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Regioselective Hydroaminomethylation of Vinylarenes by a Sol–Gel Immobilized Rhodium Catalyst

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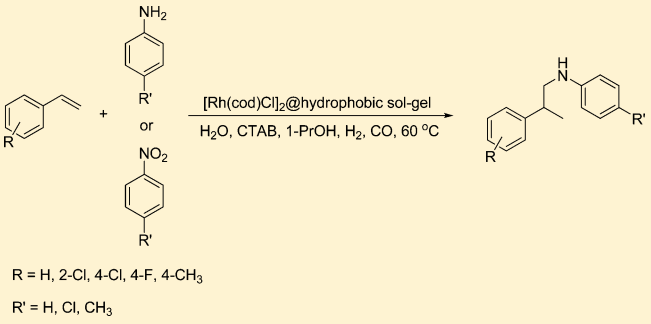
Supporting Information

ABSTRACT: In the course of our studies toward the development of new heterogeneous conditions for better controlling regioselectivity in organic reactions, we investigated the application of sol–gel immobilized organometallic catalyst for regioselective hydroaminomethylation of vinylarenes with aniline or nitroarene derivatives in an aqueous microemulsion. By immobilization of 6 mol % $[Rh(cod)Cl]_2$ within a hydrophobic silica sol–gel matrix we were able to perform efficient hydroaminomethylation under mild conditions and isolate 2-arylpropylamines with high regioselectivity. The regioselectivity of the reaction was found to be mainly dependent on the hydrophobicity of the catalyst support. It is also significantly affected by the electronic nature of the substrates, by the reaction temperature, and by syngas pressure. The heterogenized catalyst can be reused for several times.



INTRODUCTION

Hydroaminomethylation of olefins, originally discovered by Reppe and co-workers,[1] has attracted much attention as a versatile tool for the synthesis of amines and has been used in multiple applications in the pharmaceutical and chemical industry. As described, hydroaminomethylation is a one-pot tandem reaction involving hydroformylation of alkene, followed by condensation of the resulting aldehyde with a primary or secondary amine, and hydrogenation of the intermediate imine at the final stage.

From an economical and environmental point of view, one-pot synthesis of amines from alkenes seems to be a superior method over the conventional ones which comprise multistep reactions.[2] Unfortunately, multiple byproducts can be isolated from this reaction. Consequently, many efforts have been directed to improve the selectivity of the reaction. In particular, methods that ensure preferential formation of either linear or branched regioisomers have been targeted.[3] Linear amines are important intermediates and building blocks for pharmaceuticals, agrochemicals, and fine chemicals,[4] while branched amines are known to exhibit pharmacological activity such as antihistaminic and sympathomimetic properties.[5] For example, Eilbracht showed that hydroaminomethylation of styrene produces branched products with good selectivity (branched/linear (b/l) up to 16) simply with $[Rh(cod)Cl]_2$ without any ligand, although it required harsh reaction conditions.[6] Beller and Kostas reported high regioselectivity of hydroaminomethylation of styrenes and linear alkenes with either piperidine or morpholine (the ratio of b/l varies from 4/1 to 6.6/1 for styrenes and up to 99/1 for linear alkenes) under high pressures and temperatures.[7] Zwitterionic rhodium complexes developed by Alper exhibited good selectivities in the hydroaminomethylation of styrenes with primary and secondary amines (b/l up to 15/1) except for aniline (b/l = 1.9/1).[8] Later, Beller and co-workers suggested an improved protocol based on the zwitterionic rhodium complexes that achieved relatively high selectivities toward the synthesis of branched amines (b/l various from 1.4/1 to 99/1) from the hydroaminomethylation of styrenes with various amines under relatively mild conditions.[9]

Previously, we developed a new heterogeneous system for the hydroformylation of vinylarenes using immobilized $[Rh(cod)Cl]_2$ within sol–gel matrices which provided high regioselectivities toward branched aldehydes.[10] This heterogeneous system was based on combining ceramic sol–gel materials and aqueous emulsion/microemulsion systems (EST) and has been proven to be applicable in a wide variety of organic reactions.[11,12] The easily recyclable ceramic support also has the ability to perform one-pot multistep reactions in conventional organic solvents.[13] Reports on the use of microemulsions with organometallic catalysts for the hydroaminomethylation of olefins have, so far, been scarce.[14]

In this contribution we describe the application of a new heterogeneous system based on $[Rh(cod)Cl]_2$ immobilized within a sol–gel matrix as a highly efficient, regioselective, and recyclable catalyst for the hydroaminomethylation reaction of vinylarenes with aniline derivatives under mild conditions. Remarkably, we demonstrated for the first time, that anilines

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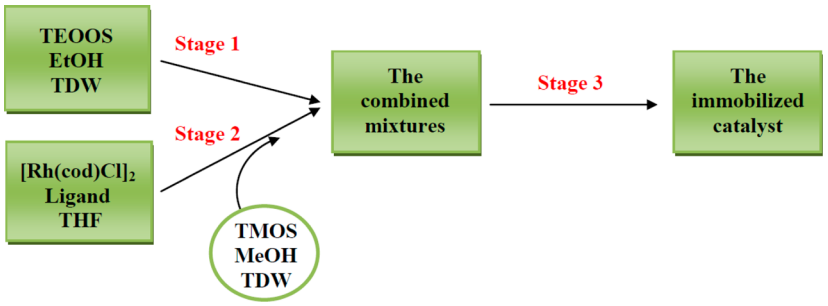
Scheme 1. Preparation of $[Rh(cod)Cl]_2$ Immobilized within Octylated Silica Sol–Gel Matrix[a]



