Duphar, B. V. (Weesp, the Netherlands) for a generous gift of vitamin D_3. E.A.K. thanks the NSF-URP for an undergraduate fellowship. We are also grateful to the National Institutes of Health (AM-16595 and AM-9012) for financial support.

Registry No. **7b**, 90079-80-4; **8a**, 90079-81-5; **8b**, 90079-82-6; **8c**, 90079-83-7; **9a**, 90079-84-8; **9b**, 90079-85-9; **9c**, 90079-86-0; **12a**, 90079-87-1; **13**, 37457-15-1; **14a**, 75154-92-6; **14b**, 75197-02-3; **15**, 75154-90-4; **16a**, 89998-52-7; **16b**, 89998-53-8; **17a**, 89998-54-9; **17b**, 89998-55-0; **18**, 90079-88-2; **19**, 75154-94-8; **20**, 90079-89-3; **21**, 89998-56-1; **22a**, 89998-57-2; **22b**, 89998-58-3; **23**, 89998-59-4; **24**, 89998-60-7; **25**, 89998-61-8; **26**, 89998-62-9; **27** (isomer 1), 89998-63-0; **27** (isomer 2), 90079-90-6; **28**, 90079-91-7; **29**, 90079-92-8; **31**, 75154-95-9; **32**, 67670-81-9; **33**, 67619-74-3; **35**, 75154-96-0; **36**, 67619-73-2; **37**, 67672-93-9.

Supplementary Material Available: Spectral and other analytical data (15 pages). Ordering information is given on any masthead page.

Defined Dimensional Alterations in Enzyme Substrates. *lin*-Naphthoadenine and *lin*-Naphthoadenosine

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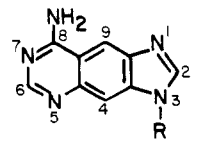
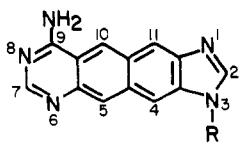
Received November 22, 1983

lin-Naphthoadenine (*lin* = linear) and *lin*-naphthoadenosine have been synthesized for the first time, on the basis of the availability of the intermediate *lin*-naphthohypoxanthine from a shortened, efficient synthesis. 5,6-Dimethylbenzimidazole, protected by a bulky group on N, was subjected to selective benzylic bromination. The tetrabromo product, when treated with sodium iodide under Finkelstein conditions, generated a dibromo-*o*-xylylene intermediate that could be trapped by maleic anhydride or *N*-hydroxymaleimide, with aromatization by loss of 2 HBr. This Diels–Alder cycloaddition approach to the otherwise difficultly available tetra-β-substituted naphthalenes was followed by stepwise conversions of the terminal anhydride or *N*-hydroxy imide ring to a suitably substituted pyrimidine ring. *lin*-Naphthoadenine and *lin*-naphthoadenosine are brilliantly fluorescent, exhibiting high fluorescent yields (Φ = 0.57, 0.64) and long lifetimes (τ = 20.5, 22.4 ns in ethanol purged of oxygen). Neither is a substrate for adenosine deaminase, showing that a lateral extension of 4.8 Å is too great for a satisfactory fit at the enzyme active site, whereas a 2.4-Å extension (*lin*-benzoadenine and *lin*-benzoadenosine) is tolerated.

The concept of utilizing defined dimensional probes for testing the spatial restrictions of enzyme binding regions for purine-containing substrates or cofactors has been advanced in this Laboratory with the synthesis and biological evaluation of laterally extended analogues of naturally occurring purines.[1] The lateral extensions are of known magnitude, brought about by the formal insertion of a benzo (2.4 Å), benzocyclobutadieno (3.9 Å), or naphtho (4.8 Å) unit between the terminal pyrimidine and imidazole rings. With synthetic dimensional probes of these types, we have been able to improve descriptions of binding and to define more accurately the spatial basis of activity and inhibition by comparison of the biochemical behavior of the synthetic analogues with those of the natural substrates and cofactors. As examples, *lin*-benzoadenine (1) and





1 R = H
2 R = β-D-Ribofuranosyl

3 R = H
4 R = β-D-Ribofuranosyl

lin-benzoadenosine (2) are excellent substrates for adenosine deaminase and show fluorescence characteristics that have made them, along with the mono-, di-, tri-, and cyclic phosphates of 2, useful in enzyme binding studies. The synthetic *lin*-naphthopurine analogues, *lin*-naphthoxanthine and *lin*-naphthohypoxanthine, which are intensely fluorescent, have been applied toward setting the spatial limits of the binding region of xanthine oxidase.[2] We have now provided a second method of synthesis of the *lin*-naphthopurine ring system that leads successfully to *lin*-naphthoadenine (3) and *lin*-naphthoadenosine (4).

The challenge of construction of the tetracyclic ring system in the *lin*-naphthopurine series lies in the synthesis of requisite tetra-β-substituted naphthalene intermediates. We have previously developed methodology for the regioselective synthesis of such intermediates via an *o*-xylylene precursor, 3,4-bis(trimethylsilyl)bicyclo[4.2.0]octa-1,3,5-triene, and an appropriate dienophile.[2] While we were convinced of the value of the Diels–Alder cycloaddition approach, we sought a more accessible substituted *o*-xylylene precursor. *o*-Xylylenes can also be obtained from substituted benzo[*c*]thiophene 2,2-dioxides by thermal cheleotropic elimination of sulfur dioxide.[3] Since these heterocycles are usually obtained from *o*-bis(bromomethyl)benzenes, which have themselves been shown to be precursors of *o*-xylylenes under the mild conditions of the Finkelstein reaction,[4] we perceived no obvious advantage in employing the thiophene dioxide route. Cava has shown that naphthalenes and anthraquinones can be synthesized from *o*-xylenes by benzylic bromination followed by dehalogenation with sodium iodide and in situ

(1) Leonard, N. J. *Acc. Chem. Res.* **1982**, *15*, 128 and references therein.

(2) Moder, K. P.; Leonard, N. J. *J. Am. Chem. Soc.* **1982**, *104*, 2613.
(3) Oppolzer, W. *Heterocycles*, **1980**, *14*, 1615.
(4) (a) Cava, M. P.; Deana, A. A.; Muth, K. *J. Am. Chem. Soc.* **1959**, *81*, 6458. (b) McOmie, J. F. W.; Perry, D. H. *Synthesis* **1973**, 416. (c) Kerdesky, F. A. J.; Ardecky, R. J.; Lakshimikantham, M. V.; Cava, M. J. *J. Am. Chem. Soc.* **1981**, *103*, 1992.

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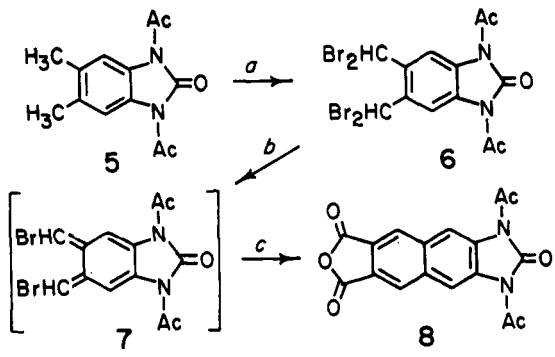
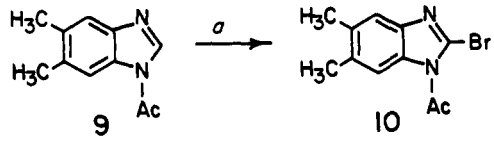
Scheme I[a]



[a] a, NBS; b, NaI, DMF; c, maleic anhydride.

Scheme II[a]



[a] a, NBS.

