Dalton Transactions

Dimerization of Terminal Alkynes Promoted by a Heterobimetallic Zr/Co Complex

Journal:	*Dalton Transactions*
Manuscript ID	DT-COM-01-2020-000334.R1
Article Type:	Communication
Date Submitted by the Author:	30-Jan-2020
Complete List of Authors:	Beattie, Jeffrey; The Ohio State Univeristy, Chemistry and Biochemistry Wang, Canning; Ohio State University Department of Chemistry and Biochemistry, Department of Chemistry and Biochemistry Zhang, Hongtu; Ohio State University Department of Chemistry and Biochemistry, Department of Chemistry and Biochemistry Krogman, Jeremy; ShanghaiTech University, Foxman, Bruce; Brandeis University, Department of Chemistry Thomas, Christine; Ohio State University Department of Chemistry and Biochemistry, Department of Chemistry and Biochemistry

Chemical Communications

COMMUNICATION

Dimerization of Terminal Alkynes Promoted by a Heterobimetallic Zr/Co Complex

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

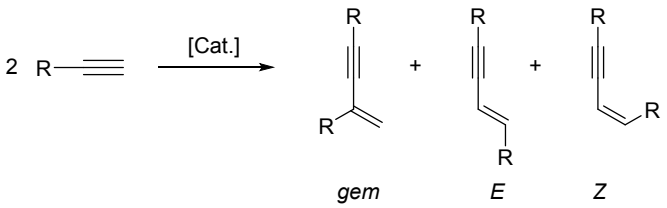
www.rsc.org

Jeffrey W. Beattie,[a] Canning Wang,[a] Hongtu Zhang,[a] Jeremy P. Krogman,[b,c] Bruce M. Foxman,[b] and Christine M. Thomas*[a]

Enynes are important synthetic intermediates that are also found in a variety of natural products and other biologically relevant molecules. The most atom economical synthetic route to enynes is via the direct coupling of readily available terminal alkyne precursors. Towards this goal, we demonstrate the formation of 1,3-enynes from terminal alkynes facilitated by a reduced Zr^{IV}/Co^{-I} heterobimetallic complex. An intermediate is trapped as a ^{t}BuNC adduct, revealing that bimetallic activation of the terminal C-H bond of the alkyne is an essential mechanistic step.

Enynes are an important building block in organic synthesis that find use in a variety of transformations such as cycloaddition and metathesis reactions.[1-3] In one recent example, 1,3-enynes have been coupled with ethylene in the catalytic formation of vinylcyclobutenes *en route* to cyclobutane derivatives,[4] highlighting the continued need for efficient and inexpensive methods to synthesize 1,3-enyne precursors. The transition metal-catalyzed dimerization of terminal alkynes to form the 1,3-enyne motif has been of particular interest owing to the reaction's atom economy combined with the regio- and stereo-control that can be imparted by transition metal catalysts.[5, 6] Most of the transition metal catalysts active for alkyne dimerization involve precious metals such as Rh, Ru, or Pd,[5-10] however, examples of catalysts containing Earth-abundant transition metals and metal-free catalytic systems have been rapidly emerging.[11-25] The homodimerization reaction proceeds by either head-to-tail coupling to generate the geminal product or by head-to-head coupling to form either *E* or *Z* alkenes (Scheme 1). The ability to control the selectivity for these three possible dimerization products is highly desirable.[20] Towards this goal, we have chosen to investigate a bimetallic approach to the dimerization of terminal alkynes, hypothesizing that two different metal binding sites may provide a unique opportunity to control the selectivity of C-C bond forming reactions by enabling new mechanistic pathways or stabilizing key intermediates in one pathway when multiple competing pathways are viable.

