DOI: 10.1002/adsc.200600404

Copper Salt-Catalyzed Azide-[3 + 2] Cycloadditions of Ynamides and Bis-Ynamides

Xuejun Zhang,[a] Hongyan Li,[a] Lingfeng You,[a] Yu Tang,[a] and Richard P. Hsung[a,*]

[a] Division of Pharmaceutical Sciences and Department of Chemistry, Rennebohm Hall, 777 Highland Avenue, University of Wisconsin, Madison, WI 53705, USA
Fax: (+1)-608-262-534; e-mail: rhsung@wisc.edu

Received: August 10, 2006; Accepted: September 19, 2006

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: A one-pot synthesis of amide-substituted triazoles from alkyl bromides and ynamides is described here along with syntheses of novel bis-ynamides and their applications in [3+2] cycloadditions with azides to construct unique bis-triazoles.

Keywords: azide-[3 + 2] cycloaddition; bis-triazoles; bis-ynamides; Cu(I) catalysis; triazoles; ynamides

Introduction

The versatility of 1,3-dipolar cycloadditions[1,2] in constructing synthetically and medicinally useful heterocycles[3] has led us to investigate [3+2] cycloadditions of ynamides.[4–8] Specifically, we have examined the classic Huisgen's azide-[3+2] cycloaddition[9–11] given its current resurgence facilitated by the "click" chemistry concept.[12] Recently, Cintrat[13] and we[14] independently communicated azide-[3 + 2] cycloadditions employing ynamides in a highly regioselective manner that favors 1,4-adducts (**1**+**2**→**3** in Figure 1). Particularly, we focused on developing tandem azidination- and hydroazidination-[3+2] cycloadditions of ynamides, leading to an array of amide-substituted triazoles.[14] We report here details of our work with copper salt-catalyzed azide-[3+2] cycloadditions of ynamides that feature a one-pot synthesis of triazoles from alkyl bromides and constructions of bis-triazoles from novel bis-ynamides.

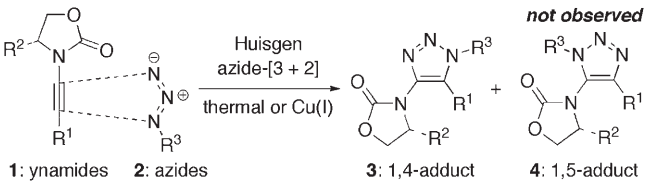
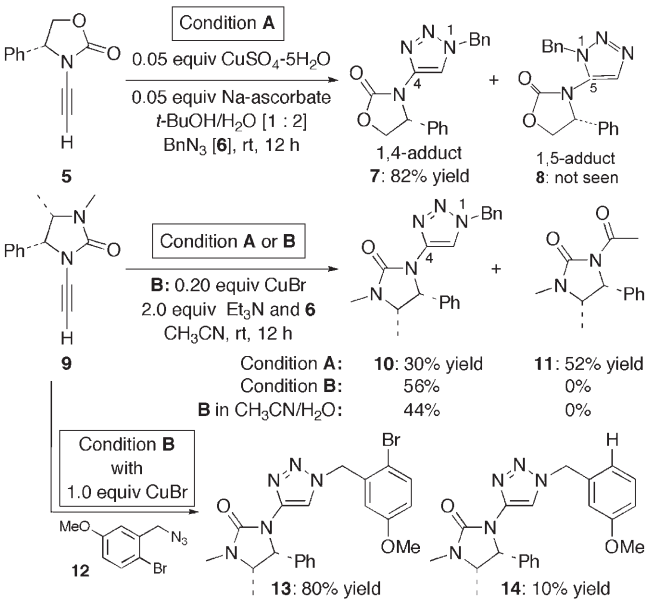


Figure 1. Ynamides in [3+2] cycloadditions.

