

Priority communication

# $\pi$ -Complexation between a mixed methylalkenylcuprate and an alkyne. Further insight into the mechanism of organocopper additions to ynoates

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## Abstract

The alkenylcopper adduct (**1**) from the conjugate addition of  $\text{Me}_2\text{CuLi} \cdot \text{LiI}$  (**3**) to methyl 4,4-dimethyl-2-pentynoate (**2**) forms a  $\pi$ -complex when exposed to an excess of the starting acetylene. The first adduct and most stable intermediate in the reaction between **2** and **3** is an alkenylcopper from a *syn*-addition as revealed by low temperature  $^{13}\text{C}$  NMR measurements. The rate of isomerization of the initially formed *E*-adduct into the *Z*-analogue through the short-lived lithium allenolate (**5**) was retarded by the removal of lithium iodide. Addition of  $\text{TMSCl}$  produces the *O*-silylated allenolate (**6**) exclusively. Neither double alkyl transfer from the cuprate to produce di-homovinyl cuprates nor a possible alkenyl transfer is observed. © 1997 Elsevier Science S.A.

**Keywords:** Copper; Alkyne; Allene;  $\pi$ -Bonding; Mechanism; Carbon-13 nuclear magnetic resonance

## 1. Introduction

Addition of organocopper reagents to functionalized acetylenic compounds for the formation of trisubstituted olefins is a thoroughly investigated and well documented method. Pioneering work on carbocuprations of terminal acetylenes [1,2] and the stereoselective additions of  $\text{R}_2\text{CuLi} \cdot \text{LiI}$  to  $\alpha,\beta$ -acetylenic esters [3–5] have provided indirect evidence of alkenylcopper intermediates as well as indicated the existence of copper or lithium allenolates. The reaction mechanism of the conjugate addition to acetylenic esters, established mainly based on electrophilic trapping of intermediates, is thought to be an initial *syn*-addition followed by an isomerization through the allenolate, thus providing the *anti*-adduct. However, to our knowledge no decisive evidence about whether an alkenylcopper or an allenolate is the most viable structure in solution has been put forward. Also, the report on double alkyl transfer from lithium dialkylcuprates to acetylenic esters, which might lead to dimeric products [6], together with the announced preference for vinyl over methyl transfer to 2-cyclopentenone [7] prompted us to further study the reaction intermediates in the conjugate addition to  $\alpha,\beta$ -acetylenic esters by NMR spectroscopy.

We have recently reported that there is an initial copper-coordination between methyl phenyl propiolate and *t*- $\text{BuCu}(\text{CN})\text{Li}$  to form a  $\pi$ -complex before the carbon–carbon bond formation produces an alkenylcopper as the main adduct. This reaction sequence was elucidated by low temperature  $^{13}\text{C}$  NMR with the use of  $^{13}\text{C}$ -labelled compounds [8].

We now wish to report on the  $\pi$ -complexation (Fig. 1) between the mixed lithium methylalkenylcuprate [*t*- $\text{Bu}(\text{Me})\text{C}=\text{C}(\text{CO}_2\text{Me})\text{Cu}(\text{Me})$ ] (**1**) and methyl 4,4-dimethyl-2-pentynoate (**2**). The mixed cuprate was obtained from addition of  $\text{Me}_2\text{CuLi} \cdot \text{LiI}$  (**3**) to **2**, and the  $\pi$ -complex (**4**) was elaborated through subsequent addition of **2** to the reaction mixture after complete consumption of **3**.

The nature of the complex was verified and new insight into the reaction mechanism was gained by low temperature  $^{13}\text{C}$  NMR shifts and  $^{13}\text{C},^{13}\text{C}$  coupling constants using **2** labelled with  $^{13}\text{C}$  at both C1 and C3 carbons.

