express our sincere appreciation to Professor Herbert C. Brown for his encouragement and valuable discussions.

Registry No. DIBAH, 1191-15-7; $CH_3(CH_2)_5OAl(i\text{-}Bu)_2$, 96503-31-0; $PhCH_2OAl(i\text{-}Bu)_2$, 41329-29-7; $CH_3CH_2CH(CH_2CH_2CH_3)OAl(i\text{-}Bu)_2$, 96503-32-1; $CH_3CH_2CH(CH_2CH_3)OAl(i\text{-}Bu)_2$, 96503-33-2; $PhOAl(i\text{-}Bu)_2$, 4165-53-1; 2,6-$(t\text{-}Bu)_2C_6H_4OAl(i\text{-}Bu)_2$, 76229-55-5; $CH_3(CH_2)_5SAl(i\text{-}Bu)_2$, 96503-34-3; $PaSAl(i\text{-}Bu)_2$, 96503-35-4; $CH_3(CH_2)_5NHAl(i\text{-}Bu)_2$, 96503-36-5; $(i\text{-}Bu)_2AlOCH_2CH_2NHAl(i\text{-}Bu)_2$, 96503-37-6; 1-hexanol, 111-27-3; benzyl alcohol, 100-51-6; 3-hexanol, 623-37-0; 3-ethyl-3-pentanol, 597-49-9; phenol, 108-95-2; 2,6-di-*tert*-butylphenol, 128-39-2; 1-hexanethiol, 111-31-9; benzenethiol, 108-98-5; *n*-hexylamine, 111-26-2; 2-aminoethanol, 141-43-5; *n*-hexanal, 66-25-1; benzaldehyde, 100-52-7; 2-heptanone, 110-43-0; norcamphor, 497-38-1; camphor, 1195-79-5; acetophenone, 98-86-2; benzophenone, 119-61-9; cinnamaldehyde, 104-55-2; methyl vinyl ketone, 78-94-4; isophorone, 78-59-1; 2-methylcyclohexanone, 583-60-8; 4-*tert*-butylcyclohexanone, 98-53-3; *p*-benzoquinone, 106-51-4; anthraquinone, 84-65-1; hexanoic acid, 142-62-1; benzoic acid, 65-85-0; crotonic acid, 3724-65-0; lithium benzoate, 553-54-8; acetic anhydride, 108-24-7; succinic anhydride, 108-30-5; phthalic anhydride, 85-44-9; hexanoyl chloride, 142-61-0; benzoyl chloride, 98-88-4; ethyl hexanoate, 123-66-0; ethyl benzoate, 93-89-0; ethyl crotonate, 10544-63-5; phenyl acetate, 122-79-2; γ-butyrolactone, 96-48-0; phthalide, 87-41-2; isopropenyl acetate, 108-22-5; *n*-octyl iodide, 629-27-6; *n*-octyl bromide, 111-83-1; *n*-octyl chloride, 111-85-3; *p*-bromotoluene, 106-38-7; 1,2-butylene oxide, 106-88-7; cyclohexene oxide, 286-20-4; styrene oxide, 96-09-3; 1-methyl-1,2-cyclohexene oxide, 1713-33-3; hexanamide, 628-02-4; benzamide, 55-21-0; *N,N*-dimethylhexanamide, 5830-30-8; *N,N*-dimethylbenzamide, 611-74-5; hexanenitrile, 628-73-9; benzonitrile, 100-47-0; acrylonitrile, 107-13-1; nitrobenzene, 98-95-3; nitropropane, 108-03-2; azobenzene, 103-33-3; azoxybenzene, 495-48-7; cyclohexanone oxime, 100-64-1; acetophenone oxime, 613-91-2; phenyl isocyanate, 103-71-9; pyridine, 110-86-1; pyridine *N*-oxide, 694-59-7; diphenyl disulfide, 882-33-7; methyl *p*-tolyl sulfide, 623-13-2; dimethyl sulfoxide, 67-68-5; diphenyl sulfone, 127-63-9; methanesulfonic acid, 75-75-2; *p*-toluenesulfonic acid, 104-15-4; *n*-octyl tosylate, 3386-35-4; cyclohexyl tosylate, 953-91-3; benzenemethanol, 100-51-6; 2-heptanol, 543-49-7; bicyclo[2.2.1]heptan-2-ol, 1632-68-4; 1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol, 10385-78-1; 1-phenylethanol, 98-85-1; diphenylcarbinol, 91-01-0; cinnamyl alcohol, 104-54-1; 3-hydroxy-1-butene, 598-32-3; 3,5,5-trimethyl-2-cyclohexen-1-ol, 470-99-5; *cis*-2-methylcyclohexanol, 7443-70-1; *trans*-2-methylcyclohexanol, 7443-52-9; *cis*-4-*tert*-butylcyclohexanol, 937-05-3; *trans*-4-*tert*-butylcyclohexanol, 21862-63-5; hydroquinone, 123-31-9; 1,4-dihydroxycyclohexadiene, 63453-92-9; 9,10-dihydro-9,10-anthracenediol, 58343-58-1; crotyl alcohol, 6117-91-5; ethanol, 64-17-5; 1,4-dihydroxybutene, 110-64-5; 1,2-benzenedimethanol, 612-14-6; 2,4-pentanediol, 625-69-4; 1,2-dihydroxybutane, 584-03-2; 1,2-dihydroxycyclohexane, 931-17-9; 2-phenylethanol, 60-12-8; 1-methylcyclohexanol, 590-67-0; 1-aminohexane, 111-26-2; benzylamine, 100-46-9; *N,N*-dimethylhexanamine, 4385-04-0; *N,N*-dimethylaniline, 121-69-7; acrylaldehyde, 107-02-8; *N*-hydroxyaniline, 100-65-2; *N*-hydroxy-1-propanamine, 627-38-3; hydrazobenzene, 122-66-7; *N*-hydroxycyclohexanamine, 2211-64-5; *N*-ethylaniline, 103-69-5; *N*-methylenebenzenamine, 100-62-9; 1,2-dihydropyridine, 22694-45-7; butyl mercaptan, 109-79-5; methyl mercaptan, 74-93-1; *p*-tolyl mercaptan, 106-45-6; dimethyl sulfide, 75-18-3; 1,4-dihydroxybutane, 110-63-4; octane, 111-65-9; cyclohexene, 110-83-8; hydrogen, 1333-74-0; di-*n*-butyl disulfide, 629-45-8; tetramethylene sulfoxide, 1600-44-8; tetramethylene sulfide, 110-01-0.

Synthesis of Pyrrolo[3,4-*d*]imidazoles. A New Fluorescent Heterocyclic System[1]

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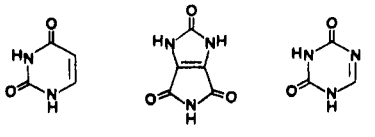
Pyrrolo[3,4-*d*]imidazoles (**9**), "stretched-up" pyrimidine analogues, have been prepared by a two-step procedure from the corresponding pyrrolo[3,4-*d*]imidazolines (**5**). The new heterocyclic system displays exceptional fluorescence properties. Large Stokes shifts are observed in both polar and nonpolar solvents, and the emission maxima are sensitive to solvent. *N*-Ribosyl derivatives have been prepared in both series (**12** and **13**). The planarity of the substituted pyrrolo[3,4-*d*]imidazole ring system has been established by X-ray crystallographic analysis.

