Efficient Syntheses of Imidazolo[1,2-*a*]pyridines and -[2,1-*a*]isoquinolines

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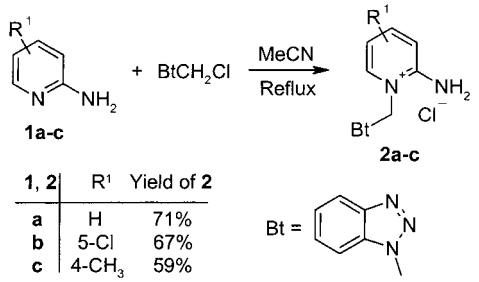
2-Aminopyridines **1a**−**c** and 1-aminoisoquinoline with 1-chloromethylbenzotriazole give 2-amino-1-[α-benzotriazol-1-ylmethyl]pyridinium chlorides **2a**−**c** and 1-amino-2-(α-benzotriazol-1-ylmethyl)-isoquinolinium chloride **12**, respectively. Compounds **2a**−**c** and **12** react with aryl aldehydes **3a**−**h** to afford imidazolo[1,2-*a*]pyridines **7a**−**k** and imidazolo[2,1-*a*]isoquinolines **13a**,**b** in good yields.

Introduction

Imidazolo[1,2-*a*]pyridines and imidazolo[2,1-*a*]isoquinolines are of interest due to their antiinflammatory,[1] potential antirhinoviral,[2] long-acting local anesthetic,[3] antiulcer,[4a,4b] and anthelmintic or bacteriostatic activities.[5] They are also versatile intermediates for synthetic transformations.[6a−c]

Imidazolo[1,2-*a*]pyridines have generally been prepared by the condensation of an α-halocarbonyl compound with a 2-aminopyridine (Chichibabin reaction).[7] Other methods based on 2-aminopyridine[8a−c] and an alternative strategy of building imidazolo[1,2-*a*]pyridines from a variety of substituted imidazoles are also recorded.[9a−c] We found three reports of the synthesis of imidazolo[2,1-*a*]isoquinolines: (i) Krohnke[10a] synthesized 2-phenylimidazolo[2,1-*a*]isoquinoline in 21% yield by the reaction of *N*-phenacylisoquinolinium bromide and hydroxylamine hydrochloride; (ii) Ito[10b] utilized α-bromoacetophenone phenylsulfonylhydrazones and isoquinoline; (iii) Tominaga[10c−d] reacted *N*-bis(alkylthio)methylene-sulfonamides with isoquinoline *N*-ylides. These methods often suffer from lengthy sequences,[8b] low overall yields,[10a,c,d] and limited ability to vary substituents[1,9a,c] or use relatively inaccessible starting materials.[10b−d] Recently, we synthesized indolizines in good yields from *N*-[α-benzotriazol-1-yl]alkylpyridinium salts via benzotriazole methodology.[11] We now extend this approach to the synthesis of substituted imidazolo[1,2-*a*]pyridines **7a**−**k** and imidazolo[2,1-*a*]isoquinolines **13a**,**b** using the condensation of 2-amino-1-[α-benzotriazol-1-ylmethyl]-pyridinium chlorides **2a**−**c** and 1-amino-2-(α-benzotriazol-1-ylmethyl)isoquinolinium chloride **12** with aryl aldehydes **3**.

Scheme 1



Results and Discussion

Preparation of 2-Amino-1-[α-benzotriazol-1-ylmethyl]pyridinium Chlorides. Previously, our group[12] showed that *N*-[α-(benzotriazol-1-yl)methyl]pyridinium chlorides were readily prepared by refluxing a mixture of pyridine and 1-chloromethylbenzotriazole in nitromethane. In the present work, 2-amino-1-[α-benzotriazol-1-ylmethyl]pyridinium chlorides **2a**−**c** were similarly prepared as crystalline solids in 59−71% yields by the reaction of the appropriate substituted 2-aminopyridines **1a**−**c** with 1-chloromethylbenzotriazole under reflux in acetonitrile (Scheme 1). These reactions gave exclusively the benzotriazol-1-yl isomers **2a**−**c**, whose structures