## 2. Results and discussion

As seen in Fig. 2, peaks due to three main species can be observed in the  $^{13}\text{C}$  NMR spectrum when methyl 4,4-dimethyl-2-pentynoate (**2**) is added at  $-90^\circ\text{C}$  to a

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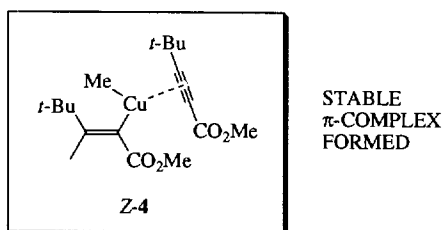


Fig. 1.

solution of 1.2 equivalents of  $\text{Me}_2\text{CuLi}(\text{LiI})$  (**3**) in diethyl ether. Noteworthy is the observation of three Me–Cu groups at ca.  $-12$  ppm which can be attributed to the three intermediates present in solution (see Table 1). The two close sets of signals (less than 0.15 ppm apart) can be attributed to two conformations of the alkenylcopper adduct (*E*-1) after a 1,2-*syn*-addition of the cuprate across the triple bond.

The two similar adducts are thought to be the *s-cis* and *s-trans* conformations of *E*-1 with restricted rotation around the C1–C2 single bond at low temperature due to lithium coordination (Scheme 1). Upon increasing the temperature from  $-90$  to  $-70^\circ\text{C}$ , these two sets of NMR signals coalesce. The third set of NMR signals are assigned the *Z*-isomer of the alkenylcopper adduct (*Z*-1), which is probably formed via isomerization of the *E*-analogue through the lithium allenolate (**5**). This conclusion is based on the fact that the formation of the *Z*-isomer can be suppressed by the removal of lithium

Table 1  
 $^{13}\text{C}$  NMR shifts for the reaction between **2** (1 equiv) and **3** (1.2 equiv)<sup>a</sup>

	<i>E</i> -1 <sup>b</sup>	<i>Z</i> -1	<b>6</b> <sup>c</sup>
C1	188.14/188.06	187.74	144.16
C2 <sup>d</sup>	156.33/156.27	155.78	176.49
C3	143.40/143.32	144.14	129.21
C4 <sup>e</sup>	37.24/37.23	37.27	36.98
<i>t</i> -Bu	31.52	31.52	29.31
OMe	55.83	56.00	54.32
Me-add <sup>f</sup>	20.63/20.49	20.71	19.72
Me–Cu	$-12.06/-12.15$	$-12.17$	–
TMS	–	–	$-0.049$

<sup>a</sup> 125.7 MHz, ca. 0.2 M solutions in diethyl ether- $d_{10}$  at  $-90^\circ\text{C}$  with the cuprate counted as monomer. The upfield resonance in diethylether- $d_{10}$  is set to 14.6 ppm. <sup>b</sup> Two conformations: *s-trans* and *s-cis*. <sup>c</sup> The *O*-silylated allene forms upon addition of TMSCl (3 equiv). <sup>d</sup> The  $^{13}\text{C},^{13}\text{C}$  coupling constants obtained for reactions with  $[3-^{13}\text{C}]$ -methyl 4,4-dimethyl-2-pentynoate:  $^1J_{2,3} = 70.2/69.9$  (*E*-1), 70.1 (*Z*-1), 110.4 (**6**). <sup>e</sup>  $^1J_{3,4} = 45.1/45.2$  (*E*-1), 44.7 (*Z*-1), 42.6 (**6**). <sup>f</sup>  $^1J_{3,\text{Me}} = 40.5/40.0$  (*E*-1), 40.1 (*Z*-1), 44.1 (**6**).

iodide. The same observation on the effect of lithium iodide on  $^{13}\text{C}$  NMR was made by Krause for the conjugate addition of **3** to 2-alkynoates [9]. For the *Z*-isomer, *s-cis* and *s-trans* conformers interconvert more rapidly than for the corresponding *E*-isomer. The broadening of the NMR signals indicates coalescence already at  $-90^\circ\text{C}$ . The equilibria strongly favour the

