

Regiospecific and Diastereoselective C–H and C–Si Bond Activation of ω -Silyl-Substituted Alkane Nitriles by “Bare” Co^+ Cations in the Gas Phase

Georg Hornung, Detlef Schröder, and Helmut Schwarz*

Contribution from the Institut für Organische Chemie der Technischen Universität Berlin, D-10623 Berlin, Germany

Received September 16, 1996[⊗]

Abstract: The unimolecular decompositions of 5-methyl-7-trimethylsilylheptanenitrile (**1**) and 6-methyl-8-trimethylsilyloctanenitrile (**2**) complexed to “bare” Co^+ cations have been investigated by means of tandem mass spectrometry. The Co^+ -mediated bond activations display a high degree of selectivity in that the major (>90%) neutral product formed is trimethylsilane. Regio- and diastereoselective labeling experiments were conducted to gain further insight into the mechanistic details, in particular, the unique regio- and stereoselectivity of the losses of trimethylsilane from **1**/ Co^+ and **2**/ Co^+ , respectively. The reaction follows a clean 1,2-elimination process, in which the building blocks of the neutral HSiMe_3 stem exclusively from activation of a C–H bond in the ($\omega - 1$) position and the Si–C bond. The observed regiospecificity can only be accounted for by invoking a metal-ion-mediated cooperation of the SiMe_3 and the CN groups in the course of the multistep reaction sequence. The examination of diastereoselectively labeled isotopologues of **1** and **2** reveals a remarkably high diastereoselectivity for the desilylation, and the steric effects (SE) clearly exceed the kinetic isotope effects (KIE) associated with C–H and C–D bond activation, respectively; i.e., $\text{KIE} = 1.6 \pm 0.1$ and $\text{SE} = 4.1 \pm 0.2$ for **1**/ Co^+ , and $\text{KIE} = 1.5 \pm 0.1$ and $\text{SE} = 3.0 \pm 0.2$ for **2**/ Co^+ . These unprecedented examples for stereoselective C–Si bond activations by Co^+ in the gas phase can be rationalized in terms of steric interactions in the different conformations of the metallacyclic intermediates.

Introduction

The role of silicon compounds in organic synthesis is of enormous importance.^{1–3} Beside the use of silyl moieties as protecting groups for heteroatom functionalities and acidic C–H bonds, silyl groups exhibit a unique variety of different electronic properties that help to steer many organic and organometallic reactions.² A hallmark in this context is the well-known β -silicon effect which stabilizes a positive charge at a carbon atom in a β -position to the silyl group.

In this contribution, we examine the effect of a silyl substituent on the course of bond activation of alkane nitriles by “bare” Co^+ cations. The ability of transition-metal cations to regioselectively activate C–H and C–C bonds in mono-functionalized alkanes at sites away from the coordinating functional group was first demonstrated by Schwarz and co-workers,⁴ and the term “remote functionalization” has been suggested in order to point out the analogy to Breslow’s seminal investigations on biomimetic synthesis.⁵ In preliminary studies it has been shown previously that the introduction of a silyl substituent at the terminus of the alkyl chain has an enormous effect on the chemo- and regioselectivity of the remote functionalization of nitriles in the gas phase, because C–H bond activation occurs exclusively and involves specifically the positions α and β to the silyl group.⁶

[⊗] Abstract published in *Advance ACS Abstracts*, February 1, 1997.
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(3) The July/August 1995 issue of *Chemical Reviews* deals exclusively with silicon chemistry; see: Michl, J. *Chem. Rev.* **1995**, *95*, 1135.

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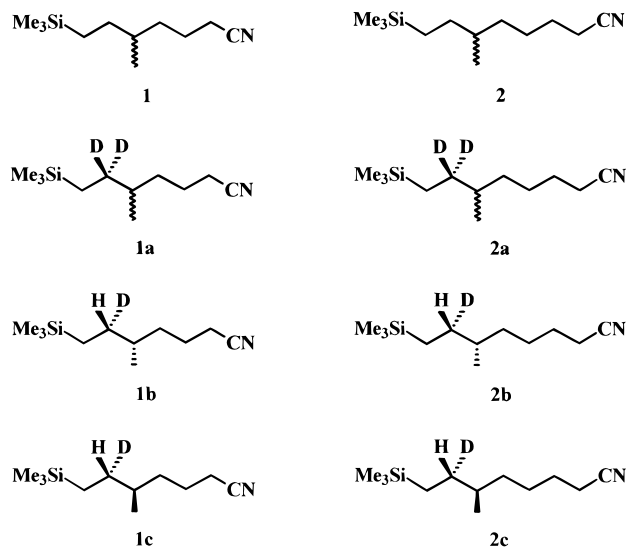


Figure 1. Model substrates as studied in the present paper: 5-methyl-7-trimethylsilylheptanenitrile (**1**), 6-methyl-8-trimethylsilyloctanenitrile (**2**), and their deuterium labeled isotopologues (**1a–c**, **2a–c**) (see ref 7).