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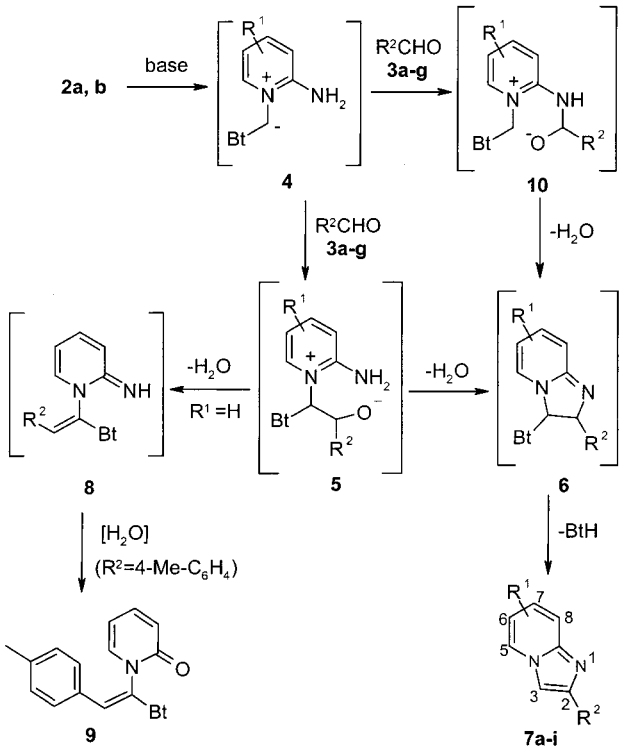
Scheme 2



R²CHO	R²	R²CHO	R²
3a	4-Me-C_6H_4	**3e**	2-Furyl
3b	4-MeO-C_6H_4	**3f**	$C_6H_5CH=C(CH_3)$
3c	2-Thienyl	**3g**	4-F-C_6H_4
3d	4-Cl-C_6H_4		

were evident from analytical and spectral data and in agreement with ^{1}H and ^{13}C NMR data for related compounds.[11]

Preparation of Imidazolo[1,2-*a*]pyridines. Treatment of **2a** with aryl aldehydes **3a**−**f** in DMF at 115 °C in the presence of DBU for 16 h gave **7a**−**f** in isolated yields of 61−75% (Scheme 2). However, to produce imidazolo[1,2-*a*]pyridines **7g**−**i** by reactions of **2b** with aryl aldehydes, stronger reaction conditions (viz heating **2b** with the appropriate aldehydes **3** at 155 °C in the presence of potassium carbonate without solvent) were required, probably because of the reduced nucleophilicity of the chloro substituted pyridine ring. Structures **7a**−**i** were supported by elemental analysis and by ^{1}H and ^{13}C NMR spectra, and in good accordance with analogues.[13] Yields and melting points of compounds **7a**−**i** are presented in Table 1. However, reaction of **2a** with **3a** under the latter reaction condition gave **7a** (48%) together with 7% of **9**. The structure of **9** was confirmed by single-crystal X-ray crystallography.

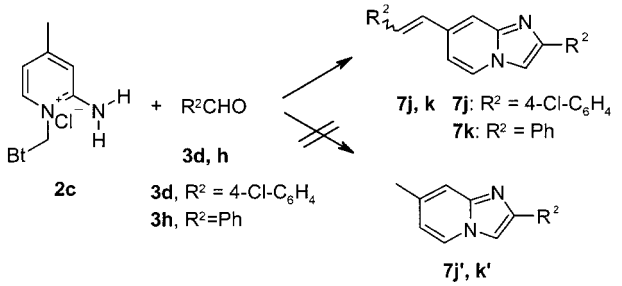
Possible mechanisms for the formation of imidazolo-[1,2-*a*]pyridines **7a**−**i** and 1-[α-(benzotriazol-1-yl)-2-(4-methylphenyl)ethenyl]-2(1*H*)-pyridinone (**9**) are shown in Scheme 2. Deprotonation of **2** forms the azomethine ylide **4** as discussed previously,[11] or alternatively occurs at the NH_2 group. Azomethine ylide **4** reacts with an aldehyde **3** to give the intermediate **5**, which could ring-close and eliminate benzotriazole to produce **7** via the intermediate **6** or undergo hydrolysis to give the product **9** via the intermediate **8**. Alternatively, an aldehyde **3** can react initially at the NH_2 group of **4** to give **10**, followed by ring-closure to **6**, and elimination of the benzotriazole molecule to generate **7**.