[a]**Stage 1:** a solution of TEOOS, TDW, and EtOH was stirred for 24 h. **Stage 2:** to a solution of $[Rh(cod)Cl]_2$, 2-(diphenylphosphino)-ethyltriethoxysilane in THF were added TMOS, MeOH, and TDW. Then, the two mixtures were combined and stirring was continued for 48 h until the gelation was complete. **Stage 3:** The resulting gel was aged for two days at 40 °C; dried at 80 °C and 0.1 Torr for 12 h. Then, it was washed with CH_2Cl_2 and dried at 80 °C and 0.1 Torr to give a constant weight.

Table 1. Hydroaminomethylation of Styrene with Aniline by $[Rh(cod)Cl]_2$ Immobilized within Differently Hydrophobicized Sol–Gel in an Aqueous Medium[a]

entry	hydrophobic moiety	hydrophobicity (%)	yield (%) of ethylbenzene[b]	yield (%) of branched (*b*) amine[b]	yield (%) of linear (*l*) amine[b]	ratio (*b*:*l*)
1[c,d]	none	–	–	76	19	4:1
2	ethyl	20	3	78	19	4:1
3	propyl	10	–	83	17	5:1
4	propyl	20	2	91	7	13:1
5	propyl	30	4	89	7	13:1
6	octyl	20	2	95	3	32:1
7	phenyl	20	5	69	26	3:1

[a]Reaction conditions: vinylarene (1.0 mmol, 0.8 wt % of the microemulsion), aniline (1.1 mmol), cetyltrimethylammonium bromide (CTAB, 3.3 wt %), *n*-propanol (PrOH, 6.6 wt %), triply distilled water (TDW, 89.3 wt %) together with heterogenized rhodium catalyst prepared from $[Rh(cod)Cl]_2$ (30 mg, 0.06 mmol, 6 mol %), 2-(diphenylphosphino)ethyltriethoxysilane (45 mg, 0.12 mmol), TEOOS (or the corresponding ethyl, propyl, or trimethoxy(phenyl)silane) (2.1 mL, 6.68 mmol, for 20% hydrophobicity) and TMOS (3.6 mL, 24.2 mmol); H_2 (200 psi), CO (100 psi); stirring rate 300 rpm; 60 °C, 12 h. [b]The percentages were determined both by GC and by ^1H NMR, and are the average of at least two experiments that did not differ by more than ±3%. [c]$[Rh(cod)Cl]_2$ immobilized within TMOS (3.6 mL, 24.2 mmol). [d]95% conversion.

can be prepared in situ from the corresponding nitroarenes in one pot over the course of the hydroaminomethylation.

RESULTS AND DISCUSSION

Although styrenes do not undergo hydroaminomethylation with anilines in pure water at 60 °C by means of the heterogenized $[Rh(cod)Cl]_2$ catalyst system, the reaction takes place upon the addition of a suitable surfactant that solubilizes the substrate. Heterogenization of the catalyst by its immobilization within a hydrophobic silica sol–gel matrix results in the formation of the corresponding branched 2-arylpropylamines in a highly regioselective fashion under mild conditions.

From our previous studies, we know that hydrophobicity of silica sol–gel matrices can affect the efficiency and the regioselectivity of chemical reactions.[10] Therefore, we investigated the influences of the hydrophobicity of the ceramic support on the hydroaminomethylation process. Thus, $[Rh(cod)Cl]_2$-containing ceramic supports modified with ethyl, propyl, octyl, or phenyl residues have been prepared by copolymerization of triethoxy(ethyl)silane, trimethoxy(propyl)-silane, triethoxy(octyl)silane (TEOOS), or trimethoxy-(phenyl)silane with tetramethyl orthosilicate (TMOS) (Scheme 1). Leaching of the rhodium catalyst from the modified matrices was studied by ICP analyses which indicated that the immobilization of the rhodium complex within silica sol–gel containing 2-(diphenylphosphino)ethyltriethoxysilane is not leachable (0.012–0.063% of rhodium per catalytic cycle). Any system in which the leaching per catalytic run exceeded 0.063% was discarded.

Optimization studies revolving around hydroaminomethylation of styrene with aniline using the aforementioned supports are summarized in Table 1. The results clearly indicate that the catalyst with the highest degree of hydrophobicity (e.g., octylated sol–gel prepared from 80 mol % of TMOS and 20 mol % of TEOOS) exhibits the highest selectivity (entry 6, Table 1). The blank hydrophilic matrix (prepared from TMOS with no alkylated comonomer), as well as matrices possessing shorter alkyl chains, results in significantly lower selectivity (entries 1, 2, 4 and 7, Table 1). The regioselectivity of the hydroaminomethylation was shown to be also influenced by the amount of the hydrophobic comonomer. For example, introducing a high amount of propyl moiety to silica sol–gel leads to a higher regioselectivity (entry 3 vs entry 4, Table 1). However, no change on the regioselectivity was obtained when higher amounts of the propyl moiety were introduced (entry 4 vs entry 5, Table 1). It should be mentioned that all the control experiments, which have been performed under the same conditions listed in Table 1, showed that hydroaminomethylation takes place only in the presence of the sol–gel immobilized $[Rh(cod)Cl]_2$ coordinated to 2-(diphenylphosphino)ethyltriethoxysilane. For example, hydroaminomethylation of styrene with aniline in the presence of 20 mol % of octylated sol–gel bearing physically immobilized $[Rh(cod)Cl]_2$ gave only the hydrogenated ethylbenzene. Also, as anticipated, no reaction was obtained when we used the 20

