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An Unusual and Diastereoselective Rearrangement during an Intramolecular Ene Reaction Involving a Disilane

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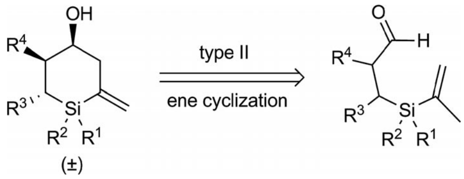
A chiral 1-isopropenyl-1-(3-oxopropyl)disilane derivative undergoes a type II ene reaction under Lewis acid catalyzed conditions to afford the silacyclic compound and an unexpected rearranged product with high diastereoselectivities. This rearrangement occurs through 1,2-migration of a trimethylsilyl group. A common intermediate was proposed to explain the formation of both products.

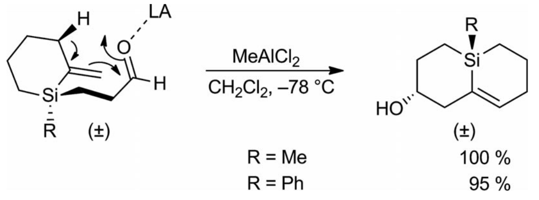
Introduction

In the course of our work on the synthesis of organosilicon cyclic compounds, we focused our attention on the preparation of a 1-trimethylsilyl-2-methylidene-1-silacyclohexanol derivative by intramolecular ene reaction from a 1-isopropenyl-1-(3-oxopropyl)disilane (Scheme 1; R^1 = $SiMe_3$, R^2 = Me, R^3 = R^4 = H). The expected cyclic compound was envisioned as a starting material to build more elaborate scaffolds after cleavage of the silicon–silicon bond.[1] Such a carbonyl ene reaction was reported by Robertson et al. for isopropenyl(3-oxopropyl)silanes. Generally, the methylaluminum dichloride-catalyzed cyclization occurs with high diastereoselectivity if at least one stereogenic center is present on the 3-oxopropyl chain (Scheme 1; R^1 = R^2 = Me, *i*Pr; R^3 = H, Me, Ph; R^4 = H, Me, *i*Pr, Bn).[2]



Scheme 1. Retrosynthesis for the preparation of 2-methylidene-1-silacyclohexanols.

In this field, we have reported the stereoselective synthesis of bicyclic compounds with a silicon atom at the ring junction, starting from 2-methylidene-1-silacyclohexanes bearing a 3-oxopropyl chain on the silicon atom.[3] The high stereoselectivity observed in this Lewis acid (LA) catalyzed ene cyclization should result from the required *cis* geometry between the transferred allylic proton and the oxopropyl chain, which thus gives rise to a hydroxy group in a *trans* relationship with the substituent on the silicon atom (Scheme 2).

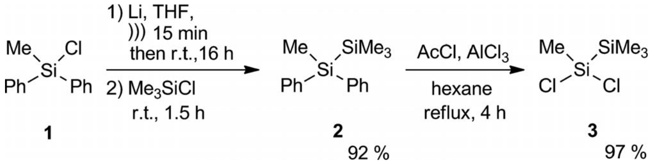


Scheme 2. Synthesis of silabicyclo[4.4.0]decenes by ene reaction.

We herein report a highly diastereoselective rearrangement concomitant with the expected ene reaction. A mechanism was proposed to rationalize these transformations, which involve a disilane with a stereogenic silicon atom.

Results and Discussion

We first investigated the preparation of isopropenyl(3-oxopropyl)disilane **9**, precursor of the ene reaction, from dichlorodisilane **3**. Treatment of chloro(methyl)diphenylsilane (**1**) with lithium in THF at room temperature (under ultrasonic agitation until precipitation of LiCl, then under magnetic stirring) followed by addition of chlorotrimethylsilane delivered 1,1,1,2-tetramethyl-2,2-diphenyldisilane (**2**) in high yield after distillation (Scheme 3).



Scheme 3. Preparation of dichlorodisilane **3**.

