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One-Pot, Selective Hydroformylation, Condensation, and Hydrogenation Processes by a Sol–Gel Entrapped Rhodium Complex, an Immobilized Base, and an Ionic Liquid

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We report on a one-pot, multistep process in which styrene derivatives are selectively hydroformylated to give branched aldehydes, which in turn, are condensed with reactive methylene compounds (malononitrile, ethyl cyanoacetate), and then hydrogenated. The process takes place at 80 °C under 20.7 bar H_2 and 20.7 bar CO in the presence of $[Rh(cod)Cl]_2$ and $Na[Ph_2P\text{-}3\text{-}(C_6H_4SO_3)]$, which have been co-entrapped within ionic liquid confined silica sol–gel together with a separately encaged base. The catalyst can be reused at least four times, but the base has to be renewed after each run.
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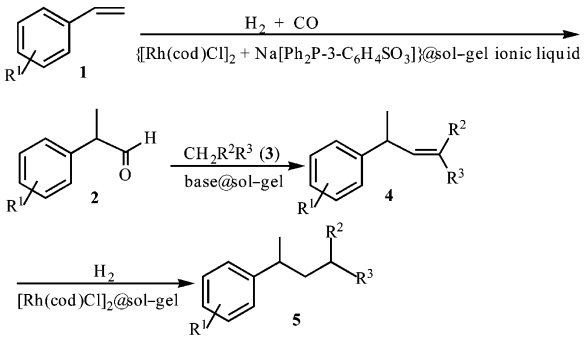
Introduction

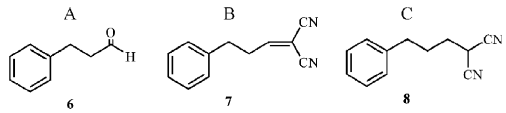
In the course of our studies on the application of the sol–gel technology to organic synthesis,[1] we have demonstrated that chemicals encaged within different ceramic matrices do not interact, even if they are of opposing nature, although they tend to react with each other in their non-heterogenized form.[2,3] In a recent study, we found that dichlorobis[(1,2,5,6-η)-1,5-cyclooctadiene]dirhodium, $[Rh(cod)Cl]_2$, that had been entrapped within an ionic liquid confined silica sol–gel promotes the hydroformylation of styrene derivatives in a highly selective manner to give mainly branched aldehydes.[4] In this paper, we show that by combining the aforementioned catalytic system with a suitable base, which may be the ionic liquid itself, it is possible to perform a one-pot, multistep process that consists of the selective hydroformylation of styrenes, a base-promoted condensation of the resulting aldehydes with active methylene compounds, and controlled hydrogenation of the unsaturated products so formed (Scheme 1).



Scheme 1.

Results and Discussion

The reaction of a mixture of 1 mmol styrene (**1**, R^1 = H), 1 mmol propanedinitrile (malononitrile, **3**, R^1 = H, R^2 = R^3 = CN), 20.7 bar H_2, and 20.7 bar CO in the presence of 2.04×10^{-2} mmol $[Rh(cod)Cl]_2$ co-entrapped with 4.01×10^{-2} mmol sodium 3-(diphenylphosphanyl)benzenesulfonate, ionic liquid confined silica sol–gel (vide infra),[4] and 10 mL of each of THF and 1,2-dichloroethane afforded, after 14 h at 80 °C, a mixture of 86% (2-phenylpropyl)propanedinitrile (**5**, R^1 = H, R^2 = R^3 = CN),[5] 7% (2-phenylpropylidene)propanedinitrile (**4**, R^1 = H, R^2 = R^3 = CN),[6] 2% (3-phenylpropylidene)propanedinitrile (**8**),[7] and traces (<0.1%) of its precursor **7**.[8] The latter two products result from the linear aldehyde **6** formed in small quantities during hydroformylation.[4] After removal of the products and addition of a new portion of the reagents and a base (vide infra), the used catalyst could be employed in a second run.



The observed selectivity of two steps in the combined process are remarkable: (a) the hydroformylation takes place only on the double bond of the styrene, but not on

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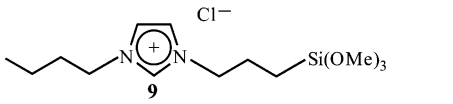
that of intermediate **4** (R^1 = H, R^2 = R^3 = CN), and (b) under our reaction conditions, hydrogenation occurs only on the internal double bond of **4** rather than on the terminal one of **1**. Moreover, despite the fact that hydrogenation reactions accompany most of the hydroformylation processes,[9] no ethylbenzene is formed as long as the pressure of H_2 and CO is roughly the same (vide infra).

