NMR Spectroscopic Investigation of the Adducts Formed by Addition of Cuprates to Ynoates and Ynones: Alkenylcuprates or Allenolates?

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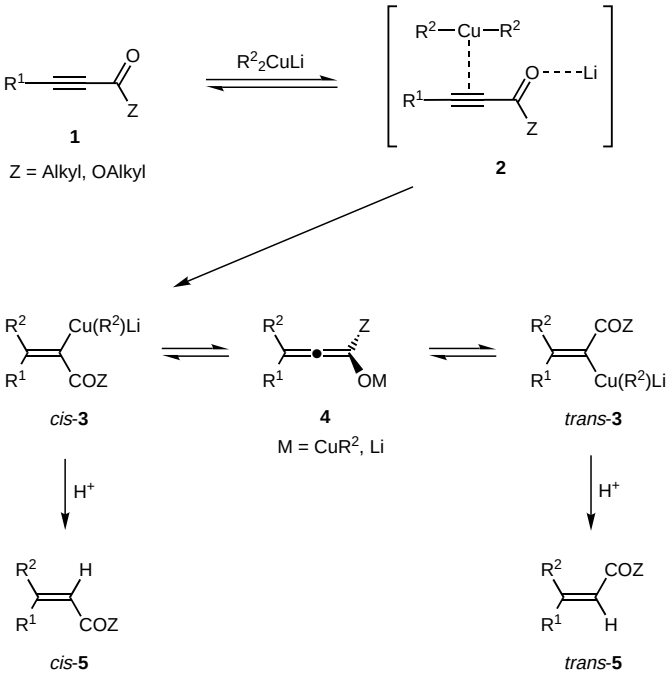
Abstract: The adducts obtained by reaction of $Me_2CuLi \cdot LiI$, *t*BuCu(CN)Li, and $tBu_2CuLi \cdot LiCN$ with ynoates and ynones were characterized by determination of their ^{13}C NMR chemical shifts and $^{13}C,^{13}C$ coupling constants. Alkenylcopper adducts were formed from ynoates and $Me_2CuLi \cdot LiI$ or *t*BuCu(CN)Li, whereas allenolates are obtained from ynoates and $tBu_2CuLi \cdot LiCN$, as well as from ynones and $Me_2CuLi \cdot LiI$. The transformations can therefore be regarded as carbocupration of an alkyne rather than a Michael addition. The equilibrium between alkenylcuprates and allenolates can be shifted towards lithium allenolates by addition of organolithium compounds. In the case of adducts formed from $Me_2CuLi \cdot LiI$, isomerization of *cis*- to *trans*-alkenylcuprates via the corresponding allenolate can be prevented by removal of LiI or by the use of THF as solvent. Whereas the protonation of alkenylcuprates to the corresponding alkenes proceeds stereospecifically, it is difficult to control the steric course of the protonation of allenolates. Addition of chlorotrimethylsilane to the adducts gives silyl ketene acetals or enol ethers in all cases.

Keywords: alkynes · carbocupration · copper · lithium · NMR spectroscopy

Introduction

The addition of organocopper reagents to activated multiple bonds is an effective way to form new carbon–carbon bonds.[1] These reactions often proceed with high chemical yields and high regio- and stereoselectivities; however, their success depends not only on the reagent, starting material, solvent,[2] and temperature, but also on the presence of additives,[2] coordinating groups,[3] and lithium salts.[4] Consequently, the search for optimal conditions may be laborious. The efficient use of these reactions would therefore benefit from an improved understanding of the mechanism.

For 30 years, the addition of organocopper reagents to acceptor-substituted alkynes **1** has been studied extensively, since this reaction offers a stereoselective route to valuable trisubstituted olefins **5**, which inter alia are useful in natural product synthesis (Scheme 1).[1, 5, 6] The addition to ynoates proceeds *cis* selectively in THF at low temperature, whereas *cis*/*trans* mixtures are obtained at higher temperature or in diethyl ether.[1, 5] The former result was explained in terms of the *cis*-alkenylcopper intermediate *cis*-**3**, and the loss of stereoselectivity was attributed to isomerization to *trans*-**3**, possibly via a copper or lithium allenolate **4**. The reactions can



Scheme 1. Reaction scheme for the formation of **5**.

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thus be regarded as the carbocupration of an alkyne[1, 7] rather than a Michael addition, which should give the enolate **4** directly. In the case of ynones, however, it is difficult to control the stereoselectivity of the cuprate addition,[6] and so far the reason for this differing behavior is unknown.

The most powerful tool for investigating the mechanism of copper-promoted transformations is NMR spectroscopy.[1, 8–10] Extensive work by several groups has shown that 1,4-additions of cuprates to enones and enoates proceed via π complexes in which the electron-rich cuprate interacts with the π system of the C–C double bond of the Michael acceptor.[1, 8] The formation of the enolate from the π complex may then take place via intermediates with a formal oxidation state of the copper center of +3. Although such σ copper(III) species have not yet been detected experimentally in conjugate cuprate additions,[11] theoretical calculations[12] support their participation in these transformations, and they also play an important role in systems of biological relevance.[13] In the case of acetylenic substrates **1**, however, little is known about the mechanism of cuprate additions; one reason is the high reactivity of these substrates, which makes it difficult to observe reaction intermediates. Earlier, the ^{13}C NMR chemical shifts of the products of the addition of Me_2CuLi to acetylenic esters were interpreted in terms of allenolate intermediates **4**.[10a] By using unreactive reactants (i.e., a *tert*-butyl-substituted ynoate and the cyanocuprate *t*BuCu(CN)Li) we recently proved the formation of a π complex of type **2**.[10b] Therefore, it seems that cuprate additions to acceptor-substituted acetylenes **1** also follow the general pathway established for enones and enoates.

