Synthesis and Chemistry of 1,3-Diazabiphenylenes

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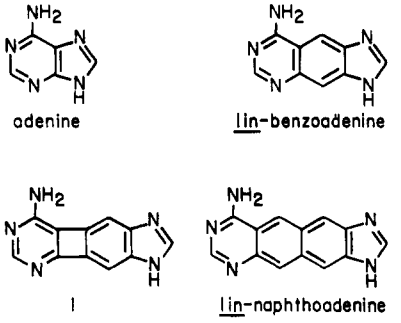
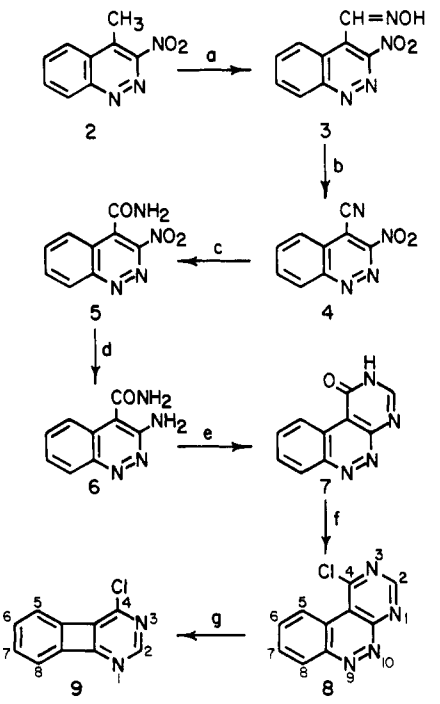
Two independent syntheses of the 1,3-diazabiphenylene ring system have been developed. The first of these involves thermal extrusion of nitrogen from a condensed pyridazine precursor, and the second utilizes a diethynylpyrimidine in a cobalt-catalyzed co-oligomerization reaction. The 1,3-diazabiphenylenes undergo facile transformations to isoquinolines upon treatment with either acid or base. The intermediacy of 1,3-benzodiazocines is proposed between a pair of electrocyclic reactions, followed by small-molecule extrusion.

Biphenylene has been the object of intense scrutiny since its first preparation in 1941,[1a] primarily because of theoretical interest in the consequences of juxtaposing an aromatic benzene ring with an antiaromatic cyclobutadiene ring.[1b,c] In recent years, much of this attention has turned to the study of biphenylene analogues in which one or both of the benzene rings is replaced by an aromatic heterocycle or some other nonbenzenoid aromatic ring.[2] Our interest in nitrogen-containing analogues of biphenylene began during a systematic study of enzyme–coenzyme interactions utilizing linearly extended nucleotide probes.[3] With the intention of fine-tuning the dimensional restrictions for such interactions, we set out to synthesize the linearly extended adenine analogue 1, which is intermediate in



width between *lin*-benzoadenine[4a] and *lin*-naphthoadenine,[4b] both of which have been prepared in this laboratory. A survey of the literature, however, revealed that the primary structural feature of 1, the 1,3-diazabiphenylene ring, was unknown. We therefore embarked on a study of the parent 1,3-diazabiphenylene ring system prior to engaging in the more demanding task of preparing 1. In this paper we report two different synthetic approaches to this ring system and describe some of the curious chemistry of these compounds.[5]

Scheme I[a]



[a] (a) *i*-AmONO, HCl, EtOH; (b) Ac_2O, 110 °C, 2 h; (c) concentrated H_2SO_4, 100 °C, 3 h; (d) $SnCl_2 \cdot 2H_2O$, aqueous HCl; (e) NaOEt, HCOOEt, EtOH; (f) $POCl_3$, $Et_4N^+Cl^-$, $PhNEt_2$, CH_3CN; (g) sublimed through quartz tube at 780–800 °C and 10^{-3} mmHg.

Results and Discussion

Our first synthetic route to a 1,3-diazabiphenylene includes the flash vacuum pyrolysis of a condensed pyridazine precursor in the final step. The construction of the pyridazine precursor started with 4-methyl-3-nitrocinnoline (2) (Scheme I), which was prepared readily from *o*-aminoacetophenone by the method of Baumgarten and

(1) (a) Lothrop, W. C. *J. Am. Chem. Soc.* **1941**, *63*, 1187. (b) Cava, M. P.; Mitchell, M. J. "Cyclobutadiene and Related Compounds"; Academic Press: New York, 1967; Chapter 10. (c) Barton, J. W. In "Nonbenzenoid Aromatics"; Snyder, J. P., Ed.; Academic Press: New York, 1969; Chapter 2.

(2) Heterocyclic biphenylenes containing sulfur: Barton, J. W.; Lapham, D. J. *Tetrahedron Lett.* **1979**, 3571. Garratt, P. J.; Neoh, S. B. *J. Org. Chem.* **1975**, *40*, 970. Garratt, P. J.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1972**, *94*, 7087. Garratt, P. J.; Holmes, A. B.; Sondheimer, F.; Vollhardt, K. P. C. *Ibid.* **1970**, *92*, 4492. Garratt, P. J.; Vollhardt, K. P. C. *Chem. Commun.* **1970**, 109. Containing nitrogen: Hull, R.; MacBride, J. A. H.; Wardleworth, M.; Wright, P. M. *J. Chem. Soc., Chem. Commun.* **1983**, 74. MacBride, J. A. H.; Wright, P. M. *Tetrahedron Lett.* **1982**, *23*, 1109. MacBride, J. A. H.; Wright, P. M.; Wakefield, B. J. *Ibid.* **1981**, *22*, 4545. Kanoktanaporn, S.; MacBride, J. A. H.; King, T. J. *J. Chem. Res., Miniprint* **1980**, 2911. Kanoktanaporn, S.; MacBride, J. A. H. *Ibid.* **1980**, 2941. Barton, J. W.; Goodland, M. C.; Gould, K. J.; McOmie, J. F. W.; Mound, W. R.; Saleh, S. A. *Tetrahedron* **1979**, *35*, 241. Barton, J. W.; Goodland, M. C.; Gould, K. J.; Hadley, J.; McOmie, J. F. W. *Ibid.* **1978**, *34*, 495. Barton, J. W.; Walker, R. B. *Tetrahedron Lett.* **1975**, 569. Gilchrist, T. L.; Nunn, E. E.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1262. Kramer, J.; Berry, R. S. *J. Am. Chem. Soc.* **1972**, *94*, 8336. Bartsch, E.-G.; Golloch, A.; Sartori, P. *Chem. Ber.* **1972**, *105*, 3463. Hünig, S.; Pütter, H. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 433. Cava, M. P.; Napier, D. R.; Pohl, R. J. *J. Am. Chem. Soc.* **1963**, *85*, 2076. Biphenylenes incorporating a carbocyclic nonbenzenoid aromatic ring: Lombardo, L.; Wege, D. *Aust. J. Chem.* **1978**, *31*, 1569. Garratt, P. J.; Vollhardt, K. P. C. *Chem. Commun.* **1971**, 1143. Cava, M. P.; Narasimhan, K.; Zeigler, W.; Radonovich, L. J.; Glick, M. D. *J. Am. Chem. Soc.* **1969**, *91*, 2378. Baxter, C. S.; Garratt, P. J.; Vollhardt, K. P. C. *Ibid.* **1969**, *91*, 7783.

(3) Leonard, N. J. *Acc. Chem. Res.* **1982**, *15*, 178 and references cited therein.

(4) (a) Leonard, N. J.; Morrice, A. G.; Sprecker, M. A. *J. Org. Chem.* **1975**, *40*, 356. (b) Stevenson, T. M.; Leonard, N. J., unpublished results.

(5) Portions of this work have been communicated: d'Alarcao, M.; Leonard, N. J. *J. Am. Chem. Soc.* **1983**, *105*, 5958. See also ref 3.

