

An Expeditious Route to Eight-Membered Heterocycles By Nickel-Catalyzed Cycloaddition: Low-Temperature $C_{sp^2}-C_{sp^3}$ Bond Cleavage**

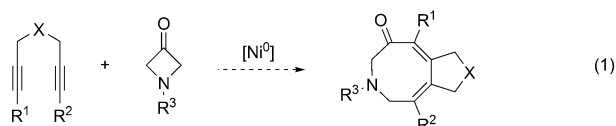
Puneet Kumar, Kainan Zhang, and Janis Louie*

In the 21st century, chemists have witnessed immense growth in the field of C–H bond activation, which represents an elegant method for constructing C–C bonds in a manner that minimizes waste.^[1] Alternatively, C–C bond activation provides another possible solution. Although significant progress has been made in the area of C–H bond activation, C–C bond activation is still in its infancy.^[2] The paucity of developments in this area can be attributed to the highly inert nature of C–C σ bond and the poor interaction of the orbitals of C–C σ bonds with transition metals.^[2a]

There is a significant amount of literature that describes the use of the inherent strain of cyclopropanes (strain energy = 27.6 kcal mol^{−1}) in transition-metal-catalyzed reactions.^[3] Before the remarkable finding of Murakami et al., the use of cyclobutanes (strain energy = 26.4 kcal mol^{−1}) in such reactions remained largely unexplored.^[4] Since then, appreciable efforts have been made in using various transition-metal catalysts to harness the latent potential of cyclobutanones.^[5] Most of these studies focused on the development of methods for accessing carbocycles that were, at the time, difficult to synthesize

Our research group has been active in developing nickel-catalyzed cycloaddition reactions. Recently, our research group and those of others independently discovered a Ni/PPh₃-catalyzed method for coupling azetidinones and alkynes to afford 3-piperidones; this method involves cleavage of the C–C bond attached to the carbonyl of the azetidinone.^[6] We surmised that if two tethered alkynes were employed instead of one, insertion of both of the alkynes into the azetidinone $C_{sp^2}-C_{sp^3}$ bond could occur, thus resulting in the formation of eight-membered N-containing heterocyclic products [Eq. (1)]. Medium-sized heterocycles are prevalent among bioactive molecules.^[7] Unfortunately, the synthesis of eight-membered rings poses a serious challenge because of enthalpic and entropic factors.^[8–10] In contrast to cyclobutanone, which was used by the research group of Murakami,^[11,12] heteroatom-substituted cyclobutanones are

prone to polymerization and decomposition.^[13] Furthermore, self-condensation of heteroatom-substituted cyclobutanones occurs under neutral as well as basic reaction conditions. Despite these challenges, we successfully developed a Ni/IPr catalyst that can effect the coupling of diynes and azetidinones to afford dihydroazocines in excellent yield.^[14] This catalytic method not only provides medium-sized eight-membered heterocycles that are normally challenging to prepare but also represents a remarkable model system for the cleavage of $C_{sp^2}-C_{sp^3}$ bonds at low temperature.