Research in our laboratory has focused on the synthesis of fluorescent and dimensionally extended analogues of adenine, adenosine, and adenosine phosphates. The interactions of these analogues with selected enzyme systems have provided insights into the geometric and electronic requirements of enzyme binding sites.[2] We are now extending such studies to include analogues of pyrimidines. Our first goal is the synthesis of a heterocycle that maintains both the array of hydrogen bond donors and acceptors found in a pyrimidine such as uracil (**1**) and the planarity of the system. The first structure targeted, pyrroloimidazole **2**, incorporates these features (albeit on both sides of the molecule), but the sites of hydrogen bonding are set apart and are at slightly different angles. We have chosen the term "stretched-up" to describe this type of analogue. Obviously, the analogy is imperfect: heterocycle **2** contains extra nitrogen and carbonyl groups. Nevertheless, the symmetry of the compound presents the same type of hydrogen-bonding potentiality on each side. Closer analogy of **2** might be to the azapyrimidine 5-azauracil (**3**), which has been found to inhibit protein synthesis and to be incorporated as its riboside into RNAs,[3] or to cyanuric acid.



1 **2** **3**

The ring structure of two fused, copolanar five-membered rings may interfere with pyrimidine metabolic processes through similar or competitive enzyme binding based on spatial requirements. At the same time, the

(1) Casteel, D. A.; Leonard, N. J. "Abstracts of Papers", 188th National Meeting of the American Chemical Society, Philadelphia, PA, Aug 1984; American Chemical Society: Washington, DC, 1984; ORGN 119.

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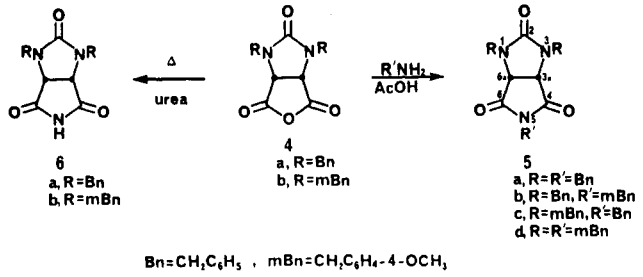
Scheme I



Bn=$CH_2C_6H_5$, mBn=$CH_2C_6H_4$-4-OCH_3

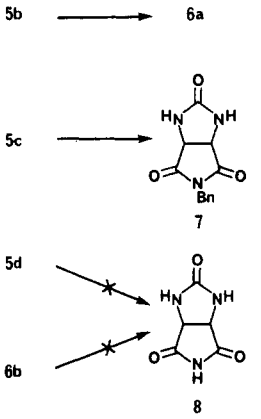
structure of the surrogate ring system is such that it would not be expected to be transformed metabolically like a pyrimidine.

Our interest in synthesis was stimulated by these biochemical motivations and by the rarity of such pyrrolo[3,4-*d*]imidazoles. Although a few compounds with this particular skeleton have been reported,[4] only more reduced examples have been studied in detail and no compounds have been reported as being fluorescent. Bimanes, which constitute another class of fluorescent 5,5-nitrogen heterocycles, have been extensively studied, however, and have found use as fluorescent labeling agents.[5]

Several clues in the literature implied that closure of the imide ring onto an imidazolone precursor might prove difficult.[6] Our synthetic strategy began, therefore, with a suitably functionalized imidazolinone, which was to be closed to the imide and then oxidized to the planar system. The intermediate **4**, used in Goldberg and Sternbach's synthesis of biotin,[7] can be prepared in four steps from fumaric acid. The stereochemistry at the methine carbons is cis, providing a meso compound. The anhydride can be converted into the protected imido compounds **5a–d** in up to 90% yield by heating with the appropriate amine in acetic acid (Scheme I).[8] Alternatively, the unprotected imido compounds **6a,b** are obtainable by urea fusion at 180–200 °C in 80–90% yields.[9]

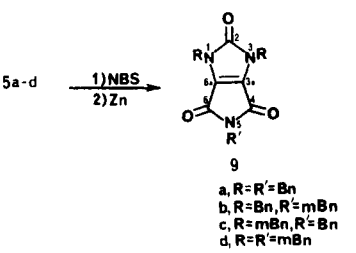
The combination of benzyl and 4-methoxybenzyl protective groups was planned to allow flexibility in deprotection. Mildly reductive conditions were ineffective in removing benzyl groups on the urea and imide functionalities. Since more drastic conditions would be unsuitable for the final, highly oxidized products, an alternative was sought. The 4-methoxybenzyl group has been reported to be selectively removable from nitrogen heterocycles in the presence of *N*-benzyl groups under oxidative conditions.[10] The suggested oxidant, ammonium cerium(IV) nitrate (CAN), was found to be less than completely satisfactory, however. The 4-methoxybenzyl group could indeed be removed selectively from either the imide (**5b** → **6a**) or the urea nitrogens (**5c** → **7**) with CAN in aqueous acetonitrile (Scheme II) within a few hours at room temperature. When either **5d** or **6b** was treated with CAN, the parent heterocycle **8** was not readily isolable even though *p*-anisaldehyde and *p*-anisic acid were formed. Careful addition of CAN to **5d** allowed the isolation of, first, the monodeprotected compound and then the dideprotected compound, both 4-methoxybenzyl groups being removed from the urea nitrogens. However, no heterocycle was recovered upon further treatment with CAN. The observation that ethyleneurea was unstable to CAN supports the supposition that compound 8 might also be unstable under the reaction conditions.

Scheme II. Deprotection with CAN



Other oxidants were examined for achieving the deprotection,[11] and while both PbO_2 and ammonium cerium(IV) sulfate (CAS)[12] effected the transformation of **5b** to **6a** in acidic solutions, treatment of **6b** with either reagent again failed to provide any compound 8.

Several methods were examined for the direct dehydrogenation of **5a**.[13] As examples, DDQ, MnO_2, NiO_2, and $Hg(OAc)_2$ under their usual reaction conditions produced, at best, fluorescent **9a** in only ~5% yield from complicated mixtures. The appearance of fluorescence was encouraging. Palladium on carbon with **5a** either in high-boiling solvents or as intimate mixtures at high temperatures produced only small quantities of fluorescent products. A two-step bromine substitution/debromination procedure for the dehydrogenation proved to be the most viable method in our hands. Reaction of **5a** with excess NBS in



CCl_4 in the dark at reflux for 1 h or less afforded (pre-

(4) (a) Sicher, J.; Rajsner, M.; Rudinger, J.; Eckstein, M.; Šorm, F. *Collect. Czech. Chem. Commun.* **1959**, *24*, 3719. (b) Wormser, H. C.; Abramson, H. N. *J. Pharm. Sci.* **1977**, *66*, 1208. (c) Wormser, H. C.; Abramson, H. N. *J. Pharm. Sci.* **1975**, *64*, 1882 and references cited therein. (d) Lown, J. W.; Landberg, B. E. *Can. J. Chem.* **1974**, *52*, 798. (e) Bowness, W. G.; Howe, R.; Rao, B. S. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2649. (f) von Dobeneck, H.; Weil, E.; Brunner, E. *Justus Liebigs Ann. Chem.* **1978**, 1424. (g) Aoki, Y.; Suzuki, H.; Akiyama, H.; Okano, S. Jpn. Kokai Tokkyo Koho JP 49/127994, 1974. (h) Aoki, Y.; Suzuki, H.; Akiyama, H.; Okano, S. Ger. Offen. 2331244 (Cl. C 07*d*), 1974.

