doi:10.1246/cl.2010.402

Design and Synthesis of New Linker Units for Covalently Immobilizing Organic Functional Molecules

Norihisa Fukaya,[1] Shun-ya Onozawa,*[1] Masae Ueda,[2] Kaori Saitou,[1] Yukio Takagi,[2]
Toshiyasu Sakakura,[1] and Hiroyuki Yasuda*[1]
[1]*National Institute of Advanced Industrial Science and Technology (AIST),*
Tsukuba Central 5, 1-1-1 Higashi, Tsukuba 305-8565
[2]*N. E. CHEMCAT CORPORATION, 678 Ipponmatsu, Numazu 410-0314*

(Received February 8, 2010; CL-100137; E-mail: h.yasuda@aist.go.jp, s-onozawa@aist.go.jp)

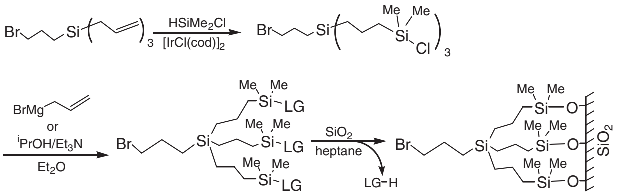
The design and synthesis of a new linker unit that will enable uniform and robust immobilization of organic functional molecules onto silica supports is described. This linker unit works as a rigid scaffold to prevent grafted organic functional moieties from leaving the support.

Hybrid organic–inorganic materials in which organic functional molecules are bound to the surface of silica have been utilized or expected to be applied in various fields, including packing materials for chromatography, chiral selectors, adsorbents, chemical sensors, and immobilized catalysts.[1] For increased stability or lifetime of these materials, strengthening the bond between organic functional groups and silica is important, as well as improving the durability of silica supports and preventing the degradation or deterioration of the organic moieties. However, the methodology for covalently binding organic functional groups to silica is mostly limited to the use of silylating reagents such as trialkoxysilanes and trichlorosilanes.

For example, the immobilization of metal complex catalysts via linkers such as a trimethylene chain on silica supports is a promising strategy to facilitate the separation of catalysts from reaction mixtures as well as for catalyst recycling,[2] whereas the elimination of metal fragments from immobilized ligands and cleavage of the bond between the ligand and support cause leaching of metal and/or ligand.[3] Employing ligands with a strong s-donating ability[4] or chelating ligands[5] effectively resolves the former problem. On the other hand, few attempts have been made to design an organic linker for fortifying ligand–support bonds.

The covalent anchoring of organic functional groups onto silica via condensation of trialkoxysilanes with surface silanol groups permits linkage through three siloxane bridges in principle. However, depending on the silanol density, monopodal and/or bipodal anchoring becomes predominant[6] (vide infra). Moreover, the residual alkoxy group occasionally reacts with unreacted trialkoxysilanes to generate complicated species on silica.[7] We hypothesized that tripodal anchoring would be realized if a silylating agent could be designed such that the Si–O–Si linkage can be formed at three independent silicon atoms. Herein we report the design and synthesis of a new linker unit, which can be tightly bound to silica by condensation of up to three allylsilyl[8] or alkoxysilyl groups in the linker with silanol groups. This new linker unit works as a rigid scaffold to prevent grafted organic functional moieties from leaving the support.

The linker compound containing three allylsilyl moieties (**1a**) was easily prepared in a one-pot process by iridium-catalyzed hydrosilylation of triallyl(3-bromopropyl)silane with dimethylchlorosilane and subsequent treatment of the resulting tris(dimethylchlorosilyl) compound with an allyl Grignard reagent. Additionally, a linker containing three isopropoxy groups (**1b**) was prepared using isopropanol and triethylamine instead of Grignard reagent in the second step (**1b**) (Scheme 1). It should be noted that not only **1a** but also **1b** could be easily purified by silica gel column chromatography at room temperature without any decomposition. In contrast to the most commonly used trimethoxy- or triethoxysilanes which are easily hydrolyzed and subsequently condensed to the corresponding siloxane compound,[8] **1b** was relatively stable under hydrolytic conditions.



1a: LG = $CH_2CH{=}CH_2$ (76%)
1b: LG = $OCH(CH_3)_2$ (87%)
2a: 0.33 mmol/g
2b: 0.38 mmol/g

Scheme 1. Synthesis and grafting on silica surface of tripodal linker compounds.