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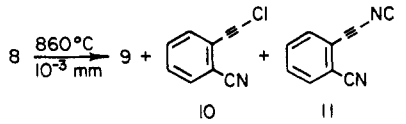
DeBrunner[6] with a modification.[7] Treatment of **2** with isoamyl nitrite in the presence of anhydrous HCl in ethanol[8] provided 3-nitrocinnoline-4-carboxaldehyde oxime (**3**) in 80% yield. Because the oxime function in **3** was not successfully converted to an amide group by the usual methods,[9] we resorted to a two-step sequence of dehydration and partial hydrolysis. This was accomplished in 76% overall yield by treating **3** with acetic anhydride[10] at 110 °C to give 4-cyano-3-nitrocinnoline (**4**), which was then hydrated to 3-nitrocinnoline-4-carboxamide (**5**) with concentrated H_2SO_4[11] at 100 °C. The reduction of the nitro group in **5** was complicated by the attendant reduction of the cinnoline nucleus. Nevertheless, selectivity was realized by treatment of **5** with exactly 3 equiv of $SnCl_2 \cdot 2H_2O$ in aqueous HCl at 0 °C, resulting in a clean reduction to 3-aminocinnoline-4-carboxamide (**6**) in 74% yield. Ring closure to the tricyclic pyrimido[6,5-*c*]-3*H*-cinnolin-4-one (**7**) proceeded in quantitative yield when compound **6** was treated with ethyl formate in ethanolic NaOEt.[12] The modified chlorination procedure reported by Robins and Uznański[13] converted **7** to 4-chloropyrimido[6,5-*c*]cinnoline (**8**) in over 85% yield.

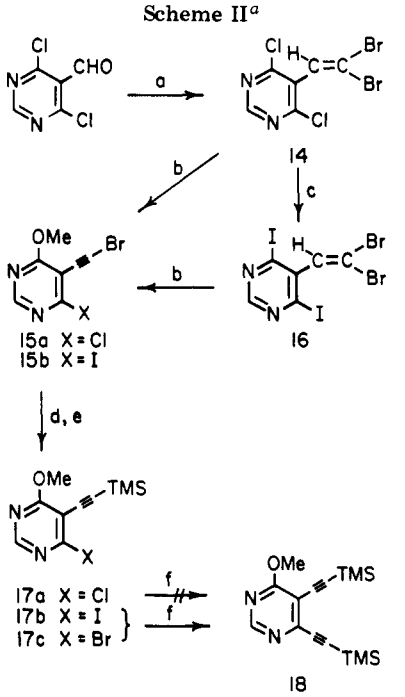
Completion of the synthesis of 4-chloro-1,3-diazabiphenylene (**9**), the first example of a new ring system, required the thermal extrusion of N_2 from compound **8** (Scheme I). To undergo a flash vacuum pyrolysis reaction successfully, the substrate must be able to sublime before decomposing. Even though the chloro compound **8** decomposed on melting at 227–228 °C at atmospheric pressure, it sublimed smoothly at 150 °C (10^{-3} mm).

Flash vacuum pyrolysis[14] of **8** was carried out in a specially constructed apparatus (see the Experimental Section) by subliming the substrate through a hot quartz tube. The yield of **9** was optimized with respect to temperature. At temperatures below 760 °C very little conversion occurred, and the starting material was recovered almost completely. The conversion was most efficient when the pyrolysis was performed at 780–800 °C; the diazabiphenylene **9** was obtained in 35–45% isolated yield. When the temperature was raised above 800 °C, two other compounds, designated A and B, were also formed. Examination of the IR spectra of A and B showed the presence of nitrile and acetylenic functions in A and of nitrile, acetylenic, and isonitrile functions in B. On the basis of IR and ^1H and ^{13}C NMR spectra, together with both low- and high-resolution electron-impact mass spectra, compounds A and B were assigned structures **10** and **11**, respectively. Compound **10** could be formed in a simple



10 11

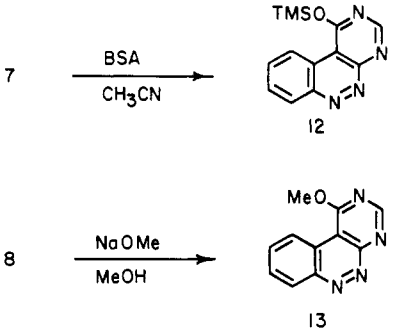
Scheme II[a]



[a] (a) CBr_4, Ph_3P, Zn, CH_2Cl_2; (b) 2NaOMe, MeOH; (c) 47% HI; (d) RLi, THF, −78 °C; (e) $(CH_3)_3SiCl$; (f) $HC{\equiv}CSiMe_3$, $(Ph_3P)_2PdCl_2$, CuI, Et_3N.

thermal electrocyclic elimination of HCN from the diazabiphenylene **9**; compound **11** could result from **9** with the loss of the elements of HCl. Indeed, compounds **10** and **11** were also formed when **9** was resubjected to the pyrolysis conditions.

In an effort to prepare the oxygen-substituted derivatives of 1,3-diazabiphenylene, we synthesized the corresponding pyrimidocinnoline precursors **12** and **13**. Thus,



the oxo compound **7** was O-trimethylsilylated with bis(trimethylsilyl)acetamide to give compound **12**. 4-Methoxypyrimido[6,5-*c*]cinnoline (**13**) was prepared by treatment of **8** with methanolic $NaOCH_3$. Although compounds **12** and **13** had lower melting points than the corresponding chloro derivative **8**, they decomposed and failed to yield diazabiphenylenes upon flash vacuum pyrolysis. The literature cites no examples of the pyrolysis of alkoxy compounds in biphenylene syntheses.

An alternative approach to the 1,3-diazabiphenylene ring system was conceived in which the pyrimidine portion of the molecule is present initially, and the carbocyclic rings are added in subsequent steps. The cobalt-catalyzed acetylene oligomerization reaction developed by Vollhardt[15] seemed especially well suited to this approach since by this method both the four-membered ring and the

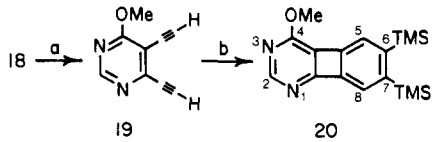
(6) Baumgarten, H. E.; DeBrunner, M. R. *J. Am. Chem. Soc.* **1954**, *76*, 3489.
(7) The smooth cyclization of nitroformaldehyde *o*-acetylphenylhydrazone to 4-methyl-3-nitrocinnoline was carried out in water in the presence of diazabicyclooctane, a modification reported by: Kanoktanaporn, S.; MacBride, J. A. H. *Tetrahedron Lett.* **1977**, 1817.
(8) Brederick, H.; Simcheu, A.; Speh, P. *Justus Liebigs Ann. Chem.* **1970**, *737*, 39.
(9) Field, L.; Hughmark, P. B.; Shumaker, S. H.; Marshall, W. S. *J. Am. Chem. Soc.* **1961**, *83*, 1983. Chattopadhyaya, J. B.; Rama Rao, A. V. *Tetrahedron* **1974**, *30*, 2899.
(10) Ogata, M. *Chem. Pharm. Bull.* **1963**, *11*, 1511.
(11) Nakagome, T.; Castle, R. N.; Murakami, H. *J. Heterocycl. Chem.* **1968**, *5*, 523.
(12) Chung, F. C.; Schram, K. H.; Panzica, R. P.; Earl, R. A.; Wotring, L. L.; Townsend, L. B. *J. Med. Chem.* **1980**, *23*, 1158.
(13) Robins, M. J.; Uznański, B. *Can. J. Chem.* **1981**, *59*, 2601.
(14) Brown, R. F. C. "Pyrolytic Methods in Organic Chemistry"; Academic Press: New York, 1980.
(15) Vollhardt, K. P. C. *Acc. Chem. Res.* **1977**, *10*, 1 and references therein.

Table I. Effect of Lithium Base on Reaction with 15b[a]

base	ratio of 17b/17c	base	ratio of 17b/17c
MeLi	1:2.5	*sec*-BuLi	2.4:1
n-BuLi	1:1.5	*t*-BuLi	4.2:1

[a] The base (0.66 mmol, 1.1 equiv) was added rapidly to a stirred solution of **15b** (200 mg, 0.592 mmol) in 5 mL THF at −78 °C. The $(CH_3)_3SiCl$ (0.10 mL, 0.80 mmol) was added after 1 min, the reaction mixture was allowed to warm to room temperature, the products were separated from unreacted **15b** by silica gel chromatography (**17b** and **17c** coelute with 50% ether-petroleum ether), and the ratio was determined by ^1H NMR.

