NMR Spectroscopic Evidence for π-Complexation and the Formation of a Vinylcopper Intermediate in the Reaction between Methyl phenylpropiolate and tBuCu(CN)Li

Karolina Nilsson,*,[†] Christina Ullenius,[†] and Norbert Krause[‡]

Department of Organic Chemistry
Chalmers University of Technology
412 96 Göteborg, Sweden
Institut für Organische Chemie und Biochemie der
Universität Bonn, Gerhard-Domagk-Strasse 1
D-53121 Bonn, Federal Republic of Germany
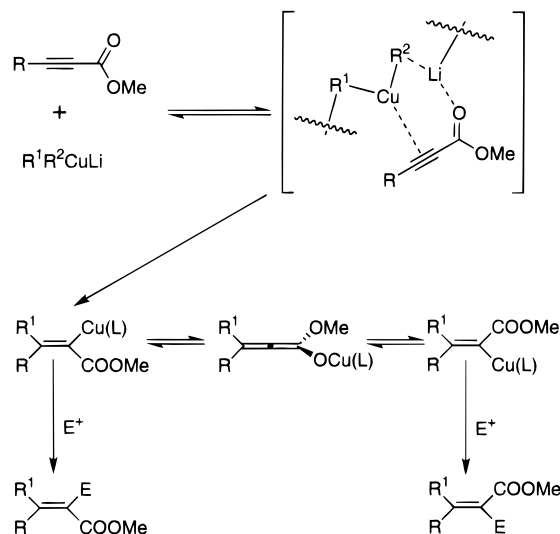
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Organocuprates have proved to be versatile tools in organic synthesis.[1] The applicability of the organocuprate reactions could be even more powerful if the mechanisms were fully understood. The mechanistic model often used for the addition to enones and enoates assumes a nucleophilic addition of the cuprate to the π-bond.[2] A transient square-planar intermediate, the controversial Cu(III) species,[3] is believed to precede the formation of the carbon−carbon bond. Alternatively, the reaction can be seen as an addition across the π-bond leading to an α-cuprio carbonyl compound.[4]

Low-temperature NMR investigations of enoates[5] and acceptor-substituted enynes[6] prove that there is a reversible coordination between copper and the C≡C bond of the substrate, i.e., a π-complexation, before carbon−carbon bond formation takes place. So far no organocopper coordination to acetylenic Michael acceptors has been detected in solution,[7] mostly because these types of substrates are far too reactive toward organocuprates. Electrophilic trapping,[8] IR measurements,[9] and NMR spectroscopy[10] of the intermediates after the C−C bond formation has taken place imply the existence of adducts with vinylcopper structures in some cases and copper allenolate structures in others (see Scheme 1).

In the present investigation, further insight into the reaction mechanism for cuprate additions to acetylenic esters was gained using ^{13}C-labeled substrates and less reactive cuprates.

The reaction of tBuCu(CN)Li[11] (**1**) with methyl phenylpropiolate (**2**) was studied by ^{13}C NMR spectroscopy using the