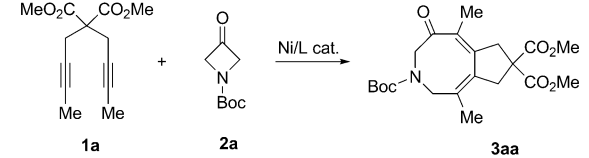
At the outset, we reasoned that self-condensation of the azetidinone could be minimized through the use of suitable protecting groups on the nitrogen atom of 3-azetidinones. The reaction between commercially available 3-Boc-protected azetidinone (**2a**) and malonate diyne **1a** was chosen as a model reaction. Given our success in using catalytic amounts of Ni/PPh₃ in toluene as reaction conditions for the coupling of azetidinones and alkynes, we initially evaluated these reactions conditions for the reaction between **1a** and **2a**. In the event, although moderate conversion of azetidinone **2a** was observed, no desired product was detected (Table 1, entry 1). Other phosphine ligands were also evaluated (Table 1, entries 2–8), but these reactions also led to little or no desired product. Notably, the reactions where some desired product was formed were those in which electron-donating phosphines were used (P(*n*Bu)₃, PCy₃, and P(Cyp)₃; Table 1, entries 5–7, respectively). A side reaction that plagues many cycloaddition reactions is the oligomerization of alkyne units to give aromatic products.^[15] We feared that this reaction was the cause of the low yields and therefore we conducted the reaction using Ni/PCy₃ as the catalyst and employing slow addition of the diyne (Table 1, entry 6). Unfortunately, a low yield of product **3aa** was still obtained. We then turned our attention to the highly σ -donating N-heterocyclic carbene (NHC) ligand, IPr, owing to our previous success in using Ni/IPr in the cycloaddition of both diyne and enynes and carbonyl compounds such as aldehydes and ketones.^[16] Murakami and co-workers also used a Ni/IPr catalyst to facilitate the cycloaddition of diynes and cyclobutanones.^[11] Ultimately, the use of IPr proved to be advantageous because the product **3aa** was obtained in

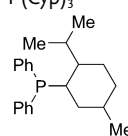
[*] P. Kumar, K. Zhang, Prof. Dr. J. Louie
Department of Chemistry, University of Utah
315 South, 1400 East, Salt Lake City, Utah 84112-0850 (USA)
E-mail: louie@chem.utah.edu
Homepage: <http://www.chem.utah.edu/faculty/louie/index.html>

[**] We acknowledge the NIH (5R01GM076125) and the NSF (0911017) for financial support. We thank Dr. J. Muller and Dr. A. Aarif of the University of Utah for providing HRMS and single-crystal X-ray crystallographic data, respectively. We also thank Ashish Thakur for the preparation of diynes **1g** and **1h**, and for the partial synthesis of **1m**.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/ange.201203521>.

Table 1: Ligand evaluation for the Ni-catalyzed cycloaddition of diyne **1a** and azetidinone **2a**.^[a]



Entry	Ligand	2a Conv. [%] ^[b]	3aa Yield [%] ^[c]
1	PPh ₃	49	n.d.
2	dppf	48	n.d.
3	binap	—	n.d.
4	PCy ₂ Ph	60	n.d.
5	P(<i>n</i> Bu) ₃	72	23
6	PCy ₃	83	37 (28) ^[d]
7	P(Cyp) ₃	81	30
8		18	n.d.
9	IPr	> 99	70 ^[e]

[a] Azetidinone **2a** (0.1 M), diyne **1a** (0.12 M), 10 mol % [Ni(cod)₂], ligand (20 mol % for entries 1, and 4–8; 10 mol % for entries 2 and 3), toluene, 100 °C, 12 h. [b] Conversion of diyne was determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. [c] Yields of isolated product. [d] Diyne **1a** was added dropwise to the reaction mixture. [e] Reaction was run at RT. binap = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, Boc = *tert*-butoxycarbonyl, cod = 1,5-cyclooctadiene, Cy = cyclohexyl, Cyp = cyclopentyl, dppf = 1,1'-bis(diphenylphosphino)ferrocene, n.d. = not detected.

70 % yield when the reaction was conducted at room temperature (Table 1, entry 9).

We surmised that the β -carbon-elimination step might be slow because the slow addition of the diyne did not lead to improved yields (see above). To facilitate this step, we conducted the reaction at higher temperatures (Table 2). Unfortunately, higher reaction temperatures proved to be deleterious to the coupling reaction and resulted in increased alkyne oligomerization. Specifically, when the reaction performed at 60 °C and at 100 °C the dihydroazocine product was obtained in 35 % and 21 % yield, respectively (Table 2, entries 2 and 3). These results suggested that lowering rather than increasing the reaction temperature might result in higher product yield. Indeed, the yield of **3aa** improved

Table 2: Temperature-effect evaluation on the Ni/IPr-catalyzed cycloaddition of **1a** and **2a** to afford **3aa**.^[a]