A consequent extension of these studies is the application of stereochemical criteria in order to further probe the mechanistic details of the silicon-enforced bond activation in nitrile/ M^+ complexes. For that purpose, we have chosen the model substrates **1** and **2** (Figure 1)⁷ and examined the unimolecular

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(7) All compounds shown in Figure 1 were prepared in racemic form. The isotopologues **1b**, **1c**, **2b**, and **2c**, though racemic mixtures, were prepared as pure diastereomers; for the sake of clarity, for each of these substrates only one stereoisomer is shown in Figure 1.

reactions of their Co^+ complexes. 5-Methyl-7-trimethylsilyl-heptanenitrile (**1**) and 6-methyl-8-trimethylsilyloctanenitrile (**2**) were chosen on the following grounds. (i) It has been shown previously that C–H and C–C bond activation of heptane- and octanenitrile by Co^+ proceeds exclusively via the mechanism of remote functionalization; thus, the chain lengths of these two nitriles are suitable for a facile activation of the alkyl backbone.^{8,9} (ii) Our earlier study on the effect of a silyl group on the regiochemistry of C–H bond activation was based on heptane- and octanenitrile, respectively.⁶ (iii) Placing a methyl group in the ($\omega - 2$) position, slightly away from the terminus of the alkyl chain, introduces a stereogenic center and implements an additional stereochemical constraint without directly involving this methyl group in the bond-activation process. (iv) In the presence of a stereogenic center, Co^+ brings about diastereoselective C–C and C–H bond activation of 5-methylheptanenitrile and 6-methyloctanenitrile.¹⁰ (v) Finally, appropriate deuterium labeling allows a direct mass-spectrometric examination of the stereochemical effects by losses of isotopic variants of the neutrals in the unimolecular dissociation of labeled $1/\text{Co}^+$ and $2/\text{Co}^+$. In fact, the use of diastereoselectively labeled compounds for the examination of the stereochemical features of bond-activation processes by transition-metal cations cannot be underestimated and has recently been successfully used in a variety of different applications, i.e., cyclic compounds,¹¹ bifunctional molecules,¹² and well-designed acyclic substrates.^{10,13} Therefore, appropriate isotopologues of **1** and **2** are expected to reveal the effect of a silyl group in the presence of a stereogenic carbon atom on the regio- and stereochemical course of remote functionalization of nitriles by bare Co^+ .

Experimental Section

The experiments were performed with a modified VG ZAB/HF/AMD four-sector mass spectrometer of BEBE configuration (B stands for magnetic and E for electric sectors) which has been previously described in detail.¹⁴ Briefly, the metal complexes were generated in a chemical ionization source (CI, repeller voltage ca. 0 V) by 100-eV electron bombardment of an approximately 5:1 mixture of $\text{Co}(\text{CO})_3$ -(NO) and the corresponding nitrile. The ions were accelerated to 8 keV kinetic energy and mass-selected by means of B(1)/E(1) at a resolution of $m/\Delta m \approx 3000$. Unimolecular fragmentations of meta-

stable ions occurring in the field-free region preceding B(2) were recorded by scanning this sector. All spectra were accumulated and on-line processed with the AMD-Intetra data system; 20 to 30 scans were averaged to improve the signal-to-noise ratio. The data for the racemic pairs of diastereomers are the average of at least three independent measurements, and for the losses of HSiMe_3 and DSiMe_3 from the Co^+ complexes of **1b**, **1c**, **2b**, and **2c**, respectively, the averaged error amounts to $\pm 2\%$. Because of the relatively high pressure that prevails in the CI source, efficient collisional cooling of the ions can be assumed, such that excited states of Co^+ ions¹⁵ are not likely to participate in the reactions observed.¹⁶

The racemic nitriles **1** and **2** as well as their isotopologues **1a** and **2a** were synthesized via (a) reaction of the dianion of propionic acid with 3-bromo-1-phenoxypropane,¹⁷ (b) reduction of the resulting acid with LiAlH_4 , for the synthesis of **1** and **2**, or LiAlD_4 (Aldrich Chemicals, >98 atom % D), for the synthesis of **1a** and **2a**, respectively, (c) tosylation of the alcohol,¹⁸ and (d) subsequent $\text{Cu}(\text{I})$ catalyzed coupling with magnesium chloromethyltrimethylsilane¹⁹ to yield as central intermediate 4-methyl-6-trimethylsilyl-1-phenoxyhexane or [5- D_2]-4-methyl-6-trimethylsilyl-1-phenoxyhexane, respectively, which have been converted to the desired nitriles by standard laboratory procedures.²⁰ The diastereospecifically labeled nitriles **1b** and **2b** were prepared in racemic form according to the routes depicted in Scheme 1, starting from [5- D_1]-4-pentyn-1-ol. The diastereospecific synthesis was achieved by (a) zirconocene-catalyzed carboalumination and quenching with H_2O ,²¹ (b) conversion of the alcohol to the methyl ether,²² (c) hydroboration with oxidative workup,²³ (d) tosylation of the obtained alcohol,¹⁸ (e) subsequent nucleophilic displacement with diethyl malonate, (f) saponification of the resulting diester with potassium hydroxide followed by thermal decarboxylation of the diacid,²⁴ (g) conversion to the acid chloride, (h) decarboxylation according to Barton,²⁵ (i) followed by nucleophilic displacement of chlorine by a trimethylsilyl group²⁶ to yield a diastereomerically pure racemic mixture of the central intermediate, i.e., (4*R*,5*S*)-[5- D_1]- and (4*S*,5*R*)-[5- D_1]-4-methyl-6-trimethylsilyl-1-methoxyhexane. This (racemic) compound has been converted to the desired nitriles **1b** and **2b** by standard laboratory procedures.²⁰ Likewise, **1c** and **2c** were prepared starting from 4-pentyn-1-ol (Aldrich Chemicals, >98%) as reactant which was carboaluminated with trimethylaluminum and subsequently quenched with D_2O (Aldrich Chemicals, >99.5 atom % D) to yield [E-5- D_1]-4-methyl-pent-4-en-1-ol as the precursor for the subsequent reactions via the same route as depicted for **1b** and **2b** in Scheme 1. All nitriles were purified by distillation and column- or gas chromatography, and fully characterized by spectroscopic means.

