

155. Oligosaccharide Analogues of Polysaccharides

Part 5

Studies on the Cross-Coupling of Alkynes and Haloalkynes

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The cross-coupling of the homopropargylic ether **1** and the halopropargylic ethers **2a** and **2b** was optimized, and aspects of the coupling mechanism were studied. Coupling promoted by Pd⁰ and Cu^I in the presence of an amine yielded a mixture of the heterodimer **3** and the homodimers **4** and **5** (Scheme 1). Optimizations were first directed at suppressing homo-coupling. Homo-coupling is partially due to a H/I exchange ($\mathbf{1} + \mathbf{2a} \rightleftharpoons \mathbf{6} + \mathbf{7}$) promoted by CuI and an amine. The exchange, but not the formation of homodimers, was largely suppressed in DMSO. The influence of phosphine ligands was also evaluated. Weaker σ -donors (with the exception of PPh₃) lead to a faster coupling and to a higher ratio of hetero- to homodimers, with P(fur)₃ leading to the cleanest reaction. Homodimers are also formed (together with I₂·(i-Pr)₂NH) by reductive dimerization of the iodoalkyne **2a** in the presence of [Pd₂(dba)₃], CuI, and (i-Pr)₂NH. Bulky and acceptor-substituted amines reduced the extent of the dimerization of **2a**, but the bulkiest amines did not promote coupling. Better results were obtained by using the bromoalkyne **2b**. Neither dimerization of **2b**, nor H/Br exchange between **1** and **2b** were observed. Coupling of **1** and **2b** was slower than the one of **1** and **2a**, but gave higher yields of the heterodimer **3**. The yield of **3** and the ratio of hetero- to homodimers was greatly improved by addition of LiI; no phosphine ligand is then required. While the oxidative addition of the iodoalkyne **2a** to [Pd(PPh₃)₄] (**2a** → **8a**) was rapid, the one of the bromoalkyne **2b** was much slower and proceeded via the η^2 -complex **9** as evidenced by ¹H-NMR spectroscopy. The rearrangement of **9** to the bromopalladium σ -complex **8b** follows first-order kinetics ($k = 0.014 \text{ min}^{-1}$). CuBr greatly increased the rate of this rearrangement. LiI caused rapid substitution of Br by I in the Pd σ -complex (**8b** → **8a**), but not in **9**, nor in **2b**. The σ -complex **8a** did not react with the alkyne **1** in the presence of (i-Pr)₂NH, unless Cu^I was added. The alkynes **10** or **1** did not react with CuI and either TMEDA or (i-Pr)₂NH to yield detectable amounts of the Cu-acetylides **11** or **12**. These observations are rationalized by the mechanism shown in Scheme 3, postulating the intermediacy of the binuclear alkyne-Pd-Cu complexes **C** and **J**, and some or all of **E**–**H**, and highlighting the role of Cu^I in this coupling.

Introduction. – Acetylenosaccharides – analogues of polysaccharides where the glycosidic O-atom is replaced completely or partially by butadiynediyl moieties [1–4] – are most efficiently prepared by a binomial synthesis [5] [6], requiring a series of orthogonal deprotections and cross-couplings of saccharide-derived alkynes and haloalkynes.

We have reported the regioselective deprotection of diynes and their use in the synthesis of an acetylenosaccharide octamer [4] as well as the synthesis of orthogonally protected dialkynes and of a dimer derived from them [3]. While these reactions proceeded well, the cross-coupling of the alkynes and iodoalkynes yielded only 50–75% of the desired diynes [2–4].

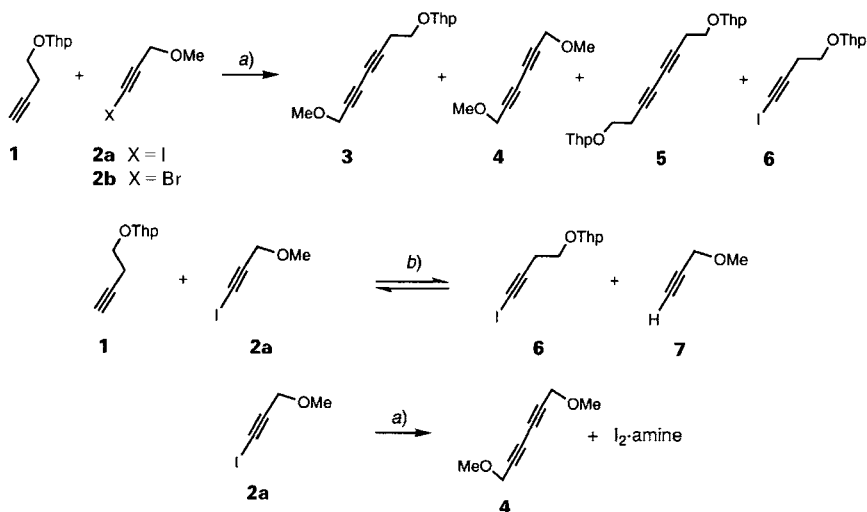
The Cu^I-catalyzed coupling of alk-1-ynes with bromoalkynes in the presence of primary amines (the reaction of Cadiot-Chodkiewicz [7]) leads to butadiynes in yields of

15–93% [8–12], and requires a high concentration ($> 0.1\text{M}$) of each coupling partner. Both the variable yields and the high concentrations are a disadvantage, particularly for the synthesis of high-molecular-weight oligomers. Lower concentrations are tolerated in the $\text{Pd}^{\text{II}}/\text{CuI}$ -promoted coupling of alk-1-yne and iodoalkynes, but the yields are also variable (12–90%) [13–15]. As reported, homo-coupling did not appear to be a serious problem in either method [7] [14], but we have obtained homodimers as major by-products by using the $\text{Pd}^{\text{II}}/\text{CuI}$ -catalyzed coupling [2–4].

The need for high yields of heterodimers prompted us to study the cross-coupling of haloalkynes and alkynes in greater detail. We report on the observations made in the course of optimizing the reaction conditions resulting in a greatly improved procedure for the cross-coupling of alkynes and bromoalkynes.

Results and Discussions. – *Optimization of the Cross-Coupling.* – We have chosen the homopropargylic acetal **1** and the iodopropargylic ether **2a** (Scheme 1) as model compounds. They are related to the 1,4-bis-ethynylated monosaccharides we have used as monomers [1], and their chemical transformations are easily monitored by gas chromatography (GC).

Scheme 1



a) Pd/Cu (cat.), ligand, amine, and solvent; for details, see text. b) CuI (0.03 equiv.), $(i\text{-Pr})_2\text{NH}$, C_6D_6 , r.t.

Cross-coupling of these model compounds led to both hetero- and homodimers, and revealed a H/I exchange between the alk-1-yne **1** and the iodoalkyne **2a** (Scheme 1). Thus, under conditions analogous to those where Wityak and Chan [14] found no homo-coupling, **1** and **2a** (1.1:1 equiv.) gave a mixture of the heterodimer **3**, the homodimers **4** and **5** [16], and a further product **6**, which was formed during the early stage of the reaction and consumed towards the end of it, as shown by GC (Table 1). The formation of **6** suggested a H/I exchange between **1** and **2a**, but **7**, which should also be formed, was not

detected by GC or $^1\text{H-NMR}$ spectroscopy. However, treatment of **1** and **2a** with CuI and $(i\text{-Pr})_2\text{NH}$ did lead to the formation of **6** and **7**; less than 3% of the coupling products were observed in the absence of a Pd catalyst¹). Neither exchange nor coupling occurred in the absence of Cu^{I} .