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(6) Compounds such as imidazole-4,5-dicarboxylic anhydride or imidazole-4,5-dicarboximide are presently unknown even though imidazole-4,5-dicarboxylic acid is available.

(7) (a) Goldberg, M. W.; Sternbach, L. H. U.S. Pat. 2489232, 1949. (b) Goldberg, M. W.; Sternbach, L. H. U.S. Pat. 2489233, 1949.

(8) Bilyard, K. G.; Garratt, P. J.; Hunter, R.; Lete, E. *J. Org. Chem.* **1982**, *47*, 4731.

(9) Crockett, G. C.; Swanson, B. J.; Anderson, D. R.; Koch, T. H. *Synth. Commun.* **1981**, *11*, 447.

(10) Yoshimura, J.; Yamaura, M.; Suzuki, T.; Hashimoto, H. *Chem. Lett.* **1983**, 1001.

(11) DDQ, PCC, $Pd(OAc)_2$, SeO_2, NiO_2, and $KMnO_4$ were all found to be unsatisfactory for the conversion of **5b** to **6a**.

(12) Periasamy, M.; Bhatt, M. Y. *Synthesis* **1977**, 330.

(13) Fu, P. P.; Harvey, R. G. *Chem. Rev.* **1978**, *78*, 317.

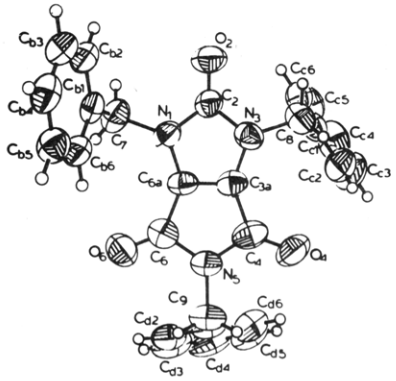

Figure 1. Perspective single ORTEP drawing of **9a** with non-hydrogen atoms represented by thermal vibration ellipsoids drawn to encompass 50% of their electron density; hydrogen atoms are represented by arbitrarily small spheres which are in no way representative of their true thermal motion.

sumably) a dibrominated derivative that was not isolated but that, after removal of succinimide, was treated immediately with zinc dust in refluxing CCl_4. Chromatography of the mixture gave **9a** in ≤30% yield along with unreacted **5a**. The exclusion of light in the first step was essential to minimize reaction at the benzylic positions, which resulted in formation of a large variety of side products.

The dehydrogenation methodology was then applied to **5b–d**. The corresponding products **9b–d** were produced in yields comparable to that of **9a** and were inherently fluorescent. The separation of the product from the starting material was much more difficult, however, in the case of the 4-methoxybenzyl-substituted derivatives. Even though **9a** and **5a** are cleanly separated by simple gravity chromatography over silica gel, the chromatographic mobilities of **9b–d** and **5b–d** are sufficiently similar to make column chromatography unsuitable for purification. Useful separations were achieved by repeated elutions of thick-layer plates in diethyl ether/petroleum ether mixtures.

Nuclear magnetic resonance spectroscopy was essential to the identification of the new fluorescent compounds. The urea benzyl protons in compounds **5a–d** showed distinctive diastereotopic doublets with J = 15 Hz. Dehydrogenation to give **9a–d** was accompanied by loss of this splitting as well as loss of the methine singlet in the ^{1}H NMR. A comparison of the ^{13}C NMR spectra of **5a** and **9a** was also helpful in confirming structures. In particular, the methine carbons of **5a**, resonating at δ 53.2 with respect to Me_4Si, were shifted downfield to δ 124.1 in **9a**. The imide carbonyl of the saturated compound appeared at δ 172.6, while in the unsaturated case the resonance was observed further upfield at δ 159.6.

An X-ray crystal structure determination of **9a** showed the heterocycle to be planar to within 0.02 Å (Figure 1). The central, conjugated double bond (C_{3a}–C_{6a}) is of standard length (1.33 Å)[14] (Table I), but the angles are compressed about those two carbons (Table II). The interior angles on the side of the imidazolone ring are 109°, while those on the side of the maleimide ring are 110–111°. The distance from C_2 to N_5 is 4.30 Å compared with 2.75 Å for C_4 to N_1 in pyrimidine[15a] and 2.74 Å in uracil[15b] and

Table I. Bond Lengths Involving Non-Hydrogen Atoms in Crystalline $C_{26}H_{21}N_3O_3$ (9a)[a]

type[b]	length, Å	type[b]	length, Å
O_2–C_2	1.195 (6)	N_1–C_2	1.408 (6)
O_4–C_4	1.232 (5)	N_1–C_{6a}	1.368 (6)
O_6–C_6	1.202 (6)	N_3–C_2	1.403 (5)
C_{3a}–C_4	1.458 (6)	N_3–C_{3a}	1.366 (6)
C_6–C_{6a}	1.457 (8)	N_5–C_4	1.402 (6)
N_1–C_7	1.479 (5)	N_5–C_6	1.421 (6)
N_3–C_8	1.490 (6)	C_{3a}–C_{6a}	1.330 (6)
N_5–C_9	1.459 (6)		

[a] The numbers in parentheses are the estimated standard deviations in the last significant digit. [b] Atoms are labeled in agreement with Figure 1. Bond lengths for the benzyl groups, which are not exceptional, are not included.

Table II. Bond Angles Involving Non-Hydrogen Atoms in Crystalline $C_{26}H_{21}N_3O_3$ (9a)[a]

type[b]	angle, deg	type[b]	angle, deg
$C_2N_1C_{6a}$	108.7 (3)	$N_3C_{3a}C_4$	140.7 (4)
$C_2N_1C_7$	122.9 (4)	$N_3C_{3a}C_{6a}$	109.2 (4)
$C_{6a}N_1C_7$	128.3 (4)	$C_4C_{3a}C_{6a}$	110.0 (4)
$C_2N_3C_{3a}$	108.8 (3)	$N_1C_{6a}C_6$	140.3 (4)
$C_2N_3C_8$	122.6 (4)	$N_1C_{6a}C_{3a}$	108.9 (4)
$C_{3a}N_3C_8$	127.9 (3)	$C_{3a}C_{6a}C_6$	110.9 (4)
$C_4N_5C_6$	112.6 (4)	$O_4C_4N_5$	127.0 (4)
$C_4N_5C_9$	121.8 (3)	$O_4C_4C_{3a}$	129.3 (4)
$C_6N_5C_9$	125.0 (4)	$N_5C_4C_{3a}$	103.7 (3)
$O_2C_2N_1$	127.3 (4)	$O_6C_6N_5$	124.3 (5)
$O_2C_2N_3$	128.3 (4)	$O_6C_6C_{6a}$	133.0 (4)
$N_1C_2N_3$	104.4 (4)	$N_5C_6C_{6a}$	102.7 (4)

[a] The numbers in parentheses are the estimated standard deviations in the last significant digit. [b] Atoms are labeled in agreement with Figure 1. Angles for the benzyl groups, which are not exceptional, are not included.

cyanuric acid.[15c,d] This geometry represents a formal upward "stretch" of 1.55 Å for the 5,5 double-ring analogues over the six-membered single-ring systems.

