Pergamon

Tetrahedron Letters, Vol. 38, No. 44, pp. 7687-7690, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10006-5

Group VI Metal-Promoted *Endo*-Azacyclizations via Alkyne-Derived Metal Vinylidene Carbenes

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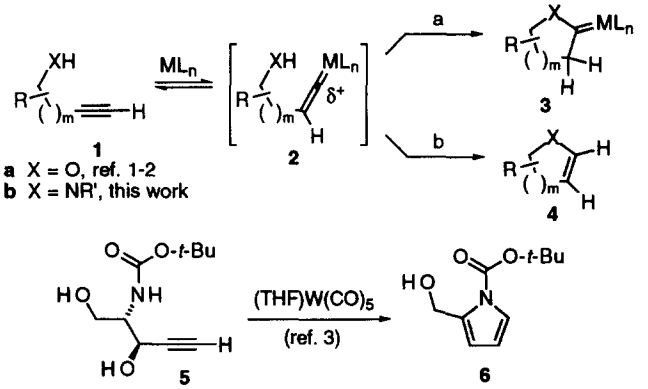
Abstract: The molybdenum-promoted cycloisomerization of terminal alkynes tethered to nitrogen nucleophiles is described. Reaction of *N*-carbamoyl alkynylamines with $(Et_3N)Mo(CO)_5$ affords cyclic enecarbamates. Similarly, cyclization of 2-ethynylaniline gives the isomeric indole heterocycle, although *N*-3-butynylaniline affords the cyclic metal azacarbene product. © 1997 Elsevier Science Ltd.

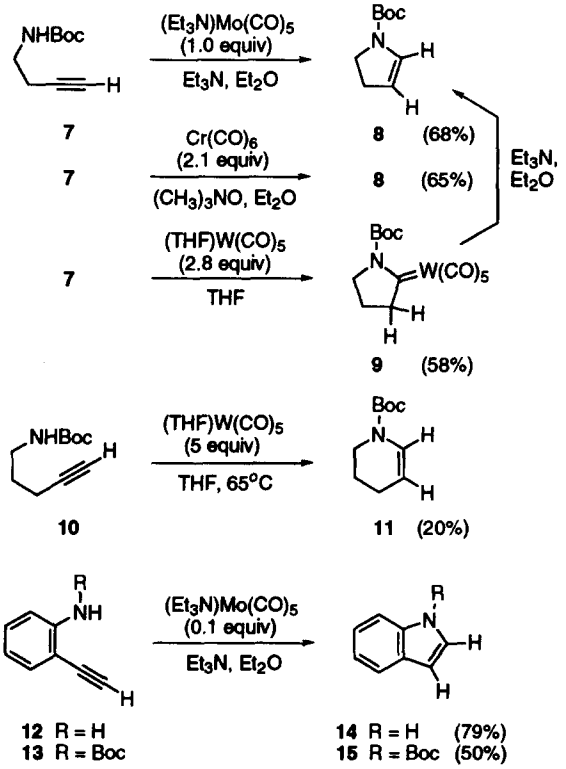
The reaction of terminal alkynes with many transition-metal complexes facilitates rearrangement to vinylidene carbene complexes. In alkyne substrates bearing hydroxyl groups (**1a**), the electrophilic sp-hybridized carbon atom of the vinylidene carbene intermediate **2a** undergoes nucleophilic addition of the oxygen atom (Scheme 1). The products of metal-promoted alkynol cyclizations are generally the stoichiometric oxacarbenes **3a** (path a),[1] although several years ago we discovered that (triethylamine)molybdenum pentacarbonyl induces a unique synthetic transformation to the cycloisomeric enol ethers **4a** (path b).[2] We are also interested in extending these cyclization reactions to the preparation of nitrogen heterocycles. Our recent inadvertent observation of pyrrole product **6** from the reaction of the *N*-carbamoyl-substituted alkynyldiol **5** with (tetrahydrofuran)tungsten pentacarbonyl[3] motivated studies of the extension of cycloisomerization reactions to carbamate-protected nitrogen nucleophiles (X = NCO_2R).[4]

