Synthesis and Reactions of Some Heterocyclic Azacyanines[1]

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Received October 16, 2000

The one-step reaction of some amino-substituted heterocycles with diiodomethane to give azacyanines is reported. This useful reaction is of wider application than initially reported and includes the synthesis of new substituted pyrido-, isoquino-, benzimadazo-, and benzothiazoazacyanines **7**. Furthermore, treatment of these azacyanines with base generally affects a facile opening of the dihydrotriazinium ring resulting in the formation of new heterocycles **10**, **11**, and **12,** which would be difficult to prepare by other means. This reaction takes an additional direction in the case of halo-substituted azacyanines **7b/c/d** where treatment with base gives rise to new interesting derivatives of dipyridotriazines **14b/c/d**.

Introduction

As a part of our interest[2] in developing small molecule drugs capable of modulating chloride-selective ion channels and being cognizant of Becq's recent report[3] that benzo[*c*]quinolizinium derivative **MPB-07** activates wild-type CFTR (the cystic fibrosis transmembrane conductance regulator membrane protein), and in view of the dipolar nature and structural similarities between **MPB-07** and azacyanines (see the Experimental Section for systematic naming with 1,3,5-triazine as the base component), we decided to explore further the method of Munavalli, Hsu, and Poziomek for the preparation of azacyanines. The interest of these authors in the synthesis of polymers with superconducting properties led them to prepare azapyridocyanines **2** with the intention of coupling these moieties to conjugated polymeric backbones.[4] Indeed, a few derivatives of *N*,*N*-methylene-2,2′-azapyridocyanines (**2**) were prepared by the reaction of 2-aminopicolines (**1**) and diiodomethane (Figure 1). Although this reaction constituted a one-step preparation of these otherwise difficult to prepare heterocycles, the authors reported that reactions fail if the pyridine ring carries electron-withdrawing groups such as bromo or nitro groups or if "2-amino-substituted five-membered diheterocyclic compounds" are used. In view of these cited difficulties, the reaction appeared to be of limited application. However, we demonstrate below that this reaction is of a wider scope than previously reported.

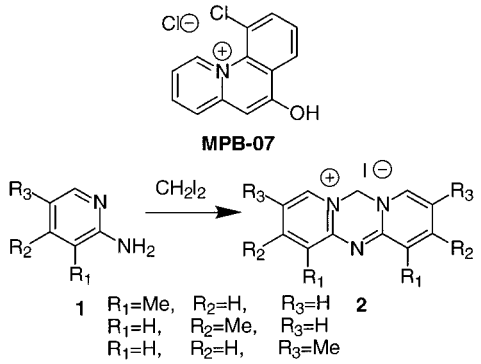

Figure 1.

Results and Discussion

Azacyanine Preparation. The rationale behind our work was to explore the reaction of diiodomethane with electron rich (π-sufficient) 2-aminoheterocycles first; our first choice was five membered heterocycles. Indeed, the reaction of 1-methyl-2-aminobenzimidazole with diiodomethane proceeded smoothly (refluxing acetonitrile) to give azacyanine **3** in 92% yield (Scheme 1). Likewise, 2-aminobenzothiazole and 6-methoxybenzothiazole gave the corresponding azacyanines **4** and **5**.[5]

Having been successful in extending this reaction to some five-membered 2-aminoheterocycles, we turned our attention to six membered (π-deficient) heterocycles with electron withdrawing groups—namely chloro-, bromo-, and even dibromo-2-aminopyridines. We were gratified to find these precursors react with diiodomethane to yield azacyanines **7a**−**e** albeit in low yields and at relatively elevated temperatures (Scheme 2). As expected, the reaction of **6f**, which is relatively electron-rich, yielded **7f**. The reaction proceeds satisfactorily with 1-aminoiso-

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(1) Dedicated to Professor Costas H. Issidorides on the occasion of his 80th birthday.

(2) Eda, M.; Kurth, M. J.; Nantz, M. H. *J. Org. Chem.* **2000**, *65*, 5131.

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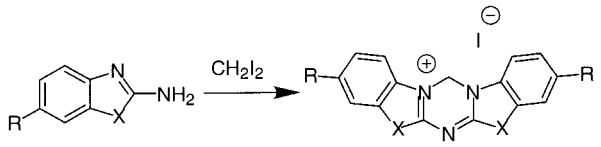
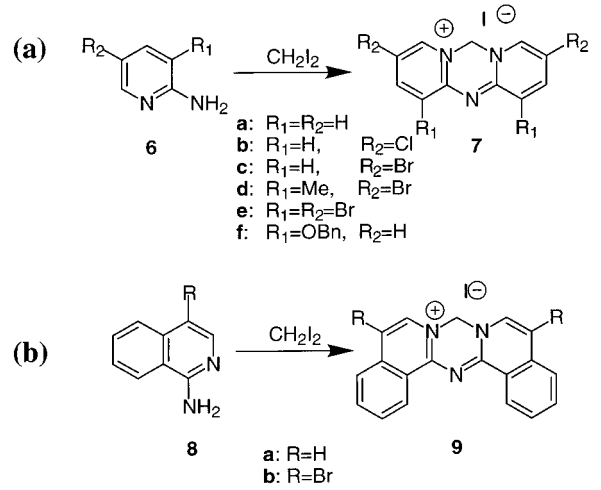
10.1021/jo001484k CCC: $20.00
Published on Web 02/01/2001

Scheme 1. Reaction of π-Sufficient 2-Aminoheterocycles with Diiodomethane



Scheme 2. Reaction of (A) 2-Aminopyridines with Diiodomethane and (B) Reaction of 1-Aminoisoquinolines with Diiodomethane



quinoline **8a** and 1-amino-4-bromoisoquinoline **8b** to give **9a** and **9b**, respectively.

All these azacyanines display a methylene singlet around δ 6.2 ppm (2H) in the ^{1}H NMR and δ 60 ppm in the ^{13}C NMR. The structure of azacyanine **9b** was confirmed by X-ray crystallography. The molecule has a 2-fold axis of symmetry passing through N(1) and C(10). The closest iodine−nitrogen approach is depicted in Figure 2.

