[18] Review: P. Lhoták, S. Shinkai, *J. Phys. Org. Chem.* **1997**, *10*, 273 – 285.
[19] a) C. A. Schalley, J. M. Rivera, J. Santamaría, G. Siuzdak, J. Rebek, Jr., *Eur. J. Org. Chem.* **1999**, *121*, 2133 – 2138; b) C. A. Schalley, T. Martín, U. Obst, J. Rebek, Jr., *J. Am. Chem. Soc.*, in press; c) for a MS study of the gas-phase ion structure of calixarene capsules containing charged guests, see C. A. Schalley, R. K. Castellano, M. S. Brody, D. M. Rudkevich, J. Rebek, Jr., *J. Am. Chem. Soc.*, in press.
[20] a) K. C. Russell, E. Leize, A. van Dorsselaer, J.-M. Lehn, *Angew. Chem.* **1995**, *107*, 204 – 208; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 209 – 213; b) X. Cheng, Q. Gao, R. D. Smith, E. E. Simanek, M. Mammen, G. M. Whitesides, *J. Org. Chem.* **1996**, *61*, 2204 – 2206; c) K. A. Jolliffe, M. Crego Calama, R. Fokkens, N. M. M. Nibbering, P. Timmerman, D. N. Reinhoudt, *Angew. Chem.* **1998**, *110*, 1294 – 1297; *Angew. Chem. Int. Ed.* **1998**, *37*, 1247 – 1250; d) P. D. Schnier, J. S. Klassen, E. F. Strittmatter, E. R. Williams, *J. Am. Chem. Soc.* **1998**, *120*, 9605 – 9613.
[21] The large number of NH protons in different chemical environments cause polymeric "calixarene polycaps" to give very broad signals in the downfield region of the ^{1}H NMR spectra; see R. K. Castellano, D. M. Rudkevich, J. Rebek, Jr., *Proc. Natl. Acad. Sci. USA* **1997**, *94*, 7122 – 7127.
[22] A denaturation by DMSO titrations was done to help determine the driving force for the formation of **C1**. Thus, [D$_6$]DMSO was added to a solution of **1** in $CDCl_3$ until the "melting point" of the assembly was reached (i.e., the assembly is in a 1:1 ratio with the dissociated monomer in solution). The approximate melting point of **C1** was determined to be 2 vol % [D$_6$]DMSO, which is roughly equivalent to the melting points measured for other calixarene systems (see references [9, 10]). In as little as 10 % DMSO, **1** exists solely as the dissociated monomer. This indicates that not enthalpy, but entropy is driving the intramolecular formation of **C1**. For a description of this technique, see M. Mammen, E. E. Simanek, G. M. Whitesides, *J. Am. Chem. Soc.* **1996**, *118*, 12614 – 12623.
[23] For another example of dissymmetric calixarene capsules, see R. K. Castellano, B. H. Kim, J. Rebek, Jr., *J. Am. Chem. Soc.* **1997**, *119*, 12671 – 12672.
[24] Only the more strongly hydrogen bound $N_\beta H$ protons adjacent to the aryl groups, as opposed to the $N_\alpha H$ protons adjacent to the calixarene, are shifted to this region in $CDCl_3$; see also J. Scheerder, Dissertation, University of Twente, **1995**, pp. 110 – 111.
[25] O. Mogck, V. Böhmer, W. Vogt, *Tetrahedron* **1996**, *52*, 12403 – 12407.

The Mechanism of 1,4- and 1,6-Cuprate Additions: The First Determination of Activation Parameters**

