

One-Step Synthesis of Symmetrical 3,3'-Substituted 2,2'-Bipyridine Ligands by Cobalt(I)-Catalyzed [2 + 2] Cycloadditions

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The design of organic ligands that, when chelated or bound to metals, assemble to form structures that may have potential for use as selective catalysts and filters,¹ or molecular wires and switches,² or electronic devices³ continues to be a major topic in the field of supramolecular chemistry.^{1a,b} Ligands particularly attractive are the oligopyridines, since they retain the well-documented ability of the 2,2'-bipyridine system to chelate a wide range of metals.⁴ Most of the methods used to synthesize functionalized oligopyridines (bipyridines, terpyridines, etc.) are based on Pd- or Ni-catalyzed heteroaryl C–C coupling reactions⁵ or on the Kröhnke-Potts⁶ or Friedländer strategies⁷ which often require multistep constructions. Here we report a one-step synthesis of symmetrical, annelated 3,3'-substituted 2,2'-bipyridines by means of cobalt(I)-catalyzed [2 + 2] cycloadditions between 5-hexynenitrile **1** and 1,3-diyne **2** (Scheme 1).⁸

Cocyclization between **1** and 1,4-bis(trimethylsilyl)-1,3-butadiyne (**2a**) catalyzed by CpCo(CO)₂ produced a 77% yield of pyridine **3**; significantly, the regioisomeric pyridine **4** (Figure 1) was not observed in the reaction mixture.⁹ We eventually used calculations (see below) to explain this unprecedented regioselectivity. It is also worth mentioning that the reaction needs

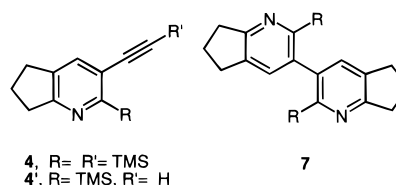
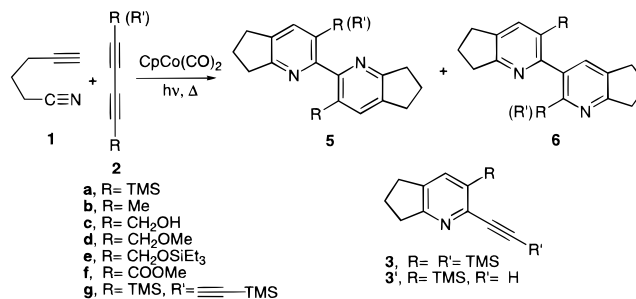


Figure 1.

Scheme 1. [CpCo(CO)₂]-Catalyzed Cycloaddition of **1** to 1,3-Diyne **2a–f** and 1,3,5-Triyne **2g**



irradiation for only 1 h and no high dilution techniques are required for its performance.^{8c}

Suspecting that steric hindrance by the TMS group at position 3 of the pyridine ring might be blocking the second cycloaddition,¹⁰ we then used the sterically less demanding 2,4-hexadiyne (**2b**). The second cocyclization now occurred as expected, producing a 1.7:1 ratio of the 2,2'-bipyridine **5b**^{11,12} and the 2,3'-bipyridine **6b** as the main reaction products in 30% and 18% isolated yields, respectively (Table 1).¹³ The 3,3'-bipyridine **7b** (R = Me, Figure 1) was not detected in the reaction mixture. To the best of our knowledge, this is the first time that a 2,2'-bipyridine is constructed from acyclic precursors in only one step.