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mol % octylated sol−gel immobilized 2-(diphenylphosphino)-ethyltriethoxysilane with no Rh precursor. Therefore, the coordination of $[Rh(cod)Cl]_2$ to the covalently bound 2-(diphenylphosphino)ethyltriethoxysilane as a ligand is obligatory for the efficient hydroaminomethylation reaction. Furthermore, by comparing the selectivities obtained from the nonhydrophobicized catalyst support with sol−gel contained micelles formed from long-chain alkyl-substituted silica precursors (entries 1 and 6, Table 1),[15] we can unequivocally conclude that the regioselectivity of the hydroaminomethylation originates from the hydrophobic nature of the sol−gel matrix but not from the organometallic complex itself. On the basis of the results of the optimization studies, we chose 20% octylated silica sol−gel-based catalyst to study the scope and limitation of the new method. Further experiments were also conducted with different loadings of the rhodium catalyst. We found that 6 mol % of $[Rh(cod)Cl]_2$ provided efficient hydroaminomethylation reaction. With a low-loading catalyst, e.g. 3 mol % $[Rh(cod)Cl]_2$, arylpropanals were isolated.

Further experimentation with the new catalyst showed that selectivity can be even improved by lowering reaction temperature (Table 2). For example, in a series of experiments

Table 2. Dependence of the Yield and of the Regioselectivity of the Hydroaminomethylation of Styrene with Aniline on the Reaction Temperature[a]

entry	temperature °C	yield (%) of branched (*b*) amine[b,c]	yield (%) of linear (*l*) amine[b,c]	ratio (*b*:*l*)
1	60	95	3	32:1
2[d]	80	82	16	5:1
3[d]	90	81	17	5:1

[a]Reaction conditions as given in Table 1 except for the temperature. [b]The data are averages of at least two experiments that did not differ by more than ±3%. [c]2% of ethylbenzene was detected. [d]Full conversion was obtained after 5 h.

at different temperatures (60−90 °C), we found dramatic changes in the *b*/*l* ratio and showed that, although at low temperatures the hydroaminomethylation is slower, selectivity is the highest (*b*/*l* = 32/1).

Another factor that influences the hydroaminomethylation of vinylarenes is the total and partial H_2 and CO pressure. The influence derived from hydroaminomethylation of styrene with aniline at 60 °C is shown in Table 3. The trend shows that the higher the pressures of CO in the syngas mixture, the lower

Table 3. Effect of the Relative H_2 and CO Pressure in the Hydroaminomethylation of Styrene with Aniline on the Regioselectivity and the Yield of the Products[a]

entry	H_2:CO (psi)	yield (%) of branched (*b*) amine[b]	yield (%) of linear (*l*) amine[b]	ratio (*b*:*l*)
1[c]	100:100	93	5	19:1
2[c]	200:100	95	3	32:1
3[c]	300:100	94	4	24:1
4[d]	100:300	77	20	4:1
5[e]	300:300	68	16	4:1

[a]Reaction conditions as given in Table 1 except for the pressures. [b]The data are averages of at least two experiments that did not differ by more than ±3%. [c]2% of ethylbenzene was detected. [d]3% of ethylbenzene was detected. [e]3% of ethylbenzene, 2% of 2-phenylpropanal, and 11% of 3-phenylpropanal were detected.

regioselectivity toward the branched amine product (entries 4 and 5). The results also indicate that optimal regioselectivity can be obtained by 2:1 H_2/CO syngas mixture (entry 2). However, lower activity and *b*/*l* ratio were obtained by raising the total pressure (e.g., entry 2 vs entry 5). Nevertheless, by increasing the H_2 pressure, the regioselectivity was hardly affected (entry 3).

Under these optimized reaction conditions we carried out the scope and limitation studies. Some typical examples of regioselective hydroaminomethylation of some vinylarenes with aniline by $[Rh(cod)Cl]_2$ immobilized within octylated sol−gel at 60 °C are summarized in Table 4. The electronic nature of the substrates has no significant effect on the reaction rate. However, a dramatic influence on the regioselectivity was observed when electron-withdrawing or -donating groups were introduced. For example, high selectivity was obtained in the hydroaminomethylation of 4-chlorostyrene (*b*/*l* = 46/1) compared to 4-methylsytene (*b*/*l* = 15/1) (entries 1, 4, and 5). Ortho-substituted substrates can also affect the regioselectivity of the reaction due to steric hindrance. Thus, 2-chlorostyrene gave lower selectivity compared to the para-substituted substrate (compare entries 3 and 4). Nevertheless, in all of the cases, including the ortho-substituted substrates summarized in Table 4, higher regioselectivity was obtained compared to those of the existing protocols.[6,8,9] Different kinds of substrates were also examined, such as heterocyclic compounds, yet no satisfying regioselectivity was obtained.

