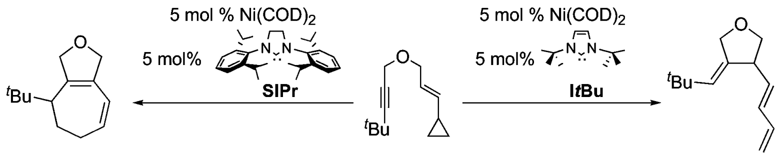
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Communication

# Selectivity in Nickel-Catalyzed Rearrangements of Cyclopropylen-ynes

Gang Zuo, and Janis Louie

*J. Am. Chem. Soc.*, **2005**, 127 (16), 5798-5799• DOI: 10.1021/ja043253r • Publication Date (Web): 05 April 2005



Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

J|A|C|S
COMMUNICATIONS

# Selectivity in Nickel-Catalyzed Rearrangements of Cyclopropylen-ynes

Gang Zuo and Janis Louie*

*Department of Chemistry, University of Utah, 315 South 1400 East, Salt Lake City, Utah 84112-0850*

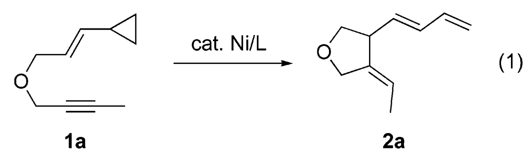
Received November 9, 2004; E-mail: louie@chem.utah.edu

Transition metal-catalyzed isomerization and rearrangement reactions of unsaturated systems provide rapid access to important heterocyclic and carbocyclic motifs. Toward this end, a variety of metal-catalyzed rearrangements have been developed over the past decade.[1] We recently discovered that the combination of Ni(0) and a sterically hindered N-heterocyclic carbene (NHC) effectively catalyzed the isomerization of vinyl cyclopropanes (VCPs) under mild conditions to afford cyclopentenes in excellent yields.[2] By tethering an alkynyl moiety to the VCP, we found that Ni/NHC systems also catalyze a rearrangement reaction to afford three different heterocyclic-based structures, two of which are distinct from those obtained employing Rh- and Ru-based catalysts.[3] Moreover, a single product can be generated selectively when an *N*-alkyl NHC is employed.

The Ni-catalyzed rearrangement of [(1*E*)-3-(2-butynyloxy)-1-propenyl]cyclopropane (**1a**) was investigated, and a variety of tertiary phosphines and NHCs[4] were explored as potential ligands (eq 1, Table 1). No rearrangement was observed in the absence of ligand or when tertiary phosphines were added as ligands (entries 1−4). Interestingly, smooth conversion of the cyclopropylen-yne **1a** was observed when an NHC was employed (entries 6−15). Furthermore, cyclopentane **2a** possessing a diene substituent was formed as the sole heterocyclic product.[5] Although almost every NHC screened ultimately afforded product **2a** in excellent yield (entries 6−17), rates were fastest with SIPr (entry 14). For example, **2a** was observed in 86, 76, and 89% after only half an hour at room temperature when I*t*Bu, IPr, and SIPr were employed, respectively (entries 8, 10, and 12). Increasing the Ni:L ratio had no significant effect on yield (entries 13−15, Table 1). In addition, toluene, benzene, pentane, THF, and ether were equally effective solvents.

Our initial investigations revolved around rearrangements catalyzed by the combination of $Ni(COD)_2$ and SIPr since rates of reaction were fastest with this system. Interestingly, as shown in Table 2, the size of the substituent on the alkyne (R) had a significant effect on the nature of the heterocyclic product that formed. Specifically, when R was small (e.g., R = Me (**1a**), entry 1), the expected cyclopentane product (**2a**) was formed exclusively. However, to our surprise, cyclopentanes **2b** and **2c** were not the sole rearrangement products from substrates **1b** and **1c** (entries 2 and 3). Instead, a mixture of heterocycles was obtained. This mixture included the expected cyclopentane (**2b** and **2c**) in addition to a bicyclic seven-membered ring (**3b** and **3c**). Furthermore, when R was large (e.g., R = *t*-Bu (**1d**) or TMS (**1e**), entries 4 and 5), isomerized seven-membered rings (**4d** and **4e**) were the sole products and were obtained in good yields.

