Inorganica Chimica Acta, 220 (1994) 85–92

Chele- and anticheleselectivity
IV*. Reaction-accelerating neighboring-group effects in the cross-coupling of vinylbromides with alkyl-transition metal reagents

Thomas Kauffmann**, Hubert Nienaber and Dirk Stach
Organisch-Chemisches Institut der Universität Münster, Correns-Strasse 40, D-48149 Münster (Germany)

(Received November 12, 1993)

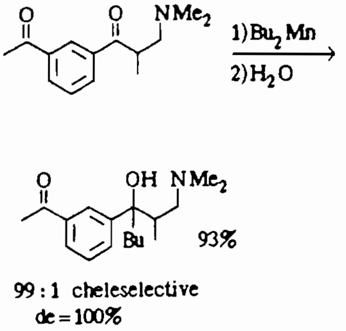
Abstract

The cross-coupling of vinylbromides with Me_4FeLi_2 or Me_4MnLi_2 is distinctly accelerated if the vinylbromide is provided with an hydroxy group in the α-, β- or γ-position to the bromine atom (compounds **2**–**4**). This was elucidated by intermolecular competition experiments and is very probably due to chelate formation as the first reaction step. Corresponding neighboring-group effects as seen in the reaction with **2**–**4** were observed by treating **2** with Bu_4MnLi_2, the α-methoxy vinylbromide (**5**) with Me_4MnLi_2, the secondary amino vinylbromide (**6**) with Me_4FeLi_2, the tertiary amino vinylbromide (**7**) with Me_4FeLi_2 or Me_4MnLi_2, and the β-cyano vinylbromide (**8**) with Me_4FeLi_2. These effects allow very chemoselective cross-coupling. The observed cross-coupling with vinylbromides are believed to occur by oxidative addition (intramolecular due to preceding chelate formation) with subsequent reductive elimination.

Key words: Alkyl-transition metal reagents; Vinylbromides; Cross-coupling; Chemoselectivity; Neighbouring-group effect

Introduction

In the alkylation of ketones with transition metal reagents, basic groups located in the α- or β-position to the keto group frequently exercise a reaction-promoting effect [1–4] which is mostly dependent on chelate formation and enables very selective ('cheleselective' [3]) alkylation (for example see Scheme 1 [5]). Such neighboring-group effects, observed in intra- and intermolecular competition experiments, can be especially anticipated in reactions which proceed rapidly at low temperature. Following the finding that alkyl-iron and alkyl-cobalt reagents react rapidly with vinylbromides at −78 °C to give cross-coupling products [6–8], we looked for analogous neighboring-group effects of these and similar reagents with functionalized vinylbromides. The results, partly reported in a short communication [5], are the object of this paper.



Scheme 1. Example of an extremely cheleselective alkylation of a diketone [5].

Results and discussion

The vinylbromide **1** was treated with the reagents in Table 1 in the presence of one equivalent of a functionalized vinylbromide (**2**–**8**). In many cases, a strongly preferred alkylation of the functionalized vinylbromide was found demonstrating the expected neighboring-group effect [9, 10]. These effects were observed with Fe and Mn reagents but not with Me_4CoLi_2 or Me_2CuLi (Tables 1 and 2). The Co reagent, which gives excellent yields in preparative cross-coupling with vinylbromides [8], is apparently too active for selective cross-coupling, while the Cu reagent is almost

---

*For Parts I–III see refs. 1, 2 and 5.

**Author to whom correspondence should be addressed.

SSDI 0020-1693(94)03859-M

TABLE 1. Competition reactions with **1** and the hydroxy vinylbromides **2–4** according to Scheme 2 (the molar ratio is given before the reagent)

Entry	Substrates	Reagent		Products and yield (%)				Selectivity	Recovery (%)	
									1	**2–4**
1[a]	**2**	0.5	Me_4FeLi_2[c]	**1a**	5	**2a**	79	6:94	66	8
2[b]	**2**	1	Me_4CoLi_2[c]	**1a**	78	**2a**	62	56:44	0	6
3[a]	**2**	1	Me_4MnLi_2	**1a**	<1	**2a**	67	1:99	71	13
4[a]	**3**	0.66	Me_4FeLi_2	**1a**	6	**3a**	48	11:89	90	25
5[a]	**3**	1	Me_4FeLi_2	**1a**	23	**3a**	70	25:75	42	0
6[b]	**3**	1	Me_4FeLi_2	**1a**	60	**3a**	72	46:54	0	0
7[b]	**3**	1	Me_4CoLi_2	**1a**	86	**3a**	78	52:48	0	0
8[b]	**3**	0.5	Me_4CoLi_2	**1a**	38	**3a**	46	45:55	45	24
9[a]	**3**	0.66	Me_4MnLi_2[c]	**1a**	14	**3a**	78	15:85	73	15
10[a]	**3**	5	Me_2CuLi	**1a**	2	**3a**	<1		50	37
11[b]	**3**	5	Me_2CuLi	**1a**	12	**3a**	1	92:8	61	44
12[a]	**4**	0.5	Me_4FeLi_2	**1a**	11	**4a**	51	18:82	85	13
13[b]	**4**	0.5	Me_4FeLi_2	**1a**	57	**4a**	19	73:27	30	10
14[a]	**4**	0.5	Me_4CoLi_2	**1a**	55	**4a**	31	64:36	35	13
15[a]	**4**	1	Me_4MnLi_2	**1a**	1	**4a**	0		90	70
16[a]	**3**	1	Bu_4FeLi_2[c]	**1b**	54	**3b**	61	47:53	34	21
17[b]	**3**	1	Bu_4FeLi_2[c]	**1b**	49	**3b**	57	47:53	29	24
18[a]	**3**	1	Bu_4MnLi_2	**1b**	10	**3b**	74	12:88	66	17

[a] Diethyl ether as solvent. [b] THF as solvent. [c] This reagent can transfer more than one Me or Bu group.

