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One-Pot Reactions with Opposing Reagents: Sol−Gel Entrapped Catalyst and Base

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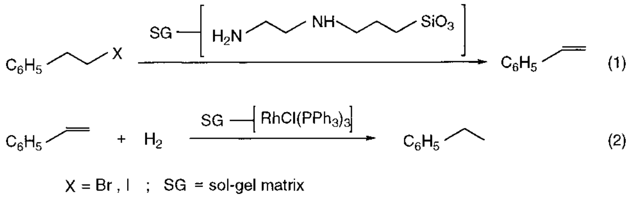
Standard multistep synthetic procedures utilizing reagents, which are destructive to each other, require consecutive product separation and isolation. Configurations which offer total avoidance of contact of reactants by placing them in different locations in the reacting vessel must be practiced in such cases, as, e.g., in electrochemical cells which require separation of the mutually annihilating redox reagents. The potential ability to carry out simultaneously in one-pot reactions with hostile reagents is therefore of great practical use. Here we offer a methodology designed to solve this inherent problem in chemical synthesis. The key to this has been the utilization of organically doped porous sol−gel oxide matrices, which have the remarkable property of being reactive practically only in their inner, diffusionally dopant-accessible regions, thus protecting the dopant from interferences which cannot penetrate the pores. This is an advantage which does not exist in most other heterogenization methods such as surface derivations of inorganic supports or the use of organic-polymer supports: In these configurations the heterogenized reagents are much more exposed, and can affect each other. Intensive activity in the field of reactive doped sol−gel materials demonstrated the generality of this heterogenization methodology, which by now has covered practically all major types of chemical reactions. These include catalysis, redox, acid/base, and complexation reactions, carried out either thermally, photochemically, electrochemically, or biochemically.[1] When it comes to multiple reagent reactions, the approach has been to isolate within the *same* matrix the various reactive species.[2] Also relevant in this context is the elegant work of Soumillion et al.,[3] who demonstrated chemical communication between derivatized silica beads in a photoredox reaction. The application developed here is tailored to the needs of chemical synthesis in the following way: First, having at hand such heterogenized, protected reagents, one has the freedom to create combinations of different reagents as required by the specific synthetic target, allowing these reagents to perform only their useful tasks without affecting each other; and second, as emphasized above, it allows one to simultaneously carry out consecutive synthetic steps.

We have decided to demonstrate this concept in the field of organometallic catalysis because of the known sensitivity of these compounds to be poisoned by various chemical species. The complex $RhCl[P(C_6H_5)_3]_3$ (Wilkinson catalyst), which is a common alkene-hydrogenation catalyst,[4] was taken for this purpose, and its substrate was synthesized with a base from the corresponding halide in the same pot. The catalyst was physically entrapped in an SiO_2 sol−gel matrix (SG-cat) as previously described.[5] The base, $H_2N(CH_2)_2NH(CH_2)_3-$, was covalently heterogenized by copolymerizing the base-$Si(OCH_3)_3$ monomer with $Si(OCH_3)_4$ (SG-base).[6,7] Using (SG-cat) and (SG-base) in one pot as a slurry in benzene at 80 °C, β-iodoethylbenzene was smoothly converted to ethylbenzene (18% after 4 h, 52% after 17 h) according to Scheme 1.[8] In benzene, the bound SG-base and SG-cat do not leach (and indeed the benzene filtrates were not reactive[8]) so that both reactions 1 and 2 are confirmed to be heterogeneous, and to take place simultaneously without interfering with each other. *The catalyst was completely deactivated (either in its homogeneous or immobilized form) in the presence of 2 equiv of the free diamines* $H_2N(CH_2)_2NH_2$ *or* $H_2N(CH_2)_2NH(CH_2)_3Si(OCH_3)_3$.[9]

Scheme 1



X = Br , I ; SG = sol-gel matrix

The rate determining step is the dehydroiodination, as is evident from the fact that styrene is, during the entire process, below the detection limit. Blank experiments confirmed that β-iodoethylbenzene is *not* converted to ethylbenzene by the catalyst in the absence of the base, but that the catalyst is capable of hydrogenating styrene.[9]

Finally, β-bromoethylbenzene could be used similarly in Scheme 1, however, along with competing polymerization of styrene. Polystyrene formation in this case may be attributed to the lower rate of dehydrobromination, compared to the dehy-

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(1) Some recent examples: (a) Fennough, S.; Guyon, S.; Jourdat, C.; Livage, J.; Roux, C. *C. R. Acad. Sci. Paris, t.2. Ser. II* **1999**, 625. (b) Lan, E. H.; Dave, B. C.; Fukuto, J. M.; Dunn, B.; Zink, J. I.; Valentine, J. S. *J. Mater. Chem.* **1999**, *9*, 45. (c) Kanti Das, T.; Khan I.; Rousseau, D. L.; Friedman, J. M. *J. Am. Chem. Soc.* **1998**, *120*, 10268. (d) Chen, Q.; Kenausis, G. L.; Heller, A. *J. Am. Chem. Soc.* **1998**, *120*, 4582. (e) Rao, M. S.; Dave, B. C. *J. Am. Chem. Soc.* **1998**, *120*, 13270. (f) Rottman, C.; Grader, G.; De Hazan, Y.; Melchior, S.; Avnir, D. *J. Am. Chem. Soc.* **1999**, *121*, 8533. (g) Blum, J.; Avnir, D.; Schumann, H. *Chemtech* **1999**, *29*, 32.

