EurJOC
European Journal of Organic Chemistry

A Journal of ChemPubSoc Europe

Accepted Article

Title: Carboboration of Alkynes with Cyclodextrin-Encapsulated N-Heterocyclic Carbene Copper Complexes

Authors: Zhonghang Wen, Yongmin Zhang, Sylvain Roland, and Matthieu Sollogoub

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201900246

Link to VoR: http://dx.doi.org/10.1002/ejoc.201900246

Supported by ACES Asian Chemical Editorial Society

WILEY-VCH

Carboboration of Alkynes with Cyclodextrin-Encapsulated *N*-Heterocyclic Carbene Copper Complexes

Zhonghang Wen,[a] Yongmin Zhang,[a] Sylvain Roland,*[a] and Matthieu Sollogoub*[a]

Abstract: The copper-catalyzed carboboration of various alkynes was investigated with a modified *N*-heterocyclic carbene-capped α-cyclodextrin copper(I) complex in which the reactive copper center is deeply encapsulated in the cyclodextrin (CD) cavity. The methylborylation of terminal alkynes was found to give linear (**L**) (*E*)-vinyl boron isomers as the major isomers, as expected from the previously proposed "perpendicular" approach of the alkyne to the Cu–B bond, and methylation of the vinyl boron copper intermediate. Under similar conditions, the intramolecular carboboration reaction with terminal alkynes functionalized by alkyl halides, led to exocyclic vinyl boronate species as the major isomer. However, an endocyclic (*Z*)-isomer was also observed in some cases. This isomer was not previously observed and is unexpected considering the "classical" mechanism. The direct generation of boron functionalized (*Z*)-alkenes by carboboration of alkynes is unprecedented.

Introduction

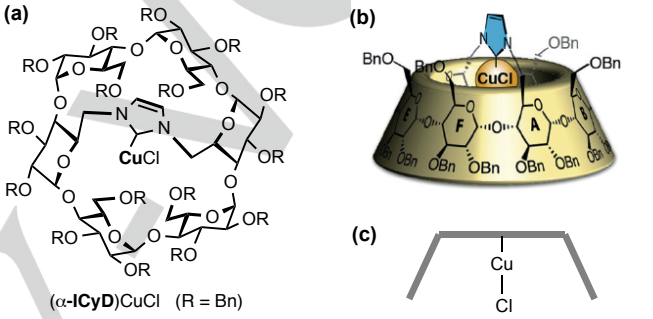
We previously described (**ICyD**)CuCl complexes in which the copper(I) center is deeply encapsulated in the cavity of a protected cyclodextrin (α or β-CD) (Figure 1).[1] The copper center is maintained in the cavity in a well-defined position through ligation by an *N*-heterocyclic carbene (NHC) ligand which covalently caps the primary rim of the CD.

Cavitand-based and other encapsulated metal complexes offer interesting opportunities to control selectivity in metal-catalyzed reactions.[2] (**α-ICyD**)CuCl, derived from benzyl-protected α-CD as cavitand, was previously shown to catalyze the formal hydroboration of terminal alkynes in the presence of $(Bpin)_2$ and MeOH, [3] to give linear (**L**) vinyl boron species as the major isomers (Scheme 1a).[4] Due to the high steric constraint imposed by the α-CD cavity, the regioselectivity in favor of the linear isomer observed with (**α-ICyD**)CuCl could not be explained by the classical "parallel" approach of the alkyne to the Cu–B bond.[5] To account for the observed regioselectivity, an alternative "perpendicular" approach was proposed which was supported by DFT calculations (Scheme 1a).[4] Interestingly, changing the nature/size of the CD from α-CD to the larger β-CD was found to induce a switch in mechanism and regioselectivity.

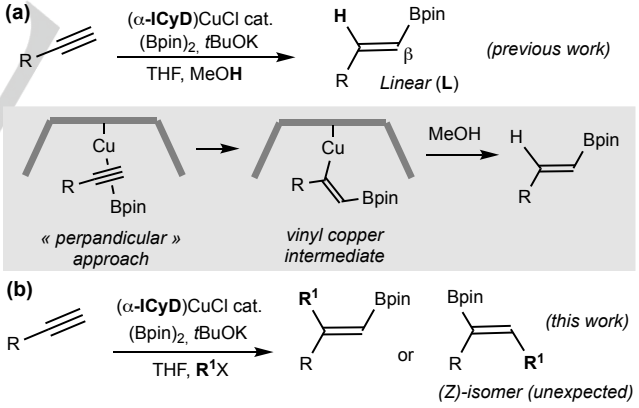
[a] Z. Wen, Dr. Y. Zhang, Dr. S. Roland and Prof. M. Sollogoub
Institut Parisien de Chimie Moléculaire UMR CNRS 8232
Sorbonne Université – Campus P. et M. Curie
4, Place Jussieu, 75005 Paris (France)
E-mail: sylvain.roland@sorbonne-universite.fr
matthieu.sollogoub@sorbonne-universite.fr
Homepage:http://ipcm.fr/-Glycochimie-Organique

Supporting information for this article is given via a link at the end of the document.

Figure 1. Representations of cyclodextrin-*N*-heterocyclic carbene copper(I) complex (**α-ICyD**)CuCl: (a) Developed structure showing the α-CD macrocycle; (b) 3-Dimensional side-view of the complex; (c) Schematic representation of the CD cavity with the encapsulated copper(I) center.



Herein we present our results concerning the carboboration reaction catalyzed by (**α-ICyD**)CuCl (Scheme 1b).[3,6,7,8] This includes investigation of the methyl borylation of a series of terminal alkynes and examples of intramolecular carboboration reactions, the latter giving in some cases unexpected results in terms of regioselectivity.

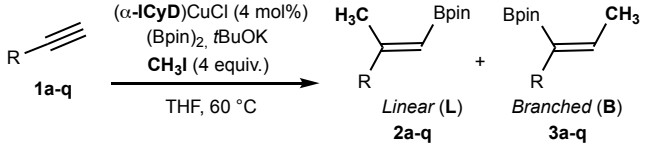


Scheme 1. Copper-catalyzed borylation of alkynes with CD-NHC-based ligands: (a) Previously reported formal hydroboration and perpendicular approach of the alkyne with (**α-ICyD**)CuCl; (b) Carboboration reactions described in the present study.

