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Reversibility of titanocene-catalyzed hydromagnesation of silylacetylenes

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Abstract

The regioisomeric silylvinylmagnesium compounds **A** and **B**, products of titanocene-catalyzed hydromagnesation of trimethylsilylacetylenes, are in a rapid dynamic equilibrium with starting acetylene and, therefore, with each other due to the reversibility of the reaction. The existence of this equilibrium is demonstrated by transfer, under the conditions of hydromagnesation, of 'HMgBr' from the vinylmagnesium compounds **A/B** to other acetylenes with regeneration of the starting acetylenes. $\text{Me}_3\text{Si}(\text{BrMg})\text{C}\equiv\text{C}(\text{H})\text{R}$ (**A**) $\rightleftharpoons$ $\text{Me}_3\text{SiC}\equiv\text{CR}$ $\rightleftharpoons$ $\text{Me}_3\text{Si}(\text{H})\text{C}\equiv\text{C}(\text{MgBr})\text{R}$ (**B**). The position of the equilibrium between **A** and **B** was determined by deuterolysis and found to depend on the substituent, being 77:23 for $\text{R} = n\text{-C}_5\text{H}_{11}$ and 95:5 for $\text{R} = \text{cyclo-CH}_2\text{C}_6\text{H}_{11}$ in diethyl ether. Reactions of the magnesium reagents **A/B** with electrophiles produce mixtures of linear (type **A**) and branched (type **B**) products. The ratios of regioisomeric products differ depending on the electrophile and the conditions (from 98:2 to 20:80). This is due to the preferential reaction of one of the regioisomers and to rapid equilibration.

Introduction

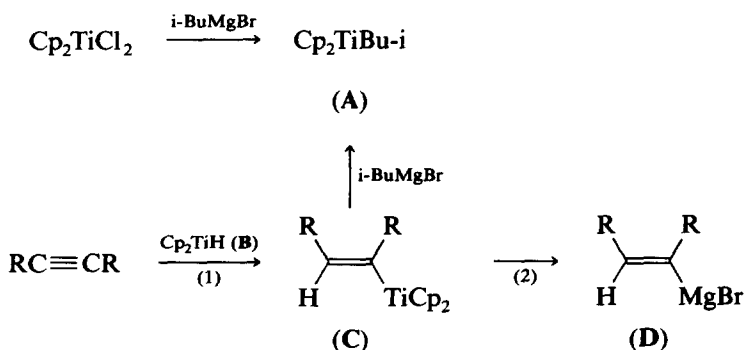
In recent years hydromagnesation of silylacetylenes catalyzed by titanocene dichloride has been increasingly used in organic synthesis. This is due to its high regio- and stereoselectivity and to the versatility of the resulting 1-(1-silylvinyl)magnesium reagents (see ref. 1 and references therein). In our investigations of the application of these reagents to the synthesis of eicosanoids, we have been faced with some results which we report below, which can be most easily interpreted by assuming the reversibility of the hydromagnesation reaction. As such a reversibility could have significant consequences for the applicability of the acetylene hydromagnesation reaction, we have studied the question in more direct experiments. Here, we report on the reversibility of silylacetylene hydromagnesation when catalyzed by

titanocene dichloride, and present examples of its influence on the reactivity of the products, the silylvinylmagnesium bromides.

Results and discussion

The accepted mechanism of titanocene-catalyzed hydromagnesation of acetylenes (see Scheme 1) [2] postulates that the latter are hydrotitanated (step 1) by the hydridotitanium(III) species **B** generated in situ by the Grignard reagent from titanocene dichloride via the intermediate titanium(III) species **A**. The product **C** exchanges titanium for magnesium (step 2) producing the final vinylmagnesium compound **D** and titanium species **A**, thus closing the catalytic cycle. After completion of the process, perhaps after all Grignard reagent has been consumed, the hydridotitanium species **B** ceases to be regenerated. However, if steps 1 and 2 are reversible, **B** continues to exist in its equilibrium concentration (which is most probably very low) and could be trapped continuously by adding another acetylene, producing new hydromagnesated species similar to **D** and regenerating the starting acetylene (see Scheme 2). Of course, this process should also be reversible. Therefore the demonstration of (reversible) hydridomagnesium transfer from species **D** to an other acetylene, with the regeneration of starting acetylene, could be regarded as a proof of the reversibility of acetylene hydromagnesation reactions.