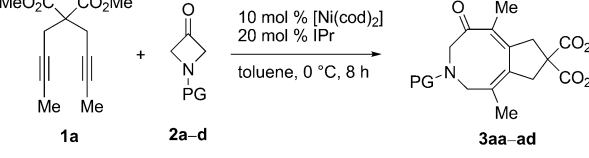
Entry	T [°C]	1a Conc. [M]	3aa Yield [%] ^[b]
1	RT	0.10	70
2	60	0.10	35
3	100	0.10	21
4	0	0.10	84
5	0	0.20	68
6	0	0.05	88

[a] Reaction conditions: azetidinone **2a** (1 equiv), diyne **1a** (1.2 equiv), 10 mol % [Ni(cod)₂], 20 mol % IPr, toluene, 8 h. [b] Yield of isolated product.

significantly when the reaction temperature was lowered to 0 °C (Table 2, entry 4).^[17] The use of a more dilute reaction mixture led to further improvement of the yield (Table 2, entries 4–6). Because previous C–C bond cleavage reactions were facilitated when they were conducted at higher temperatures, the results herein are exceptional in that the C–C bond cleavage step proceeds at 0 °C.^[18]

Other protecting groups on the nitrogen atom of 3-azetidinone were also evaluated (Table 3). The use of the methoxycarbonyl protecting group (**2b**; Table 3, entry 2)

Table 3: Effect of azetidinone protecting group on the Ni/IPr-catalyzed cycloaddition of **1a** and **2a–d**.

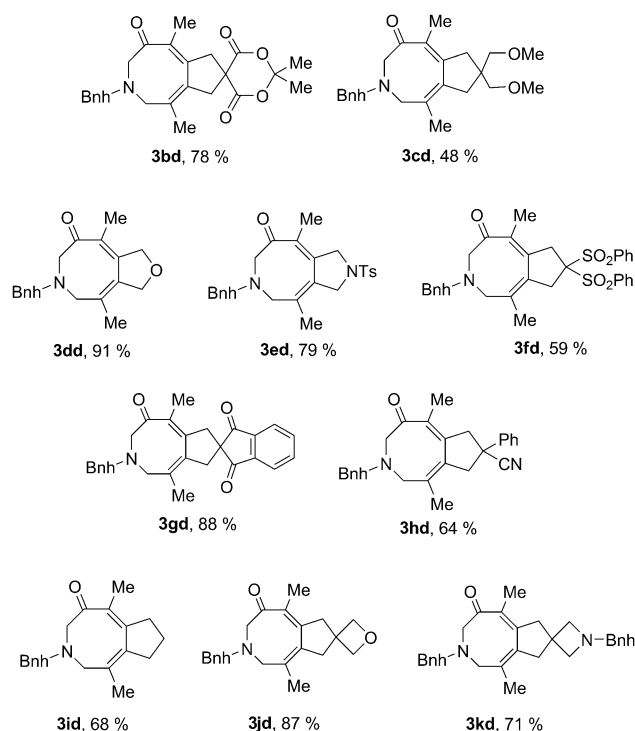


Entry	2	Protecting group (PG)	Product 3	Yield [%] 3
1	2a	Boc	3aa	88
2	2b	CO ₂ Me	3ab	69
3	2c	Ts	3ac	25
4	2d	Bnh	3ad	92

Ts = *p*-toluenesulfonyl.

resulted in a lower yield than the use of Boc-protected azetidinone (**2a**; Table 3, entry 2). The use of the tosyl (Ts) protecting group afforded the product in poor yield (**2c**; Table 3, entry 3). However, the use of the benzhydryl (Bnh) protecting group (**2d**; Table 3, entry 4) led to an excellent yield (92 %) of the corresponding dihydroazocine **3ad**.

