JOC The Journal of Organic Chemistry

NOTE

pubs.acs.org/joc

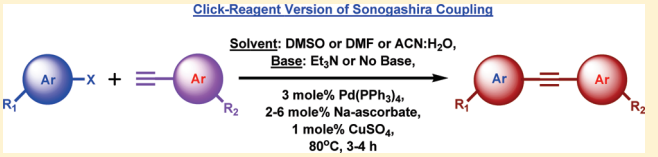
Click-Reagent Version of Sonogashira Coupling Protocol to Conjugated Fluorescent Alkynes with No or Reduced Homocoupling

Subhendu Sekhar Bag,* Rajen Kundu, and Manas Das

Bioorganic Chemistry Laboratory, Department of Chemistry, Indian Institute of Technology, Guwahati-781039, India

Supporting Information

ABSTRACT: A click-reagent version of the Sonogashira-coupling protocol has been developed. Diarylalkynes with donor and/or acceptor substituents have been synthesized via this protocol at moderate to excellent yields and with no or drastically reduced quantities of undesired homocoupled side products. This protocol is green-solvent compatible, air-insensitive, and effective under microwave conditions.



Since the discovery of Sonogashira coupling in 1975, this protocol has become a very widely used and practical tool for the generation of several terminal and internal π-conjugated acetylenic compounds that have widespread applications.[1,2] Despite its reliability, simplicity, and overall applicability, Sonogashira coupling suffers from several shortcomings, such as (a) the generation of undesired homocoupled products[3] of terminal alkynes in the presence of air, (b) the requirement of specific substrates and the skillful tailoring of reaction conditions, (c) poor coupling in the presence of mild conditions with unactivated halides, (d) the requirement of large amounts of a catalyst, and (e) low catalyst turnover.[4] Thus, there has been a tremendous research effort over the course of the past decade to overcome these limitations;[4] however, no single protocol has overcome the aforementioned shortcomings, especially the problem of homocoupling. Therefore, overcoming these limitations, especially the problem of the homocoupling side reaction, remains a challenge for researchers.

The presence of oxidizing agents or air in the reaction setup, both of which are difficult to completely remove, may oxidize nascent Pd(0) to Pd(II) and/or Cu(I) to Cu(II), which, in turn, may promote the homocoupling of terminal alkynes in CuI cocatalyzed original Sonogashira coupling.[2b,4e-g,5d] Despite several modifications,[5,6] no special steps have been taken to develop a modified version of the Cu(I) cocatalyst system so as to reduce the homocoupling reaction and facilitate a high yield of desired product; however, the reaction rate can be accelerated and applied to a wider range of reaction conditions. As a part of our ongoing research efforts toward installing a fluorescence response in a nonfluorescent precursor via a click reaction,[7] we have envisioned that Sonogashira coupling could potentially enable us to discover more conjugated and highly emissive fluorophores. Therein, the specific questions we wanted to address are as follows: (a) Can the same click-reagents serve as a source of reactive Cu(I) for Sonogashira coupling, (b) can Na-ascorbate maintain a reducing atmosphere in this system,[8] and, (c) if so, would it more effectively reduce the incidence of homocoupling in comparison to CuI or other reported

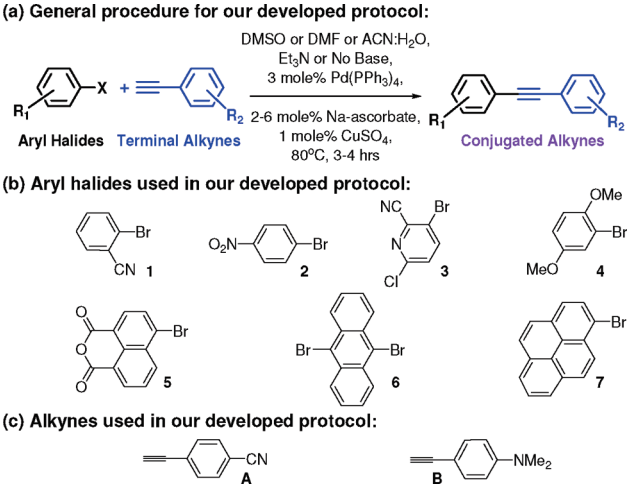


Figure 1. (a) Schematic representation of the general procedure. (b) The aryl halides and (c) alkynes that were used in our developed click-reagent version of Sonogashira coupling protocol.

modified methods?[4-6] Immediate attempts were taken to answer our curiosities, and we were successful in developing a click-reagent version of Sonogashira coupling method (Figure 1) under mild reaction conditions without any requirement of skillful reaction tailoring.

The logic behind the use of click-reagent in our strategy is the following: (a) to generate active Cu(I) in situ, (b) halt the oxidation of the generated Cu(I) into Cu(II), and (c) remove excessive air/O_2 from the reaction setup, which may damage nascent Pd(0) catalyst. Sodium ascorbate can reduce oxygen to form water in the vicinity of nascent Pd(0),[4e-g,5d] which reduces the oxygen concentration in the reaction; hence, the incidence of

Received: January 5, 2011
Published: March 08, 2011

Scheme 1. The Most Probable Mechanism of the Developed Protocol, Which Shows the Roles of the Click-Reagents