Results and Discussion

A few examples of application of (NHC)CuCl complexes in the carboboration reaction of internal or terminal alkynes have been reported.[9,10] To explore the efficiency and regioselectivity of the $(Bpin)_2$-mediated carboboration of alkynes in the cavity of (**α-ICyD**)CuCl, we first investigated the methylboration of phenyl acetylene as a model reaction (Scheme 2, R = Ph). Under the optimized conditions, a conversion of 96% was obtained by

using 4 mol % of (**α-ICyD**)CuCl and 4 equiv. of CH_3I. The linear (**L**) vinyl boron isomer **2a** was obtained with high regioselectivity (>99/1) with no detectable trace of the branched (**B**) isomer in the crude reaction mixture (Table 1, entry 1). To accelerate the conversion, the reaction was run at 60 °C. After 24 h of reaction and standard work-up, **2a** was isolated in 74% yield. Decreasing the temperature to 20 °C led to lower conversion and yield but the high regioselectivity in favor of the linear isomer is maintained (Table 1, entry 2). In contrast, with a lower catalyst charge of 2 mol%, a noticeable drop in selectivity was observed (96/4, Table 1, entry 3), although the isolated yield is slightly improved (78%).



Scheme 2. Copper-catalyzed methylboration of alkynes with the α-CD-NHC-based ligand **α-ICyD**.

Table 1. Copper-catalyzed methylboration of alkynes.[a]

Entry	**Alkyne** (R)	Convn %[b]	Yield % (**2**+**3**)[b]	ratio **2**/**3**[c]
1	**1a** (Ph)	96	74	>99/1 (**2a**:**3a**)
2[d]	**1a** (Ph)	79	51	>99/1 (**2a**:**3a**)
3[e]	**1a** (Ph)	93	78	96/4 (**2a**:**3a**)
4	**1b** (*p*-Me-Ph)	87	62	94/6 (**2b**:**3b**)
5	**1c** (*m*-Me-Ph)	92	70	95/5 (**2c**:**3c**)
6	**1d** (*p*-OMe-Ph)	60	44	91/9 (**2d**:**3d**)
7	**1e** (*m*-OMe-Ph)	65	49	97/3 (**2e**:**3e**)
8	**1f** (*o*-OMe-Ph)	47	23	98/2 (**2f**:**3f**)
9	**1g** (*p*-Cl-Ph)	99	59	98/2 (**2g**:**3g**)
10	**1h** (*m*-Cl-Ph)	90	49	96/4 (**2h**:**3h**)
11	**1i** (*o*-Cl-Ph)	>99	38	99/1 (**2i**:**3i**)
12	**1j** (*p*-F-Ph)	83	56	99/1 (**2j**:**3j**)
13	**1k** (*o*-F-Ph)	90	58	96/4 (**2k**:**3k**)
14	**1l** (*p*-CF_3-Ph)	83	50	96/4 (**2l**:**3l**)
15	**1m** (*m*-CF_3-Ph)	91	51	95/5 (**2m**:**3m**)
16	**1n** (*o*-CF_3-Ph)	>99	43	>99/1 (**2n**:**3n**)
17[e]	**1o** ($BnOCH_2$)	89	54	87/13 (**2o**:**3o**)
18[f]	**1a** (Ph)	82	56	82/18 (**2a**:**3a**)

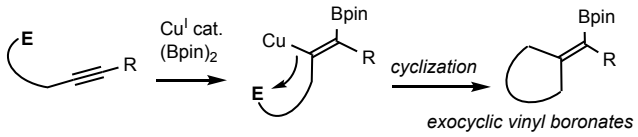
[a] 1.3 Equiv. of $(Bpin)_2$ and *t*BuOK were used, reaction time 24 h; [b] Conversion of the alkyne and NMR yield determined by ^{1}H NMR analysis of the crude reaction mixture by comparison with the internal reference (1,3,5-trimethoxybenzene, 0.33 equiv.); [c] **L**/**B** ratio determined by ^{1}H NMR analysis of the crude reaction mixture; [d] Reaction performed at 20 °C; [e] Reaction performed with 2 mol% of (**α-ICyD**)CuCl; [f] Control experiment performed with 4 mol% of (**IPr**)CuCl.

Under these optimized conditions, the scope of the methylboration reaction was investigated with a series of aromatic terminal alkynes (**1b-n**) substituted by various electron withdrawing or donating groups at the *o*, *m*, or *p* positions of the phenyl ring. In all these examples, the linear (**L**) isomer **2** was consistently obtained as the major isomer with selectivities ranging from 91/9 to >99/1 (ratio **2**/**3**). It is worth to note, that for the lowest selectivity, observed with *p*-OMe-phenyl acetylene (Table 1, entry 6), the linear isomer **2** is still strongly predominant (**2d**/**3d** = 91/9). Furthermore, the electronic properties of the aromatic substituent seem to have no direct effect on conversions and isolated yields, the best results being reached with phenylacetylene (**1a**, R = H, 74%) and *m*-methyl-substituted substrate **1c** (70%) (Table 1, entry 5), whereas **1g** (R = *p*-Cl) (Table 1, entry 9) and **1k** (R = *o*-F) (Table 1, entry 13), for instance, gave very close yields (58-59%) and similar selectivities. Substitution at the *ortho* position led in several cases (**1f**, **1i**, **1n**) to a decrease in yields but without effect on selectivity. The most significant drop in selectivity (87/13) was observed with **1o** for which the alkyne is substituted by an alkyl group (R = CH_2OBn, Table 1, entry 17). A control experiment performed with the classical bulky NHC ligand **IPr** (1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) instead of the CD-based NHC ligand **α-ICyD**, led to a significant drop in selectivity (**2a**/**3a** = 82/18) (Table 1, entry 18), thus demonstrating the importance of **α-ICyD** structure for controlling selectivity. The low sensitivity to alkyne electronic properties observed here with **α-ICyD** as ligand was already observed in the formal hydroboration reaction catalyzed by (**α-ICyD**)CuCl and with other bulky *N*-alkyl-substituted (NHC)CuCl complexes.[4,5a] To account for this effect, it was suggested that copper–alkyne coordination is the product-determining step.[11]

