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Preparation of a series of novel fluorophores, N-substituted 6-amino and 6,6″-diamino-2,2′:6′,2″-terpyridine by palladium-catalyzed amination

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Abstract—A new series of N-substituted 6-amino- and 6,6″-diamino-2,2′:6′,2″-terpyridine (6-amino- and 6,6″-diamino-tpy) was conveniently synthesized in one-step by Pd-catalyzed amination of bromo-substituted tpys with various amines. For highly coordinating tpy substrates, use of appropriate chelating phosphine ligand was critical to achieve moderate to satisfactory yield. The prepared N-substituted 6-amino- and 6,6″-diamino-tpys exhibited moderate to intense fluorescence in dichloromethane with fine-tuned fluorescence maxima ranging from 385 to 455 nm.

1. Introduction

Prompted by rapidly expanding applications of organic fluorescent materials for electroluminescence (EL), dye-lasers, sensors, probes, and phototherapeutic agents, development of new fluorescent organic compounds with high functionality has been the subject of intense study for more than a decade.[1] Though 2,2′:6′,2″-terpyridine (tpy) is an excellent metal chelate with high thermal and chemical stability,[2] tpy derivatives are not fluorescent in general.[3] We previously reported that 6-amino-2,2′:6′,2″-terpyridine (6-amino-tpy, **1**) showed intense blue fluorescence in solution ($\lambda_{fl} = 384$ nm, $\Phi = 0.70$, dichloromethane),[4] and could be a good candidate for a new functional fluorophore. However, synthesis of this compound requires laborious amination of 6-bromo-tpy with liquid ammonia under high temperature and pressure.[4] Since it is of great use to develop a series of fluorescent derivatives having different luminescence color and/or additional functional units, we extended our study to prepare a series of N-substituted 6-amino-tpy derivatives by an easily accessible method.

For this end, we tested Pd-catalyzed cross-coupling of aryl halide with various amines, which has been recognized as the convenient and useful method for preparation of a variety of arylamines.[5] However, application of this catalytic system to the synthesis of heteroarylamine is rather limited.[6] For halopyridines, (±)-BINAP ((±)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl), DPPF (1,1′-bis(diphenylphosphino)ferrocene), and other chelating phosphine ligands were used in order to suppress ligand exchange with pyridine,[6a,7] but much less has been studied for the reaction of 2,2′-bipyridine having a higher coordination ability.[8] Therefore, careful examination is required for application of this method to highly coordinating tpy. In this letter, we report that a series of *N*-alkyl- and *N*-phenyl-substituted tpys that show efficient fluorescence are conveniently synthesized in one-step by Pd-catalyzed amination of 6-bromo-tpy in the presence of appropriate phosphine ligand.

2. Synthesis

The reaction of 6-bromo- or 6,6″-dibromo-tpy with various amines (1.1 equiv) were carried out in toluene at 80 °C for 18 h in the presence of 3.0 mol % of air-stable $Pd(dba)_2$ (dba = dibenzylideneacetone) as a palladium source, 4.5 mol % of bidentate phosphine DPPF or (±)-BINAP (based on 6-bromo-tpy), and 2.6 equiv of sodium *tert*-butoxide (based on amine). Isolated yields of the amino-substituted tpys based on the bromo-tpy substrate are summarized in Tables 1 and 2, respectively.[9]

Keywords: Terpyridine; Pd-catalyzed amination; Fluorescence.
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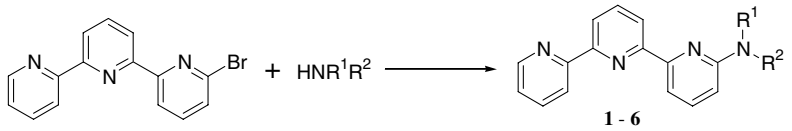
Table 1. Synthesis[a] and fluorescence maxima of N-substituted 6-amino-tpys, **1**–**6**