TABLE 2. Competition reactions with **1** and the functionalized vinylbromides **5–8** according to Scheme 2 (the molar ratio is given before the reagent)

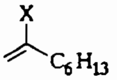
Entry	Substrates **5–8**	Reagent		Products and yield (%)				Selectivity	Recovery (%)	
									1	**5–8**
1[a]	**5**	0.5	Me_4FeLi_2[c]	**1a**	56	**5a**	62	47:53	17	25
2[b]	**5**	0.5	Me_4CoLi_2[c]	**1a**	39	**5a**	39	50:50	41	34
3[a]	**5**	1	Me_4MnLi_2	**1a**	<1	**5a**	72	<(1:99)	55	5
4[a]	**6**	0.5	Me_4FeLi_2	**1a**	5	**6a**	21	19:81	94	0
5[b]	**6**	0.5	Me_4FeLi_2	**1a**	10	**6a**	85	11:89	89	0
6[b]	**6**	0.5	Me_4CoLi_2	**1a**	29	**6a**	59	33:67	70	24
7[a]	**6**	1	Me_4MnLi_2	**1a**	0	**6a**	0		95	40
8[a]	**7**	0.5	Me_4FeLi_2	**1a**	26	**7a**	62	30:70	72	37
9[b]	**7**	0.5	Me_4CoLi_2	**1a**	56	**7a**	52	52:48	41	48
10[a]	**7**	1	Me_4MnLi_2	**1a**	1	**7a**	26	4:96	98	73
11[a]	**8**	0.5	Me_4FeLi_2	**1a**	4	**8a**	76	5:95	81	0
12[b]	**8**	0.5	Me_4FeLi_2	**1a**	3	**8a**	38	8:92	74	33
13[b]	**8**	0.5	Me_4CoLi_2	**1a**	33	**8a**	55	40:60	41	19
14[a]	**8**	1	Me_4MnLi_2	**1a**	0	**8a**	0		76	73

[a] Diethyl ether as solvent. [b] THF as solvent. [c] This reagent can transfer more than one Me group.

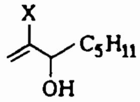
completely deactivated by the functionalized vinylbromide **3** (entries 10 and 11, Table 1). Diethyl ether was substantially more suitable as a solvent than tetrahydrofurane (THF) which strongly complexes the transition metal reagents and therefore renders coordination of the reagent to the basic group of functionalized vinylbromides more difficult.

Hydroxy group

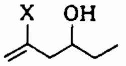
The influence of the hydroxy group was examined most closely. The best methylating reagent for the differentiation of the vinylbromide **1** and the α-hydroxy vinylbromide (**2**) with regard to yield and selectivity was Me_4MnLi_2 (entry 3, Table 1). For the differentiation of **1** and β-hydroxy vinylbromide (**3**) Me_4FeLi_2 was best suited (entry 4) but Me_4MnLi_2 also gave favorable results (entry 9), whereas by reacting **1** with the γ-hydroxy vinylbromide (**4**) only Me_4FeLi_2, applied in ether, gave a satisfactory result (entry 12; Me_4MnLi_2 is apparently deactivated by **4**). For the above mentioned reactions of alkyl-transition metal reagents with func-



