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Direct Synthesis of Imines from *gem*-Dibromomethylaryl Derivatives: Application to Unsymmetrically Substituted Bipyridine Frameworks

Nicolas Weibel, Loïc J. Charbonnière,* and Raymond F. Ziessel*

Laboratoire de Chimie Moléculaire, UMR 7008 au CNRS, Ecole de Chimie, Polymères et Matériaux (ECPM), 25 rue Becquerel, 67087 Strasbourg Cedex 02, France

ziessel@chimie.u-strasbg.fr

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Abstract: An efficient methodology for the one-pot synthesis of imines is described starting from *gem*-dibromomethylaryl compounds and primary amines. The synthesis was applied to various aliphatic mono- and polyamines as well as to electron-rich anilines. The protocol was extended to 6-bromo-5′-dibromomethyl-2,2′-bipyridine to afford the corresponding imines. With *n*-propyl- and *n*-decylamine, further conversion, in three steps, to the corresponding 6-carboxy-5′-alkylaminomethyl-2,2′-bipyridine derivatives was selectively achieved, providing new tridentate ligands that may find interesting applications for the complexation of lanthanide(III) cations in their anionic or zwitterionic form.

The synthesis of so-called Schiff bases has attracted much attention in the field of coordination chemistry. The presence of the lone pair on the nitrogen atom of the imine group enables the coordination of numerous metal cations, especially when the imine function is located at the ortho position of the heteroaromatic cycles such as pyridines. These molecules have recently found very interesting applications as ligands in various homogeneous catalytic reactions such as hydrosilation, Mukaiyama aldolization, cyclopropanation,[1] homologation of aromatic aldehydes,[2] and ethylene polymerization.[3] Furthermore, imines are also of particular interest because the hydrogenation of the C═N bond affords an alternative to the synthesis of secondary amines. Although methodologies exist for the synthesis of imines, the easiest access is probably the acid-catalyzed condensation of primary amines with aldehydes or ketones.[4] In particular, this protocol has been extensively used to produce sophisticated ligands such as polyazamacrocycles[5] or polycatenar compounds.[6] Nevertheless, this route often requires multistep synthetic schemes for generating the aldehydes or ketones, which may conflict with the presence of sensitive functionalities on the molecules. In some cases, the instability of the formyl derivatives is a major drawback.

Examples for the preparation of an imino compound from molecules where the aldehyde function is masked in the form of a *gem*-dibromomethyl derivative appeared to be rare and not specifically designed for preparative purposes.[7] However, in some cases, the intermediate imino derivative is postulated to undergo an intramolecular rearrangement, leading to substituted heterocycles such as pyrazines,[8] benzopyrazines,[9] triazines,[10] benzimidazoles,[11] and elaborated poly-heteroaromatic derivatives.[12] As a result of our recent interest in the design of ligands for complexation of lanthanide(III) cations, we have been interested in the reactivity of *gem*-dibromomethyl-functionalized aromatic compounds.[13−15] The scope of application was investigated with dibromomethylbenzene and 6-bromo-5′-dibromomethyl-2,2′-bipyridine with various primary aliphatic amines, polyamines, and aniline derivatives. Two of the bipyridine derivatives (compounds **6** and **7**) were subjected to a sequence of reactions that led to the selective formation of the secondary amine on one side and the *n*-butylcarboxylate moiety on the other side of the molecule (compounds **12** and **13**). Cleavage of the esters provided the acids, which in their anionic or zwitterionic forms are promising candidates for the complexation of lanthanide(III) cations and for their applications as luminescent devices. They afford both a chromophoric bipyridine unit for sensitization of lanthanides and an anionic carboxylate function able to bind tightly to the triply charged cation.[15]

The strategy depicted in Scheme 1 required the use of a readily available *gem*-dibromomethyl derivative displaying good stability. Dibromomethylbenzene fulfilled these requirements and was used in a first step to adjust the experimental conditions. This commercially available compound was reacted with propylamine, decylamine, triethylenetetramine, and *p*-anisidine under anhydrous

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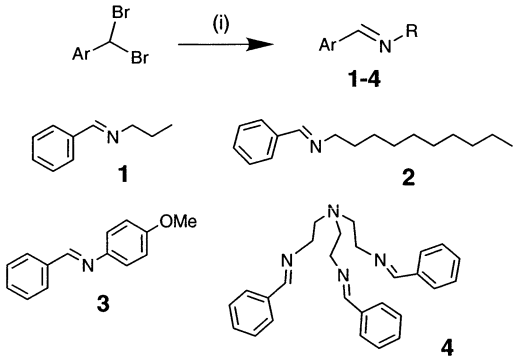
SCHEME 1. General Synthetic Methodology for the Preparation of Imines 1−4[a]



[a] Key: (i) RNH_2, CH_3CN, K_2CO_3, 80 °C.