While several selective hydroformylation reactions have already successfully been performed with rhodium catalysts and imidazolium salts,[10,11] the multistep, one-pot reaction outlined in Scheme 1 takes place efficiently only when the rhodium catalyst is entrapped within the ceramic support and the ionic liquid is chemically bound to the sol–gel backbone. Our choice for the ionic liquid was, as in the previous study, 1-butyl-3-[3-(trimethoxysilyl)propyl]imidazolium chloride (**9**) together with Na[$Ph_2P(3\text{-}C_6H_4SO_3)$].[4] Imidazolium derivatives that cannot be bound to the backbone of the support, such as the commercially available 1,3-di-*tert*-butylimidazolium tetrafluoroborate (**10**) and 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (**11**), proved to be difficult to recycle.



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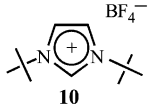

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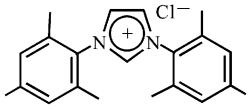

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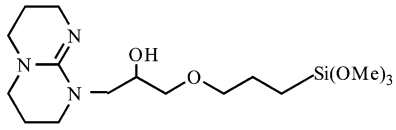
We speculate that under the aforementioned conditions the imidazole derivative serves both as a carbene ligand of the rhodium complex (and is responsible for stereoselective hydroformylation) and acts as a "base" that promotes the condensation of the aldehyde with malononitrile. Thus, a part of it is consumed during the first run of the multistep process, and a new supplement of base is required for the second run. The best results were obtained when the base was the sol–gel bound 1,5,7-triazabicyclo[4.4.0]dec-5-ene modified with (3-glycidoxypropyl)trimethoxysilane (**12**),[2d,12] although the addition of a new portion of sol–gel containing **9** to the reaction mixture in advanced runs proved to be quite satisfactory.



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In fact, there is an advantage in using the sol–gel entrapped guanidine base already in the first run. This increases the yield of **5** (R^1 = H, R^2 = R^3 = CN) from 86 to 91% at the expense of the unsaturated dinitrile **4** (R^1 = H, R^2 = R^3 = CN), which under such conditions hardly appears among the final products. Typical yields of the saturated dinitrile in the second, third, and fourth runs were 86, 80, and 82%, respectively, after 14 h at 80 °C. Attempts to recycle the system in further runs met with difficulty because of the increase in the voluminal mass of the ceramic support of the base.

In a similar manner to the transformation of **1** (R^1 = H) to **5** (R^1 = H, R^2 = R^3 = CN), we were able to convert the substituted styrenes **1** (R^1 = Cl and OMe) into the corresponding chloro- and methoxy dinitriles in ca. 90 and 57% overall yield, respectively. We were also able to perform the one-pot, multistep process with ethyl cyanoacetate. Some typical results are summarized in Table 1.

Table 1. The results of some one-pot, selective hydroformylation, condensation, and hydrogenation processes described in Scheme 1.[a]

Entry	R^1	R^2	R^3	Overall yield (**5**) [%][b]
1	H	CN	CN	83 ± 3
2	Cl	CN	CN	87 ± 7
3	CH_3O	CN	CN	57
4	H	CN	$CO_2C_2H_5$	75 ± 4

[a] Reaction conditions: 1 mmol **1**, 1 mmol **3**, sol–gel material prepared from 11 mmol prehydrolyzed $Si(OMe)_4$, 0.37 mmol **9**, 0.02 mmol $[Rh(cod)Cl]_2$, 0.04 mmol Na[Ph_2P-3-($C_6H_4SO_3$)], 1.8 mmol **12** entrapped within a non-modified sol–gel; 10 mL THF and 5 mL 1,2-dichloroethane; 20.7 bar H_2 and 20.7 bar CO; 80 °C; 14 h. [b] In the first run.

While the best solvents for the stereoselective hydroformylation are hydrocarbons and 1,2-dichloroethane,[4] the preferred medium for the combined hydroformylation, condensation, and hydrogenation process was a 1:1 mixture of 1,2-dichloroethane and THF.

