Notizen / Notes

Allenyl Enolates – A New Class of Chiral Ambident Nucleophiles, 2[1]

Reaction with Iodine and Oxidizing Agents

Norbert Krause* and Silke Arndt

Institut für Organische Chemie der Technischen Hochschule Darmstadt,
Petersenstraße 22, W-6100 Darmstadt, F.R.G.

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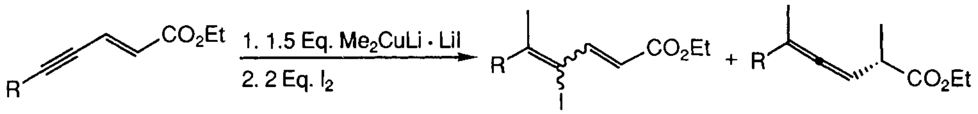
The reaction of allenyl enolates, obtained by 1,6-addition of lithium dimethylcuprate to 2-en-4-ynoates **1a**/**b**, with iodine is studied. Whereas the *n*-butyl-substituted enyne **1a** gives a mixture of vinyl iodide **2a** (48%) and methylated allene **3a** (7%), the *tert*-butyl-substituted enyne **1b** yields allene **3b** (70%) exclusively. The products **2a** and **3a** are also obtained if Br_2, O_2, or $CuCl_2$ are used to trap the allenyl enolate derived from **1a** and $Me_2CuLi \cdot LiI$. These findings are discussed with the assumption that iodo-allene **5** and the iodo-containing Gilman cuprate $[Me_2Cu(I)Li_2]_2$ are acting as intermediates.

In the preceding paper[1] we have shown that allenyl enolates derived from 1,6-addition of organocuprates to acceptor-substituted enynes react with C and Si electrophiles with remarkable regio- and stereocontrol. Another class of electrophiles that is of interest in these trapping reactions is that of the halogenes, in particular iodine. Due to the steric demand of this electrophile, one may expect high regio- and stereoselectivities in the trapping of allenyl enolates; the products may exhibit interesting reactivities for further conversions. Besides, iodine is easily reducible and can therefore act not only as electrophile but also as oxidizing agent; thus, electron transfer could play a role in the reaction with allenyl enolates. Stimulated by these prospects, we examined the reaction of iodine and other oxidizing agents with the allenyl enolates derived by 1,6-addition of lithium dimethylcuprate to 2-en-4-ynoates **1a** and **1b**[2].

Treatment of the allenyl enolate obtained by 1,6-addition of 1.5 eq. of $Me_2CuLi \cdot LiI$ to 1.0 eq. of the *n*-butyl-substituted enynoate **1a** with 2.0 eq. of iodine in diethyl ether at −20°C gave the vinyl iodide **2a** in 48% yield as a 1:5 mixture of the (2*E*,4*E*) and (2*E*,4*Z*) isomers (determined with NOE difference spectra; see Experimental Section); besides, 7% of the 2-methylated allene **3a**[3] (1:1 mixture of diastereomers) was isolated. The product ratio depends on the steric properties of the allenyl enolate: reaction of the *tert*-butyl-substituted enynoate **1b** under the same conditions furnished allene **3b** (70% yield) as the only reaction product, and no vinyl iodide was formed. The ratio of the two products obtained from enynoate