We now report the results of an extensive NMR spectroscopic investigation dedicated to the further elucidation of the mechanism of conjugate cuprate additions to ynoates and ynones. In particular, we sought to gather additional information about the solution structures of the intermediates formed in these transformations by determination of their ^{13}C NMR chemical shifts and $^{13}C,^{13}C$ coupling constants by using ^{13}C-labeled substrates. This technique has already proved rewarding for the characterization of cuprate π complexes.[9b, 10b, 14] To control the reactivity, alkynes with bulky substituents on the triple bond and less reactive copper reagents were employed in some cases. The even less reactive monoorganocopper reagents could not be used because of their heterogeneity, which renders them unsuitable for NMR studies. The structural data obtained in this study were used to account for the poorer stereoselectivity often observed in cuprate additions to acetylenic ketones.

Results and Discussion

General information: The reactions between organocuprates and ynones and ynoates were studied in diethyl ether or THF in the temperature range −100 to −20 °C. ^{13}C-Labeled substrates were used for the verification of chemical shifts and for the determination of $^{13}C,^{13}C$ coupling constants. We used three different preparation techniques for the NMR experiments (see Experimental Section), and although the variations in the results were negligible, this avoided the repetition of systematic errors in sample preparation. In the following, the organocopper reagents are denoted as monomers, irrespective of their true state of aggregation,[14, 15] and regardless of substituent priorities, the *cis*/*trans* nomenclature is used throughout to indicate the stereochemistry of cuprate addition.

Addition of $Me_2CuLi \cdot LiI$ to ynoates: First we checked the assignments of the ^{13}C NMR chemical shifts of the adducts formed by addition of $Me_2CuLi \cdot LiI$ to ynoates **6a–c** (Table 1, entries 1–3, 6, 7). The use of ^{13}C-labeled substrates would allow an unambiguous assignment; however, due to their volatility and limited stability, the synthesis of ^{13}C-labeled **6a–c** is difficult. We therefore concentrated on the *tert*-butyl- and phenyl-substituted ynoates **6d** and **6e** (Scheme 2).

The reaction of methyl 4,4-dimethyl-2-pentynoate (**6d**) with lithium dimethylcuprate in diethyl ether (Table 1,

Table 1. ^{13}C NMR chemical shifts of the adducts formed by 1,4-addition of $Me_2CuLi \cdot LiI$ to acetylenic esters **6** at −90 °C.

	Substrate	Solvent	R	Adduct	C1	C2	C3	Me (C3)	Me (Cu)
1[a,b]	**6a**	$[D_{10}]Et_2O$	H	*cis*-**7a**	188.5	162.2	125.8	23.4	−11.6
				trans-**7a**	188.3	161.7	125.8	21.6	−10.3
2[a]	**6b**	$[D_{10}]Et_2O$	Me	*cis*-**7b**	187.1	155.3	131.4	24.3	−11.8
				trans-**7b**	186.9	155.9	132.2	25.2	−9.9
3[a]	**6c**	$[D_{10}]Et_2O$	Et	*cis*-**7c**	187.0	155.2	136.7	21.5	−11.8
				trans-**7c**	187.0	154.7	137.5	24.8	−10.4
4[c]	**6d**	$[D_{10}]Et_2O$	*t*Bu	*cis*-**7d**[d]	188.0	156.3	143.3	20.6	−12.1
				trans-**7d**	187.7	155.8	144.0	20.4	−12.2
5[e]	**6e**	$[D_{10}]Et_2O$	Ph	*cis*-**7e**[d]	188.7	162.3	133.3	22.7	−11.5
				trans-**7e**	185.7	166.1	133.3	27.6	−11.0
6[a]	**6b**	$[D_8]THF$	Me	*cis*-**7b**	185.1	159.7	131.9	23.5	−11.2
7[a]	**6c**	$[D_8]THF$	Et	*cis*-**7c**	184.8	158.3	137.5	14.6	−11.1
8[f]	**6d**	$[D_8]THF$	*t*Bu	*cis*-**7d**	186.1	159.2	142.6	18.8	−11.6
9[g]	**6e**	$[D_8]THF$	Ph	*cis*-**7e**	185.8	166.8	134.0	21.3	−11.6

[a] Chemical shifts taken from ref. [10a] were reevaluated and adjusted according to the present investigation. [b] In THF, the adduct is protonated by methyl propiolate to give methyl crotonate.[10a] [c] Assignment of the chemical shifts of C1, C2 and C3 by means of experiments with [1-^{13}C]- and [3-^{13}C]-**6d**. Coupling constants: *cis*-**7d**: $^1J_{2,3} = 70$ Hz; $^1J_{3,Me} = 40$ Hz; $^1J_{3,4} = 45$ Hz; *trans*-**7d**: $^1J_{2,3} = 70$ Hz; $^1J_{3,Me} = 40$ Hz. [d] Two closely spaced sets of signals were observed and were attributed to *s-cis*/*s-trans* conformers. [e] Assignment of the chemical shifts of C1 and C2 by means of experiments with [1-^{13}C]-**6e**; $^1J_{1,2} = 48$ Hz. [f] Assignment of the chemical shifts of C1 and C2 by means of experiments with [1-^{13}C]-**6d**; $^1J_{1,2} = 48$ Hz. [g] Assignment of the chemical shifts of C1 and C2 by means of experiments with [1-^{13}C]-**6e**; $^1J_{1,2} = 47$ Hz.

