ORGANIC LETTERS

2003
Vol. 5, No. 14
2477−2480

Regioselective [2 + 2 + 2] Cycloaddition of a Nickel–Benzyne Complex with 1,3-Diynes

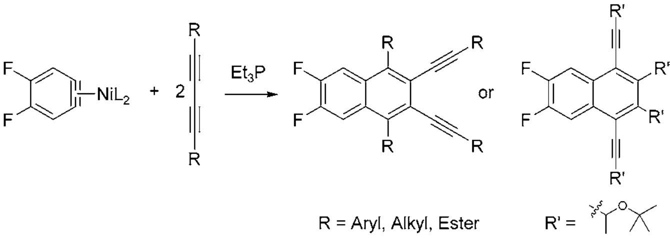
Kimberly R. Deaton and Mary S. Gin*

Department of Chemistry, University of Illinois at Urbana−Champaign,
Urbana, Illinois 61801

mgin@scs.uiuc.edu

Received April 30, 2003

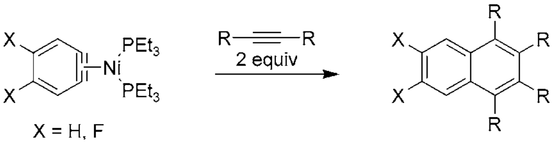
ABSTRACT



Reactions of nickel(0)–benzyne complexes with a range of symmetrically substituted 1,3-diynes in the presence of triethylphosphine lead to the regioselective formation of 2,3-dialkynyl naphthalenes. The regioselectivity can be reversed when the diyne possesses substituents of high steric bulk, allowing selective formation of either symmetric dialkynyl naphthalene.

The controlled synthesis of well-defined polyaromatic hydrocarbons is an area of increasing interest due to the unique electronic and materials properties of these compounds. Such conjugated systems have found use as, inter alia, semiconductors in electronic devices,[1] components of electronic energy transfer systems,[2] and fluorescent sensors of various environmental changes.[3]

Given the diversity of materials that incorporate aromatic rings, many methods exist for their construction from simpler starting materials. These methods include functionalization of unsubstituted ring systems,[3] cycloaromatization[4] and cyclocondensation[5] reactions, as well as metal-catalyzed trimerization of alkynes, enynes, and/or diynes.[6] Of these, metal-catalyzed alkyne trimerization is particularly attractive because of the ready availability of the alkyne precursors, and the high degree of substitution obtained in the aromatic products. An excellent example of this is the [2 + 2 + 2] cycloaddition reaction developed by Bennett in which one of the participating triple bonds is a nickel−benzyne complex that reacts with 2 equiv of an alkyne to generate substituted naphthalenes (eq 1).[6b,c]



(1)

The extension of metal-mediated cycloaddition reactions to include conjugated 1,3-diynes as substrates was historically

---

[1] (a) Würthner, F. *Angew. Chem., Int. Ed.* **2001**, *40* (6), 1037. (b) Gundlach, D. J.; Nichols, J. A.; Zhou, L.; Jackson, T. N. *Appl. Phys. Lett.* **2002**, *80* (16), 2925. (c) Shtein, M.; Mapel, J.; Benziger, J. B.; Forrest, S. R. *Appl. Phys. Lett.* **2002**, *81* (2), 268.

[2] (a) Tamura, M.; Gao, D.; Ueno, A. *Chem. Eur. J.* **2001**, *7* (7), 1390. (b) Wang, X.; Levy, D. H.; Rubin, M. B.; Speiser, S. *J. Phys. Chem. A* **2000**, *104* (28), 6558.

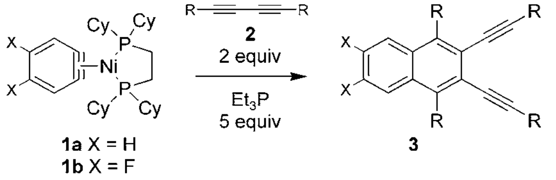
[3] (a) Isaev, R. N.; Ishkov, A. V.; Fisenko, O. V. *J. Anal. Chem.* **2001**, *56* (12), 1095. (b) Hanhela, P. J.; Paul, D. B. *Aust. J. Chem.* **1981**, *34*, 1687.