The results of the experiments observing the hydridomagnesium transfer are shown in Table 1. The first, starting acetylene **I** taken in small excess (1.06 molar equivalent), was hydromagnesated by isobutylmagnesium bromide in the presence of 8 mol% of titanocene(IV) dichloride, under the exact conditions described by Sato [2], except that excess catalyst was present, to accelerate the process. Completion of the reaction takes 20 min to 18 hours, depending on the acetylene, and results in formation of an equivalent quantity of the corresponding vinylmagnesium compound **II**. Then an equivalent of the other acetylene **I**^{*} was added and the course of the process was followed by GLC analysis of protonated aliquots. To make the diagram more clear the second, recipient acetylenes and their products bear asterisks and the corresponding formulas in Scheme 2 are in italics. In most of the **I**^{*} + **II** pairs the gradual appearance of the starting acetylene **I** was observed with concomitant formation of the new vinylmagnesium compound **II**^{*}. The forma-



Scheme 1

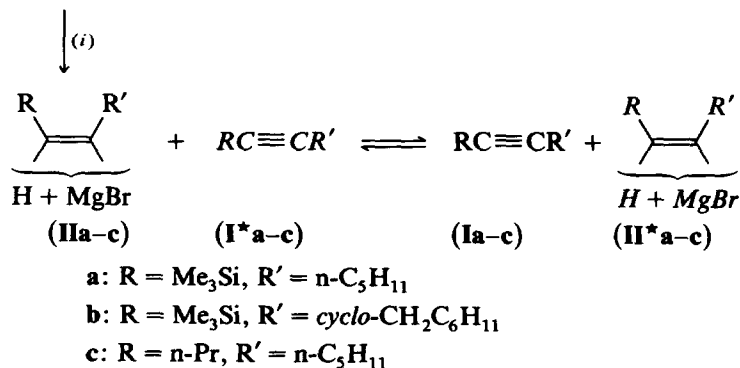
Table 1

Reactions of *trans*-hydromagnesation of vinylmagnesium bromides II and acetylenes I* (see Scheme 2)

Entry	Starting materials	Reaction time (h)	Composition of reaction mixture				Yield of II*, %'s on reacted II
			I	I*	II	II*	
1	IIa + I*b	7.5	18	87	82	13	72
		94.5	52	75	48	25	49
2	IIa + I*c	24	63	44	37	58	92
		95	91	27	9	73	80
3	IIb + I*a	4.25	29	83	71	17	58
		94.3	75	59	25	41	55
4	IIb + I*c	28.5	96	10	4	90	94
5	IIc + I*a	25	0	100	100	0	0
6	IIc + I*b	25	0	100	100	0	0

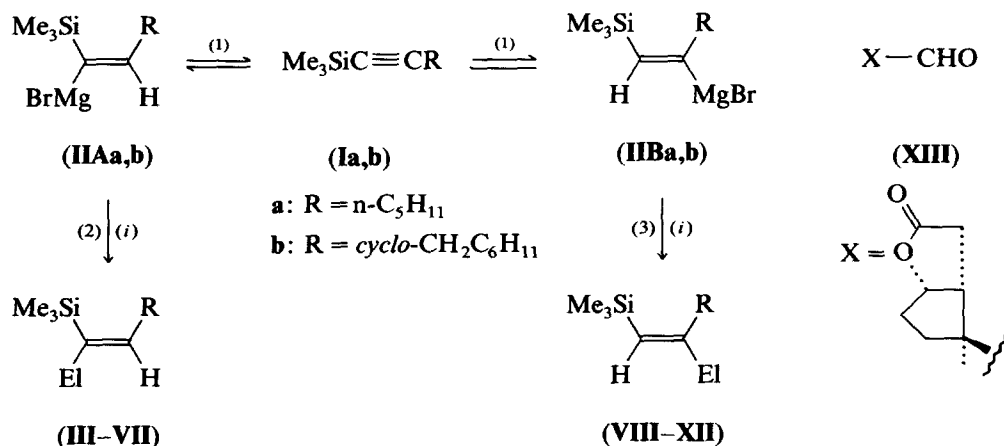
tion of the latter was demonstrated by reactions with water as well as with trimethylsilyltriflate, both of which gave the same products (*vide infra*) as obtained from the vinylmagnesium reagent synthesized by the direct hydromagnesation. The process approached equilibrium in 28–95 hours, but true equilibrium was not reached owing to deactivation of the catalyst.