Results and Discussions

Problems with the Competing Ynamide Hydrolysis

The feasibility of [3+2] cycloadditions of ynamides with organic azides could be readily established. As shown in Scheme 1, the $CuSO_4 \cdot 5\ H_2O$-catalyzed cycloaddition of terminal ynamide **5** with BnN_3 led to chiral amide-substituted triazole **7** in 82% yield as the



Scheme 1. Huisgen's azide-[3+2] cycloadditions of ynamides.

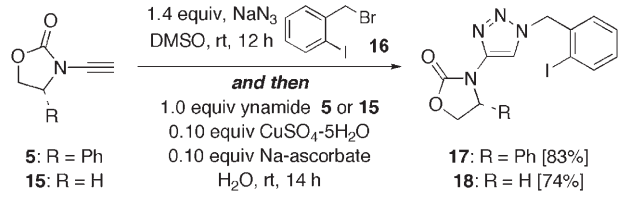
only regioisomer using Fokin–Sharpless conditions.[15] The catalytic sequence likely proceeds through a Cu(I) catalytic species generated via reduction of $CuSO_4$.[15] The high level of regioselectivity is likely a result of the copper catalysis and steric factors because of the large oxazolidinone motif.[15,16] However, there was an unresolved problem in our earlier work. When ynamides that are more prone to hydrolysis, such as **9**, were used the desired triazole **10** was obtained in only 30% yield with the hydrolysis product **11** being predominant.

To circumvent the hydrolysis problem, an improved protocol (Conditions B) was developed using 0.2 equivs. CuBr as the source of the Cu(I) catalyst along with anhydrous CH_3CN serving as the solvent and Et_3N as the base and ligand to improve the solubility of CuBr in CH_3CN. Under these new conditions, the yield of triazole **10** was improved to 56% without noticeable hydrolysis even when CH_3CN was not anhydrous, although the yield dropped to 44% (Scheme 1). The improvement was further visible in the reaction of ynamide **9** with azide **12**, which led to the desired triazole **13** in 80% yield along with intriguingly 10% of the debrominated product **14**, although 1.0 equiv. of CuBr was used. Under Conditions A, we could only observe a trace amount of **13** with hydrolysis of **9** being the major pathway.

Synthetic Scope of Organic Azides

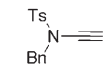
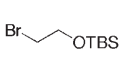
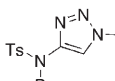
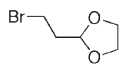
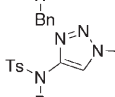
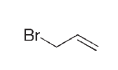
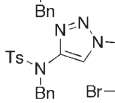
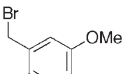
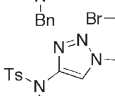
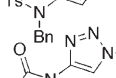
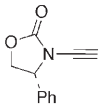
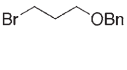
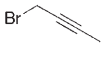
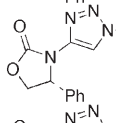
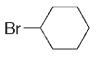
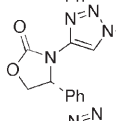
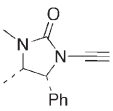
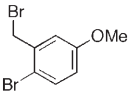
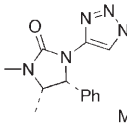
To expand the synthetic scope, we embarked on an exploration of other organic azides besides BnN_3. However, due to the difficulties in handling organic azides in general,[17] especially those with low molecular weights, we ultimately designed a one-pot syntheses of amide-substituted triazoles from alkyl bromides directly. As shown in Scheme 2, organic azides were generated *in situ* by reacting alkyl bromides with NaN_3 in DMSO solution,[18,19] and subsequently, copper salt, Na ascorbate, and terminal ynamides **5** and **15** were added without isolating the intermediate organic azides. Under this one-pot protocol, triazoles **17** and **18** were obtained in excellent yields from **5** and **15**, respectively.

The scope of this protocol was explored as shown in Table 1. In general, all primary bromides (entries 1–3, 5–7 and 10) afforded the respective triazoles in good yields, including allyl bromide (entry 3), propargyl bromide (entry 7), and benzyl bromide (entries 5 and 10). A secondary bromide (entry 8) gave slightly lower yield. Many functional groups such as silyl ether (entry 1), benzyl ether (entry 5), acetal (entry 2), aryl bromide (entries 5 and 10), alkene (entry 3), and internal alkyne (entry 7) could be tolerated.