Azacyanine Transformations. While the chemistry of azacyanines is not well explored, the triazinium structure of the central ring in these heterocycles should be susceptible to nucleophilic attack. Indeed, reaction with hydroxide ions is instantaneous at room temperature provided that the azacyanine is in solution. The extent of solubility of these interesting heterocycles is limited in most common organic solvents. However, a slurry in warm 10% methanolic KOH solution suffices and an immediate ring opening of the triazinium ring takes place to yield the corresponding 1-(2-imino-3-methyl-2,3-dihydrobenzoimidazol-1-ylmethyl)-3-methyl-1,3-dihydrobenzoimidazol-2-one **10**, and 1-(2-imino-2*H*-pyridin-1-ylmethyl)-1*H*-pyridin-2-one **11** (Scheme 3). Furthermore, **9a** gave, in high yield, **12**. The X-ray structure of **10** was determined (Figure 3). The structure shows the expected disorder between the 2-one and 2-imino groups due to the pseudo-2-fold axis of symmetry at C(1). It should be noted that **7f** was unaffected upon treatment with base. The resistance of **7f** to react with methanolic aqueous base under these conditions could be due to a combination of steric and electronic factors.

It is interesting to report that this reaction takes an additional predominant path in the case of halo substituted (X = Br, Cl) pyridoazacyanines and results in the formation of unexpected products—namely, **14b**,**c**,**d**. The structure of **14b** was confirmed by X-ray crystallography (Figure 4). The elimination of HX and the introduction of a carbonyl group at position 4 may be rationalized by the following mechanism (Scheme 4).

This mechanism involves addition of hydroxide ion to the double bond of the β-halo enamine (C_4 of structure **7**). While other mechanisms can be postulated, the depicted mechanism can explain the lack of formation of product from hydroxide attack at C_2 or C_{10}. Furthermore, this mechanism is consistent with the exclusive formation of **15** from **9b** (Scheme 5) because attack by a hydroxide ion at C_4 is not favored for it leads to an ortho quinoidal

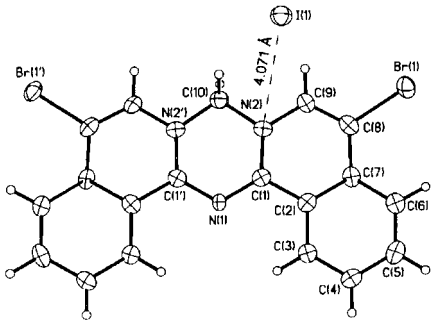


Figure 2. ORTEP diagram of **9b**.

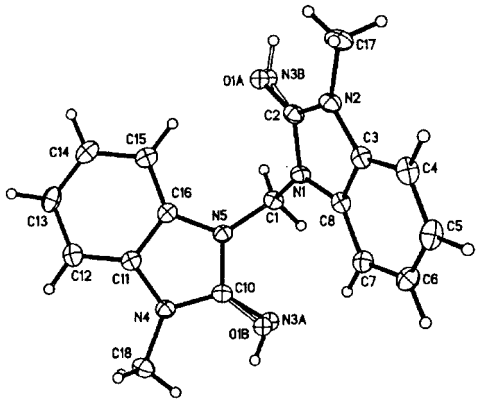
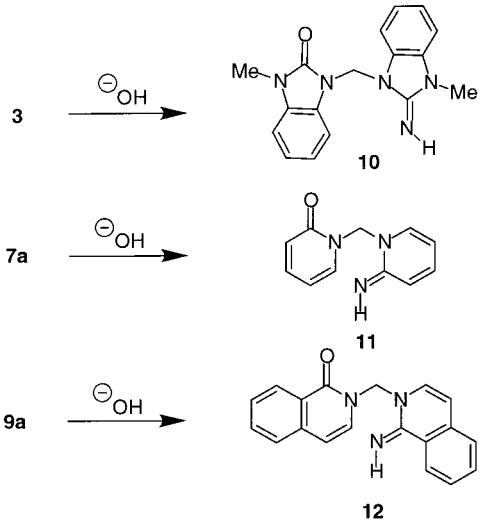


Figure 3. ORTEP diagram of **10**.

Scheme 3. Ring Opening of Azacyanines



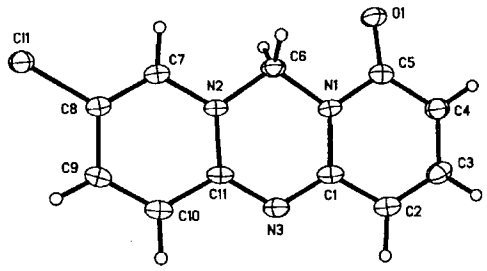
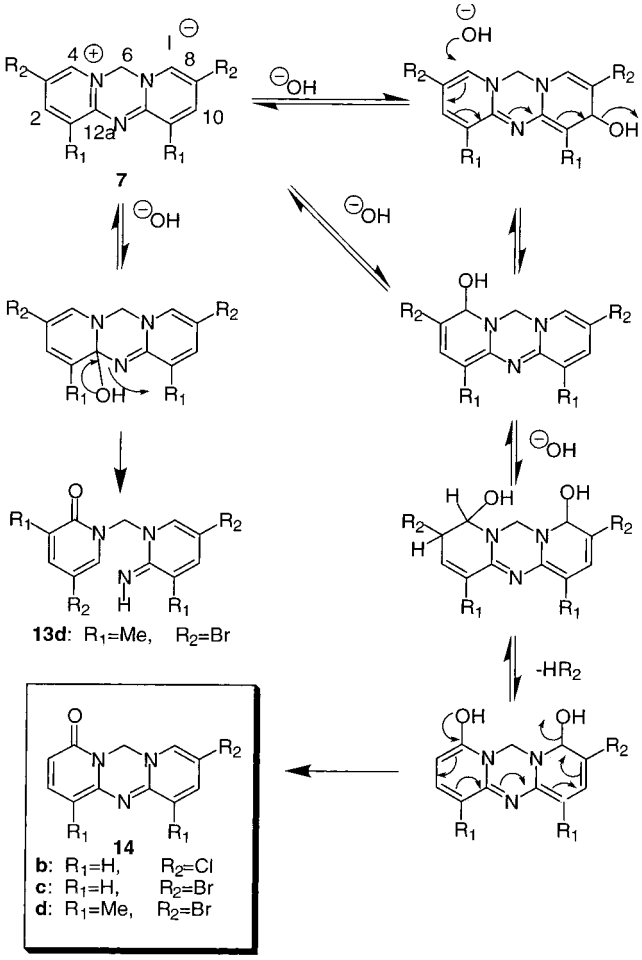
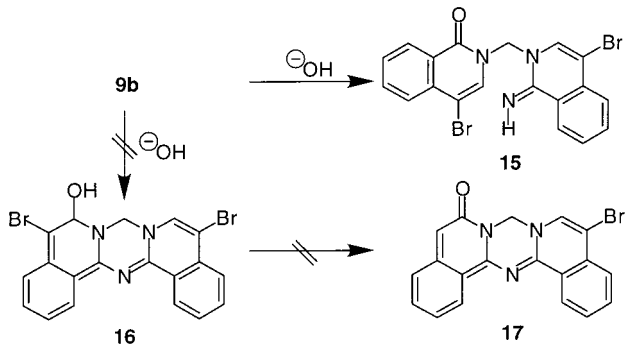