The rate of the *trans*-hydromagnesation and its extent should both depend on the relative susceptibilities to hydromagnesation of the recipient acetylenes. The determination of relative rates of hydromagnesation of the acetylenes Ia–c in competitive experiments was confounded by the exchange process (*cf.* Scheme 2). A rough estimation was obtained by comparing the reaction periods needed for a 95% hydromagnesation under standard conditions (see Experimental). These relative rates were found to be 3:1:60 for Ia–c, respectively, and correlate well with the extents of *trans*-hydromagnesation. Transfers to the most effective recipient Ic (entries 2 and 4 in Table 1) were almost complete within a short time, while no

$$RC \equiv CR' \text{ (Ia-c)}$$
Scheme 2. (i) i-BuMgBr, Cp₂TiCl₂, Et₂O.

transfer was detected from the corresponding magnesium compound **IIc** (entries 5 and 6). The transfer of magnesium from the magnesium compounds **IIa,b** to the acetylenes **Ia,b** was of medium extent, and, compared with the reverse process **IIa** $\rightarrow$ **Ib** (entry 1), the transfer to the better recipient **Ib** $\rightarrow$ **Ia** (entry 3) was significantly more complete. We consider these observations to be additional evidence of the reversible *trans*-hydromagnesation approaching an equilibrium under the chosen experimental conditions, at least in the case of trimethylsilyl-substituted acetylenes.

The reversibility of the acetylene hydromagnesation that we have discovered would be expected to have several consequences on the chemistry of the resulting vinylmagnesium compounds **II**. Firstly, a dynamic equilibrium may exist between the regioisomeric vinylmagnesium compounds **IIAa,b** and **IIBa,b** formed from silylacetylenes **Ia,b** (Scheme 3). Indeed, due to their equilibrium with the parent acetylenes **Ia,b** [reaction (1)], the regioisomers should be in equilibrium with each other, and the equilibrium position be determined solely by thermodynamics. Although *inter*-molecular *trans*-hydromagnesation (Scheme 2) takes several hours to achieve equilibrium, the analogous process in Scheme 3 could proceed intramolecularly, without dissociation of delivered hydridotitanium species from an acetylene molecule (so-called "internal return"), much more rapidly. Therefore, an equilibrium in Scheme 3 might be reached already while hydromagnesation is proceeding. Analyzing the ratios of regioisomeric **IIAa** and **IIBa** by deuteryolysis of the aliquots of the reaction mixtures during the acetylene **Ia** hydromagnesation showed the constant ratio of 77:23 after 2, 5 or 22 hours (entry 1 in Table 2). In a similar experiment with the acetylene **Ib** the ratio of the vinylmagnesium compounds **IIAb** to **IIBb** was found to be 95:5 after 22 hours (entry 2). The preponderance of the 1-silyl-1-vinylmagnesium regioisomers **IIAa,b** is to be expected from the well-known stabilisation of carbanions by silyl substituents, and the lower proportion of the minor regioisomer **IIBb** in comparison with **IIBa** is consistent with the destabilisation of the former by steric repulsion of the bromomagnesium group with the bulkier cyclohexylmethyl substituent in **IIBb**. All these data agree with the notion of



Scheme 3. (i) Electrophile.

Table 2

Selectivity of electrophile reactions with vinylmagnesium compounds **IIA/B** (see Scheme 3)

Entry	Starting material	Electrophile	T (°C)	Time (min)	EI	Codes	Products		Analysis method
							Yield (%)	Ratio	
1	IIA/Ba ^a	D ₂ O	23	1	D	IIIa + VIIIa	100 ^b	77:23	PMR
2	IIA/Bb	D ₂ O	22	1	D	IIIb + VIIIb	100 ^b	95:5	PMR
3	IIA/Ba	Me ₃ SiOTf	5	120	Me ₃ Si	IVa + IXa	72 ^b	74:26	GLC,
			23	25			80 ^b	72:28	PMR
			55	60			69 ^b	85:15	
4	IIA/Bb	Me ₃ SiOTf	5	195	Me ₃ Si	IVb + IXb	88 ^b	95:5	GLC
			23	120			87 ^b	93:7	
5	IIA/Ba	CBr ₄	23	10	Br	Va + Xa	82 ^b	98:2	GLC
6	IIA/Ba	cycloheptanone	23-25	150	hydroxy-cycloheptyl	VIa + XIa	33-44 ^c	81-88:12-19	PMR
7	IIA/Ba	XIII	-20	150	CHOHX ^d	VIIa + XIIa	65 ^c	94:6	GLC
8	IIA/Ba	CITf(OPr-i) ₃	-78	10		VIIa + XIIa	47 ^b	20:80	GLC
		+ XIII	-78	120	CHOHX ^d				

^a See Experimental. ^b GLC yield. ^c Isolated yield. ^d For meaning of X see formula.

a rapidly established equilibrium between the regioisomeric silylvinylmagnesium compounds **IIA** and **IIB**, the position of which is governed by the thermodynamic stability of the components. In his pioneering paper [2] Sato described a regioisomeric ratio of 95 : 5 for silylvinylmagnesium compounds, which was found to be slightly dependent on the procedure of hydromagnesation. Sato's ratio is close to ours for the acetylene **Ib**, but differs from that for the acetylene **Ia**, for unknown reasons. We can only suggest minor differences in the procedures influence the quantity that is generated of the active catalyst (species **B** in Scheme 1) and thus the rate of establishing the equilibrium.