TABLE 1. Experimental Conditions and Best Yields for the Synthesis of Imines 1−4 from Dibromomethylbenzene[a]

RNH_2	imine	equiv of amine	equiv of K_2CO_3	reaction time (h)	yield (%)
$^nC_3H_7NH_2$	**1**	5.0	1.0	17	98
$^nC_{10}H_{21}NH_2$	**2**	3.3	0	30	69
p-$MeOC_6H_4NH_2$	**3**	1.2	1.0	22	76
$N(C_2H_4NH_2)_3$	**4**	0.33	2.4	65	87

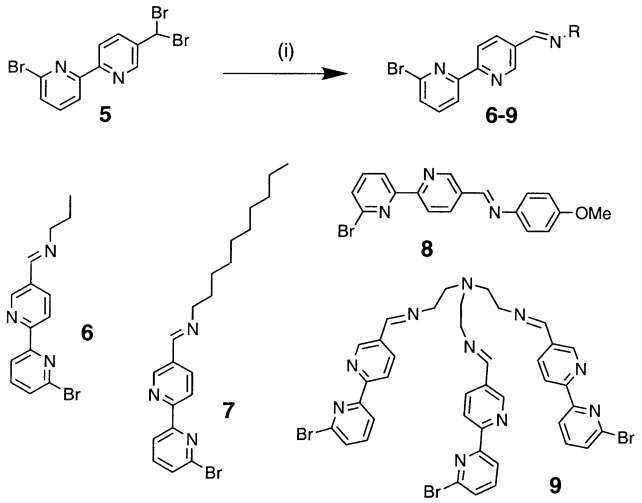
[a] In hot anhydrous acetonitrile with dry potassium carbonate. All isolated yields are given versus dibromomethylbenzene.

conditions with K_2CO_3 as base to quench the nascent hydrobromic acid (Scheme 1).

Although the use of an excess amine ensured a basic medium, it was noticed that the absence of K_2CO_3 decreased the reaction rate as well as the yield, due to the fact that an incomplete condensation took place. Furthermore, the omission of the inorganic base lead to subsequent purification problems involving the ammonium salts and the excess of free base. Selected reaction conditions and best yields are gathered in Table 1.

Compounds **1**−**4** were isolated in good yields, and their spectroscopic data are identical to those obtained by conventional condensation of aldehydes with the amines. However, in the case of **2**, the yield was much lower due to purification difficulties inherent to the in situ formation of decylammonium salts. In the case of the tris-imino derivative **4**, an X-ray molecular structure unambiguously confirmed that all three primary amine functions had indeed reacted with dibromomethylbenzene.[16] An ORTEP view is given in the Supporting Information. Crystalline compound **4** adopts a pseudo-C_3 symmetrical conformation in which the three strands are wrapped around a noncrystallographic C_3 axis. Interestingly, the lone pair of the apical nitrogen atom amines points toward the center of the cavity formed by the pendant arms. An average C═N bond distance of 1.26 Å was observed with a mean value of 117° for the C═N−CH_2 angle. Neither hydrogen bonds nor (intra- or intermolecular) stacking interactions could be evidenced from the structure, and it remains unclear why, in the solid state, such a conformation is preferred when compared to a planar one.

SCHEME 2. General Synthetic Methodology for the Preparation of Imines 6−9[a]



[a] Key: (i) RNH_2, CH_3CN, K_2CO_3, 80 °C.