(2) (a) Rabinovich, L.; Lev, O.; Tsirlina, G. A. *J. Electroanal. Chem.* **1999**, *466*, 45. (b) Gill, I.; Pastor, E.; Ballesteros, A. *J. Am. Chem. Soc.* **1999**, *121*, 9487. (c) Slama-Schwok, A.; Ottolenghi, M.; Avnir, D. *Nature* **1992**, *355*, 240.

(3) Ayadim, M.; Habib Jiwan, J. L.; Soumillion, J. Ph. *J. Am. Chem. Soc.* **1999**, *121*, 10436.

(4) E.g., see: Burgess, K.; Van der Donk, W. A. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A.. Ed.; Wiley: Chichester, 1995; Vol. 2, pp 1253−1261.

(5) Sertchook, H.; Avnir, D.; Blum, J.; Joo, F.; Kortho, A.; Schumann, H.; Weimann, R.; Wernik, S. *J. Mol. Catal. A: Chem.* **1996**, *108*, 153. Rosenfeld, A.; Blum, J.; Arnir, D. **1996**, *164*, 363.

(6) Hüsing, M.; Schubert, U.; Mezei, R.; Fratzl, P.; Riegel, B.; Kiefer, W.; Kohler, D.; Mader, W. *Chem. Mater.* **1999**, *11*, 451.

(7) A mixture of 3.0 mL of MeOH, 1.4 mL of water, and 1.0 mL of tetramethoxyorthosilicate (TMOS) was stirred at room temperature for 10 min. To this solution was added 2.0 mL of $H_2N(CH_2)_2NH(CH_2)_3Si(OCH_3)_3$, which caused rapid gelling. The gel was dried at 1 mm for 24 h at room temperature, sonicated twice in benzene, and finally dried at 1 mm for 3 h, to give 2.3 g of the sol−gel material.

(8) A miniautoclave was charged with β-iodoethylbenzene (1.6 mmol), the sol−gel base (3 mmol, 1.15 g of the material), the sol−gel encapsulated $RhCl[P(C_6H_5)_3]_3$[5] (0.018 mmol), and 15 mL of dry benzene. The reaction vessel was purged with hydrogen and the mixture was stirred magnetically at 80 °C under 200 psi of H_2. The solid material was filtered off and the products and starting material in the filtrate were analyzed by GC, ^1H NMR, and MS. The filtrate was also checked for its content of leached base and metallic compounds by elemental analysis and atomic absorption spectroscopy (detection limit of less than 1 ppm), and by its ability to dehydrohalogenate fresh samples of haloethylbenzene or to catalyze hydrogenation of styrene. The result of this blank test was negative.

(9) While a benzene solution of 1.6 mmol of styrene is reduced to ethylbenzene in quantitative yield by heating the mixture at 80 °C for 2.5 h under 200 psi of H_2 with 0.018 mmol of sol−gel encapsulated $RhCl[P(C_6H_5)_3]_3$, in the presence of 4.5 mmol of either free $H_2N(CH_2)_2NH(CH_2)_3Si(OCH_3)_3$ or of free $H_2N(CH_2)_2NH_2$, no reaction took place.

(10) Triton B was entrapped by first stirring a mixture of 2.0 mL of TMOS, 1.0 mL of water, and 2.0 mL of MeOH for 15 min at room temperature. To this solution was added 4.0 mL of 40% Triton B in MeOH. The solution gelled rapidly, and the gel was dried at 1 mm for 24 h, sonicated twice in benzene, and dried at 1 mm for 3 h. A reaction mixture of 1.6 mmol of β-bromoethylbenzene, sol−gel containing 4.5 mmol of entrapped Triton B, and 0.018 mmol of sol−gel encapsulated $RhCl[P(C_6H_5)_3]_3$ in benzene yielded after 17 h under 150 psi of H_2 at 60 °C a mixture of 18% of ethylbenzene, 29% of β-phenylethanol, and 52% of unreacted starting material. The filtrate was checked for possible ability to dehydrohalogenate the bromoethylbenzene: No reaction was detected in this blank test.

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droiodination (e.g., 6% vs 18% after 4 h). Typical reaction yield was therefore only 12% after 6.5 h. Better yields were obtained by replacing the covalently bound diamine with physically entrapped Triton B ($[C_6H_5CH_2N(CH_3)_3]^+OH^-$) which does not leach in the benzene slurry and which also proved to be friendly to the catalyst in this form.[10] With this base, nucleophilic substitution with OH^- took place along with the dehydrobromination, yielding ethylbenzene and β-phenylethanol at a ratio of 3:2.[10]

In conclusion we comment that the methodology of changing "chemical hostility" into "chemical friendliness" and compatibility, which was demonstrated here on an idea-feasibility level, is general. Other examples are indeed in preparation.

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