Figure 4. ORTEP diagram of **14b**.

Scheme 4. Proposed Mechanism for the Reaction of Halo-Substituted Azacyanines with Base[7]

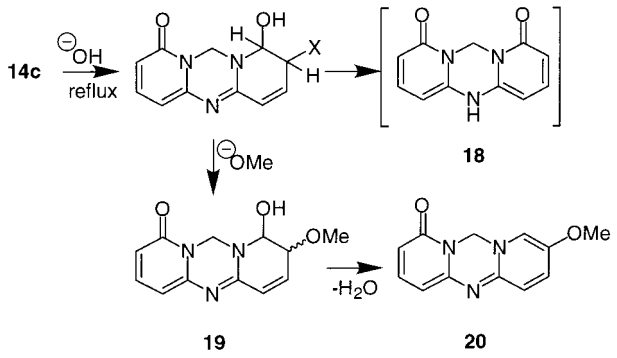


Scheme 5. Reaction of Azacyanine 9b with KOH



benzene system (**16**), and consequently no **17** can be formed.[6] Therefore, base attacks position C_{12a} and leads to **15** as the only product (86%) from **9b**.

Scheme 6. Reaction of Halo-Substituted Azacyanines with Methanolic KOH



If this assumption is operative, it was envisaged that product **14**, which contains a second β-halo enamine moiety, should also undergo a dehydrohalogenation upon further treatment with hydroxide ion. Heating of **14c** in 10% methanolic KOH and 4% water at reflux temperature led to the formation of two major products; one of which was **20** and the second was photolabile product **18**, which decomposed on further workup. It is established that thymine and uracil undergo $2\pi + 2\pi$ or $4\pi + 4\pi$ photochemical reactions, and it would not be surprising to expect **18** to polymerize by photochemical addition reactions at two sites of this structure.[8]All the azacyanines reported here are highly fluorescent and range from yellow to orange in color with the exception of **3**, which has a straw color. Absorption and fluorescence data for 10 azacyanines (**3**, **5**, **7a**−**f**, and **9a**/**b**) and three hydrolysis products (**13d**, **14c**, and **15**) are presented in Table 1.

We next turned our attention to further reactions of this interesting new heterocyclic system with test applications of the Suzuki reaction. We initially reacted **14b** with the standard palladium coupling conditions and

(6) Jones, D. W. *J. Chem. Soc. C* **1969**, *13*, 1729.

(7) We also subjected **7b** to NaOD/CD_3OD and were able to obtain deuterated **14b**.

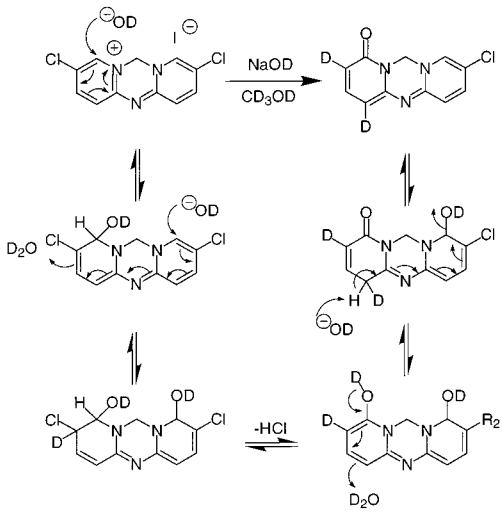


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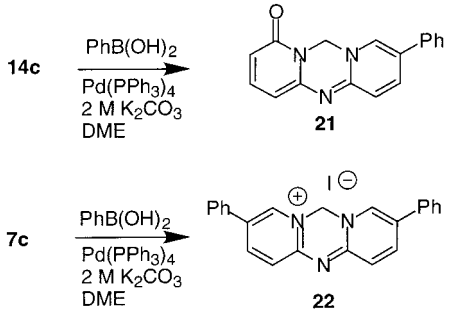
Table 1. Absorption and Emission Data for Azacyanines and Hydrolysis Products[a]

entry	λ_{max}	ϵ	log ϵ	$F\lambda_{max}$
3	339	61 996	4.79	376
5	405	43 517	4.64	470
7a	412	61 062	4.79	448
7b	433	14 480	4.16	473
7c	434	17 717	4.25	476
7d	436	17 166	4.23	502
7e[b]	449	15 079	4.17	494
7f	450	30 272	4.48	487
9a	453	38 626	4.59	474
9b	457	19 347	4.29	502
13d[c]	310	8216	3.91	*d*
14c	436	14 962	4.18	*d*
15[c]	293	9390	3.97	*d*

[a] Measured in MeOH unless otherwise indicated. [b] Measured in DMSO. [c] Measured in CH_3CO_2H. [d] Not detectable.