Scheme 1. Pathways for cyclizations via metal vinylidene complexes

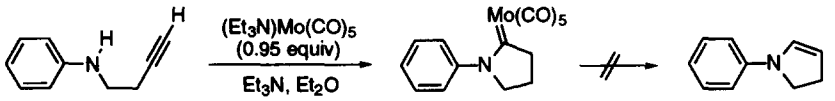


Our initial explorations on the reactions of *N*-(phenylmethyl)-3-butyn-1-amine[5] with Cr, Mo, and W carbonyl reagents gave a disappointingly complex mixture of products, whereas the *N*-(acetamido) and *N*-(*p*-toluenesulfonamido) analogs were inert to these reaction conditions.[6] However, *N*-(*t*-butoxycarbonyl)-3-butyn-1-amine (**7**)[7] exhibited the appropriate balance of nucleophilicity vs. basicity apparently required for successful cyclization with (triethylamine)molybdenum pentacarbonyl,[8] affording the cycloisomeric enecarbamate **8**[9] (Scheme 2). Cycloisomerization of **7** into the cyclic enecarbamate product **8** could also be accomplished by reaction with chromium hexacarbonyl / trimethylamine *N*-oxide (*in situ* formation of trimethylamine-chromium pentacarbonyl).[10] In contrast, the azacarbene product **9**[11,12] was obtained upon reaction with (tetrahydrofuran)-tungsten pentacarbonyl,[13] but this carbene was readily converted into enecarbamate **7** upon reaction with triethylamine. The homologous substrate **10** did not react with chromium or molybdenum pentacarbonyl reagents, but reaction with $(THF)W(CO)_5$ gave a modest yield of six-membered ring enecarbamate **11**. The 2-alkynylanilines **12** and **13**[14] also underwent facile cycloisomerization to give the corresponding indole products **14** and **15**. The high-yield cycloisomerization of **12** could be accomplished with catalytic quantities of the metal carbonyl reagent, whereas cyclizations of the aliphatic aminoalkyne substrates **7** and **10** require more equivalents of metal carbonyl reagent to obtain good yields of cyclic products. Apparently this indole synthesis is favored not only by the thermodynamic stability of the aromatic product, but also by the reduced basicity of the aniline precursor **12** relative to aliphatic amines.

Scheme 2. Cycloisomerizations of alkynylamines



However, the *N*-(3-butynyl)aniline **16**[15] underwent cyclization in the presence of one equivalent of triethylamine-molybdenum pentacarbonyl to afford only the azacarbene **17**[16] (40% yield + 55% recovered **16**), even in the presence of triethylamine. We have been unable to productively convert this carbene into a metal-free organic compound such as the corresponding enamine product **18**.



16 **17** **18**

Representative procedures for azacyclizations:

N-(*tert*-Butoxycarbonyl)-2-pyrroline (**8**): $Mo(CO)_6$ (0.5 mmol) was placed in a 18 x 150 mm borosilicate test tube; freshly distilled Et_3N (2 mL) and Et_2O (8 mL) were added and the contents dissolved by stirring. The reaction mixture was then photolyzed (350 nm, Rayonet photoreactor) for 20 min under N_2. The reaction vessel was removed from the light source, alkynyl carbamate (**7**, 0.5 mmol) was added and the reaction mixture was stirred for 20 h under N_2 at 20°C. Cyclic enecarbamate product **8** was isolated by evaporation of solvent followed by flash chromatography on silica gel (pentane / Et_2O / 2% Et_2NH). The product exhibited ^1H and ^{13}C NMR spectra which were identical to the literature.[9a]

N-(*tert*-Butoxycarbonyl)-2-tetrahydropyridine (**11**): $W(CO)_6$ (5 mmol) was placed in a 100 mL airfree reaction tube fitted with a reflux condenser and purged with N_2 for 1 h. Freshly distilled THF (25 mL) was added and the solid dissolved with stirring. The reaction mixture was then irradiated (350 nm, Rayonet photoreactor) for 2 h under N_2 with stirring. The reaction vessel was removed from the light source, alkynyl carbamate (**10**, 1.0 mmol) in THF (5 mL) was added, and the reaction mixture was stirred at room temperature for 20 h, followed by heating to reflux for two days. Enecarbamate (**11**) was isolated by evaporation of solvent under reduced pressure at 10°C followed by flash chromatography on silica gel (pentane / Et_20 / 2% Et_2NH). IR (free film from CH_2Cl_2) 2977, 2930, 2848, 1741, 1699, 1652, 1358, 1254, 1167, 1115, 1053, 994, 878, 768 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) [spectra indicated 1.5 : 1 mixture of amide rotamers] δ 6.83, 6.73 (1H, br m); 4.89, 4.87 (1H, br m), 3.53 (2H, br m), 2.02 (2H, br m), 1.82 (2H, m), 1.48 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.2, 125.7, 125.3, 105.7, 105. 3, 80.5, 42.6, 41.5, 21.8, 21.5; MS (70eV, LREI) 183, 127, 110, 83, 68, 57, 41; HRMS calcd for $C_{10}H_{17}NO_2$ 183.1259: found 183.1285.

Acknowledgment. This research was supported by the National Science Foundation (CHE-9501608). F.E.M. also acknowledges support from the Alfred P. Sloan Foundation, Lilly Research Laboratories, and the Camille and Henry Dreyfus Foundation. This paper is in memory of Timothy Fischer, whose enthusiasm and good nature will be greatly missed.