TABLE 2. Experimental Conditions and Best Yields for the Synthesis of Imines 6−9 from 6-Bromo-5′-dibromomethyl-2,2′-bipyridine[a]

RNH_2	imine	equiv of amine	equiv of K_2CO_3	reaction time (h)	yield (%)
$^nC_3H_7NH_2$	**6**	5.8	2.5	17	92
$^nC_{10}H_{21}NH_2$	**7**	3.0	2.0	26	81
p-$MeOC_6H_4NH_2$	**8**	3.0	1.0	52	85
$N(C_2H_4NH_2)_3$	**9**	0.33	3.0	91	83

[a] In hot anhydrous acetonitrile with dry potassium carbonate. All isolated yields are given versus 6-bromo-5′-dibromomethyl-2,2′-bipyridine.

To gain flexibility for the synthesis of the imine compounds and to allow the use of the resulting ligands in complexation studies with lanthanides, the same set of primary amines was reacted under similar conditions with 6-bromo-5′-dibromomethyl-2,2′-bipyridine **5**, itself prepared by a double radical bromination reaction of 6-bromo-5′-methyl-2,2′-bipyridine.[17] The imines **6**−**8** and **9** were prepared with good yields (>80%) and results from single to multiple condensations (Scheme 2). Selected reaction conditions and best yields are collected in Table 2.

To obtain tridentate chelating ligands with a 6-carboxylic-2,2′-bipyridine frame and an amino aliphatic chain at the 5′ position, compounds **6** and **7** were subjected to the following synthetic sequence of reactions (Scheme 3). In a first step, the imine function was reduced to the corresponding secondary amines (**10** and **11**) by treatment with $NaBH_4$ in hot ethanol. A quite selective carboalkoxylation protocol[18] was then applied in which the amines were reacted with bubbling CO in a $Et_3N/^nBuOH$ mixture, using 5% $[Pd(PPh_3)_2Cl_2]$ as a

(16) Crystallographic data (0.10 × 0.10 × 0.08 mm): $C_{27}H_{30}N_4$, M = 410.57, T = 173 K, monoclinic, space group 2/c, a = 29.3303(2) Å, b = 9.5854(5) Å, c = 17.1277(5) Å, β = 99.116(5)°, V = 4754.5(3) Å^3, D_{calc} = 1.15 g·cm^{-3}, Z = 8, F(000) = 1760, μ(Mo Kα)= 0.069 mm^{-1}, 15 347 data collected, 1698 with $I > 3\sigma(I)$, R_1 = 0.038, R_w = 0.041. GOF = 1.035.

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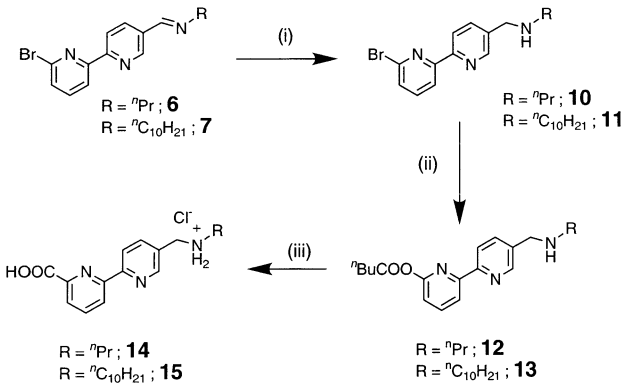
SCHEME 3[a]



[a] Key: (i) $NaBH_4$, EtOH, 80 °C, 70% for **10**, 84% for **11**; (ii) ^{n}BuOH, Et_3N, CO (1 atm), $[Pd(PPh_3)_2Cl_2]$ 5 mol %, 100 °C, 40 % for **12**, 30% for **13**; (iii) 10% aq HCl, 63% for **14**, 59% for **15**.

catalyst. Esters **12** and **13** were obtained in modest yields when compared to more conventional bromoaromatic substrates and the yields were even lower if ethanol was used. The boiling point of *n*-butanol allowed one to heat the reaction mixture higher, thus pointing to a thermodynamic barrier for formation of the esters. Interestingly, a carboamidation reaction[19] in which the secondary amine function would play the role of the nucleophile in place of the alcohol was not observed, because the alcohol is in large excess. Finally, the esters were hydrolyzed to the corresponding acids **14** and **15** by treatment with diluted HCl.