Furthermore, the low reaction rate observed with CH_3I as the electrophile, compared with MeOH (previous work),[4] suggests that the reaction of the CD-embedded vinyl boron copper intermediate with the alkyl halide might be important in the kinetics of the reaction.[12]

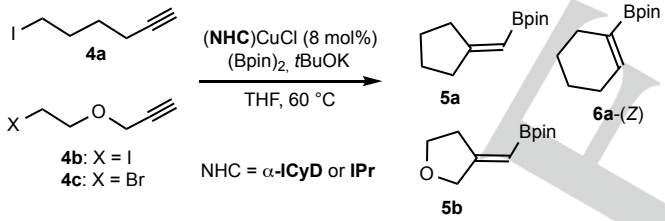
Next, the potential of (**α-ICyD**)CuCl was examined in the intramolecular copper-catalyzed carboboration reaction.[3,13] This cyclization reaction can lead either to cyclic alkylboronates or to alkenylboronates starting from alkenes or alkynes, respectively. Both structures are relevant for further synthetic transformations and are versatile intermediates for organic synthesis. A few copper-catalyzed intramolecular carboboration reactions have been described from both internal and terminal alkynes.[14] The reaction, initially reported with propargyl ethers by Lin's group in 2013,[14a] was found to give exocyclic alkenyl boronates through intramolecular reaction of the boron vinyl copper intermediate with the internal electrophile (Figure 2).

Figure 2. Intramolecular carboboration reaction. Schematic representation of the cyclization of electrophile-containing alkynes.



Our previous observations in the formal hydroboration reaction of alkynes catalyzed by (**α-ICyD**)CuCl, showed that internal alkynes reacted much slower than terminal alkynes due to important steric interactions with the CD cavity.[4] In the present study, we focussed on the cyclization of terminal alkynes for which very few examples have been reported in the literature.[14c,d]

Using simple halogenoalkyl chains (non activated electrophiles) as internal electrophiles was previously found not favourable for the intramolecular carboboration to take place. For instance, the reaction with a terminal alkyne such as 6-bromo-1-hexyne was reported by Ito's group to give low yields (8%) of cyclized compound **5a**, by using CuCl/(*o*-tol)$_3$P as catalytic system (THF, 30 °C).[14c] Similarly, the Wang and Zhao's group initially noticed that the cyclization of internal acetylenic iodides such as 6-iodo-1-phenyl-1-hexyne did not proceed with CuCl/(*n*-Bu)$_3$P as catalyst (THF, rt).[14e] The cyclization of this internal phenyl-substituted iodo alkyne (R = Ph, Figure 2) has been optimized to give the expected vinylboronate in 64% yield. However, the application of the same catalytic system to terminal alkynes was not reported.



Scheme 3. Intramolecular carboboration of alkynes catalyzed by (**α-ICyD**)CuCl or (**IPr**)CuCl. **IPr** = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene.

Table 2. (**α-ICyD**)CuCl-catalyzed intramolecular carboboration of alkynes.[a]

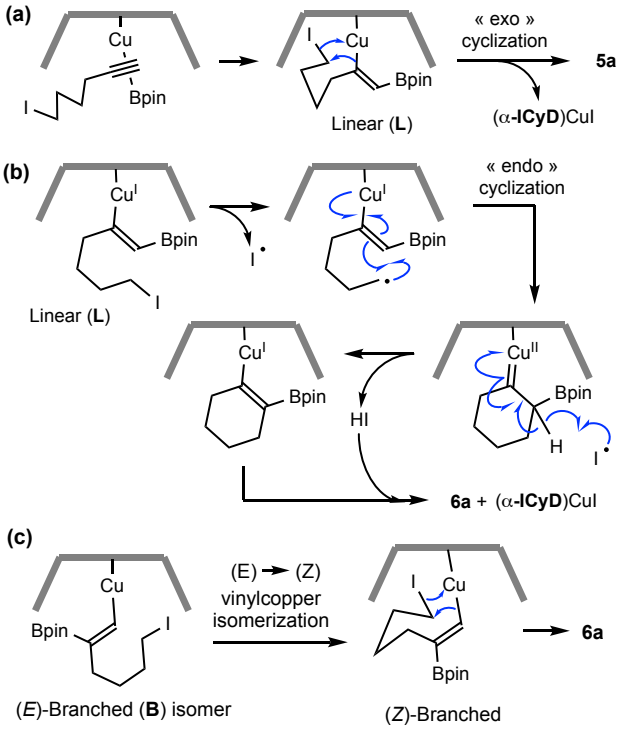
Entry	Alkyne	NHC	Convn %[a]	Yield %[b]	Ratio **5**/**6**[c]
1	**4a**	**α-ICyD**	>99	50	60:40
2[d]	**4a**	**α-ICyD**	>99	49	94:6
3	**4a**	**IPr**	>99	61	41:59
4	**4b**	**α-ICyD**	>99	40	>99:1
5	**4c**	**α-ICyD**	>99	51	>99:1
6	**4b**	**IPr**	>99	>99	>99:1

[a] 2 Equiv. of (Bpin)$_2$ and *t*BuOK were used; [b] Conversion of the alkyne determined by ^{1}H NMR analysis of the crude reaction mixture by comparison with the internal reference; [b] Isolated yield; [c] **5**/**6** ratio determined by ^{1}H NMR analysis of the crude reaction mixture; [d] The solution of base (*t*BuOK 1 M in THF) was slowly added over 1 h.

We first investigated the cyclization of the simple iodoalkyl-substituted terminal alkyne **4a** (6-iodo-1-hexyne, Scheme 3). The reaction of **4a** in the presence of 8 mol % of (**α-ICyD**)CuCl was found to give cyclized vinyl boronates **5a**/**6a** in 50 % isolated yield. The reaction is slow, and requires about 24 h of heating at 60 °C in THF to get optimized yields. Interestingly, the reaction consistently gave, in repeated experiments, a ratio of c.a. 60:40 of the expected exocyclic vinyl boronate **5a** and an endocyclic six-membered (*Z*)-vinyl boronate **6a** (Table 2, Entry 1).