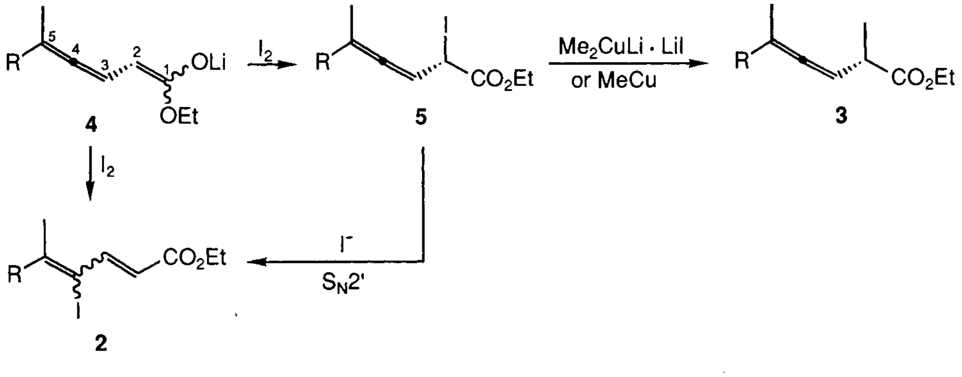


1a: R = n-Bu

1b: R = t-Bu

2a (48%, E : Z = 1 : 5) **3a** (7%, dr = 1 : 1)

— **3b** (70%, dr = 1 : 1)

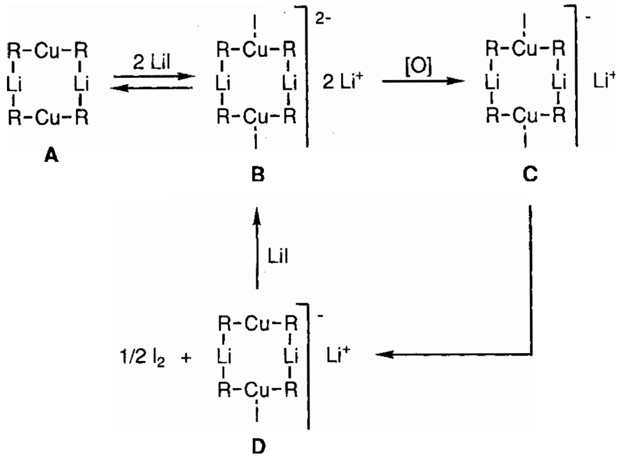


Chem. Ber. **1993**, *126*, 261–263 © VCH Verlagsgesellschaft mbH, D-6940 Weinheim, 1993 0009–2940/93/0101–0261 $ 3.50+.25/0

1a – vinyl iodide **2a** and methylated allene **3a** – was found to depend on the stoichiometry of the reactants and on the presence of additives[2]. Whereas no change of the ratio of **2a**:**3a** = 7:1 resulted when the reaction was performed with LiI-free lithium dimethylcuprate[4] or in the presence of 5.0 eq. of LiI, by the use of a larger excess of the cuprate (5.0 instead of 1.5 eq.) the ratio was shifted to **2a**:**3a** = 1:1.5, i.e. more methylated allene was formed; the same effect was observed when $n\mathrm{Bu_3P}$ was added to the mixture prior to the treatment with iodine (**2a**:**3a** = 1:3).

We explain these results by assuming that the initial trapping of the allenyl enolate **4** takes place mainly or exclusively at C-2 to give the 2-iodo-substituted allene **5**; this is the regioselectivity expected for the reaction of the allenyl enolate with a soft nucleophile[1]. Allene **5** should be highly reactive since the iodine is both in allylic and in α-position to the ester group; it can react either with excess lithium dimethylcuprate and/or methylcopper present in the mixture to give the methylated allene **3**[5] or with iodide by S_N2' substitution to give the vinyl iodide **2**. The latter is the thermodynamically more stable product[1] and does not react with cuprate anymore[5,6]. The competition between the two pathways leading to **2** and **3** is governed by the steric properties of the enolate **4** and by the amount and reactivity of the cuprate. For R = *t*Bu, reaction at C-4 is sterically disfavored; attack of I_2 at C-2 and subsequent nucleophilic substitution with cuprate gives allene **3b** exclusively. For R = *n*Bu, the product distribution depends on the amount and the reactivity of the cuprate; a larger excess of $\mathrm{Me_2CuLi \cdot LiI}$ or addition of $n\mathrm{Bu_3P}$ (giving rise to the formation of the highly reactive $\mathrm{MeCu} \cdot n\mathrm{Bu_3P}$ and $\mathrm{Me_2CuLi} \cdot n\mathrm{Bu_3P}$[7]) favor the pathway leading to the methylated allene **3a**.