Table 1. Preparation of Imidazolo[1,2-*a*]pyridines 7a−k

entry	R^1	R^2	yield[a] (%)	mp (°C)
7a	H	4-Me-C_6H_4	72	144−145
7b	H	4-MeO-C_6H_4	69	137−138 (139[14])
7c	H	2-thienyl	66	137−138
7d	H	4-Cl-C_6H_4	75	205−206 (208[15])
7e	H	2-furyl	61	92−93 (93[8b])
7f	H	$C_6H_5CH=C(CH_3)$	71	90−91
7g	6-Cl	4-Me-C_6H_4	73	223−224
7h	6-Cl	4-MeO-C_6H_4	67	227−228
7i	6-Cl	4-F-C_6H_4	78	191−192
7j	7-(4-Cl-C_6H_4)-CH=CH	4-Cl-C_6H_4	71	223−224
7k	7-C_6H_5–CH=CH	C_6H_5	66	202−204

[a] Isolated yield based on **2a**−**c**.

Scheme 3



Reactions of **2c** with 1 equiv of aldehydes **3d** and **3h** generated **7j** and 7**k**, respectively, in low yields, instead of the expected products **7j′** and **7k′** (Scheme 3), due to the reaction of a second molecule of an aldehyde with the active hydrogens of the pyridine ring methyl group. Using 2 equiv of aldehydes did increase the yields of **7j** and **7k** to 66% and 71%, respectively. The structures of the products are fully characterized by elemental analytical data and ^{1}H and ^{13}C NMR spectra.

When the starting aldehyde bears an α-proton next to the formyl group, enimine analogues are obtained instead of imidazolo[1,2-*a*]pyridines. Thus, the reaction of **2a** with aldehydes **3i**−**k** afforded **11a**−**c** in 81−87% yields (Scheme 4). Novel compounds **11a**−**c** were characterized by NMR spectroscopy and elemental analysis. In the ^{1}H NMR, the singlet CH_2 group protons between the benzotriazol-1-yl nitrogen and pyridine ring nitrogen of **11a**−**c** appear at 6.82−6.92 ppm, and the ^{1}H NMR characteristic pattern of a benzotriazol-1-yl group is observed in all compounds **11a**−**c**. The structure of **11a** was confirmed by X-ray crystallography (Figure 1), which also established the configuration (*E*,*E*) about the two double bonds. In the solid state the terminal phenyl ring is disordered over two approximately orthogonal orientations. According to the ^{1}H and ^{13}C NMR spectra, the compound **11c** is an *EZ* mixture. The reactions of **2a** with aldehydes possessing two α-hydrogens (3-phenylpropanal or hexanal) each resulted in complex mixtures.

The reaction of 2-aminothiazole with 1-chloromethylbenzotriazole gave the corresponding thiazolium salt.

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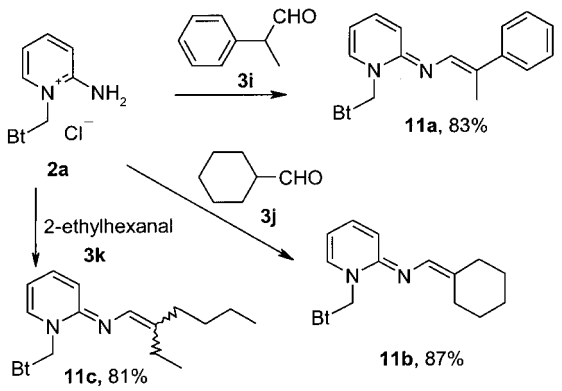
Scheme 4



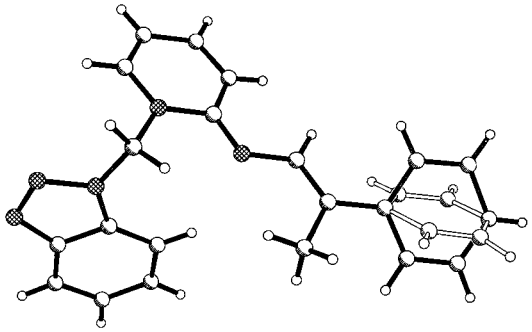
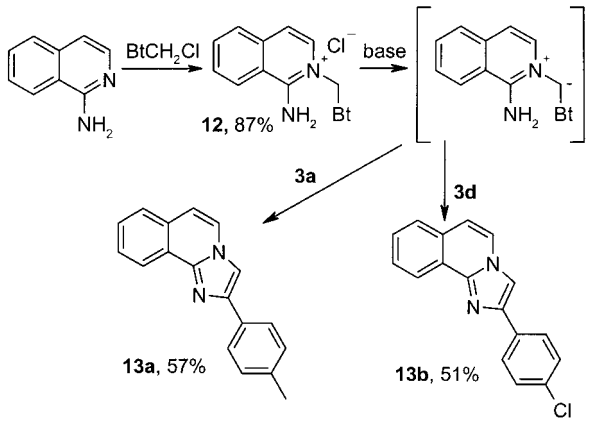


Figure 1. X-ray crystal structure of **11a**.