We should note that in the other regioselective acetylene hydromagnesations (arylacetylenes, silylarylacetylenes, propargyl alcohols) that have been described, the main regioisomer formed is the most stable thermodynamically [2–4], in other words the results could also be explained by the position of the equilibrium between the regioisomers of vinylmagnesium compounds.

The second possible consequence of the reversibility of acetylene hydromagnesation lies in the ratios of regioisomers formed in the reactions of vinylmagnesium compounds **IIA/B** with various electrophiles (reactions 2 and 3 in Scheme 3). If the rates of these reactions are both much greater than the rate of reaction 1, the ratio of linear products **III–VII** to corresponding branched ones **VIII–XII** would be equal to the ratio of magnesium compounds **IIA** and **IIB** in equilibrium. Deuterium oxide is believed to be such an electrophile. However, if the rates of reactions 2 and/or 3 are smaller than that of reaction 1, the ratio of linear and branched products should depend on the ratio of these reaction rates being different from the equilibrium ratio and influenced by the reaction conditions. We investigated the reactions of the vinylmagnesium compounds **IIA/B** with several electrophiles (see Table 2). Reactions with trimethylsilyltriflate (trimethylsilylchloride does not react) with a 77 : 23 mixture of the magnesium compounds **IIA/Ba** provided mixtures of the corresponding silylated compounds **IVa** and **IXa**, with compositions close to those of the starting mixture, with dependence on the reaction temperature (entry 3). Another extreme was found in the reaction with carbon tetrabromide which resulted in almost pure bromide **Va** with traces only of regioisomeric **Xa** (entry 5). Intermediate cases were found in reactions with aldehyde **XIII** (a prostanoid synthon [5]) and cycloheptanone (taken as an example of a ketone with hardly any tendency to enolisation) where the proportions of minor regioisomers were in the range of 6–19%, being higher for ketone (entries 6, 7). An analogous silylation of a 95 : 5 mixture of the magnesium compounds **IIA/Bb** resulted in the mixture of **IVb** and **IXb** with the same ratio of regioisomers (entry 4). The most striking result was encountered when the bromomagnesium residue in the compounds **IIA/Ba** was initially substituted for tri(isopropoxy)titanium(IV) and the resulting titanium reagent reacted with the aldehyde **XIII** (entry 8). The carbinol **XIIa**, which was the minor isomer in a corresponding reaction of the magnesium reagent **IIA/Ba**, now became by far the major isomer. One or more of the following reasons could explain this result. Selective generation of the titanium reagent of type **B**, its preponderance in equilibrium and enhanced reactivity, but the primary reason is again the dynamic equilibrium between the regioisomers of silylvinylmagnesium(titanium) compounds. It is rapid in this example at -78°C due to additional catalysis by tri(isopropoxy)titanium(IV) compounds [6] present in stoichiometric quantity.

We have demonstrated the reversibility of titanocene-catalyzed hydromagnesation

tion only in the case of silylalkylacetylenes, but see no reason why the same phenomenon could not exist with other acetylenes.

Experimental

Spectra conditions: IR, Specord IR-75 (G.D.R.), CCl_4 solutions; PMR, Tesla BS-487C (80 MHz) (C.S.S.R.), and Bruker WH-360 (360 MHz) (F.R.G.), CCl_4 solutions, internal standard: tetramethylsilane; mass-spectra (MS), LKB 2091 (Sweden), EI at 22.5 eV, in the process of chromatography on open tubular glass capillary column, 25 m $\times$ 0.36 mm, SE-30 liquid phase 0.4 micron, carrier gas (helium) velocity of 60 cm/s, column, separator and ion source temperatures 110–203°C (depending on the substance), 280°C and 250°C, respectively. GLC analyses: Chrom-5 apparatus (C.S.S.R.); condition No. 1: open tubular fused silica column, 50 m $\times$ 0.25 mm, OV-1 0.2 micron, helium 35 cm/s, 110°C for 2 min, then heating to 270°C at 20°/min; condition No. 2: same column, helium 30 cm/s, 100°C for 4 min, then heating to 270°C at 20°/min; condition No. 3: open tubular glass capillary, 25 m $\times$ 0.35 mm, SP-1000 0.3 micron, helium 50 cm/s, isothermally at 234°C. For TLC on silica gel Silufol UV-254 (C.S.S.R.) plates were used.