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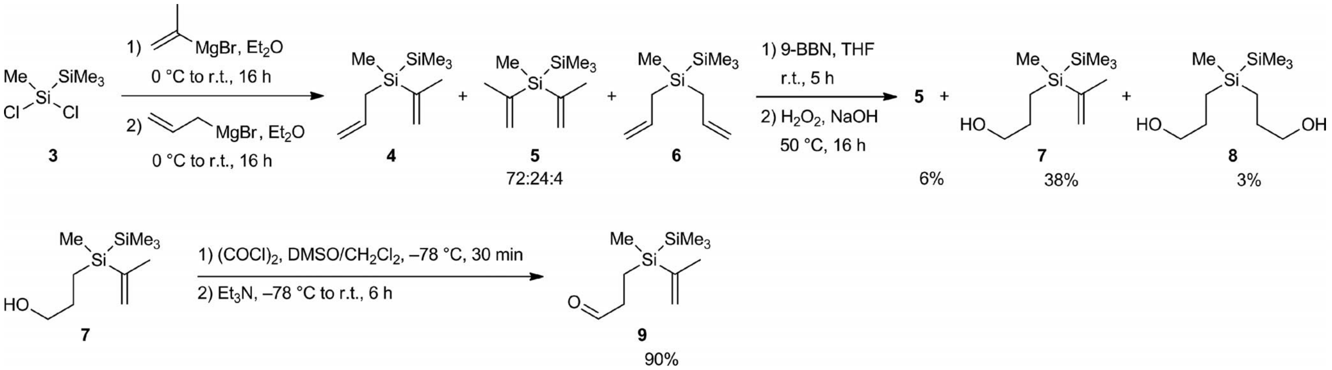
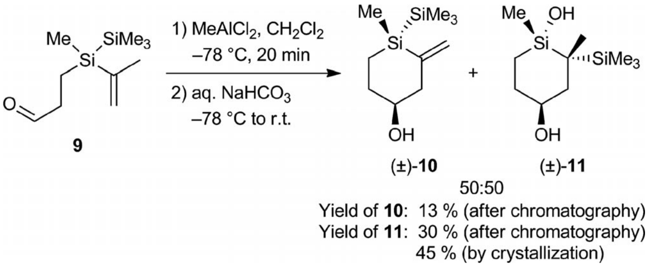


Scheme 4. Preparation of aldehyde **9** from dichlorodisilane **3**.

In our hands, all attempts of chlorodephenylation of **2** by using the standard methods ($AlCl_3$ and HCl gas from a gas cylinder or preformed from $NaCl/H_2SO_4$) failed.[4–6] Preparation of **3** was successfully achieved in an almost quantitative yield by treatment of **2** under Friedel–Crafts conditions by employing acetyl chloride and aluminum chloride in refluxing hexane (Scheme 3).[7] One-pot substitution of the chlorine atoms of **3** by successive additions of ethereal solutions of isopropenylmagnesium bromide (1 equiv.) and allylmagnesium bromide (1 equiv.) gave mainly a 75:25 mixture of allyl(isopropenyl)disilane **4** and di(isopropenyl)disilane **5**. A small amount of diallyldisilane **6** was also detected. Treatment at room temperature of this unpurified mixture with 9-borabicyclo[3.3.1]nonane (9-BBN) followed by oxidation at 50 °C with hydrogen peroxide under basic conditions led to (3-hydroxypropyl)disilane **7**, which was isolated by chromatography in 38% yield over this four-step sequence (Scheme 4). Moreover, purification allowed **5** and a small amount of bis(hydroxypropyl)disilane **8** to be obtained. Finally, subsequent oxidation of alcohol **7** under Swern conditions delivered expected aldehyde **9** in 90% yield.

Silicon-tethered ene cyclization of **9** was achieved with methylaluminum dichloride. Treatment with this Lewis acid (1.2 equiv.) followed by aqueous work-up ($NaHCO_3$ solution) resulted in the formation of a 50:50 mixture of desired silacyclohexanol **10** and unexpected rearranged product **11**. Compounds **10** and **11** were isolated after silica gel column chromatography in 13 and 30% yield, respectively. Notably, only one diastereomer for each product was formed exclusively or with high selectivity. The difference between the yields of **10** and **11** is probably due to the instability of **10** on silica gel. Under similar reaction conditions but allowing the crude reaction mixture to stand at –18 °C for 16 h, crystals of **11** were isolated in 45% yield (Scheme 5).

