Pergamon

Tetrahedron Letters 40 (1999) 4031–4034

TETRAHEDRON LETTERS

Synthesis of Aminomethyl Substituted Silacyclohexanes from Divinylsilanes: An Unusually Selective Hydroformylation / Aldol Condensation Sequence

Lars Bärfacker, David El Tom, Peter Eilbracht*

Fachbereich Chemie, Universität Dortmund, Otto-Hahn-Str. 6, D-44221 Dortmund, Germany

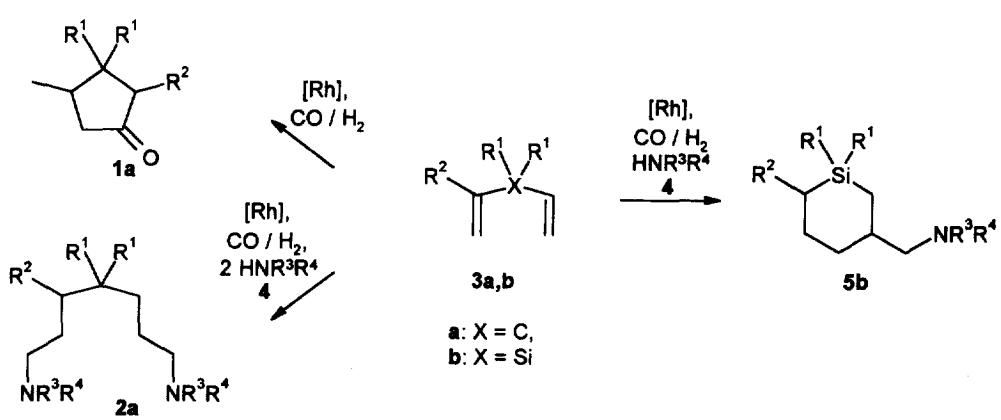
Received 3 March 1999; accepted 31 March 1999

The preparation of aminomethyl substituted silacyclohexane derivatives starting from divinylsilanes and secondary amines is achieved in a selective one-pot tandem hydroformylation / condensation sequence starting with a double olefin carbonylation and proceeding with an enamine generation followed by an aldol condensation step. Final hydrogenation leads to the silacycle in medium up to quantitative yields.

Keywords: aldol reactions, amines, carbonylation, hydroformylation, silicon heterocycles, rhodium catalysis

1,4-Dienes of type **3a** are known to react under hydroformylation conditions to form cyclopentanone derivatives **1a** [1]. If performing the hydroformylation of 1,4-dienes **3a** in the presence of secondary amines, these undergo hydroaminomethylation [2,3] at both double bonds leading to heptamethylene diamines **2a** [3b]. This overall double hydroaminomethylation of the diene as a one-pot multistep procedure includes hydroformylation, followed by condensation of the intermediate aldehyde with the secondary amine to generate the enamine and a final hydrogenation step leading to the saturated amine.

Continuing our work on hydroaminomethylation [3] of olefins, we examined the conversion of the corresponding divinylsilanes **3b** under hydroaminomethylation conditions. Surprisingly and in contrast to the reaction pathways presented above, the sila analogues **3b** under these conditions lead to silacyclohexanes of type **5b** with a new type of a CC-bond forming and ring closing tandem procedure.

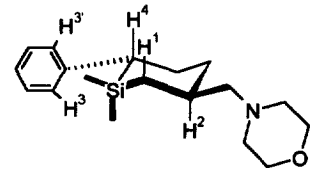


Scheme 1: Hydroformylation of diolefins in presence of secondary amines

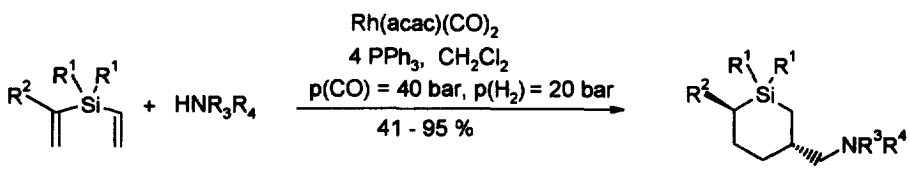
Fax: (+49)(0)231-7555363; e-mail: eilbrach@citrin.chemie.uni-dortmund.de

