 mmol), 1,2-ethanedithiol (1.4 mL, 16 mmol), and triethylamine (4.6 mL, 33 mmol) in butanol (30 mL) was heated at 110–120 °C with stirring for 2 h. After the mixture cooled, precipitates were collected, washed successively with water and acetone, and recrystallized from acetic acid to give 2.6 g (49%) of **15** as a colorless powder: mp 300 °C dec; ^{1}H NMR (60 MHz, DMSO-d_6) δ 3.70 (s, 4, SCH_2), 8.28 (s, 2, H8), 8.53 (s, 2, H2); MS 330 (M^+), 179, 166, 152, 119.

Synthesis of 3 and 4 (Coupling Reaction by Method B). To a suspension of dry potassium carbonate (0.42 g, 3.0 mmol) in DMSO (500 mL) were added dropwise a solution of **15** (1.0 g, 3.0 mmol) in DMSO (200 mL) and a solution of 1,3-dibromopropane (0.3 mL, 3.0 mmol) in DMSO (200 mL) in a period of 18 h at room temperature. After additional stirring was continued for 2 days, the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel with chloroform–methanol (19:1) and then by recrystallization from ethanol to give pure **3** (110 mg, 10%) as colorless prisms: dec pt >320 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 2.90 (m, 2, $CH_2CH_2CH_2$), 3.8–3.9 (m, 4, SCH_2), 4.0–4.8 (m, 4, NCH_2), 7.52 (s, 2, H8), 8.60 (s, 2, H2); MS, 370 (M^+). Anal. Calcd for $C_{15}H_{14}N_8S_2$: C, 48.63; H, 3.81; N, 30.25; S, 17.31. Found: C, 48.79; H, 3.80; N, 30.26; S, 17.30.

Synthesis of **4** was carried out by the similar procedure stated above. **4**: 15% yield; colorless prisms: dec pt >276 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.8–2.2 (br s, 4, NCH_2CH_2), 3.4–4.0 (br s, 4, SCH_2), 4.1–4.6 (m, 4, NCH_2), 7.54 (s, 2, H8), 8.56 (s, 2, H2); MS, 384 (M^+). Anal. Calcd for $C_{16}H_{16}N_8S_2$: C, 49.98; H, 4.20; N, 29.14; S, 16.68. Found: C, 50.04; H, 4.14; N, 29.10; S, 16.51.

6-Chloro-9-(2-chloroethyl)purine (16a). A mixture of 6-chloropurine (5 g, 32 mmol), 2-bromo-1-chloroethane (3.3 mL, 39 mmol), and potassium carbonate (4.5 g, 33 mmol) in 50 mL of DMSO was stirred for 10 h. The mixture was poured onto ice–water (200 mL), and it was extracted with chloroform. Separation by liquid chromatography and then recrystallization from ethanol gave 4.0 g (57%) of **16a**: ^{1}H NMR (60 MHz, $CDCl_3$) δ 3.92 (t, J = 11 Hz, 2, CH_2Cl), 4.60 (t, J = 11 Hz, 2, N^9CH_2), 8.10 (s, 1, H8), 8.50 (s, 1, H2); MS, 220, 218, 216 (M^+).

6-Chloro-9-(3-chloropropyl)purine (16b). The procedure is similar to that for **16a**. Crude product was purified by liquid chromatography. Without further purification the product was used for the following reaction.