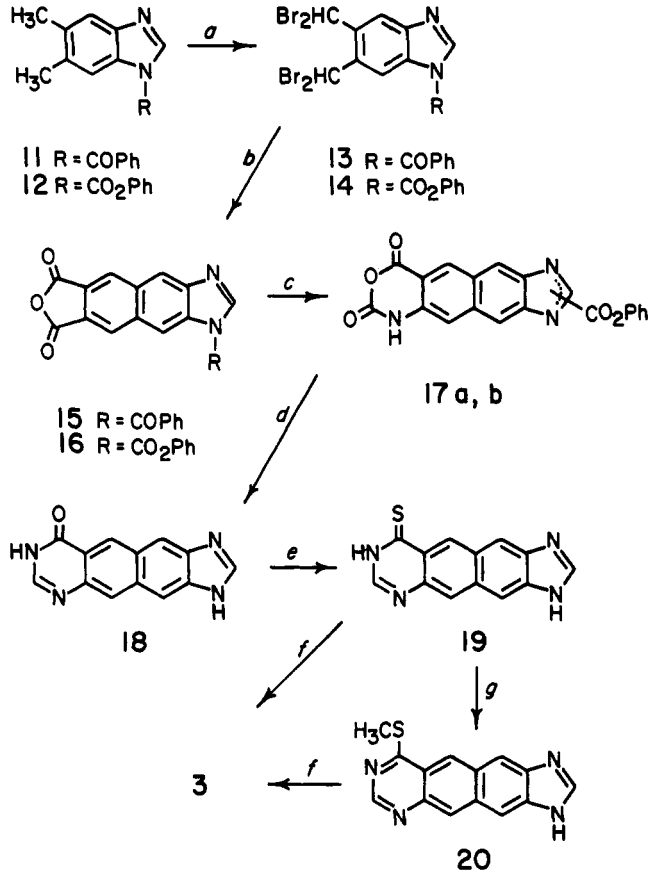
trapping with dienophiles.[4a,c]

Results and Discussion

Chemistry. Due to the difficulty encountered previously in forming the imidazole ring late in the reaction sequence leading to a *lin*-naphthopurine,[2] we planned to generate the o-xylylene with an imidazole ring already in place. Since we were aware of reports of the *N*-bromosuccinimide bromination of some N-substituted aminoxylenes on the nucleus as well as the side chain[5] and of methylimidazoles at C-2 in preference to the methyl group,[6] we first tested the application of the Finkelstein conditions to substituted benzimidazoles having a protected C-2 position. Treatment of 1,3-diacetyl-5,6-dimethyl-2*H*-benzimidazol-2-one (**5**)[7] with 4 equiv of NBS under UV radiation led exclusively to the tetrabromo derivative **6** (Scheme I). It was convenient to follow the course of the reaction by means of the ^{1}H NMR spectra. The initial signal at δ 2.3 for the methyl protons was shifted downfield to δ 4.6 ($-CH_2Br$) and finally to δ 7.0 ($-CHBr_2$). Due to its susceptibility to hydrolysis and oxidation, the tetrabromide **6** was not purified but was treated directly with sodium iodide in DMF solution in the presence of maleic anhydride to give the corresponding naphthimidazole anhydride **8** in 77% overall yield. The purpose of allowing the NBS reaction to proceed to the tetrabromo stage was to achieve the correct oxidation level through the eventual loss of 2 equiv of HBr.

While construction of the di-β-substituted naphthimidazole skeleton was thus accomplished readily under Finkelstein conditions, a protected but unsubstituted 2-position in the imidazole ring was desirable. 1-Acetyl-5,6-dimethylbenzimidazole (**9**),[8] prepared from readily available 5,6-dimethylbenzimidazole, when subjected to NBS (1 equiv) treatment in CCl_4 gave no side chain bromination but only bromination at C-2 to provide **10** (Scheme II). The conversion was followed by complete loss of the resonance for the 2-H in the ^{1}H NMR spectrum. Ring bromination was regarded as resulting from insufficient steric protection of C-2; accordingly, bulkier groups at N-1 were tried: benzoyl (**11**),[9] carbophenoxy (**12**), pivaloyl, and benzenesulfonyl. In all cases, NBS tetrabromination of the methyls was possible without effecting imidazole ring bromination. The tetrabromo products **13** and **14** from **11** and **12** behaved satisfactorily under Finkelstein conditions with sodium iodide and maleic anhydride in DMF to give the corresponding naphthimidazole anhydrides **15** and **16**, respectively, in good yield (Scheme III). The carbophenoxy-protected derivative **12** was the most suitable precursor since it gave reproducible results and the product **16** could be recrystallized conveniently from DMF. The anhydride **16** was converted to a 1:1 mixture of the corresponding isatoic anhydrides **17a** and **17b** with trimethylsilyl azide in DMF solution.[10] The lack of regiospecificity in the Curtius rearrangement was unimportant since treatment of the mixture with an excess of formamidine acetate in refluxing methyl cellosolve gave *lin*-naphthohypoxanthine (**18**)[2] directly as a result of both ring conversion and deprotection.[11] The 3*H* tautomeric form shown in **18** is in facile equilibrium with the 1*H* tautomer, and the representation is actually intended to designate the presence of both tautomers. Since reasonable quantities of *lin*-naphthohypoxanthine (**18**) were available by this shortened six-step synthesis, it was a viable precursor for conversion to *lin*-naphthoadenine (**3**) and *lin*-naphthoadenosine (**4**). Conversion of compound **18** to the more electrophilic thio derivative **19** was accomplished by

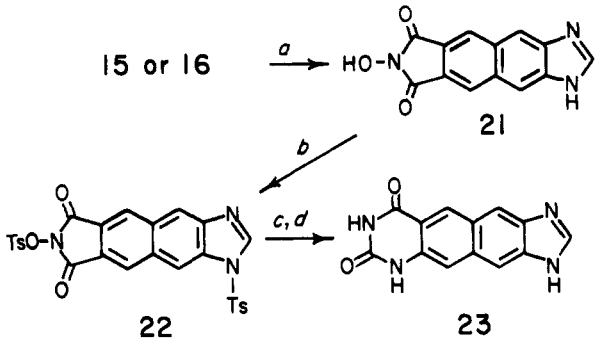
Scheme III[a]



[a] a, NBS (4 equiv); b, NaI, DMF, maleic anhydride; c, $TMSN_3$, DMF; d, formamidine acetate, 2-methoxyethanol; e, Lawesson's reagent, Pyr; f, EtOH/NH_3, 180 °C.

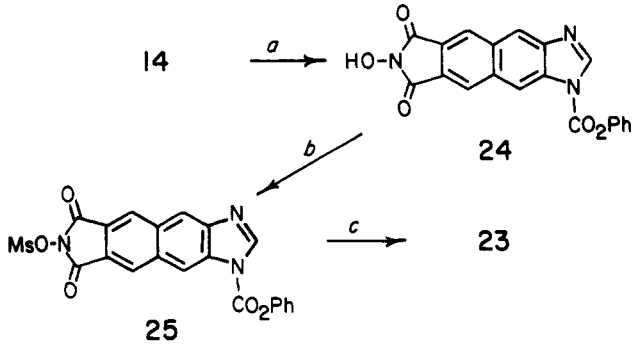
(5) Kleinschmidt, E.-G.; Bräuniger, H. *Pharmazie* **1969**, *24*, 87.
(6) Garcia-Lopez, M. T.; Herranz, R. *Eur. J. Med. Chem.* **1980**, *15*, 551.
(7) (a) Ibrahim, M. R.; Jarrar, A. A.; Sabri, S. S. *J. Heterocycl. Chem.* **1975**, *12*, 11. (b) Clark, R. L.; Pessolono, A. A. *J. Am. Chem. Soc.* **1958**, *80*, 1657.
(8) Pappalardo, L.; Elguero, J.; Fruchier, A. *An. Quim.* **1975**, *71*, 598.
(9) Hoga, M.; Ness, R. K.; Fletcher, H. G. *J. Org. Chem.* **1968**, *33*, 1810.
(10) Washburne, S. S.; Peterson, W. R.; Berman, G. A. *J. Org. Chem.* **1972**, *37*, 1738.
(11) Stevenson, T. M.; Leonard, N. J., in preparation.