Scheme 5



However, condensation with an aldehyde under the reaction conditions as used above gave no imidazolo[2,1-*b*]thiazoles.

Preparation of Imidazolo[2,1-*a*]isoquinolines. This methodology was also extended to the isoquinoline ring system. The required 1-amino-2-(α-benzotriazol-1-ylmethyl)isoquinolinium chloride (**12**) was prepared from 1-aminoisoquinoline and 1-chloromethylbenzotriazole. The reactions of **12** with **3a** and **3d** were conducted in a manner similar to that for the preparation of **7g**−**i** (Scheme 5). The ^{1}H NMR spectra and melting points of **13a** and **13b** are in agreement with the literature data.[10b]

In summary, we have developed a new facile method for the synthesis of imidazolo[1,2-*a*]pyridines **7** and imidazolo[2,1-*a*]isoquinolines **13**. The benzotriazolyl group in 2-aminopyridinium salts **2** and 1-aminoisoquinolinium salt **12** plays a dual role: (i) it activates the methylene group for easy deprotonation and stabilizes the resulting ylide by the delocalization of the negative charge; (ii) it serves as a good leaving group in the subsequent elimination step leading to the target products **7** and **13**. Benzotriazole methodology utilizes readily available starting materials, simple procedures and gives good yields.

Experimental Section

Melting points were determined using a Bristoline hot-stage microscope and are uncorrected. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a Gemini 300 NMR spectrometer in chloroform-*d* solution (with tetramethylsilane for ^{1}H and chloroform-*d* for ^{13}C as internal references), unless otherwise stated. Column chromatography was performed on silica gel. Elemental analyses were performed on a Carlo Erba-1106 instrument.

General Procedure for the Preparation of 2-Amino-1-[α-benzotriazol-1-ylmethyl]pyridinium Chlorides 2a−**c**. To a stirred solution of 1-chloromethylbenzotriazole (1.68 g, 10 mmol) in dry acetonitrile (30 mL), the appropriate 2-aminopyridine **1** (10 mmol) was added. The mixture was stirred overnight under reflux, and then the white precipitate formed was filtered off to give the corresponding 2-amino-1-(α-benzotriazol-1-ylmethyl)pyridinium chloride **2a**−**c**.

2-Amino-1-[α-benzotriazol-1-ylmethyl]pyridinium chloride (2a): colorless prisms; mp 239−240 °C; ^{1}H NMR (DMSO) δ 6.93 (t, J = 6.8 Hz, 1H), 7.24 (d, J = 8.8 Hz, 1H), 7.40 (s, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.71 (t, J = 7.6 Hz, 1H), 7.89 (t, J = 8.2 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.28−8.38 (m, 2H), 9.49 (br s, 2H); ^{13}C NMR (DMSO) δ 61.4, 110.9, 113.1, 115.9, 119.5, 124.9, 128.7, 132.5, 139.0, 143.3, 145.1, 154.7. Anal. Calcd for $C_{12}H_{12}ClN_5$: C, 55.07; H, 4.63; N, 26.77. Found: C, 55.07; H, 4.51; N, 26.89.

2-Amino-1-[α-benzotriazol-1-ylmethyl]-5-chloropyridinium chloride (2b): colorless prisms; mp 225−226 °C; ^{1}H NMR (DMSO) δ 7.34 (d, J = 7.5 Hz, 1H), 7.37 (s, 2H), 7.52 (t, J = 7.2 Hz, 1H), 7.72 (t, J = 7.2 Hz, 1H), 8.00 (d, J = 7.5 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.40 (d, J = 8.4 Hz, 1H), 8.76 (s, 1H), 9.84 (br s, 2H); ^{13}C NMR (DMSO) δ 61.6, 111.0, 117.6, 118.3, 119.6, 125.0, 128.8, 132.6, 136.6, 143.4, 145.1, 154.0. Anal. Calcd for $C_{12}H_{11}Cl_2N_5$: C, 48.67; H, 3.74; N, 23.65. Found: C, 48.55; H, 3.52; N, 23.59.