1,3-Dithia[3.3](6,9)(9',6')purinophane (6). To a solution of **16a** (0.8 g, 3.5 mmol) in 30 mL of ethanol was added thiourea (0.3 g, 3.9 mmol), and the solution was refluxed for 1 h. Precipitates of **17a** were filtered, washed with ethanol, and dried in vacuo. A solution of **17a** thus obtained in DMSO (200 mL) was added dropwise to a stirred suspension of potassium carbonate (1.5 g, 11 mmol) for 3 days at room temperature. After addition was over, stirring was continued for 2 days. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel with chloroform–methanol (19:1) and then by recrystallization from ethanol to give pure **6** (59 mg, 10%) as colorless prisms: dec pt >315 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 3.6–4.5 (m, 4, SCH_2), 4.6–4.9 (m, 4, NCH_2), 7.91 (s, 2, H8), 8.37 (s, 2, H2); MS, 356 (M^+). Anal. Calcd for $C_{14}H_{12}N_8S_2$: C, 47.18; H, 3.39; N, 31.44; S, 17.99. Found: C, 47.01; H, 3.55; N, 30.66; S, 17.95.

1,4-Dithia[4.4](6,9)(9',6')purinophane (7). This compound was prepared from 0.8 g (3.4 mmol) of **16b** and 0.25 g (3.4 mmol) of thiourea according to the procedure similar to that for **6** and yielded 120 mg (19%) as a colorless crystalline solid: mp >290 °C dec; ^{1}H NMR (100 MHz, $CDCl_3$) δ 2.68 (m, 4, $CH_2CH_2CH_2$), 3.63 (m, 4, SCH_2), 4.34 (m, 4, C9CH_2), 7.95 (s, 2, H8), 8.34 (s, 2, H2); MS, 384 (M^+). Anal. Calcd for $C_{16}H_{16}N_8S_2$: C, 49.98; H, 4.20; N, 29.14; S, 16.68. Found: C, 50.09; H, 4.28; N, 28.68; S, 16.42.

1-Imino-4-(*N*-phthalimido)-1-butanamine Hydrochloride (20). To a mixture of dioxane (100 mL) and ether (40 mL) was added 11 g (50 mmol) of **18** and 2.8 mL (50 mmol) of absolute ethanol. The solution was cooled with an ice–salt bath, and dry HCl gas was introduced. After saturation with HCl gas, the solution was allowed to stand for 1 day, and then it was concentrated until 20 mL of the solvent was left. Yielded solid was collected and dried to give quantitatively crude **19**, which was used for the subsequent reaction without further purification. To a solution of **19** in 150 mL of absolute methanol was added sodium methoxide (2.8 g, 50 mmol) and ammonium chloride (2.8 g, 50 mmol), and the mixture was allowed to stand overnight. Precipitates were filtered off, and the filtrate was concentrated. Crude product was recrystallized from methanol–ether to yield 11.3 g (83%) of **20** as colorless fine needles: mp 184–185 °C; ^{1}H NMR (60 MHz, DMSO-d_6) δ 1.7–2.2 (m, 2, $CH_2CH_2CH_2$), 2.4–2.6 (m, 2, $CH_2CH_2CH_2$), 3.53 (t, 2, NCH_2), 7.67 (s, 4, ArH), 7.3–9.0 (br s, 4, NH_2); MS, 231 (M^+).

4,6-Diamino-5-(phenylazo)-2-[3-(*N*-phthalimido)propyl]pyrimidine (21). To a stirred suspension of **20** (5.0 g, 19 mmol) and phenylazomalononitrile (3.5 g, 21 mmol) in dry butanol (100 mL) was added dropwise a solution of sodium (0.5 g, 22 mmol) in butanol (20 mL). After addition was over, the mixture was refluxed for 4 h. Precipitates were collected, washed successively with butanol and water, and recrystallized from pyridine to give 4.8 g (64%) of **21** as yellow fine needles, mp 208–211 °C.