Scheme IV[a]



[a] a, NH_2OH; b, TsCl, 4-(dimethylamino)pyridine, Pyr, Me_2SO; c, $EtOH/NH_3$; d, NaOH.

Scheme V[a]



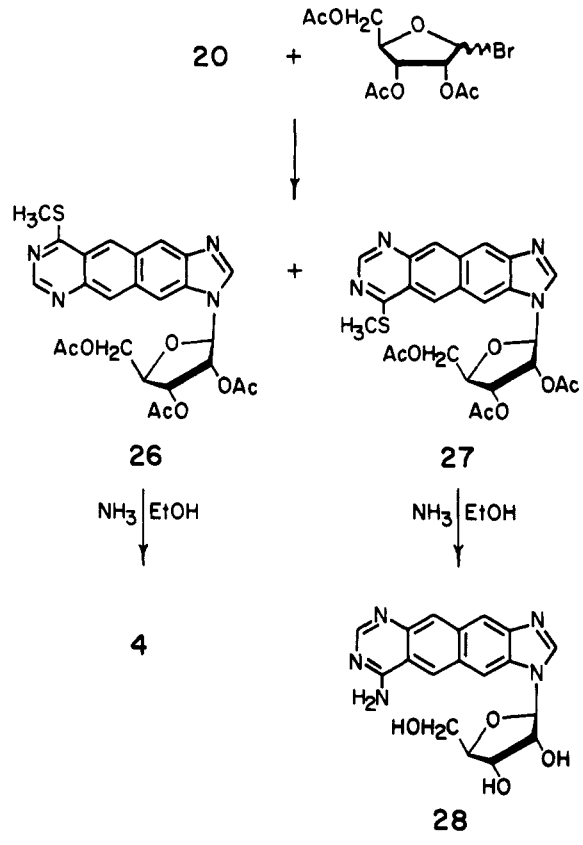
[a] a, NaI, DMF, *N*-hydroxymaleimide; b, CH_3SO_2Cl, Pyr; c, $EtOH/NH_3$.

using Lawesson's reagent[12] in large excess in refluxing anhydrous pyridine. Replacement with ethanolic ammonia was effected in a pressure bomb at elevated temperature and pressure for a first synthesis of *lin*-naphthoadenine (**3**). Another route proceeded through 9-(methylthio)-benzimidazo[5,6-*g*]quinazoline (*20*), synthesized from **19** by treatment with MeI and aqueous NaOH. The synthesis of **20** was most efficient when DMF was used as a cosolvent. Both reactivity toward nucleophilic displacement and confirmation of the site of methylation in **20** were apparent from its conversion in *lin*-naphthoadenine (**3**) by ethanolic ammonia.

Either protected naphthimidazole anhydride **15** or **16** could be used for a short synthesis of *lin*-naphthoxanthine (**23**) (Scheme IV). Reaction of either with hydroxylamine in pyridine gave the known hydroxyimide (**21**),[2] with deprotection, in greater than 90% yield. Compound **21** was converted to the ditosylated intermediate **22** as previously described[2] and thence by a Lossen rearrangement[13] with ethanolic ammonia followed by treatment with NaOH to cleave the remaining sulfonamide linkage, yielding *lin*-naphthoxanthine (**23**).[2]

The problem of accompanying N-deprotection in the synthesis of compound **21** could be circumvented by using Finkelstein conditions in the presence of N-hydroxymaleimide. *N*-Hydroxymaleimide, a readily available reagent,[14] which apparently has been overlooked as a versatile dienophile in Diels–Alder reactions, offered the solution. Indeed, when the *N*-carbophenoxy compound **14** was treated with sodium iodide and *N*-hydroxymaleimide in DMF (Scheme V), the protected hydroxyimide **24** was obtained. Treatment of **24** with methanesulfonyl chloride in pyridine to give **25** was followed by treatment with ethanolic ammonia, leading to rearrangement and concomitant deprotection, to provide *lin*-naphthoxanthine (**23**).

Scheme VI



For the synthesis of *lin*-naphthoadenosine (**4**), we drew upon previous methodology[15] and experience gained in the successful preparation of *lin*-benzoadenosine (**2**).[16] In that method, 8-(methylthio)imidazo[4,5-*g*]quinazoline was ribosidated with a protected bromo sugar. Regiospecificity was observed to the extent that the protected ribosyl group did not become attached to the deactivated pyrimidine ring but rather to the imidazole ring.[17] The position of attachment to the imidazole ring was not subject to control by the distant methylthio group, with the result that both 3-β-D-ribofuranosyl and 1-β-D-ribofuranosyl products were obtained and were isolated in pure form following separation by chromatography. The first isomer off the silica gel column with chloroform elution, the 3-isomer, was the one convertible to *lin*-benzoadenosine.[16] In the parallel reaction of 9-(methylthio)benzimidazo[5,6-*g*]quinazoline (**20**) with 2,3,5-tri-*O*-acetylribofuranosyl bromide (Scheme VI) in the presence of mercuric cyanide using nitromethane/DMF as the solvent system, two major products were obtained. Their chromatographic behavior on silica gel, with chloroform elution, was clearly parallel to that of the *lin*-benzo pair of isomers, and was deemed indicative that the first isomer off the column in the *lin*-naphtho case was the desired precursor (*26*) of *lin*-naphthoadenosine. Better separation of the isomers of presumed structures **26** and **27** was achieved by using a Waters PrepPAK-500 cartridge of silica gel and elution with ethyl acetate–acetone (vv, 7:3). Under these conditions, the same isomer moved more rapidly, as monitored by TLC on silica gel.

(12) Scheibye, S.; Pedersen, B. S.; Lawesson, S. O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 229.
(13) Bauer, L.; Exner, O. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 376.
(14) Available from Aldrich Chemical Company.
(15) Yamaoka, N.; Aso, K.; Matsuda, K. *J. Org. Chem.* **1965**, *30*, 149.
(16) Leonard, N. J.; Sprecker, M. A.; Morrice, A. G. *J. Am. Chem. Soc.* **1976**, *98*, 3987.
(17) Morrice, A. G. Ph.D. Thesis, University of Illinois, 1974.

The NMR spectra of the two positional isomers **26** and **27** were consistent with their assignments as imidazole-substituted tri-*O*-acetylribofuranosyl derivatives of 9-(methylthio)benzimidazo[5,6-*g*]quinazoline (**20**). Moreover, the significant features of the NMR spectra that were analogous to those in the spectra of the corresponding compounds in the *lin*-benzo series[16] indicated that both had the β configuration at C-1′, as shown in **26** and **27**. Separate treatment of each isomer with ethanolic ammonia for 18 h at 20 °C to effect removal of the acetyl groups and for 36 h at 150 °C to effect nucleophilic displacement of the methylthio group yielded the 3- and 1-β-D-ribofuranosyl derivatives of 9-aminobenzimidazo[5,6-*g*]quinazoline. The isomer, mp 229–231 °C, obtained from the precursor assigned structure **26**, that is, the faster moving on chromatography, showed chromatographic characteristics similar to those of *lin*-benzoadenosine (**2**) and parallel electronic absorption spectra as well. In the spectra, the three-band pattern in the longest wavelength region for this isomer was displaced to shorter wavelength in comparison with the second isomer, mp 244–246 °C, product of the slower-moving precursor assigned structure **27**. The same direction of displacement was observed in a comparison of the longest wavelength band patterns of *lin*-benzoadenosine (**2**) vs. 1-β-D–ribofuranosyl-*lin*-benzoadenine,[16] the structures of which had been determined by additional means.[18] Thus, it is entirely consistent with the chromatographic and UV spectroscopic data to assign structure **4**, that of *lin*-naphthoadenosine (or 9-amino-3-β-D-ribofuranosylbenzimidazo[5,6-*g*]quinazoline), to the compound, mp 229–231 °C, obtained from precursor **26** (greater R_f) and to assign structure **28**, that of 1-β-D-ribofuranosyl-*lin*-benzoadenine (or 9-amino-1-β-D-ribofuranosylbenzimidazo[5,6-*g*]quinazoline), to the other isomer, mp 244–246 °C. It would be prudent to seek independent confirmation of the assignments, and that is our intention.