Heterobimetallic complexes have been widely investigated both for their unique electronic structures and their ability to perform reactions with enhanced activity and selectivity compared to their monometallic analogues.[26-31] Our group has shown that the Zr/Co complex (THF)Zr(MesNP^{i}Pr$_2$)$_3$CoN$_2$ (**1**, Mes = 2,4,6-trimethylphenyl)[32] has an extensive reactivity profile that includes stoichiometric cleavage of the C=O bond in CO_2 and ketones,[33-35] and catalytic hydrosilylation and Kumada coupling reactions.[36-38] Despite the diverse reactivity already unveiled for **1**, its reactivity towards unsaturated hydrocarbons and/or C-H bonds had not been studied. Herein, we present initial investigations along these lines, specifically focusing on the reactivity of Zr/Co bimetallic complex **1** with terminal alkynes.



Scheme 1. Possible products from the homodimerization of terminal alkynes

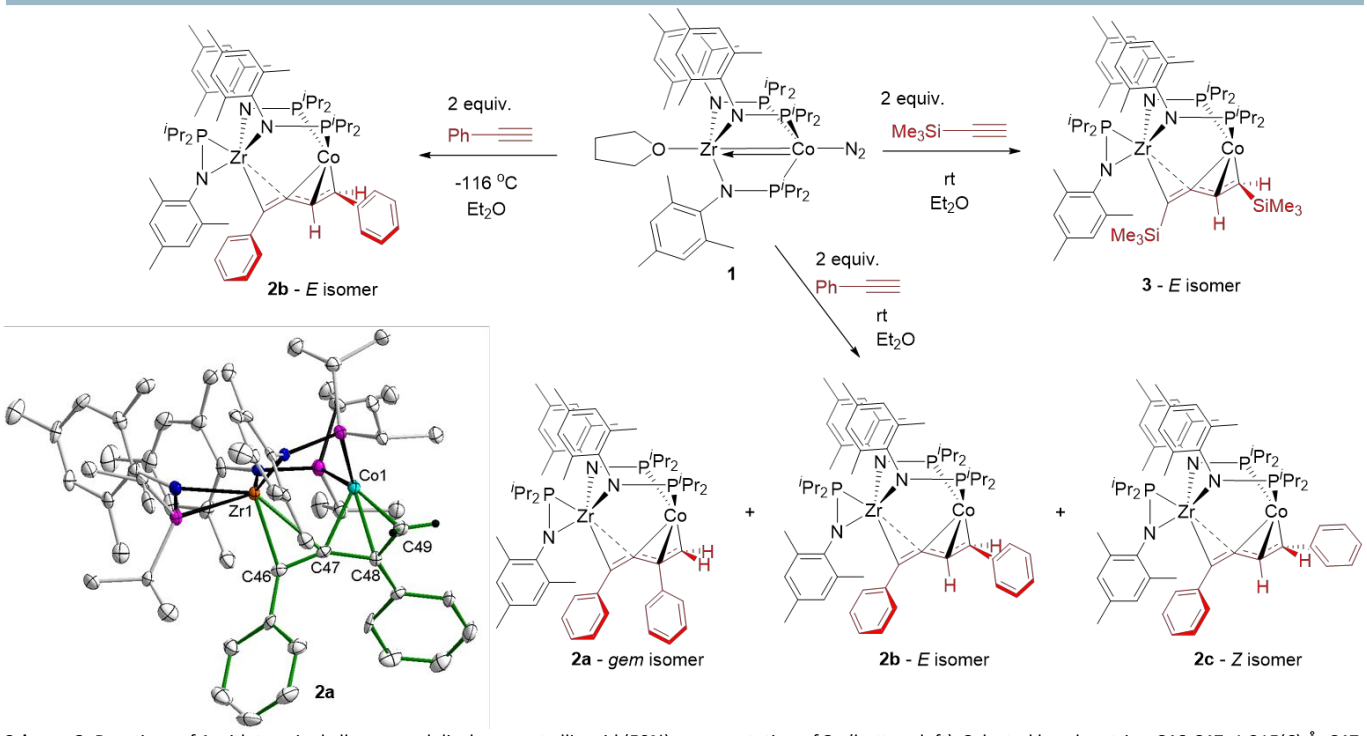
To begin probing the reactivity of **1** towards terminal alkynes, we treated **1** with two equivalents of phenylacetylene in Et_2O at room temperature (Scheme 2). Analysis of the reaction mixture by ^{1}H NMR spectroscopy showed nearly complete conversion of the alkyne to a mixture of metal-containing products (**2a-2c**). GC-MS-FID analysis revealed formation of all three possible isomers of alkyne dimerization, namely the geminal product, and *Z* and E alkenes in an approximately 1:3.5:5.5 ratio.