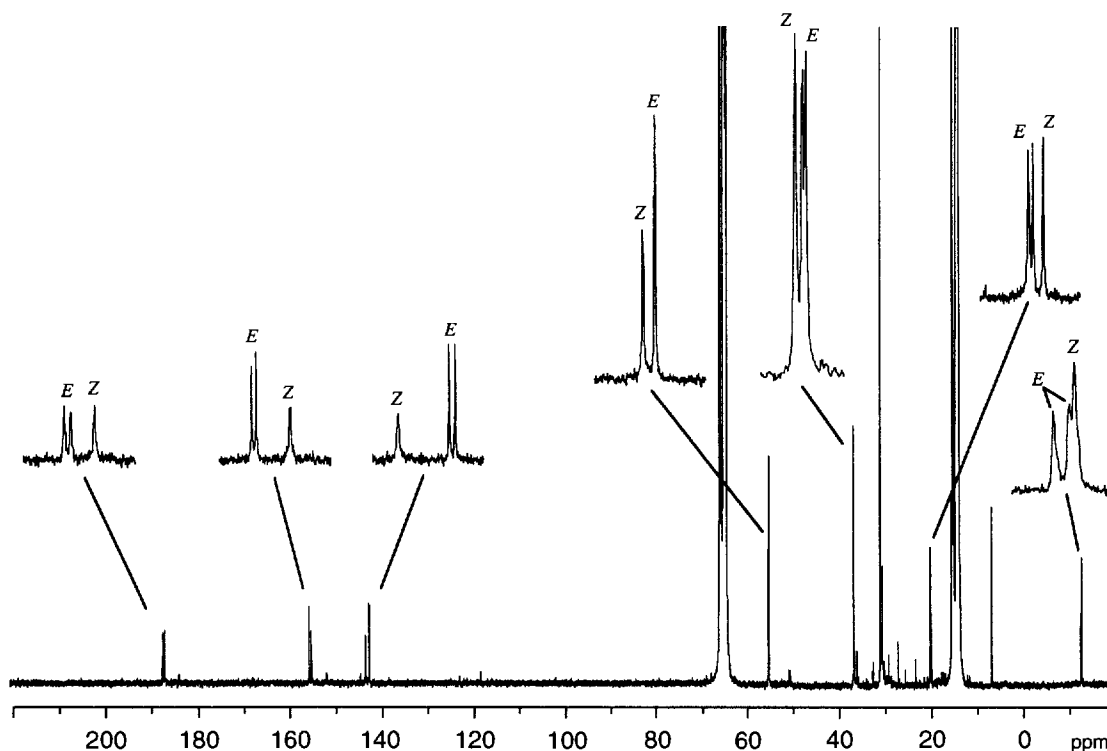


Fig. 2. 125.7 MHz  $^{13}\text{C}$  NMR spectrum observed for the addition of methyl 4,4-dimethyl-2-pentynoate (**2**) to 1.2 equiv  $\text{Me}_2\text{CuLi} \cdot \text{LiI}$  (**3**) in diethyl ether- $d_{10}$  at  $-90^\circ\text{C}$ . The two close sets represent *s-trans* and *s-cis* alkenylcopper intermediates of the *syn*-adduct (*E*-1), while the single set represents the *anti*-adduct (*Z*-1) formed through an isomerization via the lithium allenolate (**5**).

alkenylcopper adducts in the *E* to *Z* isomerization process, and the proposed lithium allenolate is not detected by NMR, due to the low concentration. Higher temperatures facilitate the isomerization and the *Z*-isomer is formed preferably at the expense of the *E*-alkenylcopper intermediate. The identification of the most stable intermediate at low temperature as an alkenylcopper adduct is based on the fact that the C1-carbon appears at the downfield shift of ca. 188 ppm, as revealed from experiments with [1-<sup>13</sup>C]-labelled **2**. Likewise, the position of the C2 and C3 carbons at ca. 156 ppm and 144 ppm, respectively, could be determined from [3-<sup>13</sup>C]-labelled **2**. There is a downfield <sup>13</sup>C NMR shift of +35 ppm for the C2-carbon when copper instead of hydrogen is directly attached. This is consistent with previous reports on alkenylcopper intermediates by Singer et al. [10] and by us [8], where the downfield shifts are 45–49 ppm and 37.7 ppm, respectively. Moreover, the observed <sup>1</sup>J<sub>2,3</sub> coupling constant of 70 Hz in **1** (Table 1), obtained from C3-labelled **2**, is within the range for olefins and is comparable with the <sup>1</sup>J<sub>2,3</sub> of 72 Hz determined for C3-labelled methyl cinnamate [11]. From these shifts and coupling constants, a copper or lithium allenolate can be ruled out as the most stable adduct in the reaction between **2** and **3**. A C2-carbon in an allene normally appears at ca. 200 ppm [12,13], and the coupling constant is approximately 100 Hz [14].