† Chalmers University of Technology.
‡ Institut für Organische Chemie und Biochemie der Universität Bonn.
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(3) Recent examples: (a) Snyder, J. P. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 80. (b) Dorigo, A. E.; Wanner, J.; Schleyer, P. v. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 476. (c) Snyder, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 11025.
(4) (a) Berlan, J.; Battioni, J.-P.; Koosha, K. *Tetrahedron Lett.* **1976**, *37*, 3355. (b) Berlan, J.; Battioni, J.-P.; Koosha, K. *J. Organomet. Chem.* **1978**, *152*, 359. (c) Yamamoto, Y.; Yamada, J.-I.; Uyehara, T. *J. Am. Chem. Soc.* **1987**, *109*, 5820.
(5) (a) Hallnemo, G.; Olsson, T.; Ullenius, C. *J. Organomet. Chem.* **1985**, *282*, 133. (b) Christenson, B.; Olsson, T.; Ullenius, C. *Tetrahedron* **1989**, *45*, 523.
(6) (a) Krause, N. *J. Org. Chem.* **1992**, *57*, 3509. (b) Krause, N.; Wagner, R.; Gerold, A. *J. Am. Chem. Soc.* **1994**, *116*, 381.
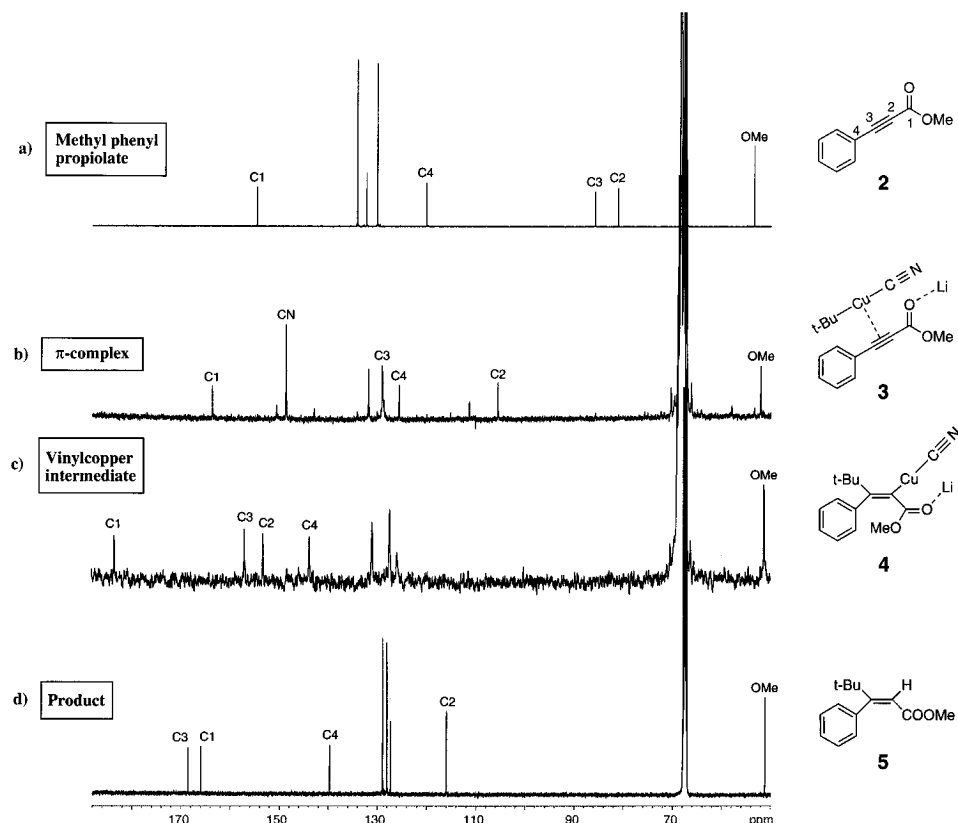(7) Copper acetylene π-complexes are well studied in the solid state: (a) Reger, D. L.; Huff, M. F. *Organometallics* **1992**, *11*, 69. (b) Brantin, K.; Håkansson, M.; Jagner, S. *J. Organomet. Chem.* **1994**, *474*, 229 and references cited therein.
(8) (a) Iodine: Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851. (b) Several examples of electrophiles: Hall, D. G.; Chapdelaine, D.; Préville, P.; Deslongchamps, P. *Synlett* **1994**, 660. (c) TMSCl: Marino, J. P.; Linderman, R. J. *J. Org. Chem.* **1981**, *46*, 3696. Fleming, I.; Perry, D. A. *Tetrahedron* **1981**, *37*, 4027.
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(11) The structure of this cuprate was suggested to be (RCuCN)⁻Li⁺ with a linear cuprate anion (Gorlier, J.-P.; Hamon, L.; Levisalles, J.; Wagnon, J. *J. Chem. Soc., Chem. Commun.* **1973**, 88) and later evidenced with ^{13}C,[13]C-couplings (Bertz, S. H. *J. Am. Chem. Soc.* **1991**, *113*, 5470.)