Scheme 7. Suzuki Reactions on Azacyanines



found the reaction did not proceed to completion. This was not suprising since aryl chlorides are known to be sluggish toward oxidative addition to Pd(0).[9] However, when **14c** was employed in the Suzuki reaction, it gave **21** in 65% yield (Scheme 7). We next employed the azacyanine salt **7c** and found that it gave **22** in good yield. Thus, preliminary Suzuki reaction experiments show that these azacyanines can be elaborated to new derivatives within this class of heterocycles.

In conclusion, it has been demonstrated that the Munavalli method for the synthesis of azacyanine is of a wider scope and these compounds undergo a number of useful reactions that result in the convenient formation of new heterocycles that are otherwise difficult to prepare.

Experimental Section

General Experimental Procedures. Unless otherwise noted, starting materials were obtained from commercial suppliers and used as received. Melting points were determined using an Electrothermal 9100 apparatus and are uncorrected. Infrared spectra were taken neat (solids) on a refractive spectrophotometer. ^{1}H NMR was measured in $CDCl_3$, CD_3CO_2D, or DMSO-d_6 at 400 or 300 MHz, and ^{13}C NMR was measured at 100 or 75 MHz. Elemental analyses were performed by Midwest Microlabs, Indianapolis, IN. UV−vis spectra were taken using an UVIKON 9410; fluorescence spectra were taken using a Perkin -Elmer 5050. Silica gel chromatography was performed according to the method of Still.[10]

General Method for the Preparation of Azacyanines. The specific 2-aminopyridine, 1-methyl-2-aminobenzimidazole, 2-aminobenzothiazole, or 1-aminoisoquinoline was dissolved in the cited solvent, and an excess of diiodomethane was added to the solution. The mixture was refluxed for the time indicated in each case. The progress of the reaction was monitored by the evolution of ammonia. The azacyanine (product) that precipitated out of the reaction mixture was collected after the reaction mixture was cooled to room temperature and was washed with CH_2Cl_2 and acetone. The systematic nomenclature of these azacyanines leads to referring to them as having a 1,3,5-triazine as the base component.

7*H*-1,13-Dimethyldibenzoimidazolo[1,2-*a*:2′,1′-*d*][1,3,5]-triazin-6-ium (Azacyanine 3).[5] The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: 1-methyl-1*H*-benzoimidazol-2-ylamine (1.5 g, 10.0 mmol), acetonitrile (20 mL) under a blanket of nitrogen, and diiodomethane (3 g, 11.2 mmol) . The mixture was refluxed for 48 h to produce **3** (1.9 g, 4.6 mmol, 92%): mp 300 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.81, (s, 6H), 6.54 (s, 2H), 7.48 (m, 4H), 7.63 (m, 2H), 7.74 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 29.4, 57.4, 110.7, 111.7, 113.7, 124.9, 125.1, 128.0, 131.5; IR (neat) 1560, 1527, 1471, 731 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 339 (4.79); fluorescent Ex/nm ($F\lambda_{max}$/nm) 339 (376).

7*H*-Dibenzothiazolo[1,2-*a*:2′,1′-*d*][1,3,5]triazin-6-ium (azacyanine 4).[5] The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: benzothiazol-2-ylamine (600 mg, 4.0 mmol) was dissolved in 2-(2-ethoxyethoxy)ethanol (5 mL), and diiodomethane (2 g, 7.5 mmol) and refluxed for 4 min to produce **4** (190 mg, 0.4 mmol, 22%): mp 380−381 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.61 (s, 2H), 7.84 (m, 8H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 60.5, 93.9, 113.2, 123.9, 124.3, 126.7, 128.6, 136.0; IR (neat) 1503, 1454, 1377, 1327, 742 cm^{-1}].

7*H*-3,11-Dimethoxydibenzothiazolo[1,2-*a*:2′,1′-*d*][1,3,5]-triazin-6-ium (Azacyanine 5). The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: 6-methoxybenzothiazolylamine (1.8 g, 10.0 mmol), 2-(2-ethoxyethoxy)ethanol (3 mL), and diiodomethane (4 g, 15 mmol). The mixture was refluxed for 3 min to produce **5** (560 mg, 3 mmol, 62%): mp 334−336 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.87 (s, 6H), 6.56 (s, 2H), 7.42 (dd, J = 9, 2 Hz, 2H), 7.82 (d, J = 9, 2H), 7.86 (d, J = 2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.1, 60.50, 97.5, 108.4, 114.1, 125.3, 129.9, 158.0, 165.0; IR (neat) 1505, 1481, 1372, 1320, 807 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 299 (4.12), 405 (4.64); fluorescent Ex/nm ($F\lambda$max/nm) 405 (470). Anal. Calcd for $C_{17}H_{14}IN_3O_2S_2$; C, 42.24; H, 2.92; N, 8.69. Found: C, 42.05; H, 3.13; N, 8.67.

5-Bromo-3-methylpyridin-2-ylamine (6d).[11] To a solution of 3-methylpyridin-2-ylamine (11 g, 102 mmol) and HBr (48%, 100 mL) was added dropwise hydrogen peroxide (30 mL, 15%) in a 1 h period at 70 °C. The solution was stirred for an additional 1 h, after which time it was poured into an ice bath, basified, filtered, and recrystallized with hot hexane to afford orange crystals **6d** (11 g, 58.81 mmol 60%); mp 92−93 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.09 (s, 3H), 4.48 (s, 2H), 7.36 (d, J = 2 Hz, 1H), 7.97 (d, J = 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4, 108.4, 118.8, 139.9, 146.1, 156.1; IR (neat) 3183, 3179, 2969, 1675, 1476, 841, 766, cm^{-1}.

6*H*-Dipyrido[1,2-*a*:2′,1′-*d*][1,3,5]triazin-5-ium (Azacyanine 7a).[5] The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: 2-aminopyridine (940 mg, 10 mmol), acetonitrile (30 mL), and diiodomethane (4 g, 15 mmol). The mixture was refluxed for 1 h to produce **7a** (390 mg, 1.2 mmol, 25%): mp 256−257 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.12 (s, 2H), 7.16 (m, 4H), 7.99 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 64.5, 116.2, 120.9, 137.6, 143.6, 151.6; IR (neat) 1589, 1490, 1330, 841 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 281 (4.59), 322 (4.35), 412(4.79); fluorescent Ex/nm ($F\lambda_{max}$/nm) 412 (448).