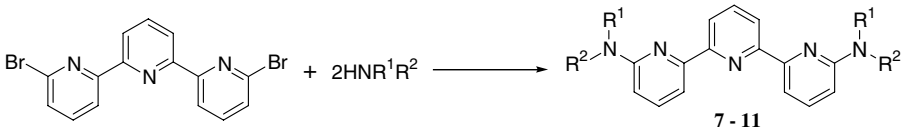


1 - 6

Compound	R^1	R^2	Ligand	Yield (%)	λ_{fl}/nm[b]
1[c]	–H	–H	DPPF	81	384[d]
2	–Et	–H	DPPF	16 (52[e])	404
				17 (40[e])[f]	
			BINAP	68 (25[e])[f]	
3	–Me	–Me	DPPF	72	427
4	–Et	–Et	DPPF	66	431
			BINAP	No reaction	
5	–Ph	–H	DPPF	90	443
6	–Ph	–Ph	DPPF	74	455

[a] Reaction conditions: 3.0 mol % $Pd(dba)_2$, 4.5 mol % ligand, *t*-BuONa, toluene, 80 °C, 18 h.
[b] In dichloromethane at 20 °C.
[c] Compound **1** was prepared by using $LiN(SiMe_3)_2$ instead of amine and *t*-BuONa, followed by hydrolysis with aq HCl solution.
[d] Taken from Ref. 4.
[e] Yield of tpy-N(Et)-tpy based on 6-bromo-tpy.
[f] Ethylamine: 5.0 equiv.

Table 2. Synthesis[a] and fluorescence maxima of N-substituted 6,6″-diamino-tpys, **7**–**11**



7 - 11

Compound	R^1	R^2	Ligand	Yield (%)	λ_{fl}/nm[b]
7[c]	–Et	–H	DPPF	31 (37[d])[e]	404
			BINAP	83 (11[d])[e]	
8	–Me	–Me	DPPF	68	422
9	–Et	–Et	DPPF	67	428
10	$-(CH_2)_2-O-(CH_2)_2-$[f]		DPPF	94	423
11	–Ph	–Ph	DPPF	88	453

[a] Reaction conditions: 6.0 mol % $Pd(dba)_2$, 9.0 mol % ligand, *t*-BuONa, toluene, 80 °C, 18 h.
[b] In dichloromethane at 20 °C.
[c] Cs_2CO_3 was used instead of *t*-BuONa as base.
[d] Yield of EtNH-tpy-N(Et)-tpy-NHEt based on 6,6″-dibromo-tpy.
[e] Ethylamine: 5.0 equiv.
[f] Morpholino group.

For amination of highly coordinating bromo-tpys, use of unidentate ligands, $P(^tBu)_3$[10] and bicyclic triaminophosphine (2,8,9-triisobutyl-2,5,8,9-tetraaza-1-phosphabicyclo[3,3,3]undecane),[11] were not effective, resulting in less than half of conversions even after prolonged reaction time. However, use of bidentate DPPF as the ligand was found to be effective, and amino-tpys (**3**–**6** and **8**–**11**) were prepared in moderate to satisfactory yields, demonstrating that the Pd-catalyzed amination was applicable even for highly coordinating tpy substrates. For the synthesis of 6-amino-tpy (**1**), $LiN(SiMe_3)_2$ (1.1 equiv) was used as an amine substrate.[10,12] Subsequent hydrolysis to remove $SiMe_3$ groups with aq HCl gave the parent compound **1** in 81%.

However, amination with ethylamine (1.1 equiv) in the presence of DPPF resulted in poor yields of ethylamino-tpys, **2** and **7**. The major products in these reactions were found to be bis(6-terpyridyl)-substituted ethylamines, indicating that further arylation of ethylamino-tpys proceeded preferentially. Use of excess amounts of ethylamine (5.0 equiv) only slightly improved the yields of the monoarylated products, and the diarylated products (yields based on bromo-tpys are given in parentheses) were still the major products (Tables 1 and 2). Unlike pyridine substrates,[6a] use of large excess amounts of amine (up to 10.0 equiv) could not effectively suppress the diarylation process, showing that DPPF was not suitable for the reaction in this case. Since Wolfe and Buchwald[13] showed that use of more bulky chelating phosphine ligand, (±)-BINAP, was effective to suppress the diarylation reaction, we tested the reaction in the presence of (±)-BINAP instead of DPPF. The diarylation reaction was appreciably suppressed, yielding **2** and **7** in 68% and 81%, respectively. Since no reaction took place when (±)-BINAP was used

for the amination with diethylamine (**4** in Table 1), the bulky (±)-BINAP ligand might prevent coordination of larger secondary amine to the Pd center, thus suppressing the further arylation of **2** and **7**.

