Direct reaction of silica gel with butyllithium

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Silica gel with a variety of surface areas is found to react directly (no $SOCl_2$ treatment required) with butyllithium to give a product with butyl groups attached. The extent of butyl group incorporation depends on available silica surface. With dehydrated 230–400 mesh silica gel, 7.4 mmoles of BuLi per g in pentane added in hexane gave silica with 2.5 mmoles of butyl groups per g provided that the silica gel was washed three times with cold water. It was found that water washing removes some unbutylated silicate increasing the apparent butyl group incorporation. The butyl-modified silica gel showed no chromatographic retention of 3-aminoquinoline in 50:50 hexane: dichloromethane or of thymol in hexane in contrast to unmodified silica gel which is known to strongly retain polar compounds, particularly basic ones. This contrast is demonstrated.

Keywords: silica, butyllithium, column chromatography, C–Si bonds

Few materials have been studied as extensively as silica. Many excellent reviews have appeared.[1-3] Although some controversy exists, the basic facts are that silica consists of a network of SiO_4 tetrahedra terminated in hydroxyl groups at the surfaces. The number of surface hydroxyl groups is given by the hydroxyl number α_{OH} which is the number of hydroxyl groups per nm.[2] The value of this parameter has been calculated theoretically using silica surfaces of known geometry by De Boer[4] and experimentally determined by Peri and Hensley[5] who extended it to silica gels.

The customary way of rendering the silica surface vulnerable to nucleophilic attack is first to convert available hydroxyl groups to chlorine atoms using thionyl chloride or other halogen-introducing reactants. Maciel[6] has examined reaction of such halogenated silica with methyl groups bonded to lithium, magnesium, aluminum and zinc and found some $Si–CH_3$ bonding. With trimethylaluminium the products are complex.[7] More recently it was found[8] that certain chlorinated silica gel reacts with a large excess of methyllithium to give completely methylated silica, 9.58 μmoles per m^2. Coverage that high had not been attained previously.[6,9,10] We now demonstrate that silica gel reacts with butyllithium in the absence of prior chlorination to attach butyl groups to the silica. To our knowledge, this has not been reported previously. Because base hydrolysis does not remove these groups, yet is known to remove alkoxy groups from silica gel,[11] we believe that attachment to silicon occurs leading to Si-C bonds. We offer an explanation.

Experimental

Materials

Silica gels were used as follows. A = 70–230 mesh, 60 Å, BET surface *ca* 500 m^2 g^{-1}, pore volume 0.75 cm^3 g^{-1}, Aldrich Chemical Co. B = 230 to 400 mesh = 40 to 63 μm, porosity = 60 Å, Sorbent Technologies. C = fumed silica, 0.07 μm, 380 m^2 g^{-1}, Aldrich Chemical Co. D = 28–200 mesh, Davison Chemical Co. Butyllithium, 2 M in pentane, was obtained from Aldrich Chemical Co. and used as received. 3-Aminoquinoline was recrystallised from hexane-dichloromethane. Apparently this can be obtained in two, presumably isomorphic, forms. We started with material melting 93–94°C[12] but obtained material melting 81–82°C[13-15] from the columns. These materials were identical by GC/MS.

General procedure for the reaction of silica with butyllithium

A three-necked round-bottomed flask containing a teflon-coated stirrer bar and having an attached pressure-equalising dropping funnel was dried by heating with a heat gun under argon flow. Distilled hexanes were added, followed by dry silica added via a curved tube. The silica was generally dried in an oven at 130°C for a least a day, followed by heating under 0.04 mbar pressure in a round-bottomed flask at an external temperature of 450°C for 15 min. The mixture of silica and hexanes was cooled in an ice bath and the appropriate amount of butyllithium (2 M in pentane) was added under argon by cannula to the previously marked dropping funnel through a rubber septum. The butyllithium solution was then added dropwise over roughly five minutes to the stirred hexane slurry kept at 0°C. The stirred mixture was allowed to warm to room temperature over 1 hr and was then treated with enough *t*-butyl alcohol to neutralise any residual butyllithium. There was generally some warming but only in the case of large-particle silica was the reaction vigorous. The silica was then separated by filtration through a funnel with a sintered glass bed and washed with hexanes. After evaporation, the hexane-soluble material was titrated to a bromocresol blue end point with 1 M HCl or past neutral pH with an Orion pH meter.