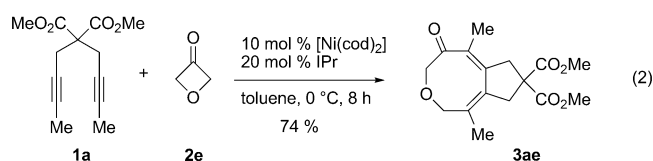
The substrate scope of this reaction was investigated with various diynes (Scheme 1). The presence of a dioxolone moiety in the diyne was well tolerated under the reaction conditions and the dihydroazocine product **3bd** was obtained in good yield. Unsurprisingly, the presence of ether functional groups was tolerated (Scheme 1; **3cd** and **3dd**).^[19] Notably, the sulfonamide-based diyne, which is not always well tolerated in Ni-catalyzed cycloaddition reactions, reacted with azetidinone to provide the pyrrolidinyl-fused dihydroazocine product **3ed** in excellent yield.^[20] The reaction of a diyne containing a sulfonyl group (**1f**) afforded product in slightly lower yield than an ester-containing diyne (**1a**). Interestingly, ketones and nitriles, which are functional groups that also undergo cycloaddition reactions with diynes, did not interfere with the coupling reaction involving the azetidinone (**3gd** and **3hd**, Scheme 1).^[11,20c,e] The success of the reaction is not dependent on the presence of the Thorpe–Ingold effect because the use of a diyne with an unsubstituted backbone afforded the corresponding dihydroazocine (**3id**) in good yield. Because ester-containing compounds often cannot be used as therapeutics, we evaluated other substrates. Inspired by the recent work of Carriera and co-workers, oxetanyl and azetidinyl diynes (**1j** and **1k**) were prepared and subjected to the optimized reaction conditions;^[21] the corresponding dihydroazocine



Scheme 1. Products derived from the Ni-catalyzed cycloaddition of diynes **1b–1k** and azetidinone **2d** (1 equiv), diyne **1b–1k** (1.2 equiv), $[\text{Ni}(\text{cod})_2]$ (10 mol %), iPr (20 mol %), toluene, 8 h.

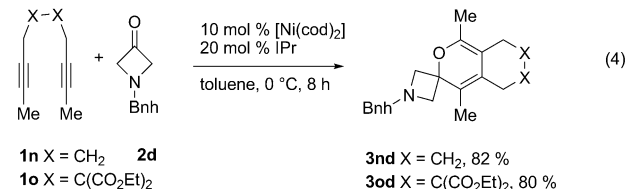
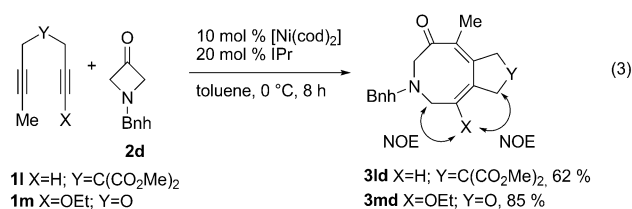
products (**3jd** and **3kd**, Scheme 1), which contain a spirocyclic backbone, were obtained in good yield.

3-oxacyclobutanone (**2e**) and diyne **1a** could also undergo the Ni/ iPr -catalyzed cycloaddition reaction using the standard reaction conditions, thus giving dihydrooxocine **3ae** in good yield [Eq. (2)].

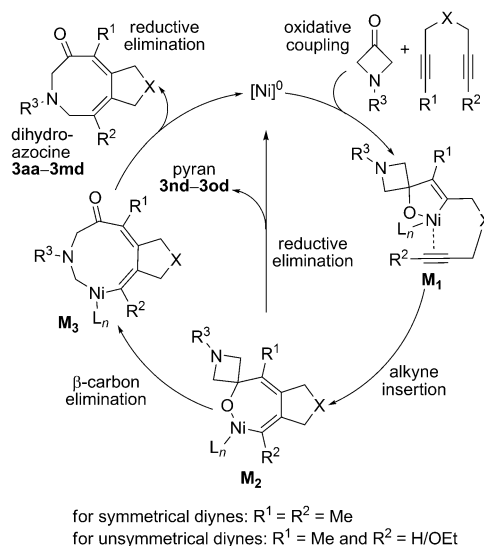


To address the question of regioselectivity when using an unsymmetrical diyne, diyne **1l**, which contains a terminal alkyne and a methyl-substituted alkyne, was subjected to the optimized reaction conditions; only one regioisomer was observed [**3ld**; Eq. (3)]. Another unsymmetrical diyne, **1m**, the termini of which differ electronically rather than sterically, was also evaluated; again, only one regioisomer was observed [**3md**, Eq. (3)].