The unequivocal method used in this laboratory for the structure confirmation of *lin*-benzoadenosine (**2**), i.e., observation of ^{15}N–^{13}C spin-spin coupling in the ^{13}C NMR spectrum between C-1′ of the ribofuranosyl moiety and a specifically labeled nitrogen-15 in the imidazole ring,[18] unfortunately cannot be applied in the case of *lin*-naphthoadenosine. Since the Curtius rearrangement of the intermediate **16** is not regiospecific, our synthetic route does not allow for the formation of unambiguously substituted model systems or for specific incorporation of nitrogen-15 in the imidazole ring.[18] Hopefully, a suitable crystalline derivative of **4** or a suitable 3-alkyl model may be found for single-crystal X-ray verification of our assignments.

Spectroscopic Properties. The electronic absorption and fluorescence emission spectra of the *lin*-naphthopurines are interesting when compared with those of the *lin*-benzopurines and of linear polycyclic aromatic hydrocarbons. Generalizations concerning the latter, which have well-defined electronic absorption bands, include (1) a decrease in absorbance with increasing wavelength and (2) displacement of the longer wavelength bands progressively with an increase in the number of rings in the linear array.[19,20] For example, the long wavelength absorptions of anthracene, related to **2**, are located between 340 and 370 nm, while those of naphthacene, related to **4**, fall between

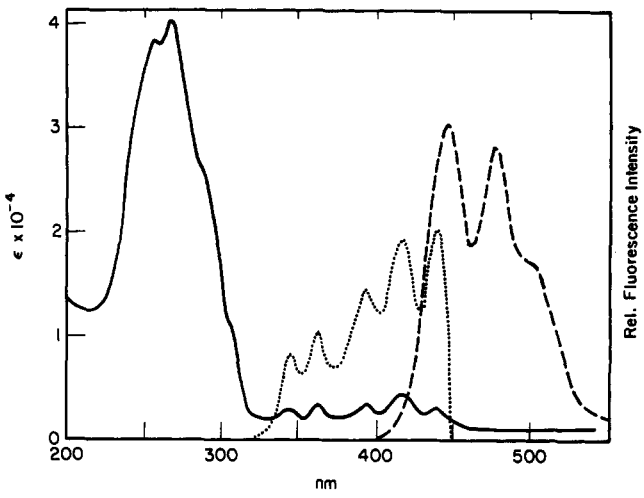


Figure 1. The fluorescence and ultraviolet spectra of *lin*-naphthoadenosine (**4**) in EtOH purged of oxygen: (—) ultraviolet absorption, (···) technical fluorescence excitation, (--) technical fluorescence emission.

415 and 470 nm.[20] The long wavelength bands of *lin*-benzoadenosine (**2**) at 305–348 nm are similarly related to those of *lin*-naphthoadenosine (**4**) at 392–438 nm (Figure 1). A displacement of the same order is observed in the spectra of *lin*-benzoadenine (**1**) and *lin*-naphthoadenine (**3**). The group of three longer wavelength bands in the electronic absorption spectrum of *lin*-naphthoadenosine (**4**) was not greatly affected by changing pH from basic to neutral to acidic media. However, the second group of bands at intermediate wavelength (340–370 nm) in the spectrum of **4** did show shifts to longer wavelength and greater absorbance upon protonation (see Experimental Section). The effect of an extra ring upon pK_a was not pronounced in going from **2** to **4** (both ~5.6), in contrast to the change from 3.5 for adenosine to 5.6 for *lin*-benzoadenosine (**2**).[22] Thus, in terms of basicity, the laterally extended analogues resemble more closely separate quinazoline and benzimidazole units than purines.[21] The site of first protonation of *lin*-naphthoadenosine (**4**), as of *lin*-benzoadenosine (**2**), is predictably on the pyrimidine ring.[22,23] Even though these analogues have higher pK_a values than that of adenosine, a direct comparison of their reactivity in the presence of specific enzymes is satisfactory at pH 7.5 or above, where all are mainly unprotonated.

The fluorescence properties of *lin*-benzoadenosine and its phosphates, i.e., quantum yield and lifetime of fluorescence and fluorescence polarization, have proved to be of great utility.[1] *lin*-Naphthoadenine (**3**) and *lin*-naphthoadenosine (**4**), like *lin*-naphthohypoxanthine (**18**) and *lin*-naphthoxanthine (**23**),[2] are brilliantly fluorescent, exhibiting high fluorescence quantum yields and long lifetimes: **3**, Φ, 0.57, τ, 20.5 ns; **4**, Φ, 0.64, τ, 22.4 ns at 25 ° C in purged ethanol. They can be excited at even longer wavelength than the *lin*-benzo analogues (e.g., **1** and **2**) and well beyond the region of absorption of proteins and nucleic acids. Thus, in cases where the *lin*-naphtho analogues exhibit activity or inhibition in specific enzyme systems, their uses as fluorescent probes will complement those of the *lin*-benzo analogues.[1,2]

Behavior with Adenosine Deaminase. Whereas *lin*-benzoadenosine (**2**) was converted by adenosine deaminase

(18) Wiemer, D. F.; Scopes, D. I. C.; Leonard, N. J. *J. Org. Chem.* **1976**, *41*, 3051.
(19) Jaffe, H. H.; Orchin, M. "Theory and Application of Ultraviolet Spectroscopy"; Wiley: New York, 1962; pp 345–375.
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(21) Keyser, G. E.; Leonard, N. J. *J. Org. Chem.* **1976**, *41*, 3529.
(22) VanDerLijn, P.; Barrio, J. R.; Leonard, N. J. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 4204.
(23) Barrio, J. R.; Liu, F. T.; Keyser, G. E.; VanDerLijn, P.; Leonard, N. J. *J. Am. Chem. Soc.* **1979**, *101*, 1564.
(24) Leonard, N. J.; Scopes, D. I. C.; VanDerLijn, P.; Barrio, J. R. *Biochemistry* **1978**, *17*, 3677.

from calf intestinal mucosa to *lin*-benzoinosine at a rate almost comparable to that for the conversion of adenosine to inosine,[16] *lin*-naphthoadenosine (4) underwent no detectable deamination under identical reaction conditions, nor did 28. If, after 18 h, to the adenosine deaminase solution containing 4 was added an equivalent amount of adenosine, its rapid conversion to inosine was observed. This indicated that the enzyme was still active and provided preliminary evidence that *lin*-naphthoadenosine was not an effective inhibitor. The absence of activity establishes that a lateral extension of 4.8 Å from the normal substrate is too great for a satisfactory fit at the enzyme active site. Since, at a 2.4-Å extension of 2, binding to the enzyme and deamination of the substrate were efficient, either that marks the dimensional limit or the limit lies somewhere between 2.4 and 4.8 Å. It would still be of interest to determine this.