0040-4039/99/$ - see front matter
PII: S0040-4039(99)00678-4

As sumarised in table 1 conversion of divinylsilanes **6** to substituted silacyclohexanes **7** can be applied to a variety of different amines and silanes. Best results are achieved with cyclic amines like morpholine, pyrrolidine and piperidine. With acyclic amines like diethylamine generally lower yields are obtained. Unsymmetrically substituted divinylsilanes **6c** and **6d** with high regioselectivity are exclusively converted to the 2,5-disubstituted silacyclohexanes **7f** and **7g** whereas the 2,3-disubstituion pattern is not observed (entry 6,7). With the *n*-butyl derivative **6c** the reaction proceeds with moderate diastereoselectivity leading to the *trans*-substituted silacycle **7f**, whereas by increasing sterical demand with a phenyl group instead of the *n*-butyl group the *trans*-isomer is formed exclusively. The relative configuration of **7g** was established by NMR spectroscopy. The large coupling constant between H^1 and H^2 ($\approx$ 13.5 Hz) indicates an antiperiplanar configuration of these atoms and consequently an equatorial position of the aminomethyl moiety. Furthermore the equatorial position of the phenyl group was established by a NOESY experiment showing interactions between the *ortho*-protons H^3, $H^{3'}$ and the protons of both $SiMe_2$ groups.



7g



6 **7**

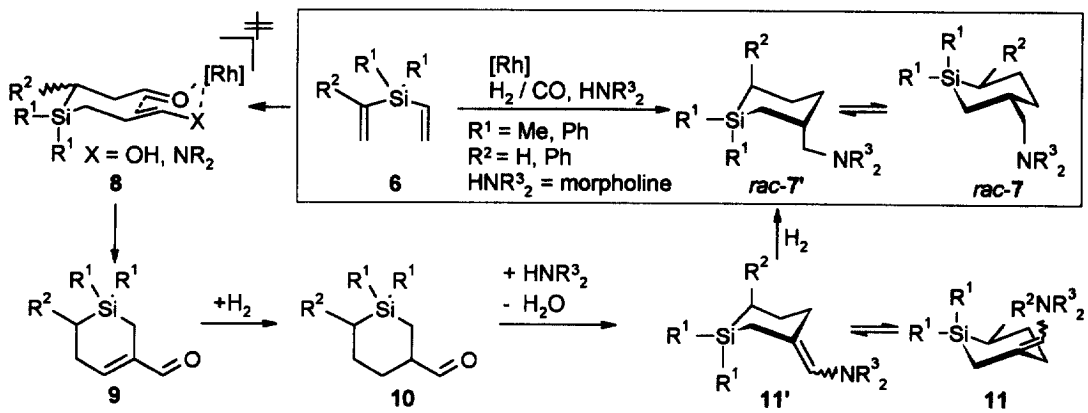
Table 1: *Hydroformylation of Divinylsilanes 1 in the Presence of Secondary Amines [4]*

entry	R^1	R^2	reactant	R^3 , R^4	conditions	product	GC-yield [%]
1	Ph	H	**6a**	$-(CH_2)_2-O-(CH_2)_2-$	2 d, 100 °C	**7a**	95
2	Ph	H	**6a**	Et Et	4 d, 90 °C	**7b**	41
3	Ph	H	**6a**	$-(CH_2)_4-$	20 h, 90 °C	**7c**	79
4	Ph	H	**6a**	$-(CH_2)_5-$	3 d, 90 °C	**7d**	54
5	Me	H	**6b**	$-(CH_2)_2-O-(CH_2)_2-$	2d, 90 °C	**7e**	92
6	Me	*n*-Bu	**6c**	$-(CH_2)_2-O-(CH_2)_2-$	3 d, 90 °C	**7f**	64 (*de* = 50)
7	Me	Ph	**6d**	$-(CH_2)_2-O-(CH_2)_2-$	20 h, 90 °C	**7g**	68 (*de* > 95)

Under mild conditions (60 °C) two key intermediates of the reaction sequence can be isolated (substrates **9** and **10**). This indicates a mechanism involving an aldol condensation as ring closing step (scheme 2). The ring closure may proceed kinetically favored as illustrated by transition state **8**, that is in good agreement to known aldol reactions of rhodium enolates [5]. This could be the reason for the suppression of the hydroaminomethylation normally observed. The overall reaction may be explained as follows.