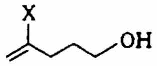
	X
1	Br
1a	Me
1b	Bu



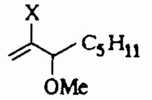
	X
2	Br
2a	Me



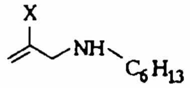
	X
3	Br
3a	Me
3b	Bu



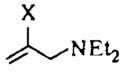
	X
4	Br
4a	Me



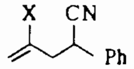
	X
5	Br
5a	Me



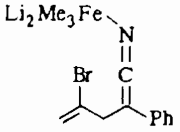
	X
6	Br
6a	Me



	X
7	Br
7a	Me



	X
8	Br
8a	Me



9

tionalized ketones, where basic groups in α- or β-positions to the keto group exercise a strong reaction-promoting effect, such a group in the γ-position was inefficient (see entry 5 in the Table of ref. 2) seems to be an exception, but the experiment is not informative because the yield is only 12% and the recovery of the unaffected ketones is poor). Therefore the 82:18 differentiation between **1** and the γ-hydroxy vinylbromide (**4**) by Me_4FeLi_2 in favor of **4** is surprising (for an explanation see 'Mechanism'). The difference in reactivity between Me_4FeLi_2 and Me_4MnLi_2 towards **4** was also observed in non-competition reactions: Me_4FeLi_2 resulted in 94% of the methylation product **4a** by treatment with 1 equiv. of **4** in ether, but Me_4MnLi_2 on the contrary was unable to produce **4a** (75% recovery of **4**) [11]. Of the two butylating reagents Bu_4MnLi_2 and Bu_4FeLi_2, only the former led to a good differentiation between **1** and the β-hydroxy vinylbromide (**3**) (entry 18). By treating the hydroxy vinylbromides **2** and **3** in ether with 1 equiv. of Me_4FeLi_2 (at −78 °C) or Me_4MnLi_2 (at −30 °C) approx. 1 equiv. CH_4 was generated in each case and the IR spectrum (at −20 °C) lacked the O−H stretching vibration bands of **2** and **3** at 3439 and 3473 cm^{-1}, respectively. It is therefore most likely that an alkoxide is formed. Since the generation of methane was rapid and occurred immediately after combining the components, the alkoxide is probably formed before the cross-coupling.

Other basic groups

Further competition reactions according to Scheme 2 demonstrated analogous reaction-accelerating effects of the groups MeO−, Hex-NH− or Et_2N− in the α-position and of NC− in the β-position to the Br atom of vinylbromides (Table 2; Hex = n-hexyl). A good differentiation between **1** and the α-methoxy vinylbromide (**5**), indicating a strong neighboring-group effect, was possible with Me_4MnLi_2 (entry 3 of Table 2), whereas this reagent was completely deactivated (Hex-NH−, NC−) or greatly reduced in activity (Et_2N−), if the basic group contained nitrogen (entries 7, 10 and 14). The reason is presumably the formation of unreactive or relatively unreactive Mn complexes. Conversely, Me_4FeLi_2 gives good discrimination between **1** and the secondary amino vinylbromide (**6**) (entry 5) or the cyano vinylbromide (**8**) (entries 11 and 12), while the discrimination between **1** and the tertiary amino vinylbromide (**7**) (entry 8) is less clear. In order to check whether the reagent becomes coordinated to the cyano group of **8** in the reaction of Me_4FeLi_2 with 1 equiv. of **8** in ether, we took a IR spectrum at −20 °C. Instead of the sharp N−C stretching vibration band of the cyano group at 2243 cm^{-1}, a very intense broad band appeared at 1959 cm^{-1} [9]. There are various IR spectroscopic indications for rapidly occurring metal-induced isomerization of aliphatic nitriles to give ketene-imines [11, 12]. The stretching vibrations of ketene-imines are at approximately 2000 cm^{-1} [13]. Considering the reduction of frequency by complexing of unsaturated groups with transition metals, it can be assumed that the band at 1959 cm^{-1} is created by a ketene-imine group, coordinated to Fe as formulated in **9**.

$$\begin{array}{c}1\ \text{Substrate A}\\+\\1\ \text{Substrate B}\end{array}\xrightarrow{x\ \text{Reagent}}\begin{array}{c}\text{Product A}'\\+\\\text{Product B}'\end{array}$$

Scheme 2. Principle of the competition experiments performed. The molar ratio is given before the reagent.

Discrimination between different functionalized vinylbromides (Table 3)

The reaction-accelerating effects of the hydroxy group in **2** and the methoxy group in **5** are so different that in competition reactions with **2** and **5** a clear differentiation was possible using Me_4FeLi_2 or Me_4MnLi_2. While Me_4FeLi_2 preferred the hydroxy vinylbromide (**2**) with 85:15 selectivity (entry 2, Table 3), Me_4MnLi_2 preferentially methylated the methoxy vinylbromide (**5**) with 82:18 selectivity (entry 5). Me_4FeLi_2 was unable to make a good distinction between **2** and the cyano vinylbromide (**8**) or between **5** and **8**. However, it is recognizable that in the first case **2** had priority over **8** and in the second case **8** over **5** (entries 6 and 9). In both cases Me_4MnLi_2 preferentially methylated the cyano vinylbromide (entries 8 and 10). From these data and from the results obtained above, decreasing electrophilicity of the compounds followed in the order **2**>**8**>**5**>**1** for Me_4FeLi_2 and **8**>**5**>**2**>**1** for Me_4MnLi_2. Me_4FeLi_2 in ether or THF showed a clear preference for the secondary amino vinylbromide (**6**) over the tertiary amino vinylbromide (**7**) and produced **6a** in excellent yield (entries 11 and 12, Table 3), whereas Me_4MnLi_2 differentiated in the reverse fashion (entry 13). The interesting preference for the α-hydroxy vinylbromide (**2**) over the β-hydroxy vinylbromide (**3**) by both reagents (entries 14 and 15) is discussed in the following section.