A variety of amines and solvents were tested in attempts to suppress the H/I exchange and to favor cross-coupling. Amines which form strong complexes with Cu^{I} , including N,N,N',N' -tetramethylethylenediamine (TMEDA), $(\text{PhNHCH}_2)_2$, naphthalene-1,8-diamine, pyridine, BuNH_2 , and morpholine suppressed the exchange to various extents; coupling (under condition B in Table 1), however, was also strongly suppressed.

Among the solvents tested, both DMPU (1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1H)-one) and DMSO considerably lowered the rate of H/I exchange between **1** and **2a** in the presence of CuI and $(i\text{-Pr})_2\text{NH}$ (Table 2). Coupling in DMPU, however, was slow and led to additional products, while homo-coupling was still a problem when DMSO was used.

A variety of ligands were then tested. As shown in Table 3, poor σ -donating phosphines – with the exception of PPh_3 ²) – led to a faster coupling, and to a higher ratio of **3/4**. Among the ligands tested, $\text{P}(\text{fur})_3$ (fur = furan-2-yl) [20] gave the best results in terms of overall yield.

The reduction of Pd^{II} to Pd^0 is accompanied by dimerization of alk-1-ynes [21], but using $[\text{Pd}_2(\text{dba})_3]$ (dba = dibenzylideneacetone) instead of Pd^{II} had only a small influence on the homo-coupling, while the ratio of $[\text{Pd}_2(\text{dba})_3]$ to CuI had an influence on the yield of **3**. Optimal results required a ratio between 0.7 and 1.4 (see also [22]). However, these conditions still failed to suppress the formation of the homodimers **4** and **5** and to significantly improve the yield (Table 3, Entry 6 vs. 5), even when air was strictly excluded.

Table 1. Ratio of Products^{a)} of the Coupling of **1** and **2a** (1.1:1 equiv.)

Entry	Conditions ^{b)}	Time [min]	1	3	4	5	6
1	A	60	13	39	22	25	1
2	B	33	18	27	24	20	11
3	B	150	1	31	31	37	0

^{a)} Mol-% as determined by GC (see *Exper. Part*).

^{b)} A: $[\text{PdCl}_2(\text{PPh}_3)_2]/\text{CuI}/(i\text{-Pr})_2\text{NH}$ 0.03:0.03:2, THF, r.t. [14]. B: $[\text{PdCl}_2(\text{PhCN})_2]/\text{CuI}/(i\text{-Pr})_2\text{NH}$ 0.03:0.03:2, benzene, r.t. [15].

Table 2. Influence of Solvents on the Exchange Reaction between **1** and **2a** (1:1 equiv., $\text{CuI}/(i\text{-Pr})_2\text{NH}$ 0.05:3.5, r.t., 30 min)

Solvent	MeCN	DMF	Et_3N	EtOH	MeCONMe_2	DMSO	DMPU
Ratio 6/1	1.1	0.24	0.16	0.088	0.046	0.0037 ^{a)}	ca. 0 ^{b)}

^{a)} After 300 min, 0.048. ^{b)} After 300 min, 0.010.

¹⁾ The Pd^{II} - and Cu^{I} -catalyzed H/I exchange between an activated iodoarene and an alk-1-yne is known [17]; an exchange between an alk-1-yne and an iodoalkyne has, to the best of our knowledge, not been reported; for CuI catalyzing the coupling of some aryl and vinyl iodides with alk-1-ynes, see [18].

Table 3. *Dependence of Product Ratios of the Coupling of 1a and 2a (1:1 equiv., [PdCl₂(PhCN)₂]/CuI/Ligand/(i-Pr)₂NH 0.03:0.035:0.062:3.5, DMSO, r.t.) upon the Ligands*

Entry	Ligand	Time [min]	1	3	4	5	3/4
1	PEtPh ₂	50	100	0	0	0	–
2	PPh ₃	50	2	63	21	14	3.0
3	P(C ₆ F ₅)Ph ₂	50	23	48	17	12	2.8
4 ^{a)}	P(C ₆ F ₅) ₃	50	2	72	17	9	4.2
5	P(fur) ₃	50	13	61	20	6	3.1
6 ^{b)}	P(fur) ₃	100	12	65	19	4	3.4
7 ^{c)}	P(fur) ₃	130	0	67	17	16	3.9

^{a)} Two unidentified by-products (ca. 8%) were also formed.

^{b)} [Pd₂(dba)₃]/CuI/P(fur)₃/(i-Pr)₂NEt 0.025:0.034:0.06:2.5 equiv.

^{c)} [Pd₂(dba)₃](CuI/P(fur)₃)/PMP 0.03:0.025:0.06:2.8 equiv.

We then discovered that the homodimer **4** was also formed by reductive dimerization of the iodoalkyne **2a** under coupling conditions (*Scheme 1*). The cross-coupling of **1** and **2a**, and the dimerization of **2a** proceeded at about the same rate in benzene or in DMSO, in the presence of [Pd₂(dba)₃], CuI, and (i-Pr)₂NH. Concomitantly, the (i-Pr)₂NH·I₂²⁾ complex was formed. Neither dimerization of **2a**, nor coupling of **1** and **2a** was observed in the absence of a base. A range of bases were then tested. Weak (bulky and acceptor-substituted) organic bases suppressed the dimerization of **2a** in the absence of **1** in the order: tetramethylurea (TMU) > (Me₃Si)₃N > 2,6-di(*tert*-butyl)-4-methylpyridine > 1,2,2,6,6-pentamethylpiperidine (PMP) ≈ Et₃NCH₂COOEt > (i-Pr)₂NEt > Et₃N > Et₂NH. TMU, (Me₃Si)₃N, and 2,6-di(*tert*-butyl)-4-methylpyridine did not promote the cross-coupling of **1** and **2a**. The best results were obtained with PMP, which promoted the cross-coupling of **1** and **2a**, and largely – but not completely – suppressed the dimerization of **2a** (*Table 3*, *Entry 7*, see also *Exper. Part*). The ratio **3/4** was slightly improved from 81:19 to 86:14 by slow addition of **2a** to **1**, and further improved to 92:8 by increasing the reaction temperature to 80°. However, these conditions did not give uniformly good results when applied to more complex alkynes [23].

To reduce the extent of the homo-coupling, we replaced **2a** by the analogous bromoalkyne **2b** (*Scheme 1*), which possesses a lower reduction potential than **2a**. Indeed, no dimerization of **2b** (in the absence of **1**, under coupling conditions), and no H/Br exchange of **2b** and **1a** (CuI/(i-Pr)₂NH in DMSO or benzene) were observed. The cross-coupling of **1** and **2b** was slower than the one of **1** and **2a** under otherwise identical conditions, but led to a higher yield of the heterodimer (*e.g. Table 4*, *Entry 1* vs. *Table 3*, *Entry 7*). The amount of the homodimer **4** was further reduced in the absence of a phosphine (*Table 4*, *Entry 4* vs. *1*). A similar influence of phosphines is known in the *Suzuki* coupling [24]. Again, higher temperatures increased the **3/4** ratio, but not the reaction rate (*Table 4*, *Entry 2* vs. *1*). Reducing the amount of the catalysts led to a much slower reaction, raised the yield of **3**, and further reduced that of the homodimers (*Entry*

²⁾ In the presence of PPh₃ (or more strongly nucleophilic analogues), there is an equilibrium between I₂·(i-Pr)₂NH and the I₂·PR₃ adduct, sequestering part of R₃P. This explains why, in these coupling reactions, Ph₃P behaves as a poorly nucleophilic phosphine.