The formation of **5a** (already observed in low yield from 6-bromo-1-hexyne),[14c] is expected from "*exo*" cyclization of the intermediate linear (**L**) copper vinyl boronate, which is expected to be the major isomer in the first reaction step (Scheme 4a). In contrast, the formation of **6a** is unexpected and unprecedented. The cyclohexyl boronate **6a** formally results from an "*endo*" cyclization of the linear (**L**) copper vinyl boronate. A radical mechanism might be proposed for its formation as shown in Scheme 4b. The formation of an alkyl radical from acetylenic halide reduction with concomitant oxidation of a copper(I)-Bpin species to copper(II) was previously proposed for the formation of **5a**.[14e] However, the primary radical that may be generated from 6-iodo-1-hexyne **4a**, is not expected to proceed into a 6-*endo* cyclization process to give **6a**. Consequently, we proposed here that an intramolecular radical cyclization takes place in the cavity of the (**α-ICyD**)CuCl catalyst from the copper vinyl boronate intermediate. This mechanism allows for regeneration of (**α-ICyD**)CuI as catalyst. It goes through a copper(II) intermediate whose formation could be favoured by the strong electron donating NHC ligand. We also observed, that decreasing the concentration of *t*BuOK in the medium by slow addition over 1 h, led to a dramatic decrease of the amount of **6a** (Table 2, Entry 2).[15] This effect of *t*BuOK concentration on **5a**/**6a** ratio could not be clearly rationalized.[16] Another possible pathway for the formation of the six-membered cycle **6a** involves (*E*)→(*Z*) isomerization of the minor branched (**B**) vinyl copper boronate isomer followed by cyclization (Scheme 4c).[17] However, our attempts to promote **6a** formation under photocatalytic conditions to favor isomerization,[17] were unsuccessful, the ratio **5a**/**6a** remaining unchanged (data not shown). To the best of our knowledge, the application of classical NHC ligands such as **IPr** in the intramolecular copper-catalyzed carboboration reaction of terminal alkynes has not been reported.[9,10] Therefore, the cyclization of **4a** was also investigated with (**IPr**)CuCl as catalyst. The reaction was found to give a mixture of cyclized vinyl boronates **5a**/**6a** in 61% yield. More interestingly, a **5a**/**6a** ratio of 41:59 was obtained, showing that the NHC ligand **IPr** not only efficiently promotes cyclization of simple terminal alkynes but also favors the formation of the unexpected six-membered vinylboronate **6a**.

Finally, based on recent results showing that intramolecular carboboration reactions gave improved yields with propargyl ether derivatives,[14c] we studied the cyclization of **4b**/**4c** with (**α-ICyD**)CuCl or (**IPr**)CuCl as catalysts. In all cases, we observed exclusively the formation of the exocyclic five-membered vinyl boronates **5a** or **5b**, with no detectable traces of six-membered endocyclic vinyl boronate (Table 2, entries 4–6).



Scheme 4. Possible mechanisms for intramolecular carboboration reactions catalyzed by (**α-ICyD**)CuCl: (a) "Classical" *exo* cyclization leading to isomer **5a**; (b) Proposed radical pathway involving *endo* cyclization to get the unexpected isomer **6a**; (c) Isomerization of the (*E*)-branched isomer and cyclization of the as-formed (*Z*) isomer to give **6a**.

Conclusions

We have shown here that the α-CD-based NHC–copper(I) complex (**α-ICyD**)CuCl, in which the reactive metallic center is deeply encapsulated in the cavity of α-CD, catalyzed the methyl boration of terminal alkynes with high selectivity in favor of linear (**L**) (*E*)-vinyl boron isomers. This selectivity is similar to that previously observed in the formal hydroboration reaction, and is consistent with the previously proposed "perpendicular" approach of the alkyne to the Cu–B bond. The reaction is relatively insensitive to the electronic properties of the alkynes and significantly slower than the formal hydroboration reaction, suggesting strong substrate/cavity interactions in the initial alkyne approach and in the reaction of alkyl halides with the encapsulated vinyl boron copper intermediate. In addition, we have demonstrated that (**α-ICyD**)CuCl catalyzed the intramolecular carboboration of challenging alkynes substrates such as simple acetylenic halides to give cyclized vinyl boron species in moderate yields. An unprecedented formal *endo*-type cyclization of a copper vinyl boronate intermediate to give a cyclohexenyl boronate was observed. This intriguing regioselectivity was also observed with the bulky NHC ligand **IPr** suggesting an effect of the NHC ligand capping the cavity. The mechanism remains to be elucidated and should be further explored.

Experimental Section

General: All reactions were performed under an argon atmosphere using well-dried reaction flask. Unless stated otherwise, reactants were purchased from commercial sources and used as received without further purification. All the solvents used as reaction media were distilled. Column chromatography was performed with silica gel (100–200 mesh). NMR spectra were recorded on a Bruker 300 MHz or 400 MHz, using the signal of the residual solvent as an internal reference. The high-resolution mass spectroscopy (HRMS) was performed on a Bruker micrOTOF spectrometer, using Agilent ESI-L Low Concentration Tuning-Mix as reference.

Starting Materials and Reagents

(**α-ICyD**)CuCl was synthesized according to our previously published procedure.[1a] Alkynes **1o**,[18] **4b**,[19] and **4c**,[20] were prepared according to reported procedures.

Standard procedure for the methylboration of alkynes catalyzed by (α-ICyD)CuCl (Table 1).

An oven-dried screwed tube was charged with (**α-ICyD**)CuCl (0.01 mmol, 29.0 mg) and bis(pinacolato)diboron ($(Bpin)_2$, 0.30 mmol, 75.2 mg). After being sealed with a septum, the tube was purged by 3 vacuum-argon cycles. THF (0.5 mL) was added and the mixture was stirred for 5 min at 20 °C. A solution of *t*BuOK 1.0 M in THF (0.3 mL) was added. After stirring for 30 min, the alkyne (0.23 mmol) was added (neat or dissolved in the minimal amount of THF if solid) followed by MeI (0.91 mmol, 56.7 μL). The tube was sealed with a screw cap and the mixture was stirred at 60 °C for 24 h. After cooling, the crude reaction mixture was filtered through a short pad of celite by rinsing with diethyl ether, and concentrated under vacuum. The crude residue was purified by silica gel chromatography (cyclohexane/diethyl ether). The conversion of the alkyne and NMR yield of the product were determined by ^{1}H NMR analysis of the crude reaction mixture by comparison with the internal reference (1,3,5-trimethoxybenzene). The regioselectivity of the reaction was determined by ^{1}H NMR analysis of the crude reaction mixture.