Scheme III[a]



19 20

[a] (a) NaOH, MeOH; (b) $Me_3SiC{\equiv}CSiMe_3$, $CpCo(CO)_2$, xylenes, $h\nu$, Δ.

second six-membered ring would be formed simultaneously.[16] The 4,5-diethynylpyrimidine that was required was prepared as outlined in Scheme II. 4,6-Dichloro-5-formylpyrimidine[17] was elaborated to 5-(2,2-dibromovinyl)-4,6-dichloropyrimidine (**14**) in 81% yield by a modification[18] of the Wittig reaction. Halide interconversion with concentrated HI provided 5-(2,2-dibromovinyl)-4,6-diiodopyrimidine (**16**) in 97% yield. Each of these compounds (**14, 16**) underwent dehydrohalogenation followed by monosubstitution when treated with 2 equiv of $NaOCH_3$ to produce **15a** and **15b** in respective yields of 73% and 97%. Although 5-(bromoethynyl)-4-chloro-6-methoxypyrimidine (**15a**) was converted cleanly (97%) to 4-chloro-6-methoxy-5-[(trimethylsilyl)ethynyl]pyrimidine (**17a**) by halogen–metal exchange of the bromine with *n*-butyllithium followed by trapping with $(CH_3)_3SiCl$, compound **17a** did not undergo the subsequent Pd-catalyzed ethynylation reaction. By contrast, 5-(bromoethynyl)-4-iodo-6-methoxypyrimidine (**15b**) did not give **17b** exclusively upon metalation and trapping, but rather a mixture of **17b** and **17c**. Fortunately, however, both of these compounds underwent the ethynylation reaction, with the iodo compound **17b** reacting more rapidly.[19] The composition of the mixture of **17b** and **17c** was dependent upon the lithium base used (Table I), as was the extent of side-product formation. The most effective experimental conditions for obtaining 4,5-bis[(trimethylsilyl)-ethynyl]-6-methoxypyrimidine (**18**) included treating compound **15b** with *n*-butyllithium, trapping with $(CH_3)_3SiCl$ to give the mixture of **17b** and **17c**, and treating this mixture with catalytic $(Ph_3P)_2PdCl_2$–CuI and an excess of (trimethylsilyl)acetylene. After removal of the trimethylsilyl groups from **18** (Scheme III), 4,5-diethynyl-6-methoxypyrimidine (**19**) was obtained in 61% yield based on initial **15b**. To our knowledge, this represents the first synthesis of an *o*-diacetylenic aromatic heterocycle.

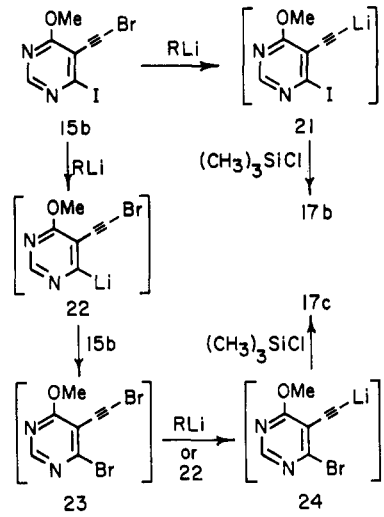
(16) Biphenylene has been prepared recently in this way: Berris, B. C.; Lai, Y.-H.; Vollhardt, K. P. C. *J. Chem. Soc., Chem. Commun.* **1982**, 953.

(17) Klötzer, W.; Herberz, M. *Monatsh. Chem.* **1965**, *96*, 1567.

(18) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

(19) When a mixture of **17b** and **17c** was subjected to the Pd-catalyzed ethynylation conditions and the reaction was allowed to proceed only to partial completion, only **17c** remained unreacted. All of the **17b** had been consumed.

Scheme IV

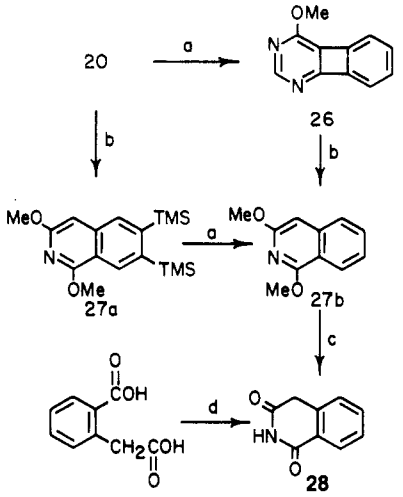


The construction of the 1,3-diazabiphenylene ring system was completed by cyclization of the deprotected diethynylpyrimidine **19** with bis(trimethylsilyl)acetylene in the presence of $CpCo(CO)_2$. Although acetylenic co-oligomerization in the hydrocarbon series is typically effected with a catalytic amount of the cobalt complex,[15] we found that this application of the organometallic reaction to the heterocyclic series functioned best with an excess of $CpCo(CO)_2$, with the formation of 6,7-bis(trimethylsilyl)-4-methoxy-1,3-diazabiphenylene (**20**) in 56% yield. This requirement is probably due to the instability of **19** at the temperature of refluxing xylenes;[5] an excess of the catalyst ensures that compound **19** can react as desired before undergoing much decomposition.

An explanation is in order for the formation of a mixture of the iodo and bromo compounds **17b** and **17c** from 5-(bromoethynyl)-4-iodo-6-methoxypyrimidine (**15b**) alone in the following reaction sequence: RLi, THF; $(CH_3)_3SiCl$. A reasonable pathway for the formation of the ring-brominated pyrimidine **17c** from the ring-iodinated compound **15b** is outlined in Scheme IV. Presumably, the rate of halogen–metal interchange of the ring iodine in **15b** is competitive with the rate of exchange of the acetylenic bromine. In this way both lithiated intermediates **21** and **22** may be formed. The latter can undergo a second halogen–metal exchange with unreacted **15b** to produce the dibromo compound **23** which would be expected to react with another molecule of RLi or **22** to produce the lithiated acetylide **24**. Trapping with $(CH_3)_3SiCl$ would produce **17b** from **21** and **17c** from **24**. Of course, the possibility that **21** is also a precursor to **24** cannot be discounted. The ratio of **17b** to **17c** in the mixtures could be estimated by the ^1H NMR spectra, and fairly pure, unreacted **17c** could be reisolated after partial reaction of the mixture of **17b** and **17c** with excess (trimethylsilyl)-acetylene.[19] As stated above, all of the mixture eventually underwent conversion to compound **18**, and this, after deprotection and co-oligomerization with bis(trimethylsilyl)acetylene, produced the 1,3-diazabiphenylene **20**.

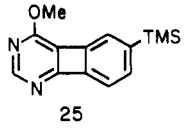
6,7-Bis(trimethylsilyl)-4-methoxy-1,3-diazabiphenylene (**20**) underwent stepwise protodesilylation when treated with CF_3SO_3H in pentane at room temperature. When the reaction was stopped after 2 min by addition of pyridine, a single (trimethylsilyl)diazabiphenylene was isolated in 68% yield. Although we have not established unequivocally the position of the remaining trimethylsilyl group in this compound, the electron-donating 4-methoxyl group and the deactivating ring nitrogens would be expected to

Scheme V[a]



[a] (a) CF_3SO_3H, pentane; (b) CF_3COOH, MeOH; (c) $(CH_3)_3SiCl$, NaI, CH_3CN; (d) ref 20.

work in concert to direct electrophiles to C-7 rather than C-6. It seems likely, therefore, that this compound has structure **25**. When the protodesilylation reaction was

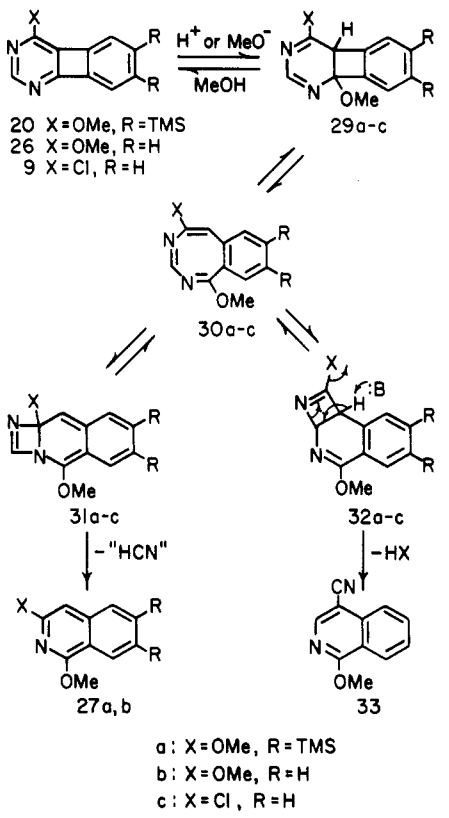


allowed to continue for 2.5 h before addition of pyridine, 4-methoxy-1,3-diazabiphenylene (**26**) was obtained in 75% yield.