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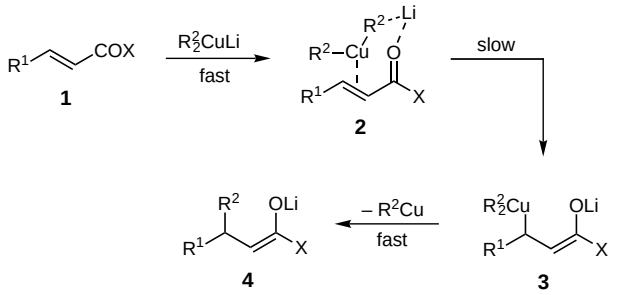
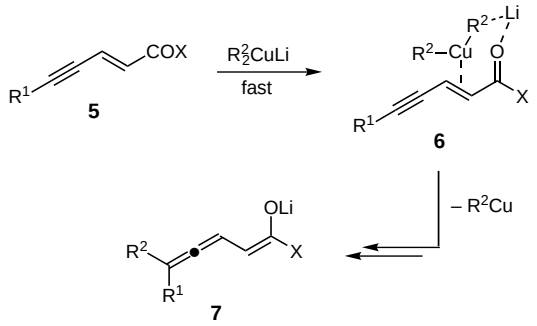
Michael additions of organocuprate reagents are among the most reliable methods for regio- and stereoselective coupling of C–C bonds. In addition to the classical 1,4-cuprate additions to enones, enoates, and acetylenic esters, recently 1,6-, 1,8-, 1,10-, and 1,12-additions to acetylenic Michael acceptors have been intensively studied.[1] The discovery of these new reaction classes, as well as advances in stereoselective cuprate additions,[2] has led to an increasing interest in the structure of organocuprate reagents[3] and the mechanisms of their reactions. Low-temperature NMR spectroscopy has been particularly well suited for mechanistic studies of these reactions,[1, 4–6] and has provided evidence for the intermediacy of π complexes **2** in the 1,4-cuprate addition to enones and enoates **1**.[4, 5] Further along the reaction pathway to product **4**, the rate-limiting step is likely an oxidative addition resulting in the formation of the σ copper(III) species **3**; this reaction pathway is in agreement with quantum-chemical calculations,[7] and recently evidence for copper(III) intermediates in biological systems has been obtained experimentally.[8]



Interestingly, 1,6-cuprate additions to electron acceptor substituted enynes **5** also result in π complexes **6** with coordination of the cuprate to the C–C double bond, even though the transfer of the alkyl moiety R^2 occurs at the acetylenic carbon atom.[6] The similarity between the π complexes **2** and **6** presumably leads to further analogies in the reaction pathways of the 1,4- and 1,6-additions, in which several short-lived intermediates take part in the formation of the 1,6-addition product **7** from the π complex **6**.[1, 6] To obtain



information about the rate-determining step of these reactions, we have performed a direct kinetic study for 1,4-additions of organocuprates to enones and 1,6-additions to enynes and determined the first set of activation parameters for these reactions.[9] These measurements indicate not only the analogies between the two reaction mechanisms, but also allow a comparison of the reactivity of various Michael acceptors.

Enone **8** and enynoate **9** were chosen as model substrates for the kinetic studies; qualitative studies had shown that these two Michael acceptors have comparable reactivities towards cuprates, allowing the kinetic measurements to be

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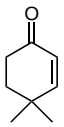

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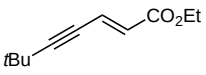

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carried out at similar temperatures. The reaction with lithium dimethylcuprate ($Me_2CuLi \cdot LiI$) was carried out in a double-walled flask between -43 and $-65\,^{\circ}C$ in diethyl ether, that is, under normal conditions for preparative application of cuprate additions (see Experimental Section). After addition of the substrate to the cuprate solution, the π complex (**2** or **6**) is immediately formed; NMR spectroscopic studies have indicated that this step is practically quantitative.[4–6] In the rate-determining step the π complex transforms into the enolate (**3** or **7**). The progress of the reaction was determined by removing aliquots at specific time intervals; the aliquots were hydrolyzed and analyzed by gas chromatography (in this way, the substrate **8** or **9** was recovered quantitatively from the remaining π complex). In an effort to minimize the systematic error in aliquot sampling and analysis, an internal standard of tetradecane was used in the reaction mixture. A typical plot of concentration versus time for these experiments is depicted in Figure 1.

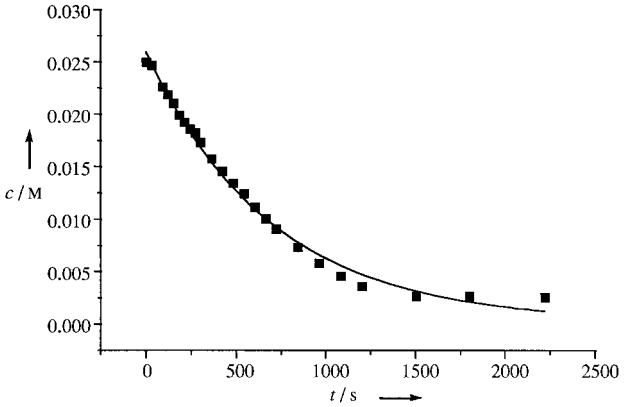


Figure 1. Time dependence of the substrate concentration for the reaction of enyne **9** with $Me_2CuLi \cdot LiI$ ($T = 219$ K; starting concentrations: c_0(cuprate) = 0.05 M, c_0(**9**) = 0.025 M in diethyl ether).