A series of comparative experiments revealed the sensitivity of the process described in Scheme 1 towards the physical nature of the various reaction components. Under homogeneous conditions, i.e. when both the rhodium catalyst and base, as well as the ionic liquid, are not entrapped in the sol–gel, the multistep process does not take place at all. Entrapment of either the base or the rhodium complex alone causes partial decomposition of the catalyst, and, consequently, only a low yield of the final product is formed. The results of these comparative experiments are listed in Table 2.

Table 2. Dependence of the multistep, one-pot process of **1** (R^1 = H) and **3** (R^2 = R^3 = CN) on the immobilization of the catalyst and the base.[a]

Entry	Rhodium catalyst[b]	Guanidine base[b]	Yield (products) [%][c] **2**	**4**	**5**	**8**
1	–	–	9.0	–	–	–
2	+	–	1.8	0.7	8.3	1.2
3	–	+	2.6	trace	17.1	1.3
4	+	+	2.2	trace	91	3.4

[a] Reaction conditions: the amounts of the reaction components, the temperature and the time as in Table 1. The yields in this series of experiments were determined by GC. [b] The signs "+" and "–" refer to the sol–gel entrapped and non-entrapped materials, respectively. [c] The yields of **6** and **7** (R^1 = H, R^2 = R^3 = CN) were in each case <0.2%. The amounts of recovered **1** (R^1 = H) have been omitted.

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Whereas an equal pressure of 13.8–20.7 bar of H_2 and CO does not lead to the formation of detectable quantities of ethylbenzene derivatives, an increase in the H_2 pressure at the expense of the CO pressure causes substantial reduction of the double bond of **1**. On the other hand, excess CO leads to an increase in the amount of the unsaturated dinitriles **4** and **7**. The results of some representative experiments are listed in Table 3.

Table 3. Dependence of the amount of ethylbenzene and the unsaturated dinitriles **4** and **7** on the H_2 and CO pressures.[a]

Entry	Initial H_2 pressure [bar]	Initial CO pressure [bar]	Yield ($C_6H_5C_2H_5$) [%]	Yield (**4** + **7**) {R^1 = H, R^2 = R^3 = CN} [%]
1	13.8	27.6	–	17
2	13.8	34.5	–	32
3	20.7	13.8	7	1.2
4	27.6	13.8	18	0.5
5	34.5	13.8	27	–

[a] Reaction conditions: except for the pressure of the gases, the same conditions as in Table 1 were employed. The yields in this series of experiments were determined by GC.

Finally, it is notable that although hydroformylation[13,14] and hydrogenation of alkenes[15] by transition-metal complexes have been shown to often involve metallic nanoparticles as reaction intermediates, thorough TEM measurements were unable to detect the presence of Rh^0 nanoparticles in our one-pot processes.

Conclusions

This study reveals that the co-entrapment of $[Rh(cod)Cl]_2$ and sulfonated triphenylphosphane within a silica sol–gel matrix confined with 1-butyl-3-[3-(trimethoxysilyl)propyl]imidazolium chloride, forms a ceramic material that catalyzes in one pot: (i) the hydroformylation of styrenes to give in high selectivity branched aldehydes; (ii) promotes the condensation of the latter products with active methylene compounds; (iii) the hydrogenation of the internal double bonds of the condensation products. The unsaturated condensation products are not further hydroformylated. We still do not have a sound explanation for the preferential hydrogenation of the sterically hindered internal double bonds over that of the terminal one of the styrene derivatives, as well as over the easily reducible aldehyde groups. As noted above, the ionic liquid which is assumed to act as a carbene ligand of the rhodium complex can promote, in the absence of an additional base, the condensation process. Thus, while the rhodium catalyst is perfectly recyclable it is necessary to renew a part of the base after each run of the multistep process.