Reduction of nitroarene derivatives to aniline is known to take place under rhodium catalysis. It was thus fascinating to test nitroarenes as "masked" anilines in the hydroaminomethylation of vinylarenes. To the best of our knowledge, the use of nitro compounds as amine precursors has never been reported in this reaction. To our delight, essentially identical efficiencies and selectivities were obtained by the employment of nitrobenzene, 1-chloro-4-nitrobenzene, and 1-methyl-4-nitrobenzene instead of their corresponding amines in the hydroaminomethylation of 4-chlorostyrene (Table 5). For example, introducing nitrobenzene in the hydroaminomethylation of 4-chlorostyrene led to approximately the same selectivity ratio obtained when aniline was used (compare entries 1 and 4). In some cases an increase in the regioselectivity was obtained by the introduction of nitro compounds instead of amine-based compounds (compare entries 3 and 6).

The recycling of the catalyst was also investigated. $[Rh(cod)Cl]_2$ immobilized within octylated silica sol−gel can be recycled only at 90 °C for at least 4 times. However, a drop in the regioselectivity was obtained during the third run, apparently, due to the enlargement of the sol−gel pores caused by hydrolysis of some Si−O bonds in the aqueous medium (Table 6). After the fourth run we were able to isolate only small amounts of phenylpropanals indicating diminished activity of the catalyst (entries 4 and 5). We assume that this decrease in activity is associated with some morphological changes in the sol−gel matrix (Si−O bond breaking) that takes place in water.[10,12a,d] Recycling of the immobilized catalyst at lower temperatures was less efficient. By recording the infrared spectra of the used immobilized catalyst, metal−carbonyl peaks were detected (1994 and 2067 cm^{-1} on KBr mulls) which may cause the drop in the catalyst activity at lower temperatures after the first catalytic run.

Finally, it is notable that although many organometallic catalysts are converted in the presence of dihydrogen or

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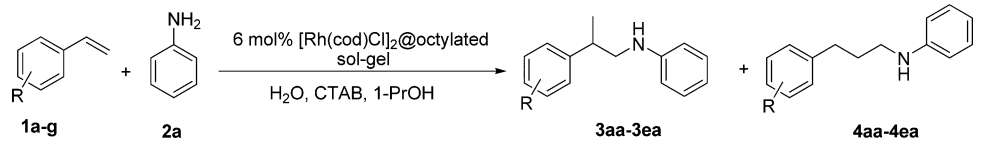
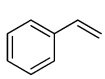
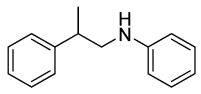
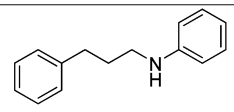
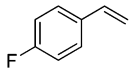
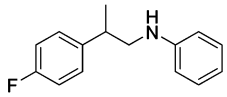
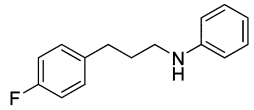
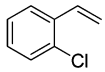
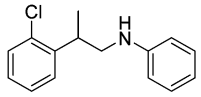
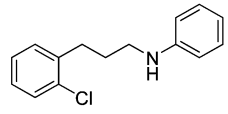
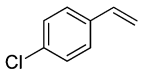
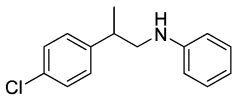
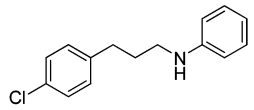
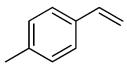
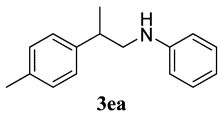
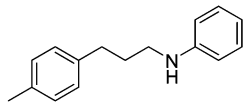
Table 4. Hydroaminomethylation of Vinylarenes with Aniline by Heterogenized $[Rh(cod)Cl]_2$ in an Aqueous Medium[a]



entry	vinylarenes	branched (*b*) product	yield of *b* (%)[b,c]	linear (*l*) product	yield of *l* (%)[b,c]	ratio (*b*:*l*)
1	 **1a**	 **3aa**	95	 **4aa**	3	32:1
2	 **1b**	 **3ba**	88	 **4ba**	5	18:1
3[d]	 **1c**	 **3ca**	78	 **4ca**	8	10:1
4	 **1d**	 **3da**	91	 **4da**	2	46:1
5	 **1e**	 **3ea**	87	 **4ea**	6	15:1

[a]Reaction conditions as given in Table 1. [b]The percentages were determined both by GC and by ^{1}H NMR, and are the average of at least two experiments that did not differ by more than ±3%. [c]Small amounts of ethylbenzene derivatives (2%) and acetophenone derivatives (5%) were detected; except for entry 1, only 2% of ethylbenzene was detected. [d]9% of 1-chloro-2-ethylbenzene and 5% of 2′-chloroacetophenoene were detected.

hydrogen donors into metallic nanoparticles particularly when an aqueous medium is employed,[12a,b,e] we were unable to detect Rh(0) species following the hydroaminomethylation processes by TEM-EDAX-EDS analyses (Figure 1).