In summary, we have developed a methodology for the direct synthesis of imines from *gem*-dibromomethylaryl or heteroaryl compounds and primary amines. The dibromomethylbenzene was chosen as a test compound, and the isolated yields are good to excellent and applicable to a few primary amines. This methodology was extended to the synthesis of 6-carboxy-2,2′-bipyridine acid substituted at the 5′ position by alkylaminomethylene groups. This synthetic protocol appears as a suitable alternative for the synthesis of imines, as well as for the easy conversion of primary amines into secondary benzylamines after reduction of the imine. Because of these notable characteristics of the reaction, one can also envisage to use these *gem*-dibromo-substituted derivatives in Wittig-type reactions. Further efforts are currently directed toward the enlargement of the scope of the reaction toward phosphorus ylides and related dibromomethyl compounds on one hand and the use of the 6-carboxy-2,2′-bipyridine acid derivatives for complexation of lanthanide(III) cations on the other hand.

Experimental Section

General Methods. The 200.1 (^{1}H) and 50.3 MHz (^{13}C) NMR spectra were recorded at room temperature using perdeuterated solvents as internal standard: δ (H) in ppm relative to residual protiated solvent; δ (C) in ppm relative to the solvent. FT-IR spectra were recorded as KBr pellets. Melting points were obtained on a capillary melting point apparatus in open-ended capillaries and are uncorrected. Chromatographic purification was conducted using 40−63 μm silica gel or aluminum oxide 90 standardized. Thin Layer Chromatography (TLC) were performed on silica gel or aluminum oxide plates coated with fluorescent indicator. Deactivated plates are previously treated with 90:10 CH_2Cl_2−Et_3N. All mixtures of solvents are given in v/v ratio. Details for the X-ray crystal structure determination for compound **4** are given in ref 16.

Materials. CH_2Cl_2 was distilled from CaH_2. THF was dried over Na/benzophenone prior to distillation. CH_3CN was filtered over aluminum oxide and distilled over P_2O_5. $[Pd(PPh_3)_2Cl_2]$ was recrystallized from hot DMSO. Et_3N and EtOH were used as purchased. Analytical and spectroscopic data for compounds **1**,[20] **2**,[21] **3**,[22] and **4**[23] are in agreement with literature data.

[(6-Bromo-2,2′-bipyridin-5′-yl)methylene]propylamine (6). A Schlenk tube under argon was successively charged with **5** (230 mg, 0.6 mmol), *n*-propylamine (272 μL, 3.3 mmol), and anhydrous K_2CO_3 (195 mg, 1.4 mmol) in 10 mL of dry acetonitrile. The suspension was heated at 80 °C during 17 h. The mixture was evaporated to dryness, 50 mL of CH_2Cl_2 and 15 mL of water were added, and the organic phase was separated. The aqueous phase was extracted twice with 50 mL of CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4, filtered, and evaporated to dryness. The residue was recrystallized with CH_2Cl_2/hexane to afford **6** (158 mg, 92%) as a yellow powder: mp 99−100 °C; R_f = 0.43 (Al_2O_3, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.97 (t, 3H, ^3J = 7.5 Hz), 1.75 (sx, 2H, ^3J = 7.5 Hz), 3.63 (td, 2H, ^3J = 7.0 Hz, ^4J = 1.0 Hz), 7.49 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.0 Hz), 7.67 (t, 1H, ^3J = 7.5 Hz), 8.20 (dd, 1H, ^3J = 8.0 Hz, ^4J = 2.0 Hz), 8.35 (s, 1H), 8.41 (dd, 1H, ^3J = 7.5 Hz, ^4J = 0.5 Hz), 8.45 (d, 1H, ^3J = 8.0 Hz), 8.88 (d, 1H, ^4J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 11.9, 24.0, 63.9, 120.1, 121.3, 128.3, 132.2, 135.5, 137.1, 139.2, 141.7, 149.6, 155.8, 157.7; IR (KBr, cm^{-1}) ν 2959, 2919, 1642, 1583, 1545, 1431, 1123; FAB$^+$-MS *m*/z 306.1 (99), 304.1 (100). Anal. Calcd for $C_{14}H_{14}N_3Br$: C, 55.28; H, 4.64; N, 13.81. Found: C, 55.02; H, 4.49; N, 13.78.