4,6-Diamino-2-(3-aminopropyl)-5-(phenylazo)pyrimidine (22). To a solution of **21** (5.0 g, 12.5 mmol) in 100 mL of pyridine–ethanol (1:1) was added hydrazine hydrate (2.0 mL, 41 mmol), and the mixture was refluxed for 10 h. After evaporation of the solvent, the residue was extracted with 60 mL of 2 N HCl and then neutralized with 10 N NaOH. Yielded yellow solid was filtered, washed thoroughly with water, and dried to give 2.8 g (84%) of crude **22**, which was used for the following reaction without further purification: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.56 (br s, 2, CNH_2), 1.90 (q, 2, $CH_2CH_2CH_2$), 2.65 (t, 2,

NCH_2), 2.79 (t, 2, $ArCH_2$), 7.3–7.6 (m, 3, o- and p-ArH), 7.6–7.8 (m, 2, m-ArH), 5.8–7.8 (br s, 4, NH_2); MS, 271 (M^+).

N^6-[3-(4,6-Diamino-5-(phenylazo)pyrimidin-2-yl)propyl]adenine (23). A mixture of **22** (1.0 g, 3.7 mmol), 6-chloropurine (0.6 g, 3.9 mmol), and triethylamine (0.6 mL, 4.3 mmol) in butanol (50 mL) was refluxed for 4 h. Precipitates were collected, washed with water and ethanol, and dried to give 1.3 g (91%) of crude **23** as a yellow solid; MS, 310 (M^+).

2,$N^{6'}$-Trimethylenebis(adenine) (24). To a stirred solution of **23** (2.0 g, 51 mmol) in acetic acid (20 mL) and 50% aqueous ethanol (50 mL) was added zinc dust (4.0 g, 61 mmol) by portions at 60–70 °C under nitrogen atmosphere. Heating and stirring were continued until the solution became colorless. The mixture was filtered, and the filtrate was concentrated. To the residue was added 50 mL of formic acid, and the mixture was heated at 80–90 °C for 1 h. After removal of formic acid under reduced pressure, 30 mL of formamide was added to the residue, and the mixture was heated at 180–190 °C for 30 min After cooling, precipitates were collected and washed with ethanol. Reprecipitation from acetic acid–ethanol gave 1.4 g (88%) of **24** as colorless solid; MS, 310 (M^+).

1-Aza[4.4](2,9)(6,9)purinophane (8). A solution of **24** (0.9 g, 2.9 mmol), and 1,3-dibromopropane (0.34 mL, 2.9 mmol) in 300 mL of DMSO was added dropwise to a stirred suspension of potassium carbonate (0.7 g, 6.0 mmol) in 500 mL of DMSO in a period of 3 days. Additional stirring was continued for 4 days. After removal of the solvent, the residue was purified by column chromatography on silica gel with chloroform–methanol (9:1) and by recrystallization from butanol to give 11 mg (1%) of **8** as a colorless powder: mp 325 °C dec; ^1H NMR (100 MHz, $CDCl_3$) δ 8.04 (s, 1, H2), 7.52 (s, 1, H8), 7.21 (s, 1, H8′); MS, 361 (M^+). Anal. Calcd for $C_{17}H_{20}N_{10}$: C, 56.03; H, 5.53; N, 38.44. Found: C, 55.87; H, 5.49; N, 38.32.

1,4-Bis[4,6-diamino-5-(phenylazo)pyrimidin-2-yl]butane (27). To a mixture of **25**[9] (2 g, 9.3 mmol) and **26**[22] (3.2 g, 19 mmol) in 30 mL of butanol was added dropwise a solution of sodium (0.44 g, 19 mmol) in butanol (30 mL). The mixture was gently refluxed for 4 h. Precipitates were collected, washed successively with ethanol and water, and then recrystallized from pyridine to yield 2.9 g (65%) of **27** as yellow plates: mp 292–293 °C dec; ^1H NMR (100 MHz, CF_3CO_2D) δ 2.16 (br s, 4, $ArCH_2CH_2$), 3.06 (br s, 4, $ArCH_2$), 7.56 (br s, 6, ArH), 7.82 (m, 4, ArH); MS, 482 (M^+). Anal. Calcd for $C_{24}H_{26}N_{12}$: C, 59.74; H, 5.43; N, 34.84. Found: C, 59.73; H, 5.25; N, 34.58.