Mechanism

As a reason for the reaction-promoting effects of basic groups in α- and β-functionalized ketones, chelate formation was indicated in various cases by the simultaneous appearance of diastereospecificity (see Scheme 1) and other findings [1–4]. Apart from theoretical considerations (see below), a corresponding reason for the neighboring-group effects of functionalized vinylbromides is suggested by the rapid generation of CH_4 at −78 °C in the reactions of Me_4FeLi_2 and Me_4MnLi_2 with hydroxy vinylbromides, the disappearance of the O−H stretching vibration band in the IR spectrum and the vanishing of the nitrile band in the IR spectrum by treating **8** with Me_4FeLi_2 in favor of a new band indicating the formation of the keteneimine derivative **9**. The question arises whether the transition metal in the assumed chelates of the hydroxy vinylbromides is coordinated in accordance with **10** to the vinyl group or according to **11** with the Br substituent ([Fe] = Fe + additional ligands). We assume the latter possibility since the vinyl group of vinylbromides is electron deficient due to the high −I-effect of the Br substituent and the ability of Br to form an electron decett (the −M-effect owing to **13** compensates or exceeds the +M-effect; compare the activating effect of Cl or Br on the carbonyl group of acyl halides). Moreover, the coordination of Fe to Br is sterically less hindered than the coordination to the vinyl group. Furthermore, chelates of type **11** are as conception attractive, being closely analogous to chelates of type **12** which are intermediates in the reactions of alkyltransition metal reagents with hydroxy ketones [4]*: the centers of the subsequent reaction, the carbon atom (which becomes more positive) of the C−Br or C=O bond and the metal atom (which becomes more negative) are activated in both cases by the −M-effect of the

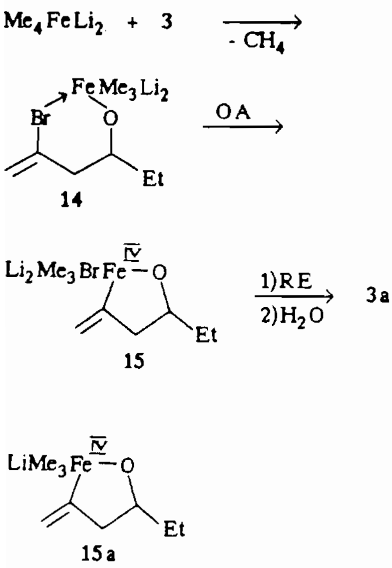
TABLE 3. Competition reactions between various functionalized vinylbromides according to Scheme 2 (the molar ratio is given before the reagent)

Entry	Substrates	Reagent		Products and yield (%)				Selectivity	Recovery (%) of substrates	
1[a]	**2+5**	1	Me_4FeLi_2[c]	**3a**	85	**5a**	31	73:27	15	58
2[a]	**2+5**	0.75	Me_4FeLi_2	**3a**	68	**5a**	12	85:15	29	79
3[a]	**2+5**	0.5	Me_4FeLi_2	**3a**	51	**5a**	11	82:18	45	81
4[a]	**2+5**	1	Me_4MnLi_2[c]	**3a**	16	**5a**	50	24:76	76	43
5[a]	**2+5**	0.75	Me_4MnLi_2	**3a**	11	**5a**	50	18:82	86	37
6[a]	**2+8**	1	Me_4FeLi_2	**3a**	87	**8a**	75	54:46	11	23
7[a]	**2+8**	1	Me_4MnLi_2	**3a**	20	**8a**	30	40:60	70	63
8[b]	**2+8**	1	Me_4MnLi_2	**3a**	4	**8a**	40	9:91	94	58
9[a]	**5+8**	1	Me_4FeLi_2	**5a**	61	**8a**	98	38:62	29	0
10[b]	**5+8**	1	Me_4MnLi_2	**5a**	1	**8a**	33	3:97	88	65
11[a]	**6+7**	0.5	Me_4FeLi_2	**6a**	91	**7a**	5	95:5	9	93
12[b]	**6+7**	0.5	Me_4FeLi_2	**6a**	98	**7a**	7	93:7	0	93
13[a]	**6+7**	1	Me_4MnLi_2	**6a**	1	**7a**	10	9:91	50	90
14[a]	**2+3**	0.5	Me_4FeLi_2	**2a**	73	**3a**	17	90:10	7	64
15[a]	**2+3**	0.5	Me_4MnLi_2	**2a**	82	**3a**	28	72:28	<1	41

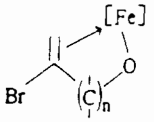
[a] Diethyl ether as solvent. [b] THF as solvent. [c] This reagent can transfer more than one Me group.

---

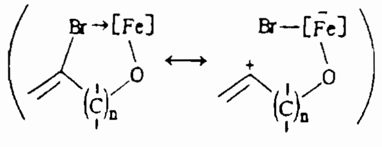
*Enhanced rates of addition of Me_2Fe or Bu_2Fe to a β-hydroxy ketone in comparison to a normal ketone [14].