The measured values were fitted using the exponential function $c = c_0 \exp(-bt)$. In the case of a first-order reaction ($v = k$[π complex]) the calculated slope b should be independent of the cuprate concentration (therefore $b = k$), whereas for a higher order reaction (for example $v = k$[π complex][cuprate]) a strong dependence on the cuprate concentration is expected. Actually, for the two Michael acceptors **8** and **9**, the values measured for b with several different initial cuprate concentrations were the same within experimental error;[10] therefore, the 1,4-addition[9a] and the 1,6-addition occur in an *intramolecular manner* from the respective π complexes.

To determine the activation parameters for the Michael addition to the model substrates **8** and **9**, the kinetic measurements were carried out at several temperatures between 204 and 230 K. The resulting rate constants[11, 12] show errors of 3–30%, with most lying within 10% of the value of k. Problems mainly occurred in runs at low temperature as the repeated withdrawal of aliquots sometimes led to decomposition of the cuprate. The rate constants result in practically parallel lines in the Arrhenius plot (Figure 2) with the following activation parameters:

- 1,4-addition of $Me_2CuLi \cdot LiI$ to enone **8**: $E_A = 76 \pm 7$ kJ mol^{-1}, $\lg A = 16 \pm 2$ (correlation coefficient $r = -0.985$)
- 1,6-addition of $Me_2CuLi \cdot LiI$ to enynoate **9**: $E_A = 70 \pm 7$ kJ mol^{-1}, $\lg A = 15 \pm 2$ (correlation coefficient $r = -0.975$)

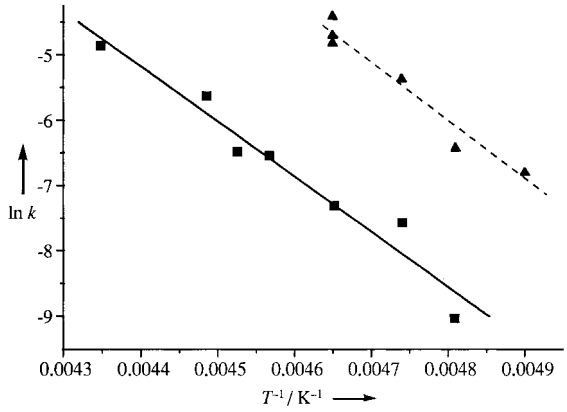
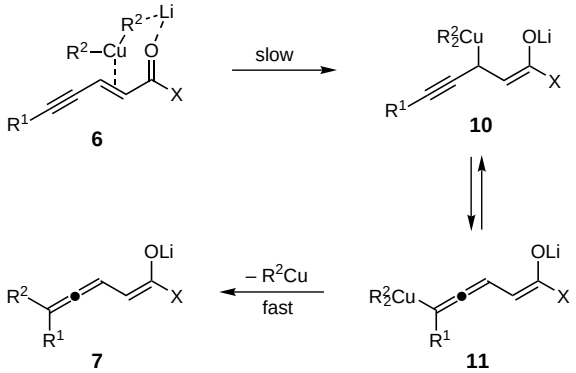


Figure 2. Arrhenius plot for the 1,4-addition of $Me_2CuLi \cdot LiI$ to enone **8** (▲) and for the 1,6-addition to enynoate **9** (■).