Results and Discussion

The fragmentations of the metastable complexes $1/\text{Co}^+$ and $2/\text{Co}^+$ (Table 1) are dominated by the unimolecular loss of neutral trimethylsilane ($\Delta m = 74$). Expulsion of HSiMe_3 can be described in terms of the concept of remote functionalization (Scheme 2), and the data of the isotopologues do completely agree with this reasoning (Table 2). As minor reaction pathways, we observe (i) dehydrogenation ($\Delta m = 2$), (ii) expulsion of methane ($\Delta m = 16$), and (iii) losses of tetramethyl

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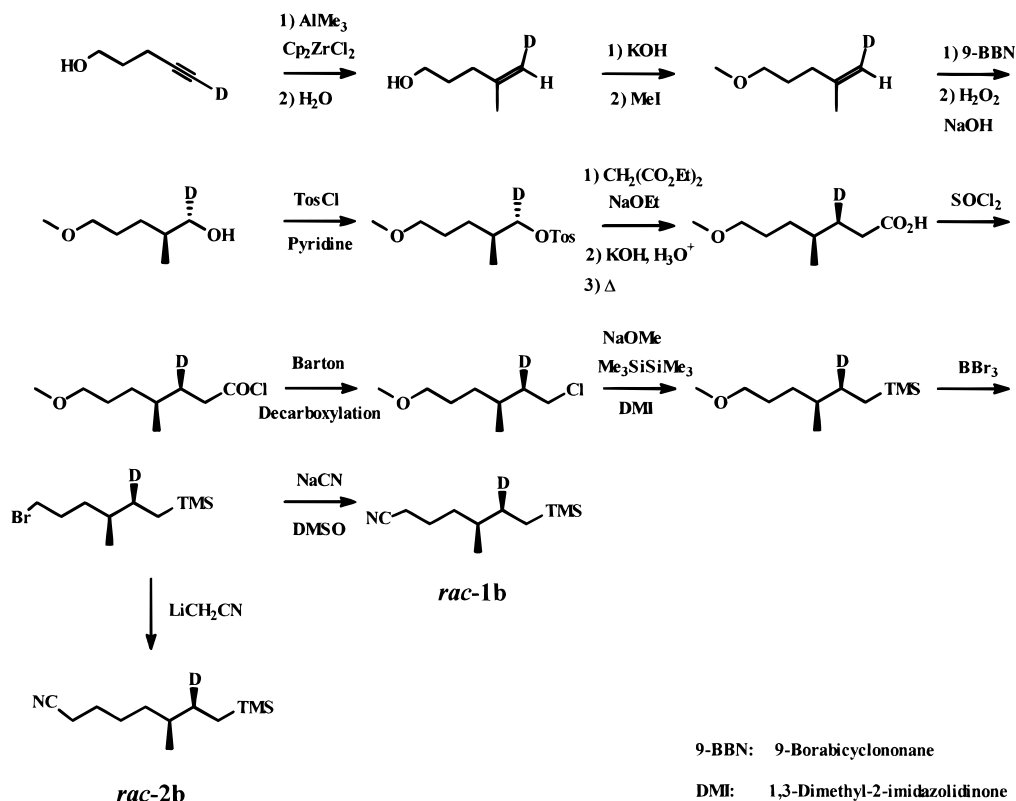
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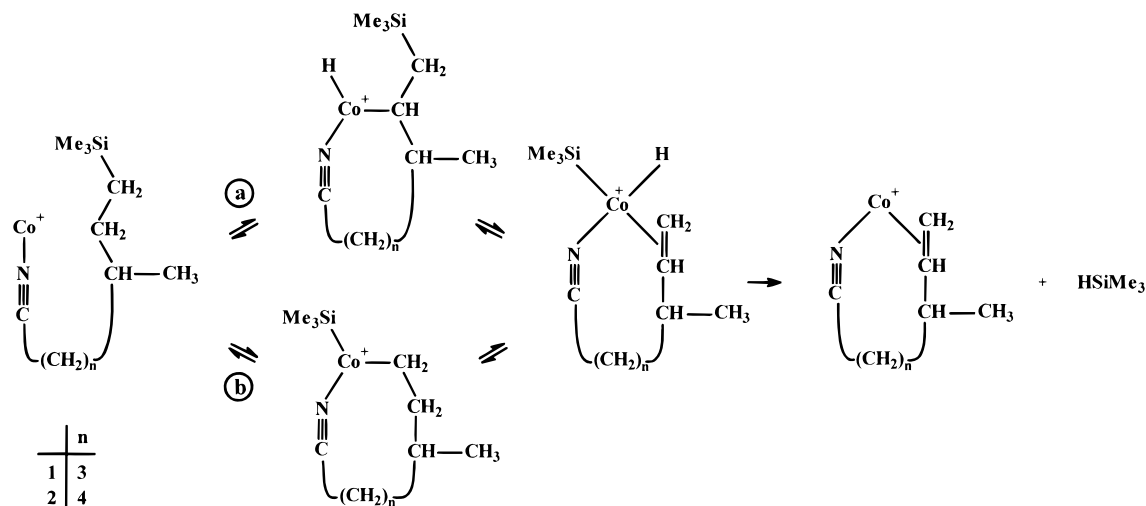
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Scheme 1