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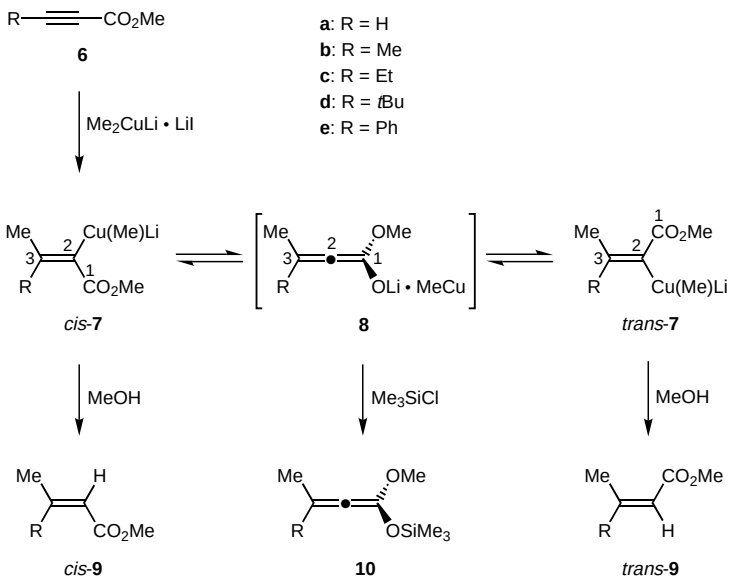

Scheme 2. Reaction scheme for the addition of $Me_2CuLi \cdot LiI$ to **6**.

entry 4) is very fast even at $-100\,^{\circ}C$, so that the NMR signals for the ynoate disappear immediately after mixing the reactants. In the ^{13}C NMR spectrum at $-90\,^{\circ}C$, signals for both alkenylcopper adducts *cis*- and *trans*-**7d** are observed. The signals for C2 and C3 appear upfield of the C1 signals, as was established by use of the C1- and C3-labeled ynoates [1-^{13}C]-**6d** and [3-^{13}C]-**6d** (Figure 1a).[16] The chemical shifts of the C2 carbon atom ($\delta = 156.3$, 155.8) and a $^1J_{2,3}$ coupling constant of 70 Hz are strong indications of an alkenylcuprate structure **7** rather than an allenolate **8**. In an allenic structure, the signal of the central carbon atom C2 would be expected downfield of the C1 and C3 signals; likewise, a coupling constant of 70 Hz is typical of alkenes, whereas values of around 100 Hz are usual for allenes.[17] Accordingly, for the silyl ketene acetal [3-^{13}C]-**10d** formed by quenching of [3-^{13}C]-**7d** with Me_3SiCl, the following chemical shifts and coupling constants were found: $\delta = 144.0$ (C1), 176.6 (C2), 128.9 (C3); $^1J_{2,3} = 110$ Hz (Figure 1b).

Similar observations were made in the ^{13}C NMR spectrum of the adduct of phenyl-substituted ynoate **6e** and $Me_2CuLi \cdot LiI$ (Table 1, entry 5). The signals of C1 appear downfield of those of C2 and C3 (verified with the labeled substrate [1-^{13}C]-**6e**), and the coupling constant of $^1J_{1,2} = 48$ Hz is also indicative of an alkenylcuprate structure **7e** (values for the corresponding silyl ketene acetal **10e**: $\delta = 145.8$ (C1), 182.8 (C2), 119.4 (C3), $^1J_{1,2} = 141$ Hz). Thus, the ^{13}C NMR chemical shifts and coupling constants of the adducts formed in diethyl ether solution from ynoates **6d/e** and lithium dimethylcuprate are interpreted as lithium alkenyl(methyl)cuprates **7d/e**, which are referred to simply as alkenylcopper adducts in the following. The quenching experiments with chlorotrimethylsilane again show that the regioselectivity of the electrophilic trapping reaction is not governed by the structure of the adduct, but rather by the HSAB principle.[18]

The assigment of the *cis*/*trans* configuration of the adducts **7** was based on the ratios for the products **9** under the assumption of equally fast stereospecific protonation of both alkenylcuprates by methanol. For example, a *cis*/*trans* ratio of 64/36 was determined for **7e** at $-94\,^{\circ}C$ in diethyl ether; as was observed for similar reactions,[10a] the *cis*/*trans* ratio changed to 42/58 on raising the temperature to $-60\,^{\circ}C$. Interestingly, the stereoselectivity of the cuprate addition to ynoates in diethyl ether also depends on the presence of lithium salts and can be improved in favor of the *cis* adduct when lithium iodide is excluded by the use of salt-free Me_2CuLi.[10a, 19] For example, addition of the salt-free cuprate to ynoate **6e** at $-90\,^{\circ}C$ in diethyl ether followed by methanolysis at this temperature furnishes exclusively *cis*-**9e**.