[4] (a) Wenk, H. H.; Winkler, M.; Sander, W. *Angew. Chem., Int. Ed.* **2003**, *42* (5), 502. (b) Zimmermann, G. *Eur. J. Org. Chem.* **2001**, 457. (c) Bowles, D. M.; Anthony, J. E. *Org. Lett.* **2000**, *2* (1), 85.

[5] (a) Qiao, X.; Padula, M. A.; Ho, D. M.; Vogelaar, N. J.; Schutt, C. E.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **1996**, *118* (4), 741. (b) Gribble, G. W.; Sibi, M. P.; Kumar, S.; Kelly, W. J. *Synthesis* **1983**, 502. (c) Oku, A.; Kakihana, T.; Hart, H. *J. Am. Chem. Soc.* **1967**, *89* (17), 4554.

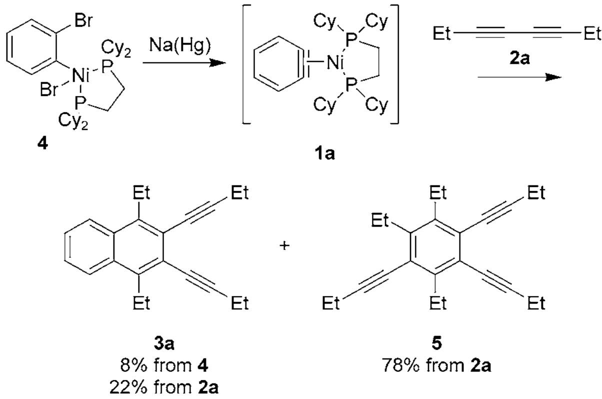
10.1021/ol034720x CCC: $25.00

limited by poor regioselectivity in the formation of benzene products, accompanied by low yields due to polymerization side reactions.[7] Recent improvements in catalyst design have led to selective incorporation of 1,3-diynes into benzene products,[8] but such substrates have not been applied to the cycloaddition with metal benzynes to form fused ring products. Herein we report the first example of the regioselective reaction of nickel−benzynes **1** and 1,3-diynes **2** to afford highly substituted dialkynyl naphthalenes (**3**, eq 2).



(2)

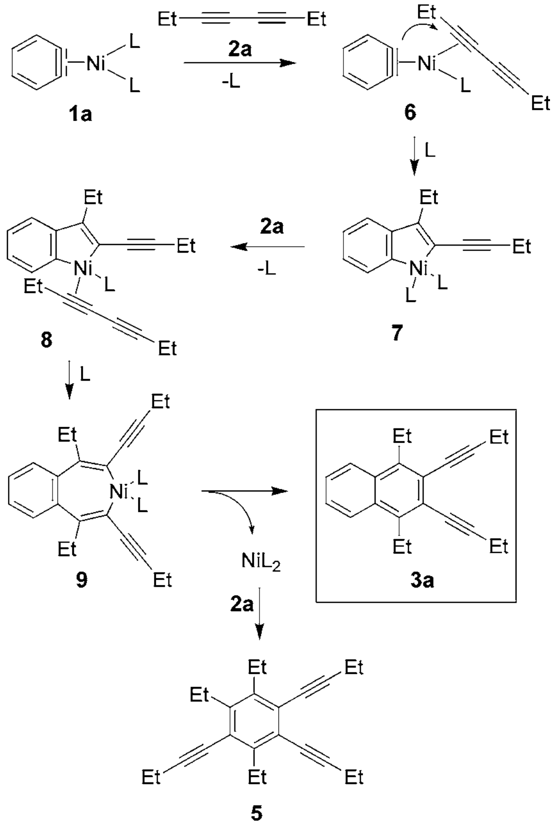
In our initial studies, nickel−benzyne **1a**,[9] prepared in situ from nickel(II) complex **4**, was reacted with 3,5-octadiyne (**2a**) to give a mixture of two products (**3a** and **5**, eq 3). The diyne was quantitatively converted to the products, but incorporation of the benzyne **1a** was low (8% from **4**). The structures for **3a** and **5** were assigned on the basis of the presence or absence of symmetry evident in the ^{1}H NMR spectrum and the mass spectrometrically determined molecular weights.