An examination of the electronic absorption and fluorescence spectra of **9a–d** reveals their exceptional properties (Table III). The absorption (or excitation) maxima and the emission maxima are widely separated in both polar and nonpolar solvents. In ethanol, a loss of energy through reorganization of the solvent shell about a dipolar excited state can be invoked to account for part of this nearly 200-nm difference (Stokes shift). Hexane would not be expected to provide such stabilization; accordingly, the 130-nm shift, still very large, observed in hexane solutions must be attributed to other factors, including possible change of geometry in the excited state. The emission maxima are solvent sensitive as well, more so than the absorption maxima, and may provide the basis for spectral probing of the polar nature of binding sites.[17] The wavelengths of emission lie in a region of the spectrum that is free from interference in biological systems, making this proposition more feasible. In spite of small molar absorptivities, the quantum yields, on the order of 0.2, are large enough to be useful. The electronic spectra were checked carefully in the long-wavelength region to discount the existence of any weak absorbance higher than the wavelength figures cited (Table III).

Compounds **9a–d** are unstable to nucleophiles and bases. Prolonged contact with alcohols results in ring opening of

(14) "Handbook of Chemistry and Physics", 57th ed.; Chemical Rubber Co.: Cleveland, OH, 1976; p F215.

(15) (a) Wheatley, P. J. *Acta Crystallogr.* **1960**, *13*, 80. (b) Parry, G. S. *Acta Crystallogr.* **1954**, *7*, 313. (c) Verschoor, G. C.; Keulen, E. *Acta Crystallogr., Sect. B* **1971**, *B27*, 134. (d) Coppens, P.; Vos, A. *Acta Crystallogr., Sect. B* **1971**, *B27*, 146.

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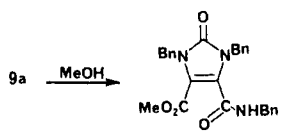
Table III. Electronic Absorption and Fluorescence

	long-wavelength absorption λ_{max} (ϵ)						
	95% EtOH	0.1 N HCl/ 95% EtOH	5% $CHCl_3$/ hexane	excitation λ_{max} hexane[b]	emission λ_{max} 95% EtOH	emission λ_{max} hexane[b]	Φ[a] hexane[c]
9a	395 (800)	395 (765)	406 (1390)	410	590	532	0.21
9b	400 (1005)	400 (1050)	408 (1310)	410	594	538.5	0.16
9c	401 (1225)	401 (1095)	408 (1500)	410.5	595.5	539	0.20
9d	402 (975)	402 (1135)	410 (1565)	410.5	599	539.5	0.17

[a] Determined relative to acridine yellow in EtOH, $\Phi = 0.47$.[16] [b] 3–10 μL of EtOH stock solutions added to 3 mL of hexane. [c] 5% $CHCl_3$ in hexane stock solutions diluted to at least 1:100 with hexane.

the imide to produce, for example, ester amide **10** almost quantitatively from **9a**. In ethanolic base, the reaction



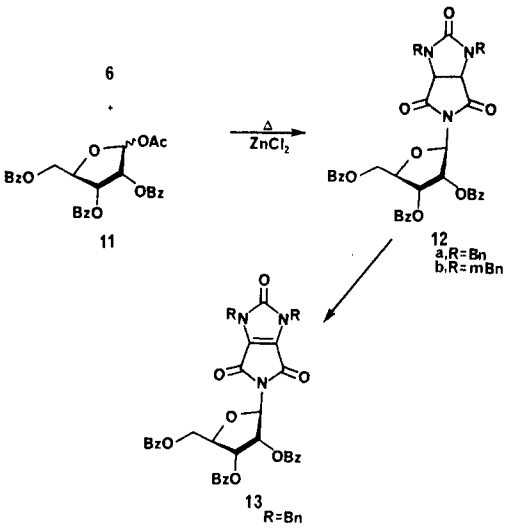
10

proceeds more rapidly, destroying the fluorescence irreversibily. The ring system is also very sensitive to the oxidative conditions of CAN, CAS, and PbO_2. When **9b** was treated with CAN in aqueous acetonitrile, the fluorescence was eliminated rapidly. The same results were observed with **9b** and CAS or PbO_2 in acidic solution and with **9a** (no 4-methoxybenzyl groups) and CAN. Chromatographic analysis (TLC) showed the absence of any mobile compounds from these reactions. CAN has been reported to interact with double bonds to give nitrate addition products[10] as well as carbon skeleton cleavage products.[18]

Cyclic voltammetry was used to examine the oxidative stability of the fluorescent system. Compound **5a** showed an irreversible oxidation wave at +1.95 V vs. SCE attributable to oxidation of the benzyl groups.[19] In contrast, the 4-methoxybenzyl group on **5b** was oxidized irreversibly at +1.66 V, demonstrating quantitatively the potential for selective removal of 4-methoxybenzyl groups in the presence of benzyl groups.[19] Compound **9a** was characterized by an irreversible oxidation wave at +1.49 V, however, much lower than that needed to oxidize either type of benzyl group. Therefore, the sensitivity of the planar heterocycles such as **9a** to chemical oxidants can be explained simply by the relatively low oxidation potential of the system. The first electron is lost from the heterocycle rather than from the benzyl or 4-methoxybenzyl protective groups.

The preparation of *N*-ribosyl derivatives of the "stretched-up" analogues was a major goal of this work. We have been able to find precedent only for the synthesis of *N*-ribosylmaleimides and -succinimides.[20] The Vorbrüggen procedure for ribosidation,[21] which was used to prepare *N*-ribosylmaleimide,[20] was unsuccessful in our systems. Recourse was then made to the fusion methodology of Shimadate.[22] Heating of **6a** with ribose derivative **11** in the presence of a Lewis acid catalyst ($ZnCl_2$) provided the substituted *N*-ribosyl derivative **12a** (Scheme III). This approach has many advantages over other possible ribosidation methods: the use of 1-*O*-acetyl sugars rather than the very sensitive 1-halo sugars, the use of the free heterocycle, and the lack of necessity for rigorously anhydrous solvents and reaction conditions. Compound **12a**, 1,3-dibenzyl-5-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline, was characterized by its FAB mass spectrum, in which the $(M + 1)^+$ peak at m/z 780 is prominent and both the heterocycle and sugar portions are observed as fragmentation peaks, m/z 334 and 445, respectively. The 200-MHz ^1H NMR spectrum shows characteristic sugar and heterocyclic resonances. The resonances attributable to the ribose protons displayed complicated coupling patterns, and the assignment of the anomeric proton was initially not clear. Anomeric protons (1′-H) generally appear downfield from the other sugar resonances (2′-, 3′-, 4′-, and 5′-H). In the case of **12a**, however, the sugar resonance farthest downfield (δ 6.0–6.11) was a multiplet integrating for two protons. What appeared to be the anomeric proton was observed slightly upfield from that (δ 5.9) as a simple doublet $J = 2$ Hz. Analysis of the coupling by 2-D FT NMR experiments allowed the assignment of the downfield multiplet as the overlapping 2′ and 3′ protons and the cited doublet as the anomeric (1′) proton. The β-configuration was confirmed on the basis of the low magnitude of the anomeric coupling constant (2 Hz)[23] and from analogy to that seen for the other *N*-ribosyl imides.[20b] Unfortunately, no comparison of the positions of the 2′- and 3′-protons in **12a** was possible since they were not

Scheme III



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reported for other *N*-ribosyl imides. The ribosidation procedure was also carried out with **6b**, yielding the substituted *N*-ribosyl derivative **12b**, 5-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,3-bis(4-methoxybenzyl)-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline, which was isolated and characterized as above.