Interestingly, when diynes **1n** and **1o**, which were expected to afford six-membered-ring-fused dihydroazocine products, were evaluated, the expected products arising from $\text{C}_{\text{sp}^2}\text{--}\text{C}_{\text{sp}^3}$ bond cleavage were not obtained. Instead, spirocyclic pyran products were formed in good yields [**3nd** and **3od**, Eq. (4)].^[16]



A proposed mechanism for the cycloaddition reaction is shown in Scheme 2. Typically, such a cycloaddition would begin with oxidative coupling between an alkyne and the carbonyl group.^[11,22,23] In this case, oxidative coupling would



Scheme 2. Proposed mechanism of the cycloaddition reaction.

afford a spirocyclic intermediate **M₁**. Subsequent insertion of the pendant alkyne would give the intermediate **M₂**, which could then undergo either reductive elimination (to afford products such as **3nd** and **3od**) or β -carbon elimination to afford metallacycle **M₃**. Finally, C–C bond forming reductive elimination occurs to give the dihydroazocine product and the catalyst. In the cycloaddition of unsymmetrical diyne **1l**, the regioselectivity is governed by the difference in the size of the substituents on the alkynes. That is, oxidative coupling between the alkyne bearing the larger group occurs first to minimize steric interactions between the group and the ligand. Indeed, this type of regioselectivity has been found in various cycloaddition reactions catalyzed by nickel complexes. However, in the cycloaddition of unsymmetrical diyne **1m**, the electronic nature of the alkyne, rather than steric

factors, dictate the observed regioselectivity. That is, the oxidative coupling of the alkyne bearing the methyl group ($R^1 = \text{Me}$) is more favored than the coupling of the alkyne with perturbed electronics ($R^2 = \text{OEt}$). This type of electronically driven regioselectivity has not been exploited extensively in cycloaddition reactions.^[24]

In conclusion, we have demonstrated that eight-membered heterocycles can be easily accessed through Ni/IPr-catalyzed coupling of 3-azetidinone (or 3-oxetanone) and diynes. The decomposition of these constrained heterocycles could be avoided by using specific reaction conditions. This method involves an interesting C–C bond cleavage step, which operates smoothly at 0°C. Further synthetic and mechanistic analysis of this reaction is currently underway.

Experimental Section

Representative procedure: In a nitrogen-filled glove box, a scintillation vial equipped with a magnetic stir bar, was charged with a solution of azetidinone (1 equiv) in toluene (0.05M) and diyne (1.2 equiv). At room temperature, a solution of the catalyst, which was prepared by stirring a mixture of $[\text{Ni}(\text{cod})_2]$ and IPr (1:2 molar ratio) in toluene for at least 6 h, was added. The vial containing the reaction mixture was immediately taken out of the glove box and sealed; the reaction mixture was then stirred at 0°C for 8 h. The solvent was removed under vacuum and the product was purified by silica-gel flash column chromatography.

Received: May 7, 2012

Published online: July 17, 2012

Keywords: azetidinones · C–C activation · cycloaddition · dihydroazocines · nickel