2-Amino-1-[α-benzotriazol-1-ylmethyl]-4-methylpyridinium chloride (2c): colorless prisms; mp 231−232 °C; ^{1}H NMR (DMSO) δ 2.30 (s, 3H), 6.85 (d, J = 6.9 Hz, 1H), 7.11 (s, 1H), 7.52 (t, J = 7.8 Hz, 1H), 7.58 (s, 2H), 7.72 (t, J = 7.2 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 8.36 (d, J = 7.2 Hz, 1H), 8.45 (d, J = 8.4 Hz, 1H), 9.55 (br s, 2H); ^{13}C NMR (DMSO) δ 21.2, 61.0, 111.0, 113.9, 115.4, 119.6, 125.0, 128.7, 132.5, 138.3, 145.1, 154.2, 155.8. Anal. Calcd for $C_{13}H_{14}ClN_5$: C, 56.63; H, 5.12; N, 25.40. Found: C, 56.61; H, 5.04; N, 25.41.

General Procedure for the Preparation of Imidazolo-[1,2-*a*]pyridines 7a−f,j,k and *N*-[(1-Benzotriazol-1-ylmethyl)-2(1*H*)-pyridinylidene]amines 11a−c. To a stirred solution of 2-amino-1-(α-benzotriazol-1-ylmethyl)pyridinium chloride **2a** (0.26 g, 1 mmol) and an appropriate aldehyde **3** (1.5 mmol) in DMF (5 mL), DBU (0.3 mL, 2 mmol) was added under nitrogen. The reaction mixture was heated at 115 °C for 16 h, and then was poured into water (10 mL) and extracted with methylene chloride. The organic layer was washed with 2 M NaOH (2 × 5 mL), dried over Na_2SO_4, and evaporated in vacuo. The crude product was purified by column chromatography using the eluent of hexanes/AcOEt (6−4/1) to give, depending on the type of an aldehyde, imidazolo[1,2-*a*]pyridines **7a**−**f** or enimines **11a**−**c**. Compounds **7j** and **7k** were obtained by reaction of 2-amino-1-[α-benzotriazol-1-ylmethyl]-4-methylpyridinium chloride (**2c**) with 2 equiv of aldehydes **3** in the similar procedure described above.

2-(4-Methylphenyl)imidazolo[1,2-*a*]pyridine (7a): colorless needles; mp 144−145 °C; ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3H), 6.73 (t, J = 6.9 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 8.4 Hz, 2H), 7.6 (d, J = 9.0 Hz, 1H), 7.79 (s, 1H), 7.84 (d, J = 8.4 Hz, 2H), 8.06 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 21.3, 107.7, 112.2, 117.3, 124.5, 125.4, 125.8, 129.4, 130.8, 137.7, 145.5,

145.8. Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.73; H, 5.82; N, 13.45. Found: C, 80.94; H, 5.88; N, 13.56.

2-(2-Thienyl)imidazolo[1,2-*a*]pyridine (7c): brown plates; mp 137−138 °C; ^{1}H NMR δ 6.76 (t, J = 7.2 Hz, 1H), 7.09 (dd, J = 5.4, 3.9 Hz, 1H), 7.15 (t, J = 6.9 Hz, 1H), 7.30 (d, J = 4.8 Hz, 1H), 7.46 (d, J = 3.6 Hz, 1H), 7.60 (d, J = 9.0 Hz, 1H), 7.75 (s, 1H), 8.06 (d, J = 6.9 Hz, 1H); ^{13}C NMR δ 107.4, 112.5, 117.3, 123.6, 124.8, 125.0, 125.4, 127.7, 137.4, 140.8, 145.4. Anal. Calcd for $C_{11}H_8N_2S$: C, 65.97; H, 4.03; N, 13.99. Found: C, 65.77; H, 3.90; N, 13.97.