(*E*)-4,4,5,5-Tetramethyl-2-(2-phenylprop-1-enyl)-1,3,2-dioxaborolane (**2a**): R_f = 0.5 (cyclohexane/diethyl ether, 12:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.47 (m, 2H), 7.36–7.26 (m, 3H), 5.76 (d, *J* = 0.9 Hz, 1H), 2.42 (d, *J* = 0.9 Hz, 3H), 1.32 (s, 12H) ppm. The NMR data are in agreement with the literature.[21]

(*E*)-4,4,5,5-Tetramethyl-2-(2-*p*-tolylprop-1-enyl)-1,3,2-dioxaborolane (**2b**): R_f = 0.35 (cyclohexane/diethyl ether, 20:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 5.74 (s, 1H), 2.40 (s, 3H), 2.34 (s, 3H), 1.31 (s, 12H) ppm. The NMR data are in agreement with the literature.[22]

(*E*)-4,4,5,5-Tetramethyl-2-[2-(*m*-tolyl)prop-1-en-1-yl]-1,3,2-dioxaborolane (**2c**): R_f = 0.35 (cyclohexane/diethyl ether, 20:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30 (d, *J* = 9.3 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 5.75 (d, *J* = 0.8 Hz, 1H), 2.40 (d, *J* = 0.8 Hz, 3H), 2.35 (s, 3H), 1.32 (s, 12H) ppm. The NMR data are in agreement with the literature.[21]

(*E*)-2-[2-(4-Methoxyphenyl)prop-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2d**): R_f = 0.4 (cyclohexane/diethyl ether, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 9.0 Hz, 2H), 6.85 (d, *J* = 9.0 Hz, 2H), 5.70 (d, *J* = 0.9 Hz, 1H), 3.81 (s, 3H), 2.39 (d, J = 0.9 Hz, 3H), 1.31 (s, 12H) ppm. The NMR data are in agreement with the literature.[21]

(*E*)-2-[2-(3-Methoxyphenyl)prop-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2e**): R_f = 0.4 (cyclohexane/diethyl ether, 10:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 7.9 Hz, 1H), 7.14–7.01 (m, 2H), 6.83 (ddd, *J* = 8.1, 2.5, 0.8 Hz, 1H), 5.76 (d, *J* = 0.8 Hz, 1H), 3.81 (s, 3H), 2.40

(d, *J* = 0.8 Hz, 3H), 1.32 (s, 12H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.58, 157.80, 145.55, 129.19, 118.55, 113.76, 111.53, 83.11, 55.37, 25.04, 20.33 ppm. HRMS (ESI, micro TOF) *m*/*z*: calcd for $C_{16}H_{23}BNaO_3$ $[M+Na]^+$ 297.1635, found 297.1635.

(*E*)-2-[2-(2-Methoxyphenyl)prop-1-en-1-yl)]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2f**): R_f = 0.4 (cyclohexane/diethyl ether, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 – 7.20 (m, 1H), 7.18 (dd, *J* = 7.4, 1.9 Hz, 1H), 6.97– 6.86 (m, 1H), 5.41 (q, *J* = 1.0 Hz, 1H), 3.80 (s, 3H), 2.34 (d, *J* = 1.0 Hz, 3H), 1.30 (s, 12H) ppm. The NMR data are in agreement with the literature.[21]

(*E*)-2-[2-(4-Chlorophenyl)prop-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2g**): R_f = 0.45 (cyclohexane/diethyl ether, 12:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 8.8 Hz, 2H), 7.28 (d, *J* = 8.8 Hz, 2H), 5.73 (d, *J* = 0.9 Hz, 1H), 2.38 (d, *J* = 0.9 Hz, 3H), 1.31 (s, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.45, 142.34, 133.91, 128.42, 127.27, 83.21, 25.03, 20.13 ppm. HRMS (ESI, micrOTOF) *m*/*z*: calcd for $C_{15}H_{20}BClNaO_2$ $[M+Na]^+$ 301.1140, found 301.1149.

(*E*)-2-[2-(3-Chlorophenyl)prop-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2h**): R_f = 0.45 (cyclohexane/diethyl ether, 12:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.43 (m, 1H), 7.39–7.33 (m, 1H), 7.26–7.22 (m, 2H), 5.75 (d, *J* = 0.8 Hz, 1H), 2.38 (d, *J* = 0.8 Hz, 3H), 1.31 (s, 12H) ppm. The NMR data are in agreement with the literature.[21]

(*E*)-2-[2-(2-Chlorophenyl)prop-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2i**): R_f = 0.45 [cyclohexane/diethyl ether (12:1)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.31 (m, 1H), 7.21–7.16 (m, 3H), 5.34 (q, *J* = 1.0 Hz, 1H), 2.33 (d, *J* = 1.1 Hz, 3H), 1.32 (s, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.83, 145.70, 131.06, 129.68, 129.27, 128.24, 126.74, 83.18, 25.08, 22.23 ppm. HRMS (ESI, micrOTOF) *m*/*z*: calcd for $C_{15}H_{20}BClNaO_2$ $[M+Na]^+$ 301.1140, found 301.1134.