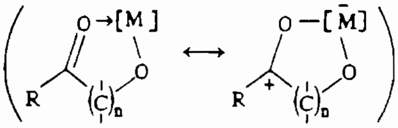
Scheme 3. Postulated 'chelation–OA–RE mechanism' exemplary formulated for the reaction of Me_4FeLi_2 with β-hydroxy vinylbromide (3) (OA = oxidative addition; RE = reductive elimination)



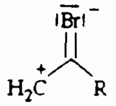
10



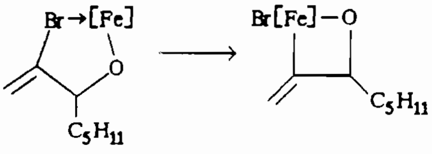
11 (n = 1-3) 11a



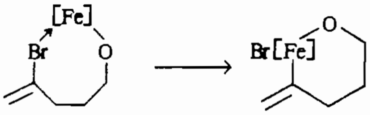
12 (n = 1 or 2) 12a



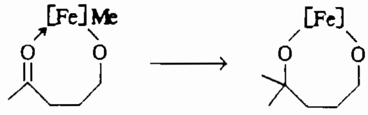
13



16 17



18 19



20 21

metal atom (see **11a** and **12a**). As to the complete mechanism of the cross-coupling with functionalized vinylbromides, in addition to the 'chelation–insertion–desinsertion mechanism', formulated in ref. 5, we considered the 'chelation–OA–RE mechanism' (OA = oxidative addition; RE = reductive elimination) which is exemplary formulated in Scheme 3 for the reaction $Me_4FeLi_2 + \mathbf{3}$ (the RE step possibly occurs with **15a** – generated from **15** by elimination of LiBr – instead of with **15**). We now give preference to the chelation–OA–RE mechanism which is analogous to the assumed mechanism for the cross-coupling of aryl halides and alkenyl halides with $MeRh(PPh_3)_3$ [15] and the well-accepted mechanism for the reaction of acyl halides with $RRh(CO)Li_2$ to give ketones [16]. The possibility that the OA step on **14** occurs not intramolecularly but intermolecularly by the reaction of a second molecule **14** cannot be excluded. In the case of the intramolecular variant, formulated in Scheme 3, the OA step is favored for entropy reasons compared to mechanisms with an intermolecular OA step.

The competition experiments 14 and 15 of Table 3 demonstrated a faster reaction of Me_4FeLi_2 or Me_4MnLi_2 with the α-hydroxy vinylbromide (**2**) compared to the β-hydroxy vinylbromide (**3**). This result is understandable with the mechanism given in Scheme 3 because a five-membered ring (e.g. **16**; [Fe] = Fe + additional ligands) is normally formed more rapidly than a corresponding six-membered ring (e.g. **14**) [17]. Certainly it must be conceded that, when starting from **16**, oxidative addition creates a four-membered ring (**17**) whereas from **14** a strainless five-membered ring (**15**) is generated. This difficulty would not occur if the intermolecular variant of the chelation–OA–RE mechanism is assumed. Finally, the chelation–OA–RE mechanism of Scheme 3 explains the surprising result that the γ-hydroxy group in **4** has a clear reaction-promoting effect in contrast to the hydroxy group in γ-hydroxy ketones. In the case of **4** the chelate **18** generates a six-membered ring **19**, whereas for γ-hydroxy ketones the chelate (e.g. **20**) reacts to give a seven-membered ring (e.g. **21**), which is less favorable due to ring tension.

Experimental

All reactions with organometallic compounds were performed under argon in dried solvents. Methyllithium was used as a 1.6 M solution in ether, butyllithium as a 1.6 M solution in hexane; the exact concentration was determined by double titration according to ref. 18. Petroleum ether: 30–60 °C. The qualitative and quantitative determination of products was accomplished by gas chromatography (GC) with the method of internal standard [19] using authentic control compounds (see (iv).

(i) Reagents

The methyl-transition metal reagents (Tables 1–3) were synthesized as in ref. 8 (stirred for 2 h at −78 °C instead of 1 h). Bu_4FeLi_2 (dark brown suspension in THF) and Bu_4MnLi_2 (yellow–brown solution in ether) were prepared analogously using butyl lithium instead of methyllithium.

(ii) Vinylbromides

1–**3**, **5** and **8** are prepared as published [8].

2-Bromo-1-pentene-5-ol (4). 5.26 g (65.0 mmol) of HBr gas were added to a suspension of 13.65 g (65.0 mmol) of tetraethyl ammonium bromide in 60 ml of CH_2Cl_2 at 0 °C, followed by addition of 5.0 g (59.5 mmol) of 4-pentine-1-ol. After 3 h stirring at 40 °C and addition of 120 ml of ether a precipitate of tetraethyl ammonium bromide was filtered off and the solvent was removed *in vacuo*. Cleaning of the raw product by flash chromatography (petroleum ether:ether = 2:1; SiO_2) and then by distillation *in vacuo* resulted in 6.28 g (64%) of **4** as an oil (b.p. 98 °C/15 Torr).

^1H NMR ($CDCl_3$): $\delta = 1.87$ (m, 2H, CH_2), 2.04 (s, 1H, OH), 2.59 (t, $^3J = 7.3$ Hz, 2H, $=C-CH_2-$), 3.72 (t, $^3J = 6.3$ Hz, 2H, CH_2-OH), 5.47 (s, 1H, $HHC=C$), 5.67 (s, 1H, $HHC=C$). ^{13}C NMR ($CDCl_3$): 31.05 (CH_2), 38.02 ($=C(Br)-CH_2$), 61.51 ($-CH_2-OH$), 117.16 ($H_2C=C$), 134.17 ($=C(Br)-$). MS (70 eV), *m*/*z* (%): 86 (10), 85 (3), 71 (55), 70 (12), 57 (11), 43 (100), 42 (73), 41 (32).