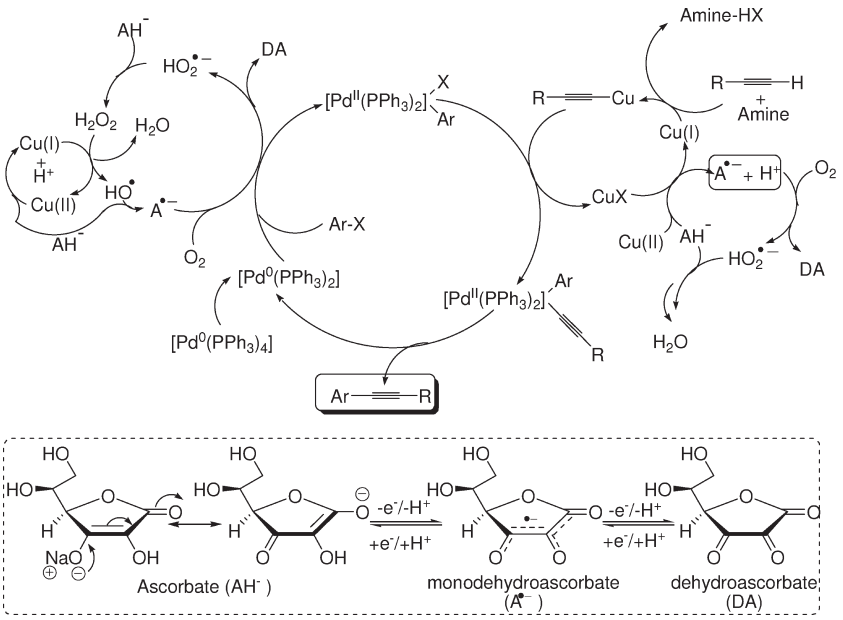
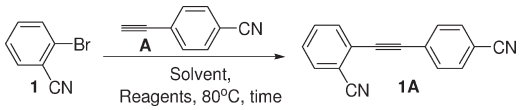


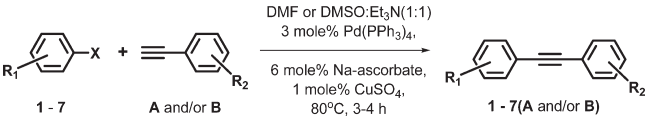
Table 1. Optimization of the Reaction Condition



	reagents (mol %)					
solvents	Pd(0)	CR1[a]	CR2[b]	base (Et_3N)	time (h)	yield (%)[c]
DMF	3	1	6	excess	4	84
	3	1	6	20 equiv	4	80
	3	1	6	10 equiv	4	70
	3	1	6	5 equiv	4	54
	3	1	6	2 equiv	4	53
	3	1	6		4	20
	3	1	5	excess	4	71
	3	1	4	excess	4	56
	3	1	3	excess	4	48
	3	1	2	excess	4	40
	3	0	6	excess	4.5	49
	3	0	6		12	22
	1	1	6	excess	5	34
DMF/H_2O (1:8)	3	1	6	excess	5	71
ACN/H_2O (1:1)	3	1	6	excess	4	82
DMF, open air	3	1	6	excess	4	40
MW, open air	3.5	1	6	excess	3.5 min	90

[a] CR1 is click-reagent 1, which is $CuSO_4$. [b] CR2 is click-reagent 2, which is sodium ascorbate. [c] Yields consist of isolated pure compounds. For all of the reactions, the conversion was 100%.

Table 2. The Synthesis of Conjugated Alkynes via the Developed Protocol



entry[a]	alkyne[b]	products[c]	yield (%)[d]	alkyne dimer (%)
1	**A**	**1A**	86 (60, 12 h)[9a,b]	
	B	**1B**	86	3
2	**A**	**2A**	91	
	B	**2B**	86	6
3[e]	**B**	**3B**	61	6
4	**A**	**4A**	72	
	B	**4B**	71	2
5	**A**	**5A**	65	
	B	**5B**	86	
6[f]	**A**	**6A**	72	
	B	**6B**	68 (50, 24 h)[9b]	1
7	**A**	**7A**	97	
	B	**7B**	92 (63, 12 h)[9c]	

[a] The reactions were performed in DMSO (for entry **1**), in DMF (for entry **2**-**5**), in 1:1:1 toluene:THF:water (for **6**; conversion was 65%), and in DMF (for entry **7**). [b] Figure 1. [c] SI, Figure S1. [d] Yields are of isolated pure compounds; yields in parentheses are of reported compounds using the original Sonogashira condition. [e] Along with **3B**, a biscoupled product **3B′** was obtained in 25% yield. [f] **6A**−**B** are monocoupled products.

undesired oxidative homocoupling is drastically diminished. Therefore, to maintain a constant reducing environment, we used six times more Na-ascorbate than Cu(II). Therefore, the most probable roles of the click-reagents in the Sonogashira coupling procedure include the in situ provision of active Cu(I) cocatalyst, maintenance of a constant reducing atmosphere in the vicinity of nascent Pd(0), and achievement of the possible