Work-up of butylated silica

In most cases, the filtered silica was stirred with cold water for 15 minutes and then refiltered. A mixture of ice and water in roughly equal amounts and totalling about 100 ml for 15 g was used. The washing procedure was repeated twice more. Each aqueous solution was titrated with 1 M HCl. After the washings over 1 mmole g^{-1} of base remained with the silica and a measured amount of the silica could then be stirred in water and titrated with 0.1 M HCl using a pH meter. In general, pH titrations of silica slurries showed an immediate low pH followed by slow return to a steady higher value. We assumed completion was reached when the pH remained constant for more than an hour. Although it was assumed that washing of basic silica with an ice-water mixture would minimise chemical reactions, some silicate was removed during these processes as evidenced by the gelling of the acidified washes. As an example, in entry 4, Table 1, 13.65 g of silica gel was treated with 75 mmoles of butyllithium in 100 ml of hexane at 0°C. After workup in the usual way, the insoluble product was washed with three separate aliquots of 150 ml cold water and then dried. Each water wash, separated from the silica material by filtration, was titrated with *ca* 1 M HCl and after evaporation down to 10 to 20 ml, started to form a gel. In addition to gel formation, the presence of silicate in the water washes was shown by IR spectra of the dried gel. After subtraction of the weight of LiCl necessarily present, approximately 2.67 g of residual dried solid was determined. As a total titration of 54.7 mmoles of HCl was required, the average equivalent weight of material, assumed to originate as anion with Li as counterion, was 49. Interestingly the dry solid from the water washes showed no C–H stretch in its IR spectrum as contrasted with the washed silica for which the C–H was quite pronounced relative to the Si–O band. Thus it seems clear that no butyl groups were removed by water washing. As an alternative workup procedure, the initial hexane-washed filtrate was treated immediately with enough 0.1 M aqueous HCl at 0°C to neutralise base present. Remarkably, 15 minutes of this treatment did not remove all base from the silica gel. However, it did lower the carbon content of the recovered silica gel as is expected if silicate is removed by the three water washes of the basic silica gel. If acid-washed silica was then treated with aqueous lithium hydroxide, silicate was removed and carbon analysis showed an increase in %C.

Chromatographic proceedure

The silica (5.1 ± 0.1 g) was slurried in hexane and added to a 25 ml burette with a teflon stopcock, glass wool and sand at the bottom. The burette was 17 cm long and had about 1 cm i.d. The silica column was topped with sand and 102 ± 2 mg of compound added in about

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Table 1 Results of treatment of various silica gels with butyllithium

Entry	Gel[a]	Wt of gel g	mmols BuLi	mmols base solv.	mmols base H_2O	mmols base gel	%C basic	%C acidic
1	A	10.1	20	–	9.0	6.9	4.19[e]	
2	A	20.0	40					5[b]
3	A	7.12	40			21.0	7.43[e]	7.54[e]
4	B	13.7	100	21.4	54.6	26.2	12.06[e]	12.76[e]
5	B	15.7	120	21.9	[c]	32.1		7.87[e]
6	B	[d]	[d]	[d]	[d]		17.44[e]	19.76[e]
7	B	22.9	60	<1	29.1	30.6	7.5[b]	
8	C	8.8	50	5.1	16.9	30.6		7.5[b]
9	D	15.6	100	117	2.6	3.1	<2[b]	

[a]See experimental section. [b]Estimated from comparison of IR spectrum with spectra of combustion analysed material. [c]Insoluble material (silica) washed immediately with aqueous acid. [d]Product from entry 5 treated with LiOH (see Experimental). [e]Analyses performed by Desert Analytics.

1 ml of the appropriate solvent. In the case of 3-aminoquinoline, it was necessary to start with a mixture of dichloromethane and hexane because of insolubility in pure hexane. Elution aliquots were 10 ml. Other more soluble compounds were also used. The full sequence was as follows: fractions 1 to 4 = pure hexane; 5 to 8 = 20% by volume of CH_2Cl_2 in hexane; 9 to 12 = 50% by volume CH_2Cl_2 in hexane; 13 to 17 = pure CH_2Cl_2; 18 to 22 = 10% by volume diethyl ether in CH_2Cl_2; 23 to 27 = 50% by volume ether in CH_2Cl_2; 28 on = pure ether. Thus 3-aminoquinoline was eluted from Aldrich silica gel (A) in fractions 25 to 34. The maximum was at fraction 28, the first fraction of 100% ether. Amounts of material were determined by evaporation and weighing. Recovery of 3-aminoquinoline was quantitative. Recovery of thymol was only 90%, probably because of evaporation.