[(6-Bromo-2,2′-bipyridin-5′-yl)methylene]decylamine (7). The same procedure as for the synthesis of **6** was used starting from **5** (200 mg, 0.5 mmol), decylamine (300 μL, 1.5 mmol), and anhydrous K_2CO_3 (135 mg, 1.0 mmol) in 5 mL of dry acetonitrile. The suspension was heated to 80 °C during 26 h. The residue was recrystallized with Et_2O to afford **7** (160 mg, 81%) as a white powder: mp 84−85 °C; R_f = 0.71 (deactivated SiO_2, 98:2 CH_2Cl_2−MeOH); ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3H, ^3J = 6.5 Hz), 1.26 (m, 14H), 1.60−1.81 (m, 2H), 3.65 (t, 2H, ^3J = 6.5 Hz), 7.49 (dd, 1H, ^3J = 7.5 Hz, ^4J = 0.5 Hz), 7.67 (t, 1H, ^3J = 7.5 Hz), 8.20 (dd, 1H, ^3J = 8.5 Hz, ^4J = 2.0 Hz), 8.35 (s, 1H), 8.41 (dd, 1H, ^3J = 7.5 Hz, ^4J = 0.5 Hz), 8.45 (d, 1H, ^3J = 7.5 Hz), 8.88 (d, 1H, ^4J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.7, 27.4, 29.3, 29.4, 29.6, 30.8, 31.9, 62.2, 120.1, 121.4, 128.3, 132.2, 135.5, 139.2, 141.7, 149.6, 155.8, 156.8, 157.6; IR (KBr, cm^{-1}) ν 2921, 2852, 1640, 1584, 1541, 1432, 1122; FAB$^+$-MS *m*/z (%) 404.2 (100), 402.2 (80), 199.2 (25). Anal. Calcd for $C_{21}H_{28}N_3Br$: C, 62.69; H, 7.01; N, 10.44. Found: C, 62.53; H, 6.98; N, 10.38.

[(6-Bromo-2,2′-bipyridin-5′-yl)methylene]-4-methoxyaniline (8). The same procedure as for the synthesis of **6** was used starting from **5** (200 mg, 0.5 mmol), *p*-anisidine (190 mg, 1.5 mmol), and K_2CO_3 (70 mg, 0.5 mmol) in 5 mL of dry acetonitrile. The solution was heated to 80 °C for 52 h. Recrystallization with CH_2Cl_2/hexane afforded **8** (154 mg, 85%) as pale green crystals: mp 195−198 °C; R_f = 0.56 (SiO_2, 97:3 CH_2Cl_2−MeOH); ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3H), 6.96 (d, 2H, ^3J = 9.0 Hz), 7.30 (d, 2H, ^3J = 9.0 Hz), 7.52 (d, 1H, ^3J = 7.5 Hz), 7.70 (t, 1H, ^3J = 7.5 Hz), 8.38 (dd, 1H, ^3J = 8.5 Hz, ^4J = 2.0 Hz), 8.45 (d, 1H, ^3J = 7.5 Hz), 8.50 (s, 1H), 8.56 (d, 1H, ^3J = 8.0 Hz), 9.03 (d, 1H, ^4J = 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 55.5, 114.5, 120.3, 121.5, 122.5, 128.4, 132.5, 135.7, 139.3, 141.8, 144.2, 150.2, 154.5, 156.1,

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156.7, 158.9; IR (KBr, cm^{-1}) ν 2956, 2833, 1619, 1505, 1432, 1123; FAB$^+$-MS *m*/z 370.2 (100), 368.2 (100), 249.2 (20), 247.2 (20). Anal. Calcd for $C_{18}H_{14}N_3OBr$: C, 58.71; H, 3.83; N, 11.41. Found: C, 58.45; H, 3.63; N, 11.30.