Scheme 2. One-pot synthesis of triazoles from alkyl bromides.

Table 1. Scope of one-pot synthesis of triazoles from alkyl bromides.

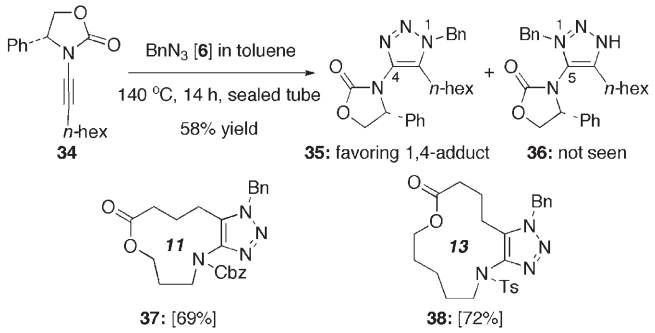
entry	ynamides		R-Br[a]		1,4-cycloadducts		yield [%][b]
1		19		20		27	70
2		19		21		28	78
3		19		22		29	67
4		19		23		30	10
5		19		23		30	80[c]
6		5		24		31	73
7		5		25		32	85
8		5		26		33	40
9		9		23		13	10
10		9		23		13	50[c]

[a] 1.4 equivs. of NaN_3, 1.3 equivs. of R-Br, DMSO, room temperature, 12 h, and then, 1.0 equiv of ynamide, 0.10 equiv of $CuSO_4 \cdot 5\ H_2O$, 0.10 equiv of Na ascorbate, H_2O, room temperature, 14 h.

[b] Isolated yields.

[c] 1.4 equivs. of NaN_3, DMSO, room temperature, 12 h, 1.3 equivs. of R-Br, and then 1.0 equivs. of ynamide, 0.20 equivs. of CuBr, 2.0 equivs. of Et_3N, CH_3CN, room temperature, 12 h.

It is noteworthy that to avoid competing hydrolysis of ynamides during the cycloaddition, when using ynamide **9**, the desired triazole **13** could be again obtained in 52% yield through the usage of new conditions [see Note c] related to Conditions B illustrated in Scheme 1 for the cycloaddition (entry 10). In addition, we found that sulfonyl-substituted ynamides such as **19** can also be problematic in terms of hydrolysis. Thus, when applicable, the cycloaddition of **19**

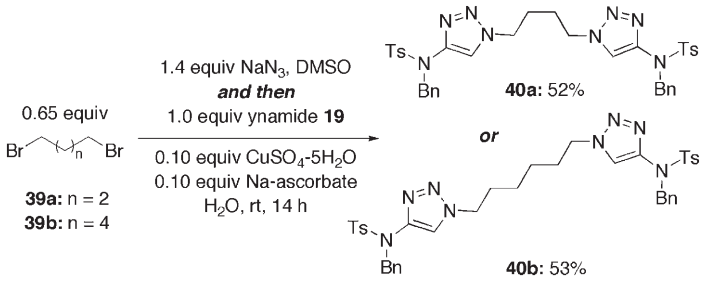


Scheme 3. Fused triazoles employing macrocyclic ynamides.

with the azide derived from bromide **23** could also be improved to 80% (entry 4 versus 5).

Syntheses of Uniquely Fused Triazoles

In our previous communication,[14] we had demonstrated that the Huisgen azide-[3 + 2] cycloaddition of internal ynamides was also feasible under thermal condition. As shown in Scheme 3, *n*-hexyl-substituted internal ynamide **34** could react with BnN_3 at 140 °C in toluene to give 1,4-disubstituted triazole **35** in 58% yield with no observable 1,5-adduct **36**.



Scheme 4. One-pot syntheses of bistriazoles from dibromides.