dx.doi.org/10.1021/jo200005n |J. Org. Chem. 2011, 76, 2332–2337

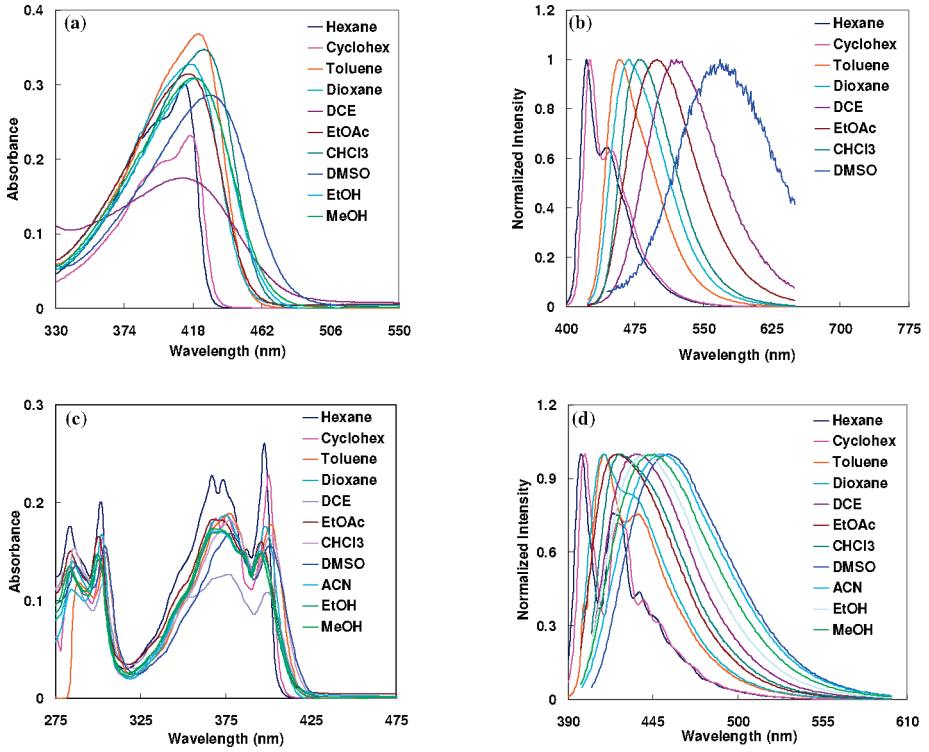


Figure 2. (a) UV−visible and (b) normalized fluorescence spectra of **3B′** and (c) UV−visible and (d) normalized fluorescence spectra of **7A** in different solvents.

acceleration of the reductive elimination step, which would result in a high yield of a desired product. Scheme 1 represents the most probable course of the reaction showing the roles of click-reagents.

In this particular article, we want to present our developed method, which was observed to result in either a tremendous decrease in or no undesired homocoupling and an enhancement in the yield of the desired heterocoupled product within a short period of time. To establish the optimum conditions of our protocol, we have investigated the possibility of coupling with varying catalytic concentrations. Thus, as is shown in Table 1, we carried out a reaction of aryl bromide **1** with alkyne **A** in various molar ratios of ascorbate, base, and Pd(0) in DMF. Thus, we have carried out the Sonogashira reaction using a $CuSO_4$/Na-ascorbate couple in a 1:6 mol % ratio as a source of active Cu(I) (1 mol %), Pd(0) (3 mol %) in a 1:1 DMF/Et_3N solvent at 80 °C, and other possible molar ratios. All of the reactions were found to be complete within 4 h. The products were isolated to purity with moderate to excellent yields via column chromatography and then characterized. We have also tested our methodology in the absence of base or copper, as well as in both copper- and base-free conditions; however, a low yield of the products (22−49%, Table 1) was obtained by applying these conditions. Finally, we observed that a minimum of 20 equiv of base is required to achieve good yields; therefore, a catalytic composition of Pd(0):$CuSO_4$:ascorbate in a ratio of 3:1:6 mol % was identified to be the optimum yielding condition (Table 1).

To test the feasibility and facilitate the generalization of our method, we used optimum yielding conditions and carried out the reactions of a series of simple aryl bromides with two terminal alkynes (Figure 1) for the synthesis of several donor−acceptor-containing conjugated alkynes; one terminal alkyne contains electron-withdrawing substituents (**A**, −CN), whereas the other has an electron-donating group (**B**, $-NMe_2$). The products were isolated to purity at good to excellent yields via column chromatography and characterized by NMR, mass spectrometry, and, in a few cases, X-ray crystallography (Table 2 and Figure S1 in the SI). We have observed that irrespective of the aryl halides, no homocoupled products with the electron-deficient alkyne **A** were formed; however, in a few cases, a negligible amount (1−6%) of homocoupled products with the electron-rich alkyne **B** was observed (Table 2). Here, it is important to mention that for 4-bromonaphthalic anhydride (entry **5A**, Table 2), due to its poor solubility in DMF or DMSO, the resulting product was isolated to purity via filtration and recrystallization from 1:1 toluene−ethanol. Therein, a loss of product resulted in a low yield of 65%. Also, in the case of dibromoanthracene, where in the reaction was carried out in 1:1:1 toluene:THF:water, an appreciable amount of unreacted starting material remained, which resulted in a moderate yield (72% for **6A**) of the product; however, most importantly, no homocoupling was observed in both of these cases. In the case of pyridine halide **3**, the yield of the desired product, **3B**, was 61%; however, along with **3B**, biscoupled product **3B′** was obtained at a 25% yield after being isolated (SI, Figure S1). This result, though it is only one example, indicates that our click-reagent version of the Sonogashira coupling procedure proceeds even when using aryl chloride.