1,4-Bis(2-adenyl)butane (28). A stirred suspension of 300 mg (0.62 mmol) of **27** in 36 mL of acetic acid–methanol–water (2:5:5) was heated at 80–85 °C. To the mixture was added by portions 820 mg of zinc powder in a period of 30 min. After cooling, the remaining zinc powder was filtered off, and the filtrate was washed with ethanol. After removal of the solvent, 15 mL of formic acid (98–100%) was added to the residue and heated at 75–80 °C for 30 min. Insoluble material was filtered and washed with ethanol. After removal of the solvent from the combined organic phase, the residue and formamide (7 mL) was heated in an ampule at 160–170 °C for 2.5 h. After the reaction was over, the yielded solid was collected and washed with ethanol to give 151 mg (75%) of crude **28**. Recrystallization from acetic acid–ethanol gave pure **28** as a white solid: dec pt >312 °C (lit.[9] mp 268 °C); IR (Nujol mull) 3100, 3270 cm^{-1}; ^1H NMR (100 MHz, CF_3CO_2D) δ 2.18 (br s, 4, $ArCH_2CH_2$), 3.22 (br s, 4, $ArCH_2$), 9.35 (s, 2, ArH); MS, 324 (M^+).

Synthesis of 9 and 10. The cyclization reaction of **28** with 1,3-dibromopropane or with 1,4-dibromobutane was carried out according to the method B described for the synthesis of **3**.

The crude product of **9** was purified by column chromatography on silica gel with methanol–chloroform (1:3) and by preparative TLC (silica gel, methanol–chloroform, 1:5) to give **9** in 28% yield. **9**: colorless prisms from ethanol, dec pt >320 °C; IR (Nujol mull) 3150, 3300 cm^{-1}; ^1H NMR (100 MHz, CF_3CO_2D) δ 2.17 (br s, 4, $ArCH_2CH_2$), 3.24 (br s, 6, $ArCH_2$ + NCH_2CH_2), 4.79 (br s, 4, NCH_2), 9.32 (s, 2, ArH); MS, 364 (M^+). Anal. Calcd for $C_{17}H_{20}N_{10}$: C, 56.02; H, 5.54; N, 38.44. Found: C, 56.10; H, 5.52; N, 38.39.

The crude product of **10** was purified by column chromatography on silica gel with methanol–chloroform (1:1) and then recrystallization from acetic acid–ethanol to give **10** in 23% yield. **10**: colorless fine needles from acetic acid–methanol; dec pt >378 °C; IR (Nujol mull) 3140, 3300 cm^{-1}; ^1H NMR (100 MHz, CF_3CO_2D) δ 2.22 (br s, 4, $ArCH_2CH_2$), 2.43 (br s, 4, NCH_2CH_2), 3.25 (br s, 4, $ArCH_2$), 3.25 (br s, 4, $ArCH_2$), 4.75 (br s, 4, NCH_2), 9.39 (s, 2, ArH); MS, 378 (M^+). Anal. Calcd for $C_{18}H_{22}N_{10}$: C, 57.12; H, 5.87; N, 37.01. Found: C, 57.12; H, 6.01; N, 37.00.

1,4-Bis(6-oxopurin-2-yl)butane (29). To a hot solution (~65 °C) of 500 mg (15 mmol) of **28** in acetic acid (25 mL) and water (30 mL) was added with stirring by portions sodium nitrite (2.13 g, 31 mmol). Stirring was continued at the same temperature for 1 h and then at room temperature overnight. Yielded white solid was collected and washed successively with water and ethanol to give 430 mg (83%) of **29**. **29**: white solid from aqueous NH_3; dec pt >329 °C; IR (Nujol mull) 1690, 3100, 3320 cm^{-1}; ^1H NMR (100 MHz, DMSO-d_6) δ 1.70–1.81 (m, 4, $ArCH_2CH_2$), 2.58–2.72 (m, 4, $ArCH_2$), 8.00 (s, 2, ArH); MS, 325 (M^+ – 1). Anal. Calcd for $C_{14}H_{14}N_8O_2$: C, 51.53; H, 4.32; N, 34.34. Found: C, 51.40; H, 4.57; N, 34.22.