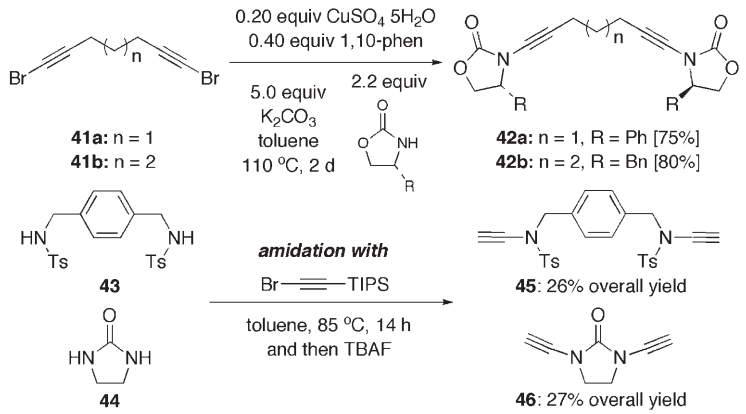
Based on this precedent, we examined cycloadditions of macrocyclic ynamides, which could be prepared through a Cu(I)-catalyzed intramolecular coupling of amides tethered to alkynyl bromides that we had reported recently.[20] As a result, novel macrocyclic fused triazoles **37** and **38** were successfully isolated in good yields when their respective macrocyclic ynamides were heated with BnN_3 at 140 °C in toluene in a sealed tube.

Novel Bis-Triazoles and Bis-Ynamides

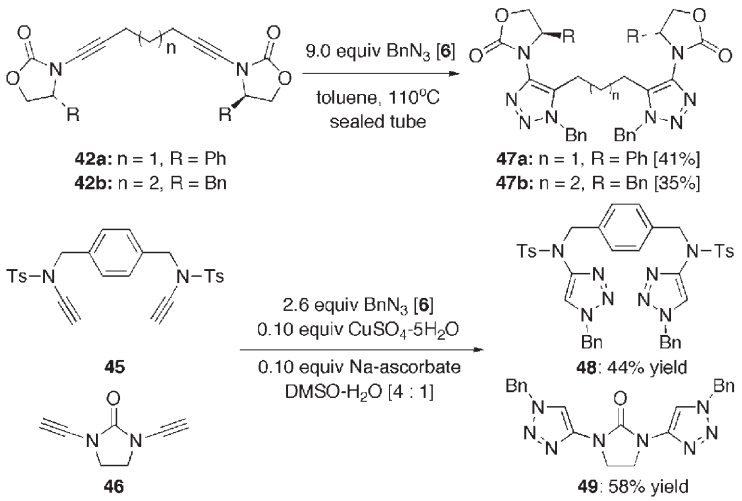
With azide-[3+2] cycloadditions of ynamide firmly established, we examined two potential approaches for achieving double cycloadditions to construct novel bis-triazoles. Two bis-triazoles could be quickly assembled in one-pot with good yields by reacting ynamide **19** with di-azides generated *in situ* from dibromides **39a** and **39b** and NaN_3, thereby providing the feasibility of the first approach (Scheme 4).

To explore the scope of the bis-triazole synthesis, we achieved the synthesis of novel bis-ynamides **42a** and **42b** by coupling the respective dialkynyl bromides **41a** and **41b** with Evans auxiliaries in good yields (Scheme 5). Another approach to the bis-ynamide synthesis was the coupling of bis-amides with monoalkynyl bromide, which was demonstrated in Scheme 5. We successfully synthesized two terminal bis-ynamides **45** and **46** in reasonable overall yields through a two-step sequence: 1) coupling of TIPS substituted alkynyl bromide with bi-sulfonamide **43** or urethane **44**, and 2) the removal of the TIPS group using TBAF. Although bis-ynamides **42a**, **42b, 45** and **46** are structurally novel, Diederich[7r] had prepared some related ynamides.

With these bis-ynamides in hand, we examined the second approach to bis-triazoles (Scheme 6). Thermally driven [3 + 2] cycloadditions of internal bis-ynamides **42a** and **42b** with BnN_3 succeeded in giving bis-triazoles **47a** and **47b** in moderate yields, while the



Scheme 5. Preparations of novel bis-ynamides.