Anal. Calc. for C_5H_9BrO ($M_r = 165.0$): C, 36.39; H, 5.50. Found: C, 36.65; H, 5.61%.

2-Bromo-1-(N-hexylamino)-2-propene (6). This compound was prepared in analogy to the method given in ref. 20. 12.0 g (60 mmol) of 2,3-dibromo-1-propene were added slowly and under ice-cooling to a solution of 12.1 g (60 mmol) of n-hexylamine in 30 ml of ether. After 12 h stirring at *c*. 20 °C, removal of the precipitated hexylamine hydrobromide, evaporation of the solvent and distillation *in vacuo* 8.58 g (65%) of **6** were obtained as an oil (b.p. 110 °C/15 Torr).

^1H NMR ($CDCl_3$): $\delta = 0.92$ (t, $^3J = 6.8$ Hz, 3H, CH_3), 1.42 (m, 9H, CH_2 and NH), 2.58 (t, $^3J = 7.1$ Hz, 2H, $N-CH_2-CH_2$), 3.48 (s, 2H, $=C(Br)-CH_2$), 5.58 (s, 1H, $HHC=$), 5.81 (s, 1H, $HHC=$). ^{13}C NMR ($CDCl_3$): $\delta = 14.23$ (CH_3), 22.82 (CH_2), 27.18 (CH_2), 30.21 (CH_2), 31.96 (CH_2), 48.10 (CH_2), 57.78 ($=C(Br)-CH_2$), 117.46 ($H_2C=$), 134.10 ($=C(Br)-$). GC/MS (70 eV), *m*/*z* (%): 221 (0.3) [M^+], 219 (0.3) [M^+], 140 (3), 71 (59), 57 (92), 43 (100).

Anal. Calc. for $C_9H_{18}BrN$ ($M_r = 220.1$): C, 49.10; H, 8.24; N, 6.36. Found: C, 49.18; H, 8.16; N, 6.47%.

2-Bromo-1-(N,N-diethylamino)-2-propene (7). **7** was prepared according to the literature method [21] in 73% yield.

^1H NMR ($CDCl_3$): $\delta = 0.89$ (t, $^3J = 7.1$ Hz, 6H, CH_3), 2.44 (q, $^3J = 7.1$ Hz, 4H, CH_2-CH_3), 3.11 (s, 2H, $=C(Br)-CH_2$), 5.41 (s, 1H, $HHC=$), 5.76 (s, 1H, $HHC=$). ^{13}C NMR ($CDCl_3$): $\delta = 12.11$ (CH_3), 47.12 (CH_2-CH_3), 61.92 ($=C(Br)-CH_2$), 117.59 ($H_2C=$), 133.09 ($=C(Br)-$).

(iii) Control compounds for GC analysis

1a–**3a**, **5a** and **8a** were prepared according to ref. 8.

2-Methyl-1-pentene-5-ol (4a). **4a** was prepared analogously to **6a** from 4 mmol of Me_4FeLi_2 and 0.66 g (4.0 mmol) of **4**. After flash chromatography (petroleum ether:ether = 2:1, SiO_2) 0.17 g (41%) of **4a** was obtained as an oil.

^1H NMR ($CDCl_3$): $\delta = 1.61$ (s, 3H, $=C-CH_3$), 1.69 (m, 3H, CH_2 and OH), 2.02 (t, $^3J = 6.9$ Hz, 2H, $=C-CH_2-$), 3.65 (m, 2H, CH_2-OH), 4.77 (s, 1H, $HHC=$), 4.87 (s, 1H, $HHC=$). ^{13}C NMR ($CDCl_3$): $\delta = 16.74$ ($=C-CH_3$), 25.78 (CH_2), 32.15 (CH_2), 65.47 (CH_2-OH), 113.42 ($H_2C=$), 143.59 ($H_2C=C$). MS (70 eV); *m*/*z* (%): 101 (0.3) [$M^+ + 1$], 100 (18) [M^+], 82 (23), 69 (43), 55 (82), 41 (100).

Anal. Calc. for $C_6H_{12}O$ ($M_r = 100.2$): C, 71.94; H, 12.08. Found: C, 72.08; H, 12.16%.

1-(N-Hexylamino)-2-methyl-2-propene (6a). 1.1 g (5 mmol) of **6** in 5 ml of THF were added to a solution of 5 mmol of Me_4FeLi_2 in THF at −78 °C. After 1 h the solution was warmed to *c*. 20 °C. Preparation according to 'AAV 2' [8] with subsequent flash chromatography (petroleum ether:ether = 5:1; SiO_2) gave 0.40 g (52%) of **6a** as an oil.

^1H NMR ($CDCl_3$): $\delta = 0.77$ (t, $^3J = 6.8$ Hz, 3H, CH_2-CH_3), 1.25 (m, 9H, CH_2 and NH), 1.62 (s, 3H,

$=C-CH_3$), 2.45 (t, $^3J=7.1$ Hz, 2H, $N-CH_2-CH_2$), 3.05 (s, 2H, $=C-CH_2-$), 4.70 (s, 1H, *H*HC=), 4.74 (s, 1H, H*H*C=). ^{13}C NMR ($CDCl_3$): $\delta=14.20$ (CH_3), 20.94 (CH_3), 22.83 (CH_2), 27.28 (CH_2), 30.34 (CH_2), 32.02 (CH_2), 49.58 (CH_2), 55.99 (CH_2), 110.58 ($H_2C=$), 144.34 ($H_2C=C-$). MS (70 eV): *m/z* (%): 156 (2) [$M^+ +1$], 155 (13) [M^+], 154 (5), 71 (60), 57 (100), 43 (87).