In comparison to the CuI cocatalyzed reaction, the yields of the cross-coupled desired products were found to have tremendously increased at the expense of the quenched incidence; of homocoupling via our protocol. We have tested our methodology in DMSO and under microwave irradiation (3.5 min, 200 W) in both DMF and DMSO. In both cases, we observed no homocoupling, and the yields were very good and comparable. From the examples listed in Table 2, it is clear that our

dx.doi.org/10.1021/jo200005n |*J. Org. Chem.* 2011, 76, 2332–2337

methodology is highly efficient with a variety of substrates, and the yields are very good to excellent, irrespective of the nature of the halides or alkynes that were utilized. Furthermore, in comparison to the reported low to moderate yields of compounds **1A** and **7B** (Table 2), which were synthesized via CuI cocatalyzed oroginal Sonogashira coupling,[9] a tremendous increase in yields was observed via our protocol, which corroborates the success of our developed methodology.

Next, we explored the capability of our methodology in the context of green solvents, such as water; however, because of the insolubility of the terminal alkynes or aryl halides in pure water, we performed the investigated reaction in 1:1:1 toluene:THF:water using aryl halide **6** (Table 2), and in ACN−water and DMF−water using aryl halide **1** as the starting halide (Table 1). Again, we found that the reaction proceeded smoothly with a comparably high yield. These findings demonstrate that this methodology can be used in the context of water-soluble alkynes and aromatic halides. Therefore, the present click-reagent version of the cross-coupling protocol appears to be compatible with several different kinds of substrates and green solvent systems, such as water.

Because an excess of ascorbate was found to maintain an excellent reducing atmosphere for the reactions to be carried out, we thought that it would be worthwhile to verify our methodology in open air without applying an inert atmosphere. Thus, we carried out a reaction of halide **1** with alkyne **A**, without degassing with N_2 gas in DMF at 80 °C and also separately under microwave irradiation. We obtained a very good yield of our desired product with no homocoupling. In these cases, all of the reactants and reagents were taken together; only a solution of 1 mol % of $CuSO_4$ in DMF was added at the end, and the reaction vessel was maintained in open atmosphere (Table 1). This observation proves the air-insensitivity of our protocol and thereby proves its versatility and practicality. Most importantly, in all cases throughout our investigation, the reducing agent, sodium ascorbate, was observed to not adversely impact susceptible functional groups, such as NO_2, −CN, or anhydride.

Finally, we studied the fluorescence photophysical properties of two of our synthesized fluorophores. Thus, in this preliminary study, the absorption spectra of the donor−acceptor acetylenes (for example, **3B′** and **7A**) are characterized by an intense, broad, and low-energy transition, which derives from the intramolecular charge-transfer transition (ICT) that results from excitationfrom the donor to the acceptor group (SI, Figures S4−S6). The observed absorption band was solvatochromic, which is characteristic of a large dipole moment change between the ground and the excited states. Furthermore, the molecules exhibited a structured emission in low polar solvents, such as hexane, dioxane, etc.; however, as the solvent polarity was increased, intense, broad, and structureless emissions at longer wavelength regions were increasingly observed, i.e., the molecules exhibited a highly solvatochromic emission from the ICT state (Figure 2).

In conclusion, we have developed a click-reagent version of Sonogashira coupling methodology that is high yielding, tolerant to a variety of substrates and functional groups, compatible with green solvents, and air-insensitive. We have exploited the known reducing behavior of sodium ascorbate to generate an active Cu(I) cocatalyst from $CuSO_4$, and we have maintained a constant reducing atmosphere to control and minimize undesired oxidative homocoupling, thereby tremendously increasing the incidence of desired cross-coupling. This is the first example of the use of click-reagents in Sonogashira coupling that yield no or drastically diminished amounts of undesired homocoupled products. Our developed protocol is also air-insensitive and effective under microwave conditions. Thus, we hope this methodology will find widespread applications in chemistry, material science, and chemical biology for the synthesis of desirable conjugated fluorescent alkynes.

EXPERIMENTAL SECTION

General Procedure for the Click-Reagent Version of Sonogashira Coupling. To a solution of aryl halide in 1:1 DMF−Et_3N under N_2, $Pd(PPh_3)_4$ followed by terminal alkyne was added. After 5 min of stirring under N_2 atmosphere, 6 mol % of a solution of sodium ascorbate in DMF was added followed by addition of 1 mol % of a solution of $CuSO_4$ in DMF. The reaction mixture was stirred for 4 h at 80 °C. After completion of the reaction monitored by TLC, the reaction mixture was extracted with ethyl acetate, washed with ammonium chloride and brine, and dried over anhydrous Na_2SO_4. The products were isolated pure by column chromatography and characterized by IR, NMR, and mass spectrometry. All the products were isolated with very good to excellent yield ranging from 70% to 97% in DMF at 80 °C within 4 h only. The synthesis and the characterization data are described below. The compounds **1A**,[1] **6B**,[2] and **7B**[3] are known compounds, and their spectral data were in agreement with those reported in the literature. The melting point of **1A** is not reported and the meltings points are in accord with the literature values for the case of compounds **6B** and **7B**. Full characterization data of unkown as well as of known compounds are also reported as was observed from our analysis.

Synthesis of 2-(2-(4-(cyano)phenyl)ethynyl)benzonitrile[9a,b] (1A): Using the general procedure, starting from 0.05 g (0.275 mmol) of 2-bromobenzonitrile **1** and 0.042 g (0.330 mmol) of 4-ethynylbenzonitrile **A**, 0.054 g (0.237 mmol) of the title compound was isolated as a white solid. Yield 86%; mp 133−135 °C; IR (KBr) 3065, 2231, 1605, 1504, 1479, 840, 768 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 7.46 (1H, t, J = 7.2 Hz), 7.59 (1H, t, J = 7.6 Hz), 7.63−7.70 (6H, m); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 89.6, 93.9, 112.7, 115.9, 117.5, 118.5, 126.3, 127.0, 129.4, 132.3, 132.5, 132.6, 132.7, 133.0; ESI-TOF-MS m/z 229 $[M + H]^+$; HRMS calcd for $C_{16}H_9N_2$ ($[M + H]^+$) 229.0765, found 229.0760.