Scheme 6. Syntheses of bis-triazoles from bis-ynamides.

Fokin–Sharpless copper salt-catalyzed cycloadditions of terminal bis-ynamides **45** and **46** proceeded well to afford bis-triazoles **48** and **49**, respectively, in good yields.

Conclusions

We have described here a one-pot regioselective synthesis of amide-substituted triazoles from alkyl bromides and ynamides, and the synthesis of novel bis-ynamides and their applications to synthesize unique bis-triazoles.

Experimental Section

Triazole 7a with Conditions A

To a vial charged with ynamide **5** (50.0 mg, 0.267 mmol) were added $CuSO_4 \cdot 5\,H_2O$ (3.3 mg, 0.0134 mmol, 0.050 equivs.), Na ascorbate (2.70 mg, 0.0134 mmol, 0.050 equivs.), benzyl azide (37.0 μL, 0.294 mmol, 1.10 equivs.), and *tert*-butyl alcohol (0.5 mL). The mixture was stirred at room temperature for 2 min before H_2O (1 mL) was added. The reaction mixture was then vigorously stirred at room temperature for 12 h under nitrogen. After TLC showed that ynamide **5** was all consumed, the reaction mixture was diluted with H_2O (8 mL) and extracted with EtOAc (3×10 mL). The combined organic layers were washed with saturated aqueous NaCl and dried over Na_2SO_4. Removal of solvent under reduced pressure gave crude triazole **7a**, which was purified *via* silica gel flash column chromatography with EtOAc/hexane as gradient eluent to yield the pure triazole **7a** as a white solid; yield: 70.0 mg (82%).

Triazole 10 with Conditions B

To a vial charged with ynamide **9** (15.0 mg, 0.070 mmol) were added CuBr (1.8 mg, 0.0035 mmol, 0.20 equivs.), BnN_3 (13.0 μL, 0.098 mmol, 1.40 equivs.), 19.5 μL Et_3N (0.14 mmol, 14.1 mg, 2.0 equivs.) and CH_3CN (1 mL). The reaction mixture was then vigorously stirred at room temperature for 12 h under nitrogen. After TLC showed that ynamide **9** was all consumed, the reaction mixture was diluted with H_2O (4 mL) and extracted with EtOAc (3×5 mL). The combined organic layers were washed with saturated aqueous NaCl and dried over Na_2SO_4. Removal of solvent under reduced pressure gave crude triazole **10**, which was purified *via* silica gel flash column chromatography with EtOAc/hexane as gradient eluent to yield the pure triazole **10** as a white solid; yield: 12.6 mg (56%).

General Procedure for Triazoles in Table 1

A stock solution of 0.5 M NaN_3 in DMSO was prepared by stirring at room temperature for 3 h. To a vial charged with 1.40 equivs. of 0.5 M NaN_3 in DMSO solution was added 1.30 equivs. of an alkyl bromide. After the mixture had been stirred for 12 h, and TLC showed that alkyl bromide was all consumed, H_2O (1/5 the total volume of DMSO used above) was added followed by 1.00 equiv. of the corresponding ynamide, 0.10 equiv. of $CuSO_4 \cdot 5\,H_2O$ and 0.10 equiv. of sodium ascorbate. After TLC showed the starting ynamide was all consumed, the reaction mixture was poured into dilute aqueous NH_4OH, and then extracted by EtOAc (3× equal volumes). The combined organic layers were washed with saturated aqueous NaCl and dried over Na_2SO_4. Removal of solvent under reduced pressure gave crude triazole, which was purified *via* silica gel column flash chromatography with EtOAc/hexane as gradient eluent.

Thermal Cycloadditions

To a sealed tube charged with an ynamide (1.00 equiv.) in toluene solution was added BnN_3 (1.30 equivs.). The reaction mixture was heated at 140 °C for 14 h. Removal of toluene under reduced pressure gave the crude triazole, which was purified *via* silica gel flash column chromatography with

using EtOAc/hexane as gradient eluent to yield the pure triazole.