Protodesilylation of **20** was performed in pentane because in nucleophilic solvents, acid induced a peculiar transformation that reorganized the diazabiphenylene (6–4–6) ring system to an isoquinoline (6–6) ring system (Scheme V). Thus, separate treatment of both **20** and **26** with CF_3COOH in CH_3OH provided **27a** and **27b**, respectively, in nearly quantitative yields. The structures of these isoquinolines were determined by their spectral properties and verified by the sequence shown in Scheme V. 6,7-Bis(trimethylsilyl)-1,3-dimethoxyisoquinoline (**27a**) obtained from **20** by this rearrangement was protodesilylated to give **27b**, which was identical with the product obtained by rearrangement of **26**. 1,3-Dimethoxyisoquinoline (**27b**) was demethylated with $(CH_3)_3SiI$ in CH_3CN to produce homophthalimide (**28**) which was identical by TLC, IR, and ^1H NMR spectra and melting point comparison to an authentic sample prepared by the method of Gabriel.[20]

The transformation of these 4-methoxy-1,3-diazabiphenylenes into isoquinolines may occur as outlined in Scheme VI. Acid-catalyzed addition of CH_3OH to **20** or **26** would be expected to produce the benzodiazocine **30a,b** by electrocyclic ring opening of the initial adduct **29a,b**.[21] A second electrocyclic reaction leading to **31a,b**, followed by acid-promoted, irreversible loss of the elements of HCN, would drive the reaction to **27a,b**.[22]

Scheme VI



Treatment of 4-chloro-1,3-diazabiphenylene (**9**) with CF_3COOH in CH_3OH led to a complicated mixture of unstable products. Perhaps the lower basicity of compound **9** compared with that of **26** allows side reactions to compete with the addition of CH_3OH (**29c**) and subsequent ring transformations (**30c**, **31c**, **27c**). By contrast, reaction of compound **9** with $NaOCH_3$ in CH_3OH gave a single product in 81% yield. The IR spectrum of this product showed a strong nitrile absorption at 2230 cm^{-1}. From ^1H and ^{13}C NMR and low- and high-resolution mass spectra we were able to conclude that the product was 4-cyano-1-methoxyisoquinoline (**33**). This structural assignment was confirmed by synthesis of **33** from 1-chloro-4-cyanoisoquinoline[23] by treatment with $NaOCH_3$ in CH_3OH.

In view of the transformation of 2-methoxy-1-azocine into benzonitrile on treatment with base,[24] it is reasonable to assume the intermediacy of benzodiazocine **30c** in the conversion of the chloro compound **9** to **33**. An electrocyclic reaction of **30c** to produce **32c**[25] followed by rapid, irreversible loss of the elements of HCl would give **33** (Scheme VI). By contrast, the methoxy compound **20**, upon treatment with methanolic $NaOCH_3$, was slowly converted to **27a** rather than **33**. This difference in behavior may be accounted for by assuming fast equilibration between **30**, **31**, and **32** and a product-determining competition between loss of "HCN" or "HX". Since methoxide is a poorer leaving group than chloride, conversion to **27** is preferred in the case of **30a,b**.

Now that we have developed two distinct methods for

(20) Gabriel, S. *Chem. Ber.* **1886**, *19*, 1653.

(21) Similar reactions have been observed with biphenylene in the presence of both a nucleophile and an electrophile: Barton, J. W. Whitaker, K. E. *J. Chem. Soc. C* **1968**, 1663.

(22) A similar sequence has been proposed to account for the conversion of uracil–alkyne photoadducts to pyridones in alkoxide medium: Kaminski, V. V.; Comber, R. N.; Wexler, A. J.; Swenton, J. S. *J. Org. Chem.* **1983**, *48*, 2337. Kaminski, V. V.; Swenton, J. S.; Cottrell, C. E. *Tetrahedron Lett.* **1982**, *23*, 4207; Comber, R. N.; Swenton, J. S.; Wexler, A. J. *J. Am. Chem. Soc.* **1979**, *101*, 5411.

(23) Braye, E.; Floy, F.; Hoogzand, C.; Lenaers, R. *Eur. J. Med. Chem.–Chim. Ther.* **1974**, *9*, 197. Wenkert, E.; Haugwitz, R. D. *Can. J. Chem.* **1968**, 46, 1160.

(24) Paquette, L. A.; Kakihana, J. *J. Am. Chem. Soc.* **1968**, *90*, 3897. For similar transformations see also: Snyder, J. P.; Lee, L.; Farnum, D. G. *J. Am. Chem. Soc.* **1971**, *93*, 3816. Wentrup, C. *Tetrahedron* **1971**, *27*, 1027.

(25) A referee has pointed out that this electrocyclic process is probably preceded by a bond-shift isomerization of **30c**.

the synthesis of 1,3-diazabiphenylenes, we are turning our attention again to the original goal, the synthesis of an adenine analogue like 1. Both the elaboration of currently available diazabiphenylenes to the imidazole-fused analogues and synthetic methods utilizing de novo biphenylene preparation are under investigation.

Experimental Section

Xylenes, Et_3N, and tetrahydrofuran (THF) were purified by distillation from Na–benzophenone. MeOH and EtOH were of anhydrous grade. *o*-Aminoacetophenone, 4,6-dihydroxypyrimidine, and $(Ph_3P)_2PdCl_2$ were obtained from Aldrich Chemical Co., bis(trimethylsilyl)acetylene and (trimethylsilyl)acetylene from Petrarch Systems Inc., and $CpCo(CO)_2$ from Strem Chemicals Inc. Petroleum ether had a boiling range of 30–60 °C. Thin-layer chromatography (TLC) was performed on Brinkmann silica gel (0.25 mm with fluorescent indicator) plates. Preparative TLC was performed on Brinkmann silica gel (2.0 mm with fluorescent indicator) plates. Column chromatography was performed on silica gel (0.05–0.2 mm) from Brinkmann. Melting points were determined on a Büchi capilary melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 337 or a Nicolet 7199 FT-IR spectrophotometer. UV absorption spectra were obtained on a Beckman Acta MVI spectrophotometer. ^1H NMR spectra were recorded on a Varian EM-390 (90 MHz) or a Nicolet NTC-360 (360 MHz) spectrometer with tetramethylsilane or deuterated organic solvents as internal standards. ^{13}C NMR spectra were recorded on a Nicolet NTC-360 (90 MHz) spectrometer. Mass spectra were obtained on a Varian MAT CH-5 instrument or a Varian MAT-731 high-resolution spectrometer coupled with a 620i computer and a STATOS recorder. Microanalyses were performed by J. Nemeth and his staff at the University of Illinois.

Apparatus for Flash Vacuum Pyrolysis. The compound to be pyrolyzed was placed in a 25-mL flask with a 14/20 male joint which was connected to a quartz tube (35 cm long and 2.5 cm o.d.) and placed in a tube furnace. The other end of the quartz tube, a 14/20 male joint, was connected to a dry ice–2-propanol trap, which in turn was connected to a liquid N_2 trap and to a vacuum pump through a two-stage oil-diffusion pump. The flask containing the sample was heated by means of an air oven formed by coiling nichrome wire around a beaker. The quartz tube was heated by the tube furnace, and the temperature was measured with a thermocouple. The pressure in the system was measured with a Sargent-Welch vacuum gauge. Liberal amounts of Apiezon grease were applied to the ground joints on both sides of the quartz tube to ensure proper sealing during the course of pyrolysis. The pressure in the system rose slightly during pyrolysis and decreased after completion. In general, each run of about 300 mg took 30 min.