■ CONCLUSION

Hydroaminomethylation of vinylarenes with aniline derivatives in a highly regioselective manner can be performed at 60 °C in the presence of $[Rh(cod)Cl]_2$ immobilized within hydrophobic silica sol–gel in aqueous microemulsions. We were able to demonstrate for the first time the use of nitroarenes as "masked" anilines in the described reaction. The efficiency and selectivity of hydroaminomethylation depend on the hydrophobic moiety of the sol–gel matrix, the reaction temperature, the H_2/CO ratio, and the electronic nature of the substrates.

■ EXPERIMENTAL SECTION

General. All reagents and solvents of commercial grade were used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded as $CDCl_3$ solutions on a 400 MHz NMR instrument. Infrared spectra were recorded on NaCl plates. Gas chromatography analyses were carried with either a 30 m long column packed with 20 M poly(ethylene glycol) in fused silica or with a 15 m long column packed with bonded cross-linked (5% phenyl) methyl polysiloxane [HP-5]. Exact mass was measured with Q-TOF LC/MS. Transmission electron microscopy was performed via scanning transmission electron microscope (STEM) operated at 200 kV and equipped with EDAX-EDS for identification of elemental compositions.

Preparation of Hydrophilic Immobilized Catalyst. Immobilization of $[Rh(cod)Cl]_2$ within hydrophilic silica sol–gel was carried out as follows. To a solution of $[Rh(cod)Cl]_2$ (30 mg, 0.06 mmol, 6 mol %), 2-(diphenylphosphino)ethyltriethoxysilane (45 mg, 0.12 mmol) in THF (2 mL) were added TMOS (3.6 mL, 24.4 mmol), MeOH (2.0 mL), and TDW (2.4 mL). Stirring was continued as long as possible (24 h), and the resulting gel was aged for two days at 40 °C, dried at 80 °C and 0.1 Torr for 12 h. The ceramic material was washed with boiling CH_2Cl_2 (2 × 15 mL) to ensure the removal of any metallic compound that was not immobilized within the sol–gel matrix, and dried again at 80 °C and 0.1 Torr to constant weight.

Preparation of Hydrophobic Immobilized Catalyst. Immobilization of $[Rh(cod)Cl]_2$ within octylated silica sol–gel was carried out as follows. To a solution of TEOOS (2.1 mL, 6.68 mmol) (alternatively, corresponding triethoxy(ethyl)silane, trimethoxy(propyl)silane or trimethoxy(phenyl)silane), TDW (0.38 mL) and EtOH (5.6 mL) was stirred for 24 h. Then, to a solution of $[Rh(cod)Cl]_2$ (30 mg, 0.06 mmol, 6 mol %), 2-(diphenylphosphino)-ethyltriethoxysilane (45 mg, 0.12 mmol) in THF (2 mL) were added TMOS (3.6 mL, 24.4 mmol), MeOH (2.0 mL) and TDW (2.4 mL). The two mixtures were combined and stirring was continued for 48–96 h until the gelation was complete. The resulting gel was aged for two days at 40 °C, dried at 80 °C and 0.1 Torr for 12 h. The ceramic

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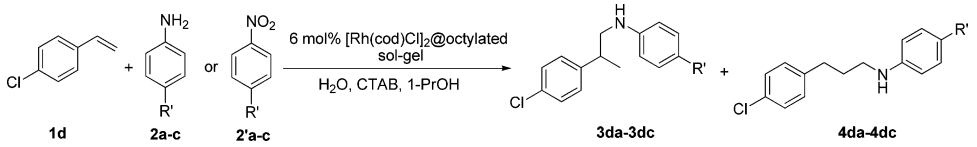
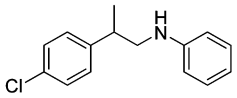
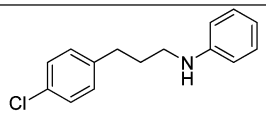
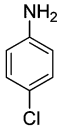
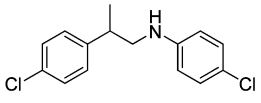
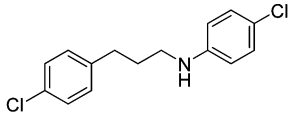
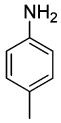
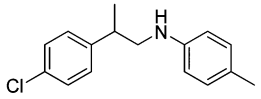
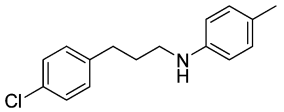
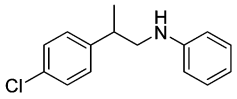
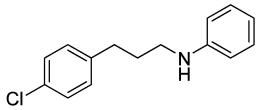
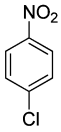
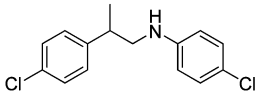
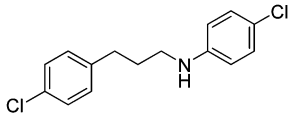
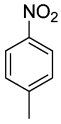
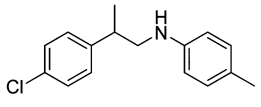
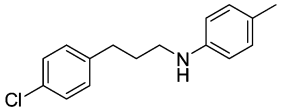
Table 5. Hydroaminomethylation of 4-Chlorostyrene with Aniline and Nitroarene Derivatives by Heterogenized $[Rh(cod)Cl]_2$ in an Aqueous Medium[a]



entry	amine	branched (*b*) product	yield of *b* (%)[b]	linear (*l*) product	yield of *l* (%)[b]	ratio (*b*:*l*)
1[c]	 **2a**	 **3da**	91	 **4da**	2	46:1
2[d]	 **2b**	 **3db**	79	 **4db**	10	8:1
3[e]	 **2c**	 **3dc**	80	 **4dc**	10	8:1
4[f]	 **2'a**	 **3da**	90	 **4da**	2	45:1
5[d]	 **2'b**	 **3db**	78	 **4db**	11	7:1
6[e]	 **2'c**	 **3dc**	82	 **4dc**	8	10:1