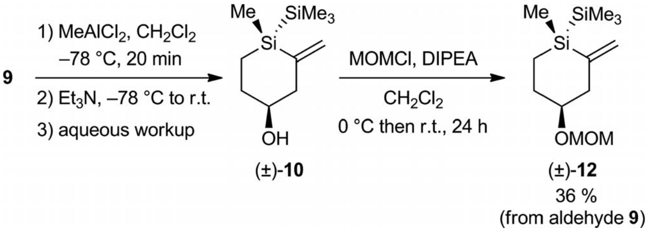
Regardless of the reaction conditions (increasing the reaction time from 20 min to 6 h, increasing the concentration of **9** from 0.013 to 0.13 M, or increasing the amount of Lewis acid from 1.2 to 2.2 equiv.), total conversion of **9** was observed and the **10/11** ratio remained roughly unchanged (the ratio was determined by ^1H NMR spectroscopy and was always between 41:59 and 54:46).



Scheme 5. Treatment of aldehyde **9** with $MeAlCl_2$.

No significant change in the **10/11** ratio was observed if the work-up was realized with 1 M HCl after reaction of **9** with methylaluminum dichloride (1.2 equiv.) under the same conditions as those described above. However, the ^1H NMR spectrum of the crude reaction product did not reveal any signals that could be attributed to **11** if Et_3N was added to the reaction mixture at –78 °C before the addition of water at room temperature. Under these conditions, the main reaction product was **10**. Nevertheless, various signals resulting from unidentified products were also present. Bulb-to-bulb distillation under low pressure (Kugelrohr distillation) allowed the isolation of **10** in 22% yield. Formation of **10** and/or **11** was not noticed in a Ti(O*i*Pr)$_4$-catalyzed reaction.

Treatment of the crude reaction product, resulting from reaction of **9** with $MeAlCl_2$ followed by addition of Et_3N before the aqueous work-up, with methoxymethyl chloride (MOMCl) in the presence of diisopropylethylamine (DIPEA) furnished methoxymethyl ether **12**. After silica gel column chromatography, **12** was thus isolated in 36% yield over this two-step sequence (Scheme 6).



Scheme 6. Preparation of methoxymethyl ether **12**.

Structure elucidation of **11** was achieved by single-crystal X-ray diffraction analysis (Figure 1).[8] This analysis supports unambiguously that the trimethylsilyl group and the OH group linked to the silicon atom are in a *trans* position relative to the OH group carried by the carbon atom.

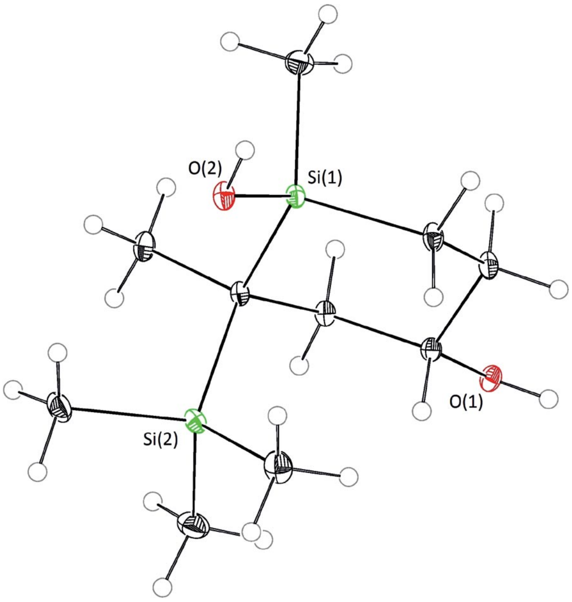


Figure 1. ORTEP structure of silacyclohexanediol **11**.[8] Ellipsoids are drawn at the 30% probability level.

The ^{1}H NMR spectrum ($CDCl_3$) of **11** shows a doublet of doublets of doublets of doublets at δ = 3.82 ppm, which can be attributed to the proton linked to the C-4 carbon atom bearing the hydroxy group. The coupling constants (two of ca. 11 Hz and two of ca. 4 Hz) are in agreement with an axial position of this proton. Thus, the trimethylsilyl group should be also in the axial position in solution.

In comparison with the spectrum of **11**, the ^{1}H NMR spectrum of **10** shows a signal at δ = 3.90 ppm with a similar coupling pattern but with two coupling constants of ca. 6 Hz and two others of ca. 3 Hz, which suggest an equatorial position of the proton carried by the C-4 carbon atom. A signal at δ = 3.71 ppm with the same shape (two coupling constants of ca. 7 Hz and two coupling constants of ca. 3 Hz) is present in the spectrum of **12**, which thus indicates that its conformation should be similar to that of **10**. NOE experiments performed on **12** showed that the protons of the trimethylsilyl group were in proximity to the two protons linked to the C-3 and C-5 carbon atoms of the silacyclohexane ring. These effects suggest the axial position of the trimethylsilyl group (Figure 2). Moreover, an NOE effect between an ethylenic proton and the protons of the methyl group linked to the cyclic silicon atom is in agreement with an equatorial position of this methyl substituent.