Having thus found that bulky substituents on the diyne partner can prevent the formation of the second pyridine ring, we decided to investigate the influence of electronic factors on the course of the reaction. Cocyclization between **1** and 2,4-hexadiyn-1,6-diol (**2c**) gave a complex mixture from which the 2,2'-bipyridine **5c** could only be isolated in 9% yield, while reaction with the methyl ether derivative **2d**^{14a} afforded a 2.7:1 ratio of the 2,2'-bipyridine **5d**¹¹ (46% yield) and the 2,3'-bipyridine **6d** (17% yield, Table 1). With a view to facilitating possible subsequent manipulation of the substituent, and to reevaluate the influence of bulkiness, the triethylsilyl ether **2e**^{14b} was also employed, giving a 4:1 ratio of the 2,2'-bipyridine **5e**¹¹ (36% yield) and the 2,3'-bipyridine **6e** (9% yield, Table 1). However, when a carbonyl group was attached to the diyne triple bonds, yields fell: the 2,4-hexadiynedioate **2f**¹⁵ gave an 18% combined yield of 2,2'-bipyridine **5f** and 2,3'-bipyridine **6f** in 1.4:1 ratio (Table 1).¹⁶

Finally, we decided to investigate the behavior of triynes. Not unexpectedly, cocyclization of **1** with 1,6-bis(trimethylsilyl)-1,3,5-

(10) 2-[(Trimethylsilyl)ethynyl]pyridine is susceptible to this type of cycloaddition. Varela, J. A.; Castedo, L.; Saá, C. *J. Org. Chem.* **1997**, *62*, 4189–4192.

(11) To distinguish between 2,2'-bipyridines **5** and 3,3'-bipyridines **7**, a combination of NOE, HMQC, and HMBC experiments were performed.

(12) This substitution pattern—3,3'-dimethylbipyridines—has been recently exploited in the design of efficient chiral catalysts, e.g., 3,3'-dimethyl-2,2'-biquinoline *N,N'*-dioxide. Nakajima, M.; Saito, M.; Shiro, M.; Hashimoto, S. *J. Am. Chem. Soc.* **1998**, *120*, 6419–6420.

(13) Small amounts of 2-(3-cyanopropyl)- and/or 3-(3-cyanopropyl)-cyclopenta[b]pyridines were also obtained.

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(16) The starting diyne was unstable, both neat and in solution.

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(9) The structure of the product was inferred from NOEs on the mono-desilylated pyridine (**3**).

Table 1. Results of Cocyclization of **1** with Dienes **2a–f** and Triyne **2g**^a

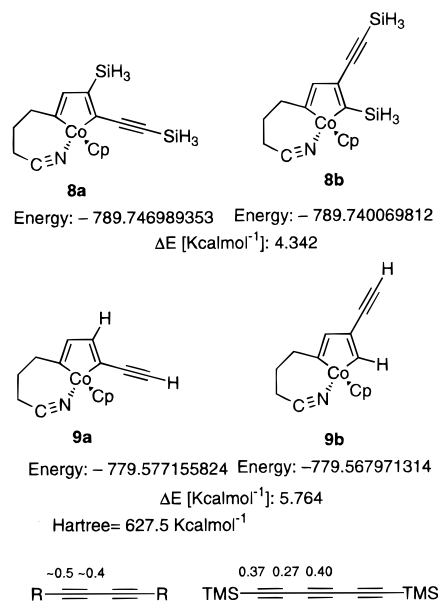
entry	diyne ^b	products ^c	ratio 5:6 ^d	yield (%) ^e
1	2a	3		77
2	2b	5b, 6b	1.7:1	48
3	2c	5c		9
4	2d	5d, 6d	2.7:1	63
5	2e	5e, 6e	4:1	45
6	2f	5f, 6f	1.4:1	18
7	2g	5g, 6g	1:2.1	31

^a Typical conditions, i.e., entry 4: A solution of **2d** (0.1 g, 0.72 mmol), **1** (0.2 g, 2.17 mmol), and [CpCo(CO)₂] (27 μL, 0.22 mmol) in toluene (10 mL) was irradiated for 1 h under Ar in a round-bottomed flask equipped with a reflux condenser. The reaction vessel was irradiated with a Philips PF 808 300W tungsten slide projector lamp placed ca. 5 cm from the center of the flask and operated at 225 W. The volatile components were removed under vacuum and the residue was chromatographed on silica gel (100:0 to 90:10 EtOAc/MeOH). ^b Typically, 0.1 g was employed. For **2b** and **2e**, reactions with 0.5 (6.41 mmol) and 2.3 g (6.8 mmol), respectively, were also carried out under the above conditions. ^c Appropriate analytical and spectral data for all compounds were obtained. ^d Both isomers are easily separable by column chromatography or preparative TLC (silica gel); i.e., *R_f* **5d**: 0.52, *R_f* **6d**: 0.37. ^e Isolated yields of **5** + **6** after separation by chromatography.