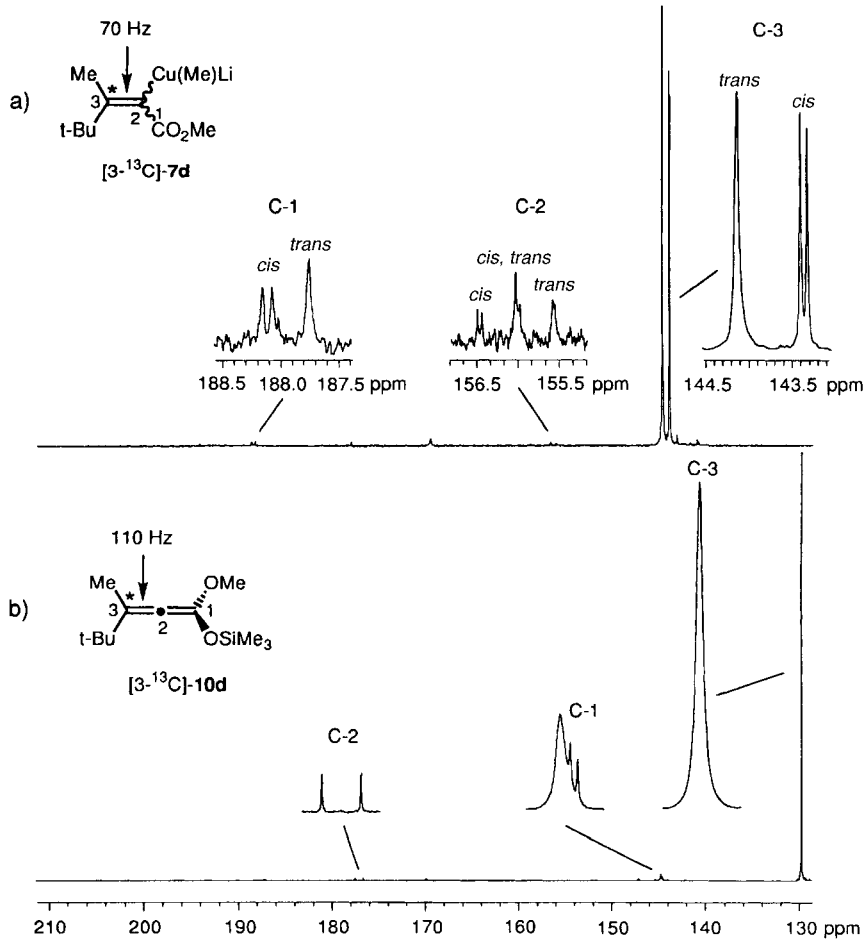

Figure 1. a) ^{13}C NMR spectrum ($-90\,^{\circ}C$) of the adducts *cis*/*trans*-[3-^{13}C]-**7d** obtained by addition of $Me_2CuLi \cdot LiI$ to [3-^{13}C]-**6d** in [D_{10}]Et_2O. b) ^{13}C NMR spectrum of silyl ketene acetal [3-^{13}C]-**10d** formed after addition of 3 equiv of Me_3SiCl to adducts [3-^{13}C]-**7d**.

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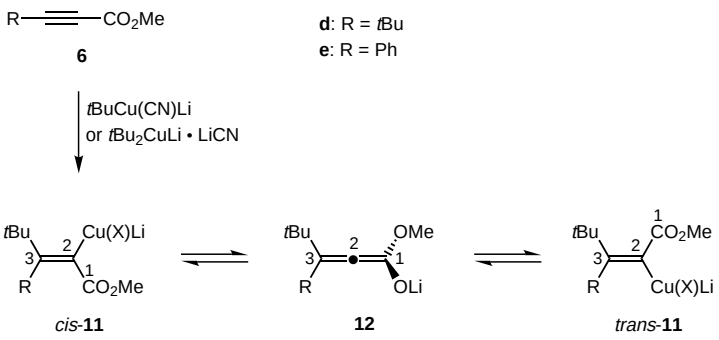
This strongly suggests that the coordination of a lithium ion to the carbonyl oxygen atom of the alkenylcuprate effectively facilitates formation of the (lithium) allenolate and hence the isomeric alkenylcopper adduct.

On the basis of the observations made with labeled ynoates for **6d** and **6e**, we can now reevaluate the earlier investigation of additions of $Me_2CuLi \cdot LiI$ to the unlabeled ynoates **6a–c**. The chemical shifts reported in ref. [10a] were reassigned in accordance with those of **7d/e** (i.e., the C1 and C2 assignments are swapped; Table 1, entries 1–3). The data in Table 1 are listed in order of increasing size of the alkyl substituent at C3 of the ynoate. A pronounced substituent effect on the chemical shift is evident for the signals of C3, which are shifted downfield with increasing size of R in the order R = H < Me < Et < *t*Bu. The corresponding value for the phenyl-substituted alkenylcuprate **7e** ($\delta = 133.3$) is additionally influenced by the electronic properties of the aromatic substituent, since it lies between those of R = Me and R = Et. This is the normal order for substituted alkenes,[20] and it also applies to the alkenes **9** that were obtained by protonation of the adducts **7**. In contrast, the chemical shifts of C1 and C2 in the adducts **7** are only slightly affected by the nature of the substituent at C3. By comparison of the chemical shifts of C2 for the alkenylcuprates **7** and the corresponding protonated alkenes **9**,[21] the substituent effect of the copper fragment Cu(Me)Li on the ^{13}C NMR chemical shifts can be deduced. The signals for C2 of **7d/e** are shifted downfield by about 50 ppm relative to those of **9d/e**, and similar downfield shifts were reported earlier by Oehlschlager et al.[22] for stannylcuprates derived from CuCN, and by us[10b] for the adduct of *t*BuCu(CN)Li to ynoate **6e**. The downfield contribution to the ^{13}C NMR shifts can be attributed to the more electrophilic character of a copper(I) center compared with a hydrogen atom.

The addition of $Me_2CuLi \cdot LiI$ to the *tert*-butyl-substituted ynoate **6d** was also carried out in THF. The solubility of the Gilman cuprate in THF is limited, and at the concentrations required for the NMR experiments (ca. 0.2 M), the cuprate already starts to precipitate at $-20\,^{\circ}C$.[10a] Therefore, the substrate was added at this temperature and the NMR samples were cooled immediately to $-90\,^{\circ}C$. This procedure gave samples that remained homogeneous, and the stereoselectivity of the addition was unaffected in spite of mixing the reactants at a higher temperature. In analogy with the earlier report on the addition of lithium dimethylcuprate to ynoates **6b** and **6c** (Table 1, entries 6 and 7),[10a] only one set of signals was found (Table 1, entry 8), and the signals were assigned by means of the labeled substrate [1-^{13}C]-**6d**. The chemical shifts are very similar to those of the adducts **7d** in diethyl ether (entry 4), and the coupling constant of $^1J_{1,2} = 48$ Hz is also typical of an alkenylcuprate. Protonation with methanol at low temperature furnished *cis*-**9d** exclusively, so that the alkenylcopper structure *cis*-**7d** can be assigned to the adduct formed from **6d** and $Me_2CuLi \cdot LiI$ in THF. Similarly, the phenyl-substituted ynoate **6e** affords the alkenylcuprate *cis*-**7e** (entry 9), and the literature values for **6b** and **6c**[10a] were corrected by exchanging the assignments of C1 and C2 (Table 1, entries 6 and 7). Possibly, the absence of the isomeric *trans*-alkenylcopper adducts reflects the solvating strength of THF for lithium cations, which is seven times stronger than that of acyclic ethers such as dimethyl ether.[23] The effect of using THF as solvent would then be similar to the removal of lithium iodide (see above), that is, the strongly solvated lithium cations can no longer induce an isomerization of the alkenylcopper adducts via a lithium allenolate.