***N*-[(6-Bromo-2,2′-bipyridin-5′-yl)methylene]-*N*′,*N*′-bis-[2-[(6-bromo-2,2′-bipyridin-5′-yl)methyleneamino]ethyl]-ethane-1,2-diamine (9).** The same procedure as for the synthesis of **6** was used starting from **5** (325 mg, 0.80 mmol), triethylenetetramine (40 μL, 0.27 mmol), and K_2CO_3 (331 mg, 2.4 mmol) in 10 mL of dry acetonitrile. The solution was heated to 80 °C for 91 h. Recrystallization from hexane afforded **9** (195 mg, 83%) as a yellow powder: mp 170−171 °C; R_f = 0.55 (Al_2O_3, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 2.99 (t, 6H, ^3J = 6.0 Hz), 3.77 (t, 6H, ^3J = 6.0 Hz), 7.48 (dd, 3H, ^3J = 7.5 Hz, ^4J = 0.5 Hz), 7.65 (t, 3H, ^3J = 8.0 Hz), 8.00 (dd, 3H, ^3J = 8.0 Hz, ^4J = 2.0 Hz), 8.25 (s, 3H), 8.32 (s, 3H), 8.36 (s, 3H), 8.75 (d, 3H, ^4J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 55.2, 60.3, 120.2, 121.3, 128.3, 131.9, 135.5, 138.6, 139.2, 141.7, 149.4, 156.7, 158.8; IR (KBr, cm^{-1}) ν 2919, 2831, 1644, 1543, 1431, 1126; FAB$^+$-MS *m*/z 883.3 (100), 881.3 (92), 662.5 (35). Anal. Calcd for $C_{39}H_{33}N_{10}Br_3$: C, 53.10; H, 3.77; N, 15.90. Found: C, 52.64; H, 3.42; N, 15.62.

[(6-Bromo-2,2′-bipyridin-5′-yl)methyl]propylamine (10). In a Schlenk tube under argon were dissolved **6** (117 mg, 0.4 mmol) and $NaBH_4$ (73 mg, 1.9 mmol) in 10 mL of ethanol. The solution was heated to 65 °C for 18 h. A few drops of water were carefully added, and the mixture was evaporated to dryness. The compound was extracted with CH_2Cl_2 and the resulting solution dried with $MgSO_4$, filtered, and evaporated to dryness. Compound **10** (82 mg, 70%) was isolated as a greenish solid: mp 31−32 °C; R_f = 0.44 (deactivated SiO_2, 97:3 CH_2Cl_2−MeOH); ^{1}H NMR ($CDCl_3$) δ 0.90 (t, 3H, ^3J = 7.5 Hz), 1.51 (sx, 2H, ^3J = 7.5 Hz), 2.58 (t, 2H, ^3J = 7.0 Hz), 3.82 (s, 2H), 7.43 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.0 Hz), 7.62 (t, 1H, ^3J = 8.0 Hz), 7.76 (dd, 1H, ^3J = 8.0 Hz, ^4J = 2.0 Hz), 8.30 (s, 1H), 8.34 (s, 1H), 8.57 (d, 1H, ^4J = 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 11.6, 23.0, 50.9, 51.2, 119.4, 121.0, 127.6, 135.3, 136.6, 139.0, 141.4, 149.0, 153.1, 157.2; IR (KBr, cm^{-1}) ν 3433, 2946, 1647, 1569, 1544, 1430, 1123; FAB$^+$-MS *m*/z 308.2 (100), 306.2 (100), 249.5 (26), 247.5 (30). Anal. Calcd for $C_{14}H_{16}N_3Br$: C, 54.92; H, 5.27; N, 13.72. Found: C, 54.76; H, 4.96; N, 13.53.

[(6-Bromo-2,2′-bipyridin-5′-yl)methyl]decylamine (11). The same procedure as for synthesis of **10** was used starting from **7** (130 mg, 0.3 mmol) and $NaBH_4$ (61 mg, 1.6 mmol) in 10 mL of ethanol. Compound **11** (110 mg, 84%) was isolated as a pale yellow powder: mp 59−60 °C; R_f = 0.54 (deactivated SiO_2, 98:2 CH_2Cl_2−MeOH); ^{1}H NMR ($CDCl_3$) δ 0.84 (t, 3H, ^3J = 6.5 Hz), 1.22 (m, 14H), 1.47 (t, 2H, ^3J = 6.5 Hz), 2.59 (t, 2H, ^3J = 7.0 Hz), 3.81 (s, 2H), 7.42 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.0 Hz), 7.61 (t, 1H, ^3J = 7.5 Hz), 7.75 (dd, 1H, ^3J = 8.0 Hz, ^4J = 2.0 Hz), 8.30 (d, 1H, ^4J = 0.5 Hz), 8.34 (d, 1H, ^4J = 0.5 Hz), 8.56 (d, 1H, ^4J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.6, 27.3, 29.2, 29.5, 30.0, 31.8, 49.4, 51.1, 119.5, 121.1, 127.7, 136.6, 136.7, 139.1, 141.5, 149.0, 153.2, 157.3; IR (KBr, cm^{-1}) ν 3440, 2923, 1620, 1568, 1543, 1431, 1384, 1122; FAB$^+$-MS *m*/z 406.2 (100), 404.3 (100), 264.2 (30), 262.3 (30). Anal. Calcd for $C_{21}H_{30}N_3Br$: C, 62.37; H, 7.48; N, 10.39. Found: C, 62.09; H, 7.26; N, 10.15.