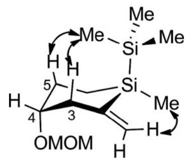
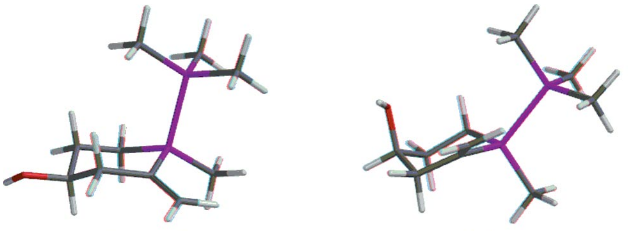


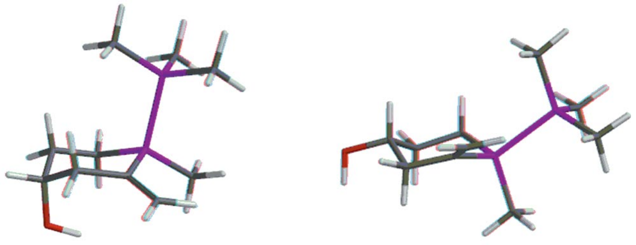
Figure 2. NOE effects observed in the spectrum of ether **12**.

By using the Merck Molecular Force Field (MMFF),[9] calculations determined the minimized molecular-modeling geometries and the relative energies of *cis*- and *trans*-**10** in the two possible chair conformations (all attempts by starting with a boat geometry converged to the chair geometry). Greater stability was found for the *trans* isomer with the trimethylsilyl and hydroxy groups in axial positions (Figure 3).



cis (OH equatorial)
E = 167.03 kJ mol^{-1}

cis (OH axial)
E = 168.14 kJ mol^{-1}



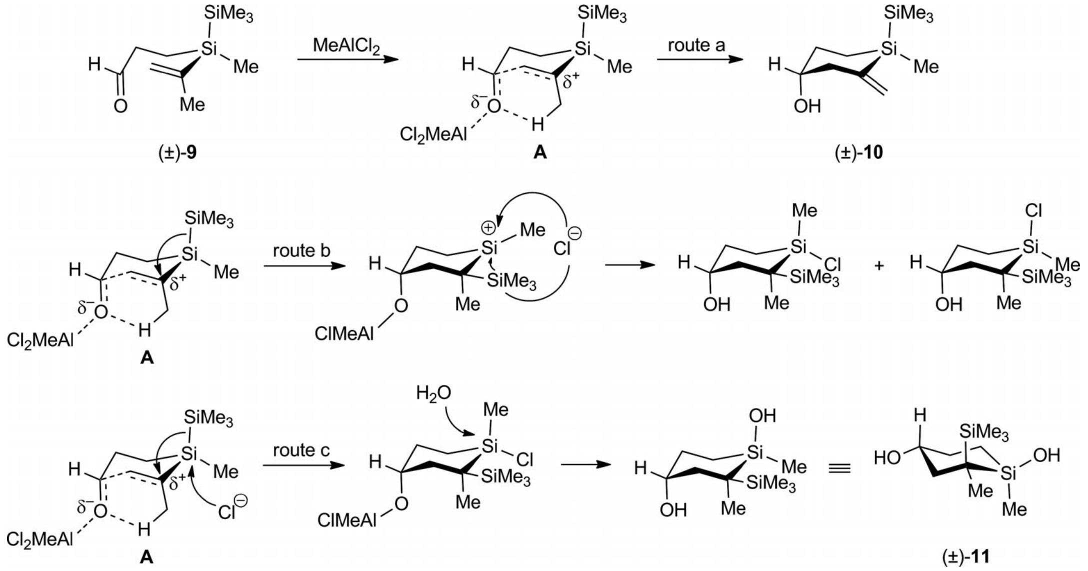
trans (OH axial)
E = 161.09 kJ mol^{-1}

trans (OH equatorial)
E = 172.31 kJ mol^{-1}

Figure 3. Calculated[9] geometries and energies of *cis*- and *trans*-silacyclohexanol **10** in the chair conformation.