4-Methyl-3-nitrocinnoline (2).[6,7] A heterogeneous mixture of nitroformaldehyde *o*-acetylphenylhydrazone[6] (31 g, 0.15 mol), diazabicyclooctane (16.8 g, 0.15 mol), and 600 mL of H_2O was heated with stirring at 65 °C for 4 h. The cooled reaction mixture was filtered, washed with H_2O, and dried. Recrystallization from EtOH yielded **2** as lustrous brown flakes: 21.2 g (75% yield); mp 190–192 °C (lit.[6] mp 188–189 °C); ^1H NMR (90 MHz) ($CDCl_3$) δ 2.85 (s, 3 H, CH_3), 7.9–8.3 (m, 3 H, Ar H), 8.6–8.75 (m, 1 H, Ar H); MS (10 eV), *m/e* (relative intensity) 189 (M^+, 100), 143 ($M^+ - NO_2$, 81), 116 (48), 44 (29).

3-Nitrocinnoline-4-carboxaldehyde Oxime (3).[8] To a stirred suspension of 4-methyl-3-nitrocinnoline (**2**; 13.0 g, 69 mmol) in ethanolic HCl (7.5 g of anhydrous HCl in 40 mL of absolute EtOH) at 0 °C was added dropwise a solution of isoamyl nitrite (7.9 g, 69 mmol) in EtOH (10 mL). The resulting mixture was stirred at 20 °C for 5 h. The precipitated product was filtered and washed with a small amount of H_2O. The dried material was recrystallized from acetone to yield **3** as pale brown flakes: 12 g (80%); mp 171–172 °C; IR (KBr) 3440, 3080, 2800, 1612, 1560, 1500, 1375, 1175, 1030, 1020, 910 cm^{-1}; ^1H NMR ($(CD_3)_2SO$) δ 8.1–8.25 (m, 2 H, Ar H), 8.65–8.82 (m, 2 H, Ar H), 8.88 (s, 1 H, N=CH); MS (10 eV), *m/e* (relative intensity) 218 (M^+, 37), 200 ($M^+ - H_2O$, 5), 172 ($M^+ - NO_2$, 100), 154 (13), 143 (19), 129 (23), 116 (82). Anal. Calcd for $C_9H_6N_4O_3$: C, 49.54; H, 2.77; N, 25.68. Found: C, 49.80; H, 2.55; N, 25.86.

4-Cyano-3-nitrocinnoline (4).[10] A solution of oxime **3** (12 g, 55 mmol) in acetic anhydride (80 mL) was heated at 110 °C for 2 h. The reaction mixture was cooled, and the precipitated yellow solid was separated by filtration. Recrystallization from EtOH provided bright yellow needles: yield 8.8 g (80%); mp 204–205 °C; IR (KBr) 2240, 1590, 1560, 1400, 1355, 820, 770 cm^{-1}; ^1H NMR ($(CD_3)_2SO$) δ 8.3–8.5 (m, 3 H, Ar H), 8.85–9.0 (m, 1 H, Ar H); MS (10 eV), *m/e* (relative intensity) 200 (M^+, 79), 154 ($M^+ - NO_2$, 86), 127 (28), 114 (36), 78 (100). Anal. Calcd for $C_9H_4N_4O_2$: C, 54.00; H, 2.01; N, 27.99. Found: C, 53.84; H, 1.92; N, 27.74.

3-Nitrocinnoline-4-carboxamide (5).[11] A solution of nitrile **4** (12.6 g, 63 mmol) in concentrated H_2SO_4 (100 mL) was heated at 100 °C for 3 h. The reaction mixture was cooled and poured over ice (400 g). The precipitated amide was filtered, washed with H_2O, and dried. An analytical sample was obtained by recrystallization from EtOH–H_2O: yield 13 g (95%); mp 299–300 °C; IR (KBr) 3360, 3160, 1685, 1615, 1550, 1355, 1220, 1190, 930, 820 cm^{-1}; ^1H NMR (90 MHz, $(CD_3)_2SO$) δ 8.2–8.5 (m, 3 H, Ar H), 8.75–8.85 (m, 1 H, Ar H); MS (34 eV), *m/e* (relative intensity) 218 (M^+, 100), 175 (7), 172 (10), 129 (10), 116 (13). Anal. Calcd for $C_9H_6N_4O_3$: C, 49.54; H, 2.77; N, 25.68. Found: C, 49.58; H, 2.52; N, 25.43.

3-Aminocinnoline-4-carboxamide (6).[6] To a stirred suspension of nitro compound **5** (8 g, 37 mmol) in 6 N HCl (40 mL) at 0 °C was added, over 30 min, a solution of $SnCl_2 \cdot 2H_2O$ (24.7 g, 109 mmol) in 12 N HCl (40 mL). The stirring was continued at 0 °C for 2 h and at 20 °C for 2 h. The resulting mixture was basified carefully with 30% KOH solution to pH 12 and cooled. The precipitated solid was filtered, washed with H_2O, and dried. Recrystallization from MeOH gave **6** as greenish yellow needles: yield 5.1 g (74%); mp 260–261 °C; IR (KBr) 3480, 3380, 3200, 1660, 1620, 1430, 1360, 1130, 1110, 1020 cm^{-1}; ^1H NMR (90 MHz) ($(CD_3)_2SO$) δ 6.48 (s, 2 H, NH_2), 7.4–7.7 (m, 2 H, Ar H), 8.0–8.2 (m, 2 H, Ar H); MS (10 eV), *m/e* (relative intensity) 188 (M^+, 100), 160 ($M^+ - N_2$, 51), 143 (17), 132 (28), 115 (25). Anal. Calcd for $C_9H_8N_4O$: C, 57.44; H, 4.29; N, 29.77. Found: C, 57.08; H, 4.10; N, 29.80.

Pyrimido[6,5-*c*]-3*H*-cinnolin-4-one (7).[12] Compound **6** (6 g, 32 mmol) was added to a solution of NaOEt prepared from 7.3 g of Na in EtOH (400 mL). Ethyl formate (11.8 g, 160 mmol) was added, and the mixture was heated at reflux for 3 h. The resulting mixture was diluted with H_2O (100 mL) to give a clear solution and was acidified with 6 N HCl to pH 3. The yellow precipitate obtained on cooling was filtered and washed with small amounts of H_2O and EtOH and dried to give **7** in quantitative yield. An analytical sample was obtained by recrystallization from aq EtOH: mp >300 °C; IR (KBr) 3460, 3090, 2920, 1700, 1615, 1540, 1390, 1315, 1235, 1170, 1110, 790 cm^{-1}; ^1H NMR (90 MHz, CF_3COOH) δ 8.45–8.7 (m, 2 H, Ar H), 8.85–8.97 (m, 1 H, Ar H), 9.03 (s, 1 H, 2 H), 9.70–9.90 (m, 1 H, Ar H); MS (10 eV), *m/e* (relative intensity) 198 (M^+, 100), 170 (5), 169 (9), 143 (29), 115 (44), 99 (9). Anal. Calcd for $C_{10}H_6N_4O$: C, 60.60; H, 3.05; N, 28.27. Found: C, 60.36; H, 2.99; N, 28.16.

4-Chloropyrimido[6,5-*c*]cinnoline (8).[13] A flask was charged with compound **7** (2 g, 10 mmol), $Et_4N^+Cl^-$ (dried at 80 °C and 1 mm; 1.84 g, 10 mmol), diethylanilne (1.6 mL, 10 mmol; distilled from CaH_2), CH_3CN (distilled from CaH_2; 10 mL), and freshly distilled $POCl_3$ (10 mL, 100 mmol). The mixture was heated at 100 °C for 15 min and then was concentrated to half volume by distillation under reduced pressure. The residue was poured slowly onto aqueous $NaHCO_3$ (50 g in 600 mL of H_2O) at 5 °C with vigorous stirring. The resultant mixture was left at room temperature for 3 h. The precipitated chloro compound was filtered, washed with H_2O, and dried. Recrystallization from benzene provided golden prisms of **8**: yield 1.8 g (85%); mp 227–228 °C dec; IR (KBr) 3140, 1600, 1560, 1530, 1425, 1390, 1320, 1210, 800 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 8.08–8.2 (m, 2 H, Ar H), 8.9–9.06 (m, 1 H, Ar H), 9.46 (s, 1 H, 2 H), 9.6–9.7 (m, 1 H, Ar H); MS (10 eV), *m/e* (relative intensity) 218 ($M^+ + 2$, 29), 216 (M^+, 100), 163 (19), 161 (57). Anal. Calcd for $C_{10}H_5ClN_4$: C, 55.44; H, 2.33; Cl, 16.36; N, 25.86. Found: C, 55.69; H, 2.40; Cl, 16.58; N, 25.98.