2-[(*Z*)-1-Methyl-2-phenylethenyl]imidazolo[1,2-*a*]pyridine (7f): yellow needles; mp 90−91 °C; ^{1}H NMR δ 2.33(s, 3H), 6.74 (t, J = 6.6 Hz, 1H), 7.16 (t, J = 8.1 Hz, 1H), 7.25 (t, J = 6.9 Hz, 1H), 7.38 (t, J = 8.1 Hz, 2H), 7.45 (d, J = 7.2 Hz, 2H), 7.59 (d, J = 9 Hz, 1H), 7.64 (s, 1H), 7.66 (s, 1H), 8.08 (d, J = 6.9 Hz, 1H); ^{13}C NMR δ 15.8, 109.0, 112.0, 117.3, 124.9, 125.5, 126.5, 127.2, 128.1, 129.2, 129.4, 137.9, 145.4, 148.3. Anal. Calcd for $C_{16}H_{14}N_2$: C, 82.01; H, 6.03; N, 11.96. Found: C, 81.70; H, 5.98; N, 11.90.

2-Phenyl-7-(2-phenylethenyl)imidazolo[1,2-*a*]pyridine (7k): yellow plates; mp 202−204 °C; ^{1}H NMR δ 7.05 (d, J = 6.9 Hz, 1H), 7.11 (d, J = 2.4 Hz, 2H), 7.26−7.48 (m, 6H), 7.54 (d, J = 7.8 Hz, 2H), 7.59 (s, 1H), 7.81 (s, 1H), 7.96 (d, J = 7.8 Hz, 2H), 8.03 (d, J = 7.2 Hz, 1H); ^{13}C NMR δ 108.4, 110.0, 115.3, 125.2, 126.0, 126.7, 126.8, 128.0, 128.2, 128.7, 128.8, 130.3, 133.7, 134.2, 136.6, 146.0, 146.5. Anal. Calcd for $C_{21}H_{16}N_2$: N, 9.45. Found: N, 9.61.

***N*-[(1-Benzotriazol-1-ylmethyl)-2(1*H*)-pyridinylidene]-*N*-[(*E*)2-phenyl-1-propenyl]amine (11a):** orange−brown needles; mp 162−163.0 °C; ^{1}H NMR δ 2.39 (s, 3H), 5.80 (t, J = 6.0 Hz, 1H), 6.74 (d, J = 9.3 Hz, 1H), 6.85−6.92 (m, 1H), 6.93 (s, 2H), 7.19 (t, J = 7.2 Hz, 1H), 7.30−7.41 (m, 4H), 7.42−7.54 (m, 4H), 8.04 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 8.7 Hz, 1H); ^{13}C NMR δ 14.7, 57.5, 104.8, 111.4, 114.3, 119.6, 124.0, 124.4, 124.9, 125.6, 128.0, 128.2, 130.5, 132.6, 135.9, 136.7, 142.7, 146.1, 151.4. Anal. Calcd for $C_{21}H_{19}N_5$: C, 73.87; H, 5.62; N, 20.52. Found: C, 73.54; H, 5.68; N, 20.57.

Crystal data for 11a: $C_{21}H_{19}N_5$, MW 341.4, triclinic, P-1, a = 4.534(3) Å, b = 10.228(8) Å, c = 19.814(14) Å, α = 101.88(1)°, β = 91.56(1)°, γ = 100.48(1)°, V = 882.1(11) Å^3, Z = 2, T = −105 °C, μ (Mo Kα) = 0.08 mm^{-1}, D_{calcd} = 1.285 g·cm^{-3}, $2\theta_{max}$ 50° (CCD area detector), wR(F^2) = 0.117 (all 3099 data), R = 0.048 (1608 data with $I > 2\sigma I$).

General Procedure for the Preparation of Imidazolo-[1,2-*a*]pyridines 7g−i. A mixture of 2-amino-1-(α-benzotriazol-1-ylmethyl)-5-chloropyridinium chloride (**2b**) (0.30 g, 1 mmol) and an appropriate aryl aldehyde **3** (1.5 mmol) in the presence of K_2CO_3 (0.28 g, 2 mmol) was heated neat at 155 °C under nitrogen for 16 h. The reaction mixture was cooled to room temperature, dissolved in 10 mL of methylene chloride, and washed with 2 M NaOH (2 × 5 mL), the organic layer was dried over Na_2SO_4, and the solvent was then removed in vacuo. The residue was purified by column chromatography using the eluent of hexanes/AcOEt (4−2/1) to give **7g−i**.

