

Nickel-Catalyzed Cycloaddition of Unsaturated Hydrocarbons and Carbonyl Compounds

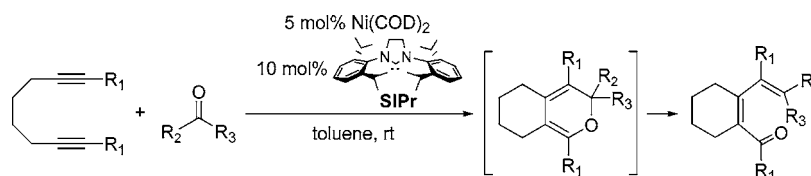
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ABSTRACT



A mild and general route for preparing pyrans and dienones from carbonyls and diynes is described. Ni imidazolylidene complexes were used to mediate cyclizations between diynes and aldehydes. The reaction of an enyne and an aldehyde afforded a mixture of cyclized products. In addition, a spiropyran was prepared from the cycloaddition of a diyne and cyclohexanone.

Transition-metal-catalyzed annulations have been used extensively to quickly construct complex cyclic systems from simple acyclic precursors.¹ We recently reported that systems based on the combination of *N*-heterocyclic carbenes (NHCs) and Ni(0)² effectively catalyze the cycloaddition of alkynes and CO₂.³ A key step in this cycloaddition protocol is the oxidative coupling of an alkyne and the C_{sp}-oxygen double bond. In contrast, analogous cycloaddition protocols that utilize C_{sp}²-oxygen double bonds are scarce. Cobalt reagents have been shown to mediate these reactions; however, stoichiometric amounts of cobalt are required.⁴ Two notable catalytic reactions based on Ni⁵ and Ru⁶ complexes have been developed; unfortunately, both systems require elevated

temperatures. In addition, only highly electron-deficient ketones can be employed as substrates with the Ru catalyst.

The efficacy of our Ni/NHC-catalyzed cycloadditions of alkynes and CO₂,³ in conjunction with recent advances in Ni-catalyzed reductive couplings of alkynes and 1,3-dienes with simple aldehydes,⁷ prompted us to investigate the Ni/NHC-catalyzed cycloaddition of diynes and aldehydes. Herein, we demonstrate these systems may also be used for catalyzing the cycloaddition between unsaturated hydrocarbons and unactivated carbonyls under mild conditions.

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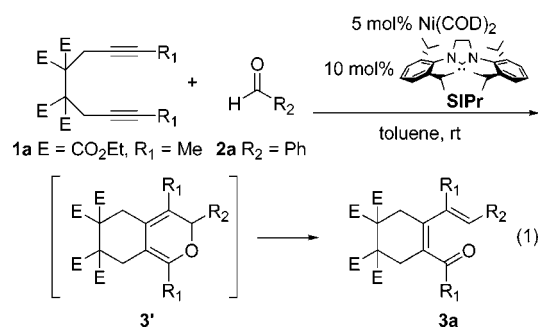
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(7) Alkynes: (a) Huang, W.; Chan, J.; Jamison, T. F. *Org. Lett.* **2000**, *2*, 4221. (b) Miller, K. M.; Huang, W.; Jamison, T. F. *J. Am. Chem. Soc.* **2003**, *125*, 3442. (c) Miller, K. M.; Luanphaisarnnont, T.; Molinaro, C.; Jamison, T. F. *J. Am. Chem. Soc.* **2004**, *126*, 4130. (d) Mahandru, G. M.; Liu, G.; Montgomery, J. J. *Am. Chem. Soc.* **2004**, *126*, 3698. (e) Ni, Y.; Amarasinghe, K. K. D.; Montgomery, J. *Org. Lett.* **2002**, *4*, 1743. 1,3-dienes: (f) Kimura, M.; Ezoe, A.; Shibata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4033. (g) Kimura, M.; Fujimatsu, H.; Ezoe, A.; Shibata, K.; Shimizu, M.; Matsumoto, S.; Tamaru, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 397. (h) Sato, Y.; Saito, N.; Mori, M. *Tetrahedron* **1998**, *54*, 1153. (i) Sato, Y.; Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2000**, *122*, 1624. (j) Sato, Y.; Sawaki, R.; Mori, M. *Organometallics* **2001**, *20*, 5510. (k) Sato, Y.; Saito, N.; Mori, M. *J. Org. Chem.* **2002**, *67*, 9310. (l) Sawaki, R.; Sato, Y.; Mori, M. *Org. Lett.* **2004**, *6*, 1131. For recent reviews, see: (m) Montgomery, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3890. (n) Ikeda, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 5120.