(*E*)-2-[2-(4-Fluorophenyl)prop-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2j**): R_f = 0.45 (cyclohexane/diethyl ether, 12:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.43 (m, 2H), 7.03–6.96 (m, 2H), 5.70 (d, *J* = 0.7 Hz, 1H), 2.38 (d, *J* = 0.9 Hz, 3H), 1.31 (s, 12H) ppm. The NMR data are in agreement with the literature.[21]

(*E*)-2-[2-(2-Fluorophenyl)prop-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2k**): R_f = 0.45 (cyclohexane/diethyl ether, 12:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (td, *J* = 7.7, 1.8 Hz, 1H), 7.22 (dddd, *J* = 8.1, 6.9, 5.0, 1.8 Hz, 1H), 7.07 (td, *J* = 7.5, 1.2 Hz, 1H), 7.01 (ddd, *J* = 11.1, 8.2, 1.1 Hz, 1H), 5.55 (s, 1H), 2.38 (dd, *J* = 1.6, 1.1 Hz, 3H), 1.31 (s, 12H) ppm. The NMR data are in agreement with the literature.[21]

(*E*)-4,4,5,5-Tetramethyl-2-{2-[4-(trifluoromethyl)phenyl]prop-1-en-1-yl}-1,3,2-dioxaborolane (**2l**): R_f = 0.5 (cyclohexane/diethyl ether, 12:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (s, 4H), 5.79 (d, *J* = 0.9 Hz, 1H), 2.41 (d, *J* = 0.9 Hz, 3H), 1.32 (s, 12H) ppm. The NMR data are in agreement with the literature.[23]

(*E*)-4,4,5,5-Tetramethyl-2-{2-[3-(trifluoromethyl)phenyl]prop-1-en-1-yl}-1,3,2-dioxaborolane (**2m**): R_f = 0.5 (cyclohexane/diethyl ether, 12:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 5.79 (d, *J* = 0.9 Hz, 1H), 2.41 (d, *J* = 0.9 Hz, 3H), 1.32 (s, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.18, 144.73, 130.73 (q, *J* = 32.1 Hz), 129.16 (d, *J* = 1.1 Hz), 128.77, 124.62 (q, *J* = 3.7 Hz), 124.33 (d, *J* = 272.3 Hz), 122.81 (q, *J* = 3.8 Hz), 83.32, 25.04, 20.12 ppm. HRMS (ESI, micrOTOF) *m*/*z*: calcd for $C_{16}H_{20}BF_3NaO_2$ $[M+Na]^+$ 335.1404, found 335.1406.

(*E*)-4,4,5,5-Tetramethyl-2-{2-[2-(trifluoromethyl)phenyl]prop-1-en-1-yl}-1,3,2-dioxaborolane (**2n**). R_f = 0.5 (cyclohexane/diethyl ether, 12:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 7.9 Hz, 1H), 7.46 (t, *J* = 7.6, 0.6 Hz, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.20 (d, *J* = 7.7 Hz, 1H), 5.25 (d, *J* = 0.7 Hz, 1H), 2.30 (d, *J* = 0.7 Hz, 3H), 1.31 (s, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.33, 146.17, 131.48, 129.11, 127.04, 126.89 (q, *J* = 30.2 Hz), 126.09 (q, J= 5.2 Hz), 124.40 (q, *J* = 273.7 Hz), 83.16, 25.04, 23.74 (q, *J* = 1.9 Hz) ppm. HRMS (ESI, micrOTOF) *m*/*z*: calcd for $C_{16}H_{20}BF_3NaO_2$ $[M+Na]^+$ 335.1404, found 335.1389.

2o and **3o** have been isolated as a mixture:

(*E*)-2-[3-(Benzyloxy)-2-methylprop-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2o**) (*major isomer*): R_f = 0.3 (cyclohexane/diethyl ether, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.24 (m, 5H), 5.50 (d, *J* = 0.5 Hz, 1H), 4.51 (s, 2H), 3.97 (d, *J* = 0.8 Hz, 2H), 2.00 (s, 3H), 1.29 (s, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.61, 138.52, 128.42, 127.67, 127.58, 82.92, 76.18, 72.18, 24.98, 18.21 ppm. HRMS (ESI, micrOTOF) *m*/*z*: calcd for $C_{17}H_{25}BKO_3$ $[M+K]^+$ 327.1531, found 327.1538.

(*E*)-2-[1-(Benzyloxy)but-2-en-2-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3o**) (*minor isomer*): R_f = 0.3 (cyclohexane/diethyl ether, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.24 (m, 5H), 6.41 (q, *J* = 6.7 Hz, 1H), 4.52 (s, 2H), 4.08 (s, 2H), 1.97 (dt, *J* = 6.9, 1.3 Hz, 3H), 1.29 (s, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.54, 139.12, 128.28, 127.71, 127.33, 83.13, 74.31, 71.92, 24.98, 17.33 ppm. HRMS (ESI, micrOTOF) *m*/*z*: calcd for $C_{17}H_{25}BKO_3$ $[M+K]^+$ 327.1531, found 327.1538.

Standard procedure for the intramolecular carboboration of alkynes catalyzed by (α-ICyD)CuCl (**Table 2**).

An oven-dried screwed tube was charged with (**α-ICyD**)CuCl (0.008 mmol, 19.4 mg) or (**IPr**)CuCl (0.008 mmol, 3.9 mg) and bis(pinacolato)diboron (0.20 mmol, 50.2 mg). After being sealed with a septum, the tube was purged by 3 vacuum-argon cycles. THF (0.3 mL) was added and the mixture was stirred for 5 min at 20 °C. A solution of *t*BuOK 1.0 M in THF (0.2 mL) was added. After stirring for 30 min, the alkyne (0.1 mmol) was added. The tube was sealed with a screw cap and the mixture was stirred at 60 °C for 24-27 h. After cooling, the crude reaction mixture was filtered through a short pad of celite by rinsing with diethyl ether, and concentrated under vacuum. The crude residue was purified by silica gel chromatography (cyclohexane/diethyl ether). The conversion of the alkyne and NMR yield of the product were determined by ^{1}H NMR analysis of the crude reaction mixture by comparison with the internal reference (1,3,5-trimethoxybenzene), and the regioselectivity of the reaction was determined by ^{1}H NMR of the crude reaction mixture.

2-(Cyclopentylidenemethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5a**): R_f = 0.4 (cyclohexane/diethyl ether, 10:1). ^{1}H NMR (400 MHz, C_6D_6) δ = 5.68 (p, *J* = 2.1 Hz, 1H), 2.76 (t, *J* = 7.3 Hz, 2H), 2.26 (t, *J* = 7.3 Hz, 2H), 1.60–1.51 (m, 2H), 1.47–1.39 (m, 2H), 1.12 (s, 12H) ppm. The NMR data are in agreement with the literature.[24]

2-(Cyclohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**6a**): R_f = 0.4 (cyclohexane/diethyl ether, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.59–6.53 (m, 1H), 2.13–2.04 (m, 4H), 1.60–1.56 (m, 4H), 1.25 (s, 12H). The NMR data are in agreement with the literature.[25]

(*E*)-2-[(Dihydrofuran-3(2H)-ylidene)methyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5b**): R_f = 0.4 (cyclohexane/diethyl ether, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.31–5.26 (m, 1H), 4.29 (d, *J* = 1.5 Hz, 2H), 3.93 (t, *J* = 7.0 Hz, 2H), 2.83–2.76 (m, 2H), 1.27 (s, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.04, 83.10, 73.24, 69.30, 33.39, 25.03 ppm. HRMS

(ESI, micrOTOF) *m*/*z*: calcd for $C_{16}H_{20}BF_3NaO_2$ $[M+Na]^+$ 233.1321, found 233.1305.