2-(4-Methylphenyl)-6-chloroimidazolo[1,2-*a*]pyridine (7g): colorless plates; mp 223−224 °C; ^{1}H NMR δ 2.38 (s, 3H), 7.10 (d, J = 9.6 Hz, 1H), 7.23 (d, J = 7.8 Hz, 2H), 7.54 (d, J = 9.6 Hz, 1H), 7.74 (s, 1H), 7.80 (d, J = 8.1 Hz, 2H), 8.10 (s, 1H); ^{13}C NMR δ 21.3, 108.1, 117.6, 120.3, 123.2, 125.8, 129.4, 130.3, 138.1, 143.9, 146.8. Anal. Calcd for $C_{14}H_{11}ClN_2$: C, 69.27; H, 4.58; N, 11.54. Found: C, 68.88; H, 4.51; N, 11.46.

2-(4-Methoxyphenyl)-6-chloroimidazolo[1,2-*a*]pyridine (7h): colorless plates; mp 227−228 °C; ^{1}H NMR (DMSO) δ 3.79 (s, 3H), 7.00 (d, J = 8.7 Hz, 2H), 7.25 (dd, J = 9.6, 2.1 Hz, 1H), 7.59 (d, J = 9.6 Hz, 1H), 7.88 (d, J = 9.0 Hz, 2H), 8.25 (s, 1H), 8.76 (s, 1H); ^{13}C NMR (DMSO) δ 55.1, 108.7, 114.2, 117.1, 118.7, 124.6, 125.4, 126.0, 127.0, 143.2, 145.4, 159.2. Anal. Calcd for $C_{14}H_{11}ClN_2O$: C, 64.99; H, 4.29; N, 10.83. Found: C, 64.69; H, 4.16; N, 10.76.

2-(4-Fluorophenyl)-6-chloroimidazolo[1,2-*a*]pyridine (7i): light yellow plates; mp 191−192 °C; ^{1}H NMR δ 6.90−7.15 (m, 3H), 7.53 (d, J = 9.6 Hz, 1H), 7.71 (s, 1H), 7.84−7.91 (m, 2H), 8.10 (dd, J = 2.1, 0.7 Hz, 1H); ^{13}C NMR δ 108.1, 155.7 (d, J = 21.6 Hz), 117.7, 120.5, 123.3, 126.1, 127.7 (d, J = 8.6 Hz), 129.4 (d, J = 3.0 Hz), 143.9, 145.9, 162.8 (d, J = 245.8 Hz). Anal. Calcd for $C_{13}H_8ClFN_2$: C, 63.30; H, 3.28; N, 11.36. Found: C, 63.30; H, 3.00; N, 11.34.

Procedure for the Preparation of 1-[α-(Benzotriazol-1-yl)-2-(4-methylphenyl)ethenyl]-2(1*H*)-pyridinone 9. A mixture of 2-amino-1-(α-benzotriazol-1-ylmethyl)pyridinium chloride (**2a**) (0.26 g, 1 mmol) and *p*-tolualdehyde (**3a**) (0.24 mL, 1.5 mmol) in the presence of K_2CO_3 (0.28 g, 2 mmol) was heated neat at 150 °C under nitrogen for 16 h. The reaction mixture was cooled to room temperature, dissolved in 10 mL of methylene chloride, and washed with 2 M NaOH (2 × 5 mL), the organic layer was dried over Na_2SO_4, and the solvent was then removed in vacuo. The residue was purified by column chromatography using the eluent of hexanes/AcOEt (4/1) to give 2-(4-methylphenyl)imidazolo[1,2-*a*]pyridine (**7a**, 48%) and 1-[α-(benzotriazol-1-yl)-2-(4-methylphenyl)ethenyl]-2(1*H*)-pyridinone (**9**, 7%) as colorless crystals.

1-[α-(Benzotriazol-1-yl)-2-(4-methylphenyl)ethenyl]-2(1*H*)-pyridinone (9): colorless clusters; mp 170−171 °C; ^{1}H NMR δ 2.35 (s, 3H), 6.28 (t, J = 6.9 Hz, 1H), 6.61 (d, J = 9.9 Hz, 1H), 7.09−7.16 (m, 5H), 7.38−7.49 (m, 3H), 7.54 (t, J = 8.4 Hz, 1H), 7.70 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 21.3, 107.2, 110.8, 120.0, 122.1, 124.5, 124.7, 128.0, 128.6, 129.7, 132.7, 137.8, 139.8, 141.2, 145.6, 161.7. Anal. Calcd for $C_{20}H_{16}N_4O$: C, 73.15; H, 4.92; N, 17.07. Found: C, 72.90; H, 4.84; N, 17.13.