Scheme 2



($\Delta m = 88$) and ethyltrimethylsilane ($\Delta m = 102$). Although Table 2 provides the complete set of data for all isotopologues studied and while a closer inspection of the results reveals the existence of significant steric effects in some of these side reactions,²⁷ the scope of the present paper is to discuss exclusively the regio- and stereoselectivity associated with the loss of neutral trimethylsilane. Therefore, we will not pursue

(27) For example, the precise ratios of H_2 and HD losses from the pairs **1b**/ Co^+ ($k_{\text{H}_2}/k_{\text{HD}} \approx 6$) and **1c**/ Co^+ ($k_{\text{H}_2}/k_{\text{HD}} \approx 2.5$) and **2b**/ Co^+ ($k_{\text{H}_2}/k_{\text{HD}} \approx 4$) and **2c**/ Co^+ ($k_{\text{H}_2}/k_{\text{HD}} \approx 2$) clearly differ from each other; as will be discussed further below, this is line with the observed diastereoselectivity for loss of trimethylsilane. However, because of the small ion currents associated with the corresponding fragment ions, the signal-to-noise ratio is quite poor. Similarly, although the losses of methane involve the ($\omega - 2$) positions, as evident from small amounts (<1%) of CH_3D formed from **1a**/ Co^+ and **2a**/ Co^+ , the signals were also too weak for a quantitative analysis. For the other processes mentioned in the text and in Tables 1 and 2, diastereoselectivity cannot be expected to play a role, because C-H(D) activation at the ($\omega - 1$) positions is not involved.

the mechanistic features of these minor processes which are, anyhow, fully in line with the concept of remote functionalization; actually, similar reactions have been discussed in previous publications at great length.^{6,10}

As already stated, the regioselectivity associated with losses of trimethylsilane from **1**/ Co^+ and **2**/ Co^+ , respectively, is clearly revealed by the [$(\omega - 1)$ - D_2]-labeled complexes **1a**/ Co^+ and **2a**/ Co^+ , both of which exclusively eliminate DSiMe_3 ($\Delta m = 75$). Thus, we conclude that loss of trimethylsilane occurs via a 1,2-elimination involving a hydrogen atom from the ($\omega - 1$) position and the trimethylsilyl unit as depicted in Scheme 2. This reaction most probably proceeds as a *syn*-elimination.^{12a} Thus, the overall reaction sequence represents the gas-phase reversal of the well-known hydrosilylation of alkenes in the condensed phase.²⁸

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Table 1. Mass Differences (in amu) Observed in the Unimolecular Fragmentations of the Metastable Ion (MI) Complexes **1**/Co⁺ and **2**/Co⁺ ^{a,b}

precursor	Δm				
	2	16	74	88	102
1	3	1	94	1	1
2	2	1	95	1	1

^a Intensities are normalized to $\sum_{\text{reactions}} = 100\%$. ^b Reactions with intensities <1% are omitted.

Table 2. Mass Differences (in amu) Observed in the Unimolecular Fragmentations of Co⁺ Complexes of the Isotopologues of **1** and **2** ^{a,b}

precursor ^c	Δm								
	2	3	16	74	75	88	102	103	104
1	3		1	94		1	1		
1a	2	2	1		92	1			2
1b	4	1	1	80	12	1		1	
1c	3	1	1	25	67	1		2	
2	2		1	95		1	1		
2a	2	2	1		93				2
2b	2	1	1	77	17	1		1	
2c	2	1	1	30	64	1		1	

^a Intensities are normalized to $\Sigma = 100\%$. ^b Reactions with intensities <1% are omitted. ^c All compounds have been measured as racemic pairs.

In this context, it is instructive to compare **1**/Co⁺ and **2**/Co⁺ with their desilylated analogues, i.e., the Co⁺ complexes of 5-methylheptanenitrile and 6-methyloctanenitrile, which exhibit a much richer gas-phase chemistry.¹⁰ For the latter, both C–H and C–C bond activation takes place resulting in the competitive generation of molecular hydrogen, methane, and (to a smaller extent) several olefins. Furthermore, for the nonsilylated nitriles, regioselectivity is limited to the Co⁺-induced loss of methane while the other products originate from several positions of the alkyl backbone. This behavior is in marked contrast to **1**/Co⁺ and **2**/Co⁺ in which the silyl group controls the reactivity by confining it by and large to just one reaction channel and, in addition, induces a remarkably high regioselectivity.⁶ These observations point toward the operation of a cooperative effect of the two functional groups; we suggest that the Co⁺ cation is anchored at the cyano group²⁹ and the electronic effects exerted by the silyl substituent¹ direct the metal toward the C–H bond in β position of the SiMe₃ group, i.e., the ($\omega - 1$) positions of the alkyl chains in **1** and **2**. The nature of the directing effect of the silyl group has been described in an ab initio MO study by Koga and Morokuma in terms of an agostic interaction.³⁰ Thus, electron donation from the Si–C σ bond into a vacant d orbital of the transition metal leads to a considerable stabilization of the organometallic species. In general, such agostic interactions are conceivable between various σ bonds and a vacant orbital of an electron-deficient metal center within a molecule; nevertheless, the agostic interaction with silicon is considerably stronger than those of C–C or C–H bonds because the electron-donating capability of the Si–C bond is more pronounced.