Addition of *t*BuCu(CN)Li and *t*Bu$_2$CuLi · LiCN to ynoates: In comparison with the Gilman reagents $R_2CuLi \cdot LiI$, the cyanocuprates RCu(CN)Li, and the cyano-Gilman reagents $R_2CuLi \cdot LiCN$[24] sometimes provide better stability as well as improved stereoselectivity and reactivity in Michael additions.[1] The fact that the cyanocuprates exist as homogeneous solutions throughout the reaction makes them especially attractive for NMR spectroscopy.[9, 10b] In order to determine whether the structure of the products of addition to acetylenic substrates depends on the type of cuprate, we examined the adducts formed by addition of *t*BuCu(CN)Li and *t*$Bu_2CuLi \cdot$ LiCN to labeled and unlabeled ynoates **6d** and **6e** (Scheme 3).



Scheme 3. Reaction scheme for the formation of **11** and **12**.

The type of cyanocuprate used for the addition indeed strongly influences the position of the equilibrium between adducts **11** and **12**. As reported previously,[10b] the reaction of ynoate **6e** with *t*BuCu(CN)Li gives exclusively the alkenylcuprate *cis*-**11e** (X = CN) (Table 2, entry 1). The assignment was based on experiments with [1-^{13}C]-**6e**, which confirmed the chemical shift of $\delta = 183.7$ for C1. This chemical shift is indicative of an alkenylcopper structure, and the same is true of the coupling constant $^1J_{1,2} = 49$ Hz for this adduct. These values are in the same range as those of adduct *cis*-**7e** (Table 1,

Table 2. ^{13}C NMR chemical shifts of the adducts formed by 1,4-addition of *t*BuCu(CN)Li or *t*$Bu_2CuLi \cdot$LiCN to acetylenic esters **6** in [D_8]THF at $-80\,^{\circ}C$.

	Substrate	Cuprate	R	Adduct	C1	C2	C3	$(CH_3)_3C$
1[a]	**6e**	*t*BuCu(CN)Li	Ph	*cis*-**11e**	183.7	153.0	157.1	31.6
2[b]	**6e**	*t*$Bu_2CuLi \cdot$LiCN	Ph	**12e**	160.7	184.6	151.7	–
3[c]	**6d**	*t*$Bu_2CuLi \cdot$LiCN	*t*Bu	**12d**	155.7	185.1	132.5	33.3

[a] For previously reported data, see ref. [10b]. Assignment of the chemical shifts of C1 and C2 by experiments with [1-^{13}C]-**6d**; $^1J_{1,2} = 49$ Hz. [b] Assignment of the chemical shift of C1 by experiments with [1-^{13}C]-**6e**; several peaks appear for each carbon atom, so that $^1J_{C,C}$ coupling constants could not be resolved. $\delta[(CH_3)_3C] = 31–32$. [c] Assignment of the chemical shifts of C1 and C2 by experiments with [1-^{13}C]-**6d**; $^1J_{1,2} = 137$ Hz.

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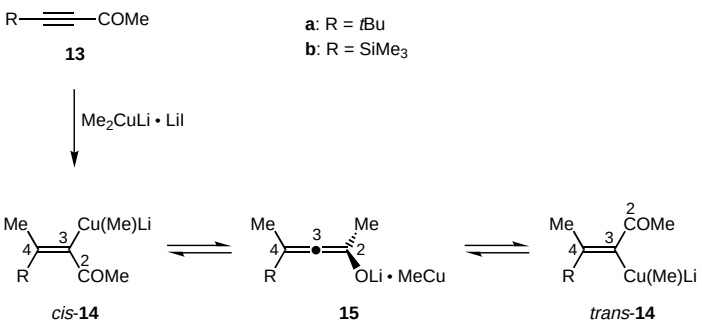
entry 9) from the corresponding addition of $Me_2CuLi \cdot LiI$. As usual, the stereochemistry of the addition was determined by methanolysis at low temperature, which gave the known alkene methyl (*Z*)-4,4-dimethyl-3-phenyl-2-pentenoate.[25, 26]

The addition of the cyano-Gilman reagent $tBu_2CuLi \cdot LiCN$ to ynoates **6d** and **6e** also gave single adducts, but with the allenolate structures **12** (Table 2, entries 2 and 3); in these cases, the second reaction product is the cuprate *t*BuCu(CN)Li, which exists as an independent species in solution.[14] The assignment is again based on experiments with the labeled substrates [1-^{13}C]-**6d/e** that allowed verification of the C1 and C2 signals; in both cases, the signals of C2 ($\delta = 184.6/185.1$) appear downfield of those of C1 ($\delta = 160.7/155.7$). This behavior strongly supports an allenic structure, as does the large coupling constant of $^1J_{1,2} = 137$ Hz for **12d**[17] (a similar value of $^1J_{1,2} = 141$ Hz was found for the silyl ketene acetal **10e**; see above).

The existence of an equilibrium between alkenylcuprates **11** and allenolates **12** was confirmed by addition of an excess of *t*BuLi to the alkenylcopper adduct *cis*-[1-^{13}C]-**11e** (X = CN), which was obtained by reaction of [1-^{13}C]-**6e** with *t*BuCu(CN)Li. This induced an upfield shift of the ^{13}C NMR signal of C1 from $\delta = 183$ to $\delta = 155$, while the signal for C2 moved downfield from $\delta = 154$ to $\delta = 185$. The coupling constant $^1J_{1,2}$ changed from about 50 to 105 Hz. Again, the appearance of the allenolate **12e** was accompanied by the simultaneous formation of the cuprate *t*BuCu(CN)Li, which can easily be recognized in the ^{13}C NMR spectrum by its characteristic cyanide signal at $\delta \approx 150$. Based on IR measurements at room temperature, Klein and Levene[6a] have also reported the formation of allenolate structures when an excess of RLi was added to the products of the addition of Gilman reagents to acetylenic Michael acceptors.