- [1] a) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; b) P. Kumar, J. Louie, *Angew. Chem.* **2011**, *123*, 10956; *Angew. Chem. Int. Ed.* **2011**, *50*, 10768; c) K. Chen, P. S. Baran, *Nature* **2009**, *459*, 824; d) C. J. Li, B. M. Trost, *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 13197; e) J.-P. Corbet, G. Mignani, *Chem. Rev.* **2006**, *106*, 2651.
- [2] For discussion on the challenges involved in C–C bond activation, see: a) M. Murakami, Y. Ito, *Top. Organomet. Chem.* **1999**, *3*, 97; b) B. Rybtchinski, D. Milstein, *Angew. Chem.* **1999**, *111*, 918; *Angew. Chem. Int. Ed.* **1999**, *38*, 870; c) C.-H. Jun, *Chem. Soc. Rev.* **2004**, *33*, 610; d) M. Miura, T. Satoh, *Top. Organomet. Chem.* **2005**, *14*, 1; e) M. Murakami, *Chem. Rec.* **2010**, *10*, 326; f) M. Murakami, T. Matsuda, *Chem. Commun.* **2011**, *47*, 1100; g) T. Seiser, T. Saget, D. N. Tran, N. Cramer, *Angew. Chem.* **2011**, *123*, 7884; *Angew. Chem. Int. Ed.* **2011**, *50*, 7740.
- [3] For transition-metal-catalyzed activation of cyclopropanes leading to carbocycles, see: for rhodium: a) P. A. Wender, A. J. Dyckman, C. O. Husfeld, D. Kadereit, J. A. Love, H. Rieck, *J. Am. Chem. Soc.* **1999**, *121*, 10442; b) P. A. Wender, C. M. Barzilay, A. J. Dyckman, *J. Am. Chem. Soc.* **2001**, *123*, 179; c) P. A. Wender, G. G. Gamber, R. D. Hubbard, L. Zhang, *J. Am. Chem. Soc.* **2002**, *124*, 2876; d) P. A. Wender, L. O. Haustedt, J. Lim, J. A. Love, T. J. Williams, J.-Y. Yoon, *J. Am. Chem. Soc.* **2006**, *128*, 6302; e) Y. Wang, J. Wang, J. Su, F. Huang, L. Jiao, Y. Liang, D. Yang, S. Zhang, P. A. Wender, Z.-X. Yu, *J. Am. Chem. Soc.* **2007**, *129*, 10060; for ruthenium: f) B. M. Trost, F. D. Toste, H. Shen, *J. Am. Chem. Soc.* **2000**, *122*, 2379; g) B. M. Trost, J. Waser, A. Meyer, *J. Am. Chem. Soc.* **2008**, *130*, 16424; for nickel: h) G. Zuo, J. Louie, *J. Am. Chem. Soc.* **2005**, *127*, 5798; i) G. Zuo, J. Louie, *Angew. Chem.* **2004**, *116*, 2327; *Angew. Chem. Int. Ed.* **2004**, *43*, 2277; for iridium: j) N. Chatani, H. Inoue, T. Morimoto, T. Muto, S. Murai, *J. Org. Chem.* **2001**, *66*, 4433.
- [4] M. Murakami, H. Amii, Y. Ito, *Nature* **1994**, *370*, 540.
- [5] For construction of carbocycles through transition-metal-catalyzed activation of cyclobutanones, see: a) M. Murakami, S. Ashida, *Chem. Commun.* **2006**, 4599; b) T. Matsuda, M. Makino, M. Murakami, *Angew. Chem.* **2005**, *117*, 4684; *Angew. Chem. Int. Ed.* **2005**, *44*, 4608; c) L. Liu, N. Ishida, M. Murakami, *Angew. Chem. Int. Ed.* **2012**, *51*, 2485; d) P. A. Wender, A. G. Correa, Y. Sato, R. Sun, *J. Am. Chem. Soc.* **2000**, *122*, 7815; e) M. M. Montero-Campillo, J. Rodríguez-Otero, E. M. Cabaleiro-Lago, *Tetrahedron* **2008**, *64*, 6215.
- [6] For Ni-catalyzed coupling of azetidinone and alkynes, see: a) P. Kumar, J. Louie, *Org. Lett.* **2012**, *14*, 2026; b) K. Y. T. Ho, C. Aïssa, *Chem. Eur. J.* **2012**, *18*, 3486.