3 vs. 1). Most significantly, the ratio **3**/**4** increased in the course of the reaction, suggesting that Br[−] had an effect on the selectivity of the coupling. Indeed, when 1.5 equiv. of LiBr was added, the yield and the ratio **3**/**4** were again significantly improved (*Entry* 5), but the reaction was much slower. LiI did not have this disadvantage, and the addition of 0.2 equiv. of LiI raised the rate of the reaction and the **3**/**4** ratio, while yields remained high (*Entry* 6).

Table 4. Cross-Coupling of **1** and **2** (1:1 equiv., [Pd₂(dba)₃]/CuI/Ligand/PMP 0.03:0.025:0.06:2.8 equiv., DMSO, r.t.)

Entry	Ligand	Time [min]	1	3	4	5	3 / 4
1	P(fur) ₃	360	5	74	16	6	4.6
2 ^{a)}	P(fur) ₃	390	18	66	11	5	6.0
3 ^{b)}	P(fur) ₃	2340	10	78	12	0	6.5
4	—	240	22	70	8	0	8.8
5 ^{c)}	—	1200	4	93	3	0	31.0
6 ^{d)}	—	180	8	90	2	0	45.0

a) 70°.

b) [Pd₂(dba)₃]/P(fur)₃/CuI/PMP 0.01:0.02:0.008:2.8 equiv. (PMP = 1,2,2,6,6-pentamethylpiperidine.)

c) LiBr 1.5 equiv.

d) LiI 0.2 equiv.

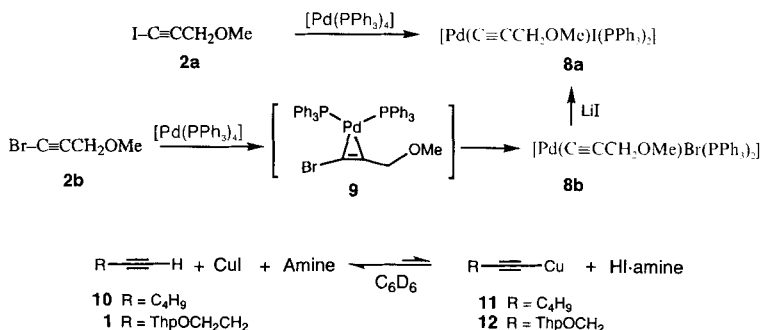
In summary, the best yields of **3** were obtained by coupling **1** and **2b** (1:1) in DMSO at r.t., and in the presence of Pd₂(dba)₃, CuI, PMP, and LiI. These conditions led to good results also in the cross-coupling of other alkynes and bromoalkynes [25].

Mechanistic Aspects of the Hetero-Coupling. The mechanism of the coupling of alk-1-ynes with aryl and vinyl halides (the *Sonogashira* reaction) [21] [26–28] might *a priori* also be valid for the cross-coupling of alkynes with haloalkynes under the conditions reported above.

The first step in the *Sonogashira* and presumably also in the Pd/Cu-catalyzed coupling of alk-1-ynes with haloalkynes is the oxidative addition of an alkyl halide to a Pd⁰ species [29–34]. In the *Sonogashira* reaction, the oxidative addition of a vinyl or aryl halide is rate-limiting [27]; it may be otherwise for the addition of haloalkynes. As monitored by ¹H-NMR spectroscopy, the oxidative addition of **2a** to [Pd(PPh₃)₄] led to [Pd(acetylide)I(PPh₃)₂] **8a** (*Scheme* 2), and the addition was completed in less than 5 min, the time required for measuring the ¹H-NMR spectrum. The analogous addition of the bromoalkyne **2b** to [Pd(PPh₃)₄] was much slower³⁾, leading, within 6 min, mostly to an intermediate which was then converted within 3.5 h to **8b**. ¹H- and ³¹P-NMR spectra suggest that the intermediate possesses the structure of a [Pd(η²-bromoalkyne)] complex **9**. While [Pt(η²-haloalkyne)] complexes are known [35], no [Pd(η²-haloalkyne)] complexes have been reported to the best of our knowledge, although attempts [35] have been made to prepare them.

³⁾ For other examples of the oxidative addition of [Pd(PPh₃)₄] to haloalkynes, see [35–37].

Scheme 2



The reaction of $[\text{Pd}(\text{PPh}_3)_4]$ with **2a** ($\rightarrow$ **8a**) was characterized by an upfield shift of the *s*'s of the MeO (3.01 $\rightarrow$ 2.68 ppm) and CH₂O (3.81 $\rightarrow$ 3.51 ppm) groups. The reaction of $[\text{Pd}(\text{PPh}_3)_4]$ with **2b** ($\rightarrow$ **9** $\rightarrow$ **8b**), however, led initially to a downfield shift of the *s*'s of the MeO (3.00 $\rightarrow$ 3.42 ppm) and CH₂O groups (3.67 $\rightarrow$ 4.15 ppm); after 3.5 h, the formation of **8b** was evidenced by *s*'s at 2.71 and 3.56 ppm. The downfield shift of the MeO and CH₂O signals of **9** is probably due to the Ph groups of the nearby PPh₃ ligand. The PPh₃ ligands of **9** are nonequivalent, as evidenced by the ³¹P-NMR spectrum ($\delta(^{31}\text{P}) = 31.68$ and 30.11 ppm; two signals with about the same intensity). The structure of **9** is also evidenced by the similar downfield shift, relative to **2b**, of the *s*'s of MeO ($\Delta\delta = 0.42$ ppm) and CH₂O ($\Delta\delta = 0.48$ ppm), suggesting a similar distance of a PPh₃ ligand from both groups. In contrast to this, the PPh₃ ligands of **8b** give rise to a single signal at 24.78 ppm, and the $\Delta\delta$ (**2b**/**8b**) values for the MeO ($\Delta\delta = 0.29$) and the CH₂O groups ($\Delta\delta = 0.11$ ppm) differ from each other.

The rearrangement of the η^2 -complex **9** to the σ -complex **8b** appears to be an intramolecular process, as evidenced by the first-order kinetics (¹H-NMR (C₆D₆), $k = 0.014 \text{ min}^{-1}$). It was greatly accelerated by Cu^I, going to completion in less than 3 min (instead of 3.5 h, see above) upon addition of CuBr to the mixture of **9** and (i-Pr)₂NH in C₆D₆. In the absence of Cu^I, (i-Pr)₂NH did not enhance the rearrangement. This shows the crucial role of Cu^I in the oxidative addition of bromoalkynes to Pd complexes, and presumably also of aryl and vinyl halides to Pd⁰.

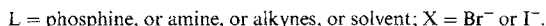
The influence of Cu^I may be rationalized by postulating the transformation of the η^2 -Pd complex of the type **B** (Scheme 3) into a binuclear Pd–Cu complex, such as **C**, and the rapid transformation of **C** into **F**, either directly or via **E** or **D**.

Addition of LiI to the bromo-Pd σ -complex **8b** in C₆D₆ caused a rapid Br/I exchange, leading to the iodo-Pd σ -complex **8a** (Scheme 2). In the absence of Cu^I, there was no Br/I exchange between LiI and the bromoalkyne **2b** (in the presence of $[\text{Pd}(\text{PPh}_3)_4]$), or between LiI and the η^2 -Pd complex **9**. The rate of the consumption of **9** ($\rightarrow$ **8a**) was slightly (< 1.5 times) increased by the addition of LiI.