Anal. Calc. for $C_{10}H_{21}N$ ($M_r=155.3$): C, 77.35; H, 16.63; N, 9.02. Found: C, 77.24; H, 13.75; N, 9.10%.

*1-(N,N-Diethylamino)-2-methyl-2-propene (**7a**).* To a solution of 5 mmol of Me_4CoLi_2 in THF, prepared as in ref. 8, 0.96 g (5.0 mmol) of **7** was added at −78 °C. After 0.5 h the solution was warmed to 20 °C. Preparation according to 'AAV 2' [8] and flash chromatography (petroleum ether:ether = 10:1) gave 0.27 g (43%) of **7a** as an oil.

^1H NMR ($CDCl_3$): $\delta=0.86$ (t, $^3J=7.1$ Hz, 6 H, CH_2-CH_3), 1.60 (s, 3H, $=C-CH_3$), 2.33 (q, $^3J=7.1$ Hz, 4H, CH_2-CH_3), 2.77 (s, 2H, $=C-CH_2$), 4.67 (s, 1H, *H*HC=), 4.73 (s, 1H, *H*HC=). ^{13}C NMR ($CDCl_3$): $\delta=11.88$ (CH_2-CH_3), 21.02 ($=C-CH_3$), 46.95 (CH_2), 60.58 (CH_2), 112.17 ($H_2C=$), 144.63 ($H_2C=C-$). MS (70 eV): *m/z* (%): 128 (4) [$M^+ +1$], 127 (32) [M^+], 126 (5), 112 (94), 86 (100), 58 (25).

Anal. Calc. for $C_8H_{17}N$ ($M_r=127.2$): C, 75.52; H, 13.47; N, 11.01. Found: C, 75.40; H, 13.42; N, 11.13%.

*2-Butyl-1-octene (**1b**).* A hexane solution (1.6 M) of 25 mmol of BuLi was added slowly at −78 °C to a solution of 0.81 g (5.0 mmol) of $FeCl_3$ in 30 ml of THF (5 mmol of the 25 mmol BuLi are necessary for the *in situ* reduction of $FeCl_3$ to give $FeCl_2$). After 2 h stirring 0.95 g (5.0 mmol) of **1** in 4 ml of THF was added slowly. After further stirring for 2 h at −78 °C, preparation according to 'AAV 2' [8] and cleaning by column chromatography (petroleum ether; SiO_2) and then by HPLC (hexane, SiO_2) 0.57 g (68%) of **1b** was isolated as an oil. Another synthesis of **1b** is described in ref. 22.

*5-Butyl-5-hexene-3-ol (**3b**).* 4.0 mmol of Bu_4FeLi_2 were reacted analogously to the synthesis of **1b** with 0.72 g (4.0 mmol) of **3**. Cleaning of the crude product by flash chromatography (petroleum ether:ether = 5:1, SiO_2) yielded 0.47 g (76%) of **3b** as an oil with $n_D^{22}=1.5661$.

^1H NMR ($CDCl_3$): $\delta=0.95$ (m, 6H, $2CH_3$), 1.39 (m, 6H, 3 CH_2), 1.76 (s, 1H, OH), 2.13 (m, 4H, $CH_2-C=$ and $=C-CH_2$), 3.63 (m, 1H, $H-C-OH$), 4.85 (m, $^2J=1.46$ Hz, 2H, $=CH_2$). ^{13}C NMR ($CDCl_3$): $\delta=10.17$ (CH_3), 14.11 (CH_3), 22.63 (CH_2), 30.03 (CH_2), 30.10 (CH_2), 35.76 (CH_2), 44.27 (CH_2), 70.34 (CH), 112.12 ($=CH_2$), 147.18 (C). MS (70 eV): *m/z* (%): 156 (0.2) [M^+], 155 (0.2), 138 (3), 127 (2), 109 (16), 98 (40), 70 (30), 69 (26), 59 (100), 57 (76), 41 (64).

Anal. Calc. for $C_{10}H_{20}O$ ($M_r=156.3$): C, 76.94; H, 12.90. Found: C, 75.89; H, 13.28%.