Addition of $Me_2CuLi \cdot LiI$ to ynones: Having found a peculiar dependence of the adduct structure on the type of cuprate used for the addition to acetylenic esters **6**, we turned our attention to the analogous reactions of ynones. It is rather difficult to control the stereoselectivity of cuprate additions to these substrates,[6] and we hoped that our NMR spectroscopic investigation might provide an explanation for this, perhaps in terms of different adducts involved in these reactions. For reasons of comparability, we studied the reactions of $Me_2CuLi \cdot LiI$ with the sterically hindered ketones **13a/b** (Scheme 4); **13b** was also prepared with a ^{13}C label at the carbonyl carbon atom ([2-^{13}C]-**13b**).



Scheme 4. Reaction scheme for the addition of $Me_2CuLi \cdot LiI$ to **13**.

In the ^{13}C NMR spectrum of the adduct obtained by reaction of lithium dimethylcuprate with the *tert*-butyl-substituted ynone **13a** in [D_{10}]diethyl ether at $-80\,^\circ$C (Table 3, entry 1), several sets of closely spaced peaks were observed, and some carbon atoms gave four equally intense signals. Hence, four different species are present, and the signals of the doubly bonded carbon atoms are centered around $\delta = 108$, 129, and 194. The same behavior was also found for the analogous reaction of silylynone **13b** (Figure 2a); in this case, the signals appeared at $\delta = 97$, 127, and 210 (Table 3, entry 2). Since the replacement of a *tert*-buty group by a trimethylsilyl substitutent at a C–C double bond usually causes an upfield shift of the α-carbon signal and a downfield shift of the signal of the β-carbon atom,[20] the chemical shifts observed here are in accordance with the assignment given in Table 3 (C2: $\delta = 129/127$; C3: $\delta = 194/210$; C4: $\delta = 108/97$). This assignment is consistent with an allenolate structure **15**, as was confirmed by experiments with the labeled ynone [2-^{13}C]-**13b**. In this case, a coupling constant of $^1J_{2,3} = 111$ Hz was determined, as is typical for an allenic structure.[17] The following chemical shifts and coupling constants were found for the silyl enol ether obtained by addition of an excess of chlorotrimethylsilane to adduct **15b**: $\delta = 120.5$ (C2), 202.2 (C3), 105.8 (C4); $^1J_{2,3} = 116$ Hz (Figure 2b).

Table 3. ^{13}C NMR chemical shifts of the adducts formed by 1,4-addition of $Me_2CuLi \cdot LiI$ to acetylenic ketones **13** in [D_{10}]diethyl ether at $-80\,^\circ$C.

	Substrate	R	Adduct	C2	C3	C4	Me (C4)	C1
1[a]	**13a**	*t*Bu	**15a**	129.66	194.02	108.78	18.21	25.91
				129.52	193.73	108.58		25.79
				129.38		108.46		
				129.26				
2[b]	**13b**	$SiMe_3$	**15b**	127.54	210.20	97.47	20.37	24.99[c]
				127.38	210.17	97.37		
				127.35	210.12[c]	97.34		
				127.18		97.21		

[a] Assignment of the chemical shifts in analogy to those of **15b**; see text. [b] Assignment of the chemical shifts of C2 and C3 by experiments with [2-^{13}C]-**13b**. [c] Coupling constants: $^1J_{1,2} = 46$ Hz; $^1J_{2,3} = 111$ Hz.

The occurence of allenolates **15** as the most stable addition products of organocopper reagents to ynones provides a simple explanation for the limited stereoselectivity of these transformations: the protonation of an allenolate with a strong protonating agent will take place at the oxygen atom to give the allenol, which then tautomerizes unselectively to the corresponding *cis*/*trans*-alkene.[27] The existence of multiple peaks in the ^{13}C NMR spectra, however, cannot easily be interpreted. The adducts **15a** and **15b** are present in the solution as racemic mixtures of enantiomers. In analogy with simpler enolates,[28] theses allenolates may exist as diastereomeric dimeric, tetrameric, or hexameric clusters. An alternative explanation invokes the hypothetical formation of isomeric copper–allenolate π complexes, which have been proposed by Corey and Boaz[29] to account for the high stereoselectivity of S_N2' displacement reactions of chiral 1,3-disubstituted bromoallenes. However, this would require the