The reaction of **1a** or **1b** with FSM-type ordered mesoporous silica (TMPS-4)[9] in heptane at reflux for 24 h gave bromopropyl-modified silica **2** (hereafter **2** refers to **2a** and **2b** derived from **1a** and **1b**, respectively). The amounts of organic moieties of **2a** and **2b** determined by elemental analysis of carbon were 0.33 and 0.38 mmol g^{-1}, respectively.[10] Figure 1A shows the ^{29}Si CP/MAS NMR spectrum of modified silica **2b**. The two signals at 2 and 14 ppm corresponded to one tetraalkyl-coordinated silicon and three trialkylmonooxygen-coordinated silicon atoms in **2b**, respectively,[11] clearly demonstrating that, as expected, **1b** is grafted onto the silica surface via three covalent Si–O–Si bonds. ^{13}C CP/MAS NMR spectroscopy further confirmed the successful grafting of **1b**. The chemical shifts observed in the ^{13}C CP/MAS NMR spectrum of **2b** agreed well with those in the ^{13}C NMR spectrum of **1b** in $CDCl_3$ except the signals of the leaving isopropoxy groups disappeared in the CP/MAS NMR spectrum (Figures 1B and 1C). Modified silica **2a** gave ^{29}Si and ^{13}C CP/MAS NMR spectra similar to Figures 1A and 1B (see Supporting Information).[12] These observations indicate that the proposed structure of **2** is reasonable. Thus, we successfully grafted linker compounds containing a bromopropyl group onto a silica surface in a well-defined uniform manner.

Stability tests were used to confirm the effectiveness of the present linker unit in minimizing leaching of organic moieties

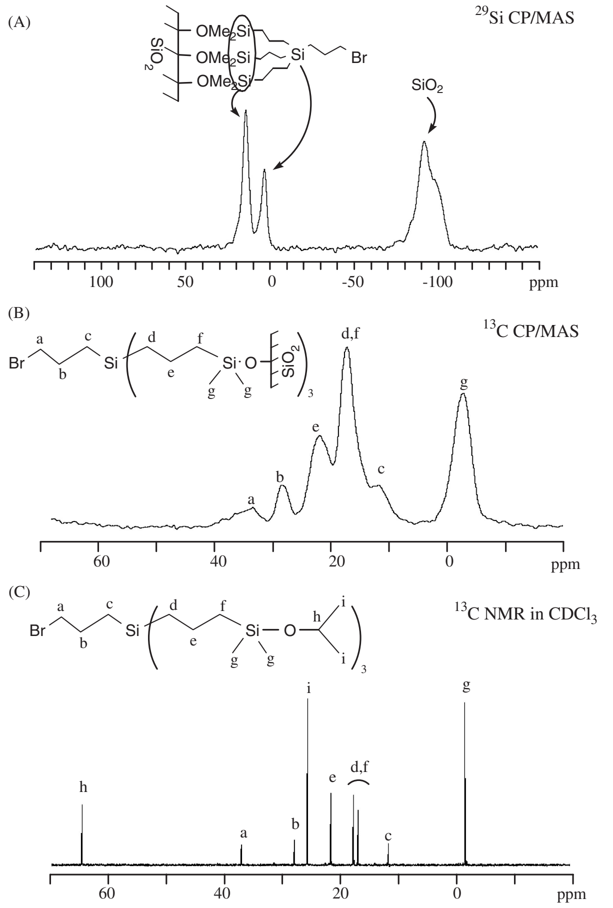
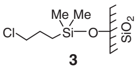
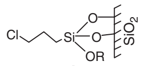


Figure 1. (A) ^{29}Si CP/MAS NMR spectrum of **2b**; (B) ^{13}C CP/MAS NMR spectrum of **2b**; and (C) ^{13}C NMR spectrum of **1b** in $CDCl_3$.

from a silica support. For comparison, we prepared chloropropyl-modified silica **3**, which involved one Si–O–Si bond, and modified silica **4** using conventional trialkoxysilane. A ^{29}Si CP/MAS NMR spectroscopic examination of the distribution of the species bound via one, two, or three siloxane bridges to silica (T^1, T^2, and T^3) in **4** revealed that T^2 is the major species (see Supporting Information).[12] Stability tests were performed by treating modified silica with water at 80 °C for 48 h and then quantifying the remaining organic moieties on silica using carbon elemental analysis. Table 1 summarizes the results. About half the organic moieties were lost for **3** and **4** by water treatment. In contrast, only 6% of **2a** leached. This difference was further corroborated by the ^{29}Si CP/MAS NMR spectra of **2a** and **4** before and after water treatment. The ^{29}Si CP/MAS NMR spectrum of **4** after water treatment showed total disappearance of the T^1 peak and decrease of the T^2 peak. In contrast, no significant changes in the ^{29}Si CP/MAS NMR peaks in the organosilane region of **2a** were observed before and after water treatment (see Supporting Information).[12] These results indicate that grafting of the present linker unit via three isolated Si–O–Si bonds is highly stable even under severe hydrolytic conditions.[3b]