3. Fluorescent properties

Structural modification frequently causes loss of their fluorescence. However, all the N-substituted 6-amino-tpy and 6,6″-diamino-tpy derivatives prepared here exhibited moderate to strong fluorescence. Their fluorescence maxima in dichloromethane solution at 20 °C are also included in Tables 1 and 2. *N*-Alkyl substitution caused bathochromic shift of fluorescence, and *N*-phenyl substitution induced larger shift. Since all the N-substituted amino-tpys showed fluorescence with slightly different fluorescence maxima, it is confirmed that N-substitution is the useful method for fine-tuning of the fluorescence maxima ranging from 385 to 455 nm without damaging the highly fluorescent nature of the parent compound **1**.

Thus, the Pd-catalyzed amination was shown to be applicable to the highly coordinating substrate, bromo-substituted tpys, by selection of the appropriate bidentate phosphine ligand, DPPF or (±)-BINAP, and a series of novel fluorescent N-substituted amino-tpys with fine-tuned fluorescence maxima were conveniently prepared in one-step in moderate to satisfactory yields.

Acknowledgments

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9. General procedure: A deaerated suspension of 6-bromo- or 6,6″-dibromo-tpy (0.5 mmol), $Pd(dba)_2$ (3.0 or 6.0 mol %, respectively), DPPF (4.5 or 9.0 mol %, respectively), amine (1.1 equiv), and sodium *tert*-butoxide (2.6 equiv to amine) in toluene (8 mL) was placed in a Schlenk tube and reacted for 18 h at 80 °C. The resultant mixture was cooled to room temperature, diluted with CH_2Cl_2 and filtered through Celite. The filtrate was evaporated in vacuo, and purified by column chromatography (aluminum oxide, benzene–acetonitrile). Compound **2**: mp 135.0–136.0 °C. Found: C, 73.67; H, 5.79; N, 20.12; calcd for $C_{17}H_{16}N_4$: C, 73.89; H, 5.84; N, 20.27. δ_H (400 MHz, $CDCl_3$) 1.31 (3H, t, CH_3), 3.42 (2H, quintet, CH_2), 4.55 (1H, br t, NH), 6.44 (1H, d, 5-H), 7.31 (1H, t, 5″-H), 7.60 (1H, t, 4-H), 7.84 (1H, t, 4″-H), 7.91 (1H, t, 4′-H), 7.92 (1H, d, 3-H), 8.38–8.40 (2H, m, 3′,5′-H), 8.62 (1H, d, 3″-H), 8.69 (1H, d, 6″-H).
Compound **3**: mp 127.4–128.3 °C (lit. 127.2–127.8 °C).[4] Found: C, 74.05; H, 5.62; N, 20.35; calcd for $C_{17}H_{16}N_4$: C, 73.89; H, 5.84; N, 20.27. δ_H (400 MHz, $CDCl_3$) 3.19 (6H, s, $(CH_3)_2$), 6.60 (1H, d, 5-H), 7.32 (1H, t, 5″-H), 7.64 (1H, t, 4-H), 7.86 (1H, t, 4″-H), 7.90–7.94 (2H, m, 3,4′-H), 8.40–8.46 (2H, m, 3′,5′-H), 8.64 (1H, d, 3″-H), 8.69 (1H, d, 6″-H).
Compound **4**: mp 82.5–83.3 °C. Found: C, 75.07; H, 6.60; N, 18.41; calcd for $C_{19}H_{20}N_4$: C, 74.97; H, 6.62; N, 18.41. δ_H (400 MHz, $CDCl_3$) 1.25 (6H, t, CH_3), 3.62 (4H, q, CH_2), 6.53 (1H, d, 5-H), 7.31 (1H, t, 5″-H), 7.59 (1H, t, 4-H), 7.84 (1H, t, 4″-H), 7.82–7.93 (2H, m, 3,4′-H), 8.36–8.43 (2H, m, 3′,5′-H), 8.64 (1H, d, 3″-H), 8.68 (1H, d, 6″-H).
Compound **5**: mp 120.5–121.5 °C. Found: C, 77.58; H, 4.90; N, 17.30; calcd for $C_{21}H_{16}N_4$: C, 77.76; H, 4.97; N, 17.27. δ_H (400 MHz, $CDCl_3$) 6.60 (1H, br, NH), 6.90 (1H, d, 5-H), 7.07 (1H, t, (Ph, *p*-H)), 7.32–7.38 (3H, m, 5″-H, (Ph, *m*-H)), 7.48 (2H, d, (Ph, *o*-H)), 7.69 (1H, t, 4-H), 7.86 (1H, t, 4″-H), 7.95 (1H, t, 4′-H), 8.10 (1H, d, 3-H), 8.38–8.45 (2H, m, 3′,5′-H), 8.64 (1H, d, 3″-H), 8.71 (1H, d, 6″-H).
Compound **6**: mp 190.5–191.5 °C. Found: C, 80.71; H, 4.91; N, 13.88; calcd for $C_{27}H_{20}N_4$: C, 80.98; H, 5.03; N, 13.99.δ_H (400 MHz, $CDCl_3$) 6.75 (1H, d, 5-H), 7.17 (2H, t, (Ph, *p*-)), 7.28–7.38 (7H, m, 5″-H, (Ph, *o*-), (Ph, *m*-)), 7.61 (1H, t, 4-H), 7.85 (1H, t, 4″-H), 7.79 (1H, t, 4′-H), 8.02 (1H, d, 3-H), 8.13 (1H, d, 3′-H), 8.36 (1H, d, 5′-H), 8.61 (1H, d, 3″-H), 8.69 (1H, d, 6″-H).
Compound **7**: mp 141.0–142.0 °C. Found: C, 71.42; H, 6.65; N, 21.98; calcd for $C_{19}H_{21}N_5$: C, 71.45; H, 6.63; N, 21.93. δ_H (400 MHz, $CDCl_3$) 1.29 (6H, t, CH_3), 3.40 (4H, quintet, CH_2), 4.56 (2H, br t, NH), 6.42 (2H, d, 5,5″-H), 7.59 (2H, t, 4,4″-H), 7.86 (1H, t, 4′-H), 7.93 (2H, d, 3,3″-H), 8.34 (2H, d, 3′,5′-H).
Compound **8**: mp 197.0–198.0 °C. Found: C, 71.44; H, 6.49; N, 21.82; calcd for $C_{19}H_{21}N_5$: C, 71.45; H, 6.63; N,