All experiments with organometallic compounds were performed in the static atmosphere of purified argon in diethyl ether purified by distillation from benzophenone-sodium. Usual treatment of reaction mixtures consisted in dilution by hexane or diethyl ether, separation of the aqueous phase, additional extraction by the same organic solvent, washing of combined extracts with brine, drying with anhydrous Na_2SO_4 , and rotoevaporation at aspirator vacuum. Isobutylmagnesium bromide in ether was prepared by a standard method [7].

Synthesis of starting materials

1-Trimethylsilylhept-1-yne (Ia). Prepared from commercial 1-heptyne according to ref. 8, yield 89%, b.p. 75–76°C/20 mmHg, n_D^{20} 1.4342 (lit. [8]: b.p. 176°C, n_D^{20} 1.4344).

1-Trimethylsilyl-3-cyclohexylprop-1-yne (Ib). 8.6 ml of 1.4 M solution (12.0 mmol) of n-butyllithium were added to a stirred solution of 1.7 ml (12.1 mmol) of diisopropylamine in 20 ml abs. ether at –20°C and after 15 min a solution of 1.22 g (10.0 mmol) of cyclohexylallene (prepared according to ref. 9, b.p. 50–51°C/17 mmHg, n_D^{24} 1.4789) was added. The reaction mixture was maintained at 30–36°C. After 4.5 h GLC analysis (condition No. 1) of the water-quenched reaction mixture demonstrated the conversion into the 8:2 mixture of 3-cyclohexylprop-1-yne and presumed 3-cyclohexylprop-2-yne, retention times (RT) being 3.93 and 4.29 min, respectively, for starting allene 4.18 min. The bright-yellow reaction mixture was cooled to –78°C, 1.7 ml (13.4 mmol) of trimethylsilylchloride were added, the mixture was heated for 15 min to 23°C and maintained at this temperature for 1.5 h, which resulted in the formation of a white precipitate. Reaction was quenched at 0°C by adding 25 ml of saturated aqueous ammonium chloride solution and treated in the usual manner (ether). Fractional distillation isolated 1.43 g (74%) of silylacetylene **Ib**, b.p. 93–98.5°C/9 mmHg, $n_D^{23.5}$ 1.4619. IR (cm^{-1}): 2127, 1450, 1251, 1029, 843. PMR (CDCl_3 , 80 MHz), δ , ppm: 0.137 s (9H, SiMe_3), 2.06 d (2H, J 6.2 Hz, $\text{CH}_2\text{C}\equiv\text{C}$). MS, m/z (rel. intensity, %): 194 (5, $[M]^+$), 179 (100, $[M - \text{Me}]^+$),

120 (5, $[M - \text{HSiMe}_3]^+$), 112 (11, $[\text{Me}_3\text{SiC}\equiv\text{CMe}]^+$), 83 (5, $[\text{C}_6\text{H}_{11}]^+$), 73 (16, $[\text{Me}_3\text{Si}]^+$).

Titanocene-catalyzed hydromagnesation of acetylenes Ia–c.

A. For use in transfer hydromagnesation reactions. To the suspension of 10 mg (0.04 mmol) of finely ground titanocene dichloride in solution of 0.50 mmol of an alkyne and 25–27 mg of *n*-decane (internal standard for GLC analysis) in 0.5 ml of abs. ether was added an ether solution of isobutylmagnesium bromide (2.16 *M*, 0.22 ml, 0.47 mmol) under stirring at 23°C. The reaction mixture turned out to be brown–blackish with a complete dissolution of titanocene. The course of the reaction was followed by GLC analysis of aliquots quenched by pouring into a hexane–phosphate buffer solution (pH 6.8), using the percentage of the corresponding (*Z*)-olefine formed after protonation as a measure of hydromagnesation completeness. Data for the acetylenes **Ia–c**: reaction times 5–6 h, 18 h, 15–20 min; conversions 95%, 90–95%, 94–95%; RT (condition No. 2) of starting acetylenes 5.92, 9.00, 5.57 min, of resulting (*Z*)-olefins 6.09, 9.29, 5.49 min, resp. *Spectral data for protonation products.* 1-Trimethylsilylhept-1(*Z*)-ene. IR (cm^{-1}): 1611, 1250, 853, 836. PMR (80 MHz), δ , ppm: 0.10 s (9H, SiMe_3), 0.89 t (3H, J 4.5 Hz, Me), 2.04 q (2H, J 6.5 Hz, C^3H_2), 5.39 dt [1H, J 14.5 + 1 Hz (compare with [10]), C^1H], 6.24 dt (1H, J 14.5 + 7.2 Hz, C^2H). MS, m/z (%): 170 (3, $[M]^+$), 155 (100, $[M - \text{Me}]^+$), 114 (37, $[\text{Me}_3\text{SiCH}=\text{CHMe}]^+$), 99 (32, $[114 - \text{Me}]^+$), 95 (20), 85 (15), 73 (64, $[\text{Me}_3\text{Si}]^+$), 59 (52, $[\text{Me}_2\text{SiH}]^+$). 1-Trimethylsilyl-3-cyclohexylprop-1(*Z*)-ene. IR (cm^{-1}): 1606, 1448, 1258, 1248, 854, 833, 686. PMR (80 MHz), δ , ppm: 0.10 s (3H, SiMe_3), 1.93 t (2H, J 6.5 Hz, C^3H_2), 5.42 dt (1H, J 14 + 1 Hz, C^1H), 6.25 dt (1H, J 14 + 7 Hz, C^2H). MS, m/z (%): 196 (0.5, $[M]^+$), 181 (100, $[M - \text{Me}]^+$), 153 (19), 114 (89, $[\text{Me}_3\text{SiCH}=\text{CHMe}]^+$), 99 (20, $[\text{Me}_3\text{SiCH}=\text{CH}]^+$), 83 (20, $[\text{C}_6\text{H}_{11}]^+$), 73 (89), 59 (19). 4(*Z*)-Decene. IR (cm^{-1}): 1656, 715. PMR (80 MHz), δ , ppm: 0.89 t (6H, J 6.5 Hz, $2 \times \text{Me}$), 1.95 q (4H, J 5 Hz, $2 \times \text{CH}_2\text{C}=\text{}$), 5.24 m (2H, $\text{CH}=\text{CH}$).