Synthesis of 2-(2-(4-(*N*,*N*-dimethylamino)phenyl)ethynyl)benzonitrile (1B): Using the general procedure, starting from 0.06 g (0.3296 mmol) of 2-bromobenzonitrile **1** and 0.057 g (0.3955 mmol) of 4-ethynyl-*N*,*N*-dimethylbenzenamine **B**, 0.070 g (0.2845 mmol) of the title compound was isolated as a lime solid. Yield 86%; mp 125−126 °C; IR (KBr) 3060, 2902, 2817, 2204, 2173, 1603, 1590, 1520, 1365, 1143, 815, 755 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 2.98 (6H, s), 6.63 (2H, d, J = 8.8 Hz), 7.30 (1H, ddd, J = 1.2, 7.6 Hz), 7.46 (2H, d, J = 9.2 Hz), 7.49−7.55 (2H, m), 7.60 (1H, dd, J = 0.4, 8.0 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 40.2, 84.5, 98.3, 108.6, 111.8, 114.7, 118.1, 127.3, 128.4, 131.7, 132.4, 132.7, 133.4, 133.8, 150.8; ESI-TOF-MS m/z 247 $[M + H]^+$; HRMS calcd for $C_{17}H_{15}N_2$ ($[M + H]^+$) 247.1235, found 247.1230.

Synthesis of 4-(2-(4-nitrophenyl)ethynyl)benzonitrile (2A): Using the general procedure, starting from 0.070 g (0.3465 mmol) of 1-bromo-4-nitrobenzene **2** and 0.053 g (0.4173 mmol) of 4-ethynylbenzonitrile **A**, 0.078 g (0.3145 mmol) of the title compound was isolated as a lime solid. Yield 91%; mp 212−214 °C; IR (KBr) 3075, 2226, 1604, 1592, 1511, 1339, 836 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 7.61−7.68 (6H, m), 8.23 (2H, d, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 91.4, 92.5, 112.7, 118.4, 123.9, 127.1, 129.2, 132.4, 132.5, 132.7, 147.7; ESI-TOF-MS m/z 249 $[M + H]^+$; HRMS calcd for $C_{15}H_9N_2O_2$ ($[M + H]^+$) 249.0664, found 249.0667.

Synthesis of *N*,*N*-dimethyl-4-(2-(4-nitrophenyl)ethynyl) benzenamine (2B): Using the general procedure, starting from 0.100 g (0.4950 mmol) of 1-bromo-4-nitrobenzene **2** and 0.0790 g

dx.doi.org/10.1021/jo200005n |*J. Org. Chem.* 2011, 76, 2332–2337

(0.5448 mmol) of 4-ethynyl-*N*,*N*-dimethylbenzenamine **B**, 0.1135 g (0.4267 mmol) of the title compound was isolated as a red solid. Yield 86%; mp 209−212 °C; IR (KBr) 3095, 2909, 2208, 1609, 1586, 1529, 1508, 1371, 1336, 1104, 820 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 3.00 (6H, s), 6.65 (2H, d, J = 8.8 Hz), 7.41 (2H, d, J = 8.4 Hz), 7.57 (2H, d, J = 9.2 Hz), 8.16 (2H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 40.3, 86.6, 97.3, 111.9, 123.8, 128.7, 128.8, 131.8, 132.1, 132.2, 132.3, 133.4, 133.8, 146.4, 150.9; ESI-TOF-MS m/z 267 $[M + H]^+$; HRMS calcd for $C_{16}H_{15}N_2O_2$ ($[M + H]^+$) 267.1134, found 267.1130.

Synthesis of 6-chloro-3-(2-(4-(*N*,*N*-dimethylamino)phenyl) ethynyl)picolinonitrile (3B): Using the general procedure, starting from 0.05 g (0.2299 mmol) of 3-bromo-6-chloropicolinonitrile **3** and 0.04 g (0.2758 mmol) of 4-ethynyl-*N*,*N*-dimethylbenzenamine **B**, 0.0393 g (0.1396 mmol) of the title compound was isolated as a yellow solid. Yield 61%; mp 142−145 °C; IR (KBr) 2923, 2853, 2193, 1606, 1560, 1527, 1369, 1156, 1023, 808 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 3.01 (6H, s), 6.64 (2H, d, J = 8.8 Hz), 7.42−7.47 (3H, m), 7.77 (1H, d, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 40.2, 81.3, 103.3, 107.4, 111.8, 115.5, 125.6, 127.6, 130.4, 133.7, 140.9, 149.4, 151.3; ESI-TOF-MS m/z 282 $[M + H]^+$; HRMS calcd for $C_{16}H_{13}N_3Cl$ ($[M + H]^+$) 282.0798, found 282.0789.