Table 1. Data for the leaching of linkers from the silica support

Modified SiO_2	Immobilized organic group		Remained organic group after water treatment		Leaching /%
	Loading /mmol g^{-1}	Organic moiety on 1 g of SiO_2/g	Loading /mmol g^{-1}	Organic moiety on 1 g of SiO_2/g	
2a	0.33	0.17	0.31	0.16	6
 **3**	1.23	0.20	0.66	0.098	51
 **4**	1.19	0.17	0.70	0.094	45

In summary, we have developed a new linker unit that will enable uniform and robust immobilization of organic functional molecules onto silica supports. Various functional groups can be attached to the bromopropyl moiety in the linker. Further multipodal anchoring may be possible by replacing the six methyl moieties with leaving groups. Hence, we believe that the present method has great potential in the development of various organic-functionalized silica materials including silica-immobilized molecular catalysts. Such efforts are currently underway in our group.

This research was financially supported by Development of Microspace and Nanospace Reaction Environment Technology for Functional Materials Project of NEDO, Japan.

References and Notes

1 a) Special Issue on Organic–Inorganic Nanocomposites: *Chem. Mater.* **2001**, *13*, No. 10. b) *Functional Hybrid Materials*, ed. by C. Sanchez, P. G. Romero, Wiley-VCH, Weinheim, Germany, **2004**. c) *Hybrid Materials, Synthesis, Characterization and Applications*, ed. by G. Kickelbick, Wiley-VCH, Weinheim, Germany **2007**. d) A. P. Wight, M. E. Davis, *Chem. Rev.* **2002**, *102*, 3589. e) A. Corma, H. Garcia, *Adv. Synth. Catal.* **2006**, *348*, 1391. f) Special Issue on Functional Hybrid Materials: *J. Mater. Chem.* **2005**, *15*, No. 35–36.

2 a) J. A. Gladysz, *Chem. Rev.* **2002**, *102*, 3215. b) J. Y. Ying, C. P. Mehnert, M. S. Wong, *Angew. Chem., Int. Ed.* **1999**, *38*, 56. c) D. Brunel, A. C. Blanc, A. Galarneau, F. Fajula, *Catal. Today* **2002**, *73*, 139. d) J. H. Clark, D. J. Macquarrie, *Chem. Commun.* **1998**, 853. e) A. Corma, H. Garcia, *Adv. Synth. Catal.* **2006**, *348*, 1391.

3 a) C. Merckle, J. Blümel, *Chem. Mater.* **2001**, *13*, 3617. b) E. A. Smith, W. Chen, *Langmuir* **2008**, *24*, 12405.

4 a) G. Hamasaka, A. Ochida, K. Hara, M. Sawamura, *Angew. Chem., Int. Ed.* **2007**, *46*, 5381. b) K. Hara, R. Akiyama, S. Takakusagi, K. Uosaki, T. Yoshino, H. Kagi, M. Sawamura, *Angew. Chem., Int. Ed.* **2008**, *47*, 5627.

5 a) S. Reinhard, K. D. Behringer, J. Blümel, *New J. Chem.* **2003**, *27*, 776. b) C. Merckle, J. Blümel, *Adv. Synth. Catal.* **2003**, *345*, 584. c) M. Bogza, T. Oeser, J. Blümel, *J. Organomet. Chem.* **2005**, *690*, 3383.

6 K. Behringer, J. Blümel, *J. Liq. Chromatogr. Relat. Technol.* **1996**, *19*, 2753.

7 D. W. Sindorf, G. E. Maciel, *J. Am. Chem. Soc.* **1983**, *105*, 3767.

8 a) T. Shimada, K. Aoki, Y. Shinoda, T. Nakamura, N. Tokunaga, S. Inagaki, T. Hayashi, *J. Am. Chem. Soc.* **2003**, *125*, 4688. b) K. Aoki, T. Shimada, T. Hayashi, *Tetrahedron: Asymmetry* **2004**, *15*, 1771.

9 FSM-type ordered mesoporous silica (TMPS-4) was supplied by Taiyo Kagaku Co., Ltd. The surface area (BET), pore volume ($P/P_0 = 0.99$), and the average pore diameter (BJH) were 1039 $m^2 g^{-1}$, 1.46 $cm^3 g^{-1}$, and 3.8 nm, respectively.

10 Based on elemental analysis of bromine, the loading amounts of **2a** and **2b** were 0.31 and 0.33 mmol g^{-1}, respectively. These results were in general agreement with carbon analysis.

11 G. Engelhardt, H. Jancke, E. Lippmaa, A. Samoson, *J. Organomet. Chem.* **1981**, *210*, 295.

12 Supporting Information is available electronically on the CSJ-Journal Website, http://www.csj.jp/journals/chem-lett/index.html.