[(6-Carbutoxy-2,2′-bipyridin-5′-yl)methyl]propylamine (12). A solution of **10** (191 mg, 0.6 mmol) and [Pd(PPh_3)$_2$Cl$_2$] (26 mg, 37 μmol) in a mixture of 15 mL of ^{n}BuOH and 10 mL of Et_3N was heated at 100 °C for 19 h, under a continuous flow of CO at atmospheric pressure. After the solution was cooled to rt, the solvents were distillated under reduced pressure, and the resulting solid was purified by flash column chromatography (SiO_2, 100:0−95:5 CH_2Cl_2−MeOH) to give compound **12** (82 mg, 40%) as a yellowish gum: R_f = 0.63 (deactivated SiO_2, 95:5 CH_2Cl_2−MeOH);^{1}H NMR ($CDCl_3$) δ 0.93 (t, 3H, ^3J = 7.5 Hz), 0.92 (t, 3H, ^3J = 7.5 Hz), 1.33−1.58 (m, 2H), 1.66−1.91 (m, 4H), 2.95 (t, 2H, ^3J = 7.5 Hz), 4.20 (s, 2H), 4.39 (t, 2H, ^3J = 6.5 Hz), 7.90 (t, 1H, ^3J = 7.5 Hz), 8.05 (d, 1H, ^3J = 7.5 Hz), 8.15 (dd, 1H, ^3J = 8.0 Hz, ^4J = 2.0 Hz), 8.25−8.45 (m, 2H), 8.87 (s, br, 1H); ^{13}C NMR ($CDCl_3$) δ 11.3, 13.7, 19.1, 20.4, 30.6, 49.0, 49.8, 65.9, 121.6, 124.5, 125.1, 129.3, 138.1, 139.2, 147.6, 150.8, 155.0, 155.5, 165.3; IR (KBr, cm^{-1}) ν 3438, 2926, 1738, 1640, 1589, 1457, 1141, 1077; FAB$^+$-MS *m*/z 328.2 (100), 254.2 (30). Anal. Calcd for $C_{19}H_{25}N_3O_2$: C, 69.70; H, 7.70; N, 12.83. Found: C, 69.51; H, 7.39; N, 12.69.

[(6-Carbutoxy-2,2′-bipyridin-5′-yl)methyl]decylamine (13). A solution of **11** (156 mg, 0.4 mmol) and [Pd(PPh_3)$_2$Cl$_2$] (16 mg, 23 μmol) in a mixture of 12 mL of ^{n}BuOH and 8 mL of Et_3N was heated at 100 °C for 15 h under a CO atmosphere. The solution was cooled to rt and filtered over Celite. The solvents were distilled under reduced pressure, and the resulting solid was purified by flash column chromatography (SiO_2, 100:0−97:3 CH_2Cl_2−MeOH) to give **13** (50 mg, 30%) as a beige solid: mp 40−41 °C; R_f = 0.60 (deactivated SiO_2, 97:3 CH_2Cl_2−MeOH); ^{1}H NMR ($CDCl_3$) δ 0.84 (t, 3H, ^3J = 6.5 Hz), 0.98 (t, 3H, ^3J = 7.5 Hz), 1.21 (m, 14H), 1.39−1.70 (m, 4H), 1.72−1.89 (m, 2H), 2.73 (t, 2H, ^3J = 7.5 Hz), 3.97 (s, 2H), 4.41 (t, 2H, ^3J = 6.5 Hz), 7.91 (t, 1H, ^3J = 8.0 Hz), 7.95 (dd, 1H, ^3J = 8.0 Hz, ^4J = 2.5 Hz), 8.07 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.0 Hz), 8.44 (d, 1H, ^3J = 7.5 Hz), 8.51 (dd, 1H, ^3J = 7.5 Hz, ^4J = 1.0 Hz), 8.69 (d, 1H, ^4J = 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.7, 14.1, 19.2, 22.6, 27.1, 28.8, 29.2, 29.3, 29.5, 30.7, 31.8, 48.8, 50.2, 121.4, 124.1, 124.8, 133.6, 137.7, 137.8, 147.7, 149.7, 154.5, 156.0, 165.3; IR (KBr, cm^{-1}) ν 3439, 2927, 1739, 1641, 1588, 1466, 1157, 1087; FAB$^+$-MS *m*/z 426.2 (100), 368.2 (20). Anal. Calcd for $C_{26}H_{39}N_3O_2$: C, 73.37; H, 9.24; N, 9.87. Found: C, 73.00; H, 8.99; N, 9.64.