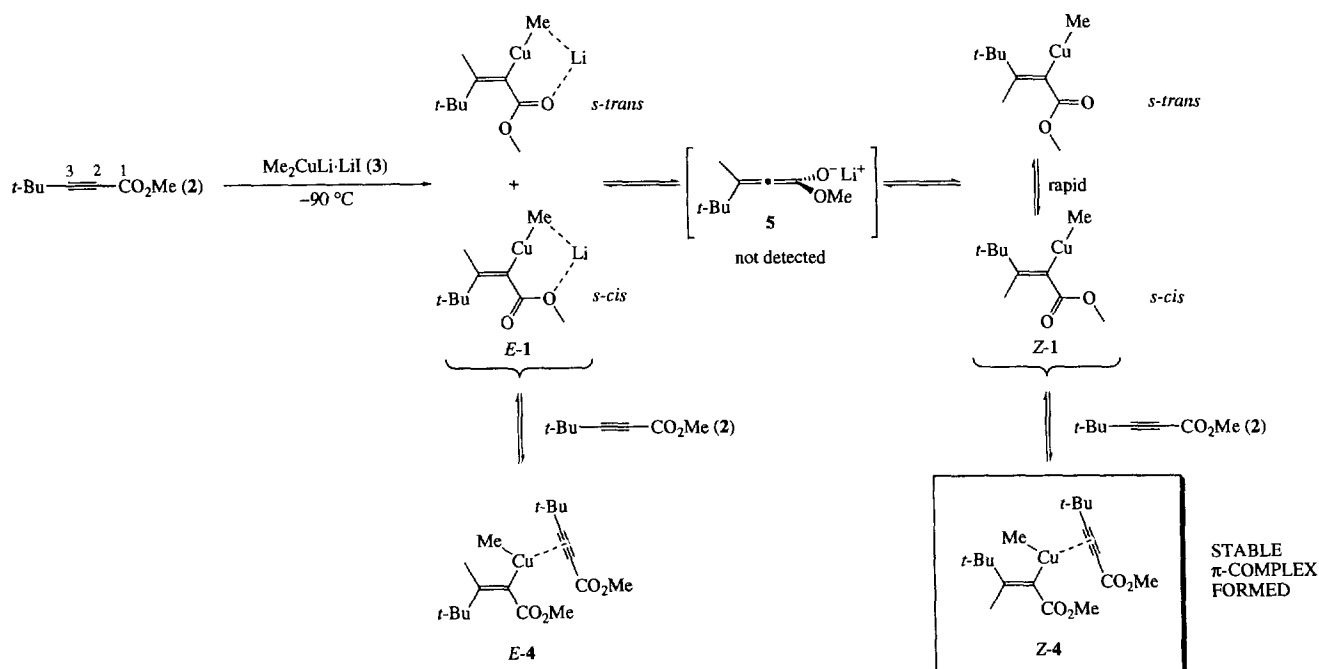
When three equivalents of TMSCl are added to a solution of the alkenylcopper adducts, only one product

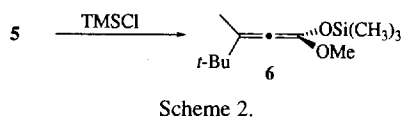
can be seen in the NMR spectrum. From its C2-carbon shift at 176.49 ppm and the <sup>1</sup>J<sub>2,3</sub> coupling constant of 110.4 Hz together with the C1 and C3 chemical shifts (144.16 and 129.21 ppm, respectively), it can be concluded that an *O*-silylated allenolate (**6**) forms upon addition of TMSCl to **2** (Scheme 2).