lin-Naphthoadenine (3) was also inactive as a substrate for adenosine deaminase, thus exhibiting behavior similar to adenine itself and to the bent benzo derivatives, *prox*-benzoadenine and *dist*-benzoadenine.[16] By contrast, *lin*-benzoadenine (1) was as good a substrate as the corresponding ribonucleoside analogue 2. Among the bases, *lin*-benzoadenine is thus unique. While it helps define the limits of size and shape for satisfactory binding and reaction at the base level, it leaves open the question as to why the tricyclic base bears enzyme-behavioral resemblance to adenosine, in which the pendant ribosyl group is required for activity.[16] The present findings provide an additional application of the *lin*-naphthopurines for defining the enzyme binding sites for purines, since we have already shown by their use that the limiting lateral extension of the substrate for xanthine oxidase (hypoxanthine and xanthine are the normal substrates) to be able to act on the imidazole ring appears to lie between 2.4 and 4.8 Å.[1,2] Synthesis of the *lin*-benzocyclobutadieno analogues of the purine bases (3.9-Å extension) and their ribosyl derivatives may assume greater importance as we attempt further fine-tuning of the spatial limits of the binding regions of adenosine deaminase and xanthine oxidase.

Experimental Section

General Comments. Thin-layer chromatography was performed on Merck precoated silica gel f-254 plates with fluorescent backing. NMR spectra were recorded on a Varian Associates EM-390 or XL-200 or on a Nicolet NTC-360 spectrometer. Melting points were determined on a Büchi melting point apparatus and are uncorrected. UV absorption spectra were obtained on a Beckman Acta MVI spectrophotometer. Electron-ionization mass spectra (EIMS) were obtained on a Varian MAT CH-5 instrument, high-resolution electron ionization mass spectra (HREIMS) were obtained on a Varian MAT-731 high-resolution spectrometer coupled with a 620i computer and a STATOS recorder, and fast atom bombardment mass spectra (FABMS) and high-resolution mass spectra (HRFABMS) were obtained on a VG ZAB-1F instrument equipped with a high-field magnet and a VG 11/250 data system, all by J. Carter Cook and his staff. Microanalyses were performed by Josef Nemeth and his staff, who also weighed samples for electronic absorption spectra. Medium-pressure liquid chromatography was performed on a Waters PrepPAK-500 system using a silica gel cartridge (360 g) by Robb Gutowsky. Technical fluorescence emission and excitation spectra were obtained on a microprocessor-controlled photon-counting spectrophotometer described by Gratton and Limkeman.[25] Adenosine deaminase (Adenosine aminohydrolase; EC 3.5.4.4), grade I from calf intestinal mucosa, was purchased from Sigma Chemical Co.

(25) Gratton, E.; Limkeman, M. *Rev. Sci. Instrum.* **1983**, *54*, 294.

1,3-Diacetyl-2,3-dihydro-2-oxo-1*H*-naphth[2,3-*d*]imidazole-6,7-dicarboxylic Anhydride (8). A solution of 5[7a] (3.4 g, 13.8 mmol) in 250 mL of carbon tetrachloride was treated with *N*-bromosuccinimide (9.8 g, 55 mmol) and a few milligrams of benzoyl peroxide. The mixture was refluxed under irradiation from a 250-W flood lamp for 4 h. After the mixture had cooled, the succinimide was filtered and the solvent was removed in vacuo to provide a yellow solid (6). The residue was dissolved in 75 mL of anhydrous DMF and treated with maleic anhydride (6.5 g, 66 mmol) and sodium iodide (12 g). The dark suspension was stirred at 80 °C for 2 h under vacuum (100 mmHg), then diluted with aqueous 10% sodium bisulfite solution (125 mL), and filtered. The solid was washed with water (50 mL), ethanol (50 mL), and acetone (50 mL). Drying gave 8 (3.8 g, 82%) as a yellow powder: mp 258–260 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 2.71 (s, 6, CH_3), 8.41 (s, 2, Ar H), 8.63 (s, 2, Ar H); mass spectrum, 10 eV, *m/e* (relative intensity) 338 (26, M^+), 296 (43), 254 (100); high-resolution MS, *m/e* 338.0546; M^+ calcd for $C_{17}H_{10}N_2O_6$, 338.0539.

1-Benzoyl-5,6-dimethyl-1*H*-benzimidazole (11). 5,6-Dimethyl-1*H*-benzimidazole (4.2 g, 28 mmol) was suspended in $CHCl_3$ (70 mL) and treated with triethylamine (10 mL). This mixture was then treated dropwise with benzoyl chloride (3.5 mL, 29 mmol). After the initial exothermic reaction, the mixture was stirred at room temperature for 1 h and then washed with 1 N NaOH (50 mL). The organic layer was dried (Na_2SO_4), concentrated, and recrystallized from hexane/acetone to provide 11 in two crops (5.9 g, 82%): mp 132–133 °C (lit.[9] mp 132–134 °C); ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 6, CH_3), 7.25 (m, 5, COC_6H_5), 7.58 (s, 1, Ar H), 7.85 (s, 1, Ar H), 8.52 (s, 1, Im–CH).

1-Benzoyl-1*H*-naphth[2,3-*d*]imidazole-6,7-dicarboxylic Anhydride (15). A suspension of 11 (2.0 g, 8.1 mmol) and *N*-bromosuccinimide (2.9 g, 16.3 mmol) in carbon tetrachloride (150 mL) was heated at reflux under irradiation from a 250-W flood lamp with a few mg of benzoyl peroxide. After 1 h, more *N*-bromosuccinimide (2.9 g, 16.3 mmol) was added and refluxing with irradiation was continued for 1.5 h longer. The mixture was then cooled and filtered to remove succinimide. The crude tetrabromide 13 was obtained by concentration: ^{1}H NMR (CCl_4) δ 7.1 (br, 2, $CHBr_2$), 7.53 (m, 5, COC_6H_5), 8.01 (s, 1, Ar H), 8.20 (s, 1, Ar H), 8.40 (s, 1, Im–CH). The residue was dissolved in DMF (25 mL) and treated with maleic anhydride (1.3 g, 13.3 mmol) and sodium iodide (10.5 g). The deeply colored mixture was stirred at 80 °C under vacuum (100 mmHg) for 1.5 h. The semisolid mass was treated with aqueous 10% sodium bisulfite solution (100 mL) and filtered. The solid was washed with water (60 mL) and acetone (50 mL) and dried to provide 1.4 g (52%) of 15 as a tan powder. An analytical sample was obtained by recrystallization from DMF: mp >300 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 7.72 (m, 3, Ph H), 7.96 (m, 2, Ph H), 8.83 (s, 1, Ar H), 8.84 (s, 1, Ar H), 8.98 (s, 1, Ar H), 9.09 (s, 1, Ar H), 9.19 (s, 1, Ar H); mass spectrum, 70 eV, *m/e* (relative intensity) 342 (2, M^+), 238 (4), 166 (5), 105 (45), 44 (85), 28 (100).

Anal. Calcd for $C_{20}H_{10}N_2O_4$: C, 70.17; H, 2.94; N, 8.18. Found: C, 70.13; H, 2.74; N, 8.00.