21.93. δ_H (400 MHz, $CDCl_3$) 3.18 (12H, s, CH_3), 6.58 (2H, d, 5,5″-H), 7.62 (2H, t, 4,4″-H), 7.87 (1H, t, 4′-H), 7.94 (2H, d, 3,3″-H), 8.40 (2H, d, 3′,5′-H).

Compound **9**: mp 132.2–133.2 °C. Found: C, 73.46; H, 7.79; N, 18.80; calcd for $C_{23}H_{29}N_5$: C, 73.57; H, 7.78; N, 18.65. δ_H (400 MHz, $CDCl_3$) 1.25 (12H, t, CH_3), 3.62 (8H, q, CH_2), 6.52 (2H, d, 5,5″-H), 7.58 (2H, t, 4,4″-H), 7.86 (1H, t, 4′-H), 7.88 (2H, d, 3,3″-H), 8.36 (2H, d, 3′,5′-H).

Compound **10**: mp 228.0–229.0 °C. Found: C, 68.29; H, 6.33; N, 17.38; calcd for $C_{23}H_{25}N_5O_2$: C, 68.47; H, 6.25; N, 17.36. δ_H (400 MHz, $CDCl_3$) 3.63 (8H, t, CH_2), 3.89 (8H, t, CH_2), 6.70 (2H, d, 5,5″-H), 7.69 (2H, t, 4,4″-H), 7.87 (1H, t, 4′-H), 8.04 (2H, d, 3,3″-H), 8.36 (2H, d, 3′,5′-H).

Compound **11**: mp 261.0–262.0 °C. Found: C, 82.44; H, 5.05; N, 12.40; calcd for $C_{39}H_{29}N_5$: C, 82.51; H, 5.15; N, 12.34. δ_H (400 MHz, $CDCl_3$) 6.74 (2H, d, 5,5″-H), 7.16 (4H, t, (Ph, *p*-)), 7.28 (8H, d, (Ph, *o*-)), 7.35 (8H, t, (Ph, *m*-)), 7.60 (2H, t, 4,4″-H), 7.62 (1H, t, 4′-H), 7.93 (2H, d, 3,3″-H), 8.13 (2H, d, 3′,5′-H).

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