[a]Reaction conditions as given in Table 1, except for entries 4, 5 and 6, the reaction was performed at 70 °C. [b]The data are the average of at least two experiments that did not differ by more than ±3%. [c]2% of 1-chloro-4-ethylbenzene and 5% of 4′-chloroacetophenone were detected. [d]5% of 1-chloro-4-ethylbenzene and 6% of 4′-chloroacetophenone were detected. [e]5% of 1-chloro-4-ethylbenzene and 5% of 4′-chloroacetophenone were detected. [f]4% of 1-chloro-4-ethylbenzene and 4% of 4′-chloroacetophenone were detected.

material was washed with boiling CH_2Cl_2 (2 × 15 mL) to ensure the removal of any metallic compound that was not immobilized within the sol–gel matrix, and dried again at 80 °C and 0.1 Torr to give a constant weight.

Emulsification of the Substrates. A mixture of the vinylarene (1 mmol, 0.8 wt.% of the desired microemulsion), aniline derivative (1.1 mmol), TDW (89.3 wt.%), CTAB (3.3 wt.%), cosurfactant (PrOH, 6.6 wt.%) and 5–7 mg of 2,5-di-*tert*-butyl hydroquinone was agitated at room temperature. The mixture was then degassed by bubbling Ar through it for 20 min and mixed with the heterogenized catalyst.

Emulsification of 4-Chlorostyrene and *p*-Toluidine or 4-Chloroaniline. A mixture of the 4-chlorostyrene (0.138 g, 1 mmol, 0.8 wt.% of the desired microemulsion), either *p*-toluidine (0.12 g, 1.1 mmol) or 4-chloroaniline (0.14 g, 1.1 mmol), TDW (15.4 mL, 89.3 wt.%), CTAB (0.56 g, 3.3 wt.%), PrOH (1.4 mL, 6.6 wt.%) and 5–7 mg of 2,5-di-*tert*-butyl hydroquinone was agitated at 50 °C. The mixture was then degassed by bubbling Ar through it for 20 min and mixed with the heterogenized catalyst.

Emulsification of 4-Chlorostyrene and Nitrobenzene. A mixture of the 4-chlorostyrene (0.138 g, 1 mmol, 0.8 wt.% of the desired microemulsion), nitrobenzene (0.135 g, 1.1 mmol), TDW (15.4 mL, 89.3 wt.%), CTAB (0.56 g, 3.3 wt.%), PrOH (1.4 mL, 6.6 wt.%) and 5–7 mg of 2,5-di-*tert*-butyl hydroquinone was agitated at room temperature. The mixture was then degassed by bubbling Ar through it for 20 min and mixed with the heterogenized catalyst.

Emulsification of 4-Chlorostyrene and 1-Methyl-4-nitrobenzene or 1-Chloro-4-nitrobenzene. A mixture of the 4-chlorostyrene (0.138 g, 1 mmol, 0.8 wt.% of the desired microemulsion), either 1-methyl-4-nitrobenzene (0.15 g, 1.1 mmol) or 1-chloro-4-nitrobenzene (0.172 g, 1.1 mmol), TDW (15.4 mL, 89.3 wt.%), CTAB (0.56 g, 3.3 wt.%), PrOH (1.4 mL, 6.6 wt.%) and 5–7 mg of 2,5-di-*tert*-butyl hydroquinone was agitated at 70 °C. The mixture

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Table 6. Effect of Catalyst Recycling in the Hydroaminomethylation of Styrene on the Yield and on the Regioselectivity in an Aqueous Medium[a]

run no.	conversion (%)	yield of ethylbenzene(%)[b]	yield of bbranched (*b*) amine (%)[b]	yield of linear (*l*) amine (%)[b]	ratio (*b*:*l*)
1	100	2	81	17	5:1
2	100	2	80	16	4:1
3	100	3	63	34	2:1
4[c]	98	4	31	48	1:2
5[d]	88	4	24	44	1:2

[a]Reaction conditions as given in Table 1 except the hydroaminomethylation was performed at 90 °C. [b]The data are the average of at least two experiments that did not differ by more than ±3%. [c]8% of 2-phenylpropanal and 7% of 3-phenylpropanal was detected. [d]11% of 2-phenylpropanal and 5% of 3-phenylpropanal was detected.

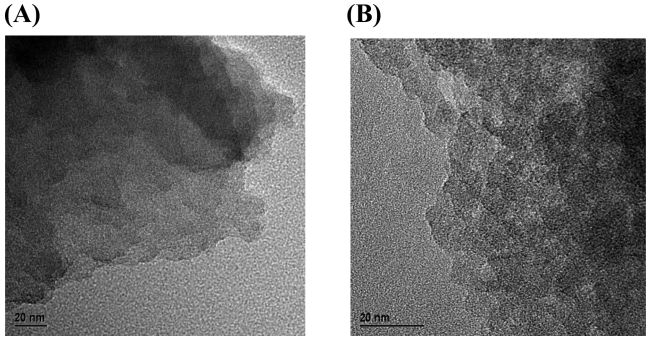

Figure 1. TEM micrograph of a typical 20% octylated silica sol–gel support immobilized Rh complex (A) before and (B) after the hydroaminomethylation reaction of styrene and aniline at the same conditions listed in Table 1

was then degassed by bubbling Ar through it for 20 min and mixed with the heterogenized catalyst.