1,4-Bis(6-chloropurin-2-yl)butane (30). To a hot stirred mixture (65 °C) of **29** (100 mg, 0.31 mmol) and DMF (3 mL) was added dropwise thionyl chloride (4.25 mL, 59 mmol) in a period of 15 min. After additional stirring at 65 °C for 8 h, the solvent was removed and the residue was washed well with dichloromethane. Crude solid (90 mg, 80%) was purified by column chromatography on silica gel with methanol–chloroform (1:3) and then recrystallization from DMSO–water to give pure **30** as colorless fine needles: dec pt >285 °C; ^1H NMR (100 MHz, DMSO-d_6) δ 1.79–1.88 (m, 4, $ArCH_2CH_2$), 2.90–3.02 (m, 4, $ArCH_2$), 8.56 (s, 2, ArH); MS, 366, 364 (M^+), 362, 329 (M^+ – Cl), 327 (M^+ – Cl). Anal. Calcd for $C_{14}H_{12}N_8Cl_2$: C, 46.30; H, 3.33; N, 30.85; Cl, 19.52. Found: C, 46.31; H, 3.43; N, 30.61; Cl, 19.64.

1,4-Diaza[4.4](2,6)purinophane (31). A solution of **30** (400 mg, 1.1 mmol) in DMSO (150 mL) and a solution of ethylenediamine (0.089 mL, 2.7 mmol) in water (150 mL) were simultaneously added dropwise into 150 mL of hot DMSO (~90 °C) under nitrogen atmosphere with stirring in a period of 20 h. Additional stirring and heating were continued for 2 days. After removal of the solvent, the residue was washed with water and purified by column chromatography on silica gel with methanol–chloroform (1:3) to give 97 mg (25%) of **31**. Further purification was done by recrystallization from acetic acid and then sublimation at 300 °C (<10^{-4} mmHg). **31**: white solid; dec pt >327 °C; IR (Nujol mull) 3280 cm^{-1}; ^1H NMR (100 MHz, DMSO-d_6) δ 1.78–1.88 (m, 4, $ArCH_2CH_2$), 2.64–2.78 (m, 4, $ArCH_2$), 3.62–3.74 (m, 4, $NHCH_2$), 7.64 (br s, 2, $NHCH_2$), 7.99 (s, 2, ArH), 12.6 (br s, 2, NH); MS, 350 (M^+). Anal. Calcd for $C_{16}H_{18}N_{10}$: C, 54.83; H, 5.19; N, 39.98. Found: C, 54.38; H, 5.20; N, 39.39.

6,6′-Dichloro[3.4](2,9)purinophane (32). Following the procedure of method B described for the synthesis of **3**, cyclization of **30** with 1,3-dibromopropane was carried out. Crude product was purified by column chromatography on silica gel with methanol–chloroform (1:5) to give **32** in 28% yield. Further purification by preparative TLC (silica gel, methanol–chloroform, 1:9) followed by recrystallization from ethanol gave **32** as colorless prisms: dec pt >243 °C; ^1H NMR (100 MHz, $CDCl_3$) δ 1.72–1.99 (m, 4, $ArCH_2CH_2$), 2.93 (quint, J = 7 Hz, 2, NCH_2CH_2), 3.05–3.13 (m, 4, $ArCH_2$), 4.25 (t, 4, NCH_2), 8.03 (s, 2, ArH). Anal. Calcd for $C_{17}H_{16}N_8Cl_2$: C, 50.63; H, 4.00; N, 27.79; Cl, 17.58. Found: C, 50.49; H, 3.76; N, 27.55; Cl, 17.35.