Although complexes **2a**-**2c** could not be separated, cooling a Et_2O solution of the product mixture to -35 °C resulted in the formation of a single crystal of one of the three products, the metal-bound geminal enyne species **2a**. X-ray diffraction

[a] *Department of Chemistry and Biochemistry, The Ohio State University, 100 W 18th Ave. Columbus, OH 43210 U.S.A.*
[b] *Department of Chemistry, Brandeis University, 415 South Street Waltham, MA 02454 U.S.A.*
[c] *School of Physical Science and Technology, ShanghaiTech University, Pudong, Shanghai, 201210, China*

Chemical Communications

COMMUNICATION



Scheme 2. Reactions of **1** with terminal alkynes, and displacement ellipsoid (50%) representation of **2a** (bottom left). Selected bond metrics: C46-C47, 1.315(6) Å; C47-C48, 1.430(6) Å; C48-C49, 1.436(7) Å; Zr-C46, 2.203(5) Å; Zr-C47, 2.487(5) Å; Co-C47, 1.950(5) Å; Co-C48, 2.040(5) Å; Co-C49, 1.994(5) Å; Zr-Co, 2.7502(8) Å.

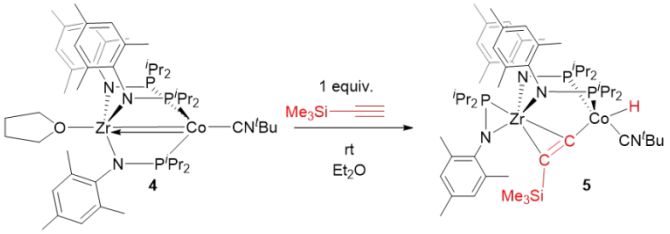
revealed the product to be an asymmetric Zr/Co complex with one of the three phosphinoamide ligands bound η^2 to Zr to accommodate the bridging enyne (Scheme 2). The enyne nominally binds via attachment of the C≡C triple bond to Zr and the terminal alkene to Co, although the bond distances reveal significant π-backbonding and resonance delocalization. The C-C triple (1.315(6) Å) and C-C double (1.436(7) Å) bond distances of the enyne fragment are elongated by roughly 0.1 Å compared to related free enynes (1.20 Å and 1.33 Å, respectively),[39, 40] as would be expected as a result of metal binding. The C-C single bond (1.430(6) Å), on the other hand, remains unchanged compared to the corresponding distance in free enynes (1.43 Å). The Zr-Co distance has lengthened significantly from 2.36(1) Å in **1** to 2.7502(8) Å in **2a**,[32] which indicates the loss of metal-metal bonding in the complex as electron density is diminished upon back-bonding to the bound enyne.