The most remarkable result of the present study represents the *diastereoselectivity* associated with the loss of neutral trimethylsilane from the Co⁺ complexes of **1** and **2**. As becomes obvious from inspection of the normalized data given in Table 3, the ratio of HSiMe₃ versus DSiMe₃ losses is

(29) Extensive ab initio MO studies (ref 9a) clearly demonstrate that RCN and atomic ground-state M⁺ (M = Fe, Co) form exclusively *end-on* complexes RCN–M⁺; the isomeric *side-on* complexes do not correspond to minima on the potential-energy surface, which is rather shallow with regard to the distortion of the RCN–M⁺ moiety from linearity.

(30) Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1988**, *110*, 108.

Table 3. Normalized Data for the Unimolecular Losses of HSiMe₃ and DSiMe₃ from the Co⁺ Complexes of **1b**, **1c**, **2b**, and **2c**^a

precursor ^b	HSiMe ₃	DSiMe ₃	HSiMe ₃ /DSiMe ₃
1b	87 ± 1	13 ± 1	6.7 ± 0.3
1c	29 ± 1	71 ± 2	0.4 ± 0.02
2b	82 ± 2	18 ± 1	4.6 ± 0.2
2c	33 ± 1	67 ± 2	0.5 ± 0.02

^a Intensities are normalized to the sum of trimethylsilane loss $\Sigma = 100\%$. ^b The diastereomers have been measured as racemic pairs.

significantly larger for the complexes **1b**/Co⁺ and **2b**/Co⁺ than that for their diastereoisomers **1c**/Co⁺ and **2c**/Co⁺, respectively. The effect is rather large and far beyond any possible experimental uncertainty. Owing to the fact that the only structural difference between the pairs **1b**/**1c** and **2b**/**2c**, respectively, is the relative stereochemistry of the methyl group at the ($\omega - 2$) position, a significant diastereoselective discrimination in the course of the 1,2-elimination of trimethylsilane must be operative.

Irrespective of the stereochemical effects (SEs), the losses of HSiMe₃ and DSiMe₃ are also associated with kinetic isotope effects (KIEs). Although separation of different kinetic effects is often difficult, the particular situation provided by the comparison of compounds, which only differ in their relative stereochemistry at one stereogenic center, allows one to solve the set of differential equations for the pairs **1b**/**1c** and **2b**/**2c**, respectively.³¹ As a result, the measured intensities of HSiMe₃ and DSiMe₃ losses can be separated in the two relevant components, and we obtain: KIE = 1.6 ± 0.1 and SE = 4.1 ± 0.2 for **1**/Co⁺, and KIE = 1.5 ± 0.1 and SE = 3.0 ± 0.2 for **2**/Co⁺, respectively. Thus, for the Co⁺ complexes of both silyl-substituted nitriles strong steric effects are operative which point in the same direction favoring loss of HSiMe₃ over that of DSiMe₃ from the racemic pairs of (*S,R*) (**1b** and **2b**) and (*R,S*) enantiomers (**1'b** and **2'b**) as compared to the pairs of (*R,R*) (**1c** and **2c**) and (*S,S*) enantiomers (**1'c** and **2'c**), respectively. Under the reasonable assumption that ions as large as **1**/Co⁺ and **2**/Co⁺ are approximately equilibrated to the temperature of the ion source (473 K) when formed via chemical ionization,³² these steric effects can be converted to $\Delta\Delta G^\ddagger$ of about 1 kcal/mol for bond activation in the pairs of diastereoisomers. We note in passing that the sheer existence of diastereoselectivity clearly demonstrates that the reactions occur in the vicinity of their corresponding thermochemical thresholds for bond activation.

A straightforward analysis of these experimental results is hampered by the fact that the loss of neutral trimethylsilane may be rationalized via two different mechanistic scenarios (paths ③ and ④ in Scheme 2) which cannot be distinguished by isotopic labeling studies.^{6,33}

Mechanism 1. The first route is depicted in Scheme 3 and assumes an initial insertion of the Co⁺ cation into the C–H or the C–D bond at the ($\omega - 1$) position to generate **3** or **4**, respectively.³⁴ These insertion steps are followed by exocyclic β -silyl transfer steps from the ω positions to the metal center,