1,4-Diaza[4.4.3](2,6,9)purinophane (11). To a stirred solution of **32** (250 mg, 0.62 mmol) in butanol (200 mL) was added a solution of ethylenediamine (0.05 mL, 0.75 mmol) and tripropylamine (0.24 mL, 1.3 mmol) in 150 mL of butanol in a period of 31 h at a bath temperature of 90–95 °C. Additional stirring and heating were continued for 35 h. After removal of the solvent, the residue was extracted with methanol–chloroform (1:3). Crude product from the extracts was purified by column chromatography on silica gel with methanol–chloroform (1:3), followed by liquid chromatography, by preparative TLC (silica gel, methanol–chloroform, 1:3), and finally by recrystallization from 2-propanol to give 20 mg (8%) of pure **11** as colorless microcrystals: mp 303–305 °C; ^1H NMR (100 MHz, $CDCl_3$) δ 1.88–2.67 (m, 10, CH_2), 3.67–4.71 (m, 8, NCH_2), 5.47–5.59 (m, 2, NH), 7.28 (s, 2, H8); MS, 390 (M^+). Anal. Calcd for $C_{19}H_{22}N_{10}$: C, 58.45; H, 5.68; N, 35.87. Found: C, 58.89; H, 5.86; N, 35.23.

1,4-Diaza[4.4.4](2,6,9)purinophane (12). The reaction of **31** (81 mg, 0.23 mmol) and 1,4-dibromobutane (0.025 mL, 0.23 mmol) was carried out by method B. Crude product was purified by column chromatography on silica gel with methanol–chloroform (1:5), followed by liquid chromatography to yield 24 mg (26%) of **12**. Further purification was done by recrystallization from chlorobenzene and by sublimation at 300 °C (<4×10^{-4} mmHg). **12**: white microcrystals; ^1H NMR (100 MHz, $CDCl_3$) δ 1.84–2.28 (m, 8, CH_2), 2.68 (br s, 4, ArH), 3.64–3.81 (m, 4, NCH_2), 4.23–4.45 (m, 4, NCH_2), 5.91 (br s, 2, NH), 7.24 (s, 2, H8); MS, 404 (M^+). Anal. Calcd for $C_{20}H_{24}N_{10}$: C, 59.39; H, 5.98; N, 34.63. Found: C, 59.18; H, 6.24; N, 34.60.

N^6,$N^{6'}$-Dimethyl-9,9′-trimethylenebis(adenine) (33). A mixture of **34** (0.5 g, 1.3 mmol), monomethylamine (1.0 mL, 13.0 mmol), and water (1 mL) in an ampule was heated at 130 °C for 20 h. After being cooled, precipitated white solid was collected, washed successively with water and acetone, and recrystallized from ethyl acetate to yield 0.3 g (68%) of **33** as a colorless crystalline solid: mp 241–242 °C; ^1H NMR (100 MHz, $CDCl_3$) δ 2.54 (q, J = 6.6 Hz, 2, $CH_2CH_2CH_2$), 3.27 (d, J = 6.6 Hz,

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4, N^6CH_3), 4.26 (t, J = 6.6 Hz, 4, N^9CH_2), 6.1 (br s, 2, NH), 7.92 (s, 2, H8), 8.40 (s, 2, H2). Anal. Calcd for $C_{15}H_{18}N_{10}$: C, 53.24; H, 5.37; N, 41.39. Found: C, 53.29; H, 5.41; N, 40.84.