Charcterization data for triazoles and bis-triazoles prepared can be found in the Supporting Information.

Acknowledgements

The authors thank NIH-NIGMS [GM066055], UW-Madison, and the UW-Cancer Center for financial support.

References

[1] For general reviews, see: a) I. Coldham, R. Hufton, *Chem. Rev.* **2005**, *105*, 2765; b) K. Rueck-Braun, T. H. E. Freysoldt, F. Wierschem, *Chem. Soc. Rev.* **2005**, *34*, 507; c) A. I. Kotyatkina, V. N. Zhabinsky, V. A. Khripach, *Russ. Chem. Rev.* **2005**, *34*, 507; d) M. Harmata, P. Rashatasakhon, *Tetrahedron* **2003**, *59*, 2371; e) H. M. L. Davies, in: *Advances in Cycloaddition*, (Ed.: M. Harmata), JAI Press, Greenwich, **1998**, Vol. 5, pp. 119–164; f) K. V. Gothelf, K. A. Jørgensen, *Chem. Rev.* **1998**, *98*, 863; g) F. G. West, in: *Advances in Cycloaddition*, (Ed.: M. Lautens), JAI Press, Greenwich, **1997**, Vol. 4, p. 1; h) J. H. Rigby, F. C. Pigge, *Org. React.* **1997**, *51*, 351; i) A. Padwa, in: *Comprehensive Organic Synthesis* (Ed.: B. M. Trost), Pergamon Press, Oxford, **1991**, Vol. 4, pp. 1069–1109.

[2] For related reviews, see: a) J. A. Varela, C. Saá, *Chem. Rev.* **2003**, *103*, 3787; b) M. Rubin, A. W. Sromek, V. Gervorgyan, *Synlett* **2003**, 2265; c) C. Aubert, O. Buisine, M. Malacria, *Chem. Rev.* **2002**, *102*, 813; d) S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901.

[3] For a review, see: W.-Q. Fan, A. R. Katritzky, in: *Comprehensive Heterocyclic Chemistry*, (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon Press, Oxford, **1996**, Vol. 4, pp. 101–126.

[4] For reviews on ynamides, see: a) C. A. Zificsak, J. A. Mulder, R. P. Hsung, C. Rameshkumar, L.-L. Wei, *Tetrahedron* **2001**, *57*, 7575; b) J. A. Mulder, K. C. M. Kurtz, R. P. Hsung, *Synlett* **2003**, 1379; c) A. R. Katritzky, R. Jiang, S. K. Singh, *Heterocycles* **2004**, *63*, 1455; d) M. R. Tracey, R. P. Hsung, J. Antoline, K. C. M. Kurtz, L. Shen, B. W. Slafer, Y. Zhang, in: *Science of Synthesis Houben-Weyl Methods of Molecular Transformations*, (Ed.: S. M. Weinreb), Georg Thieme Verlag, Stuttgart, Chapter 21.4, **2005**.

[5] For the synthesis of ynamides, see: a) M. O. Frederick, J. A. Mulder, M. R. Tracey, R. P. Hsung, J. Huang, K. C. M. Kurtz, L. Shen, C. J. Douglas, *J. Am. Chem. Soc.* **2003**, *125*, 2368; b) Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, *Org. Lett.* **2004**, *6*, 1151; see also: c) J. R. Dunetz, R. L. Danheiser, *Org. Lett.* **2003**, *5*, 4011; d) S. Couty, M. Barbazanges, C. Meyer, J. Cossy, *Synlett* **2005**, 906.

[6] For a special issue dedicated to the chemistry of ynamides, see: *Tetrahedron-Symposium-In-Print:* "Chemistry of Electron-Deficient Ynamines and Ynamides." *Tetrahedron* **2006**, *62*, Issue No. 16.