In an effort to selectively form a single enyne isomer, the alkyne dimerization reaction was carried out at low temperature. The addition of phenylacetylene to a frozen solution of **1** in Et_2O led to formation of primarily the *E* isomer **2b** upon thawing. The $^{31}P\{^1H\}$ NMR spectrum **2b** consists of three resonances, including two broad signals at 51.8 and 51.4 ppm corresponding to inequivalent bridging phosphinoamide ligands and a sharp singlet at 24.9 ppm for the phosphinoamide ligand bound η^2 to the Zr center. Although X-ray quality crystals of **2b** could not be obtained, the identity of the metal-bound enyne isomer was confirmed by thorough NMR analysis. The ^1H NMR spectrum revealed two doublets at 7.84 and 6.96 ppm with coupling constants of J = 16 Hz, assigned to the alkene protons. These signals were found to be shifted downfield upon metal binding when compared to the free *E*-enyne, but with a similar coupling constant.[41] Further, analysis of the ^1H-^{13}C HSQC NMR spectrum revealed that each alkene proton is attached to a unique carbon atom (Figure S12), ruling out the geminal product **2a**. As would be expected for an *E*-alkene, the ^1H-^1H NOESY NMR spectrum revealed no through-space interaction between the two alkene protons. The one- and two-dimensional NMR data taken together with the solid-state structure of **2a**, which is presumed to have a similar enyne binding mode, allows us to assign the major alkyne dimerization product formed at low temperature as **2b**, the *E* enyne-bound isomer.

The reaction of **1** with two equivalents of trimethylsilylacetylene was carried out in order to expand the scope of the reaction. Analysis by ^1H and ^{31}P NMR spectroscopy revealed complete consumption of the TMSC≡CH and formation of a single product (**3**, Scheme 2). Similar to **2b**, three $^{31}P\{^1H\}$ signals were observed for **3** including a singlet at 21.7 ppm for the phosphinoamide ligand bound η^2 to Zr and two broad singlets at 50.2 and 47.9 ppm for the two inequivalent

bridging phosphinoamide ligands. All attempts to grow suitable crystals for X-ray crystallographic analysis were unsuccessful, as the product exhibits high solubility in even the most nonpolar solvents. However, a suite of one- and two-dimensional NMR experiments were again used to confirmed the connectivity of the enyne product, revealing spectroscopic features largely similar to those of **2b** (see Figures S14-S19) and allowing for the assignment of **3** as the metal-bound *E*-enyne product resulting from head-to-head dimerization of TMSC≡CH.

To better understand the mechanism of alkyne dimerization promoted by **1**, we next sought to isolate an intermediate. Reactions of **1** with one equivalent of either terminal alkyne reagent afforded a 50:50 mixture of starting material **1** and enyne product **2**/**3**, as evident from integration of $^{31}P\{H\}$ NMR spectra obtained (Figure S24). Since this indicated that any intermediate species were highly reactive towards addition of a second equivalent of alkyne, we posited that replacement of the labile N_2 ligand with *tert*-butylisocyanide, which has been shown to bind irreversibly and effectively block the Co coordination site,[42, 43] would block the binding and insertion of a second equivalent of terminal alkyne. To test this hypothesis, (THF)Zr(MesNP^{i}Pr$_2$)$_3$CoCN^{t}Bu (**4**) was treated with one equivalent of TMSC≡CH, resulting in the clean formation of a single new product (**5**, Scheme 3). The ^1H NMR spectrum of **5** showed a well-defined triplet at -12.79 ppm corresponding to a cobalt-bound hydride. Similar to **2** and **3**, complex **5** also appears to have one ligand that is now bound exclusively to Zr, as evident by a sharp resonance at 8.02 ppm in the $^{31}P\{^1H\}$ NMR spectrum. However, in this case, both bridging phosphinoamide ligands are significantly downfield-shifted and equivalent on the NMR timescale, resulting in one broad signal at 107.8 ppm. X-ray quality crystals of **5** were grown from a concentrated diethyl ether solution at -35°C, and single crystal X-ray diffraction revealed a terminal cobalt hydride and a bridging acetylide ligand that adopts a binding mode that is κ^1 to Co and η^2 to Zr (Figure 1).



Scheme 3. Reaction of **4** with TMSC≡CH.