- [7] For selected biologically important compounds containing reduced azocine moieties, see: a) J. D. Winkler, A. T. Londregan, M. T. Hamann, *Org. Lett.* **2006**, *8*, 2591; b) J. D. Winkler, A. T. Londregan, J. R. Ragains, M. T. Hamann, *Org. Lett.* **2006**, *8*, 3407; c) E. Vedejs, R. J. Galante, P. G. Goekjian, *J. Am. Chem. Soc.* **1998**, *120*, 3613.
- [8] For construction of eight-membered carbocycles through transition metal catalyzed cycloaddition, see: a) P. A. Wender, N. C. Ihle, *J. Am. Chem. Soc.* **1986**, *108*, 4678; b) P. A. Wender, M. J. Tebbe, *Synthesis* **1991**, 1089; c) P. A. Wender, J. M. Nuss, D. B. Smith, A. Suárez-Sobrin, J. Vågberg, D. Decosta, J. Bordner, *J. Org. Chem.* **1997**, *62*, 4908; d) P. A. Evans, J. E. Robinson, E. W. Baum, A. N. Fazal, *J. Am. Chem. Soc.* **2002**, *124*, 8782; e) S. R. Gilbertson, B. DeBoef, *J. Am. Chem. Soc.* **2002**, *124*, 8784; f) J. A. Varela, L. Castedo, C. Saa, *Org. Lett.* **2003**, *5*, 2841; g) P. A. Evans, E. W. Baum, *J. Am. Chem. Soc.* **2004**, *126*, 11150; h) P. A. Evans, E. W. Baum, A. N. Fazal, M. Pink, *Chem. Commun.* **2005**, 63; i) S. I. Lee, S. Y. Park, Y. K. Chung, *Adv. Synth. Catal.* **2006**, *348*, 2531; j) P. A. Wender, J. P. Christy, *J. Am. Chem. Soc.* **2006**, *128*, 5354; k) B. DeBoef, W. R. Counts, S. R. Gilbertson, *J. Org. Chem.* **2007**, *72*, 799; l) G. Hilt, J. Janikowski, *Angew. Chem.* **2008**, *120*, 5321; *Angew. Chem. Int. Ed.* **2008**, *47*, 5243.
- [9] For a ring-closing-metathesis route to medium-sized heterocycles, see: a) A. Deiters, S. F. Martin, *Chem. Rev.* **2004**, *104*, 2199; for a Rh-catalyzed reaction forming dihydroazocines, see: b) R. T. Yu, R. K. Friedman, T. Rovis, *J. Am. Chem. Soc.* **2009**, *131*, 13250.
- [10] A. Michaut, J. Rodriguez, *Angew. Chem.* **2006**, *118*, 5870; *Angew. Chem. Int. Ed.* **2006**, *45*, 5740.
- [11] For studies on the synthesis of carbocycles by methods involving nickel-catalyzed β -carbon elimination, see: a) M. Murakami, S. Ashida, T. Matsuda, *J. Am. Chem. Soc.* **2005**, *127*, 6932; b) M. Murakami, S. Ashida, T. Matsuda, *J. Am. Chem. Soc.* **2006**, *128*, 2166; c) M. Murakami, M. Makino, S. Ashida, T. Matsuda, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1315; d) S. Ashida, M. Murakami, *Bull. Chem. Soc. Jpn.* **2008**, *81*, 885.
- [12] For prior work with cyclobutenones, see: a) L. S. Liebeskind, S. L. Baysdon, M. S. South, S. Iyer, J. P. Leeds, *Tetrahedron* **1985**, *41*, 5839; b) L. S. Liebeskind, R. Chidambaram, D. Mitchell, B. Foster, *Pure Appl. Chem.* **1988**, *60*, 2734; c) M. A. Huffman, L. S. Liebeskind, *J. Am. Chem. Soc.* **1991**, *113*, 2771; d) M. A. Huffman, L. S. Liebeskind, *J. Am. Chem. Soc.* **1993**, *115*, 4895; e) L. S. Liebeskind, A. Bombrun, *J. Org. Chem.* **1994**, *59*, 1149.
- [13] a) Y. Dejaegher, N. M. Kuz'menok, A. M. Zvonok, N. De Kimpe, *Chem. Rev.* **2002**, *102*, 29; b) D. De Smaele, Y. Dejaegher, G. Duvey, N. De Kimpe, *Tetrahedron Lett.* **2001**, *42*, 2373.
- [14] This synthetic technology is the subject of a patent application submitted by us in Aug. **2011** (P. Kumar, J. Louie, 61-528,739).