hexatriyne (**2g**)¹⁷ afforded only the 2,2'-bipyridine **5g** (10%) and the 2,3'-bipyridine **6g** (21%),¹⁸ the third cycloaddition presumably being prevented by steric hindrance impeding access to the triple bond remaining in **5g** and **6g**.

A common feature of all the above cycloadditions is their high regioselectivity in the initial cyclization. If the commonly accepted mechanism is operating, during the oxidative coupling reaction (metallacycle formation), it seems that the electronic influence of the adjacent alkyne completely overrides the electronic and/or steric properties of the other substituent. To gain further understanding of these experimental results, we used two calculational approaches involving semiempirical methods¹⁹ on the starting diyne and B3LYP/LANL2DZ ab initio calculations²⁰ on the metallacycle. Since Hoffmann et al. have suggested that the alkyne partner enters the intermediate metallacycle with the biggest lobe of its LUMO β to the metal,²¹ we calculated LUMO coefficients for the various diynes. All the diynes had their biggest LUMO lobe at position 1 (Figure 2), which explains why no 3,3'-bipyridines were obtained.²²

To investigate the influence of steric and electronic factors on metallacycle formation, we also performed B3LYP/LANL2DZ ab initio calculations to estimate the energies of the intermediate metallacycles in the reactions of **2a** and its desilylated analogue (Figure 2).²³ From the results, it may be concluded that the type **a** cobaltacycle with the triple bond α to the cobalt is energetically favored for both **8** and **9**. Assuming that both electronic and steric factors are operative in **8** whereas only electronic factors are important in **9**, and that electronic and steric factors have opposite

**Figure 2.** Energies (hartree) of intermediate cobaltacycles and relative magnitudes of LUMO coefficients.

regiodirective influence, it would appear that the electronic factor is responsible for the observed regioselectivity.²⁴ To our knowledge, this would be the first case of a [2 + 2 + 2] cycloaddition reaction in which regiochemical outcome is completely controlled by the electronic influence of the alkyne partner (here, the diyne).²⁵

Finally, as a first demonstration of the ligand capabilities of the new 3,3'-substituted 2,2'-bipyridines **5b** and **5e**, we prepared the corresponding four-coordinate complexes [Cu^IL₂]₂,²⁶ which were formed in almost quantitative yield as yellow/orange crystalline hexafluorophosphate salts when [Cu^I(CH₃CN)]PF₆ was added to solutions of **5b** and **5e** in CH₂Cl₂ at room temperature.²⁷

To sum up, we have developed a new, one-step method for synthesizing annelated symmetric 3,3'-substituted 2,2'-bipyridines from acyclic precursors. This method relies on the regioselective Co(I)-catalyzed cocyclization between 5-hexynenitrile with 1,3-diynes and reverses the usual strategy in bipyridine synthesis, the future biaryl bond being present prior to the construction of either of the two aryl rings. Studies of coordination complexes of these ligands are currently being carried out and will be the subject of forthcoming reports.

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Supporting Information Available: Experimental details and characterization data of compounds **5b**, **5e**, **6b**, **6e**, [Cu^I(**5b**)₂]PF₆, and [Cu^I(**5e**)₂]PF₆ as well as HMQC and HMBC spectra of compounds **5b** and **5e** (22 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(22) For triyne **2g**, the LUMO coefficients of positions 1 and 3 are similar. It seems likely that the first cycloaddition involves the central triple bond and the second either of the others.

(23) For brevity, calculations were performed for SiH₃ rather than the trimethylsilyl group.

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