3,9-Dichloro-6*H*-dipyrido[1,2-*a*:2′,1′-*d*][1,3,5]triazin-5-ium (Azacyanine 7b).[5] The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: 2-amino-5-chloropyridine (8.6 g, 67

(9) (a) Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972. (b) Suzuki, A. *Pure and Appl. Chem.* **1985**, *57*, 1749. For the use of Ar−Cl in Suzuki coupling, see: (a) Buchwald, S. L.; Fox, J. M. *Strem Chem.* **2000**, *18*, 1. (b) Bei, X.; Turner, H. W.; Weinberg, W. H.; Guram, A. S. *J. Org. Chem.* **1999**, *64*, 6797 and references therein.

(10) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *14*, 2923.

(11) Dunn, A. D.; Currie, A.; Hayes, L. E. *J. Prakt. Chem.* **1989**, *331*, 369.

mmol), 2-(2-ethoxyethoxy)ethanol (8 mL), and diiodomethane (35 g, 131 mmol). The mixture was refluxed for 1 h to produce **7b** (4.5 g, 11.7 mmol, 36%): mp 323−324 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.35 (s, 2H), 7.29 (m, 2H), 8.12 (m, 2H), 8.48 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 65.0, 121.9, 122.5, 136.1, 144.0, 150.6; IR (neat) 1501, 1492, 1331, 1325, 847 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 289 (4.03), 339 (3.59), 433 (4.16); fluorescent Ex/nm ($F\lambda_{max}$/nm) 433 (473)].

3,9-Dibromo-6*H*-dipyrido[1,2-*a*:2′,1′-*d*][1,3,5]triazin-5-ium (Azacyanine 7c).[5] The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: 2-amino-5-bromopyridine (10 g, 58 mmol), 2-(2-ethoxyethoxy)ethanol (30 mL), and diiodomethane (30 g, 113 mmol). The mixture was refluxed for 1 h to produce **7c** (3.5 g, 7.5 mmol, 26%): mp 300 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.31 (s, 2H), 7.20 (d, J = 9 Hz, 2H), 8.17 (dd, J = 9, 2 Hz, 2H), 8.48 (d, J = 2 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 65.4, 109.1, 123.1, 138.6, 146.7, 151.1; IR (neat) 1500, 1490, 1331, 1324, 1117, 827 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 287 (4.15), 434 (4.25); fluorescent Ex/nm ($F\lambda_{max}$/nm) 434 (476).

3,9-Dibromo-1,11-dimethyl-6*H*-dipyrido[1,2-*a*:2′,1′-*d*][1,3,5]triazin-5-ium (Azacyanine 7d). The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: 5-bromo-3-methylpyridin-2-ylamine **6d** (2 g, 12 mmol), 2-(2-ethoxyethoxy)ethanol (2 mL), and diiodomethane (6 g, 23 mmol). The mixture was refluxed for 1 h to produce **7d** (570 mg, 1.2 mmol, 20%): mp 350−351 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.32 (s, 6H), 6.28 (s, 2H), 8.16 (s, 2H), 8.33 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 17.1, 65.4, 108.7, 132.5, 135.9, 144.7, 150.2; IR (neat) 1494, 1336, 1316, 1289, 836, cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 284 (4.10), 436 (4.23); fluorescent Ex/nm ($F\lambda_{max}$/nm) 436 (502). Anal. Calcd for $C_{13}H_{12}Br_2IN_3$; C, 31.42; H, 2.43; N, 8.46. Found: C, 31.39; H, 2.44; N, 8.39.

1,3,911-Tetrabromo-6*H*-dipyrido[1,2-*a*:2′,1′-*d*][1,3,5]triazin-5-ium (Azacyanine 7e).[5] A 25 mL flask equipped with a magnetic stir bar was charged with 2-amino-3,5-dibromopyridine (1.2 g, 5 mmol) and diiodomethane (3 g, 11 mmol) as solvent. Under a blanket of N_2, this solution was refluxed to 240 °C for 15 min. An additional amount of diiodomethane (1 g, 5 mmol) was then added via syringe to this hot solution, and the refluxing was continued for 30 min, after which time the solution was cooled to room temperature. The paste was filtered and washed with CH_2Cl_2, acetone, and MeOH and dried to produce a red solid **7e** (520 mg, 0.840 mmol, 35%): mp 300−301 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.34 (s, 2H), 8.59 (d, J = 2 Hz, 2H), 8.79 (d J = 2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 66.3, 109.0, 117.5, 138.6, 148.9, 149.4; IR (neat) 1493, 1475, 1331, 1309, 1190, 833 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (DMSO) 296 (4.48), 371 (4.22), 449 (4.18); fluorescent Ex/nm ($F\lambda_{max}$/nm) 449 (494).

1,11-Benzyloxy-6*H*-dipyrido[1,2-*a*:2′,1′-*d*][1,3,5]triazin-5-ium (Azacyanine 7f).[5] The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: 3-benzyloxy-pyridin-2-ylamine (2 g, 10 mmol), 20 mL of dioxane, and diiodomethane (3 g, 12 mmol). The mixture was refluxed for 48 h to produce **7f** (360 mg, 0.70 mmol, 14%): mp 250−252 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.29 (s, 4H), 6.45 (s, 2H), 7.16 (dd, J = 11, 9 Hz, 2H), 7.35 (m, 6H), 7.47 (m, 4H), 7.65 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 70.0, 76.2, 121.3, 127.4, 132.9, 133.5, 133.9, 134.2, 141.3, 150.7, 153.6; IR (neat) 1508, 1502, 1351, 1282, 1253, 743, 730 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 281 (3.98), 321 (4.05), 450 (4.48); fluorescent Ex/nm ($F\lambda_{max}$/nm) 450 (487).