Isolation of **5** suggests that the first step in the alkyne dimerization process is C-H activation. Coordination and insertion of a second equivalent of alkyne into either the Co-C or Co-H bond, followed by reductive elimination would then form the *E* or *gem* enyne isomers depending on the orientation of the incoming alkyne, with steric effects largely favouring formation of the *E* isomer. The formation of the *Z* enyne isomer is not possible through such an alkyne insertion step, but could proceed via formation of a cobalt vinylidene intermediate following the C-H activation and alkyne coordination steps. A similar vinylidene intermediate was invoked for Milstein's Z-selective alkyne dimerization catalysed by cobalt.[12] Notably, neither mechanistic pathway alone could account for the formation of all three enyne isomers (*E*, *Z*, *gem*) so, at least in the case of PhC≡CH, more than one mechanistic route is accessible at room temperature. In the case of **5**, ^{t}BuNC does not prevent the initial C-H activation step, but serves to prevent binding of an additional alkyne, halting the dimerization process. Indeed, no reaction is observed upon treatment of **5** with additional equivalents of TMSC≡CH. Isolation of **5** indicates that one role of the Zr center in this bimetallic transformation is to stabilize the acetylide fragment generated upon oxidative addition of the C-H bond.

With information about stoichiometric reactions in hand, the potential for catalytic turnover was probed. Addition of a large excess of PhC≡CH to a stirring solution of complex **1** afforded an orange solid whose ^1H NMR and IR spectra were consistent with polyphenylacetylene (Figures S25-S26).[44, 45] We hypothesize that formation of the polymer is the result of the strong binding of the enyne moiety to the metal centres. Without dissociation of this moiety, subsequent binding and C-H activation of PhC≡CH units leads to lengthening of the polymer chain rather than loss of bound enyne and turnover to restart a potential catalytic cycle. Indeed, addition of excess PhC≡CH to complex **2b** also led to the formation of polyphenlyacetylene, further confirming the proposed mechanism. In contrast, addition of excess TMSC≡CH to complex **1** led only to the formation of complex **3**, leaving excess TMSC≡CH in solution. This is most likely due to the greater steric hindrance around the metal centers in **3**, which precludes the approach of additional equivalents of TMSC≡CH to initiate polymerization.

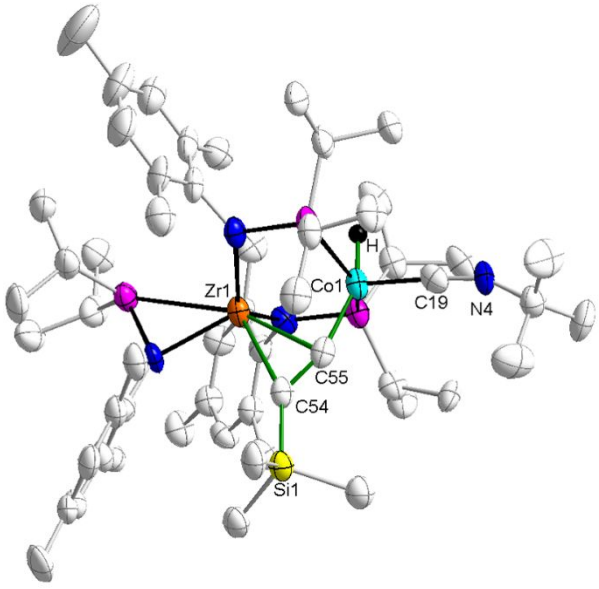


Figure 1. Displacement ellipsoid (50%) representation of **5**. Selected bond metrics: C55-C54, 1.290(11) Å; Co-C55, 1.795(9) Å; Zr-C55, 2.379(8) Å; Zr-C54, 2.417(9) Å; Zr-Co, 2.7898(13) Å.