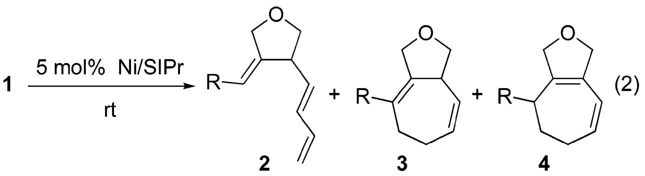
**Table 1.** Ni-Catalyzed Rearrangement of Cyclopropylen-yne **1**[a]



| entry | L | Ni:L | time (h) | % conv. of **1a**[b] | % **2a**[b] |
|---|---|---|---|---|---|
| 1 | none | n/a | 12 | 0 | 0 |
| 2 | $PPh_3$ | 1:1 | 12 | 23 | 0 |
| 3 | $PCy_3$ | 1:1 | 12 | 100 | 0 |
| 4 | P*t*$Bu_3$ | 1:1 | 12 | 100 | 0 |
| 5 | ICy | 1:1 | 2 | 0 | 0 |
| 6 | IAd | 1:1 | 2 | 73 | 65 |
| 7 | IMes | 1:1 | 2 | 100 | 72 |
| 8 | I*t*Bu | 1:1 | 0.5 | 88 | 86 |
| 9 | I*t*Bu | 1:1 | 2 | 100 | 89 |
| 10 | IPr | 1:1 | 0.5 | 100 | 76 |
| 11 | IPr | 1:1 | 2 | 100 | 84 |
| 12 | SIPr | 1:1 | 0.5 | 100 | 89 |
| 13 | SIPr | 1:1 | 2 | 100 | 91 |
| 14 | SIPr | 1:2 | 0.5 | 100 | 86 |
| 15 | SIPr | 1:3 | 0.5 | 100 | 89 |

[a] Reaction conditions: 5 mol % $Ni(COD)_2$, toluene, room temperature. [b] Determined by GC using naphthalene as an internal standard.

**Table 2.** Product Distribution in the Ni-Catalyzed Rearrangement of **1**[a]



| entry | substrate | **2**:**3**:**4**[b] | % yield[c] |
|---|---|---|---|
| 1 | R = Me (**1a**) | 1:0:0 | 54% (**2a**) |
| 2 | R = Et (**1b**) | 3:2:0 | 34% (**2b**)<br>27% (**3b**) |
| 3 | R = *i*-Pr (**1c**) | 1:2:0 | 28% (**2c**)<br>38% (**3c**) |
| 4 | R = *t*-Bu (**1d**) | 0:0:1 | 82% (**4d**) |
| 5 | R = TMS (**1e**) | 0:0:1 | 88% (**4e**) |

[a] Reaction conditions: 5 mol % $Ni(COD)_2$, 5 mol % SIPr, toluene, ambient temperature. [b] Determined by GC using naphthalene as an internal standard. [c] Isolated yield (average of two runs).

A mechanism that diverges at a common intermediate and may account for the product distributions is shown in Scheme 1.[6] Reaction between the Ni catalyst and cyclopropylen-yne **1** would ultimately afford eight-membered intermediate **6**.[7,8] $\beta$-Hydride elimination and reductive elimination would afford cyclopentane product **2**. In contrast, if both the ligand and R are large, $\beta$-hydride would be inhibited and direct reductive elimination would yield seven-membered ring **3**. Product **4** would arise from further isomerization of **3**.[9]

Gratifyingly, we discovered the cyclopentane product (**2**) can be prepared *selectively* from cyclopropylen-yne substrates, regardless of substituent size (e.g., R), when I*t*Bu[10] was employed (eq 3). As shown in Table 3, cyclopentene products (**2a**−**d**, entries 1−4) were formed exclusively under mild conditions. As expected, the Ni/NHC catalyst system tolerated both amino (**8**) and ester (**10**)