A variety of conditions were evaluated using diyne **1a** and benzaldehyde (**2a**) as model substrates for the cycloaddition reaction (eq 1). Ultimately, a protocol similar to the one



found effective for the cycloaddition of alkynes and CO₂ cleanly afforded dienone **3a**, derived from electrolytic ring opening of the initial pyran **3'**.⁸ Excellent yields (as determined using gas chromatography) were obtained using 5 mol % of Ni(COD)₂, 10 mol % of SIPr,⁹ a diyne concentration of 0.1 M in toluene, and a slight excess (1.25 equiv) of aldehyde at room temperature.

As illustrated in Table 1, the Ni/SIPr combination catalyzes the cycloaddition reaction of diynes and various aldehydes.

Table 1. Ni-Catalyzed Cycloaddition of Diynes **1** and Aldehydes **2**^a

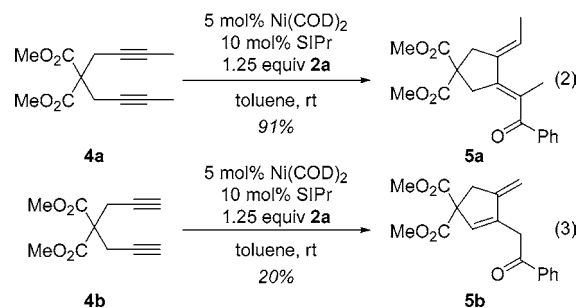
entry	diyne	aldehyde	dienone product	% yield ^b
1	1a , R ₁ = Me	2a , R ₂ = C ₆ H ₅	3a	78
2	1a	2b , R ₂ = 4-MeO-C ₆ H ₄	3b	91
3	1a	2c , R ₂ = 4-CF ₃ -C ₆ H ₄	3c	65 ^c
4	1a	2d , R ₂ = <i>i</i> -Pr	3d	58 ^{d,e}
5	1a	2e , R ₂ = <i>n</i> -Pr	3e	72 ^{d,e}
6	1b , R ₁ = Et	2a	3f	80

^a Reaction conditions: 0.1 M diyne, 0.125 M aldehyde, 5 mol % of Ni(COD)₂, 10 mol % of SIPr, room temperature. ^b Isolated yields (average of two runs). ^c 10 mol % of Ni(COD)₂, 20 mol % of SIPr. ^d 10 mol % of Ni(COD)₂, 10 mol % of SIPr. ^e Product exists as an equilibrium mixture of dienone (major) and ether (minor).

For example, benzaldehyde cyclized smoothly at room temperature with diynes **1a** and **1b** to afford dienones **3a** and **3f** in good yields (entries 1 and 6, respectively). The cycloaddition of an aryl aldehyde bearing an electron-donating group (*p*-OMe) afforded the dienone product in a

higher yield than the reaction of an aryl aldehyde possessing an electron-withdrawing group (*p*-CF₃) (entries 2 and 3, respectively). Aliphatic aldehydes also underwent facile cycloaddition (entries 4 and 5) using slightly modified conditions (10 mol % of Ni(COD)₂ and 10 mol % of SIPr). In addition, excess butyraldehyde (5 equiv) was necessary to ensure complete dienone formation (entry 5).¹⁰

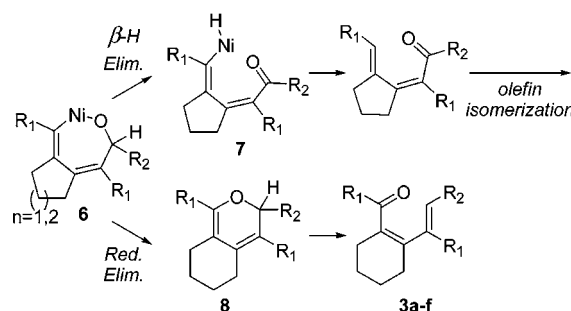
Diynes **4a** and **4b**, which possess a three carbon linkage between the alkynes, also underwent coupling with benzaldehyde **2a** (eqs 2 and 3). Surprisingly, the connectivity of



these dienones was different with those obtained from diynes possessing a four-carbon linkage. Specifically, the Ph group of benzaldehyde remains connected to the carbonyl in dienones **5a** and **5b**. In contrast, this bond has been cleaved in dienones **3a–f**.