[7] For recent reports on ynamides in the last three years, see: a) J. R. Dunetz, R. L. Danheiser, *J. Am. Chem. Soc.* **2005**, *127*, 5776; b) N. Riddell, K. Villeneuve, W. Tam, *Org. Lett.* **2005**, *7*, 3681; c) Y. Zhang, *Tetrahedron Lett.* **2005**, *46*, 6483; d) M. F. Martinez-Esperon, D. Rodriguez, L. Castedo, C. Saá, *Org. Lett.* **2005**, *7*, 2213; e) M. Bendikov, H. M. Duong, E. Bolanos, F. Wudl, *Org. Lett.* **2005**, *7*, 783; f) F. Marion, J. Coulomb, C. Courillon, L. Fensterbank, M. Malacria, *Org. Lett.* **2004**, *6*, 1509; g) M. Rosillo, G. Domínguez, L. Casarrubios, U. Amador, J. Pérez-Castells, *J. Org. Chem.* **2004**, *69*, 2084; h) S. Couty, B. Liégault, C. Meyer, J. Cossy, *Org. Lett.* **2004**, *6*, 2511; i) D. Rodríguez, L. Castedo, C. Saá. *Synlett* **2004**, 783; j) D. Rodríguez, L. Castedo, C. Saá, *Synlett* **2004**, 377; k) S. Hirano, R. Tanaka, H. Urabe, F. Sato, *Org. Lett.* **2004**, *6*, 727; l) M. Klein, B. König, *Tetrahedron* **2004**, *60*, 1087; m) F. Marion, C. Courillon, M. Malacria, *Org. Lett.* **2003**, *5*, 5095; n) B. Witulski, C. Alayrac, L. Tevzaadze-Saeftel, *Angew. Chem. Int. Ed.* **2003**, *42*, 4257; o) R. Tanaka, S. Hirano, H. Urabe, F. Sato, *Org. Lett.* **2003**, *5*, 67; p) B. Witulski, J. Lumtscher, U. Bergsträber, *Synlett* **2003**, 708; q) S. Naud, J.-C. Cintrat, *Synthesis* **2003**, 1391; r) F. Denonne, P. Paul Seiler, F. Diederich, *Helv. Chim. Acta* **2003**, *86*, 3096; s) see ref.[4] for chemistry before 2003.

[8] For our work on ynamides since 2003, see: a) K. C. M. Kurtz, R. P. Hsung, Y. Zhang, *Org. Lett.* **2006**, *8*, 231; b) K. C. M. Kurtz, M. O. Frederick, J. A. Mulder, R. P. Hsung, *Tetrahedron* **2006**, *62*, 3928; c) Y. Zhang, R. P. Hsung, X. Zhang, J. Huang, B. W. Slafer, A. Davis, *Org. Lett.* **2005**, 7, 1047; d) M. R. Tracey, Y. Zhang, M. O. Frederick, J. A. Mulder, R. P. Hsung, *Org. Lett.* **2004**, *6*, 2209; e) L. Shen, R. P. Hsung, *Tetrahedron Lett.* **2003**, *44*, 9353; f) M. O. Frederick, R. P. Hsung, R. H. Lambeth, J. A. Mulder, M. R. Tracey, *Org. Lett.* **2003**, *5*, 2663; g) J. A. Mulder, K. C. M. Kurtz, R. P. Hsung, H. A. Coverdale, M. O. Frederick, L. Shen, C. A. Zificsak, *Org. Lett.* **2003**, *5*, 1547.

[9] a) R. Huisgen, *Angew Chem.* **1963**, *75*, 604; b) R. Huisgen, G. Szeimies, L. Moebiu, *Chem. Ber.* **1967**, *100*, 2494; c) R. Huisgen, in: *1,3-Dipolar Cycloaddition Chemistry*, (Ed.: A. Padwa), Pergamon Press, Oxford, **1984**, pp. 1–176.