The mechanism proposed for the *Sonogashira* reaction [27] suggests that the step following oxidative addition of the haloalkyne **A** to Pd⁰ (Scheme 3) is the alkynylation of **F** by **I** to form the *trans*- and *cis*-[Pd^{II} bis(acetylide)] **L** and **M**. This step requires Cu^I [38] [39]. The role of Cu^I in the *Sonogashira* reaction is not clear [27]; it has been proposed

⁴) For a discussion of the role of Cu^I in some related reactions, see: for the *Stille* coupling, [41]; for carbonylations, [42] and ref. cited there; for the activation of alkynes, [43] [44] and ref. cited there. For some cases of an alkynylation without Cu^I and amine, see [45].

Scheme 3



- 5) The only change of the ^1H - and ^{13}C -NMR spectra of **10** or **1** in the presence of CuI, and either TMEDA (1–4 equiv.) [48], or (i-Pr) $_2\text{NH}$ (4 equiv.) in C_6D_6 , even after keeping the samples for a month in sealed tubes, was the decrease of the intensity of the $\text{H}-\text{C}\equiv\text{C}$ signals (1→0.8–0.4 H), and the disappearance of the $\text{HC}\equiv\text{C}$ signals, probably due to the much longer relaxation time (T_1) in the absence of O_2 , while the other C and H signals remained sharp and identical to those observed in the control experiments run in the absence of CuI. These changes were observed independently of the amount of CuI (1–2 equiv.), and the presence of (i-Pr) $_2\text{NEt}$ (up to 6 equiv.) or of piperidine (3 equiv.).
- 6) Complexes where Pd^{II} and Cu^{I} are simultaneously π -bonded to a single alkyne ligand have not been described. However, complexes where two Cu^{I} centres are π -bonded to a single alkyne are known, and have been obtained even in the presence of excess alkyne [51] [52]; most transition metals form stable complexes of the type $[\text{MM}'(\mu\text{-alkyne})]$ [53] [54]; for a discussion of perpendicular and parallel acetylene-transition-metal complexes, see [55].

(Scheme 3). Such binuclear $[\text{CuPd}(\text{acetylene})]$ intermediates are expected to be more highly acidic than a $[\text{Cu}(\text{acetylene})\text{I}]$ complex. The subsequent intramolecular transformation of **J** to the $[\text{Pd}^{\text{II}}\text{bis}(\text{acetylides})]$ **M** and **L** should be fast; if these species are indeed formed *via J*, one has also to consider the intermediacy of a complex **K**. The formation of $[\text{CuPd}(\text{acetylene})]$ intermediates is in agreement with the dependency of the rate of the coupling on the nature of the phosphine (Table 3) and on the concentration of the Pd/Cu catalysts (Table 4, Entry 6 vs. 2). The stronger σ -donating phosphines favor the oxidative addition of a haloalkyne to Pd^0 , but compete with the alkynyl moiety as ligands for Cu and Pd, impairing the formation of the bimetallic complexes **E–J**. Strong σ -donor ligands in **J** will also slow the deprotonation.

The following step (Scheme 3), reductive elimination (**M** $\rightarrow$ **N**), has been extensively discussed [56–59]. Cu^{I} may also play a role in this step, *e.g.* by promoting the isomerization of the $[\text{Pd}^{\text{II}}\text{bis}(\text{acetylides})]$ **L** $\rightarrow$ **M**, *e.g.* *via* the π -complex **K**⁷⁾. That coupling of **1** with the bromoalkyne **2b** at a higher temperature increased the ratio of the hetero- to homodimers (Table 4, Entries 3 and 4 vs. 1 and 2) without influencing the coupling rate can be rationalized by assuming that higher temperatures accelerate the reductive elimination of **M**, but also lower the concentration of the binuclear species **E–J** (Scheme 3).

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Experimental Part

General. Solvents were removed under reduced pressure (rotatory evaporator). DMSO was distilled under vacuum. CuI (Fluka) and $[\text{Pd}_2(\text{dba})_3]$ (Aldrich) were used without purification. Reactions were run under N_2 , and solvents were degassed. Gas chromatography (GC): Fractovap 4160 series (Carlo Erba), flame ionization detector, carrier gas H_2 , Waters 746 (Millipore) integrator, column # 3566-01D, Supelco 2-4026 SPBTM-1, 15m $\times$ 0.25 mm; 50 $\rightarrow$ 240°, 10°/min, 240°, 5 min. *f* Values (mmol/area): **1** 7.63, **3** 6.00, **4** 7.41, **5** 7.38, **6** 6.37. The mol-%⁸⁾ of **3** from **1** and **3–6** = $f_3A_3/f_1A_1 + f_3A_3 + f_4A_4 + f_5A_5 + f_6A_6$; the others were calculated accordingly, manipulations for air-sensitive reactions and of NMR samples were according to [62].

H/I Exchange between 1 and 2a. A soln. of **1** and **2a** (0.1 mmol each) in degassed C_6D_6 (1 ml) was added to CuI (0.50 mg, 0.0026 mmol), followed by $(i\text{-Pr})_2\text{NH}$ (5 μl , 0.035 mmol). The mixture was stirred for 30 min. The resulting light yellow soln. was transferred by syringe to a NMR tube under N_2 (¹H-NMR monitoring after 40 min, 2 and 15 h). ¹H-NMR (200 MHz, C_6D_6 ; ratio of **6/1** = $\text{HC}\equiv\text{CCH}_2\text{OMe}/\mathbf{2a}$: 40 min 48:52; 2 h 55:45; 15 h 52:48): 4.50 (*t*, *J* = 3.3, OCHO of **6**); 4.45 (*t*, *J* = 3.3, OCHO of **1**); 3.83 (*s*, CH_2OMe of **2a**); 3.74 (*d*, *J* = 2.4, $\text{HC}\equiv\text{CCH}_2\text{OMe}$); 3.80–3.62 (*m*), 3.44–3.23 (*m*, CH_2O of **1** and **6**); 3.08 (*s*, MeO of **2a**); 3.02 (*s*, $\text{HC}\equiv\text{CCH}_2\text{OMe}$); 2.38 (*t*, *J* $\approx$ 7.5, $\text{C}\equiv\text{CCH}_2$ of **6**); 2.30 (*td*, *J* = 7.0, 2.7, $\text{C}\equiv\text{CCH}_2$ of **1**); 2.02 (*t*, *J* = 2.4, $\text{HC}\equiv\text{CCH}_2\text{OMe}$); 1.76 (*t*, *J* = 2.7, $\text{HC}\equiv\text{C}$ of **1**).

Attempted H/Br Exchange between 1 and 2b. As described above, with **1** and **2b**, 3 h in DMSO or 3.5 h in benzene. GC showed only the signal of **1** (the signal of **2b** overlapped with that of the solvent).

General Procedure for Coupling Reactions (solvent, catalysts, ligands, amines, LiBr or LiI , and the reaction times are specified in the Tables or in the text). A soln. of **1** and **2a** or **2b** (0.1 mmol each) in the indicated solvent (1 ml) was added to the stirred catalysts and ligand under N_2 . The mixture was stirred for *ca.* 5 min, and treated with the indicated amount of the amine. GC: 0.1 ml of the mixture was diluted with Et_2O (0.5 ml), neutralized, washed ($3 \times \text{H}_2\text{O}$), dried (MgSO_4), and passed through a silica gel pipette column (AcOEt , 4 ml).

⁷⁾ For a review on bridging ligands in bimetallic alkynyl complexes, see [49]; for $[\text{Cu}^{\text{I}}(\mu\text{-alkyne})_2]$ in Cu–Pt complexes, see [60]; in Cu–Ir and Cu–Rh; see [40] [50] [61].

⁸⁾ The peaks of **2a**, **2b**, and methyl propargyl ether (**7**) overlapped with that of the solvent; their mol percentages were not taken into account.