1-Amino-4-bromoisoquinoline (8b).[12] A 250 mL round-bottom flask equipped with a magnetic stir bar was charged with 1-aminoisoquinoline (1 g, 7 mmol) and acetic acid (35 mL). To this was added dropwise a solution of bromine (1 g 7 mmol) in CCl_4 (70 mL) during a 45 min period, and the solution was stirred for an additional 1 h until TLC showed no starting material. The solution was poured onto 250 mL of ice, basified with KOH solution, and stirred for 1 h. The aqueous layer was separated and extracted with 3 × 50 mL of chloroform and then with benzene. The combined organic layers were dried with Na_2SO_4, filtered, concentrated, and recrystallized from benzene to give **8b** (1.35 g, 6.05 mmol, 88%): mp 152−153 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.57 (s, 2H), 7.50 (m, 1H), 7.69 (m, 2H), 8.02 (d, J = 8 Hz, 1H), 8.07 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.6, 119.2, 123.1, 126.8, 127.2, 131.5, 135.7, 142.7, 155.8; IR (neat) 3473, 3292, 3074, 1575, 1556, 1425, 1285, 897 cm^{-1}.

8*H*-Diisoquinolino[1,2-*a*:2′,1′-*d*][1,3,5]triazin-7-ium (Azacyanine 9a).[5] The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: isoquinolin-1-ylamine (720 mg, 5 mmol), diiodomethane (3.6 g, 13 mmol), and 2-(2-ethoxyethoxy)ethanol (2 mL), were refluxed for 3 min to produce **9a** (650 mg, 12.59 mmol, 65%): mp 320 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.61 (s, 2H), 7.64 (dd, J = 10, 1 Hz, 2H), 7.85 (m, 4H), 8.00 (m, 4H), 8.97 (dd, J = 11, 1 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 65.1, 115.6, 122.9, 126.9, 126.9, 129.3, 129.6, 134.8, 136.7, 151.2; IR (neat) 1559, 1523, 1427, 788 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 321 (4.18), 453 (4.59); fluorescent Ex/nm ($F\lambda_{max}$/nm) 453 (474).

5,11-Dibromo-8*H*-diisoquinolino[1,2-*a*:2′,1′-*d*][1,3,5]-triazin-7-ium (Azacyanine 9b). The general procedure for the preparation of azacyanines was employed with the following reagents and quantities: bromoisoquinoline **8b** (260 mg, 1 mmol), 2-(2-ethoxyethoxy)ethanol (1 mL), and diiodomethane (870 mg, 320 mmol). The mixture was refluxed to produce **9b** (100 mg, 1.15 mmol, 30%): mp 380−381 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.51 (s, 2H), 8.14 (m, 6H), 8.43 (s, 2H), 9.16 (d, J = 8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 65.0, 110.3, 124.2, 126.7, 128.8, 131.3, 131.5, 135.9, 137.2, 151.8; IR (neat) 1613, 1583, 1295, 754, 496 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 457 (4.29); fluorescent Ex/nm ($f\lambda_{max}$/nm) 457 (502). Anal. Calcd for $C_{19}H_{12}Br_2IN_3$; C, 40.10; H, 2.13; N, 7.38. Found: C, 40.22; H, 2.24; N, 7.05.

General Method for the Reaction of Azacyanines with Base. The azacyanine (1−0.5 g scale) was mixed with 10% methanolic KOH (20 mL containing 2 mL of water). The slurry was magnetically stirred at room temperature, and the disappearance of the highly fluorescent starting material was monitored by TLC (3:7 MeOH/EtOAc). The product is not fluorescent and moves very slowly on TLC. Because of the limited solubility of the starting material, the slurry was stirred for 2−3 days at room temperature (or specified) after which the mixture was diluted with water and the resulting solid was collected by suction filtration, washed with water, dried, and recrystallized from CH_2Cl_2/MeOH.

1-(2-Imino-3-methyl-2,3-dihydrobenzoimidazol-1-ylmethyl)-3-methyl-1,3-dihydrobenzoimidazol-2-one (10). The general procedure for the reaction of azacyanines with base was employed with the following reagents and quantities: azacyanine **3** (650 mg, 1.56 mmol) was warmed to 50 °C for 2 d to yield **10** as shiny gray needles (410 mg, 1.33 mmol 86%): mp 256−258 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.31 (s, 3H), 3.44 (s, 3H), 5.00 (s, 1H), 6.03 (s, 2H), 6.76 (m, 1H), 6.92 (m, 1H), 6.99 (m, 2H), 7.07 (m, 2H), 7.52 (m, 1H), 7.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 27.7, 47.5, 105.9, 107.3, 108.5, 110.6, 121.2, 121.3, 121.7, 122.0, 128.2, 129.9, 130.2, 131.9, 154.4, 154.9; IR (neat) 3310, 1689, 1642, 1495, 1303, 1014, 900, 732 cm^{-1}. Anal. Calcd for $C_{17}H_{17}N_5O$; C, 66.43; H, 5.58; N, 22.79. Found: C, 66.65; H, 5.65; N, 22.89].

1-(2-Imino-2*H*-pyridin-1-ylmethyl)-1*H*-pyridin-2-one (11). The general procedure for the reaction of azacyanines with base was employed with the following reagents and quantities: azacyanine **7a** (650 mg, 1.6 mmol)was warmed to 50 °C for 2 d to yield **11** as shiny white needles (410 mg, 1.3 mmol 86%): mp 256−258 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67 (m, 1H), 5.93 (s, 2H), 6.13 (m, 1H), 6.22 (m, 1H), 6.54 (m, 1H), 6.68 (m, 1H), 7.32 (m, 1H), 7.66 (m, 1H), 8.29 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 60.5, 102.5, 105.3, 120.8, 121.4, 134.5, 139.1, 140.6, 140.7, 160.5, 163.7; IR (neat) 3680, 1659, 1650, 1056, 720 cm^{-1}.