From the same reaction mixture we were able to isolate 0.0224 g (0.0574 mmol) of dihalide (Br and Cl) substituted compound, 3,6-bis(2-(4-(*N*,*N*-dimethylamino)phenyl)ethynyl)picolinonitrile, **3B′** as a yellow solid. Yield 25%; mp 210−212 °C; IR (KBr) 2922, 2852, 2201, 1604, 1530, 1447, 1365, 1157, 816 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 2.99 (12H, d, J = 1.6 Hz), 6.63 (4H, d, J = 8.8 Hz), 7.45 (2H, d, J = 3.2 Hz), 7.47 (2H, d, J = 3.2 Hz), 7.50 (1H, d, J = 8.4 Hz), 7.73 (1H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 40.3, 82.7, 86.7, 95.5, 102.8, 107.9, 108.0, 109.9, 111.9, 116.2, 124.1, 128.8, 133.7, 133.8, 135.5, 138.4, 142.9, 151.1, 151.2; ESI-TOF-MS m/z 391 $[M + H]^+$; HRMS calcd for $C_{26}H_{23}N_4$ ($[M + H]^+$) 391.1922, found 391.1930.

Synthesis of 4-(2-(2,5-dimethoxyphenyl)ethynyl)benzonitrile (4A): Using the general procedure, starting from 0.030 g (0.1382 mmol) of 2-bromo-1,4-dimethoxybenzene **4** and 0.021 g (0.1653 mmol) of 4-ethynylbenzonitrile **A**, 0.026 g (0.0988 mmol) of the title compound was isolated as a white semisolid. Yield 72%; IR (KBr) 2924, 2853, 2227, 1602, 1494, 1458, 1261, 1021, 840, 805, 699 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 3.77 (3H, s), 3.86 (3H, s), 6.84 (1H, s), 6.88 (1H, d, J = 2.8 Hz), 7.01 (1H, d, J = 3.2 Hz), 7.60 (4H, m); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 56.0, 56.6, 90.5, 91.8, 111.5, 112.0, 112.3, 116.9, 118.4, 118.8, 128.6, 132.2, 132.3, 133.2, 153.5, 154.9; ESI-TOF-MS m/z 264 $[M + H]^+$; HRMS calcd for $C_{17}H_{14}NO_2$ ($[M + H]^+$) 264.1024, found 264.1030.

Synthesis of 4-(2-(2,5-dimethoxyphenyl)ethynyl)-*N*,*N*-dimethylbenzenamine (4B): Using the general procedure, starting from 0.050 g (0.2304 mmol) of 2-bromo-1,4-dimethoxybenzene **4** and 0.0367 g (0.2534 mmol) of 4-ethynyl-*N*,*N*-dimethylbenzenamine **B**, 0.046 g (0.1637 mmol) of the title compound was isolated as a lime semisolid. Yield 71%; IR (KBr) 2924, 2853, 2830, 2207, 1603, 1521, 1499, 1356, 1225, 1197, 1042, 821, 712 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 2.97 (6H, s), 3.76 (3H, s), 3.85 (3H, s), 6.66 (2H, d, J = 7.6 Hz), 6.79 (2H, d, J = 1.6 Hz), 7.01 (1H, d, J = 3.6 Hz), 7.42 (2H, d, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 41.4, 55.9, 56.7, 83.7, 94.9, 110.5, 111.9, 112.4, 114.2, 115.1, 118.1, 124.5, 124.6, 133.0, 150.3, 153.5, 154.4; ESI-TOF-MS m/z 282 $[M + H]^+$; HRMS calcd for $C_{18}H_{20}NO_2$ ($[M + H]^+$) 282.1494, found 282.1488.

Synthesis of 4-(2-(4-(cyano)phenyl)ethynyl)-1,8-naphthalic anhydride (5A): Using the general procedure, starting from 0.08 g (0.2888 mmol) of 4-bromo-1,8-naphthalicanhydride **5** and 0.0404 g (0.3176 mmol) of 4-ethynylbenzonitrile **A**, 0.061 g (0.1888 mmol) of the title compound was isolated pure by filtration followed by washing with water and ethanol as a yellow solid. Yield 65%; mp >312 °C (it became black); IR (KBr) 2223, 1778, 1758, 1601, 1588, 1043, 832 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 7.46−7.52 (4H, m), 7.67 (1H, t, J = 7.6 Hz), 7.77 (1H, d, J = 7.6 Hz), 8.30 (1H, d, J = 8.0 Hz), 8.38 (1H, d, J = 6.8 Hz), 8.51 (1H, d, J = 8.0 Hz); ESI-TOF-MS m/z 324 $[M + H]^+$; HRMS calcd for $C_{21}H_{10}NO_3$ ($[M + H]^+$) 324.0660, found 324.0653.

Synthesis of 4-(2-(4-(*N*,*N*-dimethylamino)phenyl)ethynyl)-1,8-naphthalic anhydride (5B): Using the general procedure, starting from 0.06 g (0.2166 mmol) of 4-bromo-1,8-naphthalicanhydride **5** and 0.0345 g (0.2382 mmol) of 4-ethynyl-*N*,*N*-dimethylbenzenamine **B**, 0.0635 g (0.1862 mmol) of the title compound was isolated as a red solid. Yield 86%; mp 288−292 °C; IR (KBr) 2917, 2862, 2188, 1752, 1730, 1604, 1585, 1575, 1524, 1371, 1169, 1010, 781 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 3.06 (6H, s), 6.82 (2H, bs), 7.55 (2H, d, J = 7.6 Hz), 7.84−7.92 (2H, m), 8.53 (1H, d, J = 7.6 Hz), 8.64 (1H, d, J = 7.2 Hz), 8.81 (1H, d, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 40.1, 85.2, 103.8, 107.9, 110.6, 111.7, 112.1, 112.8, 118.9, 125.3, 127.5, 129.5, 130.5, 132.8, 133.5, 134.2, 135.0, 153.4, 160.4, 160.8; ESI-TOF-MS m/z 342 $[M + H]^+$; HRMS calcd for $C_{22}H_{16}NO_3$ ($[M + H]^+$) 342.1130, found 342.1125.