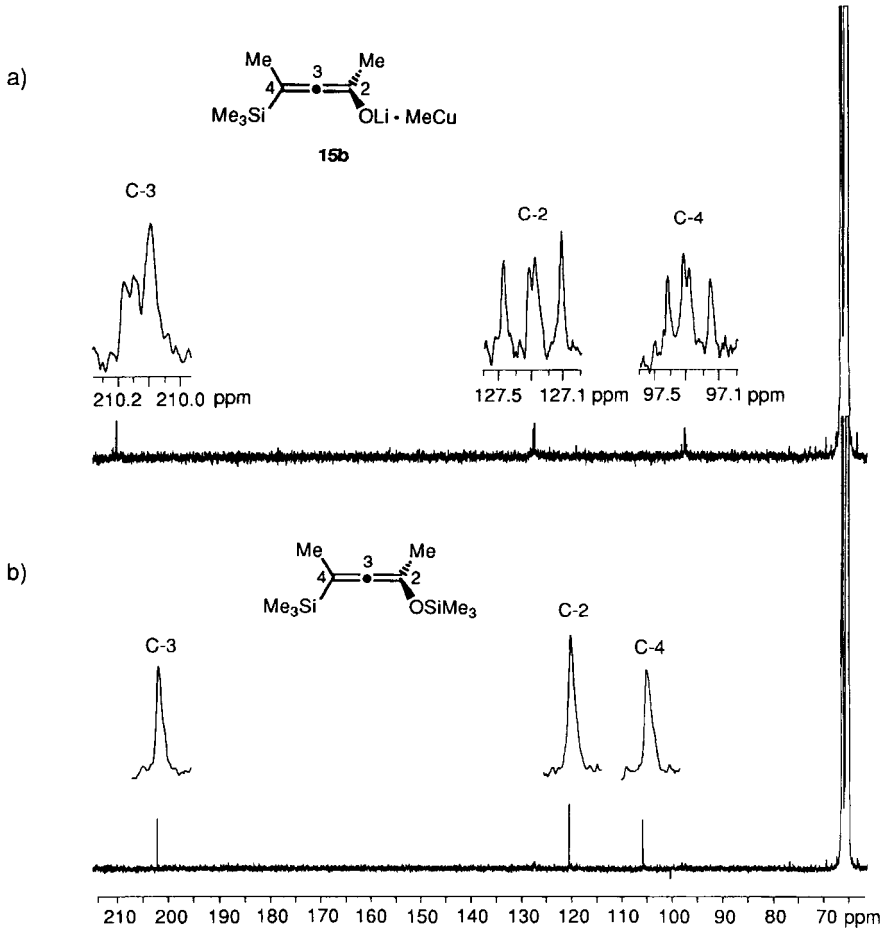


Figure 2. a) ^{13}C NMR spectrum ($-80\,^{\circ}C$) of the adduct **15b** obtained by addition of $Me_2CuLi \cdot LiI$ to **13b** in $[D_{10}]Et_2O$. b) ^{13}C NMR spectrum of the corresponding silyl enol ether formed after addition of 3 equiv of Me_3SiCl to adduct **15b**.

weakly nucleophilic methylcopper to act as π complexation agent, and attempts to detect π complexes of monoorganocopper reagents with enones and enoates by NMR spectroscopy were unsuccessful so far.[30]

Conclusions

We have used ^{13}C NMR chemical shifts and $^{13}C,^{13}C$ coupling constants to characterize the adducts of organocuprates to ynones and ynoates. Alkenylcopper adducts are formed from ynoates and $Me_2CuLi \cdot LiI$ or *t*BuCu(CN)Li, whereas allenolates are obtained from ynoates and $tBu_2CuLi \cdot LiCN$, as well as from ynones and $Me_2CuLi \cdot LiI$. The presence of an equilibrium between the *cis*- and *trans*-alkenylcopper adducts via the lithium allenolate was also established. Together with the earlier observation of a π complex of type **2**, these results allow the formulation of a mechanistic model which is in accordance with all experimental data currently available (Scheme 1).

Thus, the addition of organocuprates to ynoates gives the π complex **2** as primary intermediate, which is then converted into the *cis*-alkenylcuprate *cis*-**3** by regio- and stereoselective carbocupration[1, 7] of the alkyne. Isomerization to the *trans* adduct *trans*-**3** takes place via the lithium allenolate **4** and can be prevented by removal of the lithium ions or their complexation with solvents such as THF. In cases in which the allenolate is the more stable species, it is probably also formed via *cis*-**3** and subsequent rearrangement.[31]

The protonation of the isomeric alkenylcuprates proceeds rapidly and stereospecifically to give the corresponding alkenes, so that the *cis*/*trans* ratio of the isolated products reflects the *cis*/*trans* ratio of the intermediate alkenylcopper adducts. In contrast, the stereoselectivity of the protonation of allenolates is difficult to control, since it may depend on the acidity and steric properties of the proton source and can take place via the corresponding allenol. Thus, reaction conditions which favor the formation of alkenylcuprates rather than allenolates should be used to optimize the stereoselectivity of the addition reaction. Hard electrophiles such as silyl halides, however, always react in accordance with the HSAB principle to give silyl ketene acetals or enol ethers, regardless of the ratio of alkenylcopper and allenolate adducts in solution.

Experimental Section

General: All reactions were carried out under argon and in oven-dried glassware. Nondeuterated solvents were distilled from sodium/benzophenone under a nitrogen atmosphere before use. Deuterated solvents were either used without purification or stored over Deporex (Fluka) and freshly distilled. Unless stated otherwise, commercially available chemicals were used without further purification. Solutions of MeLi (ca. 1.6 M in diethyl ether), *n*BuLi (ca. 2.5 M in hexane) and *t*BuLi (ca. 1.7 M in pentane) were titrated prior to use.[32] In some cases, CuI was purified via its dimethyl sulfide complex ($CuI \cdot 0.75\,Me_2S$[33]), but in general commercially available CuI (99.999%) and CuCN (98%) were used. Chlorotrimethylsilane was distilled and then stored under argon at 8 °C. Low-temperature NMR experiments were carried out on a Varian Unity 500 spectrometer with $[D_{10}]Et_2O$ ($\delta = 14.6$) or $[D_8]THF$ ($\delta = 25.4$) as solvent and internal standard, and routine ^{13}C NMR spectra were recorded with a Varian XL 400 MHz (100.6 MHz) or a Bruker AC-300 spectrometer (75.5 MHz) with $CDCl_3$ as solvent and internal standard ($\delta = 77.0$).