- [15] P. A. Wender, J. P. Christy, *J. Am. Chem. Soc.* **2007**, *129*, 13402.
- [16] For Ni-catalyzed cycloaddition of diynes and enynes with carbonyl compounds, see: a) T. N. Tekevac, J. Louie, *Org. Lett.* **2005**, *7*, 4037; b) T. N. Tekavec, J. Louie, *J. Org. Chem.* **2008**, *73*, 2641.
- [17] When PCy₃ was used as a ligand in a reaction conducted at 60 °C and RT, yields of **1a** were 47 % and 24 %, respectively.
- [18] Y. Nakao, T. Hiyama, *Pure Appl. Chem.* **2008**, *80*, 1097.
- [19] The structure of **3dd** was unambiguously determined by single crystal X-ray crystallography (see the Supporting Information). CCDC 890696 (**3dd**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [20] For examples of where a diyne containing an NTs group in the backbone can be a poorly effective coupling partner in nickel-catalyzed cycloaddition reactions, see: a) J. Louie, J. E. Gibby, M. V. Farnworth, T. N. Tekavec, *J. Am. Chem. Soc.* **2002**, *124*, 15188; b) T. N. Tekavec, A. M. Arif, J. Louie, *Tetrahedron* **2004**, *60*, 7431; c) M. M. McCormick, H. A. Duong, G. Zuo, J. Louie, *J. Am. Chem. Soc.* **2005**, *127*, 5030; d) P. Kumar, D. M. Troast, R. Cella, J. Louie, *J. Am. Chem. Soc.* **2011**, *133*, 7719; e) P. Kumar, S. Prescher, J. Louie, *Angew. Chem.* **2011**, *123*, 10882; *Angew. Chem. Int. Ed.* **2011**, *50*, 10694.
- [21] J. A. Burkhard, G. Wuitschik, M. Rogers-Evans, K. Müller, E. M. Carreira, *Angew. Chem.* **2010**, *122*, 9236; *Angew. Chem. Int. Ed.* **2010**, *49*, 9052.
- [22] a) K. M. Miller, W.-S. Huang, T. F. Jamison, *J. Am. Chem. Soc.* **2003**, *125*, 3442; b) J. Montgomery, G. J. Sormunen, *Top. Curr. Chem.* **2007**, *279*, 1; c) H. A. Malik, G. J. Sormunen, J. Montgomery, *J. Am. Chem. Soc.* **2010**, *132*, 5966; d) P. R. McCarren, P. Liu, P. H.-Y. Cheong, T. F. Jamison, K. N. Houk, *J. Am. Chem. Soc.* **2009**, *131*, 6654; e) P. Liu, P. McCarren, P. H.-Y. Cheong, T. F. Jamison, K. N. Houk, *J. Am. Chem. Soc.* **2010**, *132*, 2050.
- [23] Based on the recent DFT calculations, the possibility of initial oxidative coupling of two alkyne units cannot be ruled out completely. J.-Y. Tao, D.-C. Fang, G. A. Chass, *Phys. Chem. Chem. Phys.* **2012**, *14*, 6937.
- [24] a) F. E. McDonald, H. Y. H. Zhu, C. R. Holmquist, *J. Am. Chem. Soc.* **1995**, *117*, 6605; b) J. Castro, H. Sorensen, A. Riera, C. Morin, A. Moyano, M. A. Pericas, A. E. Greene, *J. Am. Chem. Soc.* **1990**, *112*, 9388; c) T. Hanazawa, K. Sasaki, Y. Takayama, F. Sato, *J. Org. Chem.* **2003**, *68*, 4980; d) Y. Komine, A. Kamisawa, K. Tanaka, *Org. Lett.* **2009**, *11*, 2361.