(3)

The formation of these two products can be rationalized on the basis of the mechanism proposed for the nickel−benzyne alkyne cycloaddition reaction (Scheme 1).[6b,c] Following coordination of the diyne **2a** to give **6**, alkyne insertion into the benzyne−nickel bond gives nickelaindene **7**. Coordination to give **8** and insertion of a second equivalent of diyne gives a seven-membered-ring metallacycle **9** that, following reductive elimination of the zero-valent nickel fragment NiL$_2$, affords the naphthalene product **3a**. The extruded nickel(0) (NiL$_2$) is responsible for further trimerization of the diyne to afford the benzene product **5**.[10]

Scheme 1. Mechanism of Nickel−Benzyne + Diyne Cycloaddition



The low yield of naphthalene **3a** isolated is attributed to two factors: (1) the reduction of nickel(II) complex **4** proceeds in ca. 50% yield, affording the nickel−benzyne **1a** of variable purity, and (2) trimerization to form benzene **5** consumes the diyne at a faster rate than reaction with nickel−benzyne **1a**. To overcome these problems, we made two changes. First, the more stable 4,5-difluorobenzyne nickel complex **1b**[6c] was employed. In contrast to the nonfluorinated complex **1a**, complex **1b** can be readily recrystallized and even manipulated in air for brief periods of time. The second improvement involved the addition of excess triethylphosphine to the reaction mixture to sequester the expelled nickel(0), thus preventing the formation of the benzene product arising from diyne trimerization.[6b] Indeed, these two changes led to the selective formation of 2,3-dialkynyl naphthalene **3** as the major isolable product (Table 1).

The reaction protocol involves adding freshly recrystallized nickel benzyne **1b** (1 equiv) to a solution of diyne **2** (2.2 equiv) and triethylphosphine (5 equiv) in degassed toluene under an atmosphere of argon. The solution is then heated to 60 °C. Following removal of the solvent, the

---

[6] (a) Takahashi, T.; Li, Y.; Stepnicka, P.; Kitamura, M.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **2002**, *124* (4), 576. (b) Bennett, M. A.; Wenger, E. *Organometallics* **1996**, *15* (26), 5536. (c) Bennett, M. A.; Wenger, E. *Organometallics* **1995**, *14* (4), 1267. (d) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1985**, *23* (8), 539.

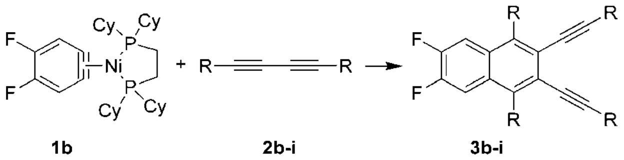
[7] (a) Hübel, W.; Merényi, R. *Chem. Ber.* **1963**, *96* (4), 930. (b) Hubert, A. J.; Dale, J. *J. Chem. Soc.* **1965**, 3160.

[8] (a) Gevorgyan, V.; Radhakrishnan, U.; Takeda, A.; Rubina, M.; Rubin, M.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66* (8), 2835. (b) Sugihara, T.; Wakabayashi, A.; Nagai, Y.; Takao, H.; Imagawa, H.; Nishizawa, M. *Chem. Commun.* **2002**, 576.

[9] Bennett, M. A.; Hambley, T. W.; Roberts, N. K.; Robertson, G. B. *Organometallics* **1985**, *4* (11), 1992.

[10] Chalk, A. J.; Jerussi, R. A. *Tetrahedron Lett.* **1972**, *13* (1), 61.