Conclusions

In summary, we have demonstrated that the Zr/Co bimetallic complex **1** is capable of binding and subsequently

dimerizing terminal alkynes to form desirable 1,3-enyne motifs. The resulting enyne product bridges between the metal centers in an unusual η^2-Zr,η^3-Co orientation. By exchanging the labile N_2 ligand in **1** with the more tightly binding *tert*-butylisocyanide ligand in **4**, we were able to isolate a C-H activated complex **5** as a model of a key intermediate in the dimerization process. Future work will focus on further exploration of the alkyne dimerization mechanism and efforts to induce catalytic turnover and extend this reactivity to alkyne cross-dimerization reactions.

This research was supported by the U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences, Catalysis Science Program, under Award No. DE-SC0019179.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1. S. Saito and Y. Yamamoto, *Chem. Rev.*, 2000, **100**, 2901-2916.
2. P. Wessig and G. Müller, *Chem. Rev.*, 2008, **108**, 2051-2063.
3. B. Kang, D.-h. Kim, Y. Do and S. Chang, *Org. Lett.*, 2003, **5**, 3041-3043.
4. V. V. Pagar and T. V. RajanBabu, *Science*, 2018, **361**, 68-72.
5. B. M. Trost and J. T. Masters, *Chem. Soc. Rev.*, 2016, **45**, 2212-2238.
6. Y. Zhou, Y. Zhang and J. Wang, *Org. Biomol. Chem.*, 2016, **14**, 6638-6650.
7. C. J. Pell and O. V. Ozerov, *ACS Catal.*, 2014, **4**, 3470-3480.
8. W. Weng, C. Guo, R. Çelenligil-Çetin, B. M. Foxman and O. V. Ozerov, *Chem. Commun.*, 2006, DOI: 10.1039/B511148J, 197-199.
9. C. Yang and S. P. Nolan, *J. Org. Chem.*, 2002, **67**, 591-593.
10. R. Azpíroz, L. Rubio-Pérez, R. Castarlenas, J. J. Pérez-Torrente and L. A. Oro, *ChemCatChem*, 2014, **6**, 2587-2592.
11. Q. Liang, K. M. Osten and D. Song, *Angew. Chem. Int. Ed.*, 2017, **56**, 6317-6320.
12. O. Rivada-Wheelaghan, S. Chakraborty, L. J. W. Shimon, Y. Ben-David and D. Milstein, *Angew. Chem. Int. Ed.*, 2016, **55**, 6942-6945.
13. G. C. Midya, B. Parasar, K. Dhara and J. Dash, *Org. Biomol. Chem.*, 2014, **12**, 1812-1822.
14. G. C. Midya, S. Paladhi, K. Dhara and J. Dash, *Chem. Commun.*, 2011, **47**, 6698-6700.
15. F. Xue, X. Song, T. T. Lin, K. Munkerup, S. F. Albawardi, K.-W. Huang, T. S. A. Hor and J. Zhao, *ACS Omega*, 2018, **3**, 5071-5077.
16. D. Xu, Q. Sun, Z. Quan, X. Wang and W. Sun, *Asian J. Org. Chem.*, 2018, **7**, 155-159.
17. N. Gorgas, B. Stöger, L. F. Veiros and K. Kirchner, *ACS Catal.*, 2018, **8**, 7973-7982.
18. M. Bhunia, S. R. Sahoo, G. Vijaykumar, D. Adhikari and S. K. Mandal, *Organometallics*, 2016, **35**, 3775-3780.
19. X. Zhuang, J.-Y. Chen, Z. Yang, M. Jia, C. Wu, R.-Z. Liao, C.-H. Tung and W. Wang, *Organometallics*, 2019, **38**, 3752-3759.
20. Q. Liang, K. Sheng, A. Salmon, V. Y. Zhou and D. Song, *ACS Catal.*, 2019, **9**, 810-818.