The orientation of the OH bond in the direction of the C=C bond is suggestive of an intramolecular H-bonding in the most stable conformer of the *trans* isomer of **10**. The 3607 cm^{-1} absorption band in the IR spectrum of a dilute solution of **10** is not in disagreement with a weak H-bonding. The axial positions of the trimethylsilyl and methoxymethyloxy groups seem to be maintained in **12**. To avoid the probably less accurate parameters of the silicon atom, further calculations in the MMFF field made with the chair-conformed methylidenecyclohexane derivatives show the same orientation of the OH bond with respect to the C=C bond. An equatorial position of the trimethylsilyl group introduces strong allylic1,3-strain. The axial position of this bulky group, which decreases the interaction with the exocyclic C=C bond, should be the main reason why *trans*-**10** and **12** remain in this conformation.

The mechanism of the ene reaction is frequently reported as the asynchronous formation of a C–C bond followed by migration of the hydrogen atom.[10] In the case of **9**, with the hypothesis of a chair-like transition state, the formation of the C–C bond should give a carbenium ion or a partially positively charged carbon atom in the α position of the ring silicon atom (and in the β position relative to the $SiMe_3$ group).[11] With the hypothesis of a concerted mechanism, C–C bond formation is only possible if the carbonyl group and the methyl substituent of the isopropenyl group are in axial positions. A strong stabilizing interaction of the posi-



Scheme 7. Possible mechanisms for the reaction of aldehyde **9**.

tive charge with the Si–Si bond should occur if the trimethylsilyl group is in an axial position.[12] Therefore, the reaction with a conformer in which the $SiMe_3$ group is in an equatorial position seems less likely (Scheme 7). From intermediate **A** with such an axial trimethylsilyl group, transfer of the hydrogen atom according to the classical ene reaction mechanism should deliver **10** with the OH group in a *trans* relationship to the trimethylsilyl group (Scheme 7, route a). Also from **A**, 1,2-migration of the trimethylsilyl group could give a silylium ion, which could react with a chloride ion to yield a chlorosilane (Scheme 7, route b). Whatever the mechanism of this shift, with[13] or without[14] formation of an intermediate silyl-bridged cation, it should be suprafacial. A similar 1,2-migration of a trimethylsilyl group occurred when 3-[tris(trimethylsilyl)silyl]prop-2-en-1-ol derivatives were treated with BF_3, HCl, or H_2SO_4.[15] In these examples, formation of a silylium ion by migration of the silyl group on the carbenium center after the first ionization step was postulated. Ab initio calculations showed a greater stabilization (ca. 40 $kJ\,mol^{-1}$) of the silylium ion compared to the carbenium ion.[16] We cannot exclude a stereoselective addition of the chloride anion to the intermediate silylium ion, but formation of two diastereomeric chlorosilanes seems more likely, and the presence of two diastereomeric silacyclohexanediols could be expected after hydrolysis (Scheme 7, route b). Simultaneous addition of the chloride anion on the ring silicon atom and migration of the trimethylsilyl group to the positively charged carbon center of **A**[17] would deliver a single chlorosilane (Scheme 7, route c). Hydrolysis of this chlorosilane should occur with inversion of configuration of the silicon center,[18] which would give rise to **11** only after a change in conformation.

Conclusions

The methylaluminum dichloride-catalyzed ene reaction of a 1-isopropenyl-1-(3-oxopropyl)disilane with a chiral Si center allowed a 1-silacyclohexan-4-ol to be obtained as a single diastereomer. Unexpected 1,2-migration of the trimethylsilyl group yielded a 1-silacyclohexane-1,4-diol with three stereogenic centers. These noteworthy highly diastereoselective reactions highlight the few examples reported in the literature in which the configuration of a silicon atom induces efficient control of the creation of stereogenic centers.[19] We postulate the formation of both products via a unique intermediate, which could evolve by the usual ene reaction mechanism or by migration of the silyl group.

Supporting Information (see footnote on the first page of this article): Full experimental details including procedures and characterization data for all compounds, crystallographic data, and copies of the NMR spectra.