Dimerization of 2a to 4. a) As described above, with **2a** (0.1 mmol) in DMSO (1 ml), [Pd(dba)₃] (1.35 mg, 0.003 mmol), CuI (0.45 mg, 0.0024 mmol), P(fur)₃ (1.35 mg, 0.006 mmol), (i-Pr)₂NEt (50 µl, 0.3 mmol), 50 min: 100% **4**. b) As in a, but in benzene: 50% **4**. c) As in a, but with PMP as the base, 50 min: 16% **4**; 6 h → 100% **4**. d) As in a, but with CuI (0.96 mg, 0.005 mmol), (i-Pr)₂NEt (20 µl, 0.12 mmol), in (D₆)DMSO (1 ml) without P(fur)₃. ¹H-NMR (300 MHz; **2a/4**: 40 min, 1:2.5; 130 min, 0): 4.21 (s, CH₂ of **4**); 4.18 (s, CH₂ of **2a**); 3.7–3.4 (br., I₂·MeCH₂N(CHMe₂)₂); 3.24 (s, MeO of **4**); 3.21 (s, MeO of **2a**); 3.3–3.0 (br., I₂·MeCH₂N(CHMe₂)₂); 1.4–0.9 (br., m, 5 Me of I₂·(i-Pr)₂NEt and (i-Pr)₂NEt). ¹H-NMR (300 MHz; (i-Pr)₂NEt (17.5 µl) in (D₆)DMSO): 2.97 (dq, 2 Me₂CH); 2.42 (q, CH₂); 0.95 (t, CH₂Me); 0.95 (d, Me). ¹H-NMR (300 MHz; (i-Pr)₂NEt (17.5 µl) and CuI (ca. 1.5 mg) in (D₆)DMSO (1 ml)): δs the same as above and signals slightly broadend. ¹H-NMR (300 MHz; (i-Pr)₂NEt (17.5 µl, 0.3 mmol) and I₂ (24.5 mg, 0.1 mmol) in (D₆)DMSO (1 ml)): 3.70–3.50 (m, I₂·MeCH₂N(CHMe₂)₂); 3.20–3.03 (m, I₂·MeCH₂N(CHMe₂)₂); 1.30–1.17 (m, 5 Me of I₂·(i-Pr)₂NEt and (i-Pr)₂NEt).

Attempted Dimerization of 2b to 4. a) As described above under a, with **2b** (0.1 mmol), PMP (50 µl, 0.28 mmol), 2 h: 0% **4** (GC). b) As in a, but in benzene and with (i-Pr)₂NH (50 µl, 0.36 mmol) as the base, 190 min: 0% **4** (GC).

Interaction of PPh₃ with I₂·(i-Pr)₂NH in the Presence of (i-Pr)₂NH. *Soln. 1:* PPh₃ (2 mg, 0.08 mmol), (i-Pr)₂NH (50 µl, 0.35 mmol), and (D₆)DMSO (1 ml). ¹H-NMR (300 MHz): 7.43–7.44 (m, PPh₃); 2.80 (sept., (Me₂CH)₂NH); 2.51 (m, DMSO); 0.93 (d, (Me₂CH)₂NH). *Soln. 2:* I₂ (25 mg, 0.1 mmol) was added to *Soln. 1*. ¹H-NMR (300 MHz): 7.50–7.70 (m, I₂·PPh₃); 5.05 (br. s, (Me₂CH)₂NH·I₂); 3.05 (m, (Me₂CH)₂NH); 2.50 (m, DMSO); 1.05 (d, 4 Me of I₂·(i-Pr)₂NH and (i-Pr)₂NH).

Slow Addition of 2a to the Reaction Mixture. A soln. of **1** and **2a** (0.062 mmol each) in DMSO (0.5 ml) was added to [Pd₂(dba)₃] (9.39 mg, 0.021 mmol), P(fur)₃ (9.51 mg, 0.041 mmol), and CuI (4.43 mg, 0.023 mmol) under N₂. The brown soln. was stirred for 2 min, treated with **1** (226 mg, 1.465 mmol), stirred for 1 min, treated with PMP (0.6 ml, 3.32 mmol), and heated to 80° for 2 min. A soln. of **2a** (287 mg, 1.465 mmol) in DMSO (5.5 ml) was added via a syringe pump (3 ml/h for 2 h, then 0.3 ml/h) to the stirred mixture. Samples were taken for GC analysis at the indicated time (Table 3).

Tetrahydro-2-(7-methoxyhepta-3,5-diynoxy)-2H-pyran (3). A soln. of **1** (0.47 ml, 3.0 mmol) and **2a** (0.3 ml, 3.0 mmol) in DMSO (20 ml, degassed) was added to [Pd₂(dba)₃] (41.4 mg, 0.090 mmol), P(fur)₃ (42 mg, 0.18 mmol), and CuI (15 mg, 0.079 mmol) under N₂, followed by PMP (1.2 ml, 6.64 mmol). The mixture was stirred at r.t. for 8 h, diluted with Et₂O, washed with 0.1N HCl (45 ml), and H₂O (4×), dried (MgSO₄), and filtered through a pad of silica gel (AcOEt). Evaporation and distillation (ca. 200°/1 Torr, the residue turned dark during distillation) gave **3** (200 mg, 30%). Yellow oil, turning brown upon standing. IR (CHCl₃): 3007s, 2946s, 2879s, 2853s, 2826m, 2259m, 1465m, 1453m, 1442m, 1416w, 1377m, 1356s, 1334w, 1324w, 1276m, 1261s, 1178m, 1155s, 1135s, 1122s, 1097s, 1080s, 1068s, 1032s, 998m, 978s, 905s, 869m, 845w, 818w. ¹H-NMR (200 MHz, CDCl₃): 4.64 (br. t, J ≈ 3.0, OCHO); 4.15 (s, CH₂OMe); 3.90–3.77 (m, CH₂O); 3.63–3.45 (m, CH₂O); 3.38 (s, MeO); 2.59 (br. t, J ≈ 7.0, CH₂C≡C); 1.90–1.47 (m, 6 H). ¹³C-NMR (100 MHz, CDCl₃): 98.84 (d, OCHO); 77.95 (s, C≡C); 71.96 (s, C≡C); 71.36 (s, C≡C); 65.40 (s, C≡C); 65.08 (t, CH₂O); 62.24 (t, CH₂O); 60.22 (t, CH₂O); 57.74 (q, MeO); 30.52 (t); 25.41 (t); 20.87 (t); 19.35 (t). EI-MS: 222 (0.3, M⁺), 221 (0.4), 191 (0.8, [M – MeO]⁺), 138 (4, [M – Thp + 2]⁺), 107 (12, [M – Thp – MeO + 2]⁺), 91 (12), 85 (100, Thp⁺), 77 (23), 55 (23). Anal. calc. for C₁₃H₁₈O₃ (222.28): C 70.24, H 8.16; found: C 70.21, H 8.16.