Surprisingly, treatment the allenyl enolate derived from **1a** and $\mathrm{Me_2CuLi \cdot LiI}$ with bromine, oxygen, and copper(II) chloride, respectively, furnished the same product mixture as the trapping reaction with iodine, i.e. vinyl iodide **2a** and allene **3a** in a ratio of 7:1. In these cases, the iodine source is the lithium iodide which is produced in the preparation of the cuprate from CuI and MeLi. The vinyl iodide **2a** was also obtained in 31% yield when the allenyl enolate was formed from **1a** and the cyanocuprate $\mathrm{Me_2Cu(CN)Li_2}$ and then treated with I_2. In contrast, no allene **3a** was formed when **1a** was treated with $\mathrm{Me_2Cu(CN)Li_2}$ and $\mathrm{Br_2}$ and $\mathrm{O_2}$, respectively; thus, in accordance with the rationalizations made above, the presence of iodine in the mixture is prerequisite for the formation of the methylated allene **3a**.



The results obtained with $\mathrm{Me_2CuLi \cdot LiI}$ and bromine, oxygen, and copper(II) chloride may be explained by initial oxidation of the LiI to I_2 which is then acting as electrophile; however, O_2 and $\mathrm{CuCl_2}$ are too weak oxidizing agents to oxidize I^- to I_2 in aqueous medium[8]. Rather, it seems that the cuprate takes part in this oxidation[9]. Here, NMR-spectroscopic investigations of CuI-derived Gilman cuprates[4,10] have to be taken into account, which have been interpreted in terms of an equilibrium between $\mathrm{(R_2CuLi \cdot LiI)_2}$ (structure **A**[11], free lithium iodide) and $\mathrm{[R_2Cu(I)Li_2]_2}$ (structure **B**, iodide bound to the copper in analogy to higher-order cyanocuprates[12]). Oxidation of the electron-rich complex **B** could give species **C**; the latter bears electrophilic iodine and could transfer this to the allenyl enolate to give the trapping products **2**/**3**, or it could eliminate iodine which then reacts as electrophile with the enolate. The cuprate **D** could again add lithium iodide to yield **B**. Thus, the trapping reactions studied here can be explained by assuming that iodo-allene **5** and the iodo-containing Gilman cuprate $\mathrm{[Me_2Cu(I)Li_2]_2}$ are acting as intermediates; besides, they are also interesting from the preparative point of view, as is shown by the selective formation of allene **3b**.

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Experimental

General Information: See ref.[13] – The NMR data for the major isomer of a mixture are marked with an asterisk (*).

Ethyl (2E,4E)- and (2E,4Z)-4-Iodo-5-methyl-2,4-nonadienoate (**2a**) *and Ethyl 2,5-Dimethyl-3,4-nonadienoate* (**3a**) *from* **1a** *and* $\mathrm{Me_2CuLi \cdot LiI/I_2}$: To a suspension of 0.86 g (4.5 mmol) of copper(I) iodide in 20 ml of diethl ether was added dropwise at 0°C 6.0 ml (9.0 mmol) of methyllithium (1.5 M solution in diethyl ether). After stirring for 15 min at 0°C the mixture was cooled to −20°C, and a solution of 0.54 g (3.0 mmol) of **1a** in 10 ml of diethyl ether was added dropwise. Stirring at −20°C was continued for 1 h, followed by addition of a solution of 1.52 g (6.0 mmol) of iodine in 15 ml of diethyl ether. After stirring for another 1 h at −20°C the mixture was poured into vigorously stirred 2 N $\mathrm{H_2SO_4}$ (15 ml). The copper salts and excess of acid were removed by filtration through Celite; the filtrate was dried with $\mathrm{MgSO_4}$ and concentrated in vacuo. The crude product consists of a 7:1 mixture of **2a** and **3a** (^{1}H-NMR spectroscopy) and was separated by column chromatography ($\mathrm{SiO_2}$, diethyl ether/hexane, 1:20) to give 0.46 g (48%) of **2a** [1:5 mixture of the (2*E*,4*E*) and (2*E*,4*Z*) isomers] and 0.04 g (7%) of **3a** (1:1 mixture of diastereomers)[1] as slightly yellow oils.