Results

We tried the reaction of dehydrated, not chlorinated, silica gel with butyllithium and were surprised to find that alkylation took place as shown by the antagonism of the product to water (creeping and floating) and by analysis. Addition of 20 mmoles of butyllithium in pentane to 10.1 g of 70–230 mesh Aldrich chromatographic grade silica gel in 50 ml hexane at 0°C gave hexane and water-washed product which, after titration to acidic pH, filtration and drying gave %C = 4.19 and %H = 1.89 (see entry 1 in Table 1). Addition of 40 mmoles of butyllithium to 7.2 g of silica gel gave %C = 7.43 and %H = 1.39 (1.55 mmoles/g based on %C) after treatment with *t*-butyl alcohol to remove unreacted butyllithium, hexane washing, water washing and dehydration. This product was still basic but acidification by titration with 0.1 M HCl followed by filtration and dehydration resulted in silica gel with %C = 7.54 and %H = 1.75. (See entry 3 in Table 1). IR spectra of these materials showed C–H stretching at 2971, 2943 and a doublet centred at about 2880 cm^{-1} (accuracy *ca* ± 2 cm^{-1}). A similar experiment was tried with fumed silica (0.07 μm – Aldrich, entry 8 in Table 1). Butyllithium was added at 5.65 mmoles per g. Butyl groups were incorporated although in lower amount than in the low particle size silica gel. The IR spectrum of this material was indistinguishable from that obtained with Aldrich chromatographic grade silica (analysed by combustion, entry 3, Table 1) suggesting roughly 7% carbon (est. 1.5 mmoles butyl per g).

Other entries in Table 1 show that higher surface area leads to higher butyl group incorporation. Large particle size, low surface area silica resulted in little or no butyl incorporation (entry 9). Water washing of the initially obtained filtrate removes some silicate resulting in an effectively higher butyl group incorporation. In agreement, the removed silicate shows no C–H presence by IR. The same effect may be accomplished by acidification of the initially filtered silica containing a moderate amount of carbon, followed by aqueous lithium hydroxide treatment resulting in a large increase (entries 5 and 6). A lower initial ratio of butyllithium resulted in lower carbon content (entry 7).

It was thought that this procedure would place other alkyl groups on the silica surface if the corresponding alkyllithiums were available. The elegant procedure published by Bailey and Punzalan[16] and by Negishi, *et al.*[17] was tried. Heptyl and octadecyl groups were incorporated but the extent is uncertain at present.

Simple column chromatography was carried out using the silica gel from entry 4. The mobile phase graduated from hexane to dichloromethane to diethyl ether. The 12.06 % carbon material, corresponding to 2.6 mmoles of butyl per g, did not retain either 3-aminoquinoline or thymol whereas these moved relatively slowly down untreated silica gels or even commercial C_{18} material. Facilities for reversed-phase gas-liquid chromatography were not available.

Discussion

While the surface geometry of silica gel is complex, a first assumption might be that there was one hydroxyl group for every silicon atom. This is the assumption made by De Boer and despite the fact that he dealt with a flat surface the fact that the hydroxyl number is similar for silica gels plus the difficulty of envisaging surface silicon atoms with no hydroxyl groups make this a reasonable picture. It is reasonably assumed that butyllithium would readily react with such surface hydroxyl groups to form salt-like lithium oxygen bonds and subsequent reaction with butyllithium might then be avoided. Such is not the case with carboxylic acids whence initially formed lithium carboxylates react with another molecule of alkyllithium at carbon.[18] In fact, butyllithium reacts with hexanoic acid to give a good yield of decan-5-one after quenching.[19] An analogous process for silica is shown in Figure 1 and is a possible explanation for the observed phenomenon.

Conclusions

Silica reacts with butyllithium to introduce butyl groups. Reaction of the product with lithium hydroxide removes silicate, but not butyl. Thus the butyl groups are attached to silicon atoms and these remain part of the polymer. The degree

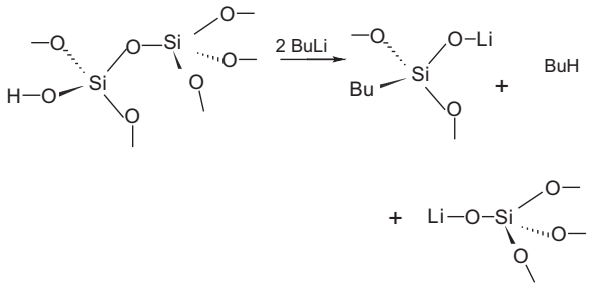

Fig. 1

of incorporation depends on the amount of surface and even the small, nonporous,[20] spherical particles present in fumed silica react at their surfaces. It is clear that nucleophiles attack silicon atoms in a variety circumstances.[21-23] The mechanism of this reaction may involve 5-coordinate silicon atoms.[24-26] There do not seem to be any reports of permanent nucleophilic attachment of groups to the silicon atoms of unmodified silica. The data in this paper indicate that once butyl groups are attached to silica by our procedure, they are not removed by subsequent hydrolysis despite other reactions of the silica.

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