1-Carbophenoxy-5,6-dimethyl-1*H*-benzimidazole (12). To a stirred suspension of 5,6-dimethyl-1*H*-benzimidazole (20.0 g, 13.7 mmol) and triethylamine (50 mL) in methylene chloride (400 mL) was slowly added phenyl chloroformate (23 mL, 180 mmol). The suspension dissolved slowly and after 1 h at room temperature, the mixture was washed with 0.5 N NaOH. The organic layer was dried (Na_2SO_4) and passed through a plug of silica gel (100 g) and washed with methylene chloride (200 mL). Concentration of the solution gave a viscous residue that was recrystallized from cyclohexane to afford 12 (26.5 g, 71%): mp 108–109 °C; ^{1}H NMR ($CDCl_3$) δ 2.46 (s, 6, CH_3), 7.36 (m, 5, C_6H_5), 7.57 (s, 1, Ar H), 7.83 (s, 1, Ar H), 8.50 (s, 1, Im–CH); mass spectrum, 10 eV, *m/e* (relative intensity) 266 (90, M^+), 173 (92), 94 (100).

Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.23; H, 5.59; N, 10.65.

1-Carbophenoxy-1*H*-naphth[2,3-*d*]imidazole-6,7-dicarboxylic Anhydride (16). A suspension of 12 (5.1 g, 19 mmol) and *N*-bromosuccinimide (6.9 g, 39 mmol) in CCl_4 (300 mL) was treated with benzoyl peroxide (spatula tip) and heated at reflux under irradiation from a 250-W flood lamp for 1 h. The mixture was cooled and treated with more *N*-bromosuccinimide (6.9 g,

39 mmol), and refluxing under irradiation was continued for an additional 1.5 h. After the reaction mixture had cooled to room temperature, it was filtered and concentrated to provide the crude tetrabromide **14**: ^{1}H NMR (CCl_4) δ 7.16 (s, 1, $CHBr_2$), 7.18 (s, 1, $CHBr_2$), 7.45 (m, 5, C_6H_5), 8.05 (s, 1, Ar H), 8.31 (s, 1, Ar H), 8.52 (s, 1, Im–CH). The residue was dissolved in DMF (120 mL) and treated with maleic anhydride (4.5 g, 46 mmol). Addition of sodium iodide (19 g) caused a deep coloration of the mixture which was then heated at 80 °C for 1.5 h under vacuum (100 mmHg). The suspension was decolorized with 10% aqueous sodium bisulfite (170 mL), filtered, and washed with water (3 × 100 mL), ethanol (2 × 100 mL), and ether (2 × 100 mL). After air drying, the solid was recrystallized from DMF to give **16** (3.85 g, 56%) as a faintly yellow powder: mp 291–292 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 7.54 (m, 5, C_6H_5), 8.83 (s, 1, Ar H), 8.94 (s, 1, Ar H), 8.99 (s, 1, Ar H), 9.06 (s, 1, Ar H), 9.28 (s, 1, Ar H); mass spectrum, 10 eV *m/e* (relative intensity) 358 (8, M^+), 238 (14), 194 (8), 166 (20), 94 (50), 44 (100).

Anal. Calcd for $C_{20}H_{10}N_2O_5$: C, 67.04; H, 2.81; N, 7.82. Found: C, 66.71; H, 2.61; N, 7.71.

3*H*-Benzimidazo[5,6-*g*]quinazolin-9(8*H*)-one (18). A suspension of **16** (3.65 g, 10 mmol) in DMF (200 mL) was heated at 120 °C until dissolution occurred. The resulting solution was cooled to 60 °C, trimethylsilyl azide (7.5 mL) was added, and stirring at this temperature was continued until nitrogen evolution ended (2 h). The mixture was heated to 100 °C for 5 min and then allowed to cool to room temperature. Removal of the solvent at reduced pressure provided **17a** and **17b**: mp 268 °C dec; ^{1}H NMR ($(CD_3)_2SO$) δ 7.57 (m, 5, C_6H_5), 8.27–9.09 (m, 5, Ar H); mass spectrum, 10 eV, *m/e* (relative intensity) 373 (6, M^+), 339 (12), 94 (100). The residue was suspended in methyl cellosolve and treated with formamidine acetate (4.5 g, 43 mmol). The suspension dissolved upon being heated to reflux and after 1 h was cooled to 0 °C. The precipitated solid was filtered and washed with water (20 mL) and ether (20 mL). Drying at 110 °C (1 mmHg) for 12 h provided 2.13 g (90%) of **18** as a yellow powder: mp >320 °C (lit.[2] mp >300 °C); ^{1}H NMR ($(CD_3)_2SO$) δ 7.98 (s, 1, Ar H), 8.26 (s, 1, Ar H), 8.33 (s, 1, Ar H), 8.49 (s, 1, Ar H), 8.61 (s, 1, Ar H), 8.98 (s, 1, Ar H).

3*H*-Benzimidazo[5,6-*g*]quinazoline-9(8*H*)-thione (19). A suspension of **18** (2.08 g, 8.8 mmol) and Lawesson's reagent (11.5 g, 28 mmol) in pyridine (100 mL) was heated at reflux for 18 h. The hot solution was poured into 400 mL of water and then boiled until crystallization occurred. After standing at 0 °C overnight, the precipitate was filtered and washed with water (3 × 100 mL). The solid was dried for 24 h at 137 °C (0.5 mmHg) to give **19** (1.96 g, 88%) as an orange powder: mp >320 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 8.01 (s, 1, Ar H), 8.32 (s, 1, Ar H), 8.42 (s, 1, Ar H), 8.55 (s, 1, Ar H), 8.64 (s, 1, Ar H), 9.37 (s, 1, Ar H); mass spectrum, 10 eV, *m/e* (relative intensity) 252 (100, M^+), 219 (27); high-resolution MS, *m/e* 252.0476; M^+ calcd for $C_{13}H_8N_4S$, 252.0473.

9-(Methylthio)-3*H*-benzimidazo[5,6-*g*]quinazoline (20). A solution of **19** (792 mg, 3.1 mmol) in 35 mL of DMF at 10 °C was treated with 0.1 N NaOH solution (33 mL). To the resulting red solution was added MeI (0.2 mL, 3.2 mmol) with stirring. After 2 min a yellow solid began to precipitate. The suspension was stirred for 1 h and diluted with water (100 mL). The solid was filtered and dried to provide **20** (730 mg, 86%). An analytical sample was obtained by recrystallization from DMF/ethanol: mp 319–321 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 2.80 (s, 3, SCH_3), 8.41 (s, 1, Ar H), 8.56 (s, 1, Ar H), 8.68 (s, 1, Ar H), 8.73 (s, 1, Ar H), 8.89 (s, 1, Ar H), 8.98 (s, 1, Ar H); mass spectrum, 10 eV, *m/e* 266 (100, M^+).

Anal. Calcd for $C_{14}H_{10}N_4S$: C, 63.14; H, 3.78; N, 21.04; S, 12.04. Found: C, 63.05; H, 3.51; N, 20.98; S, 11.89.

***lin*-Naphthoadenine or 9-Amino-3*H*-benzimidazo[5,6-*g*]quinazoline (3). Method A.** A solution of **19** (65 mg, 0.25 mmol) in 30 mL of ethanol containing excess ammonia at −78 °C was sealed in a 125-mL steel bomb and heated for 16 h at 170 °C. After the bomb was cooled, the ethanol was degassed with nitrogen to remove excess ammonia. Filtration provided **3** (47 mg, 78%) as an orange powder: mp >320 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 8.29 (s, 1, Ar H), 8.33 (s, 1, Ar H), 8.39 (s, 1, Ar H), 8.50 (s, 1, Ar H), 8.62 (s, 1, Ar H), 8.8 (br, 2, NH_2), 9.18 (s, 1, Ar H); mass spectrum, 10 eV, *m/e* (relative intensity) 235 (100, M^+); high-resolution MS, *m/e* 235.0854; M^+ calcd for $C_{13}H_9N_5$, 235.0850; λ_{max} (95% EtOH) 255 nm (31 000), 261 (sh), 340 (5340), 359 (5590), 392 (5300), 414 (3800), 441 (4700); λ_{max} (0.1 N HCl) 242 (21 000), 252 (26 300), 264 (28 800), 288 (17 900), 300 (13 800), 336 (5180), 352 (8680), 390 (4220), 409 (4860), 434 (3690); λ_{max} (0.1 N NaOH) 247 (20 500), 296 (32 000), 308 (sh), 358 (8960), 371 (9100).