Table 1. Nickel−Benzyne + 1,3-Diyne Cycloadditions[a]



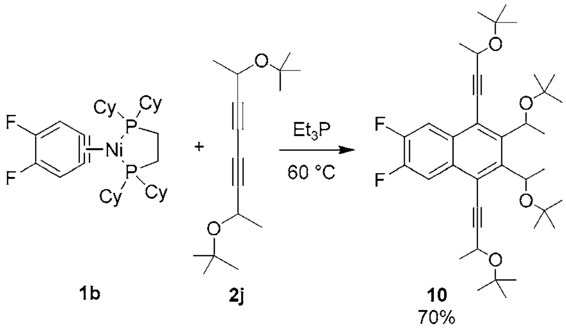
entry	diyne	R	product	% yield **3**[b]
1	**2b**	Ph	**3b**	85
2[c]	**2c**	CO_2Et	**3c**	82
3	**2d**	CH_2CH_2OTBS	**3d**	74
4	**2e**	*n*-Bu	**3e**	68
5[d]	**2f**	CH_2OMe	**3f**	40
6	**2g**	$CH_2CH_2CO_2Me$	**3g**	36
7	**2h**	CH_2OAc	**3h**	27
8	**2i**	$SiMe_3$	**3i**	21

[a] Conditions: 1 equiv of **1b**, 2.2 equiv of **2**, 5 equiv of Et_3P, toluene, 60 °C. [b] Isolated yield. [c] Reaction was performed at −78 to 23 °C with 10 equiv of **2c** in the absence of Et_3P. [d] Et_3P was omitted from the reaction.

products are purified by silica gel column chromatography to give the dialkynyl naphthalenes **3** as yellow oils or white solids. The highest yields of naphthalene were obtained using diynes with relatively electroneutral phenyl (Table 1, entry 1) or noncoordinating *n*-alkyl substituents (entries 3 and 4). With the more reactive conjugated diester **2c**, low yields were initially obtained due to competitive decomposition of the diyne.[11] To circumvent this, the reaction was performed at a lower temperature and the diyne was used in excess, resulting in 82% yield of naphthalene **3c** (entry 2). In some cases (entries 2 and 5) triethylphosphine was not added, as the diynes were reactive toward the phosphine.

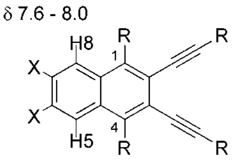
We interpret the lower yields observed for entries 5−8 to indicate restricted approach of diynes **2f−i** to the metal center. Of particular note is the lower yield for reaction of diyne **2g** (entry 6) when compared with the much higher yield for **2d** (entry 3), as the two diynes differ only in remote substituents ($CH_2CH_2CO_2Me$ versus CH_2CH_2OTBS, respectively). This suggests that the Lewis basic oxygens of the esters in **2g** coordinate to the metal center, preventing productive reaction (vide supra, Scheme 1). Such side chain coordination cannot occur with the sterically shielded oxygen of **2d**. This can also explain the lower yields observed for the oxygen-containing methyl ether **2f** (entry 5) and acetate **2h** (entry 7). For trimethylsilyl-substituted diyne **2i**, steric hindrance is likely the cause of the lower yield obtained (entry 8).

A further exploration of sterically demanding diyne substituents led us to react 2,5-di-*tert*-butoxyhexadiyne **2j** with nickel−benzyne **1b**. Although we were expecting little or no yield of naphthalene product because of the steric congestion at the terminal carbon of the diyne, we were surprised to find that a 70% yield of the 1,4-dialkynyl naphthalene **10** was formed (eq 4). This result is particularly intriguing, as it indicates that the regioselectivity can be controlled by judicious choice of diyne substitution.