10.1021/ja043253r CCC: $30.25 © 2005 American Chemical Society

***Scheme 1.*** Proposed Mechanism for the Rearrangement of **1**

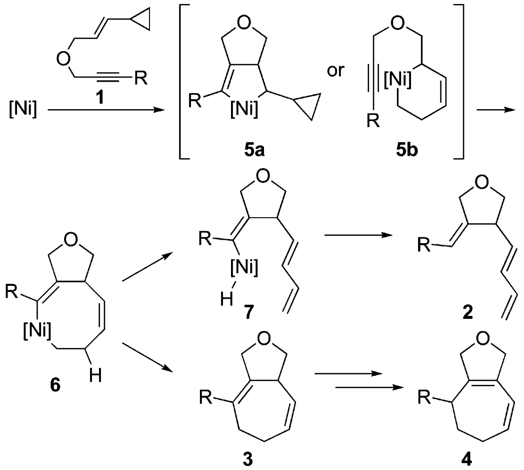
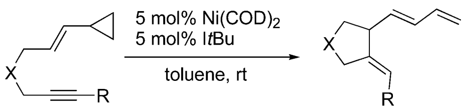
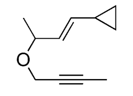
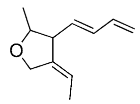
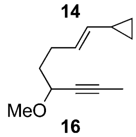
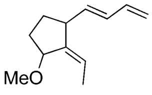
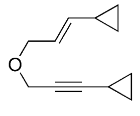
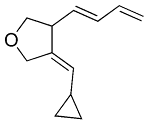


***Table 3.*** Selective Formation of Cyclopentanes[a]



(3)

| Entry | Cyclopropylen-yne | Product | % Yield[b] |
|---|---|---|---|
| 1 | X=O, R=Me (**1a**) | **2a** | 54% |
| 2 | X=O, R=Et (**1b**) | **2b** | 52% |
| 3 | X=O, R=*i*-Pr (**1c**) | **2c** | 65% |
| 4 | X=O, R=*t*-Bu (**1d**) | **2d** | 79% |
| 5 | X=C(CO$_2$Me)$_2$, R=Me (**8**) | **9** | 71%[c] |
| 6 | X=NTs, R=Me (**10**) | **11** | 86%[c] |
| 7 | X=O, R=CH$_2$OMe (**12**) | **13** | 64% |
| 8 |  **14** |  **15** | 61% |
| 9 |  **16** |  **17** | 55%[c,d] |
| 10 |  **18** |  **19** | 61% |

[a] Reaction conditions: 5 mol % Ni(COD)$_2$, 5 mol % I*t*Bu, toluene, room temperature. [b] Isolated yields (average of two runs). [c] SIPr was used as the ligand instead of I*t*Bu. [d] Reaction was run at 40 °C.

functionality (entries 5 and 6). Furthermore, internal substitution did not effect the rearrangement (entries 8 and 9). Interestingly, rearrangement of **18** afforded a tetrahydrofuran product (**19**) possessing a VCP moiety that resisted further isomerization to a spirocyclopentane (entry 10).[11]

We have discovered a variety of conditions based on Ni/NHC systems for the rearrangement of cyclopropylen-ynes to afford cyclopentane- and cycloheptene-based heterocycles. However, the use of I*t*Bu led to the selective formation of the cyclopentane products. Investigations focused on developing protocols for selective cycloheptene formation and understanding the mechanistic details of the rearrangements are currently underway.

**Acknowledgment.** We gratefully acknowledge the University of Utah, ACS (PRF Type G), and the NSF (Career Award) for support of this research.