Flash Vacuum Pyrolysis of 4-Chloropyrimido[6,5-*c*]cinnoline (8). 4-Chloro-1,3-diazabiphenylene (9). Compound **8** (300 mg, 1.4 mmol) was subjected to flash vacuum pyrolysis (780–800 °C, 10^{-3} mmHg) in the apparatus described above. The

product was leached with warm $CHCl_3$. The $CHCl_3$ extract was concentrated to 0.5 mL and spotted as a band on a preparative TLC plate. The plate was developed with ether–petroleum ether (1:1 v/v). The yellow band (R_f ~0.4) was collected, and the product was extracted with $CHCl_3$. Recrystallization from ether–hexane gave analytically pure **9** as a yellow solid: yield varied from 35% to 45%; mp 84–86 °C; IR (KBr) 1660, 1570, 1400, 1260, 1140, 860, 750, 670 cm^{-1}; UV (EtOH) λ_{max} 243 nm (log ϵ 4.45), 258 (4.26), 314 (3.54), 323 (3.71), 340 (3.80); ^1H NMR (360 MHz, $CDCl_3$) δ 7.0–7.16 (m, 4 H, Ar H), 8.34 (s, 1 H, 2 H); ^{13}C (90 MHz, $CDCl_3$) δ 120.9 (d), 121.9 (d), 130.5 (d), 132.9 (d), 140.2 (s), 143.6 (s), 150.0 (s), 150.5 (s), 158.3 (d), 182.1 (s); MS (10 eV), *m/e* (relative intensity) 190 (M^+ + 2, 30), 188 (M^+, 85), 163 (34), 161 (100). Anal. Calcd for $C_{10}H_5ClN_2$: 63.68; H, 2.67; Cl, 18.80; N, 14.85. Found: C, 63.54; H, 2.38; Cl, 18.79; N, 14.50.

When the pyrolysis was carried out at 850 °C (10^{-3} mmHg), two other products were obtained along with 4-chloro-1,3-diazabiphenylene (**9**). The pyrolysate was leached with warm $CHCl_3$, and the products were separated by preparative TLC ($CHCl_3$/EtOAc, 3:2). At the higher pyrolysis temperature, **8** (250 mg) yielded **9** (15 mg, 7%; R_f 0.4), **10** (25 mg, 13%; R_f 0.6), and **11** (15 mg, 9%; R_f 0.5) in a typical run.

Compound A, 2-(chloroethynyl)benzonitrile (10): mp 64–65 °C; IR (KBr) 3450, 2230, 2225, 1640, 1485, 1450, 760 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.4–7.7 (AA′ BB′ m); ^{13}C NMR (90 MHz, $CDCl_3$) δ 67.6 (s, acetylenic C), 77.6 (s, acetylenic C), 115.5 (s, CN), 116.8 (s), 121 (s), 131.6 (d), 132.4 (d), 133 (d), 134.3 (d); MS (10 eV), *m/e* (relative intensity) 163 (32), 161 (100), 126 (4); HREIMS, exact mass calcd for C_9H_4ClN (M^+) *m/e* 161.0032, obsd 161.0037.

Compound B, 2-(isocyanoethynyl)benzonitrile (11): mp 88–90 °C; IR (KBr) 3460, 2280, 2270, 2145, 1475, 1445, 770, 670 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.6–7.8 (AA′ BB′ m); ^{13}C NMR (90 MHz, $CDCl_3$) δ 65.8 (s, acetylenic C), 75.2 (s, acetylenic C), 115.6 (s, CN), 117.2 (s), 125.9 (s), 128.7 (d), 132.4 (d), 132.7 (d), 132.9 (d), 154.2 (s, NC); MS (10 eV), *m/e* (relative intensity) 152 (100); HREIMS, exact mass calcd for $C_{10}H_4N_2$ (M^+) *m/e* 152.0374, found *m/e* 152.0379.

4-(Trimethylsiloxy)pyrimido[6,5-*c*]cinnoline (12). A mixture of oxo compound **7** (400 mg, 2 mmol), bis(trimethylsilyl)acetamide (10 mL), and dry CH_3CN (25 mL) was heated at reflux under dry N_2 for 30 min. The clear solution was evaporated under reduced pressure to a green solid: 420 mg (77%); mp 153–155 °C ($CHCl_3$–hexane; ^1H NMR (90 MHz, $CDCl_3$) δ 0.7 (s, 9 H, $Si(CH_3)_3$), 7.9–8.1 (m, 2 H, Ar H), 8.75–8.9 (m, 1 H, Ar H), 9.0–9.2 (m, 2 H, Ar H); MS (10 eV), *m/e* (relative intensity) 270 (M^+, 100), 255 ($M^+ - CH_3$, 59), 227 (6), 200 (7), 147 (8), 73 (Me_3Si^+, 31).

4-Methoxypyrimido[6,5-*c*]cinnoline (13). To a solution of Na in CH_3OH (230 mg in 25 mL) was added compound **8** (217 mg, 1 mmol), and the resulting clear solution was stirred at 20 °C for 4 h and at reflux for 10 min. Then, the solution was cooled, diluted with H_2O (75 mL), acidified with 3 N HCl, and extracted with $CHCl_3$ (3 × 30 mL). The $CHCl_3$ extract was dried (Na_2SO_4) and evaporated to a bright greenish yellow solid: 180 mg (85%); mp 189–191 °C (hexane–$CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 4.36 (s, 3 H, CH_3), 7.9–8.1 (m, 2 H, Ar H), 8,7–8.9 (m, 1 H, Ar H), 8.95–9.10 (m, 1 H, Ar H), 9.16 (s, 1 H, 2 H); MS (10 eV), *m/e* (relative intensity) 212 (M^+, 100), 183 (5), 169 (10), 157 (12). Anal. Calcd for $C_{11}H_8N_4O$: C, 62.25; H, 3.80; N, 26.40. Found: C, 62.50; H, 3.70; N, 26.51.

5-(2,2-Dibromovinyl)-4,6-dichloropyrimidine (14). A 2-L flask fitted with a reflux condenser topped with a $CaSO_4$ drying tube was charged with CBr_4 (200 g, 0.60 mol), Ph_3P (157 g, 0.60 mol), Zn dust (39.2 g, 0.60 mol), and CH_2Cl_2 (1 L).[18] After an initial exothermic reaction the suspension was cooled to 20 °C and stirred for 23 h. To this was added solid 4,6-dichloro-5-formylpyrimidine[17] (46.7 g, 0.26 mol) slowly enough, in portions, to keep the ensuing exothermic reaction under control. The resulting suspension was stirred at 20 °C for 22 h and then poured into 3 L of petroleum ether. The tarry precipitate which formed was removed by filtration, resuspended in CH_2Cl_2 (750 mL), and poured into 2 L of fresh pet ether. The tarry precipitate was again removed by filtration, and the combined filtrates were evaporated to dryness. The residue was crystallized from EtOH–H_2O (~350 mL) to give pure product (66.2 g, mp 98–100 °C). A second crop was obtained by concentration of the mother liquor (4.7 g, mp 96–98 °C). The combined product was suitable for use in the next reaction (total yield 70.9 g, 81%); ^1H NMR ($CDCl_3$) δ 9.04 (s, 1 H, pyrimidine CH), 7.51 (s, 1 H, vinyl CH); ^{13}C NMR ($CDCl_3$) δ 99.9 (s), 128.6 (d), 129.2 (s), 157.2 (d), 160.5 (s); MS (10 eV), *m/e* (relative intensity) 336 (31), 334 (81), 332 (91), 330 (40), 255 (50), 253 (100), 251 (74). Anal. Calcd for $C_6H_2Br_2Cl_2N_2$: C, 21.65; H, 0.61; N, 8.42; Br, 48.02; Cl, 21.30. Found: C, 21.71; H, 0.61, N, 8.07; Br, 47.72; Cl, 20.99.