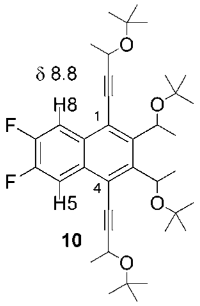


(4)

The structural assignments of dialkynyl naphthalenes **3** and **10** were originally based primarily on the ^1H NMR spectrum. The number of signals revealed that symmetric products had formed in both cases. Because of the proximity of the 1,4-substituents to the 5,8-protons, the two constitutional isomers can be distinguished by the different shielding effects of an alkyl versus an alkynyl group. The observed chemical shifts of δ 7.6−8.0 ppm for naphthalenes **3** are similar to the shifts for H8 of 1-alkyl naphthalenes reported in the literature.[12] In contrast, the δ 8.8 ppm shift observed for H8 in **10** is indicative of a 1,4-dialkynyl naphthalene.[13]



3



10

To confirm our structural assignments further, we were gratified to find that cycloadduct **3b** formed a crystalline product that could be analyzed by X-ray diffraction, which confirmed our NMR structural analysis (Figure 1).

Because of its higher stability, the nickel-4,5-difluorobenzyne **1b** could be isolated and purified, which enabled the precise determination of the yield of the cycloaddition reactions. However, the ability to access nonfluorinated 2,3-dialkynyl naphthalenes would constitute a more general method. Knowing that 1,4-diphenylbutadiyne **2b** gave the highest yield of the cycloadduct, nickel−benzyne **1a**, prepared in situ from complex **4**, was reacted with an excess of

---

(11) Varela, J. A.; Castedo, L.; Maestro, M.; Mahía, J.; Saá, C. *Chem. Eur. J.* **2001**, *7* (23), 5203.

(12) (a) Rigaudy, J.; Lachgar, M.; Saad, M. M. A. *Bull. Soc. Chim. Fr.* **1994**, *131* (2), 177. (b) Brown, R. F. C.; Browne, N. R.; Coulston, K. J.; Eastwood, F. W. *Aust. J. Chem.* **1990**, *43* (11), 1935. (c) Best, W. M.; Collins, P. A.; McCulloch, R. K.; Wege, D. *Aust. J. Chem.* **1982**, *35* (4), 843.

(13) (a) Pschirer, N. G.; Bunz, U. H. F. *Tetrahedron Lett.* **1999**, *40* (13), 2481. (b) John, J. A.; Tour, J. M. *Tetrahedron* **1997**, *53* (45), 15515. (c) Butler, I. R.; Soucy-Breau, C. *Can. J. Chem.* **1991**, *69* (7), 1117. (d) Klusener, P. A. A.; Hanekamp, J. C.; Brandsma, L.; Schleyer, P. v. R. *J. Org. Chem.* **1990**, *55* (4), 1311.

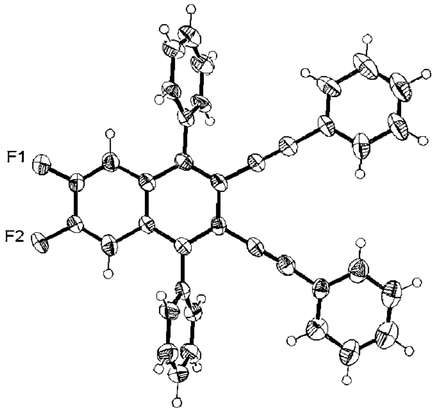
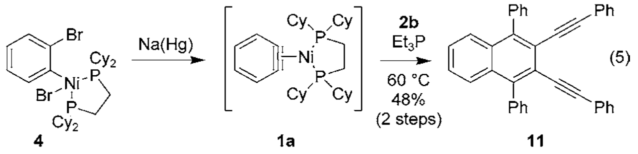


Figure 1. ORTEP diagram of 2,3-dialkynyl naphthalene **3b**.

1,4-diphenylbutadiyne **2b**, which afforded a 48% yield of **11** for the two-step sequence (eq 5). As the reduction of nickel(II) complex **4** to nickel(0)−benzyne **1a** typically proceeds in ca. 50% yield, this result indicates a high yield for the cycloaddition reaction. Crystals of **11** were also suitable for X-ray analysis, and the structure data obtained was nearly identical to that of **3b** (see Supporting Information).