General Procedure for Catalytic Hydroaminomethylation. The emulsion or microemulsion containing the substrate (usually 15–20 mL) was placed in a glass-lined Parr bomb equipped with a mechanical stirrer, together with the immobilized rhodium catalyst. The autoclave was sealed and purged three times with hydrogen and then pressurized to the desired pressure of H_2 and CO. The reaction mixture was kept at the desired temperature for the required period of time. The reaction vessel was cooled to room temperature, the gases were released and the remaining mixture was filtered. The filtrate was treated with NaCl (1 g), which caused the mixture to separate into two phases. The sol–gel material, as well as the aqueous layer, were extracted with CH_2Cl_2 (2 × 10 mL) to ensure complete removal of the products. The combined organic solutions were dried ($MgSO_4$), filtrated over silica column, concentrated and analyzed by GC, ^{1}H NMR and ^{13}C NMR. The heterogenized catalyst was dried at 80 °C and 0.1 Torr for 5 h in order to be ready for use in the next run.

***β*-Methyl-*N*-phenylbenzene Ethanamine (3aa):**[9] yield 95% (0.200 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 2H), 7.23 (m, 3H), 7.15 (t, J = 7.8 Hz, 2H), 6.68 (t, J = 7.3 Hz, 1H), 6.56 (dd, J = 0.9, 8.6 Hz, 2H), 3.56 (br s, 1H), 3.34 (m, 1H), 3.22 (m, 1H), 3.05 (sextet, J = 7.1 Hz, 1H), 1.33 (d, J = 7.0 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 148.1, 144.5, 129.2, 128.6, 127.2, 126.6, 117.3, 112.9, 50.9, 39.2, 19.7; IR (NaCl, chloroform, ν_{max}, cm^{-1}): 3422, 3009, 2967, 1599, 1501, 1311, 1244, 760, 682.

4-Fluoro-*β*-methyl-*N*-phenylbenzene Ethanamine (3ba): yield 88% (0.201 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (m, 4H), 7.00 (t, J = 8.8 Hz, 2H), 6.68 (dt, J = 1.1, 7.3 Hz, 1H), 6.55 (dd, J = 1.1, 7.9 Hz, 2H), 3.53 (br s, 1H), 3.32 (m, 1H), 3.19 (m, 1H), 3.02 (sextet, J = 7.2 Hz, 1H), 1.30 (d, J = 6.9 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 161.5 (d, J = 244.2 Hz), 147.9, 140.1 (d, J = 3.2 Hz), 129.2, 128.6 (d, J = 7.8 Hz), 117.4, 115.4 (d, J = 21.1 Hz), 112.9, 50.9 (d, J = 0.8 Hz), 38.5 (d, J = 0.5 Hz), 19.8 (d, J = 0.7 Hz); IR (NaCl, chloroform, ν_{max}, cm^{-1}): 3409, 2963, 2932, 2870, 1601, 1505, 1319, 1256, 1223, 1096, 832; HRMS (ESI) calcd for $C_{15}H_{17}FN$, $(M + H)^+$ 230.1345, found 230.1344.

2-Chloro-*β*-methyl-*N*-phenyl-benzene Ethanamine (3ca): yield 78% (0.191 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, J = 0.3, 1.3 Hz, 1H), 7.26 (m, 2H), 7.15 (m, 3H), 6.68 (tt, J = 1.0, 7.3 Hz, 1H), 6.60 (dd, J = 1.0, 8.6 Hz, 2H), 3.64 (br sextet, J = 7.0 Hz, 2H), 3.37 (m, 1H), 3.26 (m, 1H), 2.22 (s, 3H), 1.33 (d, J = 6.9 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 148.1, 141.7, 134.1, 129.7, 129.2, 127.6, 127.3, 127.2, 117.3, 112.8, 49.7, 35.3, 18.7; IR (NaCl, chloroform, ν_{max}, cm^{-1}): 3398, 2929, 2868, 1600, 1502, 1444, 1254, 1096, 1022, 840, 669; HRMS (ESI) calcd for $C_{15}H_{17}ClN$, $(M + H)^+$ 246.1049, found 246.1045.

4-Chloro-*β*-methyl-*N*-phenylbenzene Ethanamine (3da).[9] Reaction with aniline or nitrobenzene afforded yields of 91% (0.223 g) and 90% (0.221 g), respectively; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.5 Hz, 2H), 7.15 (m, 4H), 6.69 (tt, J = 1.0, 7.3 Hz, 1H), 6.56 (dd, J = 1.0, 8.7 Hz, 2H), 3.53 (br s, 1H), 3.33 (m, 1H), 3.19 (m, 1H), 3.04 (sextet, J = 7.1 Hz, 1H), 1.31 (d, J = 6.9 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 147.9, 143.0, 132.2, 129.2, 128.7, 128.6, 117.5, 112.9, 50.8, 38.6, 19.6; IR (NaCl, chloroform, ν_{max}, cm^{-1}): 3417, 2964, 1603, 1505, 1320, 1256, 1218, 1094, 1013, 828, 772, 746, 693.