[(6-Carboxy-2,2′-bipyridin-5′-yl)methyl]propylammonium Chloride (14). A solution of **12** (69 mg, 0.2 mmol) in 1 mL of concentrated HCl (37%) and 9 mL of water was heated to 70 °C for 2 h. The mixture was evaporated to dryness, and recrystallization of the residue with a mixture of MeOH/Et_2O afforded **14** (43 mg, 63%) as a white powder: mp >230 °C dec; ^{1}H NMR (CD_3OD) δ 1.07 (t, 3H, ^3J = 7.5 Hz), 1.83 (sx, 2H, ^3J = 7.5 Hz), 3.17 (t, 2H, ^3J = 7.5 Hz), 4.58 (s, 2H), 8.28−8.47 (m, 2H), 8.72 (dd, 1H, ^3J = 7.5 Hz, ^4J = 1.5 Hz), 8.84−9.02 (m, 2H), 9.28 (s, br, 1H); ^{13}C NMR ($CDCl_3$) δ 11.3, 20.8, 48.3, 51.0, 125.7, 127.2, 129.1, 133.1, 141.8, 146.1, 148.7, 149.2, 149.6, 150.4, 167.4; IR (KBr, cm^{-1}) ν 3448, 2969, 2768, 1749, 1635, 1465, 1263, 1188; FAB$^+$-MS *m*/z 272.5 (80). Anal. Calcd for $C_{15}H_{18}N_3O_2Cl\cdot H_2O$: C, 55.30; H, 6.19; N, 12.90. Found: C, 55.25; H, 6.01; N, 12.75.

[(6-Carboxy-2,2′-bipyridin-5′-yl)methyl]decylammonium Chloride (15). A solution of **13** (24 mg, 56 μmol) in 1 mL of concentrated HCl (37%) and 4 mL of water was heated to 70 °C for 3 h. The mixture was evaporated to dryness, and recrystallization of the residue with a mixture of MeOH/Et_2O afforded **15** (14 mg, 59%) as a white powder: mp >185 °C dec;^{1}H NMR (CD_3OD) δ 0.89 (t, 3H, ^3J = 6.5 Hz), 1.29 (m, 14H), 1.71−1.91 (m, br, 2H), 3.21 (t, 2H, ^3J = 8.0 Hz), 4.59 (s, 2H), 8.26−8.46 (m, 2H), 8.72 (dd, 1H, ^3J = 7.0 Hz, ^4J = 1.5 Hz), 8.86−9.03 (m, 2H), 9.31 (s, 1H); ^{13}C NMR (CD_3OD) δ 14.4, 23.7, 27.4, 27.6, 30.2, 30.4, 30.5, 30.6, 33.0, 48.2, 49.6, 125.7, 127.1, 129.0, 133.1, 141.8, 146.1, 148.7, 149.2, 149.6, 150.4, 167.4; IR (KBr, cm^{-1}) ν 3441, 2923, 2775, 1700, 1636, 1466, 1257; FAB$^+$-MS *m*/z 370.4 (70). Anal. Calcd for $C_{22}H_{32}N_3O_2Cl\cdot H_2O$: C 62.32, H 8.08, N 9.91. Found: C 62.19, H 7.88, N 9.72.

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Supporting Information Available: Experimental details for compounds **1**−**4**, crystallographic data for compound **4**, and an ORTEP view. This material is available free of charge via the Internet at http://pubs.acs.org.

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