The dialkynyl naphthalene products are all chromophoric and fluorescent, with absorption bands at 258−305 nm and molar absorptivities of 3 × 10^4−1.5 × 10^5 M^{-1} cm^{-1} (Figure 2). The fluorescence emission bands appear at 363−407 nm (see Supporting Information for additional spectra). Of particular interest is the efficiency of fluorescence for phenyl-susbtituted naphthalene **11**. Whereas the majority of fluorescence spectra were obtained at optical densities of 0.1, naphthalene **11** required a 10-fold lower optical density in order to stay within the limits of the detector, suggesting that these may be useful fluorescent materials.

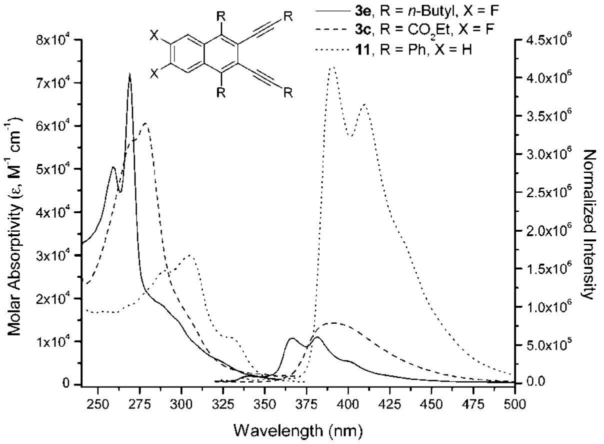


Figure 2. Absorption and emission spectra of **3e** (−), **3c** (- - -), and **11** (···) in chloroform.

The observed regioselectivity for the nickel−benzyne + diyne cycloaddition can be rationalized by considering the electronic factors that influence the course of the reaction. Because the benzyne carbon acts as the nucleophile toward the electrophilic diyne, the regioselectivity of the reaction is dictated by the relative sizes of the LUMO coefficients on the diyne. For symmetric diynes, the electronic contributions of the conjugated bonds dominate over those of the substitutents, placing the larger coefficient on the terminal carbons of the diyne regardless of the substituents.[14] Consistent with this argument, we observe the same regioselectivity with both electron-donating alkyl substituents (e.g., Table 1, entry 4) and electron-withdrawing ester groups (Table 1, entry 2). The only exception occurs when the steric congestion at the more electrophilic site prohibits reaction at that center (eq 4).

Although the electronic nature of the diyne substituents does not affect the regioselectivity of the reaction, it does influence the rate of reaction. This is most notable in the case of diester **2c**, which affords the naphthalene product **3c** after 4 h at −78 to 23 °C. In contrast, the more electron-rich dibutyl diyne **2e** yields naphthalene **3e** after 4 h at 60 °C. Thus, not surprisingly, we observe that better electrophiles react faster than less electrophilic diynes.

In conclusion, we have shown for the first time that conjugated 1,3-diynes react regioselectively with nickel−benzyne complexes in a formal [2 + 2 + 2] cycloaddition reaction to give highly substituted dialkynyl naphthalenes. The regiochemical course of the reaction is typically dictated by the electronics of the diyne to afford 2,3-dialkynyl naphthalenes; however, this electronic preference can be overcome when the diyne substituents are particularly bulky, resulting in the formation of 1,4-dialkynyl naphthalene. This allows for the selective formation of either symmetric dialkynyl naphthalene by simply choosing the appropriate diyne substituent. The naphthalenes reported herein may find utility as fluorescent materials, and further studies on their photophysical properties are currently underway.

Acknowledgment. Financial support from The donors of the Petroleum Research Fund, administered by the American Chemical Society (ACS-PRF # 36426-G1), and from the University of Illinois is gratefully acknowledged.

Supporting Information Available: Experimental and spectroscopic data for all new compounds and X-ray crystallographic data for **3b** and **11** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

OL034720X

---

[14] Varela, J. A.; Castedo, L.; Saá, C. *J. Am. Chem. Soc.* **1998**, *120* (46), 12147.