The fluorescent, planar **13**, 1,3-dibenzyl-5-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-2,4,6-trioxopyrrolo[3,4-*d*]-imidazole, was prepared from **12a** according to the methodology developed for the simple heterocycles (**5** → **9**). The product was difficult to purify because the chromatographic mobilities of **12a** and **13** are nearly identical. *N*-Ribosyl derivative **13** was identified by its high-resolution FAB-MS and by its characteristic fluorescence. The deprotection of the ribose moiety in the presence of the base-sensitive aglycone remains a challenge in this work and suggests the alternative of protection with acid-removable groups.[20]

In conclusion, we have synthesized a new heterocyclic system and have recorded some of its unique physical properties, especially its fluorescence. We have also prepared the *N*-ribosyl derivatives, "stretched-up" analogues of substituted uridines, as a prelude to the study, by fluorescence spectroscopy, of biological interactions (either activity or inhibition) and binding.

Experimental Section

Analytical thin-layer chromatography was performed on plastic-backed Brinkmann silica gel plates (0.25 mm, with fluorescent indicator). Preparative TLC was performed on glass-backed Brinkmann silica gel plates (2.0 mm, with fluorescent indicator). Petroleum ether was the low-boiling (35–60 °C) fraction. Melting points were determined on a Thomas-Hoover Unimelt apparatus and are uncorrected. ^{1}H NMR spectra of the simple heterocycles were recorded on a Varian EM-390 (90 MHz) spectrometer. ^{1}H NMR spectra of the ribosides, 2-D NMR, and ^{13}C NMR were recorded on a Varian XL-200 spectrometer. Tetramethylsilane was used as an internal standard. Electron impact mass spectra were obtained on a Varian MAT CH-5 low-resolution instrument coupled with a 620i computer and STATOS recorder. Fast atom bombardment mass spectra were obtained on either a Varian 311A or a ZAB-HF spectrometer, and the field desorption spectra on a Varian 731 spectrometer. Absorption spectra were obtained on a Beckman Acta MVI or a Hewlett-Packard 8451A spectrophotometer. Fluorescence excitation and emission spectra were obtained on a Spex Datamate spectrophotometer. Cyclic voltammetry was performed on a cybernetic potentiostat built at the University of Illinois by Peixin He and recorded on a Houston Instruments digital plotter. Microanalyses were performed by Josef Nemeth and his staff at the University of Illinois. The crystal structure was solved by Dr. Cynthia Day at Crystalytics Co. in Lincoln, NB.

1,3,5-Triaralkyl-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline (5). The appropriate anhydride **4** (2.2 g) was stirred overnight at room temperature in 40 mL of glacial AcOH containing 1.2 equiv of the desired benzylamine. The heterogeneous mixture was brought to reflux for 1 h and then cooled and poured onto 400 mL of ice. The precipitate was collected and washed with H_2O. An ether solution of the solid was extracted with 2 × 50 mL of saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated on a steam bath. The colorless needles were collected by filtration. Concentration of the filtrate and/or addition of petroleum ether afforded additional product.

1,3,5-Tribenzyl-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline (5a):[24] 2.5 g (90%) in four crops; mp 125–126.5 °C; ^{1}H NMR ($CDCl_3$) δ 3.95 (s, 2, CH), 4.23 (d, 2, *J* = 15 Hz, urea Bn CH_2), 4.62 (s, 2, imide Bn CH_2), 5.01 (d, 2, *J* = 15 Hz, urea Bn CH_2), 7.28 (s, 5, aromatic), 7.33 (s, 10, aromatic); ^{13}C NMR ($CDCl_3$) δ 42.6, 46.3 (Bn), 53.2 (methine), 127.9, 128.3, 128.8, 134.6, 135.6 (aromatic), 157.4 (urea carbonyl), 172.6 (imide carbonyl). Anal. Calcd for $C_{26}H_{23}N_3O_3$: C, 73.39; H, 5.45; N, 9.88. Found: C, 73.19; H, 5.46; N, 9.64.

1,3-Dibenzyl-5-(4-methoxybenzyl)-2,4,6-trioxopyrrolo-[3,4-*d*]imidazoline (5b): 2.4 g (81%) in three crops; mp 122–123 °C; ^{1}H NMR ($CDCl_3$) δ 3.76 (s, 3, OCH_3), 3.94 (s, 2, CH), 4.21 (d, 2, *J* = 15 Hz, urea Bn CH_2), 4.57 (s, 2, imide mBn CH_2), 5.06 (d, 2, *J* = 15 Hz, urea Bn CH_2), 6.79 (d, 2, *J* = 9 Hz, substituted aromatic), 7.25 (d, 2, *J* = 9 Hz, substituted aromatic), 7.35 (s, 10, aromatic). Anal. Calcd for $C_{27}H_{25}N_3O_4$: C, 71.19; H, 5.53; N, 9.23. Found: C, 71.31; H, 5.55; N, 9.19.

1,3-Bis(4-methoxybenzyl)-5-benzyl-2,4,6-trioxopyrrolo-[3,4-*d*]imidazoline (5c): 0.60 g (82%) from 0.60 g of **4b** in two crops; mp 122–123.5 °C; ^{1}H NMR ($CDCl_3$) δ 3.79 (s, 6, OCH_3), 3.92 (s, 2, CH), 4.15 (d, 2, *J* = 15 Hz, urea mBn CH_2), 4.60 (s, 2, imide Bn CH_2), 4.96 (d, 2, *J* = 15 Hz, urea mBn CH_2), 6.78 (d, 4, *J* = 9 Hz, substituted aromatic), 7.24 (d, 4, *J* = 9 Hz, substituted aromatic), 7.30 (s, 5, aromatic). Anal. Calcd for $C_{28}H_{27}N_3O_5$: C, 69.26; H, 5.61; N, 8.86. Found: C, 69.56; H, 5.59; N, 8.64.

1,3,5-Tris(4-methoxybenzyl)-2,4,6-trioxopyrrolo[3,4-*d*]-imidazoline (5d): 2.22 g (77%) in three crops; mp 128–129.5 °C; ^{1}H NMR ($CDCl_3$) δ 3.77 (s, 9, OCH_3), 3.96 (s, 2, CH), 4.12 (d, 2, *J* = 15 Hz, urea mBn CH_2), 4.53 (s, 2, imide mBn CH_2), 4.94 (d, 2, *J* = 15 Hz, urea mBn CH_2), 6.70–6.90 (m, 6, substituted aromatic), 7.18–7.32 (m, 6, substituted aromatic). Anal. Calcd for $C_{29}H_{29}N_3O_6$: C, 67.56; H, 5.67; N, 8.15. Found: C, 67.62; H, 5.79; N, 8.04.