The activation parameters for the Michael acceptors **8** and **9** are identical within the limits of error. Comparable data for other copper-mediated reactions are not available; it is noteworthy, however, that the values measured here for the preexponential term ($\lg A = 15-16$) lie in the region typical for the opening of small rings.[13] Direct conclusions concerning analogous rate-determining steps based upon the similarity of activation parameters are not possible; nevertheless, it seems conceivable that both the 1,4-cuprate addition to enone **8** and the 1,6-addition to enyne **9** proceed through the oxidative addition of the substrate to produce a σ copper(III) species. On this premise the following mechanistic model arises for the 1,6-addition to acceptor-substituted enynes: In the rate-determining step of the reaction the copper π complex **6** decomposes into the copper(III) species **10**, which



6 **10** **7** **11**

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could be in equilibrium with the allenecopper compound **11**. The two intermediates can undergo reductive elimination to produce the 1,4-addition product from **10** and the 1,6-adduct from **11**. The experimentally observed exclusive formation of the 1,6-addition product may indicate that the hypothetical equilibrium lies on the side of intermediate **11**, or that the reductive elimination of **11** occurs much faster than from **10**.[14]

In conclusion, it is noted that kinetic investigations provide useful insight into the mechanistic pathways of the cuprate additions. The activation parameters determined here for the first time indicate that strong analogies exist between the reactions of various Michael acceptors.

Experimental Section

The kinetic measurements were conducted under an argon atmosphere in a double-walled flask with a double-walled dropping funnel; both were cooled with a Kryomat RUK 90 made by Lauda. The temperature in the reaction flask was measured using a PT-100 thermometer and held constant to within ±0.5 K. $Me_2CuLi \cdot LiI$ was prepared in the double-walled flask by addition of MeLi (2 equiv, salt-free; ca. 1.5 M solution in diethyl ether) to a suspension of CuI (1 equiv) in diethyl ether. The cuprate solution was cooled to the reaction temperature, and a solution of the Michael acceptor and the internal standard tetradecane was likewise cooled in the dropping funnel. At the timepoint $t = 0$ the substrate was added in one shot to the cuprate (end volume: 40 mL; starting concentration of substrate and cuprate: 0.02–0.10 M); warming due to the formation of the π complex could be held to within 0.5 K. Aliquots were withdrawn at specific time intervals with a pipet that was precooled in liquid nitrogen; the aliquots were immediately hydrolyzed and analyzed by gas chromatography.