21. T. Sakurada, Y.-k. Sugiyama and S. Okamoto, *The Journal of Organic Chemistry*, 2013, **78**, 3583-3591.
22. Y. Ueda, H. Tsurugi and K. Mashima, *Angew. Chem. Int. Ed.*, 2020, **59**, 1552-1556.
23. J.-C. Grenier-Petel and S. K. Collins, *ACS Catal.*, 2019, **9**, 3213-3218.
24. J. Ahmed, A. K. Swain, A. Das, R. Govindarajan, M. Bhunia and S. K. Mandal, *Chem. Commun.*, 2019, **55**, 13860-13863.
25. M. Hasenbeck, T. Müller and U. Gellrich, *Catalysis Science & Technology*, 2019, **9**, 2438-2444.
26. P. Buchwalter, J. Rosé and P. Braunstein, *Chem. Rev.*, 2015, **115**, 28-126.
27. B. G. Cooper, J. W. Napoline and C. M. Thomas, *Cat. Rev. - Sci. Eng.*, 2012, **54**, 1-40.
28. M. K. Karunananda and N. P. Mankad, *ACS Catal.*, 2017, **7**, 6110-6119.
29. N. P. Mankad, *Chem. Eur. J.*, 2016, **22**, 5822-5829.
30. R. C. Cammarota, L. J. Clouston and C. C. Lu, *Coord. Chem. Rev.*, 2017, **334**, 100-111.
31. C. M. Farley and C. Uyeda, *Trends in Chemistry*, 2019, **1**, 497-509.
32. B. P. Greenwood, G. T. Rowe, C.-H. Chen, B. M. Foxman and C. M. Thomas, *J. Am. Chem. Soc.*, 2010, **132**, 44-45.
33. H. Zhang, B. Wu, S. L. Marquard, E. D. Litle, D. A. Dickie, M. W. Bezpalko, B. M. Foxman and C. M. Thomas, *Organometallics*, 2017, **36**, 3498-3507.
34. S. L. Marquard, M. W. Bezpalko, B. M. Foxman and C. M. Thomas, *J. Am. Chem. Soc.*, 2013, **135**, 6018-6021.
35. J. P. Krogman, B. M. Foxman and C. M. Thomas, *J. Am. Chem. Soc.*, 2011, **133**, 14582-14585.
36. W. Zhou, J. W. Napoline and C. M. Thomas, *Eur. J. Inorg. Chem.*, 2011, **2011**, 2029-2033.
37. W. Zhou, S. L. Marquard, M. W. Bezpalko, B. M. Foxman and C. M. Thomas, *Organometallics*, 2013, **32**, 1766-1772.
38. J. Coombs, D. Perry, D.-H. Kwon, C. M. Thomas and D. H. Ess, *Organometallics*, 2018, **37**, 4195-4203.
39. K. L. Evans, F. R. Fronczek and R. D. Gandour, *Acta Crystallographica Section C*, 1991, **47**, 2729-2731.
40. Y. Odabachian, X. F. Le Goff and F. Gagosz, *Chem. Eur. J.*, 2009, **15**, 8966-8970.
41. N. Kakusawa, K. Yamaguchi and J. Kurita, *J. Organomet. Chem.*, 2005, **690**, 2956-2966.
42. J. P. Krogman, M. W. Bezpalko, B. M. Foxman and C. M. Thomas, *Dalton Trans.*, 2016, **45**, 11182-11190.
43. H. Zhang, G. P. Hatzis, C. E. Moore, D. A. Dickie, M. W. Bezpalko, B. M. Foxman and C. M. Thomas, *J. Am. Chem. Soc.*, 2019, **141**, 9516-9520.
44. F. Cataldo, G. Strazzulla and S. Iglesias-Groth, *Radiat. Phys. Chem.*, 2009, **78**, 244-250.
45. O. Trhlíková, J. Zedník, J. Vohlídal and J. Sedláček, *Polym. Degrad. Stab.*, 2011, **96**, 1310-1320.

Table of Contents Synopsis:

A reduced Zr^{IV}/Co^{-I} heterobimetallic complex facilitates the formation of 1,3-enynes from terminal alkynes through a cooperative bimetallic C-H activation process.