2-(1-Imino-1*H*-isoquinolin-2-ylmethyl)-2*H*-isoquinolin-1-one (12). The general procedure for the reaction of azacya-

(12) Sanders, G. M.; van Dijk, M.; den Hertog, H. J. *Rec. Trav. Chim.* **1974**, *93*, 273.

nines with base was employed with azacyanine **9a (**400 mg, 10 mmol) for 4 h to produce **12** as white needles (290 mg, 9.49 mmol, 99%): mp 193−195 °C; ^{1}H NMR (300 MHz, CD_3CO_2D) δ 6.60 (s, 2H), 6.91 (d, J = 8 Hz, 1H), 7.34 (d, J = 8 Hz, 1H), 7.65 (m, 2H), 7.81 (m, 3H), 7.96 (m, 2H), 8.11 (d, J = 8 Hz, 1H), 8.43 (d, J = 8 Hz, 1H), 8.52 d, J = 8 Hz, 1H); ^{13}C NMR (75 MHz, CD_3CO_2D) δ 61.0, 109.9, 113.6, 118.7, 124.9, 125.7, 126.9, 128.0, 128.0, 128.1, 129.7, 130.4, 131.8, 134.2, 135.5, 136.4, 137.6, 155.2, 164.1; IR (neat) 3310, 1653, 1624, 1331, 1146, 752 cm^{-1}. Anal. Calcd for $C_{19}H_{15}N_3O$; C, 75.73; H, 5.02; N, 13.94. Found: C, 75.62; H, 5.03; N, 13.90.

5-Bromo-1-(5-bromo-2-imino-3-methyl-2*H*-pyridin-1-ylmethyl)-3-methyl-1*H*-pyridin-2-one (13d). The general procedure for the reaction of azacyanines with base was employed with azacyanine **7d** (0.429 g, 0.863 mmol). The mixture was warmed for 4 h to produce **13d** as white crystals (230 mg, 590 mmol, 69%): mp 239−242 °C; ^{1}H NMR (400 MHz, CD_3CO_2D): δ 2.15 (s, 3H), 2.31 (s, 3H), 6.41 (s, 2H), 7.55 (s, 1H), 7.82(s, 1H), 8.21 (s, 1H), 8.51 (s, 1H); ^{13}C NMR (100 MHz, CD_3CO_2D): δ 16.2, 16.9, 64.7, 101.3, 105.8, 126.7, 131.9, 135.2, 137.5, 142.9, 144.8, 153.9, 163.1; IR (neat) 3400, 1660, 1645, 1573, 1330, 1139, 886 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (CH_3CO_2H) 266 (2.67), 310 (3.91). Anal. Calcd for $C_{13}H_{13}Br_2N_3O$; C, 40.34; H, 3.39; N, 10.86. Found: C, 39.96; H, 3.34; N, 10.57.

General Method for the Reaction of Haloazacyanines 7b,c,d with Base. The haloazacyanine (0.5−2.0 g scale) was mixed with 10% methanolic KOH (20 mL containing 2 mL of water). The slurry was magnetically stirred at room temperature, and formation of the orange product with disappearance of the highly fluorescent starting material were monitored by TLC (7:3 MeOH: EtOAc). The reaction is normally finished within 2 h, however, warming the alcoholic solution (50 °C) leads to product in 5−10 min. The solution is diluted with water (80 mL) and extracted with CH_2Cl_2 (4 × 10 mL). The yellow orange CH_2Cl_2 solution is dried (Na_2SO_4), filtered, and evaporated to give an orange solid which was recrystallized from ethyl acetate.

9-Chloropyridin-4-one-6*H*-pyrido[6,1-*a*:2′,1′-*d*][1,3,5]triazine (14b). The general procedure for the reaction of haloazacyanines with base was employed with azacyanine **7b** (1 g, 2.63 mmol; 2 d) to produce **14b** (200 mg, 860 mmol, 33%): R_f = 0.25; mp 257−258 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (s, 2H), 5.91, (dd, J = 8, 1 Hz, 1H), 6.19 (dd, J = 9, 1 Hz, 1H), 6.75 (d, J = 9 Hz, 1H), 7.27 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.3, 98.9, 111.8, 117.2, 123.1, 131.9, 139.2, 142.2, 147.0, 149.3, 161.3; IR (neat) 1641, 1550, 1495, 1137, 769 cm^{-1}. Anal. Calcd for $C_{11}H_8ClN_3O$; C, 56.54; H, 3.45; N, 17.98. Found: C, 56.34; H, 3.48; N, 17.60.

9-Bromopyridin-4-one-6*H*-pyrido[6,1-*a*:2′,1′-*d*][1,3,5]triazine (14c). The general procedure for the reaction of haloazacyanines with base was employed with azacyanine **7c** (1.80 g, 3.84 mmol; 12 h), and flash column chromatography (20% methanol in ethyl acetate) afforded **14c** as orange crystals (840 mg, 3.0 mmol, 79%): mp 261−263 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78 (s, 2H), 5.87 (d, J = 8 Hz, 1H), 6.17 (d, J = 9 Hz, 1H), 6.71 (d, J = 10 Hz, 1H), 7.23 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.2, 98.9, 102.8, 111.9, 123.3, 134.1, 141.1, 142.1, 147.0, 149.3, 161.3; IR (neat) 1635, 1564, 1490, 1134, 776 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 281 (4.07), 358 (4.14), 436 (4.18). Anal. Calcd for $C_{11}H_8BrN_3O$: C, 47.51; H, 2.90; N, 15.11. Found: C, 47.64; H, 2.97; N, 15.10.

9-Bromo-1,11-dimethyl-pyridin-4-one-6*H*-pyrido[6,1-*a*:2′,1′-*d*][1,3,5]triazine (14d). The general procedure for the reaction of haloazacyanines with base was employed with azacyanine **7d** (0.429 g, 0.863 mmol). The mixture was refluxed until the solution turned colored and purified by flash column chromatography (30% methanol in ethyl acetate) to afford **14d** as a colorless oil (50 mg, 0.20 mmol, 19%): R_f = 0.35; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.09 (s, 3H), 2.19 (s, 3H), 5.77 (s, 2H), 5.92 (d, J = 7 Hz, 1H), 7.17 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.0, 17.8, 56.8, 99.0, 101.9, 121.3, 131.7, 132.4, 138.3, 139.9, 145.1, 148.8, 161.3; IR (neat) 1635, 1558, 1491, 777 cm^{-1}.