1,6-Dimethoxyhexa-2,4-diyne (4). A soln. of methyl propargyl ether (1.7 ml, 20 mmol), CuCl (99 mg, 1 mmol) and N,N,N',N'-tetramethylethylenediamine (TMEDA, 0.15 ml, 1 mmol) in acetone (14 ml) was stirred for 3 h under a stream of O₂ [16]. The solvent was evaporated. A soln. of the residue in Et₂O was washed with 0.1N aq. HCl and 3× with H₂O, and passed through a pad of silica gel (AcOEt). Evaporation and distillation (ca. 50°/0.5 Torr) gave **4** (970 mg, 70%). Yellow liquid, turning brown upon standing. IR (CHCl₃): 2999s, 2934s, 2887s, 2827s, 2184w, 2142w, 1987w, 1464s, 1450s, 1434m, 1378m, 1352s, 1278m, 1178m, 998s, 936s, 902s, 840w, 572m. ¹H-NMR (200 MHz, CDCl₃): 4.17 (s, 2 CH₂); 3.89 (s, 2 Me). ¹³C-NMR (50 MHz, CDCl₃): 75.49 (s, C≡C); 70.70 (s, C≡C); 60.36 (q, MeO); 58.05 (t). EI-MS: 138 (4, M⁺), 123 (30), 95 (77), 79 (30), 78 (20), 77 (100), 76 (23), 75 (33), 74 (43), 67 (50), 65 (55), 64 (39), 63 (72), 62 (26), 61 (13), 53 (28), 51 (49), 50 (45), 41 (44), 39 (26), 29 (11), 28 (35).

2,2'-(Octa-3,5-diyne-1,8-diyl)bis(oxy)bis(tetrahydro-2H-pyran) (5). As described for **4**, with **1** (500 mg, 3.24 mmol), CuCl (16 mg, 0.16 mmol), TMEDA (20 mg, 0.16 mmol), and acetone (3 ml); 6 h; ca. 230°/0.5 Torr): **5** (244 mg, 50%). Oil. IR (CHCl₃): 3007s, 2947s, 2878s, 2854s, 1466w, 1455m, 1442m, 1416w, 1385w, 1367m, 1353m, 1324w, 1286w, 1276w, 1261w, 1178, 1155s, 1135s, 1122s, 1079s, 1068s, 1032s, 981s, 936w, 918m, 906m, 869s, 845w, 818w. ¹H-NMR (200 MHz, CDCl₃): 4.63 (t, J = 3.2, OCHO); 3.93–3.76 (m, CH₂O); 3.62–3.41 (m, CH₂O); 2.56 (t, J = 7.0, C≡CCH₂); 1.85–1.48 (m, 3 CH₂). ¹³C-NMR (50 MHz, CDCl₃): 99.09 (d, OCHO); 74.75 (s, C≡C); 66.37 (s, C≡C); 65.50 (t, CH₂O); 62.45 (t, CH₂O); 30.72 (t); 25.60 (t); 20.95 (t); 19.53 (t). EI-MS: 305 (0.1, [M – 1]⁺), 221 (0.6, [M – Thp + 1]⁺), 85 (100, Thp⁺), 77 (10), 55 (12). Anal. calc. for C₁₈H₂₆O₄ (306.40): C 70.56, H 8.55; found: C 70.59, H 8.26.

Tetrahydro-2-(4-iodobut-3-ynoxy)-2H-pyran (6). A soln. of **1** (1.20 g, 7.78 mmol) in THF (6 ml) was treated dropwise with BuLi (2.5M in hexane, 3.0 ml, 7.5 mmol) at -76° under N_2 , stirred for 0.5 h at -76° to -68° and 15 min at -68 to 0° , treated with a soln. of I_2 (1.87 g, 7.5 mmol) in THF (3 ml) in one portion, stirred at -76 to -20° for 20 min, diluted with Et_2O , washed with 0.1N aq. HCl and ($3 \times H_2O$), and processed as usual. Distillation (ca. 150°/0.5 Torr) gave **6** (1.80 g, 86%). Oil. IR ($CHCl_3$): 3007s, 2947s, 2877s, 2853s, 2192w, 1466w, 1454m, 1442m, 1385w, 1368m, 1353m, 1325w, 1276w, 1261m, 1178w, 1156m, 1134s, 1122s, 1080s, 1069s, 1032s, 982s, 965m, 906m, 868m, 845w, 818w, 556w, 518w. 1H -NMR (300 MHz, $CDCl_3$): 4.64 (br. t, $J \approx 3.4$, OCHO); 3.91–3.81 (m, CH_2O); 3.78–3.48 (m, CH_2O); 2.67 (t, $J = 7.0$, $CH_2C \equiv C$); 1.85–1.50 (m, 3 CH_2). ^{13}C -NMR (75 MHz, $CDCl_3$): 98.76 (d, OCHO); 91.48 (s, $C \equiv C$); 65.46 (t, CH_2O); 62.22 (t, CH_2O); 30.54 (t); 25.43 (t); 22.25 (t); 19.38 (t); -5.53 (s, $IC \equiv C$). EI-MS: 279 (1.5, $[M - 1]^+$), 224 (26), 179 (45), 178 (63), 115 (17), 85 (100, Thp^+), 67 (10), 52 (10).

1-Bromo-3-methoxypropyne (2b). At -5 to 0° , Br_2 (31.1 g, 0.19 mol) was added dropwise within 15 min to a stirred soln. of KOH (29.2 g, 0.52 mol) in H_2O (78 ml). At 0 – 3° , the pale yellow soln. was added to stirred methyl propargyl ether (15.0 g, 0.21 mol) within 30 min. The mixture was stirred for 30 min at 0 – 17° . The lower oily layer was separated, dried ($MgSO_4$) for 30 min and filtered. The filtrate was distilled through a short column (52°/ca. 55 Torr) to give **2b** (25.5 g, 90%). Colorless liquid, turning light yellow on standing. 1H -NMR (300 MHz, $CDCl_3$): 4.12 (s, CH_2O); 3.38 (s, MeO). 1H -NMR (300 MHz, C_6D_6): 3.65 (s, CH_2O); 2.98 (s, MeO). ^{13}C -NMR (75 Hz, $CDCl_3$): 76.36 (s, $C \equiv CBr$); 60.84 (q, MeO); 57.96 (t, CH_2O); 46.27 (s, $BrC \equiv C$).

trans-Iodo(3-methoxyprop-1-ynyl)bis(triphenylphosphine)palladium(II) (8a): Oxidative Addition of 2a to $[Pd(PPh_3)_4]$. A stirred soln. of $[Pd(PPh_3)_4]$ (158 mg, 0.14 mmol) in C_6D_6 (5 ml) was treated with **2a** (12 μ l, 0.18 mmol) at r.t. After 0.5 min, 0.7 ml of the soln. was transferred to a NMR tube, and measured immediately. 1H -NMR (300 MHz, C_6D_6 ; **8a/2a** 77:23): 7.93 (br. s, 12 H of $Pd(PPh_3)_2$); 7.39 (br. s, 12 H of 2 PPh_3); 7.04–6.98 (m, 32 H); 3.81 (s, CH_2 of **2a**); 3.51 (s, CH_2 of **8a**); 3.01 (s, MeO of **2a**); 2.68 (s, MeO of **8a**). ^{31}P -NMR (121 MHz, C_6D_6): 25.04 (O=PPh₃); 23.39 (br., $Pd(PPh_3)_2$); -5.32 (br., PPh_3).