1,3-Diaralkyl-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline (6). The appropriate anhydride **4** was intimately mixed with 1.1 equiv of urea. The fine powder was heated in an oil bath at 175–200 °C until foaming ceased. Upon cooling, the glass was dissolved in hot $CHCl_3$, filtered, and allowed to cool. The colorless crystals were collected by filtration. Additional material could be obtained by concentration of the filtrate.

1,3-Dibenzyl-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline (6a): 3.62 g of **4a** produced 3.39 g (90%) in two crops; mp 220–221 °C; ^{1}H NMR ($CDCl_3$) δ 3.95 (s, 2, CH), 4.20 (d, 2, *J* = 15 Hz, Bn CH_2), 5.04 (d, 2, *J* = 15 Hz, Bn CH_2), 7.32 (s, 10, aromatic). Anal. Calcd for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 68.32; H, 5.19; N, 12.79.

1,3-Bis(4-methoxybenzyl)-2,4,6-trioxopyrrolo[3,4-*d*]-imidazoline (6b): 0.72 g of **4b** produced 0.59 g (82%) in two crops; mp 203–205 °C; ^{1}H NMR ($CDCl_3$) δ 3.80 (s, 6, OCH_3), 3.95 (s, 2, CH), 4.13 (d, 2, *J* = 15 Hz, mBn CH_2), 4.99 (d, 2, *J* = 15 Hz, mBn CH_2), 6.83, 7.25 (two d, 8, *J* = 9 Hz, aromatic). Anal. Calcd for $C_{21}H_{21}N_3O_5$: C, 63.79; H, 5.35; N, 10.63. Found: C, 63.62; H, 5.43; N, 10.73.

1,3-Dibenzyl-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline (6a) from 5b. Compound **5b** (100 mg) was stirred at room temperature in 7 mL of CAN solution (0.33 M in H_2O/CH_3CN, 1:3 v/v) for 5 h. The reaction mixture was extracted with $CHCl_3$ (4 × 2.5 mL). The organic layer was dried (Na_2SO_4), filtered, and evaporated in vacuo. The residue was applied to a thick-layer plate and developed with 2% MeOH in $CHCl_3$. The product band (R_f 0.1–0.2) was eluted to yield 45 mg (61%) of **6a**, which was identical in all respects with the material prepared from **4a**.

5-Benzyl-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline (7). Compound **5c** (100 mg) was stirred at room temperature for 4 h in 7 mL of CAN solution (0.33 M in H_2O/CH_3CN, 1:3 v/v). The solution was then extracted with $CHCl_3$ (4 × 2.5 mL). The organic layer was dried (Na_2SO_4), filtered, and evaporated in vacuo. The residue was triturated in Et_2O, filtered, and washed well with Et_2O to give 40 mg (80%) of a tan solid. The solid could be recrystallized from MeOH to provide pure product: mp 265–267 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 4.47 (s, 2, methine), 4.56 (s, 2, Bn CH_2), 7.23 (s, 5, aromatic), 7.44 (s, 2, NH); MS (10 eV), *m/z* (relative intensity) 245 (M^+, 66), 202 (47), 91 (Bn^+, 40), 84 (100). Anal. Calcd for $C_{12}H_{11}N_3O_3$: C, 58.77; H, 4.52; N, 17.14. Found: C, 58.56; H, 4.23; N, 16.99.

1,3,5-Triaralkyl-2,4,6-trioxopyrrolo[3,4-*d*]imidazole (9). Compound **5** (100 mg) was brought to reflux in 60 mL of CCl_4 containing 300 mg of NBS for 1 h in the dark. The solution was cooled in ice and filtered, 0.21 g of Zn dust was added, and the

(24) Compound **5a** has been previously reported: Mikhno, S. D.; Kulachkina, N. S.; Berezovskii, V. M. *Zh. Org. Khim.* **1970**, *6*, 81. Their described preparation by the reaction of **4a** with benzylamine in refluxing xylenes for 30 min provided a very high melting material (mp 247–248 °C) which was characterized only by elemental analysis. We are currently exploring this discrepancy.

reaction was heated at reflux overnight in the dark. After filtration through Celite and evaporation, the residue was chromatographed by preparative TLC in benzene (**9a**) or ether/petroleum ether (1:1, v/v) (3× for **9b–d**). The fast-running, yellow, fluorescent band was collected, eluted with $CHCl_3$ or ether, and evaporated. The residue was carefully crystallized from CH_3OH or ether/petroleum ether. Unreacted starting material could be recovered by collecting the band running just slower than product.

1,3,5-Tribenzyl-2,4,6-trioxopyrrolo[3,4-*d*]imidazole (9a): 32 mg; mp 113.5–115 °C; ^1H NMR (CCl_4) δ 4.47 (s, 2, imide Bn CH_2), 4.81 (s, 4, urea Bn CH_2), 7.05–7.60 (m, 15, aromatic); ^{13}C NMR ($CDCl_3$) δ 41.5, 47.0 (Bn), 124.1 (ring junction), 127.9, 128.5, 128.7, 128.8, 128.9, 135.8, 136.6 (aromatic), 155.0 (urea carbonyl), 159.6 (imide carbonyl); MS (10 eV), *m/z* (relative intensity) 423 (M^+, 57), 424 ($(M + 1)^+$, 16), 425 ($(M + 2)^+$, 3), 91 (Bn^+, 100). Anal. Calcd for $C_{26}H_{21}N_3O_3$: C, 73.74; H, 5.00; N, 9.92. Found: C, 73.64; H, 4.95; N, 9.76.

1,3-Dibenzyl-5-(4-methoxybenzyl)-2,4,6-trioxopyrrolo[3,4-*d*]imidazole (9b): 39 mg; mp 111–112 °C; ^1H NMR ($CDCl_3$) δ 3.76 (s, 3, OCH_3), 4.50 (s, 2, imide mBn CH_2), 4.93 (s, 4, urea Bn CH_2), 6.70–6.87, 7.13–7.54 (m, 14, aromatic); MS (10 eV), *m/z* (relative intensity) 453 (M^+, 15), 454 ($(M + 1)^+$, 5), 455 ($(M + 2)^+$, 1), 121 (mBn^+, 33), 91 (Bn^+, 100). Anal. Calcd for $C_{27}H_{23}N_3O_4$: C, 71.51; H, 5.11; N, 9.27. Found: C, 71.13; H, 5.47; N, 9.20.

1,3-Bis(4-methoxybenzyl)-5-benzyl-2,4,6-trioxopyrrolo[3,4-*d*]imidazole (9c): 109 mg from 500 mg of **5c** (200 mg recovered); mp 115–116 °C; ^1H NMR (CCl_4) δ 3.69 (s, 6, OCH_3), 4.45 (s, 2, imide Bn CH_2), 4.73 (s, 4, urea mBn CH_2), 6.64–6.81, 7.05–7.46 (m, 13, aromatic); MS (10 eV), *m/z* (relative intensity) 483 (M^+, 16), 484 ($(M + 1)^+$, 6), 485 ($(M + 2)^+$, 1), 121 (mBn^+, 100). Anal. Calcd for $C_{28}H_{25}N_3O_5$: C, 69.55; H, 5.21; N, 8.69. Found: C, 69.37; H, 5.12; N, 8.62.