5-(Bromoethynyl)-4-chloro-6-methoxypyrimidine (15a). A solution of Na (700 mg, 30.4 mmol) in CH_3OH (100 mL) was added dropwise over 1 h to a solution of **14** (5.0 g, 15 mmol) in CH_3OH (100 mL). The reaction was stirred at room temperature for 3 h and then evaporated to dryness. The residue was washed thoroughly with H_2O and recrystallized from EtOH–H_2O (~100 mL) to give white, crystalline product: mp 134–136 °C; ^1H NMR ($CDCl_3$) δ 4.09 (s, 3 H, OCH_3), 8.50 (s, 1 H, pyrimidine CH); IR ($CHCl_3$) 2200, 1380, 1125 cm^{-1}. Anal. Calcd for $C_7H_4BrClN_2O$: C, 33.97; H, 1.63; N, 11.32; Br, 32.29; Cl, 14.33. Found: C, 34.18; H, 1.41; N, 11.24; Br, 32.40; Cl, 14.37.

5-(2,2-Dibromovinyl)-4,6-diiodopyrimidine (16). A suspension of **14** (9.4 g, 28 mmol) in 47% HI (150 mL) was stirred in a stoppered vessel wrapped with foil to exclude light for 5 h at room temperature. The reaction mixture was poured onto 1 L of crushed ice, the ice was allowed to melt, and the pale yellow product was collected by filtration and washed with H_2O, yielding **16** (14.1 g, 97%). An analytically pure sample was obtained by recrystallization from CCl_4: mp 155–158 °C; ^1H NMR ($CDCl_3$) δ 8.57 (s, 1 H, pyrimidine CH), 7.35 (s, 1 H, vinyl CH); ^{13}C NMR ($CDCl_3$) δ 101.3 (s), 130.2 (s), 137.5 (d), 143.9 (s), 156.4 (d). MS (10 eV), *m/e* (relative intensity) 518 (40), 516 (80), 514 (42), 435 (43), 387 (53). Anal. Calcd for $C_6H_2Br_2I_2N_2$: C, 13.97; H, 0.39; N, 5.43; I, 49.21. Found: C, 13.99; H, 0.32; N, 5.19; I, 48.93.

5-(Bromoethynyl)-4-iodo-6-methoxypyrimidine (15b). A solution of Na (1.25 g, 54.4 mmol) in dry CH_3OH (300 mL) was added dropwise over ~45 min to a suspension of **16** (14.0 g, 27.1 mmol) in CH_3OH (300 mL). Halfway through the addition, the starting material had dissolved, and toward the end of the addition a new precipitate (NaBr) had appeared. The reaction mixture was stirred for 1 h after the addition was complete and then evaporated to dryness. The residue was washed thoroughly with H_2O and collected by filtration to give a white powder suitable for use in the subsequent reaction: 8.9 g (97%); mp 129–135 °C. A portion of this was recrystallized twice from EtOH–H_2O: mp 135–136.5 °C; ^1H NMR ($CDCl_3$) δ 8.34 (s, 1 H, pyrimidine CH), 4.09 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 55.1 (q), 62.7 (s), 75.0 (s), 114.8 (s), 133.9 (s), 155.1 (d), 168.5 (s); IR (KBr) 2200, 1535, 1480, 1410, 1380, 1330, 1016, 879 cm^{-1}. Anal. Calcd for $C_7H_4BrIN_2O$: C, 24.81; H, 1.19; H, 8.26; Br, 23.58; I, 37.44. Found: C, 24.62; H, 1.03; N, 8.01; Br, 23.94; I, 37.58.

4-Chloro-6-methoxy-5-[(trimethylsilyl)ethynyl]pyrimidine (17a). A solution of **15a** (500 mg, 2.03 mmol) in THF (20 mL) was cooled in a dry ice–acetone bath under N_2, and a hexane solution of *n*-butyllithium (2.2 M, 0.93 mL, 2.05 mmol) was added. This was stirred for 5 min at 78 °C, quenched by addition of $(CH_3)_3SiCl$ (0.38 mL, 3.00 mmol), and allowed to warm for ca. 5 min. Aqueous 0.1 M HCl (10 mL) was added, the layers were separated, the aqueous phase was extracted with ether (20 mL), and the combined organics were dried ($MgSO_4$) and evaporated to give 472 mg (97%) of crude product as a yellow oil. An analytical sample was obtained by Kugelrohr distillation, but this results in extensive decomposition in the pot and is not suitable for general purification: bp ~ 100 °C (1.0 mm); ^1H NMR ($CDCl_3$) δ 0.34 (s, 9 H, $Si(CH_3)_3$), 4.04 (s, 3 H, OCH_3), 8.39 (s, 1 H, pyrimidine CH); MS (10 eV), *m/e* (relative intensity) 242 (15), 240 (44), 227 (37), 225 (100). Anal. Calcd for $C_{10}H_{13}ClN_2OSi$: C, 49.88; H, 5.44; N, 11.63; Cl, 14.72. Found: C, 50.10, H, 5.16; N, 11.70; Cl, 14.46.

4-Bromo-6-methoxy-5-[(trimethylsilyl)ethynyl]pyrimidine (17c) and 4-Iodo-6-methoxy-5-[(trimethylsilyl)ethynyl]pyrimidine (17b). *n*-Butyllithium (2.2 M in hexane) was allowed to react with **15b** as described in Table I. After chromatography, the coeluting mixture of **17b** and **17c** was collected: ^1H NMR ($CDCl_3$) δ 0.30 (s, 5.4 H, $Si(CH_3)_3$, **17c**), 0.31 (s, 3.6 H, $Si(CH_3)_3$, **17b**), 4.04 (s, 1.2 H, OCH_3, **17b**), 4.06 (s, 1.8 H, OCH_3, **17c**), 8.33 (s, 0.4 H, pyrimidine CH, **17b**), 8.41 (s, 0.6 H, pyrimidine CH, **17c**).

Assignments were made by comparison with a fairly pure sample of **17c** obtained by allowing the mixture of **17b** and **17c** to react with excess (trimethylsilyl)acetylene as described in the following paragraph, but with reisolation of the unreacted **17c** at partial completion.[19] This sample of **17c** gave the following in addition to the ^{1}H NMR signals listed above: MS (10 eV), *m/e* (relative intensity) 286 (39), 284 (37), 271 (99), 269 (100). Anal. Calcd for $C_{10}H_{13}BrN_2OSi$: C, 42.11; H, 4.59; N, 9.82; Br, 28.02. Found: C, 44.56; H, 4.91; N, 9.56; Br, 28.22.

4,5-Diethynyl-6-methoxypyrimidine (19). A solution of **15b** (5.00 g, 14.8 mmol) in THF was cooled to −78 °C under N_2, and 7.39 mL of 2.2 M *n*-butyllithium was added. The reaction mixture was stirred for 5 min, and then $(CH_3)_3SiCl$ (2.60 mL, 20.0 mmol) was added. After additional stirring for 15 min, the reaction mixture was allowed to warm to room temperature, and 50 mL of 0.1 M HCl was added. The layers were separated, the aqueous portion was extracted with ether (2 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and evaporated to a brown oil. This residue was flushed with Ar, $(Ph_3P)_2PdCl_2$ (250 mg, 0.25 mmol) and CuI (250 mg, 1.25 mmol) were added, and Et_3N (30 mL) containing $HC{\equiv}CSi(CH_3)_3$ (10 mL, 71 mmol) was added by syringe. After being stirred under Ar at 20 °C for 22 h, the reaction mixture was evaporated, dissolved in 10 mL of $CHCl_3$, and passed through a 250-g silica gel column (elution with $CHCl_3$). All material beginning with a fluorescent compound and ending when a dark solution began to elute was collected and evaporated to a dark oil. This was dissolved in CH_3OH (100 mL), 3.0 mL of 0.1 M NaOH was added, and the reaction mixture was stirred at room temperature for 20 min. The reaction mixture was evaporated to a semisolid, dissolved in ether (200 mL), and evaporated onto silica gel. This was dry loaded onto a 200-g silica gel column packed in 20% ether–petroleum ether and eluted with the same solvent. The major component (R_f 0.55; TLC with 50% ether–petroleum ether) was collected by evaporation (≤30 °C) of the appropriate fractions to give pure **19** as a heat-sensitive solid (stable at −20 °C for several months): ^{1}H NMR ($CDCl_3$) δ 3.61 (s, 1 H, C≡CH), 3.75 (s, 1 H, C≡CH), 4.16 (s, 3 H, OCH_3), 8.70 (s, 1 H, pyrimidine CH); MS (10 eV), *m/e* (relative intensity) 158 (100), 103 (50); IR (mineral oil) 3240, 2100, 1555, 1530, 1315, 1060, 850, 800 cm^{-1}. Anal. Calcd for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.02; H, 3.86; N, 17.25.