Anal. Calcd for $C_{13}H_9N_5 \cdot H_2O$: C, 61.65; H, 4.38; N, 27.66. Found: C, 61.27; H, 4.27; N, 27.27.

Method B. A solution of **20** (70 mg, 0.26 mmol) in 25 mL of ethanolic ammonia (saturated at −78 °C) was sealed in a 125-mL steel bomb and heated for 18 h at 160 °C. The reaction mixture was degassed with nitrogen and the precipitate was filtered and dried to give **3** (53 mg, 85%), identical with that prepared above.

***N*-Hydroxy-1*H*-naphth[2,3-*d*]imidazole-6,7-dicarboximide (21). Method A.** Hydroxylamine hydrochloride (1.3 g, 19 mmol) was added to a suspension of **15** (575 mg, 1.7 mmol) in dry pyridine (15 mL). The mixture was stirred at 80 °C for 12 h. After cooling, the precipitated solid was filtered and washed with water (3 × 25 mL). The product was dried to provide 385 mg (90%) of **21**, identical with an authentic sample: mp >300 °C (lit.[2] mp >300 °C).

Method B. Identical treatment of **16** with hydroxylamine hydrochloride gave **21** in 90% yield.

1-Carbophenoxy-*N*-hydroxy-1*H*-naphth[2,3-*d*]imidazole-6,7-dicarboximide (24). *N*-bromosuccinimide (2.7 g, 15 mmol) and **12** (2.0 g, 14 mmol) were suspended in carbon tetrachloride (200 mL) and treated with benzoyl peroxide (spatula tip). The mixture was brought to reflux under irradiation from a 250-W flood lamp for 1 h. *N*-bromosuccinimide (2.7 g, 15 mmol) was added and the mixture was heated at reflux for 1 h further. The suspension was allowed to cool to room temperature and the succinimide was filtered. Concentration afforded an orange residue which was dissolved in DMF (50 mL) and treated with *N*-hydroxymaleimide (750 mg, 6.5 mmol) and sodium iodide (20 g). The dark mixture was heated to 80 °C under vacuum (100 mmHg) for 1.25 h. Dilution with aqueous 10% sodium bisulfite (50 mL) and filtration gave crude **24**, which was crystallized from DMF to give **24** (1.2 g, 44%) as a white powder: mp >300 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 7.50 (m, 5, C_6H_5), 8.49 (s, 1, Ar H), 8.60 (s, 2, Ar H), 8.75 (s, 1, Ar H), 9.10 (s, 1, Ar H), 10.8 (br, 1, N–OH); mass spectrum, 10 eV, *m/e* (relative intensity) 373 (5, M^+), 357 (10), 94 (100); high-resoltuion MS, *m/e* 373.0700; M^+ calcd for $C_{20}H_{11}N_3O_5$, 373.0698.

1-Carbophenoxy-*N*-(methylsulfonyl)-1*H*-naphth[2,3-*d*]imidazole-6,7-dicarboximide (25). A suspension of **24** (750 mg, 2 mmol) in dimethylacetamide (10 mL) and pyridine (3 mL) was treated with methanesulfonyl chloride (0.22 mL, 3.6 mmol). The reaction mixture was stirred at 100 °C until dissolution occurred and then was allowed to cool to room temperature. After 1 h the solution was poured into water (75 mL), filtered, and washed with water (3 × 25 mL). The crude solid was taken up in ethanol/DMF and reprecipitated by addition of water to give **25** (790 mg, 87%): mp 274–276 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 3.72 (s, 3, CH_3), 7.51 (m, 5, C_6H_5), 8.70 (s, 1, Ar H), 8.83 (s, 1, Ar H), 8.85 (s, 1, Ar H), 9.16 (s, 1, Ar H); mass spectrum, 10 eV, *m/e* (relative intensity) 451 (15, M^+), 373 (5), 357 (35), 314 (20), 94 (100); high resolution MS, *m/e* 451.0469; M^+ calcd for $C_{21}H_{13}N_3O_7S$, 451.0464.

Anal. Calcd for $C_{21}H_{13}N_3O_7S$: C, 55.87; H, 2.70; N, 9.31; S, 7.10. Found: C, 55.43; H, 3.02; N, 9.21; S, 7.28.

3*H*-Benzimidazo[5,6-*g*]quinazoline-7,9-(6*H*,8*H*)-dione (23). A suspension of **25** (300 mg, 0.67 mmol) in ethanolic ammonia (saturated at −20 °C) was heated at reflux for 3 h. During this time a canary yellow solid was deposited which, after cooling, was filtered to give **23** (146 mg, 87%), identical with an authentic sample: mp >300 °C (lit.[2] mp >300 °C).

***lin*-Naphthoadenosine (4) and 1-β-D-Ribofuranosyl-*lin*-naphthoadenine (28).** A suspension of **20** (1.5 g, 5.6 mmol) and $Hg(CN)_2$ (1.8 g, 7.1 mmol) in DMF/nitromethane (1:3, 200 mL) was heated at reflux for 3.5 h, and then 40 mL of solvent was distilled to insure dryness. When the heterogeneous mixture had cooled to 40 °C, a freshly prepared solution of 1-bromo-2,3,5-triacetylribofuranose (prepared from D-1,2,3,5-tetra-*O*-acetylribofuranose (4.5 g, 15 mmol))[16] in dry dichloromethane (20 mL) was added under a stream of dry nitrogen along with 5 g of Linde 4-Å molecular sieves. The mixture was heated at 50 °C for 2 h and then at 100 °C for 12 h. Filtration, followed by concentration of the solvent, gave a dark residue that was dissolved in ethyl

Table I. Fluorescence Spectral Data for *lin*-Naphthoadenine (3) and *lin*-Naphthoadenosine (4) in Ethanol[a]

compd	excitation > 320, nm (uncor)	emission, nm (uncor)	τ, ns[b]	Φ[c]
lin-naphthoadenine (3)	345, 361, 393, 413, 440	451, 477, 506 (sh)	20.5	0.57
lin-naphthoadenosine (4)	342, 360, 393, 414, 439	447, 474, 502 (sh)	22.4	0.64

[a] Purged of oxygen. [b] For fluorescence lifetime see Experimental Section. [c] Quantum yields determined relative to quinine in 0.1 N H_2SO_4 (Φ = 0.70).

acetate (200 mL) and chloroform (300 mL). The organic layer was washed with 30% aqueous KI (3 × 50 mL) and dried (Na_2SO_4). After removal of the solvent, the residue was dissolved in ethyl acetate/acetone (7:3, 20 mL) and applied to a Waters PrepPAK-500/silica cartridge and eluted with the same solvent system. Concentration of the first main fraction gave **26** as a red glass: ^{1}H NMR ($CDCl_3$) δ 2.03–2.26 (m, 9, $COCH_3$), 2.75 (s, 1, SCH_3), 4.21 (m, 2, 5′-CH_2), 4.4 (m, 4′-CH), 5.45 (m, 1, 3′-CH), 5.73 (m, 1, 2′-CH), 6.16 (d, 1, 1′-CH, J = 6 Hz), 8.02 (s, 1, Ar H), 8.32 (s, 1, Ar H), 8.43 (s, 1, Ar H), 8.54 (s, 1, Ar H), 8.65 (s, 1, Ar H), 8.83 (s, 1, Ar H); λ_{max} (95% EtOH) 266, 354, 372, 403, 425, 444 nm. Concentration of the second main fraction gave **27** as a red brown foam: ^{1}H NMR ($CDCl_3$) δ 2.05–2.25 (m, 9, $COCH_3$), 2.71 (s, 3, SCH_3), 4.32 (m, 2, 5′-CH_2), 4.4 (m, 1, 4′-CH), 5.41 (m, 1, 3′-CH), 5.64 (m, 1, 2′-CH), 6.15 (d, 1, 1′-CH, J = 6 Hz), 8.01 (s, 1, Ar H), 8.19 (s, 1, Ar H), 8.33 (s, 1, Ar H), 8.42 (s, 1, Ar H), 8.46 (s, 1, Ar H), 8.73 (s, 1, Ar H); λ_{max} (95% EtOH) 264, 308 (sh), 352, 368, 404, 427, 448 nm.