In the initial step a double *n*-selective hydroformylation of **6** leads to the dialdehyde. In a subsequent conversion the α,β-unsaturated aldehyde **9** is generated via aldol condensation presumably supported by morpholine as a base and probably passing transition state **8** (X=OH). Alternatively, the cyclisation can interpreted to proceed via an enamine of **8** ($X=NR_2$). This assumption is supported by a control experiment with triethylamine instead of a secondary amine (no formation of enamines), that exlusively leads to a complex product mixture.

In all cases the α,β-unsaturated aldehyde **9** then undergoes hydrogenation to the silacyclohexane derivative **10**, that subsequently forms **11** by enamine condensation. A final hydrogenation then concludes the multi-step reaction sequence with the generation of *rac*-**7**.



Scheme 2: Proposed mechanism for the generation of rac-7

Based on this mechanism the observed regioselectivity in the case of silanes **6c,d** is reasonable. Here, the first carbonylation proceeds at the less hindered vinyl moiety with a fast formation of the corresponding enamine. The consecutive hydroformylation predetermines the choice of the electrophilic and nucleophilic centres for the condensation step defining the 2,5-disubstitution pattern of product **7f,g**. The hydrogenation of **11** to *rac*-**7** obviously determines the diastereoselectivity of the overall reaction. Stereochemical consideration supported by MM2 force field calculation illustrate, that no matter which conformer of **11** or **11'** reacts, the final reaction step should force the aminomethyl group to occupy the axial position. Therefore it can be concluded, that the thermodynamically less favored conformer **11'** reacts predominantly to silacycle **7'**, which then interconverts to adopt the all-equatorial *trans*-situation in **7**. This unexpected result may be due to a stereodirecting effect of the phenyl group precoordinating the catalyst. This interpretation is in line with the observed lower selectivity if butyl as substituent is used instead of phenyl. The reaction described above represents one of the rare examples [6] of a selective hydroformylation / aldol condensation sequence. Usually condensation reactions following hydroformylation of olefins are only unintended and unselective side reactions [7].

In conclusion we here report a new and effective procedure of a tandem hydroformylation/ condensation sequence which is not observed with carbon analogues and should be applicable to other double unsaturated silanes.

Silacyclohexanes have attracted interest from both pharmaceutical and synthetical points of view, since they proved to be of high spasmolytical [8] and antiarthritic [9] activity. Furthermore silacycloalkanes serve e. g. as reactants for ring enlargement reactions [10] or as synthons for the generation of silylenolether [11]. Several approaches for the generation of functionalised silacyclohexanes have been made [12]. Therefore our approach represents a promising additional new entry to this class of compounds, with the option to introduce aminofunctionalities in a stereoselective way.

Acknowledgements: Financial support of this work by the Fonds der Chemischen Industrie and the state of Nordrhein-Westfalen is gratefully acknowledged. We also thank the Degussa AG, Hanau for donation of chemicals.

References and Notes:

(1) (a) Eilbracht, P.; Acker, M.; Hüttmann, G.; Winkels, I.; *Chem. Ber.* **1989**, *122*, 159-168. (b) Eilbracht, P.; Acker, M.; Hädrich, I.; *Chem. Ber.* **1989**, *122*, 519-524.

(2) (a) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpaintner, C. W.; *J. Mol. Catal. A* **1995**, *104*, 17-85. (b) Baig, T.; Molinier, J.; Kalck, P.; *J. Organomet. Chem.* **1993**, *455*, 219-224. (c) Jones, M. D.; *J. Organomet. Chem.* **1989**, *366*, 403-408. (d) Jachimowicz, F.; Raksis, J. W.; *J. Org. Chem.* **1982**, *47*, 445-447.