6,7-Bis(trimethylsilyl)-4-methoxy-1,3-diazabiphenylene (20). A solution of bis(trimethylsilyl)acetylene (50 mL) in xylenes (50 mL) was warmed to reflux under a stream of argon. To this was added $CpCo(CO)_2$ (2.0 mL) followed by a solution of **19** (0.50 g, 3.2 mmol) in xylenes (50 mL). The reaction was stirred at reflux under irradiation by a 250-W sunlamp for 10 min and then opened to the air and allowed to cool to room temperature. This was evaporated onto a small amount of silica gel and dry-loaded onto a 200 g silica gel column. Elution with 10% ether–petroleum ether provided a pale yellow solid product: 0.58 g (56%); R_f 0.13 (TLC, 10% ether–petroleum ether). Two recrystallizations (EtOH–H_2O) afforded an analytical sample: mp 95.5–96 °C; ^{1}H NMR (CCl_4) δ 0.40 (s, 18 H, $Si(CH_3)_3$), 3.89 (s, 3 H, OCH_3), 6.97 (s, 1 H, benzene ring CH), 7.11 (s, 1 H, benzene ring CH), 8.17 (s, 1 H, pyrimidine ring CH); ^{13}C NMR ($CDCl_3$) δ 1.95 (q), 2.02 (q), 54.8 (q), 123.8 (d), 125.1 (d), 127.7 (s), 148.1 (s), 149.7 (s), 150.4 (s), 152.6 (s), 156.0 (s), 158.5 (d), 183.4 (s); MS (10 eV), *m/e* (relative intensity) 328 (66), 313 (33), 199 (39), 171 (88), 158 (98), 103 (100), 76 (31), 74 (33), 73 (26); IR (mineral oil) 1650, 1575, 1550, 1310, 1245, 1020, 850, 760 cm^{-1}; UV (EtOH) λ_{max} 262 nm (log ε 4.56), 314 (3.40), 328 (3.61), 344 (3.66). Anal. Calcd for $C_{17}H_{24}N_2OSi_2$: C, 62.14; H, 7.36; N, 8.53. Found: C, 62.16; H, 7.15; N, 8.73.

4-Methoxy-6-(trimethylsilyl)-1,3-diazabiphenylene (25). To a solution of **20** (70 mg, 0.21 mmol) in 25 mL of pentane was added CF_3SO_3H (0.14 mL). The resulting red, heterogeneous reaction mixture was stirred vigorously for 2 min, pyridine (0.3 mL) was added, and stirring was continued until all of the red color disappeared. The salt was removed by filtration, and the filtrate was evaporated and chromatographed on a small silica gel column (elution with 50% ether–petroleum ether). The product was obtained as a yellow oil: 37 mg (68%); R_f 0.41 (TLC, 50% ether–petroleum ether); ^{1}H NMR (CCl_4) δ 0.26 (s, 9 H, $Si(CH_3)_3$), 3.90 (s, 3 H, OCH_3), 6.75–7.05 (m, 3 H, benzene ring CH), 8.13 (s, 1 H, pyrimidine CH); MS (10 eV), *m/e* (relative intensity) 256 (100), 241 (84); HREIMS, calcd for $C_{14}H_{16}N_2OSi$ *m/e* 256.1032, found *m/e* 256.1035.

4-Methoxy-1,3-diazabiphenylene (26). A solution of **20** (50 mg, 0.15 mmol) in 10 mL of pentane was stirred vigorously with 0.2 mL of CF_3SO_3H for 2.5 h, and then pyridine (0.4 mL) was added. The reaction mixture was shaken until all of the red color had disappeared and then filtered to remove the salt. The filtrate was evaporated onto a small amount of silica gel and dry-loaded onto a silica gel column packed in 10% ether–petroleum ether. Elution with the same solvent provided product: 21 mg (75%); mp 70–73 °C; R_f 0.67 (TLC, 75% ether–petroleum ether); ^{1}H NMR (CCl_4) δ 3.90 (s, 3 H, OCH_3), 6.60–6.95 (m, 4 H, benzene ring CH), 8.17 (s, 1 H, pyrimidine ring CH); MS (10 eV), *m/e* (relative intensity) 184 (100), 157 (31), 114 (28); HREIMS, calcd for $C_{11}H_8N_2O$ *m/e* 184.0637, found *m/e* 184.0635.

6,7-Bis(trimethylsilyl)-1,3-dimethoxyisoquinoline (27a). A solution of **20** (100 mg, 0.30 mmol) and CF_3COOH (0.05 mL, 0.67 mmol) in MeOH (50 mL) was stirred at room temperature for 1.25 h and then evaporated to dryness. A ^{1}H NMR spectrum of this crude material indicated that the reaction had proceeded quantitatively to product. The residue was recrystallized twice from EtOH–H_2O to yield an analytical sample: 75 mg (75%); mp 100–100.5 °C; ^{1}H NMR (CD_3OD) δ 0.39 (s, 9 H, $Si(CH_3)_3$), 0.40 (s, 9 H, $Si(CH_3)_3$), 3.95 (s, 3 H, OCH_3), 4.09 (s, 3 H, OCH_3), 6.25 (s, 1 H, pyridine ring CH), 7.93 (s, 1 H, benzene ring CH), 8.38 (s, 1 H, benzene ring CH); ^{13}C NMR ($CDCl_3$) δ 1.43 (q), 1.65 (q), 53.6 (q), 54.2 (q), 90.8 (d), 114.2 (s), 130.7 (d), 132.4 (d), 139.27 (s), 139.30 (s), 147.9 (s), 159.7 (s), 160.1 (s); MS (10 eV), *m/e* (relative intensity) 333 (100), 318 (28), 302 (40). Anal. Calcd for $C_{17}H_{17}NO_2Si_2$: C, 61.21; H, 8.16; N, 4.20. Found: C. 61.13; H, 8.18; N, 4.31.

The conversion of **27a** to **27b** was effected under the same conditions as described above for **20** → **26**. Compound **27b** was demethylated with $(CH_3)_3SiI$ in CH_3CN to the known homophthalimide **8**[20] and was compared directly (TLC, IR, ^{1}H NMR, mp, mmp) with an authentic sample.

4-Cyano-1-methoxyisoquinoline (33). To a solution of $NaOCH_3$ in CH_3OH (23 mg of Na in 3 mL) was added compound **9** (25 mg, 0.13 mmol). The clear solution obtained was stirred at 20 °C for 2 h. The reaction mixture was then diluted with H_2O (15 mL) and extracted with $CHCl_3$ (3 × 10 mL). The $CHCl_3$ extract was washed with H_2O, dried ($MgSO_4$), and evaporated to a colorless solid that was purified by preparative TLC: yield 20 mg (81%); mp 110–111 °C; IR (KBr) 2230, 1570, 1450, 1380, 1220, 1090, 960, 760 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.66–7.70 (dd, 1 H, Ar H), 7.84–7.88 (dd, 1 H, Ar H), 8.05–8.08 (d, 1 H, Ar H), 8.31–8.33 (d, 1 H, Ar H), 8.45 (s, 1 H, 3 H); ^{13}C NMR (90 MHz, $CDCl_3$) 54.7 (q, OCH_3), 99.8 (s), 116.8 (s, CN), 118.8 (s), 123.9 (d), 124.8 (d), 128.4 (d), 132.6 (d), 135.9 (s), 147.5 (d), 163.4 (s); MS (10 eV), *m/e* (relative intensity) 184 (M^+, 100), 183 (29), 155 (24), 154 (16); HREIMS, exact mass calcd for $C_{11}H_8N_2O$ (M^+) *m/e* 185.0637, found *m/e* 184.0629.

1-Chloro-4-cyanoisoquinoline[23] was converted to **33** as an authentic sample under similar $NaOCH_3/CH_3OH$ conditions, identical with the product from **9** (IR, ^{1}H NMR, mp, and mmp).

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