Synthesis of 4-(2-(9-bromoanthracen-10-yl)ethynyl)benzonitrile (6A): Using the general procedure, starting from 0.070 g (0.2083 mmol) of 9,10-dibromoanthracene **6** and 0.0265 g (0.2083 mmol) of 4-ethynylbenzonitrile **A**, 0.040 g (0.1190 mmol) of 9,10-dibromoanthracene was isolated as unreacted and 0.0245 g (0.0641 mmol) of the title compound was isolated as a yellow solid. Yield 72%; mp 214−215 °C; IR (KBr) 2222, 2198, 1620, 1602, 1502, 837, 752 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 7.62−7.64 (4H, m), 7.70 (2H, dd, J = 1.6, 8.2 Hz), 7.80 (2H, dd, J = 1.2, 8.0 Hz), 8.55−8.60 (4H, m); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 90.6, 100.0, 112.0, 118.7, 127.0, 127.5, 127.8, 128.4, 128.7, 129.1, 130.5, 132.2, 132.5, 133.4, 142.5; ESI-TOF-MS m/z 383, 385 $[M + H]^+$; HRMS calcd for $C_{23}H_{12}N$ ($[M - Br]$) 302.0970, found 302.0960.

Synthesis of 4-(2-(9-bromoanthracen-10-yl)ethynyl)-*N*,*N*-dimethylbenzenamine[9c] (6B): Using the general procedure, starting from 0.060 g (0.1785 mmol) of 9,10-dibromoanthracene **6** and 0.0258 g (0.1785 mmol) of 4-ethynyl-*N*,*N*-dimethylbenzenamine **B**, 0.016 g (0.0476 mmol) of 9,10-dibromoanthracene was isolated as unreacted and 0.0305 g (0.0763 mmol) of the title compound was isolated as a yellow solid. Yield 68%; mp 234−236 °C (reported 236 °C);[9c] IR (KBr) 2924, 2854, 2192, 1634, 1605, 1520, 1348, 1188, 811, 752 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 3.03 (6H, s), 6.73 (2H, d, J = 8.4 Hz), 7.56−7.64 (6H, m), 8.53 (2H, d, J = 8.0 Hz), 8.70 (2H, d, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 40.5, 84.5, 96.2, 103.8, 112.3, 123.0, 126.6, 127.3, 127.6, 127.8, 128.3, 130.6, 132.9, 133.1, 152.8; ESI-TOF-MS m/z 401, 403 $[M + H]^+$; HRMS calcd for $C_{24}H_{19}BrN$ ($[M + H]^+$) 400.0701, found 400.0697.

Synthesis of 4-(2-(pyren-1-yl)ethynyl)benzonitrile (7A): Using the general procedure, starting from 0.055 g (0.1957 mmol) of 1-bromopyrene **7** and 0.0273 g (0.2152 mmol) of 4-ethynylbenzonitrile **A**, 0.062 g (0.1896 mmol) of the title compound was isolated as a yellow solid. Yield 97%; mp 201−203 °C; IR (KBr) 3037, 2229, 2202, 1604, 1512, 1497, 854, 825, 718, cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 7.65 (2H, d, J = 8.0 Hz), 7.72 (2H, d, J = 8.4 Hz), 8.01−8.04 (2H, m), 8.09−8.12 (2H, m), 8.16−8.24 (4H, m), 8.56 (1H, d, J = 9.2 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 93.4, 93.6, 111.6, 116.7, 118.8, 124.4, 124.7, 124.8, 125.4, 126.2, 126.6, 127.4, 128.6, 128.9, 130.0, 131.2, 131.4, 132.2, 132.3; ESI-TOF-MS m/z 328 $[M + H]^+$; HRMS calcd for $C_{25}H_{14}N$ ($[M + H]^+$) 328.1126, found 328.1130.

Synthesis of *N*,*N*-dimethyl-4-(2-(pyren-1-yl)ethynyl)benzenamine[9d] (7B): Using the general procedure, starting from 0.055 g (0.1957 mmol) of 1-bromopyrene **7** and 0.0312 g (0.2152 mmol) of 4-ethynyl-*N*,*N*-dimethylbenzenamine **B**, 0.062 g (0.1797 mmol) of the title compound was isolated as a bright yellow solid. Yield 92%; mp 168−169 °C (reported 169 °C);[9d] IR (KBr) 3035, 2922, 2853, 2196,

2182, 1606, 1594, 1520, 1355, 1152, 845, 819, 711 cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 3.02 (6H, s), 6.76 (2H, d, J = 7.6 Hz), 7.60 (2H, d, J = 8.8 Hz), 7.98−8.10 (4H, m), 8.14−8.20 (4H, m), 8.68 (1H, d, J =8.8 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ 40.6, 87.0, 96.8, 112.4, 119.1, 124.7, 124.8, 125.4, 125.5, 126.0, 126.3, 127.5, 127.9, 128.2, 129.5, 130.9, 131.4, 131.6, 131.7, 133.0, 150.3; ESI-TOF-MS m/z 346 $[M + H]^+$; HRMS calcd for $C_{26}H_{20}N$ ($[M + H]^+$) 346.1595, found 346.1589.