Scheme 1

unlabeled as well as [1-^{13}C]-labeled methyl phenylpropiolate for the correct assignment of NMR shifts. For the NMR experiment, **1** was prepared in THF by addition of 1 equiv of tBuLi to CuCN at −40 °C. The ^{13}C NMR spectrum of the cuprate was recorded before a precooled solution of the substrate in THF was added at −100 °C. The ^{13}C NMR spectra were recorded from −100 to −40 °C at 20 °C intervals. After the reaction was allowed to go to completion at −40 °C, the sample was recooled to −100 °C and the spectrum of the adduct **4** was obtained. This adduct was then quenched with water, and MS[12] and NMR spectra of the product **5** were recorded (*cf.* Figure 1d).

On copper coordination to the double bond in enoates[5a] and enynoates,[6b] the upfield shifts observed for the C2 and C3 carbons have been attributed to a rehybridization from sp2 toward sp3 for the C≡C carbons. In analogy with this, the sp-hybridized carbons of a triple bond would be shifted downfield upon π-complexation. This effect is indeed observed (*cf.* Table 1); i.e., a downfield shift of +24.6 ppm occurs for C2 while the difference is +43.1 ppm for C3 in **3**. The downfield shift of +9.1 ppm for the carbonyl carbon (C1) is in the same range as that obtained for enoates[5] and enynes[6] and is attributed to the coordination between a lithium ion and the carbonyl oxygen. In the [6]Li NMR spectrum a new signal at 1.25 ppm appears when methyl phenylpropiolate is added to **1**, which implies a lithium coordination to **2**.[13] For [1-^{13}C]-methyl phenylpropiolate, the coupling constant $^1J_{1,2}$ decreases from 127.3 Hz in **2** to 104.2 Hz in π-complex **3**, i.e., a decrease of 23.1 Hz attributed to a rehybridization of C2 from sp toward sp2 (*cf.* Table 1).

The formation of π-complex **3** is reversible and is characterized by the observation of starting material when the temperature is increased. The π-complex reappears on recooling the NMR sample. The irreversible adduct formation starts when the temperature is raised above −70 °C, and the ^{13}C NMR spectrum of the primary adduct **4** formed is in accordance with an olefin where the copper is σ-bonded to C2. A carbon resonance of a C≡C bond typically shows a shift of +45−49 ppm when covalently bound to copper relative to hydrogen.[14] This can be compared with the downfield shift of +37.7 ppm for C2 in adduct **4**. The only product seen after protonation, **5**, has the

(12) High-resolution mass spectra were recorded on a VG ZabSpecFPD-(EI+). Calcd for C₁₄H₁₈O₂: 218.130680. Found: 218.130659.
(13) The [6]Li NMR spectra were referenced to external 0.3 M [6]LiCl in methanol-d_4 (δ = 0.0). The observed shift for the tBu-cyanocuprate in the reaction mixture was −0.67 ppm.
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Figure 1. ^{13}C NMR spectra of the reaction sequence on mixing $^{t}BuCu(CN)Li$ (**1**) and methyl phenylpropiolate (**2**) in tetrahydrofuran/pentane at −100 °C. The upfield resonance in THF-d_8 is set to 25.37 ppm. (a) ^{13}C NMR spectrum of **2** in THF-d_8. (b) Spectrum, interpreted to be a copper acetylene π-complex (**3**), after mixing **1** and **2** at −100 °C. Excess cuprate used (2:1) is labeled as CN. (c) After the temperature is raised to −40 °C and then recooled to −100 °C, the spectrum of the primary adduct (**4**) is observed. Due to considerable broadening, the CN signals of **3** and **4** are not observed in the spectra. (d) Spectrum of the hydrolyzed reaction mixture (**5**) in THF-d_8. Phenyl peaks appear in the range 125−135 ppm.