1,3,5-Tris(4-methoxybenzyl)-2,4,6-trioxopyrrolo[3,4-*d*]imidazole (9d): 22 mg; mp 122.5–123 °C; ^1H NMR (CCl_4) δ 3.71 (s, 9, OCH_3), 4.40 (s, 2, imide mBn CH_2), 4.74 (s, 4, urea mBn CH_2), 6.60–6.73, 7.06–7.42 (m, 12, aromatic); MS (10 eV), *m/z* (relative intensity) 513 (M^+, 10), 514 ($(M + 1)^+$, 4), 515 ($(M + 2)^+$, 0.6), 121 (mBn^+, 100). Anal. Calcd for $C_{29}H_{27}N_3O_6$: C, 67.82; H, 5.30; N, 8.18. Found: C, 67.56; H, 5.29; N, 8.09.

X-ray Structural Determination of 9a. Yellow crystals of **9a** were grown from methanol. A crystal of approximate dimensions 0.2 × 0.3 × 0.8 mm was selected for analysis. It displayed monoclinic symmetry, space group $P2_1/c$-C_{2h}^5 (No. 14), with a = 9.881 (3) Å, b = 26.537 (7) Å, c = 9.048 (4) Å, β = 110.54 (2)°, V = 2222 (1) Å^3, and d_{calcd} = 1.27 g cm^{-3} for Z = 4 ($C_{26}H_{21}N_3O_3$, M_n = 423.5). The intensity data were collected on a computer-controlled four-circle Nicolet autodiffractometer using the ω-scan technique and graphite-monochromated Mo K_α radiation (λ = 0.71073 Å). Of the 3048 independent reflections collected, 1481 had $I \geq 3\sigma(I)$ and were utilized in the determination after corrections for Lorenz and polarization effects. The 32 non-hydrogen atoms were located by using the SHELXTL direct methods programs. The 21 hydrogen atoms were included in the structure factor calculations as idealized atoms (assuming sp^3 or sp^2 hybridization of the carbon atom and a C–H bond length of 0.96 Å) "riding" on their respective carbon atoms. The isotropic thermal parameter of each hydrogen atom was fixed at 1.2 times the equivalent isotropic thermal parameter of the carbon atom to which it is covalently bonded. The final discrepancy indices are R = 0.049, R_w = 0.043, and "goodness-of-fit" = 1.74. There were no peaks present in the final difference Fourier above the noise level (0.19 e$^-$/Å^3). For bond lengths and bond angles, see Tables I and II. Atomic coordinates, anisotropic thermal parameters, and torsion angles are presented as supplementary material.

Fluorescence Studies. Quantitative solutions in EtOH were prepared in anhydrous EtOH and diluted to 95% with either distilled H_2O or 2 N HCl. Concentrations of stock solutions in EtOH were considered valid only on the day of preparation. Quantitative stock solutions in hexane were prepared by dissolution in $CHCl_3$ (Mallinckrodt, SpectrAR, 5% total volume) to ensure solubility and were then diluted with hexane (J. T. Baker, Photrex). Further dilutions were made with hexane. The appropriate blanks were run to show that the residual $CHCl_3$ did not affect the data. The excitation/emission program was written by Dr. R. D. Bindal, University of Illinois. No long-wavelength absorptions (ϵ >10) were observed to 800 nm. The absorption spectrum of a concentrated sample is unchanged by exposure to the fluorometer excitation beam. Acridine yellow in ethanol was used as the Φ standard with Φ = 0.47;[16] quantum yields for acridine yellow in ethanol and our analogues in hexane were determined at λ_{ex} = 425 nm.

Cyclic Voltammetry. Voltammegrams were obtained with a three-electrode cell and 0.1 M $LiClO_4$ in CH_3CN as the electrolyte. A BAS glassy carbon disk electrode was the working electrode, a platinum wire was the counter electrode, and a saturated calomel electrode was the reference electrode. Solutions for analysis were made up to ~2 mM in **5a**, **5b**, or **9a**. Potentials were scanned from 0 to +2.0 V for **5b** and **9a** and 0 to 2.5 V for **5a** at 100 mV/s. Oxidation waves for all three compounds were irreversible.

Methyl 4-(*N*-Benzylcarbamoyl)-1,3-dibenzyl-2-oxoimidazole-5-carboxylate (10). Compound **9a** was heated in MeOH as for recrystallization. The originally yellow solution became colorless and, upon cooling, silky crystals formed, which were collected by filtration. Alternatively, a methanolic solution of **9a**, after standing at 25 °C for 1 week, deposited colorless crystals: mp 174–176 °C; ^1H NMR ($CDCl_3$) δ 3.53 (s, 3, OCH_3), 4.33, 4.39 (2 s, 2 total, amide Bn CH_2, syn and anti), 5.12, 5.22 (two s, 4 total, urea Bn CH_2), 7.22 (s, 15, aromatic); MS (10 eV), *m/z* (relative intensity) 455 (M^+, 74), 106 (83), 91 (Bn^+, 100).

1,3-Dibenzyl-5-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline (12a). Crystalline **6a** (1.0 g) was intimately mixed with 1.5 g of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**11**), and the powder was placed in a round-bottomed flask with ~10 mg of anhydrous $ZnCl_2$. The solid mixture was heated at 145–160 °C in vacuo (rotary evaporator, water aspirator) for 2 h. After cooling, the black residue was dissolved in $CHCl_3$ and chromatographed over silica gel with $CHCl_3$. The fraction with R_f 0.16 (TLC in $CHCl_3$) was collected to give a crude yield of 0.49 g of riboside **12a**. Further elution of the column yielded unreacted **6a**, 0.64 g. Riboside **12a** could be purified further by preparative TLC in $CHCl_3$ and then by crystallization from CH_2Cl_2/Et_2O/petroleum ether: mp 181–183 °C; ^1H NMR ($CDCl_3$) δ 4.04 (s, 2, methine), 4.16 (d, 1, J = 15 Hz, Bn CH_2), 4.27 (d, 1, J = 15 Hz, Bn CH_2), 4.52–4.84 (m, 3, 4′-H and 5′-H), 5.04 (d, 1, J = 15 Hz, Bn CH_2), 5.11 (d, 1, J = 15 Hz, Bn CH_2), 5.88 (d, 1, J = 2 Hz, 1′-H), 6.01–6.11 (m, 2, 2′-H and 3′-H), 7.25–7.60 (m, 19, C_6H_5, meta and para Bz H's), 8.11, 7.98, 7.87 (three d, 6, J = 8 Hz, ortho Bz H's); MS (FAB), *m/z* (relative intensity) 780 ($(M + 1)^+$, 15.4), 445 ($Rib(OBz)_3^+$, 34.1), 334 (het^+, 9.7); HRMS (FAB), exact mass observed 780.2560 ($C_{45}H_{38}N_3O_{10}$ ($M + 1^+$), 780.2563). This compound has no fluorescence emission in $CHCl_3$/hexane solution when irradiated at 408 nm. Anal. Calcd for $C_{45}H_{37}N_3O_{10}$: C, 69.31; H, 4.78; N, 5.39. Found: C, 69.16; H, 4.92; N, 5.34.