2a: IR: $\tilde{\nu}$ = 1720 cm^{-1} (s, C=O), 1610 (s, C=C). – ^{1}H NMR: δ = 0.87–0.97 (m, 3H, 9-H), 1.28–1.55 (m, 4H, 7-, 8-H), 1.30/1.31* (2 t, 3H, 2 × *J* = 7.0 Hz, $\mathrm{OCH_2C}H_3$), 2.17 (d, 3H, *J* = 2.4 Hz, 5-$\mathrm{CH_3}$), 2.44–2.58 (m, 2H, 6-H), 4.21/4.22* (2 q, 2H, 2 × *J* = 7.0 Hz, $\mathrm{OCH_2}$), 5.80 (d, *J* = 14.8 Hz, 2-H), 6.18* (d, *J* = 15.6 Hz, 2-H), 7.33* (dd, *J* = 2.4/15.6 Hz, 3-H), 7.87 (d, *J* = 14.8 Hz, 3-H). NOE difference spectra (irradiation at → intensity enhancement at): 2.17 (5-$\mathrm{CH_3}$) → 7.33* (3-H); 7.33* (3-H) → 2.17 (5-$\mathrm{CH_3}$); 6.18* (2-H) → no effect. – ^{13}C NMR: δ = 13.8/14.2 (2+, C-9, $\mathrm{OCH_2CH_3}$), 20.0/31.7* (2+, 5-$\mathrm{CH_3}$), 22.2/22.5 (2-, C-8), 29.3/30.8 (2-, C-7), 35.5/45.9 (2-, C-6), 60.3 (–, $\mathrm{OCH_2}$), 96.6/98.0* (2×, C-4), 125.8*/126.1 (2+, C-2), 141.5*/142.0 (2+, C-3), 154.5/155.5* (2×, C-5), 166.9 (×, C-1). – MS, *m/z* (%): 322 (40) [M^+], 95 (100). – The vinyl iodide **2a** is rather unstable; even after repeated purification a correct elemental analysis could not be obtained.

$\mathrm{C_{12}H_{19}IO_2}$ (322.2) Calcd. C 44.74 H 5.94
Found C 46.91 H 6.26

2a *from* **1a** *and* $\mathrm{Me_2Cu(CN)Li_2/I_2}$: From 0.13 g (1.5 mmol) of CuCN in 10 ml of diethyl ether, 2.0 ml (3.0 mmol) of MeLi (1.5 M solution in diethyl ether), 0.18 g (1.0 mmol) of **1a** in 10 ml of diethyl ether, and 0.51 g (2.0 mmol) of I_2 in 10 ml of diethyl ether according to the above procedure. Yield: 0.10 g (31%) of **2a** as 1:5 mixture of the (2*E*,4*E*) and (2*E*,4*Z*) isomers.

Ethyl 2,5,6,6-Tetramethyl-3,4-heptadienoate (**3b**): From 1.33 g (7.0 mmol) of CuI in 30 ml of diethyl ether, 9.3 ml (14.0 mmol) of MeLi (1.5 M solution in diethyl ether), 0.72 g (4.0 mmol) of **1b** in 10 ml of diethyl ether, and 2.03 g (8.0 mmol) of iodine in 20 ml of diethyl ether according to the above procedure; yield: 0.59 g (70%) of **3b** (1:1 mixture of diastereomers)[1].

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[231/92]

CAS Registry Numbers

1a: 64576-91-6 / **1b**: 54599-49-4 / **2a** (2*E*,4*E*): 143193-02-6 / **2a** (2*E*,4*Z*): 143193-03-7 / **3a** (*R**,*R**): 143193-04-8 / **3a** (*R**,*S**): 143289-16-1 / **3b** (*R**,*S**): 143215-14-9 / **3b** (*R**,*R**): 143290-25-9