Starting materials: The unlabeled acetylenic esters **6a–e** are either commercially available, or were prepared by esterification of the corresponding acid[34] or methoxycarbonylation of the terminal alkyne.[35] Ketones **13a** and **13b**[36] were obtained by acetylation of the corresponding acetylenes.[37]

The C1-labeled ynoates [1-^{13}C]-**6d** and [1-^{13}C]-**6e** were prepared from lithiated 3,3-dimethyl-1-butyne or lithiated phenylacetylene by treatment with $^{13}CO_2$ (from $Ba^{13}CO_3$) and esterification of the crude acids with diazomethane; overall yield: 31% of [1-^{13}C]-**6d** and 56% of [1-^{13}C]-**6e**.[9b, 14, 38] [1-^{13}C]-**6d**: ^{13}C NMR ($CDCl_3$): $\delta = 154.7$ (C1), 97.1 (C3, $^2J_{1,3} = 19$ Hz), 71.6 (C2, $^1J_{1,2} = 127$ Hz), 52.8 (OMe), 30.1 ($C(CH_3)_3$), 27.7 (C4). [1-^{13}C]-**6e**: ^{13}C NMR ($CDCl_3$): $\delta = 154.6$ (C1), 133.1, 130.8, 128.7 (Ph), 119.6 (C4), 86.7 (C3, $^2J_{1,3} = 20$ Hz), 80.5 (C2, $^1J_{1,2} = 128$ Hz), 52.9 (OMe).

The C3-labeled ynoate [3-^{13}C]-**6d** was prepared according to the procedure of Hamper et al.[39] by treatment of *t*BuLi with $^{13}CO_2$ (from $Ba^{13}CO_3$), conversion of the labeled pivalic acid into the acid chloride with $SOCl_2$, and

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reaction of the latter with methoxycarbonylmethyltriphenylphosphonium bromide. Pyrolysis of the resulting methyl [3-^{13}C]-4,4-dimethyl-3-oxo-2-(triphenylphosphoranylidene)pentanoate gave [3-^{13}C]-**6d** in an overall yield of 19%.[9b, 14, 38] [3-^{13}C]-**6d**: ^{13}C NMR ($CDCl_3$): $\delta = 154.7$ (C1, $^2J_{1,3} =$ 19 Hz), 97.1 (C3), 71.6 (C2, $^1J_{2,3} = 175$ Hz), 52.8 (OMe), 30.2 ($C(CH_3)_3$), 27.7 (C4, $^1J_{3,4} = 64$ Hz).

[2-^{13}C]-4-Trimethylsilyl-3-butyn-2-one ([2-^{13}C]-**13b**) was prepared in 73% yield according to the procedure of Walton and Waugh[36] from [1-^{13}C]-acetyl chloride. ^{13}C NMR ($CDCl_3$): $\delta = 184.6$ (C2), 102.5 (C3, $^1J_{2,3} = 81$ Hz), 97.6 (C4, $^2J_{2,4} = 10$ Hz), 32.7 (C1, $^1J_{1,2} = 47$ Hz), -0.6 ($Si(CH_3)_3$).

Preparation of the NMR samples

Method A: A solution of *t*BuCu(CN)Li was prepared, in a round-bottomed flask (equipped with an argon inlet and septum), by addition of *t*BuLi (0.5 mmol) to a slurry of CuCN (0.5 mmol) in THF (1 mL) at $-40\,^\circ$C. After stirring for 30 min at $-40\,^\circ$C, the solution was cooled to $-80\,^\circ$C, and [D_8]THF (0.5 mL) was added. Equal amounts of the cuprate solution were transferred into two NMR tubes, which were also equipped with septa, cooled to $-80\,^\circ$C; for the transfer, commercially available Teflon tubing (2 mm internal diameter) was used and was inserted directly into the septa. The ^{13}C NMR spectrum of the cuprate was recorded at $-90\,^\circ$C and then a precooled solution ($-90\,^\circ$C) of the substrate (ca. 0.10 mmol in 0.2 mL [D_8]THF) was added. ^{13}C NMR spectra of the mixture were then recorded in the range $-100\,^\circ$C to $-20\,^\circ$C with stepwise temperature increases of 20 °C. In some cases, the temperature was alternately increased and decreased to check for reversible processes. Adducts of the cyano-Gilman cuprate $t\mathrm{Bu_2CuLi \cdot LiCN}$ were prepared analogously with 2 equiv of *t*BuLi.

Method B: A 0.5 mmol solution of *t*BuCu(CN)Li or $t\mathrm{Bu_2CuLi \cdot LiCN}$ in THF was prepared at $-40\,^\circ$C according to method A, but in a two-necked round-bottomed flask equipped with an argon inlet, septum and an attached NMR tube. After stirring for 30 min at $-40\,^\circ$C, the solution was cooled to $-90\,^\circ$C and the substrate (0.5 mmol in 0.5 mL THF) was added. About half of the mixture was removed, quenched with methanol, and analyzed by GC. After the addition of [D_8]THF (0.2 mL) to the remainder of the reaction mixture, the solution was degassed with three freeze/thaw/pump cycles. The mixture was then transferred into the precooled NMR tube, which was then cooled in liquid nitrogen and sealed under vacuum. NMR samples prepared with this method can be stored in liquid nitrogen for months without decomposition.

Method C: In some cases, application of methods A and B to the Gilman cuprate $\mathrm{Me_2CuLi \cdot LiI}$ caused partial decomposition when the reagent was transferred into the NMR tubes. Therefore, the samples were prepared directly in the NMR tubes; however, it is difficult to mix the starting materials thoroughly under these conditions. Thus, CuI (0.14 mmol) was weighed directly into an NMR tube, which was then flushed with nitrogen and equipped with a septum. After addition of [D_{10}]Et_2O (0.4 mL), the tube was cooled to $-40\,^\circ$C and MeLi (0.28 mmol) was added slowly. The NMR tube was then sonicated for 1 min at 0 °C and recooled to $-40\,^\circ$C; this procedure was repeated until the copper salt was completely dissolved (usually three times). The ^{13}C NMR spectrum of the cuprate was recorded at $-90\,^\circ$C, and then the substrate (ca. 0.10 mmol in 0.2 mL [D_{10}]Et_2O) was added at $-90\,^\circ$C. Adducts were prepared analogously in [D_8]THF; however, the substrate was added at $-20\,^\circ$C before cooling the mixture to $-90\,^\circ$C.

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