[10] For recent reviews on azide-alkyne cycloadditions, see: a) V. D. Bock, H. Hiemstra, J. H. Van Maarseveen, *Eur. J. Org. Chem.* **2006**, 51; b) A. R. Katritzky, Y. Zhang, S. K. Singh, *Heterocycles.* **2003**, *60*, 1225; c) S. T. Abu-Orabi, *Molecule.* **2002**, *7*, 302; d) H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 2004.

[11] For reviews on chemistry of organic azides, see: a) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.* **2005**. *44*, 5188; b) C.-K. Sha, A. K. Mohanakrishnan, *Chemistry of Heterocyclic Compounds,* (Eds.: A. Padwa, W. H. Pearson), John Wiley, New York, **2002**, *Vol. 59*, Chapter 9, pp. 623–679.

[12] For some recent examples, see: a) V. D. Bock, R. Perciaccante, T. P. Jansen, H. Hiemstra, J. H. van Maarseveen, *Org. Lett.* **2006**, 919; b) F. Francesca Pagliai, T. Pirali, E. D. Grosso, R. D. Brisco, G. C. Tron, G. Sorba, A. A. Genazzani, *J. Med. Chem.* **2006**, *49*, 467; c) V. O. Rodionov, V. V. Fokin, M. G. Finn, *Angew. Chem. Int.*

Ed. **2005**, *44*, 2210; d) L. Zhang, X. Chen, P. Xue, H. H. Y. Sun, I. D. Williams, K. B. Sharpless, V. V. Fokin, G. Jia, *J. Am .Chem. Soc.,* **2005**, *127*, 15998; e) F. Himo, T. Lovell, R. Higraf, V. V. Rostovstsev, L. Noodleman, K. B. Sharpless, V. V. Fokin, *J. Am. Chem. Soc* . **2005**, *127*, 210; f) J. F. Billing, U. Nilsson, *J. Org. Chem.* **2005**, *70*, 4847; g) V. Gracias, D. Darczak, A. F. Gasiecki, S. W. Djuric, *Tetrahedron. Lett.* **2005**, *46*, 9053; h) H. Yanai, T. Taguchi, *Tetrahedron. Lett.* **2005**, *46*, 8639; i) C. Chowdhury, S. B. Mandal, B. Achari, *Tetrahedron. Lett.* **2005**, *46*, 8531; j) Y. Angell, K. Burgess, *J. Org. Chem.* **2005**, *70*, 9595.

[13] M. IJsselstijin, J.-C. Cintrat, *Tetrahedron* **2006**, *62*, 3837.

[14] X. Zhang, R. P. Hsung, L. You, *Organic Biomol. Chem.* 2006, 4, 2679.

[15] a) V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596; b) P. Wu, A. K. Feldman, A. K. Nugent, C. J. Hawker, A. Scheel, B. Voit, J. Pyun, J. M. J. Frechet, K. B. Sharpless, V. V. Fokin, *Angew. Chem. Int. Ed.* **2004**, *43*, 3928; c) Q. Wang, T. R. Chan, R. Hilgraf, K. B. Sharpless, V. V. Fokin, *J. Am. Chem. Soc.* **2003**, *125*, 3192; d) A. K. Feldman, B. Colasson, V. V. Fokin, *Org. Lett.* **2004**, *6*, 3897.

[16] a) D. J. Hlasta, J. A. Ackerman, *J. Org. Chem.* **1994**, 59, 6184; b) S. J. Howell, N. Spencer, D. Philp, *Tetrahedron* **2001**, 57, 4945; c) J. Chen, J. Rebek, Jr., *Org. Lett.* **2002**, 4, 327.

[17] E. F. V. Scriven, K. Turnbull, *Chem. Rev.* **1988**, *88*, 297.

[18] S. G. Alvarez, M. T. Alvarez, *Synthesis* **1997**, 413.

[19] K. Kacprzak, *Synlett* **2005**, 943.

[20] X. Zhang, Y. Zhang, J. Huang, R. P. Hsung, K. C. M. Kurtz, J. Oppenheimer, M. E. Petersen, I. K. Sagamanova, M. R. Tracey, *J. Org. Chem.* **2006**. *71*, 4170.