(iv) Evaluation of cross-coupling by GC

The reaction conditions, reagent/substrate ratios, solvents and reaction temperatures are given in Tables 1–3 or in the corresponding legends. The reactions (normally with 0.25 mmol transition metal reagent) and preparations were performed as in 'AAV 2' of ref. 8 with the following modifications: reaction time at −78 °C 2 h instead of 0.5 h; in the case of Me_2CuLi hydrolysis with 10 ml of a saturated solution of NH_4Cl in water in order to destroy stable Cu complexes. The yield was determined by GC with a fused silica capillary column FS-SE 52 (= column A) or HP-5 (= column B) from Macherey-Nagel (Düren, Germany) and with 2-octanol as internal standard. The GC conditions are stated in the following order: column/starting temperature (°C)/pause (min)/heating rate (°C/min)/end temperature (°C). **1a** + **2a**: A/60/0/6/260; **1a** + **3a**: A/50/0/5/260; **1a** + **4a**: B/80/0/8/280; **1a** + **5a**: A/60/0/6/260; **1a** + **6a**: B/80/0/8/280; **1a** + **7a**: B/80/0/8/280; **1a** + **8a**: A/60/0/6/260; **1b** + **3b**: A/60/0/5/260; **2a** + **3a**: A/50/0/5/260.

(v) Determination of CH_4

To the ether solution of Me_4FeLi_2 or Me_4MnLi_2, prepared as given in (i), 1 mol equiv. of **2** or **3** was added at −78 °C (Me_4FeLi_2) or −30 °C (Me_4MnLi_2), then warmed to 20 °C. The gas generated was measured as described in ref. 23. The number of mols was calculated taking the solubility of CH_4 in ether into consideration. CH_4 was identified by GC with authentic CH_4. Results: Me_4FeLi_2 + **2**: 0.87 equiv. CH_4; Me_4FeLi_2 + **3**: 0.97 equiv. CH_4; Me_4MnLi_2 + **2** or **3**: 0.89 equiv. CH_4.

Acknowledgements

This work was supported by the Volkswagen-Stiftung and the Deutsche Forschungsgemeinschaft.

References

1 T. Kauffmann, T. Möller, H. Rennefeld, S. Welke and R. Wieschollek, *Angew. Chem., 97* (1985) 351; *Angew. Chem., Int. Ed. Engl., 24* (1985) 348.
2 T. Kauffmann, K. Abel, W. Bonrath, M. Kolb, T. Möller, C. Pahde, S. Raedeker, M. Robert, M. Wensing and B. Wichmann, *Tetrahedron Lett., 27* (1986) 5351.
3 T. Kauffmann in H. Werner and G. Erker (eds.), *Organometallics in Organic Synthesis 2*, Springer, Berlin, 1989, p. 161; T. Kauffmann, C. Beirich, A. Hamsen, T. Möller, C. Philipp and D. Wingbermühle, *Chem. Ber., 125* (1992) 157; T. Kauff-

mann, C. Neiteler and S. Robbe, *Chem. Ber., 126* (1992) 2418.

4 M.T. Reetz, *Acc. Chem. Res., 26* (1993) 462; X. Chen, E.R. Hortelano, E.L. Eliel and S.V. Frye, *J. Am. Chem. Soc., 114* (1992) 1778.

5 T. Kauffmann and D. Stach, *Angew. Chem., 103* (1991) 1683; *Angew. Chem., Int. Ed. Engl., 30* (1991) 1684.

6 T. Kauffmann, B. Laarmann, D. Menges, K.-U. Voss and D. Wingbermühle, *Tetrahedron Lett., 31* (1990) 507.

7 T. Kauffmann, G. Hopp, B. Laarmann, D. Stegemann and D. Wingbermühle, *Tetrahedron Lett., 31* (1990) 511.

8 T. Kauffmann and D. Stach, *Chem. Ber., 125* (1992) 913.

9 D. Stach, *Dissertation,* Universität Münster, Germany, 1991.

10 H. Nienaber, *Dissertation,* Universität Münster, Germany, prospectively 1994.

11 I.N. Juchnovski, J.S. Dimitrova, I.G. Binev and J. Kaneti, *Tetrahedron, 34* (1978) 779.

12 I.N. Juchnovski and I.G. Binev, *J. Organomet. Chem., 99* (1975) 1.

13 D.H. Williams and I. Fleming, *Spektroskopische Methoden zur Strukturaufklärung (A)*, Thieme, Stuttgart, 3rd edn., 1975, p. 59.

14 D. Menges, *Dissertation,* Universität Münster, Germany, 1991.

15 M.F. Semmelhack and L. Ryono, *Tetrahedron Lett.,* (1973) 2967.

16 J.P. Collman and L.S. Hegedus, *Principles and Applications of Organotransition Metal Chemistry,* Oxford University Press, Mill Valley, CA, 1980, p. 569.

17 J. March, *Advanced Organic Chemistry,* Wiley, New York, 3rd edn., 1985, p. 186; L. Mandolini, *J. Am. Chem. Soc., 100* (1978) 550.

18 H. Gilman and F.K. Cartledge, *J. Organomet. Chem., 2* (1964) 447.

19 R. Kaiser, *Chromatographie in der Gasphase,* Part 4, Bibliographisches Institut, Mannheim, 2nd edn., 1969, p. 211.

20 C.B. Pollard and R.F. Parcell, *J. Am. Chem. Soc., 73* (1951) 2925.

21 R.F. Parcell and C.B. Pollard, *J. Am. Chem. Soc., 72* (1950) 2385.

22 A.R. Chamberlin, J.E. Stemke and F.T. Bond, *J. Org. Chem., 43* (1978) 147.

23 F. Pregel and H. Roth, *Quantitative organische Mikroanalyse,* Springer, Vienna, 7th edn., 1958, p. 233.