Table 1. ^{13}C NMR Chemical Shifts[a] (δ) and $^{13}C,^{13}C$ Coupling Constants (Hz) in the Reaction between $^{t}BuCu(CN)Li$ (**1**)[b] and Methyl Phenylpropiolate (**2**) in Tetrahydrofuran/Pentane

	C1	C2	C3	C4	OMe	$^{1}J_{1,2}$
2	154.6	81.1	85.8	120.1	53.4	127.3
π-complex (**3**)[c]	163.6	105.6	128.8	125.6	52.0	104.2
adduct (**4**)	183.5	153.3	157.1	143.8	51.2	49.3
product (**5**)	166.8	115.6	168.5	139.2	51.2	75.8

[a] δ monitored at −100 °C and referenced to the upfield resonance in THF-d_8 at 25.37 ppm. [b] The CN ligand in the cuprate appears at 148.58 ppm. [c] C3 and C4 peaks in **3** have been assigned in analogy with π-complex **7** obtained from C3-labeled **6**.

Z-configuration.[15] This indicates that the intermediate adduct **4** is obtained through a stereoselective syn addition.[8a,16] The assignment of chemical shifts in the spectra above (Figure 1) was further supported by the NMR investigations of **1** with methyl 4,4-dimethyl-2-pentynoate (**6**) and its two ^{13}C-labeled analogues, labeled at C1 and C3, respectively.[17] The decrease of 62 Hz in $^{1}J_{2,3}$ upon π-complex formation (**7**) firmly

establishes that the triple bond is coordinated to the cuprate. Accordingly, the coupling constants $^{1}J_{2,3}$ of enoates and enynoates experience a decrease of 23 Hz upon π-complex formation.[6b] The coupling constant ($^{1}J_{2,3}$) of 94.5 Hz[17] for **7** indicates a hybridization state more like sp^2 than sp. No characterization of the adduct could be made since the reaction of **1** with **6** was too slow even at −20 °C,[18] possibly due to steric hindrance.

In conclusion, the addition of $^{t}BuCu(CN)Li$ (**1**) to methyl phenylpropiolate (**2**) is suggested to start by the reversible formation of a π-complex at temperatures below −90 °C. Data for the adduct formed at higher temperatures corresponds well to data for vinylcopper compounds. Further work is underway, including a wider range of cuprates with labeled acetylenic esters as well as the evaluation of ^6Li NMR.

Supporting Information Available: Experimental procedure and low-temperature ^{13}C and ^6Li NMR spectra of substrates, reaction course, and products (11 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(17) ^{13}C NMR chemical shifts (δ, ppm) and $^{13}C,^{13}C$ coupling constants (*J*, Hz) at −100 °C with THF-d_8 as internal standard [δ = 25.37] follow. Methyl 4,4-dimethyl-2-pentynoate (**6**): δ = 28.2 (C(**C**H$_3$)$_3$), 29.9 (C4), 53.0 (OCH$_3$), 72.4 (C2), 95.5 (C3), 154.4 (C1); $^{1}J_{1,2}$ = 126.9, $^{1}J_{2,3}$ = 174.5. π-complex **7**: δ = 30.9 (C(**C**H$_3$)$_3$), 32.7 (C4), 51.7 (OCH$_3$), 94.7 (C2), 132.5 (C3), 163.8 (C1); $^{1}J_{1,2}$ = 108.8, $^{1}J_{2,3}$ = 94.5. Changes in shift and in $^{13}C,^{13}C$ coupling constants upon π-complexation: $\Delta\delta$ = 9.4 (C1), 22.3 (C2), 37.1 (C3), 4.4 (C4), 0.9 (C(**C**H$_3$)$_3$), −1.3 (OCH$_3$); $\Delta^{1}J_{1,2}$ = −18.1, $\Delta^{1}J_{2,3}$ = −62.2.

(18) After the NMR sample was kept for several days in a freezer at −20 °C, no characteristic peaks assignable to an adduct could be observed.