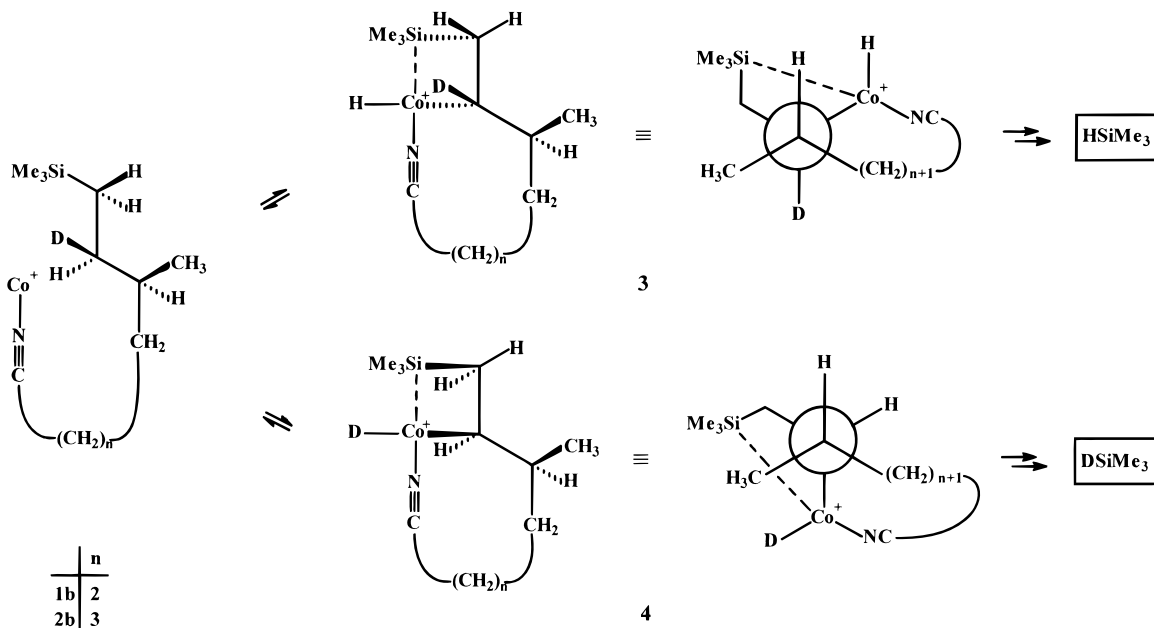
(31) Assuming that the steric effect on the magnitudes of the KIEs can be neglected, the following equations can be derived: $k_{\text{HSiMe}_3}/k_{\text{DSiMe}_3}(\mathbf{1b}/\text{Co}^+) = \text{KIE} \cdot \text{SE} = 6.7$; $k_{\text{HSiMe}_3}/k_{\text{DSiMe}_3}(\mathbf{1c}/\text{Co}^+) = \text{KIE}/\text{SE} = 0.4$; $k_{\text{HSiMe}_3}/k_{\text{DSiMe}_3}(\mathbf{2b}/\text{Co}^+) = \text{KIE} \cdot \text{SE} = 4.1$; $k_{\text{HSiMe}_3}/k_{\text{DSiMe}_3}(\mathbf{2c}/\text{Co}^+) = \text{KIE}/\text{SE} = 0.5$. Here, KIE stands for the ratio of $k_{\text{H}}/k_{\text{D}}$ for H and D transfer, respectively, and SE for the steric effect which is operative. For further details, see: Schröder, D., Ph.D. Thesis, Technische Universität Berlin D83, 1992.

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(34) For the sake of clarity, in Schemes 3 and 4 only the reactions of one diastereomer of the racemic pairs **1b** and **2b** are shown. For **1c** and **2c** all the essential features are identical, except that the H/CH₃ substituents in the ($\omega - 2$) positions are interchanged.

Scheme 3



preferentially involving planar, four-centered intermediates as indicated in Scheme 3. The reaction is then completed by reductive eliminations of HSiMe_3 or DSiMe_3 , respectively. Note that a direct elimination of trimethylsilane from the insertion products **3** and **4**, respectively, is also feasible and would circumvent the formation of intermediates containing a high-valent $(\text{H})\text{Co}(\text{SiMe}_3)^+$ unit which may not correspond to a minima on the potential-energy surface;³⁵ however, this question does not affect our stereochemical analysis to be discussed next. With respect to the experimentally observed diastereoselective discrimination, the dominating losses of HSiMe_3 from **1b**/ Co^+ and **2b**/ Co^+ , respectively, can be assigned to the preferential formation of the sterically less congested eclipsed conformer **3**, while formation of DSiMe_3 has to proceed via the sterically more demanding eclipsed conformer **4**. The steric demands of these two conformers are best illustrated by their Newman projections (Scheme 3) which reveal that in intermediate **3** the methyl group at $\text{C}(\omega - 2)$ is *gauche* to the $\text{C}(\omega) - \text{C}(\omega - 1)$ bond, whereas intermediate **4** has to adopt a sterically less favorable conformation, displaying *gauche* interactions between the methyl group at $\text{C}(\omega - 2)$ and the $\text{C} - \text{Co}^+$ as well as the $\text{C}(\omega) - \text{C}(\omega - 1)$ bonds. In addition to these steric effects, elimination of HSiMe_3 via intermediate **3** profits from a primary kinetic isotope effect (see above); consequently, for **1b**/ Co^+ and **2b**/ Co^+ the loss of HSiMe_3 is favored over the elimination of DSiMe_3 both in terms of a preferred conformation of the intermediate and the operation of a kinetic isotope effect. In contrast, in the analogous intermediates derived from the diastereoisomers **1c** and **2c**, the stereochemical effect (SE) and the isotope effect oppose each other. Owing to the fact that for both nitriles SE is much larger than the KIE (see above), the loss of DSiMe_3 is now favored over that of HSiMe_3 . Thus, although $\text{C} - \text{D}$ bond activation of **1c**/ Co^+ and **2c**/ Co^+ is hampered by a KIE, this is overcompensated by the formation of the sterically favorable stereoisomer associated with formation of DSiMe_3 , such that the loss of the heavier isotopic variant prevails.