Acknowledgments

ZW thanks the China Scholarship Council for PhD grant.

Keywords: Catalysis • copper • cyclodextrins • regioselectivity • supramolecular chemistry

[1] a) M. Guitet, P. Zhang, F. Marcelo, C. Tugny, J. Jiménez-Barbero, O. Buriez, C. Amatore, V. Mouriès-Mansuy, J. Goddard, L. Fensterbank, Y. Zhang, S. Roland, M. Ménand, M. Sollogoub, *Angew. Chem. Int. Ed.* **2013**, *52*, 7213-7218; b) P. Zhang, C. Tugny, J. Meijide Suárez, M. Guitet, E. Derat, N. Vanthuyne, Y. Zhang, O. Bistri, V. Mouriès-Mansuy, M. Ménand, S. Roland, L. Fensterbank, M. Sollogoub, *Chem* **2017**, *3*, 174-191.

[2] *For reviews, see:* a) S. H. A. M. Leenders, R. Gramage-Doria, B. de Bruin, J. N. H. Reek, *Chem. Soc. Rev.* **2015**, *44*, 433-448; b) T. Iwasawa. *Tetrahedron Lett.* **2017**, *58*, 4217-4226; c) S. Roland, J. Meijide Suárez, M. Sollogoub, *Chem. Eur. J.* **2018**, *24*, 2-12; d) I. Sinha Partha, S. Mukherjee, *Inorg. Chem.* **2018**, *57*, 4205-4221; e) J. Yang, B. Chatelet, D. Hérault, J.-P. Dutasta, A. Martinez, *Eur. J. Org. Chem.* **2018**, *41*, 5618-5628; f) M. Otte, *ACS Catal.* **2016**, *6*, 6491-6510; g) M. Raynal, P. Ballester, A. Vidal-Ferran, P. W. N. M. Van Leeuwen, *Chem. Soc. Rev.* **2014**, *43*, 1734-1787; h) C. J. Brown, F. D. Toste, R. G. Bergman, K. N. Raymond, *Chem. Rev.* **2015**, *115*, 3012-3035; i) L. J. Jongkind, X. Caumes, A. P. T. Hartendorp, J. N. H. Reek, *Acc. Chem. Res.* **2018**, *51*, 2115-2128; j) C. Tan, Dandan Chu, X. Tang, Y. Liu, W. Xuan, Y. Cui, *Chem. Eur. J.* **2019**, 25, 662-672; k) C. Deraedt, D. Astruc, *Coord. Chem. Rev.* **2016**, *324*, 106-122.

[3] *For reviews, see:* a) H. Yoshida, *ACS Catal.* **2016**, *6*, 1799-1811; b) J. Yun, *Asian J. Org. Chem.* **2013**, *2*, 1016-1025; c) D. Hemming, R. Fritzemeier, S. A. Westcott, W. L. Santos, P. G. Steel, *Chem. Soc. Rev.* **2018**, *47*, 7477-7494.

[4] P. Zhang, J. Meijide Suárez, T. Driant, E. Derat, Y. Zhang, M. Ménand, S. Roland, M. Sollogoub, *Angew. Chem Int. Ed.* **2017**, *56*, 10821-10825.

[5] a) H. Jang, A. R. Zhugralin, Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2011**, *133*, 7859-7871; b) J. H. Moon, H.-Y. Jung, Y. J. Lee, S. W. Lee, J. Yun, J. Y. Lee, *Organometallics*, **2015**, *34*, 2151-2159; c) D. S. Laitar, E. Y. Tsui, J. P. Sadighi, *Organometallics*, **2006**, *25*, 2405-2408.

[6] The copper-catalyzed carboboration of alkynes was initially reported in 2012, see: a) L. Zhang, J. Cheng, C. B. Carry, Z. Hou, *J. Am. Chem. Soc.* **2012**, *134*, 14314-14317; b) R. Alfaro, A. Parra, J. Alemán, J. L. G. Ruano, M. Tortosa, *J. Am. Chem. Soc.* **2012**, *134*, 15165-15168.

[7] *For other examples of carboboration, see*: a) H. Yoshida, I. Kageyuki, K. Takaki, *Org. Lett.* **2013**, *15*, 952-955; b) C.-C. Tai, M.-S. Yu, Y.-L. Chen, W.-H. Chuang, T.-H. Lin, G. P. A. Yap, T.-G. Ong, *Chem. Commun.* **2014**, *50*, 4344-4346.

[8] *For a review, see:* Y. Shimizu, M. Kanai, *Tetrahedron Lett.* **2014**, *55*, 3727-3737.

[9] For references with internal alkynes, *see*: a) C.-C. Tai; M.-S. Yu; Y.-L. Chen; W.-H. Chuang; T.-H. Lin; G. P. A. Yap; T.-G. Ong, *Chem. Commun.* **2014**, *50*, 4344-4346; b) Y. D. Bidal; F. Lazreg; C. S. J. Cazin, *ACS Catal.* **2014**, *4*, 1564-1569; c) T. Itoh, Y. Shimizu, M. Kanai, *J. Am. Chem. Soc.* **2016**, *138*, 7528-7531.

[10] For terminal alkynes, *see*: B. Mun, S. Kim, H. Yoon, K. H. Kim, Y. Lee, *J. Org. Chem.* **2017**, *82*, 6349-6357.

[11] With *N*-adamantyl-substituted NHC-Cu complexes, it was suggested that copper–alkyne coordination is the product-determining step, rather than alkyne insertion into Cu–B bond. This could account for the low sensitivity of regioselectivity to substrate electronic effect, *see* ref. 5a.