6,6'-Bis(methylthio)-9,9'-trimethylenebis(purine) (34). To a stirred mixture of 6-methylthiopurine (2.0 g, 12.4 mmol) in DMSO (20 mL) was added at 30 °C 1,3-dibromopropane (0.65 mL, 6.2 mmol). Stirring was continued at 30 °C for 16 h. After the reaction was over, water (50 mL) was added to the mixture, and yielded precipitates were collected, washed successively with water and acetone, and then recrystallized from ethyl acetate to give 1.1 g (47%) of **34** as colorless prisms: mp 236-237 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 2.59 (q, J = 6.8 Hz, 2, $CH_2CH_2CH_2$), 2.74 (s, 6, SCH_3), 4.32 (t, J = 6.8 Hz, 2, N^9CH_2), 8.12 (s, 2, H8), 8.73 (s, 2, H2); MS, 372 (M^+). Anal. Calcd for $C_{15}H_{16}N_8S_2$: C, 48.37; H, 4.33; N, 30.08; S, 17.22. Found: C, 48.38; H, 4.36; N, 29.82; S, 17.04.

1,4-Bis(N^6,9-dimethyladenin-2-yl)butane (35). Under a nitrogen atmosphere was added 60% NaH (132 mg, 3.3 mmol) to a stirred solution of **30** (500 mg, 1.4 mmol) in DMF (10 mL). After being stirred for 10 min, methyl iodide (0.26 mL, 4.1 mmol) was added to the solution, and stirring was continued at room temperature for 3 h. After the reaction was over, the mixture was chromatographed on silica gel with methanol-chloroform (1:3) and purified with preparative TLC (silica gel) with methanol-chloroform (1:9) to give the N^9,N^9-dimethyl derivative of **30** in 54% yield. Recrystallization from 2-propanol gave the pure compound as white microcrystals: mp 223 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.89-2.06 (m, 4, $ArCH_2CH_2$), 2.96-3.17 (m, 4, $ArCH_2$), 3.89 (s, 5, CH_3), 8.01 (s, 2, ArH); MS, 394, 392, 390 (M^+), 357, 355 (M^+ - Cl).

To a solution of the above described compound (210 mg, 0.54 mmol) in 1-butanol was added a 40% aqueous solution of monomethylamine (0.46 mL) and triethylamine (0.18 mL, 1.3 mmol), and the mixture was gently refluxed for 5.5 h. During the reaction, each 0.46 mL of monomethylamine aqueous solution was added five times to the reaction mixture. After the reaction was over, the solvent was removed and crude product was purified by preparative TLC (silica gel) with methanol-chloroform (1:5) to give 61 mg (30%) of **35**. Further purification from 1-butanol gave pure **35** as white microcrystals: mp 262-265 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.88-2.03 (m, 4, $ArCH_2CH_2$), 2.82-2.91 (m, 4, $ArCH_2$), 3.22 (d, J = 4.9 Hz, 6, $NHCH_3$), 3.77 (s, 6, NCH_3), 5.54 (br s, 2, $NHCH_3$), 7.62 (s, 2, ArH); MS, 380 (M^+). Anal. Calcd for $C_{18}H_{24}N_{10}$: C, 56.83; H, 6.36; N, 36.81. Found: C, 56.59; H, 6.64; N, 36.53.

N^6,9-Dimethyladenine (36). A mixture of **37** (0.2 g, 1.1 mmol), 40% monomethylamine (0.5 mL, 6.4 mmol), and water (0.5 mL) in an ampule was heated at 130 °C for 20 h. After being cooled, the solvent was removed and the residue was chromatographed on silica gel with methanol. Recrystallization from benzene gave 0.10 g (55%) of **36** as colorless prisms: mp 181.5-182.5 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 3.23 (d, J = 5.1 Hz, 3, N^6CH_3), 3.82 (s, 3, N^9CH_3), 5.80 (br s, 1, NH), 7.71 (s, 1, H8), 8.43 (s, 1, H2); MS, 163 (M^+). Anal. Calcd for $C_7H_9N_5$: C, 51.52; H, 5.56; N, 42.92. Found: C, 51.57; H, 5.39; N, 42.67.