The difference in the reactivity of diynes **4a,b** (where *n* = 1) may be attributed to a slower rate of reductive elimination, relative to β -hydride elimination, from nickelacycle **6** to form a strained fused [5,6] ring system (Scheme 1). However when *n* = 2, as in diynes **1a,b**, the rate of

Scheme 1. β -H Elimination or Reductive Elimination from Intermediate **6**



reductive elimination to form the less strained [6,6] ring system **8** is more facile, ultimately producing the observed electrolytic ring opened cycloadducts (**3a–f**). Previous reports have invoked a [1,5] sigmatropic shift from metalacycle **6** or pyran **8** rather than β -H elimination to account for the formation of products similar to **5**.¹¹ However, cyclization of enyne **9** and benzaldehyde **2a** produced

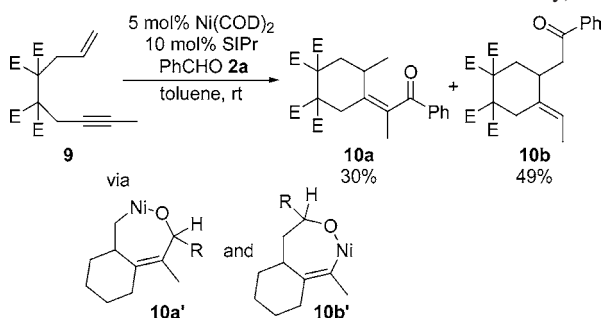
(8) The thermal electrocyclic isomerization of fused α -pyrans is common; see: (a) Trost, B. M.; Rudd, M. T.; Costa, M. G.; Lee, P. I.; Pomerantz, A. E. *Org. Lett.* **2004**, *6*, 4235. (b) Marvell, E. N.; Chadwick, T.; Caple, G.; Gosink, T.; Zimmer, G. *J. Org. Chem.* **1972**, *37*, 2992. (c) Kluge, A. F.; Lillya, C. P. *J. Org. Chem.* **1971**, *36*, 1979. (d) Marvell, E. N.; Caple, G.; Gosink, T. A.; Zimmer, G. *J. Am. Chem. Soc.* **1966**, *88*, 619.

(9) Unsaturated analogue IPr gave slightly lower yields under identical reaction conditions (84% vs 56% for SIPr and IPr, respectively). Other NHCs such as IrBu and IMes led to incomplete conversion of the diyne or low yields. (IrBu = 1,3-di-*tert*-butylimidazol-2-ylidene; IMes = 1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene; IPr = 1,3-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene; SIPr = 1,3-bis-(2,6-diisopropylphenyl)-4,5-dihydroimidazol-2-ylidene.)

(10) We have recently discovered that NHCs, such as SIPr, catalyze the cyclotrimerization of linear aliphatic aldehydes. This cyclotrimerization competes with the annulation reaction of diynes and aliphatic aldehydes.

carbocycles **10a** and **10b** in good overall yield (79%, 1:1.6 ratio, Scheme 2). This supports β -H elimination as the more

Scheme 2. Cycloaddition of Enyne **9** (Esters Have Been Omitted from Intermediates **10a'** and **10b'** for Clarity)



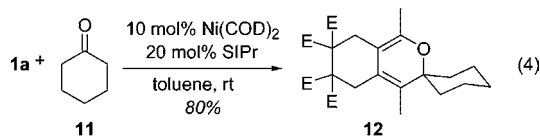
plausible mechanism since a [1,5] sigmatropic rearrangement is *not* possible from either metallacycles **10a'** or **10b'** nor from their respective pyrans. In addition, carbocycle **10b** represents a rare example of the preferential reaction between an aldehyde and an alkene over an alkyne.^{12,13}

(11) See refs 4a and 5. Alternatively, two sequential metal-mediated [1,3] rearrangements are possible; see: Karel, K. J.; Brookhart, M.; Aumann, R. *J. Am. Chem. Soc.* **1981**, *103*, 2695.

(12) For an example of oxidative coupling between an alkene and an aldehyde, see: Ogoshi, S.; Oka, M.; Kurosawa, H. *J. Am. Chem. Soc.* **2004**, *126*, 11802.

(13) Miller and Jamison reported that in the reductive coupling of an enyne and an aldehyde, the tethered alkene influences the regioselectivity of the oxidative coupling but remains *intact* in the products obtained. See: Miller, K.; Jamison, T. F. *J. Am. Chem. Soc.* **2004**, *126*, 15342.

Unactivated ketones also cleanly cyclized with diynes under mild conditions.¹⁴ For example, subjecting **1a** and cyclohexanone **11** to a slightly higher catalyst loading (10 mol % of $\text{Ni}(\text{COD})_2$ and 20 mol % of SIPr) afforded pyran **12** in good isolated yield (80%, eq 4).



The combination of SIPr and a Ni(0) precursor successfully catalyzed the cycloaddition between C_{sp}^2 carbonyls and diynes under mild conditions. The connectivity of the cyclized products obtained was dependent on the number of carbons linking the two alkynes. Furthermore, enynes and ketones also served as cycloaddition substrates. Work is currently underway to expand the scope of ketones and enynes available for this reaction.

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Supporting Information Available: ^1H NMR, ^{13}C NMR, and IR data for all compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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