trans-Bromo(3-methoxyprop-1-ynyl)bis(triphenylphosphine)palladium(II) (8b) and [1-2- η -(1-Bromo-3-methoxyprop-1-ynyl)]bis(triphenylphosphine)palladium(0) (9): Oxidative Addition of 2b to $[Pd(PPh_3)_4]$ and Kinetic Measurement of the Rearrangement of 9 to 8b. A soln. of $[Pd(PPh_3)_4]$ (32 mg, 0.028 mmol) in C_6D_6 (1 ml) was added to **2b** (0.3M in C_6D_6 ; 0.12 ml, 0.036 mmol) at 25° . 1H -NMR (300 MHz, C_6D_6 ; **2b/9/8b** 28:66:6): after 6 min (including 0.5 min acquisition time): 7.55–6.85 (m, PPh_3); 4.15 (s, CH_2 of **9**); 3.67 (s, CH_2 of **2b**); 3.56 (s, CH_2 of **8b**); 3.42 (s, MeO of **9**); 3.00 (s, MeO of **2b**); 2.71 (s, MeO of **8b**); after 210 min: **2b/8b** 28:72: 7.90–6.90 (m, PPh_3); 3.67 (s, CH_2 of **2b**); 3.56 (s, CH_2 of **8b**); 3.00 (s, MeO of **2b**); 2.72 (s, MeO of **8b**). ^{31}P -NMR (121 MHz, C_6D_6): after 13 min (including 4 min acquisition time): 31.68 (br.), 30.11 (br., $Pd(PPh_3)_2$ of **9**); 25.09 (O=PPh₃); 24.78 (br., $Pd(PPh_3)_2$ of **8b**); -5.06 (br., PPh_3); after 190 min: 25.09 (O=PPh₃); 25.04 (br., $Pd(PPh_3)_2$ of **8b**); -5.39 (br., PPh_3). ^{31}P -NMR (121 MHz, PPh_3 in C_6D_6): -5.26 . ^{31}P -NMR (121 MHz, $[Pd(PPh_3)_4]$ in C_6D_6): 24.98 (O=PPh₃); 17.11 ($[Pd(PPh_3)_4]$).

For kinetic studies, 12 1H -NMR spectra (300 MHz) of the above sample were measured at 25° between 6 to 200 min (including 0.5 min acquisition time). The integrals of the signals of **9** in these spectra were divided by those of **2b**. Raw data were processed using the 'Cricket Graph' programs on a Macintosh PC.

Influence of CuBr and (i-Pr)₂NH on the Oxidative Addition of 2b to $[Pd(PPh_3)_3]$. As described for (**8b**), (i-Pr)₂NH (12 μ l, 0.08 mmol) was added 40 s after mixing **2b** and $[Pd(PPh_3)_4]$. After 11 min, 1H -NMR (300 MHz, C_6D_6): **2b/8b/9** 28:5:67. After 14 min, CuBr (ca. 4 mg, 0.028 mmol) was added. After 17 min (3 min after the addition of CuBr), 1H -NMR (300 MHz, C_6D_6): **2b/8b/9** 29:71:0.

Influence of LiI on the Oxidative Addition of 2b to $[Pd(PPh_3)_4]$. As described for **8b**, LiI (ca. 20 mg) was added 30 min after mixing **2b** and $[Pd(PPh_3)_4]$. 10 min after the addition, 1H -NMR (300 MHz, suspension in C_6D_6): **9/2b/8a/8b** 43:29:28:0; 100 min after the addition, **9/2b/8a/8b** 61:29:10:0.

Attempted Formation of Dialkynylpalladiums by Treatment of 8a with 10 and Et₃N in C₆D₆. A soln. of **8a** (0.12 mmol) and **2a** (0.034 mmol) in C_6D_6 (4.3 ml) was treated with **10** (12 μ l, 0.1 mmol) and Et₃N (0.14 mmol) for 6 h at r.t. 1H -NMR (300 MHz; **8a/2a/10** 47:14:39): 3.81 (s, CH_2 of **2a**); 3.51 (s, CH_2 of **8a**); 3.01 (s, MeO of **2a**); 2.68 (s, MeO of **8a**); 1.94 (td, $CH_2C \equiv C$ of **10**); 1.77 (t, 0.5 $HC \equiv C$ of **10**); 1.31–1.20 (m, 2 CH_2 of **10**); 0.73 (m, Me of **10**). 1H -NMR (300 MHz, **10** in degassed C_6D_6 in N_2): 1.77 (t, 0.4–0.6 $HC \equiv C$ of **10**); δ s of the other signals are identical to those above.

Attempted Formation of Alkynylcoppers by Treatment of 10 or with CuI and Amines in C₆D₆. At r.t. and under N_2 , a soln. of CuI and the amines (specified below) in C_6D_6 (degassed, 0.5 ml) was treated with a soln. of **10** or **1** (0.054 mmol) in C_6D_6 (degassed, 0.1 ml), according to the molar ratios given below.

For **10**: a) CuI/TMEDA/**10** 1.1:2.2:1, 14 h. b) CuI/TMEDA/**10** 1.1:1.1:1, one month in a sealed tube. c) CuI/TMEDA/**10** 1.1:4.4:1, 24 h. d) CuI/TMEDA/EtN(i-Pr)₂/**10** 1.1:1.1:3:1, 3 h. e) CuI/TMEDA/**10** 2.2:2.2:1, 1 h. f) CuI/TMEDA/EtN(i-Pr)₂/**10** 2.2:2.2:6.6:1, one month in a sealed tube. g) CuI/TMEDA/piperidine/**10**

1.1:1.1:3.3:1, 5 h. $^1\text{H-NMR}$ (300 MHz, **10** in *a-g*); integration of the signals of $\text{CH}_2\text{C}\equiv\text{C}$ of **10** in *a-g*) and the CH_2 of the amines were in keeping with the molar ratios given above): 1.94 (*m*, $\text{CH}_2\text{C}\equiv\text{C}$ of **10**); 1.77 (*t*, 0.4–0.8 $\text{HC}\equiv\text{C}$ of **10**); 1.31–1.20 (*m*, 2 CH_2 of **10**); 0.73 (*m*, Me of **10**). $^1\text{H-NMR}$ (300 MHz, **10** in degassed C_6D_6 in N_2): 1.77 (*t*, 0.4–0.6 $\text{HC}\equiv\text{C}$ of **10**); δ s of the other signals were identical to those above. $^{13}\text{C-NMR}$ (75 MHz, signals of **10** in *a-g*) were identical to those of **10** in degassed C_6D_6 under N_2): 68.46 (*d*, $\text{HC}\equiv\text{C}$); 30.50 (*t*, $\text{C}\equiv\text{CCH}_2$); 21.71 (*t*); 18.00 (*t*); 13.32 (*q*). $^{13}\text{C-NMR}$ (75 MHz, **10** in C_6D_6 containing air): 84.42 (*s*, $\text{HC}\equiv\text{C}$); δ s of the other signals were identical to those above.

For **1**: $\text{CuI}/(\text{i-Pr})_2\text{NH}/\mathbf{1}$ 1:5:1, 5 h. $^1\text{H-NMR}$ (200 MHz, $\mathbf{1}/(\text{i-Pr})_2\text{NH}$ 1:5): 4.49 (*t*, $J = 3.3$, OCHO of **1**); 3.85–3.67 (*m*), 3.44–3.26 (*m*, 2 OCH_2 of **1**); 2.78 (*dq*, $(\text{Me}_2\text{CH})_2\text{NH}$); 2.30 (*td*, $J = 7.0, 2.7$, $\text{C}\equiv\text{CCH}_2$ of **1**); 1.76 (*t*, $J = 2.7$, 0.7 $\text{HC}\equiv\text{C}$ of **1**); 1.56–1.1 (*m*, 8 H of **1**); 0.98 (*d*, $(\text{Me}_2\text{CH})_2\text{NH}$).