Mechanism II. A second possible reaction pathway (Scheme 4) commences with an insertion of the Co^+ cation into the $\text{Si} - \text{C}$ bond at the ω positions to generate **5** and **6**, respectively.³⁴ Elimination of HSiMe_3 or DSiMe_3 must then proceed via an endocyclic β -H (D) transfer; note, that the optimal planar arrangement of the four-centered intermediates cannot be achieved in an endocyclic situation.^{9b,36} In analogy to the arguments raised for the intermediates **3** and **4**, we assume that the system will preferentially populate the conformationally favored intermediate **5** rather than the more sterically demanding metallacycle **6**. Again, this is best illustrated in the corresponding Newman projections of the conformers **5** and **6**. Thus, the metallacyclic intermediate **6** is disfavored by *gauche* interactions between the methyl group at $\text{C}(\omega - 2)$ and the $\text{C}(\omega) - \text{C}(\omega - 1)$ bond, while the latter *gauche* interaction is absent in conformer **5** which is therefore expected to be more stable. Following this reasoning, the same interplay of SE and KIE as outlined above for mechanism I can rationalize the different amounts of HSiMe_3 and DSiMe_3 formed from the diastereoisomeric complexes.

From a conceptual point of view, both mechanisms I and II equally account for the experimentally observed diastereoselective discrimination. According to simple thermochemical considerations, mechanism II should be preferred because insertion of Co^+ into a $\text{Si} - \text{C}$ bond is more facile than in a $\text{C} - \text{H}$ bond; i.e., the bond dissociation energy (BDE) in $\text{Me}_3\text{Si} - \text{CH}_2\text{CH}_3$ amounts to 85 kcal/mol as compared to ca. 99 kcal/mol for a secondary $\text{C} - \text{H}$ bond,³⁷ while $\text{BDE}(\text{Co}^+ - \text{H})$ and $\text{BDE}(\text{Co}^+ - \text{SiH}_3)$ are very similar (45.7 and 45.2 kcal/mol, respectively).³⁸ However, a series of high-level ab initio studies^{9,35} have recently demonstrated that the initial insertion step is not rate determining for M^+ -induced losses of $\text{R} - \text{H}$ molecules ($\text{R} = \text{H}$, alkyl; here, silyl) from alkanes. Thus, although neither the experimental findings nor the stereochemical features permit a decision whether mechanism I or II is operative, two arguments are in favor of an initial $\text{C} - \text{H}$ bond

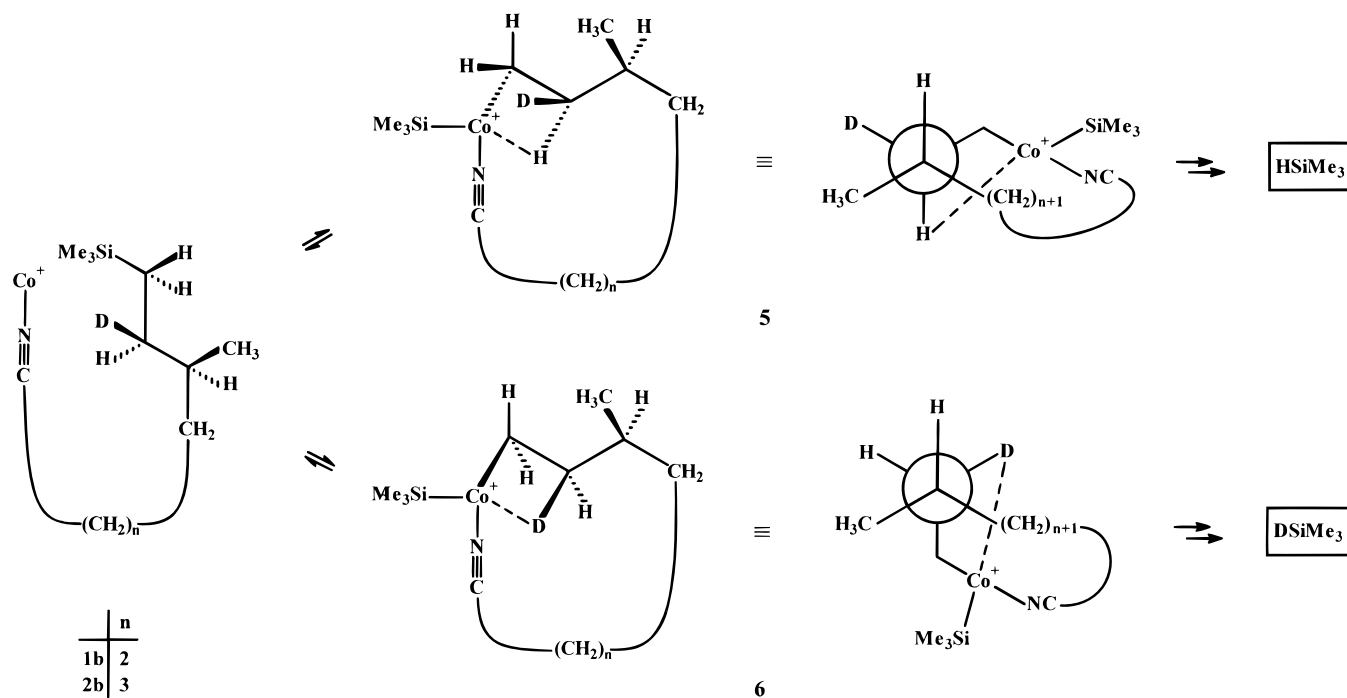
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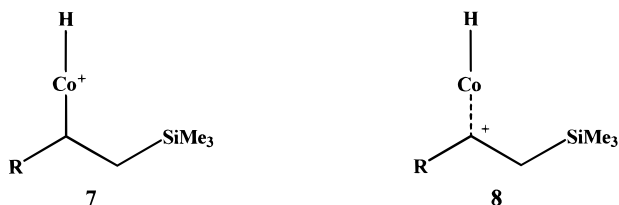
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Scheme 4