B. For use in reactions with electrophiles. Procedure as above but using 0.02 mmol of titanocene dichloride and 0.85 mmol of isobutylmagnesium bromide and reaction times (for **Ia,b**) of 18–20 h.

Reactions of transfer hydromagnesation

To the solution of alkenylmagnesium bromide prepared as described above a solution of the equivalent quantity (0.50 mmol) of an acetylene **Ia–c** in 0.3 ml abs. ether was added and the course of *trans*-hydromagnesation was followed by GLC analysis (condition No. 2) of aliquots quenched by pouring into the mixture of phosphate buffer (pH 6.8) and hexane. For the results see Table 1.

Reactions of the alkenylmagnesium bromides IIa,b with electrophiles (conditions and results see Table 2)

A. IIa with deuterium oxide. The aliquots (0.5 mmol) of the reaction mixture in the synthesis of magnesium reagent **IIa** were withdrawn and quenched by pouring them into the mixture of deuterium oxide (1 ml) and hexane. Usual work-up followed by filtration in hexane through 0.2 g Kieselgel 60 (ASTM) provided the mixtures of the deuterated olefines **IIIa** + **VIIIa** for analysis by PMR.

B. IIb with deuterium oxide. A portion of the magnesium reagent **IIb** (0.5 mmol) was quenched by deuterium oxide (1 ml) and the product isolated as above.

C. *IIa* with trimethylsilyl trifluoromethanesulphonate. To the solution of 0.50 mmol of *IIa* (see above) 1.20 ml of a 30% solution of silyl reagent in benzene were added and the reaction was followed by GLC. After quenching with phosphate buffer (pH 6.8), usual treatment and filtration in hexane through a small Kieselgel 60 column the mixtures of 1,1- and 1,2-bis(trimethylsilyl)hept-1(*E*)-enes (*IVa* + *IXa*) were isolated. IR of the mixture (cm^{-1}): 1573, 1246, 859, 836, 686. Compound *IVa*. GLC (condition No. 3), RT: 8.09 min. PMR (80 MHz), δ , ppm: 0.06 s (9H, *cis*-SiMe₃), 0.14 s (9H, *trans*-SiMe₃), 0.87 t (3H, *J* 5 Hz, Me), 2.10 m (2H, C³H₂), 6.59 t (1H, *J* 7 Hz, C²H). Compound *IXa*. GLC: 7.57 min. PMR: 0.06 s (9H, C¹SiMe₃), 0.11 s (9H, C²SiMe₃), 5.94 b.s (1H, C¹H) (compare with [11]). MS, *m/z* (% for *IVa* and *IXa*, respectively): 242 (5, 0.3, [*M*]⁺), 227 (41, 6, [*M* - Me]⁺), 186 (25, 41, [(Me₃Si)₂C=CHMe]⁺), 153 (100, 29, [227 - HSiMe₃]⁺), 98 (54, 48), 73 (70, 100, [SiMe₃]⁺); metastable ions 143.0 (242 → 186), 103.1 (227 → 153), 62.8 (153 → 98).