Probably, an allenolate adduct is silylated by TMSCl with the depletion of the alkenylcopper concentrations. The isolation of the *O*-silylated allenolates is often precarious, and instead the olefin esters are obtained after work-up. To our knowledge, the only successful trapping of these allenolates from conjugate additions to α,β-acetylenic esters includes the use of HMPA [15].

To evaluate the effect of the substrate:cuprate ratio used in these reactions, subsequent aliquots of **2** were added to a diethyl ether solution of **3** in an NMR-tube. The <sup>13</sup>C NMR-spectra for substrate:cuprate ratios of 1:2, 1:1, 1.5:1, 2:1 and 2.5:1 were obtained (Table 2, cuprate counted as a monomer). Ratios of up to 1:1 produced only the *E*- and *Z*-alkenylcopper intermediates at –70°C, while stable π-complexes started to form when the ratio exceeded 1:1. At the 1.5:1 ratio, the alkenylcopper intermediates formed π-complexes with **2**, keeping the *E*:*Z* ratio unperturbed initially. This ratio later changed slowly in preference for the π-complexed *Z*-adduct (see Table 2, 2:1 ratio).

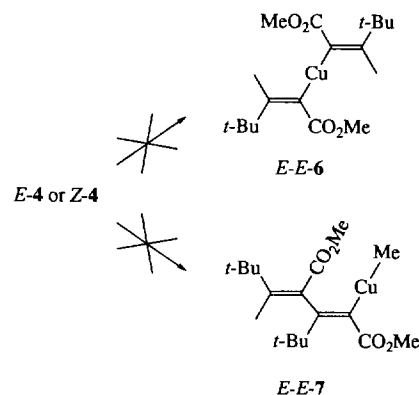
Quantum chemical calculations with the semi-empirical method PM3(tm) also suggest the π-complexed *Z*-adduct to be more stable than its *E*-analogue by 5.2 kcal mol<sup>-1</sup> [16,17].





By finally adding C3-labelled **2** to the fully complexed 2:1-solution, the  $\pi$ -complex (**4**) formation was determined to be a reversible process, while the formation of **1** from **2** and **3** apparently is not. The C3-labelled **2** readily exchanged with unlabelled **2**, and the C3- and the C2-carbon for the acetylene in **4** could be assigned to the peaks at 126.99 ppm and 104.83 ppm, respectively (Table 2). These shifts agree well with the previously reported shifts for the  $\pi$ -complex between **2** and *t*-BuCu(CN)Li (132.5 ppm for C3 and 94.7 ppm for C2) [8]. The observed  $^{13}\text{C},^{13}\text{C}$  coupling constant  $^1J_{2,3}$  of 107.2 Hz indicates a weakening of the triple bond and change in the hybridisation from  $sp$  toward  $sp^2$ .

It has been reported that both alkyl groups (e.g., *n*-butyl) of a di-*n*-alkylcuprate can be added to acetylenic esters [6]. The possibility of a second transfer of a methyl group from **1** to the excess of **2** to produce a di-homoalkenylcuprate (**6**) can be ruled out in this case, as the NMR signal for the methyl group attached to



copper can be observed throughout the reaction until TMSCl is added (Scheme 3). This NMR-peak ( $-11.1$  ppm) is assigned to **4** as the  $^{13}\text{C}$  NMR shift is different from  $\text{Me}_2\text{CuLi} \cdot \text{LiI}$  ( $-9.5$  ppm [18]) and  $\text{MeCu} \cdot \text{LiI}$  ( $-7.7$  ppm [19]). The difference from the work of Anderson et al. [6] probably lies in the choice of the alkyl group. In 1,4-additions, the transfer ability in mixed cuprates decreases in the order: *n*-alkyl  $\approx$  *s*-alkyl  $>$  *t*-alkyl  $>$  Ph  $\approx$  vinyl  $\approx$  Me  $>$  alkynyl [20]. A butyl

Table 2  
 $^{13}\text{C}$  NMR data<sup>a</sup> for the stepwise addition of **2** to **3**<sup>b</sup>