Acknowledgments

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[1] A. Giros, *Synlett* **2012**, *23*, 805–806.
[2] a) J. Robertson, G. O'Connor, D. S. Middleton, *Tetrahedron Lett.* **1996**, *37*, 3411–3414; b) J. Robertson, G. O'Connor, T. Sardharwala, D. S. Middleton, *Tetrahedron* **2000**, *56*, 8309–8320.
[3] S. Díez-González, R. Paugam, L. Blanco, *Eur. J. Org. Chem.* **2008**, 3298–3307.
[4] W. H. Campbell, T. K. Hilty, Eur. Pat. Appl. 0325248(A2), **1989**.
[5] E. Hengge, G. Bauer, E. Brandstätter, G. Kollmann, *Monatsh. Chem.* **1975**, *106*, 887–892.
[6] M. Ishikawa, T. Fuchikami, M. Kumada, *J. Organomet. Chem.* **1976**, *118*, 139–153.
[7] U. Herzog, G. Roewer, *J. Organomet. Chem.* **1997**, *544*, 217–223.
[8] CCDC-921760 (for **11**) contains the supplementary crystallographic data for this paper. These data can be obtained free of

charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[9] Semi-empirical calculations were run with *Spartan 08* (version 1.2), Molecular Modeling Package, Wavefunction, Inc., Irvine, CA, **2008**.

[10] a) K. Mikami, M. Shimizu, *Chem. Rev.* **1992**, *92*, 1021–1050; b) H. M. R. Hoffmann, *Angew. Chem.* **1969**, *81*, 597–618; *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 556–577; c) J. Cai, A. G. Davies, *J. Chem. Soc. Perkin Trans. 2* **1992**, 1743–1746.

[11] A. Barbero, F. J. Pulido, M. C. Sañudo, *ARKIVOC* **2007**, *4*, 220–233.

[12] J. B. Lambert, *Tetrahedron* **1990**, *46*, 2677–2689.

[13] A. W. P. Jarvie, A. Holt, J. Thompson, *J. Chem. Soc. B* **1969**, 852–855.

[14] M. A. Cook, C. Eaborn, D. R. M. Walton, *J. Organomet. Chem.* **1970**, *24*, 301–306.

[15] K. Schmohl, D. Wandschneider, H. Reinke, A. Heintz, H. Oehme, *Eur. J. Inorg. Chem.* **2002**, 597–601.

[16] a) A. C. Hopkinson, M. H. Lien, *J. Org. Chem.* **1981**, *46*, 998–1003; b) Y. Apeloig, M. Karni, A. Stanger, H. Schwarz, T. Drewello, G. Czekay, *J. Chem. Soc., Chem. Commun.* **1987**, 989–991; c) T. Drewello, P. C. Burgers, W. Zummack, Y. Apeloig, H. Schwarz, *Organometallics* **1990**, *9*, 1161–1165; d) R. Bakhtiar, C. M. Holznagel, D. B. Jacobson, *J. Am. Chem. Soc.* **1992**, *114*, 3227–3235.

[17] a) K. Tamao, M. Kumada, *J. Organomet. Chem.* **1971**, *30*, 329–337; b) G. Märkl, M. Horn, W. Schlosser, *Tetrahedron Lett.* **1986**, *27*, 4019–4022; c) K. Sternberg, H. Oehme, *Eur. J. Inorg. Chem.* **1998**, 177–181.

[18] a) R. J. P. Corriu, G. Royo, *J. Organomet. Chem.* **1968**, *14*, 291–307; b) R. J. P. Corriu, G. Royo, *Bull. Soc. Chim. Fr.* **1972**, 1490–1497; c) R. J. P. Corriu, F. Larcher, G. Royo, S. Olive, *J. Organomet. Chem.* **1976**, *104*, 161–171; d) L. H. Sommer, C. L. Frye, G. A. Parker, K. W. Michael, *J. Am. Chem. Soc.* **1964**, *86*, 3271–3276.

[19] a) A. G. Brook, W. W. Limburg, *J. Am. Chem. Soc.* **1963**, *85*, 832–833; b) A. G. Brook, J. D. Pascoe, *J. Am. Chem. Soc.* **1971**, *93*, 6224–6227; c) R. G. Daniels, L. A. Paquette, *Organometallics* **1982**, *1*, 1449–1453; d) S. Bienz, A. Chapeaurouge, *Helv. Chim. Acta* **1991**, *74*, 1477–1488; e) A. Chapeaurouge, S. Bienz, *Helv. Chim. Acta* **1993**, *76*, 1876–1889; f) P. J. Coelho, L. Blanco, *Eur. J. Org. Chem.* **2000**, 3039–3046.

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