D. *IIb* with trimethylsilyl trifluoromethanesulphonate. Magnesium reagent *IIb*, treated analogously to the above procedure, produced 1,1-bis(trimethylsilyl)-3-cyclohexylprop-1-ene (*IVb*) with a small (see Table 2) admixture of 1,2-bis(trimethylsilyl)-3-cyclohexylprop-1(*E*)-ene (*IXb*). GLC (condition No. 2), RT: 8.86 and 8.42 min, resp. Spectra of the mixture. IR (cm^{-1}): 1566, 1450, 1262, 1250, 893, 856, 833, 683. PMR (80 MHz), δ , ppm: 0.06 s (9H, *cis*-SiMe₃), 0.15 s (9H, *trans*-SiMe₃), 2.06 t (2H, *J* 6.5 Hz, C³H₂), 6.62 t (1H, *J* 7.2 Hz, C²H) (signals of the minor isomer could not be identified as they coincided with signals of impurities, mainly protonation product). MS, *m/z* (% for major and minor isomer, resp.): 268 (6, 0, [*M*]⁺), 253 (39, 6, [*M* - Me]⁺), 186 (45, 65, [(Me₃Si)₂C=CHMe or isomer]⁺), 179 (100, 9, [253 - HSiMe₃]⁺), 98 (91, 64), 73 (64, 100).

E. *IIa* with carbon tetrabromide. To a solution of 0.49 mmol of *IIa* a solution of 185 mg (0.56 mmol) CBr₄ in 0.3 ml abs. ether was added at ambient temperature. Exothermic reaction resulted in red-brown discoloration. The quenching by phosphate buffer and usual treatment (ether) afforded after filtration in hexane through a small Kieselgel 60 column a mixture of 1- and 2-bromo-1-trimethylsilylhept-1(*E*)-enes (*Va* + *Xa*), a yellow oil, with 15–20% of *Ia*, protonated and unidentified compounds as impurities. IR of the mixture (cm^{-1}): 1604, 1470, 1460, 1250, 1106, 853, 839, 696, 673, 626. Compound *Va*. GLC (condition No. 2), RT: 8.29 min. PMR (80 MHz), δ , ppm: 0.26 s (9H, SiMe₃), 0.90 t (3H, *J* 5 Hz, Me), 2.04 q (2H, *J* 6.5 Hz, C³H₂), 6.71 t (1H, *J* 8.2 Hz, C²H). Compound *Xa*. GLC: 7.95 min. PMR: 0.17 s (9H, SiMe₃), 5.88 b.s (1H, C¹H). MS, *m/z* (% for *Va* and *Xa*, resp., ions with ⁸⁹Br): 248 (3, 15, [*M*]⁺), 153 (5, 7, [*M* - Me - HBr]⁺), 137 (99, 88, [BrSiMe₂]⁺), 95 (45, 39, [*M* - HBr - SiMe₃]⁺), 73 (84, 81, [SiMe₃]⁺), 67 (11, 7).

F. *IIa* with cycloheptanone. 199 mg (1.63 mmol) of cycloheptanone in 1.2 ml of abs. ether were used for 2 mmol of magnesium compound *IIa*. Quenching with saturated aqueous NH₄Cl solution, usual treatment (ether) and chromatography using 20 g of silica gel (Woelm, TSC) and hexane as eluent resulted in the isolation of 201 mg (44%) of the mixture of 1-[1'-(trimethylsilyl)hept-1'(*Z*)-en-1'-yl]cycloheptan-1-ol (*VIa*) and 1-[1'-(trimethylsilyl)hept-1'(*E*)-en-2'-yl]cycloheptan-1-ol (*XIa*), a light-yellow oil. IR of the mixture (cm^{-1}): 3607, 3485, 1603, 1460, 1448, 1250, 1023, 853, 839. Compound *VIa*. TLC (hexane-ethylacetate, 9:1), *R_f* 0.42. GLC (condition No. 2), RT: 14.09 min. PMR (80 MHz), δ , ppm: 0.20 s (9H, C^{1'}SiMe₃), 0.89 t (3H, *J* 5.5 Hz, Me), 2.06 q (2H, *J* 7 Hz, C^{3'}H₂), 6.01 t (1H, *J* 7.4

Hz, C^{2'}H). Compound **XIa**. TLC: 0.34. GLC: 13.73 min. PMR: 0.10 s (9H, SiMe₃), 5.78 s (1H, C^{2'}H). MS, *m/z* (% for **VIa** and **XIa**, resp.): 282 (24, 2, [M]⁺), 267 (14, 10, [M - Me]⁺), 266 (14, 1), 264 (40, 5, [M - H₂O]⁺), 249 (21, 16, [M - Me - H₂O]⁺), 223 (40, 1), 209 (42, 9, [M - Bu - H₂O]⁺), 208 (29, 8), 197 (71, 4), 195 (42, 3), 191 (28, 2, [M - H₂O - SiMe₃]⁺), 190 (29, 2), 155 (55, 60, [Me₂SiCH=CHAm]⁺), 153 (31, 10), 136 (16, 33), 121 (16, 39), 114 (13, 14, [Me₃SiCH=CHMe]⁺), 113 (55, 45, [Me₃SiCH=CHCH₂]⁺), 95 (17, 19, [cycloheptenyl]⁺), 75 (68, 23), 73 (100, 100).