***β*-Methyl-*N*-phenylbenzene Ethanamine (3ea):**[16] yield 87% (0.196 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (m, 6H), 6.67 (t, J = 7.3 Hz, 1H), 6.56 (d, J = 8.7 Hz, 3H), 3.56 (br s, 1H), 3.31 (m, 1H), 3.19 (m, 1H), 3.01 (sextet, J = 7.1 Hz, 1H), 2.33 (s, 3H), 1.31 (d, J = 7.0 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 148.1, 141.4, 129.3, 129.2, 127.1, 117.2, 112.9, 50.8, 38.7, 21.0, 19.8; IR (NaCl, chloroform, ν_{max}, cm^{-1}): 3419, 2963, 2950, 1603, 1505, 1320, 1220, 818, 639.

4-Chloro-*N*-(2-(4-chlorophenyl)propyl)aniline (3db). Reaction with 4-chloroaniline or 1-chloro-4-nitrobenzene afforded yields of 79% (0.221 g) and 78% (0.218 g), respectively; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.9 Hz, 2H), 6.46 (d, J = 8.9 Hz, 2H), 3.53 (br s, 1H), 3.29 (m, 1H), 3.16 (m, 1H), 3.01 (sextet, J = 7.1 Hz, 1H), 1.30 (d, J = 6.9 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 145.6, 143.1, 132.2, 129.7, 128.7, 128.6, 126.7, 113.1, 51.2, 38.6, 20.3, 19.6; IR (NaCl, chloroform, ν_{max}, cm^{-1}): 3415, 2964, 2874, 1598, 1499, 1247, 1092, 1010, 818, 690, 543; HRMS (ESI) calcd for $C_{15}H_{16}Cl_2N$, $(M + H)^+$ 280.0659, found 280.0655.

4-Chloro-*N*-(3-(4-chlorophenyl)propyl)aniline (4db). Reaction with 4-chloroaniline or 1-chloro-4-nitrobenzene afforded yields of 10% (0.028 g) and 11% (0.030 g), respectively; mp = 89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (m, 2H), 7.10 (m, 4H), 6.48 (d, J = 8.9 Hz, 2H), 3.60 (br s, 1H), 3.09 (t, J = 7.0 Hz, 2H), 3.17 (t, J = 7.6 Hz, 2H), 1.90 (pentet, J = 7.4 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 146.7, 139.8, 131.7, 129.7, 129.1, 128.5, 121.8, 113.7, 43.3, 32.6, 30.8; IR (NaCl, chloroform, ν_{max}, cm^{-1}): 3335, 2927, 2868, 1601, 1490, 1448, 1365, 1251, 1094, 1018, 830, 690; HRMS (ESI) calcd for $C_{15}H_{16}Cl_2N$, $(M + H)^+$ 280.0659, found 280.0653.

***N*-(2-(4-Chlorophenyl)propyl)-4-methylaniline (3dc).** Reaction with *p*-toluidine or 1-methyl-4-nitrobenzene afforded yields of 80% (0.207 g) and 82% (0.213 g), respectively; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 8.3 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H), 6.97 (d, J = 8.5 Hz, 2H), 6.49 (d, J = 8.5 Hz, 2H), 3.41 (br s, 1H), 3.30 (m, 1H), 3.17 (m, 1H), 3.03 (sextet, J = 7.2 Hz, 1H), 2.22 (s, 3H), 1.30 (d, J = 6.8 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 145.6, 143.1, 132.2, 129.7, 128.7, 128.6, 126.7, 113.1, 51.2, 38.6, 20.3, 19.6; IR (NaCl, chloroform, ν_{max}, cm^{-1}): 3411, 2929, 2870, 1615, 1519, 1489, 1370, 1094, 1011, 827; HRMS (ESI) calcd for $C_{16}H_{19}ClN$, $(M + H)^+$ 260.1206, found 260.1201.

***N*-(3-(4-Chlorophenyl)propyl)-4-methylaniline (4dc).** Reaction with *p*-toluidine or 1-methyl-4-nitrobenzene afforded yields of 10% (0.025 g) and 8% (0.020 g), respectively; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 8.5 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 6.53 (d, J = 8.4 Hz, 2H), 3.54 (br s, 1H), 3.13 (t, J = 7.0 Hz, 2H), 3.17 (t, J = 7.6 Hz, 2H), 1.93 (pentet, J = 7.5 Hz, 2H); ^{13}C

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NMR (400 MHz, $CDCl_3$) δ 145.6, 140.1, 131.6, 129.7, 128.5, 126.6, 113.0, 43.6, 32.7, 31.0, 20.3; IR (NaCl, chloroform, ν_{max}, cm^{-1}): 3358, 2930, 2872, 1605, 1499, 1436, 1250, 1022, 830; HRMS (ESI) calcd for $C_{16}H_{19}ClN$, $(M + H)^+$ 260.1206, found 260.1197.

■ ASSOCIATED CONTENT

Supporting Information

^1H NMR and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org

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Notes

The authors declare no competing financial interest.

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