9-Methyl-6-(methylthio)purine (37). A mixture of 6-methylthiopurine (1.0 g, 6.2 mmol), potassium carbonate (0.6 g, 4.3 mmol), and methyl iodide (0.4 mL, 7.4 mmol) in DMSO (10 mL) was stirred at 30 °C for 16 h. The solvent was removed under reduced pressure, and the residue was extracted with chloroform. Crude product was passed through a short column of silica gel with methanol and then purified by column chromatography on alumina with benzene-chloroform, followed by recrystallization from benzene to give 0.65 g (58%) of **37** as colorless prisms: mp 167-167.5 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 2.74 (s, 3, SCH_3), 3.88 (s, 3, NCH_3), 7.93 (s, 1, H8), 8.74 (s, 1, H2); MS, 180 (M^+). Anal. Calcd for $C_7H_8N_4S$: C, 46.65; H, 4.47; N, 31.09; S, 17.79. Found: C, 46.94; H, 4.38; N, 31.19; S, 17.73.

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The First Silylenium Ions in Solution

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Abstract: The first silylenium ions (R_3Si^+) have been produced in solution. They are generated in polar solvents of low nucleophilicity, including CH_2Cl_2, $ClCH_2CH_2Cl$, CH_3CN, and sulfolane. Tris(alkylthio)silyl cations [$(R'S)_3Si^+$, R' = Me, Et, *i*-Pr] are produced by treatment of the corresponding silane with trityl perchlorate. The covalent form is unambiguously eliminated as the structure in dilute solution by the conductance and molecular weight. A dicationic bridged dimer is eliminated by the molecular weight and by crossover experiments. Complexation with solvent is inconsistent with the ^{1}H and ^{13}C resonance positions. Similar treatment of triphenylsilane yields a solution of low conductance in CH_2Cl_2 and $ClCH_2CH_2Cl$ and of high conductance in CH_3CN and sulfolane. Molecular weight measurements show that triphenylsilyl perchlorate in dilute sulfolane is unambiguously in the two-particle ionic form, whereas the azide is in a one-particle covalent or ion-paired form. Carbon-13 analysis of the phenyl resonances in all solvents substantiates an ionic or ion-paired form. Conductance and ^{35}Cl experiments demonstrate that the ionic form is favored at low concentrations but that association occurs at high concentrations. The ^{13}C and ^{15}N resonance positions of CH_3CN and sulfolane eliminate the possibility that they are forming tetravalent complexes in CH_2Cl_2 and $ClCH_2CH_2Cl$.

Silylenium ions[2] have been known and studied in the gas phase for over 20 years. Electron impact mass spectrometry gave values of the appearance potential of Me_3Si^+ in the early 1960s.[3] Fragmentation studies indicated reasonable stability for silylenium ions,[4-6] which were found to be more stable than analogous carbenium ions, as judged from the fragment intensities. The ion Me_2PhSi^+ represented 50% of the total ion current in the mass spectrum of (trimethylsilyl)benzene.[5] Several ion cyclotron resonance studies have been carried out on silylenium ions,[7-9] with

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(2) Even the nomenclature for trivalent, positive silicon (R_3Si^+) has been controversial. The earliest term was *siliconium*, but, like its strict analogue *carbonium*, it denotes hypervalency and is best reserved for pentacoordinate silicon, R_5Si^+. We and others have used the term *silicenium*, by loose analogue to *carbenium*. This term, however, seems to have no linguistic basis. The term *carbenium* is derived from the divalent species *carbene*. Thus, since the divalent silicon species is *silylene*, the trivalent, positive form should be *silylenium*. The general term *carbocation* finds analogy with *silyl* cation. Pronunciation of all these terms varies according to the side of the Atlantic, with Americans preferring the initial *i* long (except in *siliconium* because of the close analogy to *silicon*). Individual species are best named as derivatives of silanes, so that Me_3Si^+ becomes trimethylsilylenium or trimethylsilyl.

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