G. IIa with 2-oxa-cis-bicyclo[3.3.0]octane-3-one-6-exo-carbaldehyde (XIII). 227 mg (1.47 mmol) of the aldehyde **XIII** in 1.5 ml of abs. THF were added at -78°C to the solution of 2.14 mmol of the magnesium compound **IIa**, the mixture was stirred for 150 min at -20°C and quenched with saturated aqueous NH₄Cl solution. Usual treatment (ethyl acetate) and high-performance flash chromatography (HPFC) [12] yielded a mixture of epimeric/isomeric alcohols α + β-**VIIa** and α + β-**XIIa**, separable by GLC (condition No. 3), RT: 13.2, 13.8, 12.0 and 12.6 min, ratio 15.0:78.5:1.4:5.1, resp. (stereochemistry determination will be published elsewhere in due course). The mixture of epimeric alcohols α + β-**VIIa** was isolated by repeated HPFC, R_f 0.57 and 0.50, respectively (methylene chloride-acetone-hexane, 8:1:1). IR (cm⁻¹): 3602, 3440, 1773, 1661, 1613, 1251, 1172, 1047, 852, 837. PMR (360 MHz), δ, ppm: 0.18 s (9H, SiMe₃), 0.90 t (3H, J 6.8 Hz, Me), 4.00 d and 4.10 d (total 1H, J 7.4 and 6.1 Hz, C^{1'}H), 4.94 t and 4.96 t (total 1H, J 6.3 and 6.5 Hz, C^{1'}H), 6.18 td and 6.21 td (total 1H, J 7.6 + 0.8 and 7.6 + 1.0 Hz, C^{3'}H). MS, *m/z* (% for α- and β-epimer, resp.) 324 (1.5, 1.6, [M]⁺), 309 (0.4, 0.3, [M - Me]⁺), 306 (0.5, 0.5, [M - H₂O]⁺), 291 (2, 2, [309 - H₂O]⁺), 253 (3, 3, [M - Am]⁺), 225 (2, 2), 199 (20, 21, [AmCH=CSiMe₃CHOH]⁺), 183 (100, 100), 129 (8, 2), 113 (10, 9), 75 (18, 16), 73 (14, 16); metastable ion: 168.2 (199 → 183).

H. IIa with tri(isopropoxy)titanium(IV) chloride followed by aldehyde XIII. An ether solution of 2.76 mmol of the magnesium compound **IIa** was cooled at -78°C under stirring and 1.30 ml of a 2.12 M hexane solution (2.76 mmol) of tri(isopropoxy)titanium(IV) chloride were added, followed by the solution of 100 mg (0.65 mmol) of aldehyde **XIII** in 1.4 ml of abs. THF after 10 min. The mixture was stirred at the same temperature for 2 h, heated to 23°C and, after 30 min, diluted by saturated aqueous NaHCO₃ solution and ether, and filtered. After usual treatment (ether) and flash chromatography the mixture of the alcohols α + β-**VIIa** and α + β-**XIIa** (ratio 5.4:14.6:33.6:46.4, respectively) was isolated, yield 98 mg (47%). IR of the mixture (cm⁻¹): 3590, 3470, 1788, 1613, 1253, 1162, 1045, 855, 835. PMR (360 MHz), δ, ppm (signals of epimeric α- and β-**XIIa**): 0.12 s (9H, SiMe₃), 0.90 t (3H, J 6.7 Hz, Me), 3.97 d (1H, J 5.8 Hz, C^{1'}H), 4.93 m (1H, C^{1'}H), 5.51 s (1H, SiC^{1''}H). MS, *m/z* (% for α- and β-epimer, resp.): 324 (12, 12), 309 (3, 3), 291 (27, 18), 267 (7, 8, [M - Bu]⁺), 253 (19, 14), 251 (8, 7, [M - SiMe₃]⁺), 199 (28, 24), 183 (22, 22), 153 (13, 11), 143 (30, 23), 133 (36, 26), 127 (42, 35), 126 (30, 24), 119 (24, 17), 118 (21, 16), 75 (97, 81), 73 (100, 100) (interpretation of the ions as above).

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