4-Bromo-2-(4-bromo-1-imino-3-1*H*-isoquinolin-2-ylmethyl)-2*H*-isoquinolin-1-one (15). Azacyanine **9b (**380 mg, 6.68 mmol) was dissolved in 20 mL of a 10% methanolic KOH solution and 2 mL of water, and a white precipitate formed immediately. After 1 h of stirring, the solids were collected by filtration, washed with CH_2Cl_2, and dried to produce **15** as white needles (260 mg, 0.57 mmol, 86%): mp 250−251 °C; ^{1}H NMR (400 MHz, CD_3CO_2D) δ 6.57 (s, 2H), 7.70 (m, 1H), 7.89 (m, 1H), 7.92 (m, 2H), 8.09 (m, 1H), 8.15 (m, 1H), 8.27 (s, 1H), 8.48 (d, J = 8 Hz, 1H), 8.52 (s, 1H), 8.61 (d, J = 8 Hz, 1H); ^{13}C NMR (100 MHz, CD_3CO_2D) δ 64.0, 103.0, 107.2, 119.3, 125.4, 126.3, 126.8, 127.1, 128.8, 129.1, 130.5, 131.5, 132.5, 134.9, 135.0, 136.0, 136.5, 151.2, 163.5; IR (neat) 3300, 1650, 1612, 1099, 916 cm^{-1}; UV−vis λ_{max}/nm (log ϵ) (methanol) 293 (3.97). Anal. Calcd for $C_{19}H_{13}Br_2N_3O$: C, 50.03; H, 2.85; N, 9.15. Found: C, 50.41; H, 2.99; N, 9.04.

9-Methoxypyridin-4-one-6*H*-pyrido[6,1-*a*:2′,1′-*d*][1,3,5]triazine (20). Haloazacyanine **14c** (300 mg, 1.08 mmol) was dissolved in 50 mL of a 10% methanolic KOH and 5 mL of water and refluxed for 12 h. The solution was diluted with water (50 mL) and extracted with CH_2Cl_2 (4 × 10 mL). The organic solution was dried (Na_2SO_4), filtered, and evaporated by rotatory evaporation. Purification by column chromatography (10% MeOH; EtOAC) produced **20** as a clear oil (30 mg, 0.13 mmol, 12%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.70 (s, 3H), 5.84 (s, 2H), 5.87 (d, J = 7 Hz, 1H), 6.12 (d, J = 9 Hz, 1H), 6.66 (d, J = 3 Hz, 1H), 6.83 (d, J = 10 Hz, 1H), 7.17 (dd, J = 10, 3 Hz, 1H), 7.31 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.4, 57.1, 98.1, 110.2, 114.8, 123.4, 133.7, 139.1, 142.4, 147.7, 148.9, 161.6; IR (neat) 1637, 1579, 1497, 778 cm^{-1}.

9-Phenylpyrdin-4-one-6*H*-pyrido[6,1-*a*:2′,1′-*d*][1,3,5]triazine (21). A 250 mL round-bottom flask equipped with a magnetic stir bar was charged with halo-azacyanine **14c** (40 mg, 0.14 mmol), DME (10 mL), phenylboronic acid (140 mg, 1.2 mmol), $Pd(PPh_3)_4$ (90 mg, 0.081 mmol), and 0.70 mL of a 2 M K_2CO_3. This solution was slowly refluxed for 2 h and quenched with 5 mL or water. The organic layer was separated, dried with Na_2SO_4, filtered, concentrated, and purified by flash column chromatography (20% methanol in ethyl acetate) to afford **21** as red needles (25 mg, 0.091 mmol, 65%): R_f = 0.35; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.92 (s, 2H), 6.17 (d, J = 9 Hz, 1H), 6.90 (d, J = 9 Hz, 1H), 7.39 (m, 8H), 7.59 (dd, J = 9, 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.6, 98.5, 110.7, 122.1, 124.9, 125.6, 128.3, 129.3, 129.3, 131.63 135.0, 138.2, 142.2, 150.0, 161.5; IR (neat) 1643, 1558, 1498, 1477, 758 cm^{-1}.

3,9-Diphenyl-6*H*-dipyrido[1,2-*a*:2′,1′-*d*][1,3,5]triazin-5-ium (22). Azacyanine **7c** (90 mg, 0.2 mmol) was dissolved in DME (10 mL), phenylboronic acid (280 mg, 2.4 mmol), $Pd(PPh_3)_4$ (180 mg, 0.162 mmol), and 1.40 mL of a 2 M K_2CO_3. This solution was refluxed for 4h and quenched with 5 mL or water. The organic layer was, separated, dried with Na_2SO_4, filtered, and concentrated. The solid was washed with CH_2Cl_2 and acetone to produce **22** (60 mg, 0.13 mmol 68%): mp 361−363 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.52 (s, 2H), 7.34 (d, J = 9 Hz, 2H), 7.44 (m, 2H), 7.53 (m, 4H), 7.74 (m, 4H), 8.38 (dd, J = 9, 2 Hz, 2H), 8.52 (d, J = 2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 65.9, 122.0, 126.8, 129.0, 129.5, 130.1, 134.7, 135.8, 142.5, 151.0; IR (neat) 1532, 1480, 1330, 1318, 823 cm^{-1}. Anal. Calcd for $C_{23}H_{18}IN_3 \cdot {}^1/_2H_2O$ C, 58.49; H, 4.05; N, 8.90. Found: C, 58.52; H, 3.93; N, 8.71.

Acknowledgment. We are grateful to the Cystic Fibrosis Foundation and the National Science Foundation for financial support of this research. The 400 and 300 MHz NMR spectrometers used in this study were funded in part by a grant from NSF (CHE-9808183). M.J.H. is grateful to the American University of Beirut for a Sabbatical leave at the University of California, Davis.

Supporting Information Available: Copies of ^{1}H NMR, ^{13}C NMR, and IR for compound **11**/**14d**/**21** and ^{1}H NMR and IR for compound **20**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO001484K