References and Notes

1. Reviews: (a) Chisholm, M. H.; Clark, H. C. *Acc. Chem. Res.* **1973**, *6*, 241. (b) Bruce, M. I.; Swincer, A. G. *Adv. Organomet. Chem.* **1983**, *22*, 59. (c) Bruce, M. I. *Chem. Rev.* **1991**, *91*, 197. For more recent examples of path a processes, see: (d) McDonald, F. E.; Bowman, J. L. *Tetrahedron Lett.* **1996**, *37*, 4675, and references therein.
2. McDonald, F. E.; Gleason, M. M. *J. Am. Chem. Soc.* **1996**, *118*, 6648, and references therein.
3. McDonald, F. E.; Zhu, H. Y. H. *Tetrahedron* **1997**, *53*, 11061.
4. Thia- and azacarbenes have been prepared by *inter*molecular addition of sulfur and nitrogen nucleophiles to cationic iron vinylidene carbenes. (a) Boland-Lussier, B. E.; Churchill, M. R.; Hughes, R. P.; Rheingold, A. L. *Organometallics* **1982**, *1*, 628. (b) Boland-Lussier, B. E.; Hughes, R. P. *Organometallics* **1982**, *1*, 635.
5. Arnold, H.; Overman, L. E.; Sharp, M. J.; Witschel, M. C. *Org. Synth.* **1992**, *70*, 111.
6. These experiments were conducted by Mr. Alexander Vazquez, Northwestern University, 1994.
7. Compound **7** was prepared by *t*-butoxycarbonylation of 3-butyn-1-amine: (a) Taylor, E. C.; Macor, J. L.; Pont, J. L. *Tetrahedron* **1987**, *43*, 5145. (b) Keller, O.; Keller, W. E.; van Look, G.; Wersin, G. *Org. Synth.* **1984**, *63*, 160.
8. McDonald, F. E.; Schultz, C. C. *J. Am. Chem. Soc.* **1994**, *116*, 9363.
9. Compound **8** was previously prepared by Rh or Pd-catalyzed isomerization of *N*-(*t*-butoxycarbonyl)-3-pyrroline: (a) Stille, J. K.; Becker, Y. *J. Org. Chem.* **1980**, *45*, 2139. (b) Sonesson, C.; Hallberg, A. *Tetrahedron Lett.* **1995**, *36*, 4505.
10. (a) Koelle, U. *J. Organomet. Chem.* **1977**, *133*, 53. (b) Maher, J. M.; Beatty, R. P.; Cooper, N. J. *Organometallics* **1985**, *4*, 1354.
11. Other syntheses of similar cyclic azacarbene compounds require strongly basic and pyrophoric reagents. Schwindt, M. A.; Lejon, T.; Hegedus, L. S. *Organometallics* **1990**, *9*, 2814.
12. Tungsten azacarbene (**9**): IR (free film from CH_2Cl_2) 2981, 2066, 1920, 1767, 1700, 1396, 1276, 1145, 910, 579 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.01 (2H, t, J = 7.7 Hz), 3.45 (2H, t, J = 7.7 Hz), 1.91 (2H, dd, J = 7.7, 7.7 Hz), 1.62 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.5, 198.1, 151.2, 86.3, 61.4, 58.5, 29.8, 27.7; MS (70eV, LREI) 495, 493, 492, 491, 467, 465, 464, 463, 409, 381, 353, 325, 296, 268, 240, 212, 184, 112, 57, 41; HRMS calcd for $C_{13}H_{15}O_6N^{182}W$ 463.0382: found 463.0398 (M^+ - CO).
13. (a) Arndt, L. W.; Bischoff, C. J.; Darensbourg, M. Y. *Inorg. Synth.* **1989**, *26*, 335. (b) Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 1154.
14. Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1989**, *30*, 2581.
15. Compound **16** was prepared by reaction of 3-butynyl-1-methanesulfonate with aniline.
16. Molybdenum azacarbene (**17**): IR (free film from CH_2Cl_2) 2987, 2883, 2060, 1948, 1599, 1514, 1455, 1300, 1073, 843, 759, 697, 592 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55 - 7.27 (5H, m), 4.09 (2H, t, J = 7.8 Hz), 3.59 (2H, t, J = 7.8 Hz), 2.10 (2H, quintet, J = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.4, 206.5, 145.0, 129.9, 129.2, 125.9, 65.2, 57.8, 21.8; MS (70eV, LREI) 383, 355, 299, 271, 243, 212, 184, 169, 145, 130, 104, 91, 77, 51, 39; HRMS calcd for $C_{15}H_{11}NO_5{}^{98}Mo$ 382.9697: found 382.9690.

(*Received in USA* 16 *July* 1997; *revised* 25 *August* 1997; *accepted* 26 *August* 1997)