■ ASSOCIATED CONTENT

Supporting Information. General experimental details, crystallographic data, crystallographic information files (CIFs), copies of selected UV and fluorescence spectra, and copies of ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*Fax: (+)91-361-258-2324. E-mail: ssbag75@iitg.ernet.in.

■ ACKNOWLEDGMENT

The authors thank DST (SR/SI/OC-69/2008), and CSIR [01(2330)/09/EMR-II], Government of India, for financial support. R.K. thanks IIT Guwahati for a fellowship.

■ REFERENCES

(1) (a) Sonogashira, K. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., de Meijera, A., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. 1, p 319. (b) Sengupta, S. *Synlett* **2004**, 1191. (c) Li, Y.; Soni, P. B.; Liu, L.; Zhang, X.; Liotta, D. C.; Lutz, S. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 841. (d) Seela, F.; Ingale, S. A. *J. Org. Chem.* **2010**, *75*, 284. (e) Bozdemir, O. A.; Buyukcakir, O.; Akkaya, E. U. *Chem.—Eur. J.* **2009**, *15*, 3830. (f) Saito, Y.; Motegi, K.; Bag, S. S.; Saito, I. *Bioorg. Med. Chem. Lett.* **2008**, *16*, 107. (g) Bag, S. S.; Saito, Y.; Hanawa, K.; Kodate, S.; Suzuka, I.; Saito, I. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 6338. (h) Wang, C.; Plsson, L.-O.; Batsanov, A. S.; Bryce, M. R. *J. Am. Chem. Soc.* **2006**, *128*, 3789. For reviews see:(i) Basak, A.; Mandal, S.; Bag, S. S. *Chem. Rev.* **2003**, *103*, 4077. (j) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979. (k) Chinchilla, R.; Najera, C. *Chem. Rev.* **2007**, *107*, 874.

(2) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467. (b) Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46.

(3) (a) Glaser, C. *Ber. Dtsch. Chem. Ges.* **1869**, *2*, 422. (b) Hay, A. S. *J. Org. Chem.* **1962**, *27* (7), 3320. (c) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632.

(4) (a) Wang, R.; Piekarski, M. M.; Shreeve, J. M. *Org. Biomol. Chem.* **2006**, *4*, 1878. (b) Gil-Molto, J.; Karlstrom, S.; Najera, C. *Tetrahedron* **2005**, *61*, 12168. (c) Juo, Y.; Gao, H.; Li, Y.; Huang, W.; Lu, W.; Zhang, Z. *Tetrahedron* **2006**, *62*, 2465. (d) Corma, A.; Garcia, H.; Leyva, A. J. *J. Catal.* **2006**, *240*, 87. (e) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632 and references cited therein. (f) Batsanov, A. S.; Collings, J. C.; Fairlamb, I. J. S.; Holland, J. P.; Howard, J. A. K.; Lin, Z.; Marder, T. B.; Parsons, A. C.; Ward, R. M.; Zhu, J. *J. Org. Chem.* **2005**, *70*, 703. (g) Merkul, E.; Urselmann, D.; Müller, T. J. J. *Eur. J. Org. Chem.* **2011**, 238.

(5) (a) Tong, L. H.; Pascu, S. I.; Jarrosson, T.; Sanders, J. K. M. *Chem. Commun.* **2006**, 1085. (b) Cheng, J.; Sun, Y.; Wang, F.; Guo, M.; Xu, J.-H.; Pan, Y.; Zhang, Z. *J. Org. Chem.* **2004**, *69*, 5428. (c) Palimkar, S. S.; Kumar, P. H.; Lahoti, R. J.; Srinivasan, K. V. *Tetrahedron* **2006**, *62*, 5109. (d) Elangovan, A.; Wang, Y.-H.; Ho, T.-I. *Org. Lett.* **2003**, *5*, 1841.

(6) (a) Amatore, C.; Bensalem, S.; Ghalem, S.; Jutand, A.; Medjour, Y. *Eur. J. Org. Chem.* **2004**, 366. (b) Leadbeater, N. E.; Marco, M.; Tominack, B. J. *Org. Lett.* **2003**, *5*, 3919.

(7) (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596. (b) Meldal, M.; Tornoe, C. W. *Chem. Rev.* **2008**, *108*, 2952.

(8) (a) Strizhak, P. E.; Basylchuk, A. B.; Demjanchyk, I.; Fecher, F.; Schneider, F. W.; Munster, A. F. *Phys. Chem. Chem. Phys.* **2000**, *2*, 4721. (b) Halliwell, B. *Free Radical Res.* **1996**, *25*, 439. (c) Buettner, G. R.; Jurkiewicz, B. A. *Radiat. Res.* **1996**, *145*, 532.

(9) (a) Michael, R.; Alexander, T.; Valdimir, G. *J. Am. Chem. Soc.* **2005**, *127*, 10243. (b) Hirsch, K. A.; Wilson, S. R.; Moore, J. S. *J. Am. Chem. Soc.* **1997**, *119*, 10401. (c) Ha-Thi, M.-H.; Souchon, V.; Hamdi, A.; Metivier, R.; Alain, V.; Nakatani, K.; Lacroix, P. G.; Genet, J.-P.; Michelet, V.; Leray, I. *Chem.—Eur. J.* **2006**, *12*, 9056. (d) Kim, H. M.; Lee, Y. O.; Lim, C. S.; Kim, J. S.; Cho, B. R. *J. Org. Chem.* **2008**, *73*, 5127.