**Supporting Information Available:** Detailed experimental procedures and compound characterization data are available (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

## References

(1) (a) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (b) López, F.; Delgado, A.; Rodríguez, J. R.; Castedo, L.; Mascareñas, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 10262. (c) Cadran, N.; Cariou, K.; Hervé, G.; Aubert, C.; Fensterbank, L.; Malacria, M.; Marco-Contelles, J. *J. Am. Chem. Soc.* **2004**, *126*, 3408. (d) Ni, Y.; Montgomery, J. *J. Am. Chem. Soc.* **2004**, *126*, 11162. (e) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813. (f) Trost, B. M.; Toste, F. D.; Pinkerton, A. B. *Chem. Rev.* **2001**, *101*, 2067. (g) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49.

(2) (a) Zuo, G.; Louie, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 2277. In contrast, the Ir-catalyzed cyclization of cyclopropylen-ynes provides 1,3-dienes with the cyclopropyl ring intact. See: (b) Chatani, N.; Inoue, H.; Morimoto, T.; Muto, T.; Murai, S. *J. Org. Chem.* **2001**, *66*, 4433.

(3) For Rh, see: (a) Wender, P. A.; Barzilay, C. M.; Dyckman, A. J. *J. Am. Chem. Soc.* **2001**, *123*, 179. (b) Wender, P. A.; Sperandio, D. A. *J. Org. Chem.* **1998**, *63*, 4164. (c) Binger, P.; Wedermeann, P.; Kozhushkov, S. I.; de Meijere, A. *Eur. J. Org. Chem.* **1998**, *113*, 3. (d) Wender, P. A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc.* **1995**, *117*, 4720. For Ru, see: (e) Trost, B. M.; Toste, F. D.; Shen, H. *J. Am. Chem. Soc.* **2000**, *122*, 2379.

(4) For leading reviews on NHCs, see: (a) Arduengo, A. J., III. *Acc. Chem. Res.* **1999**, *32*, 913. (b) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290. (c) Bourissou, D.; Guerret, O.; Gabbaï, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39. [ICy = 1,3-dicyclohexylimidazol-2-ylidene; IAd = 1,3-diadamantylimidazol-2-ylidene; I*t*Bu = 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-dihydroimidazolin-2-ylidene.]

(5) Pinke, P. A.; Stauffer, R. D.; Miller, R. G. *J. Am. Chem. Soc.* **1974**, *96*, 4229.

(6) Rearrangements proceeded smoothly in the presence of a variety of radical traps (e.g., 2,6-di-*tert*-butyl-4-methylphenol, 1,4-cyclohexadiene, phenyl disulfide, glavinoxyl).

(7) It is unclear at this time whether **6** would result from **5a** or **5b**. A variety of Ni compounds are known to catalyze cycloaddition reactions of enynes via initial oxidative coupling between an alkene and alkyne (see ref 8). Thus, a similar pathway could led to the formation of **6** via intermediate **5a**. Indeed, a similar mechanism has been proposed for analogous Rh- and Ru-catalyzed chemistry (see ref 3). However, we recently discovered that the Ni/NHC catalyst system mediates the isomerization of VCPs. Consequently, **6** may be derived from the initial isomerization of the VCP (**5b**) and subsequent insertion of the alkyne (see ref 2a).

(8) (a) Zhang, M.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 4498. (b) Wender, P. A.; Smith, T. E. *J. Org. Chem.* **1995**, *60*, 2962. (c) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 1286.

(9) It is possible that isomerization to form **4** occurs via the generation of a Ni−H complex (see ref 5). Indeed, the addition of catalytic amounts of HBF$_4$ (10 mol %) to Ni/I*t*Bu-catalyzed reactions of **1d** led to complete conversion and formation of **4d**. We are currently investigating the isomerization mechanism.

(10) Dorta, R.; Stevens, E. D.; Scott, N. M.; Costabile, C.; Cavallo, L.; Hoff, C. D.; Nolan, S. P. *J. Am. Chem. Soc.* **2005**, *127*, 2485.

(11) When Ni/SIPr was used as the catalyst, further isomerization occurred to give a mixture of products. As shown in Table 1, Ni/I*t*Bu is a less active catalyst system than Ni/SIPr, which allows for the selective formation of **19**.

JA043253R