New silica-immobilised chiral aminoalcohol for the enantioselective addition of diethylzinc to benzaldehyde

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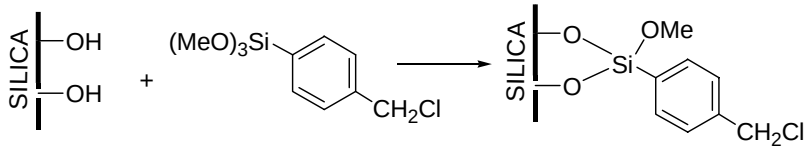
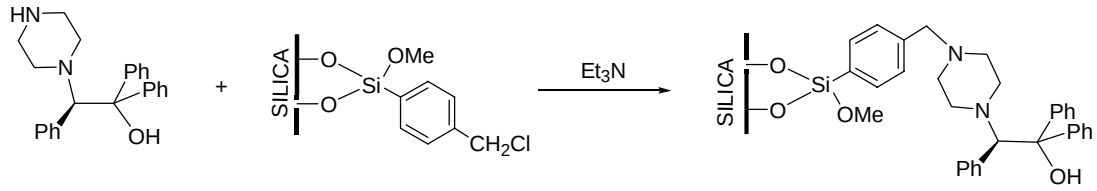


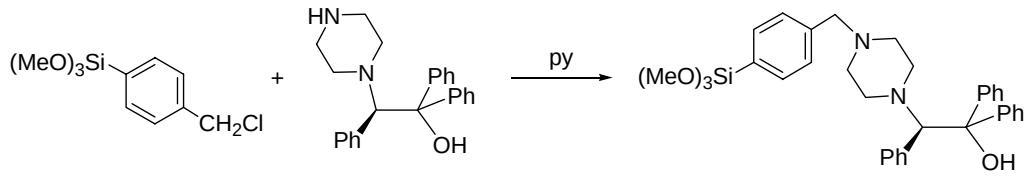
Silica (Merck 60) was dried under vacuum overnight at 140ºC prior to use. *p*-Trimethoxysilylbenzyl chloride (535 mg, 2.17 mmol) was added dropwise on a suspension of silica (2 g) in anhydrous toluene (10 mL) under Ar. The resulting suspension was heated under reflux for 1.5 h and a toluene/methanol mixture (about 2.5 mL) was distilled off. The same volume of toluene was added and the heating and distillation were repeated once. The solid was filtered off, thoroughly washed with anydrous toluene and dried under vacuum at 50ºC overnight. The functionalization of the solid was estimated from the carbon content: 7.07% C, 0.74 mmol of C_8H_9Cl per g silica.

Grafting of (R)-1,1,2-triphenyl-2-(piperazin-1-yl)ethanol



A mixture of chlorobenzylated silica (0.5 g, 0.37 mmol of chlorobenzyl groups), (*R*)-1,1,2-triphenyl-2-(piperazin-1-yl)ethanol (157 mg, 0.44 mmol), triethylamine (44 mg, 0.44 mmol) and anhydrous toluene (7 mL) was heated under reflux for 20 h. After cooling, the solid was filtered off, thoroughly washed with toluene, diethyl ether and methanol, and dried under vacuum at 50ºC overnight. The functionalization of the solid was estimated from the nitrogen content: 16.86% C, 1.36% N, 0.49 mmol of aminoalcohol per g silica.

Synthesis of (R)-1,1,2-triphenyl-2-[4-(p-trimethoxysilylbenzyl)piperazin-1-yl]ethanol



A solution of (*R*)-1,1,2-triphenyl-2-(piperazin-1-yl)ethanol (100 mg, 0.28 mmol) and *p*-trimethoxysilylbenzyl chloride (69 mg, 0.28 mmol) in anhydrous pyridine (3 mL) was stirred at room temperature for 7 days under Ar. Water (4 mL) was added and the solution was extracted with ethyl acetated (3 × 5 mL). The combined organic layers were dried over sodium sulfate and the solvent was eliminated under reduced pressure. (*R*)-1,1,2-triphenyl-2-[4-(p-trimethoxysilylbenzyl)piperazin-1-yl]ethanol was obtained as a yellow oil (87 mg, 0.15 mmol, 55% yield) that was used without further purification. ^{1}H-NMR ($CDCl_3$, 300 MHz, δ/ppm relative to TMS): 7.75 (d, 2H, J = 8.4 Hz), 7.4-7.0 (m, 17H), 5.40 (bs, 1H), 4.66 (s, 1H), 3.54 (s, 9H), 3.44 (s, 2H), 2.5-2.3 (m, 8H).

Sol-gel synthesis

To a solution of dodecylamine (2.03 g, 11mmol) in ethanol (15 mL) and water (21 mL) was added a solution of Si(OEt)4 (7.52 g, 36 mmol) and (*R*)-1,1,2-triphenyl-2-[4-(p-trimethoxysilylbenzyl)piperazin-1-yl]ethanol (74 mg, 0.13 mmol) in ethanol (3 mL). The mixture was vigorously stirred for 24 h. The solid was filtered off, thoroughly washed with ethanol and dried under vacuum at 50ºC overnight. Weight of solid: 1.986 g (90% yield). The functionalization of the solid was estimated from the nitrogen content: 10.39% C, 0.52% N, 0.19 mmol of aminoalcohol per g silica.

End-capping procedure

To a suspension of the solid (1 g) in anhydrous toluene (4 mL) was added hexamethyldisilazane (0.7 mL) and the mixture was heated under reflux for 1 h. After cooling the solid was filtered off, thoroughly washed with toluene, acetone, water, ethanol and acetone, and dried under vacuum at 50ºC overnight.

Addition of diethylzinc to benzaldehyde

To a suspension of the catalyst (required amount for 0.06 mmol aminoalcohol) in anhydrous toluene (3 mL) under Ar at –15ºC, was added freshly distilled benzaldehyde (106 mg, 1 mmol) and the mixture was stirred for 30 min. In the case of reactions promoted by BuLi, the required amount (see Table 2 of the manuscript) was added and then diethylzinc (2.73 mL, 1.1M in toluene, 3 mmol). The mixture was stirred at –15ºC for 24 h. After this time the solution was obtained *via* syringe, the solid in the flask was throughly washed with anhydrous toluene and the combined extraction solutions were treated with saturated NH_4Cl (3 mL). The organic layer was separated and dried over sodium sulfate. The reaction mixture was analyzed by GC: He as carrier gas (20 p.s.i.); injector temperature: 230 °C; FID detector temperature: 250 °C. Cross-linked methyl silicone column (25 m × 0.2 mm × 0.33 μm); oven temperature program: 50ºC (3 min), 25ºC/min, 250ºC (5 min); retention times: benzaldehyde 4.64 min, benzyl alcohol 5.46 min, 1-phenyl-1-propanol 6.52 min. Cyclodex B column (30 m × 0.25 mm × 0.25 μm); oven temperature: 115ºC (isotherm); retention times: (*R*)-1-phenyl-1-propanol 15.93 min, (*S*)-1-phenyl-1-propanol 16.85 min.