(3) (a) Rische, T.; Eilbracht, P.; *Synthesis* **1997**, 1331-1337. (b) Kranemann, C. L.; Eilbracht, P.; *Synthesis* **1998**, 71-77. (c) Rische, T.; Kitsos-Rzychon, B.; Eilbracht, P. *Tetrahedron* **1998**, *54*, 2723-2742. (d) Bärfacker, L.; Hollmann, C.; Eilbracht, P. *Tetrahedron* **1998**, *54*, 4493-4506. (e) Rische, T.; Eilbracht, P. *Tetrahedron* **1998**, *54*, 8441-8450. (f) Rische, T.; Eilbracht, P. *Tetrahedron* **1999**, *55*, 1915-1920. (g) Rische, T.; Bärfacker, L.; Eilbracht, P. *Eur. J. Org. Chem.*, accepted for publication. (h) Kranemann, C. L.; Kitsos-Rzychon, B.; Eilbracht, P. *Tetrahedron*, accepted for publication.

(4) A typical experiment is as follows: A mixture of divinylsilane **6d** (5.31 mmol), morpholine (14.35 mmol), triphenylphosphine (4 mol-% mmol) and $Rh(acac)(CO)_2$ (1 mol-%, based to the amount of silane) in 15 ml of dry CH_2Cl_2 was placed in an autoclave. After flushing the autoclave with argon the reactor was pressurised with 20 bar CO and additional 40 bar of H_2. The reaction mixture was magnetically stirred at 90 °C for 4 d. The residue was dissolved in methyl *t*-butyl ether and filtered through neutral alumina. The isolation of the silacyclohexanes **7** was carried out by column chromatography on alumina with petrol ether 30/60 : methyl t-butyl ether (40 : 1) as the eluent affording 370 mg (11.28 mmol, 24 %) of silacyclohexane **7g** as an oil. Spectral data of **7g**: ^1H NMR (400 MHz, $CDCl_3$, 20 °C): δ [ppm] = -0.12 (s, 3H), 0.00 (s, 3H), 0.24 (t*, 1H, J = 13.5 Hz), 0.96 (m, 2H), 1.75 (m, 1H), 1.93 (m, 1H), 2.07 (m, 3H), 2.18 (m, 2H), 2.42 (m, 4H), 3.74 (m, 4H), 7.01 (d, 2H, ^3J = 7.5 Hz), 7.09 (t*, 1H, ^3J = 7.5 Hz) , 7.25 (t*, 2H, ^3J = 7.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C): δ [ppm] = -7.1 (CH_3), -3.3 (CH_3), 19.5 (CH_2), 29.9 (CH_2), 33.4 (CH), 34.5 (CH_2), 36.3 (CH), 54.1 (CH_2), 67.0 (CH_2), 69.1 (CH_2), 124.0 (CH) 126.6 (CH) 128.0 (CH) 144.9 (Cq). IR (neat): $\tilde{\nu}$ [cm^{-1}] = 2956 s, 1454 m, 1295 s, 1119 s, 699 s. MS (EI, 70 eV): m/z = 303 (M^+, 9%), 230 (1%), 135 (2%), 127 (3%), 100 (100%), 91 (3%), 77 (1%), 59 (5%). Anal. Calcd. for $C_{18}H_{29}NOSi$: C, 71.2; H, 9.6; N, 4.6. Found: C, 71.4; H, 9.9; N, 4.5.

(5) Slough, G. A.; Bergman, R. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1989**, *111*, 938-949.

(6) Knifton, J. F.; Lin, J. J.; *J. Mol. Catal.* **1993**, *81*, 27-36.

(7) Cornils, B. in *New Syntheses with Carbon Monoxide*; Falbe, J. Ed.; Springer-Verlag, Berlin, 1980, pp 1-225.

(8) R. Tacke, U. Wannagat, *Top. Curr. Chem.* **1979**, *84*, 1-75.

(9) A. M. Badger, D. A. Schwartz, D. H. Picker, J. W. Dorman, F. C. Fontaine, *J. Med. Chem.* **1990**, *33*, 2963-2970.

(10) Matsumoto, K.; Aoki, Y.; Oshima, K. ; Utimoto, K. ; *Tetrahedron* **1993**, *49*, 8487-8502.

(11) Tanaka, Y.; Yamashita, H.; Tanaka, M.; *Organometallics* **1996**, *15*, 1524-1526.

(12) for reviews, see: a) Hermanns, J.; Schmidt, B.; *J. Chem. Soc., Perkin Trans. I* **1998**, 2209-2230. a) Hermanns, J.; Schmidt, B.; *J. Chem. Soc., Perkin Trans. I* **1999**, 81-102.