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[1] Recent review: N. Krause, A. Gerold, *Angew. Chem.* **1997**, *109*, 194–213; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 186–204.
[2] a) B. L. Feringa, M. Pineschi, L. A. Arnold, R. Imbos, A. H. M. de Vries, *Angew. Chem.* **1997**, *109*, 2733–2736; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2620–2623; b) N. Krause, *Angew. Chem.* **1998**, *110*, 295–297; *Angew. Chem. Int. Ed.* **1998**, *37*, 283–285.
[3] Review: a) G. van Koten, S. L. James, J. T. B. H. Jastrzebski in *Comprehensive Organometallic Chemistry II*, *Vol. 3* (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson), Pergamon, Elsevier, Oxford, **1995**, pp. 57–133; b) G. Boche, F. Bosold, M. Marsch, K. Harms, *Angew. Chem.* **1998**, *110*, 1779–1781; *Angew. Chem. Int. Ed.* **1998**, *37*, 1684–1686; c) C. M. P. Kronenburg, J. T. B. H. Jastrzebski, A. L. Spek, G. van Koten, *J. Am. Chem. Soc.* **1998**, *120*, 9688–9689; d) C.-S. Hwang, P. P. Power, *J. Am. Chem. Soc.* **1998**, *120*, 6409–6410; e) N. Krause, *Angew. Chem.* **1999**, *111*, 83–85; *Angew. Chem. Int. Ed.* **1999**, *38*, 79–81.
[4] K. Nilsson, T. Andersson, C. Ullenius, A. Gerold, N. Krause, *Chem. Eur. J.* **1998**, *4*, 2051–2058, and references therein.
[5] Formation of π complexes in 1,4-cuprate additions to acetylenic esters: a) K. Nilsson, C. Ullenius, N. Krause, *J. Am. Chem. Soc.* **1996**, *118*, 4194–4195; b) K. Nilsson, T. Andersson, C. Ullenius, *J. Organomet. Chem.* **1997**, *545–546*, 591–595.
[6] N. Krause, *J. Org. Chem.* **1992**, *57*, 3509–3512; b) N. Krause, R. Wagner, A. Gerold, *J. Am. Chem. Soc.* **1994**, *116*, 381–382.
[7] a) A. E. Dorigo, J. Wanner, P. von R. Schleyer, *Angew. Chem.* **1995**, *107*, 492–494; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 476–478; b) E. Nakamura, S. Mori, K. Morokuma, *J. Am. Chem. Soc.* **1997**, *119*, 4900–4910; see, however, c) J. P. Snyder, *J. Am. Chem. Soc.* **1995**, *117*, 11025–11026; d) S. H. Bertz, G. Miao, B. E. Rossiter, J. P. Snyder, *J. Am. Chem. Soc.* **1995**, *117*, 11023–11024.
[8] A. P. Cole, D. E. Root, P. Mukherjee, E. I. Solomon, T. D. P. Stack, *Science* **1996**, *273*, 1848–1850; b) W. B. Tolman, *Acc. Chem. Res.* **1997**, *30*, 227–237.
[9] Previous kinetic investigations of 1,4-cuprate additions: a) S. R. Krauss, S. G. Smith, *J. Am. Chem. Soc.* **1981**, *103*, 141–148 (measurement at room temperature; under these conditions cuprates and enolates decompose); b) S. H. Bertz, G. Miao, M. Eriksson, *Chem. Commun.* **1996**, 815–816 (logarithmic reactivity scales); c) D. E. Frantz, D. A. Singleton, J. P. Snyder, *J. Am. Chem. Soc.* **1997**, *119*, 3383–3384 (kinetic isotope effects).
[10] Typical results for the 1,4-addition of $Me_2CuLi \cdot LiI$ to the enone **8** at 215 K with $c_0(\text{enone}) = 0.025$ M: $k = 0.012 \pm 0.001$ s^{-1} ($c_0(\text{cuprate}) = 0.025$ M); 0.009 ± 0.001 s^{-1} ($c_0(\text{cuprate}) = 0.050$ M); 0.0080 ± 0.0005 s^{-1} ($c_0(\text{cuprate}) = 0.075$ M); 0.009 ± 0.001 s^{-1} ($c_0(\text{cuprate}) = 0.10$ M).
[11] Rate constants k for the 1,4-addition of $Me_2CuLi \cdot LiI$ to the enone **8**: 0.0011 ± 0.0002 s^{-1} (204 K), 0.0016 ± 0.0005 s^{-1} (208 K), 0.0046 ± 0.0003 s^{-1} (211 K), 0.009 ± 0.001 s^{-1} (215 K), 0.0080 ± 0.0005 s^{-1} (215 K), 0.009 ± 0.001 s^{-1} (215 K), 0.012 ± 0.001 s^{-1} (215 K).
[12] Rate constants k for the 1,6-addition of $Me_2CuLi \cdot LiI$ to the enyne **9**: 0.00012 ± 0.00004 s^{-1} (208 K), 0.00052 ± 0.00008 s^{-1} (211 K), 0.00067 ± 0.00008 s^{-1} (215 K), 0.00145 ± 0.00008 s^{-1} (219 K), 0.00154 ± 0.00005 s^{-1} (221 K), 0.0036 ± 0.0009 s^{-1} (223 K), 0.0078 ± 0.0003 s^{-1} (230 K).
[13] a) P. J. Robinson, K. A. Holbrook, *Unimolecular Reactions*, Wiley, London, **1972**, pp. 189–205; b) R. H. DeWolfe in *Comprehensive Chemical Kinetics, Vol. 9* (Eds.: C. H. Bamford, C. F. H. Tipper), Elsevier, Amsterdam, **1973**, pp. 460–481.
[14] Analogous mechanistic models can be designed for cuprate additions to any other Michael acceptor in which further rearrangement steps of the type **10** → **11** are necessary to produce the experimentally observed regioisomer.[1]

η^5-Phospholylgallium: The First Monomeric Polyhapto Compound between a Phospholyl Ligand and a Main Group Metal**

Andreas Schnepf, Gregor Stößer, Duncan Carmichael, François Mathey,* and Hansgeorg Schnöckel*

Metastable, donor-stabilized Ga^I halide solutions are important precursors for subvalent gallium species.[1] For instance, Ga^I chloride solutions have provided access to the first organometallic compounds of gallium(I), GaCp[2] and GaCp*[3] ($Cp = C_5H_5$, $Cp^* = C_5Me_5$), which incorporate highly symmetrically bound η^5-Cp ligands. Simple neutral complexes involving main group elements bound to an aromatic

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