Substrate:cuprate	<i>T</i> (°C)	<i>E</i> -1	<i>Z</i> -1	$\pi$ -complex		$\pi$ -complex		excess alkynoate ( <b>2</b> )	allene ( <b>6</b> )
				<i>E</i> -4 alkenyl	<i>Z</i> -4 alkynoate	<i>E</i> -4 alkenyl	<i>Z</i> -4 alkynoate		
<b>1:2</b>	-90	Major	Minor						
C1		188.16/188.09	187.78						
C2		156.32/156.26	155.74						
C3		143.47/143.40	144.24						
<b>1:1</b>	-70	Major	Minor						
C1		188.19	187.73						
C2		156.43	155.98						
C3		143.55	144.27						
<b>1.5:1</b>	-70	Major	Minor	Major	Major	Minor	Minor		
C1		188.14	187.75	184.62	168.26	185.70	170.91		
C2		156.45	155.97	155.74	102.68	157.80	104.88		
C3		143.57	144.30	139.09	127.57	137.86	127.02		
<b>2:1</b>	-70			Minor	Minor	Major	Major		
C1				184.62	168.24	185.68	170.88	154.77	
C2				155.74	102.68	157.78	104.88	72.25	
C3				139.07	127.57	137.84	127.02	95.91	
<b>2.5:1<sup>c</sup></b>	-70								
C1						185.66	170.85	154.73	
C2						157.78	104.83 <sup>d</sup>	72.24 <sup>e</sup>	
C3						137.83	126.99	95.87	
<b>+ TMSCl</b>	-70								
C1								154.21	144.16
C2								72.29	176.70
C3								95.22	128.92

<sup>a</sup> 125.7 MHz, in diethyl ether- $d_{10}$  with the upfield resonance set to 14.6 ppm. <sup>b</sup> Portions of 0.11 mmol of **2** were added to 0.22 mmol of **3**. A total of 0.55 mmol of **2** was added. <sup>c</sup> The final addition was 0.11 mmol [3- $^{13}\text{C}$ ]-methyl 4,4-dimethyl-2-pentynoate (**2**). <sup>d</sup>  $^{13}\text{C},^{13}\text{C}$ -coupling constant for C3-labelled **2**,  $^1J_{2,3} = 107.2$  Hz. <sup>e</sup>  $^1J_{2,3} = 175.6$  Hz.

group is more readily transferred than a methyl group. Also, lithium methyl(vinyl)cuprate is reported to selectively transfer the vinyl group in its reactions with 2-cyclopentenone [7]. The possible formation of **7** from **1** and **2** should be revealed by the  $^{13}\text{C}$  NMR shifts when C3-labelled **2** is used. There is no alkenylcopper-core formed from the C3-labelled **2**. The  $^{13}\text{C}$  NMR shifts for C2 and C3 (104.83 and 126.99 ppm, respectively) clearly corresponds to a  $\pi$ -bonded triple bond and not to a double bond (Table 2). No **7** has been observed. Together these facts excludes both alkenyl and methyl transfer from **1** to **2** at  $-70^\circ\text{C}$  (Scheme 3).

When the  $\pi$ -complex (**4**) is treated with TMSCl, the major product formed is the *O*-silylated allenolate **6** (Scheme 2) and only a small fraction of the former excess of starting material **2** remains. The excess of **2** can be consumed by the reaction with either MeCu · LiI alone [21] or with an activated form of methylcopper, MeCu · LiI/TMSCl [22]. The methylcopper is thought to be released from **4** when the TMS-allenolate is formed. A previous NMR study has shown that MeCu is fully compatible with TMSCl [19]. The activating effect is believed to be the formation of iodotrimethylsilane (TMSI) from TMSCl and LiI [23,24].

The formation of  $\pi$ -complex **4** was further confirmed by the addition of two equivalents of **2** to one equivalent of **3** in a separate NMR-experiment. This NMR-spectrum was the same as the one obtained in the titration experiment with the same ratio (see Table 2, 2:1 ratio).

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