Each fraction was dissolved separately in ethanolic ammonia ((30 mL) saturated at −78 °C) and sealed in a 125-mL steel bomb. After 18 h at room temperature, the bomb was heated to 150 °C for 36 h. Upon cooling, the mixtures were filtered and the filtrates were concentrated to 10 mL, cooled to 4 °C overnight, and filtered. The combined solids were collected in each case to afford **4** and **28**, respectively. *lin*-Naphthoadenosine (4) was recrystallized from water as silky yellow fibers (290 mg, 14%): mp 229–231 °C dec; ^{1}H NMR ($(CD_3)_2SO$) δ 3.72 (m, 2, 5′-CH_2), 4.11 (m, 1, 4′-CH), 4.26 (m, 1, 3′-CH), 4.52 (m, 1, 2′-CH), 5.2 (br, 2, OH), 5.5 (br, 1, OH), 6.03 (d, 1, 1′-CH, J = 6 Hz), 8.01 (br, 2 NH_2), 8.33 (s, 2, Ar H), 8.38 (s, 1, Ar H), 8.41 (s, 1, Ar H), 8.79 (s, 1, Ar H), 9.10 (s, 1, Ar H); mass spectrum, FAB, m/e, positive ion spectrum, 368 (M^+ + H); high-resolution MS, FAB m/e 368.1351; (M^+ + H) calcd for $C_{18}H_{18}N_5O_4$, 368.1359; λ_{max} (95% EtOH) 257, (38 500), 266 (41 900), 344 (3300), 362 (3800), 392 (4400), 414 (5890), 438 nm (4090); λ_{max} (95% EtOH, 0.1 N HCl) 241 (28 500), 266 (30 900), 289 (sh), 297 (sh), 335 (4760), 352 (8100), 387 (4480), 408 (5710), 433 nm (4280); λ_{max} (95% EtOH; 0.1 N NaOH) 264 (34 800), 347 (1900), 362 (2620), 392 (3140), 414 (4950), 439 nm (3800).

Anal. Calcd for $C_{18}H_{17}N_5O_4 \cdot {}^2/_3H_2O$: C, 56.98; H, 4.87; N, 18.46. Found: C, 56.91; H, 4.87; N, 18.46.

Compound **28** was crystallized from water to give a yellow amorphous powder (80 mg, 4%): mp 244–246 °C dec; ^{1}H NMR ($(CD_3)_2SO$ δ 3.72 (m, 2, 5′-CH), 4.06 (m, 1, 4′-CH), 4.24 (m, 1, 3′-CH), 4.52 (m, 1, 2′-CH), 5.2–5.7 (br, 3 OH), 6.03 (d, 1, 1′-CH J = 6 Hz), 8.1 (br, 2, NH_2), 8.27 (s, 1, Ar H), 8.36 (s, 1, Ar H), 8.44 (s, 2, Ar H), 8.79 (s, 1, Ar H), 9.02 (s, 1, Ar H); mass spectrum, FAB, positive ion spectrum, m/e 368 (M^+ + H); high-resolution MS, FAB, m/e 368.1351; (M^+ + H) calcd for $C_{18}H_{18}N_5O_4$, 368.1359; λ_{max} (95% EtOH) 256 (46 300), 277 (28 100), 341 (3500) 357 (3100), 396 (3300), 418 (4540), 442 nm (3300); λ_{max} (95% EtOH; 0.1 N HCl) 246 (39 000), 267 (32 500), 338 (6500), 354 (9540), 389 (4510), 411 (4330), 436 nm (3040); λ_{max} (95% EtOH, 0.1 N NaOH) 256 (31 700), 272 (sh), 340 (2170), 358 (3300), 396 (4080), 419 (5640), 445 nm (5200).

Fluorescence. The technical fluorescence data were recorded at 25 °C and were not corrected for monochrometer efficiency and photomultiplier response. The absolute quantum yields of compounds **3** and **4** were determined by comparison with the fluorescence emission of quinine sulfate (quantum yield 0.70 in 0.1 N H_2SO_4)[26] in ethanol solutions purged of oxygen (dry nitrogen was passed through each solution at the rate of 1 bubble per second for 20 min immediately before each experiment).

Fluorescence lifetimes were determined at 23 °C in solutions purged of oxygen using a continuously variable frequency cross-correlation phase fluorometer.[27] The exciting light was modulated at various frequencies (1-50 MHz) through a monochrometer and a CS-3-72 Corning filter (see Table I).

Adenosine Deaminase. Solutions of adenosine, *lin*-benzoadenosine (**2**), *lin*-naphthoadenosine (**4**), compound **28**, and *lin*-naphthoadenine (**3**) were made in 0.05 M phosphate buffer. To a given amount of substrate in 3.0 mL of buffer was added 1 unit of enzyme. The reactions were monitored for change in OD. For the adenosine (monitored at 265 nm) and *lin*-benzoadenosine (monitored at 345 nm), the reactions were essentially complete in 6 min and 60 min, respectively. No change in OD was observed for **3**, **4**, or **28** (monitored at 440, 438, and 443 nm, respectively) over a 6-h period. Treatment with additional enzyme at the end of that time resulted in no change in OD over a 12-h period.

Acknowledgment. This work was supported by Research Grant GM-05829 from the National Institutes of Health. High-resolution mass spectral data were obtained in part under a grant from the National Institutes of Health, National Institute of General Medical Sciences (GM-27029). NMR data were obtained in part with support from the University of Illinois NSF Regional Instrumentation Facility, Grant NSF CHE 79-16100. We are pleased to acknowledge our colleagues Professor Enrico Gratton and Mark Limkeman for their help and guidance with the fluorescence studies and Marc d'Alarcao for his assistance in obtaining NMR spectra.

Registry No. **3**, 90108-76-2; **4**, 90108-79-5; **5**, 51360-47-5; **6**, 90108-66-0; **8**, 90108-67-1; **9**, 3245-29-2; **10**, 90108-83-1; **11**, 16109-46-9; **12**, 90108-69-3; **13**, 90108-84-2; **14**, 90108-70-6; **15**, 90108-68-2; **16**, 90108-71-7; **17a**, 90108-72-8; **17b**, 90108-73-9; **18**, 80964-04-1; **19**, 90108-74-0; **20**, 90108-75-1; **21**, 80964-17-6; **22**, 80976-40-5; **23**, 80964-05-2; **24**, 90108-77-3; **25**, 90108-78-4; **26**, 90108-81-9; **27**, 90108-82-0; **28**, 90108-80-8; adenosine deaminase, 9026-93-1; maleic anhydride, 108-31-6; 5,6-dimethyl-1*H*-benzimidazole, 582-60-5; 1-bromo-2,3,5-triacetylribofuranose, 39110-68-4; D-1,2,3,5-tetra-*O*-acetylribofuranose, 28708-32-9.

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