Crystal data for 9: $C_{20}H_{16}N_4O$, MW 328.4, triclinic, P-1, a = 8.953(2) Å, b = 9.936(3) Å, c = 10.739(3) Å, α = 66.272(3)°, β = 79.212(4)°, γ = 70.412(3)°, V = 822.4(4) Å^3, Z = 2, T = −110 °C, μ (Mo Kα) = 0.09 mm^{-1}, D_{calcd} = 1.326 g·cm^{-3}, $2\theta_{max}$ 53° (CCD area detector), wR(F^2) = 0.093 (all 3254 data), R = 0.035 (2943 data with $I > 2\sigma I$).

Procedures for the Preparation of 1-Amino-2-(α-benzotriazol-1-ylmethyl)isoquinolinium Chloride 12 and Imidazolo[2,1-*a*]isoquinolines 13a,b. To a stirred solution of 1-chloromethylbenzotriazole (1.66 g, 10 mmol) in dry acetonitrile (30 mL), 1-aminoisoquinoline (1.44 g, 10 mmol) was added. The mixture was stirred overnight under reflux, and then the white-off precipitate formed was filtered off to give 1-amino-2-(α-benzotriazol-1-ylmethyl)isoquinolinium chloride **12**.

A mixture of 1-amino-2-(α-benzotriazol-1-ylmethyl)isoquinolinium chloride **12** (0.31 g, 1 mmol) and an appropriate aryl aldehyde **3** (2 mmol) in the presence of K_2CO_3 (0.28 g, 2 mmol) for **13a**, DBU (0.45 mL, 3 mmol) for **13b** was heated neat at 160 °C under nitrogen for 16 h. The reaction mixture was cooled to room temperature, dissolved in 10 mL of methylene chloride, washed with 2 N NaOH (2 × 5 mL), the organic layer was dried over Na_2SO_4, and the solvent was then removed in vacuo. The residue was purified by column chromatography using the eluent of hexanes/AcOEt (10/1) to give 2-(4-methylphenyl)imidazolo[2,1-*a*]isoquinoline (**13a**) and hexanes/AcOEt (5/1) to give 2-(4-chlorophenyl)imidazolo[2,1-*a*]isoquinoline (**13b**).

1-Amino-2-(α-benzotriazol-1-ylmethyl)isoquinolinium chloride (12): colorless prisms; mp 244−245 °C; ^{1}H NMR (DMSO) δ 6.37 (d, J = 7.2 Hz, 1H), 6.56 (t, J = 7.2 Hz, 1H), 6.64 (s, 2H), 6.76 (t, J = 7.5 Hz, 1H), 6.86 (t, J = 6.6 Hz, 1H), 6.95−7.07 (m, 2H), 7.12 (d, J = 7.2 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.1 Hz, 1H), 9.51 (br s, 2H); ^{13}C NMR δ 61.6, 111.0, 112.5, 118.6, 119.6, 125.0, 126.4, 127.7, 128.6, 129.3, 131.5, 132.6, 135.3, 135.6, 145.1, 154.6. Anal. Calcd for $C_{16}H_{14}ClN_5$: C, 61.63; H, 4.54; N, 22.47. Found: C, 61.64; H, 4.47; N, 22.47.

2-(4-Methylphenyl)imidazolo[2,1-*a*]isoquinoline (13a): light yellow plates; mp 156−157 °C (lit.[10b] mp 159−160 °C); ^{1}H NMR δ 2.40 (s, 3H), 7.03 (d, J = 7.2 Hz, 1H), 7.24−7.28 (m, 3H), 7.53−7.65 (m, 2H), 7.68 (t, J = 8.1 Hz, 1H), 7.80 (s, 1H), 7.88−7.93 (m, 3H); ^{13}C NMR δ 21.3, 109.4, 113.0, 122.9, 123.5, 123.8, 125.7, 126.9, 128.0, 129.1, 129.4, 129.7, 129.8, 130.2, 137.3. Anal. Calcd for $C_{18}H_{14}N_2$: C, 83.68; H, 5.47; N, 10.85. Found: C, 84.00; H, 5.21; N, 10.54.

Supporting Information Available: Characterization data for compounds **7b**,**d**−**e**,**j**, **11b**,**c**, and **13b**; figure of the X-ray crystal structure for **9**; table of X-ray crystallographic data for **9** and **11a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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