1,3-Bis(4-methoxybenzyl)-5-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-2,4,6-trioxopyrrolo[3,4-*d*]imidazoline (12b). Compound **12b** was prepared in the same manner as **12a** by using 0.30 g of **6b** and 0.75 g of **11**. A total of 126 mg of **12b** was obtained after chromatography; recrystallization from CH_2Cl_2/Et_2O/petroleum ether: mp 138–140 °C; ^1H NMR ($CDCl_3$) δ 3.80 (s, 6, CH_3O), 4.01 (s, 2, methine), 4.06 (d, 1, J = 15 Hz, mBn CH_2), 4.17 (d, 1, J = 15 Hz, mBn CH_2), 4.52–4.86 (m, 3, 4′-H and 5′-H), 4.97 (d, 1, J = 15 Hz, mBn CH_2), 5.04 (d, 1, J = 15 Hz, mBn CH_2), 5.82 (d, 1, J = 2 Hz, 1′-H), 6.01–6.14 (m, 2, 2′-H and 3′-H), 6.87 (d, 4, meta mBn H's), 7.26–7.57 (m, 13, ortho mBn, meta and para Bn H's), 7.88, 7.98, 8.12 (three d, 6, J = 8 Hz, ortho Bn H's); FDMS (13 mA), *m/z* 839, 840 (M^+, ($M + 1$)$^+$). Anal. Calcd for $C_{47}H_{41}N_3O_{12}$: C, 67.22; H, 4.92; N, 5.00. Found: C, 67.01; H, 5.03; N, 4.85.

1,3-Dibenzyl-5-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-2,4,6-trioxopyrrolo[3,4-*d*]imidazole (13). Crystalline riboside **12a** (0.10 g) was heated at reflux in 60 mL of CCl_4 containing 0.30 g of NBS for 45 min in the dark under N_2. After cooling, the solution was filtered, ~0.2 g of Zn dust was added, and the reaction was refluxed overnight in the dark under N_2. The reaction was again cooled, filtered through Celite, and concentrated in vacuo. The fluorescent residue was chromatographed on a preparative TLC plate in $CHCl_3$ three times. The fluorescent band was cut, eluted, and rechromatographed as above. Product band yielded 26 mg which contained **13** by MS: MS (FAB), *m/z*

(relative intensity) 779 (**12a** M^+, 5), 777 (**13** M^+, 2.5); HRMS (FAB), exact mass observed 778.2408 ($C_{45}H_{36}N_3O_{10}$ $(M + 1)^+$, 778.2415). A mixed sample containing **12a** and **13** in $CHCl_3$/hexane solution displays a fluorescence emission maximum at 495 nm with an excitation maximum at 399.5 nm.[25]

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Registry No. **4a**, 26339-42-4; **4b**, 96666-59-0; **5a**, 26511-17-1; **5b**, 96666-45-4; **5c**, 96666-46-5; **5d**, 96666-47-6; **6a**, 96666-48-7; **6b**, 96666-49-8; **7**, 96666-50-1; **9a**, 96666-51-2; **9b**, 96666-52-3; **9c**, 96666-53-4; **9d**, 96666-54-5; **10**, 96666-55-6; **11**, 14215-97-5; **12a**, 96666-56-7; **12b**, 96666-57-8; **13**, 96666-58-9; $NH_2CH_2C_6H_5$, 100-46-9; $NH_2CH_2C_6H_4$-4-OCH_3, 2393-23-9.

Supplementary Material Available: Tables of atomic coordinates, anisotropic thermal parameters, and torsion angles from X-ray structure determination of **9a** (10 pages). Ordering information is given on any current masthead page.

(25) Since **12a** and **13** proved to be difficult to separate, methods for the preparation of **13** by another route are being explored, one that would not require such a separation in the final step.

Synthesis of Imidazo[4,5-*h*]-1,3-diazabiphenylene (*lin*-Benzocyclobutadienopurine), a Ring System Having a Benzocyclobutadieno Spacer between the Terminal Rings of Purine[1]

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Two distinct syntheses of the pyrimido[6,5-*i*]imidazo[4,5-*g*]cinnoline ring system have been accomplished. The first of these began with 2-acetamido-4-chloro-5-nitroacetophenone, which was elaborated sequentially by fusion of the imidazole, pyridazine, and pyrimidine rings to provide the tetracyclic system. The second synthesis made use of a Pd-catalyzed cross-coupling reaction of (4,6-dimethoxypyrimidin-5-yl)zinc chloride and 3,4-dinitrobromobenzene, followed by closure of the imidazole and pyridazine rings. The flash vacuum pyrolysis (810–860 °C, 10^{-3} torr) of the unsubstituted tetracyclic compound, pyrimido[4,5-*i*]imidazo[4,5-*g*]cinnoline, resulted in the extrusion of nitrogen to provide imidazo[4,5-*h*]-1,3-diazabiphenylene (*lin*-bcb-purine), the parent molecule to a new class of linearly extended purine analogues.

Recent work in this laboratory has suggested that the dimensional probe *lin*-naphthoadenine (Figure 1), widened by 4.8 Å with respect to adenine, exceeds the space limitations of the active site in calf adenosine deaminase.[2] The related *lin*-naphthohypoxanthine, which is only monooxidized in the buttermilk xanthine oxidase system, exceeds the limits for the usual second stage oxidation (of hypoxanthine).[3] By contrast, *lin*-benzoadenine (Figure 1) and *lin*-benzoadenosine, in which the lateral extension with respect to adenine is 2.4 Å, are readily accepted within the active site of adenosine deaminase. Moreover, *lin*-benzohypoxanthine and *lin*-benzoinosine are oxidized in both terminal rings in the xanthine oxidase system.[4] To define more precisely the spatial restrictions on the activity of these enzymes it remains a desirable goal to prepare a dimensional probe having a lateral extension intermediate between 2.4 Å and 4.8 Å. For this purpose, derivatives of *lin*-benzocyclobutadienopurine (*lin*-bcb-purine) (**2**)[1] such as *lin*-bcb-adenine (Figure 1), in which the benzocyclobutadieno spacer separates the terminal rings by 3.9 Å, were chosen. In this paper, we report two independent syntheses of the pyrimido[6,5-*i*]imidazo[4,5-*g*]cinnoline ring system (e.g., **3**) and the gas-phase thermolysis of the unsubstituted parent to produce *lin*-bcb-purine (**2**).

Results and Discussion

Previous experience has shown[5] that the synthesis of **2** by elaboration of a 1,3-diazabiphenylene such as **1** (Figure 2, path a) may be complicated by facile rearrangement of this ring system to an isoquinoline upon attempted electrophilic or nucleophilic substitution. Accordingly, we decided to follow path b, which utilizes a thermal, gas-phase nitrogen-extrusion reaction of a fused pyridazine precursor **3** in the ultimate step.

Two distinct synthetic strategies leading to the requisite pyridazine precursors were employed, one utilizing a sequential ring-elaboration approach, and the other, a ring-coupling, ring-elaboration approach. The first of these, diagrammed in Scheme I, began with the substituted acetophenone **4**, prepared by an improvement[6] of the lit-

(1) *lin*-bcb-Purine (*lin*-benzocyclobutadienopurine) is the trivial name we are suggesting for the imidazo[4,5-*h*]-1,3-diazabiphenylene ring system having a benzocyclobutadiene spacer between the pyrimidine and imidazole rings of purine (e.g., **2**). This choice is consistent with the names of the other nucleoside base analogues, e.g., *lin*-benzoadenine and *lin*-naphthoadenine, in which the terminal rings are separated by benzo and naphtho spacers, respectively.

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