REFERENCES

- [1] J. Alzeer, C. Cai, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 242.
- [2] J. Alzeer, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 177.
- [3] C. Cai, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 732.
- [4] J. Alzeer, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 1219.
- [5] E. Igner, O. I. Paynter, D. J. Simmonds, M. C. Whiting, *J. Chem. Soc., Perkin Trans. 1* **1987**, 2447.
- [6] J. Zhang, J. S. Moore, Z. Xu, R. A. Aguirre, *J. Am. Chem. Soc.* **1992**, *114*, 2273.
- [7] P. Cadiot, W. Chodkiewicz, in 'Chemistry of Acetylenes', Ed. H. G. Viehe, Marcel Dekker, New York, 1969, p. 614.
- [8] J. M. J. Tronchet, A. Bonenfant, *Helv. Chim. Acta* **1977**, *60*, 892.
- [9] J. M. J. Tronchet, A. Bonenfant, *Helv. Chim. Acta* **1981**, *64*, 1893.
- [10] D. Grandjean, P. Pale, J. Chucho, *Tetrahedron Lett.* **1992**, *33*, 5355.
- [11] Y. Rubin, S. S. Lin, C. B. Knobler, J. Anthony, A. M. Boldi, F. Diederich, *J. Am. Chem. Soc.* **1991**, *113*, 6943.
- [12] S. Ohba, J. F. J. Engbersen, *Tetrahedron* **1991**, *47*, 9947.
- [13] S. Y. Mhaskar, G. Lakshminarayana, *Synth. Commun.* **1990**, *20*, 2001.
- [14] J. Wityak, J. B. Chan, *Synth. Commun.* **1991**, *21*, 977.
- [15] D. Elbaum, T. B. Nguyen, W. L. Jorgensen, S. L. Schreiber, *Tetrahedron* **1994**, *50*, 1503.
- [16] A. S. Hay, *J. Org. Chem.* **1962**, *27*, 3320.
- [17] P. Nguyen, Z. Yuan, L. Agocs, G. Lesley, T. B. Marder, *Inorg. Chim. Acta* **1994**, *220*, 289.
- [18] K. Okuro, M. Furuue, M. Enna, M. Miura, M. Nomura, *J. Org. Chem.* **1993**, *58*, 4716.
- [19] V. Farina, B. Krishnan, *J. Am. Chem. Soc.* **1991**, *113*, 9585.
- [20] D. W. Allen, B. G. Hutley, M. T. J. Mellor, *J. Chem. Soc., Perkin Trans. 2* **1972**, 63.
- [21] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, 4467.
- [22] R. Singh, G. Just, *J. Org. Chem.* **1989**, *54*, 4453.
- [23] R. Bürli, A. Vasella, unpublished results.
- [24] T. I. Wallow, B. M. Novak, *J. Org. Chem.* **1994**, *59*, 5034.
- [25] A. Ernst, A. Vasella, unpublished results.
- [26] R. Heck, 'Palladium Reagents in Organic Synthesis', Academic Press, New York, 1985, p. 299.
- [27] I. B. Campbell, in 'Organocopper Reagents. A Practical Approach', Ed. R. J. K. Taylor, Oxford University Press, Oxford, 1994, p. 217.
- [28] M. Schlosser, 'Organometallics in Synthesis', John Wiley & Sons, New York, 1994, p. 385.
- [29] J. K. Stille, K. S. Y. Lau, *Acc. Chem. Res.* **1977**, *10*, 434.
- [30] P. Fitton, E. A. Rick, *J. Organomet. Chem.* **1971**, *28*, 287.
- [31] C. Amatore, A. Jutand, F. Khalil, M. A. M'Barki, L. Mottier, *Organometallics* **1993**, *12*, 3168.
- [32] C. Amatore, A. Jutand, A. Suarez, *J. Am. Chem. Soc.* **1993**, *115*, 9531.
- [33] M. Portnoy, D. Milstein, *Organometallics* **1993**, *12*, 1665.
- [34] S. G. Wilkinson, F. G. A. Stone, E. W. Abel, 'Comprehensive Organometallic Chemistry', Pergamon Press, Oxford, 1982, Vol. 6, p. 455.
- [35] J. Burgess, M. E. Howden, R. D. W. Kemmitt, N. S. Sridhara, *J. Chem. Soc., Dalton Trans.* **1978**, 1577.
- [36] H.-F. Klein, B. D. Zettel, *Chem. Ber.* **1995**, *128*, 343.
- [37] B. Voort, A. L. Spek, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1987**, *43*, 2311.
- [38] K. Sonogashira, T. Yatake, A. Tohda, S. Takahashi, N. Hagihara, *J. Chem. Soc., Chem. Commun.* **1977**, 291.

- [39] D. Villemin, E. Schigecko, *J. Organomet. Chem.* **1988**, 346, C24.
- [40] A. M. Sladkov, I. R. Gol'ding, *Russ. Chem. Rev. (Engl. Transl.)* **1979**, 48, 868.
- [41] V. Farina, S. Kapadia, B. Krishnan, C. Wang, L. S. Liebeskind, *J. Org. Chem.* **1994**, 59, 5909.
- [42] T. Satoh, K. Kokubo, M. Miura, M. Nomura, *Organometallics* **1994**, 13, 4431.
- [43] J. S. Thompson, J. F. Whitney, *Inorg. Chem.* **1984**, 23, 2813.
- [44] K. Brantin, M. Håkansson, S. Jagner, *J. Organomet. Chem.* **1994**, 474, 229.
- [45] J. H. Nelson, A. Verstuyft, J. D. Kelly, H. B. Jonassen, *Inorg. Chem.* **1974**, 13, 27.
- [46] S. G. Wilkinson, F. G. A. Stone, E. W. Abel, 'Comprehensive Organometallic Chemistry', Pergamon Press, Oxford, 1982, Vol. 2.
- [47] F. Bohlmann, H. Schönowsky, E. Inhoffen, G. Grau, *Ber. Dtsch. Chem. Ges.* **1964**, 97, 794.
- [48] L. M. Engelhardt, R. I. Papasergio, A. H. White, *Aust. J. Chem.* **1984**, 37, 2207.
- [49] S. Lotz, P. H. v. Rooyen, R. Meyer, *Adv. Organomet. Chem.* **1995**, 37, 219.
- [50] A. Camus, N. Marsich, G. Nardin, L. Randaccio, *Inorg. Chim. Acta* **1977**, 23, 131.
- [51] D. L. Reger, M. F. Huff, *Organometallics* **1992**, 11, 69.
- [52] H. Lang, K. Köhler, L. Zsolnai, *Chem. Ber.* **1995**, 128, 519.
- [53] E. Sappa, A. Tiripicchio, P. Braunstein, *Chem. Rev.* **1983**, 83, 203.
- [54] J. R. Berenguer, J. Forníes, E. Lalinde, F. Martinez, *J. Chem. Soc., Chem. Commun.* **1995**, 1227.
- [55] D. M. Hoffman, R. Hoffmann, C. R. Fisel, *J. Am. Chem. Soc.* **1982**, 104, 3858.
- [56] J. J. Low, W. A. Goddard III, *J. Am. Chem. Soc.* **1986**, 108, 6115.
- [57] A. Gillie, J. K. Stille, *J. Am. Chem. Soc.* **1980**, 102, 4933.
- [58] J. M. Brown, N. A. Cooley, *Chem. Rev.* **1988**, 88, 1031.
- [59] E.-I. Negishi, T. Takahashi, K. Akiyoshi, *J. Organomet. Chem.* **1987**, 334, 181.
- [60] J. Forníes, E. Lalinde, A. Martin, M. T. Moreno, *J. Organomet. Chem.* **1995**, 490, 179.
- [61] O. M. A. Salah, M. I. Bruce, *Aust. J. Chem.* **1976**, 29, 531.
- [62] D. F. Shriver, M. A. Drezdson, 'The Manipulation of Air-sensitive Compounds', John Wiley & Sons, New York, 1986.
- [63] J. K. Terlouw, P. C. Burgers, H. Hommes, *Org. Mass Spectrom.* **1979**, 14, 387.