Scheme 5



activation as depicted in Scheme 3. First, an initial C–H bond insertion leads to an intermediate which can be stabilized by the previously mentioned β -C–Si agostic interaction, which would not be possible in the case of a primary C–Si bond activation. Further, an intermediate arising from C–H bond insertion may experience stabilization owing to the better possibility for the distribution of the overall positive charge, in terms of the bonding mnemonics **7** and **8** depicted in Scheme 5. Here, **7** corresponds to the classical formulation of an transition-metal insertion intermediate in which the positive charge is located at the metal center. Single electron transfer to the metal leads to structure **8**, in which the positive charge is located at the carbon atom β to the silyl group. In view of the significant stabilization of carbocations due to the β -silicon effect,³⁹ contribution of a resonance structure resembling **8** stabilizes the insertion intermediates and thus favors C–H bond activation. Further, the stabilization of **8** via the β -silicon effect would coincide with a weakening of the Me₃Si–C bond at the ω position, thus facilitating the migration of the silyl group.

Second, while mechanism I is followed by an exocyclic β -silyl migration, initial C–Si bond insertion in terms of mechanism II requires an endocyclic β -H migration. Though the latter reaction is by no means impossible,^{9a} the activation barriers associated with endocyclic group transfer are significantly higher than those for the corresponding exocyclic processes, because the required planarity for an optimal arrangement of the participating atoms in a four-membered ring is more difficult if not impossible to achieve, and the endocyclic pathway induces more strain in the backbone of the chain.^{9,36}

For the time being, we cannot ultimately decide between mechanisms I and II. However, the stereochemical features reported here may stimulate further experimental and theoretical efforts to clarify this particular issue and by such provide deeper insight into the role of silicon for steering bond-activation processes. In particular, these further studies should also provide an answer for the intriguing question in which way the silyl substituent affects the chemoselectivity which is entirely different in the nonsilylated analogues of **1**/Co⁺ and **2**/Co⁺, respectively.¹⁰

Finally, it should be pointed out that the qualitative model we apply to rationalize the observed diastereoselectivity is entirely based on the steric 1,2-interactions of the substituents at the carbon atoms in the $(\omega - 1)$ and $(\omega - 2)$ positions. However, steric constraints along the C($\omega - 1$)/C($\omega - 2$) axis are by no means the only factors that govern the stereoselectivity, and certainly also the conformations of the metallacyclic intermediates and of the associated transition structures, which can be regarded as bicyclic systems with either *cis* or *trans* fusion, play important roles. These aspects are in part reflected by the differences between **1**/Co⁺ and **2**/Co⁺, for which regio- and chemoselectivities as well as the KIE are very similar, while the steric effects differ quite significantly. As already mentioned, the SE decreases with increasing chain length; i.e., **2b**/Co⁺ exhibits a smaller preference for the generation of HSiMe₃ as compared to the homologous complex **1b**/Co⁺. Thus, the ring sizes of the metallacyclic intermediates have a notable influence on the magnitude of the diastereoselective discrimination. To a first approximation the lower SE for **2**/Co⁺ can be attributed to the fact that the metallacyclic intermediates formed are more flexible than those derived from the lower homologue **1**/Co⁺, such that the steric interactions diminish and the diastereoselectivity decreases upon elongation of the alkyl chain.

Conclusions

The application of stereochemical criteria provides a powerful tool for a detailed examination of organometallic reaction mechanisms by mass spectrometric means. Obviously, many kinetic phenomena which are difficult to assess experimentally

(39) (a) Apeloig, Y. In ref 1, p 59. (b) Schwarz, H. In ref 1, p 446.

can be neglected in the comparison of a pair of diastereoisomers. In fact, the diastereospecifically labeled silyl nitriles **1b/1c** and **2b/2c** represent suitable model systems to probe the diastereoselectivity in the Co⁺-mediated remote functionalization of carbon–silicon and carbon–hydrogen bonds in the gas phase. As compared to the nonsilylated nitriles, the effect of silyl substituent is rather large, and the analysis of the unimolecular fragmentation patterns of these Co⁺ complexes reveals remarkable increases in chemo-, regio-, and stereoselectivity resulting in an almost exclusive generation of neutral trimethylsilane. As suggested earlier,^{6,30} this effect can be attributed to the interaction of silicon with the Co⁺ cation; however, the precise nature of this interaction needs to be clarified by adequate theoretical treatment.

The observed diastereoselectivity can be explained in terms of steric interactions of the two stereogenic carbon atom centers in the metallacycles formed from the pairs **1b/1c** and **2b/2c**, respectively, after initial bond activation by Co⁺. However,

even extensive isotopic labeling techniques in combination with tandem mass spectrometry are not powerful enough to yield a satisfying, detailed mechanistic picture, namely, a distinction between the mechanisms I and II as depicted in Schemes 3 and 4. Hence, theoretical modeling is desirable in order to unravel further mechanistic details, such as the energetically preferred primary site of insertion of the metal ion (i.e., initial C–H versus C–Si bond activation), the associated transition structures, and their conformational features, influences of rotational barriers along the reaction path, and last, but not least, the influence of the ring size on the diastereoselective discrimination.

Acknowledgment. Financial support by the Deutsche Forschungsgemeinschaft, the Volkswagen-Stiftung, and the Fonds der Chemischen Industrie is acknowledged. We are grateful to Professor Wolfram Koch and Dr. Max C. Holthausen for helpful comments and communication of unpublished results.

JA963254M