[12] Previous calculations on the copper-catalyzed alkene carboboration reaction by Yu and Fu's group suggested that the reaction with alkyl halides is the rate-determining step *see*: Z.-Y. Xu, Y.-Y. Jiang, W. Su, H.-Z. Yu, Y. Fu, *Chem. Eur. J.* **2016**, *22*, 14611-14617.

[13] *For initial examples of alkene cyclization, see*: a) C.-T. Yang, Z.-Q. Zhang, H. Tajuddin, C.-C. Wu, J. Liang, J.-H. Liu, Y. Fu, M. Czyzewska, P. G. Steel, T. B. Marder, L. Liu, *Angew. Chem. Int. Ed.* **2012**, *51*, 528-532; b) K. Kubota, E. Yamamoto, H. Ito, *J. Am. Chem. Soc.* **2013**, *135*, 2635-2640.

[14] a) *Intramolecular addition on conjugated ketones:* P. Liu, Y. Fukui, P. Tian, Z. T. He, C. Y. Sun, N. Y. Wu, G. Q. Lin, *J. Am. Chem. Soc.* **2013**, *135*, 11700-11703; b) *Intramolecular cyclization on silicon-tethered alkylbromides:* K. Kubota, H. Iwamoto, E. Yamamoto, H. Ito, *Org. Lett.* **2015**, *17*, 620-623; c) *Intramolecular cyclization of propargyl ethers and amines linked to alkylhalides:* H. Iwamoto, Y. Ozawa, K. Kubota, H. Ito, *J. Org. Chem.* **2017**, *82*, 10563-10573; d) *Formal allylboration of alkynes, S_N2'-type intramolecular cyclization:* F. Zhang, S. Wang, Z. Liu, Y. Bai, G. Zhu, *Tetrahedron Lett.* **2017**, *58*, 1448-1452; e) *Intramolecular cyclization of aryl-subtituted internal alkynes:* S. Zhou, F. Yuan, M. Guo, G. Wang, X. Tang, W. Zhao, *Org. Lett.* **2018**, *20*, 6710-6714; f) *Intramolecular addition on epoxides and conjugated esters:* S.-H. Kim-Lee, I. Alonso, P. Mauleón, R. Gómez Arrayás, J. C. Carretero, *ACS Catal.* **2018**, *8*, 8993-9005.

[15] The effect of NaO*t*Bu on the mechanism of the copper-catalyzed carboboration reaction was studied in details by Mauleón, Arrayás and Carretero, *see* ref. 14f. In contrast to ref. 14e, a nonradical process was proposed for "exo" cyclization with an internal epoxide as electrophile and $CuCl/PCy_3$ as catalyst.

[16] It is conceivable that a competitive radical "endo" cyclization leads to **6a** formation. Decreasing the *t*BuOK concentration could decrease the concentration of (**L**)-Cu^I–Bpin species which could be involve in the formation of a primary alkyl radical, *see* ref. 14e.

[17] *Photocatalytic E/Z isomerizations have been recently described, see*: a) J. J. Molloy, J. B. Metternich, C. G. Daniliuc, A. J. B. Watson, R. Gilmour, *Angew. Chem.* **2018**, *130*, 3222-3226; b) W. Cai, H. Fan, D. Ding, Y. Zhang, W. Wang, *Chem. Commun.* **2017**, *53*, 12918-12921.

[18] T. Ishikawa, T. Mizuta, K. Hagiwara, T. Aikawa, T. Kudo, S. Saito, *J. Org. Chem.* **2003**, *68*, 3702-3705.

[19] T. Harada, K. Muramatsu, K. Mizunashi, C. Kitano, D. Imaoka, T. Fujiwara, H. Kataoka, *J. Org. Chem.* **2008**, *73*, 249-258.

[20] J. Breitenfeld, J. Ruiz, M. D. Wodrich, X. Hu, *J. Am. Chem. Soc.* **2013**, *135*, 12004-12012.

[21] J. J. Molloy, J. B. Metternich, C. G. Daniliuc, A. J. B. Watson, R, Gilmour, *Angew. Chem. Int. Ed.* **2018**, *130*, 3222-3226.

[22] R. Alfaro, A. Parra, J. Aleman, J. L. G. Ruano, M. Tortosa, *J. Am. Chem. Soc.* **2012**, *134*, 15165-15168.

[23] C. Wang, C. Wu, S. Ge, *ACS Catal.* **2016**, *6*, 7585-7589.

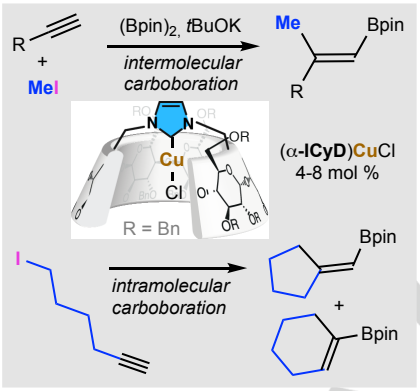
[24] I. A. I. Mkhalid, R. B. Coapes, S. N. Edes, D. N. Coventry, F. E. S. Souza, R. L. Thomas, J. J. Hall, S. Bi, Z. Lin, T. B. Marder, *Dalton Trans.* **2008**, *8*, 1055-1064.

[25] N. Selander, B. Willy, K. J. Szabó, *Angew. Chem. Int. Ed.* **2010**, *49*, 4051-4053.

Entry for the Table of Contents

FULL PAPER

The carboboration of terminal alkynes was studied with a *N*-heterocyclic carbene-capped α-cyclodextrin copper(I) complex as catalyst. The intermolecular reaction with CH_3I gave linear (**L**) vinyl boron isomers with high selectivity. The intramolecular reaction with terminal alkynes led to exocyclic vinyl boronates and to an unexpected endocyclic (*Z*)-isomer, suggesting an unusual mechanism promoted by the ligand.



Encapsulated Catalyst*

Zhonghang Wen, Yongmin Zhang, Sylvain Roland, Matthieu Sollogoub**

Page No. – Page No.

Carboboration of Alkynes with Cyclodextrin-Encapsulated *N*-Heterocyclic Carbene Copper Complexes