Experimental Section

General: The various styrenes, propanedinitrile, ethyl acetoacetate, 2- and 3-phenylpropanecarboxaldehyde, 2-phenylpropanol, and 1-butylimidazole were purchased from Sigma–Aldrich. (3-Chloropropyl)trimethoxysilane and tetramethoxysilane were obtained from Gelest Silanes and Silicons. Di-μ-chlorobis[(1,2,5,6-η)-1,5-cyclooctadiene]dirhodium,[16] 1-butyl-3-[3-(trimethoxysilyl)propyl]imidazolium chloride,[4] sodium 3-(diphenylphosphanyl)benzenesulfonate,[17] (2-phenylpropylidene)propanedinitrile,[6] (3-phenylpropylidene)propanedinitrile,[7] (2-phenylpropyl)propanedinitrile,[5] (3-phenylpropyl)propanedinitrile,[7] and ethyl α-cyano-γ-methylbenzene butanoate[18] were prepared according to literature procedures. The immobilization of the catalyst was performed essentially as described previously.[4] The following analytical instruments were used: Bruker Vector 22, FTIR spectrometer, Bruker DRX-400 NMR instruments, Hewlett Packard model Agilent 4890 D gas chromatograph, Hewlet Packard model 4989A mass spectrometer equipped with an HP gas chromatograph model 5890 series II, and a Q-TOF-II (Micromass, UK) spectrometer that enabled direct injection by nanoelectrospray through a glass capillary at 1200 V. A Perkin–Elmer model ELAN DRC II instrument was used for inductively coupled plasma (ICP) measurements. Transmission electron microscopy was carried out with a Scanning Transmission Electron Microscope (STEM) Tecani G^2 F20 (FEI Company, USA) operated at 200 kV and equipped with EDAX-EDS for identification of the elemental composition. Initial powders were dispersed in ethanol and dropped onto a standard 400 mesh carbon-coated copper TEM gird.

General Procedure for the One-Pot, Multistep Process: Typically, a 100 mL glass-lined mini-autoclave equipped with a mechanical stirrer and a sampling device was charged with the styrene derivative **1** (1 mmol: 104 mg for R^1 = H; 138.5 mg for R^1 = Cl; 134 mg for R^1 = CH_3O), nitrile **3** (1 mmol: 66 mg for R^2 = R^3 = CN; 113 mg for R^2 = CN, R^3 = $CO_2C_2H_5$), the heterogenized catalyst {containing $[Rh(cod)Cl]_2$ (10 mg, 0.02 mmol), $Na[Ph_2P\text{-}3\text{-}C_6H_4SO_3]$ (14.6 mg, 0.04 mmol) within the ceramic material from $Si(OMe)_4$ (5 mL) and ionic liquid **9** (260 mg, 0.8 mmol)}, together with the guanidine base **12** (675 mg, 1.8 mmol) within a separate ionic liquid-free sol–gel matrix from $Si(OC_2H_5)_4$ (4.5 mL), 1,2-dichloroethane (10 mL), and THF (10 mL).[4] The autoclave was sealed, perched with N_2, and then pressurized with H_2 and CO (usually 20.7 bar of each of the gases). The reaction mixture was stirred and heated at 80 °C for 14 h. After cooling to 0 °C, the excessive gases were released, and the remaining mixture filtered. The solid was washed with CH_2Cl_2 (2 × 15 mL). The filtrate was concentrated and analyzed by GC, mass spectrometry, and NMR spectroscopy and, when possible, compared with authentic samples. The solid was refluxed with CH_2Cl_2 (20 mL) and sonicated with the same solvent for 15 min. The combined washings were concentrated and subjected to ICP analysis. The solids were dried at room temperature for 5 h and then mixed with a fresh portion of **12** (1.8 mmol) entrapped within a non-modified sol–gel before use in a second catalytic run.

Under these conditions **1** (R^1 = H) and **3** (R^2 = R^3 = CN) afforded up to 158 mg (86%) (2-phenylpropyl)propanedinitrile (**5**, R^1 = H, R^2 = R^3 = CN), which proved to be identical with an authentic sample.[5] Likewise, **1** (R^1 = H) and **3** (R^2 = CN, R^3 = $CO_2C_2H_5$) gave up to 180 mg (78%) ethyl 2-cyano-(2-phenylpropyl)acetate [**5**, R^1 = H, R^2 = CN, R^3 = $(O_2C_2H_5)$].[18] [2-(4-Chlorophenylpropyl)]-propanedinitrile (**5**, R^1 = H, R^2 = R^3 = CN) was obtained in 87–94% yield as a pale yellow viscous oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (d, J = 7 Hz, 3 H), 2.18 (m, 1 H), 2.37 (m, 1 H), 3.03 (m, 1 H), 3.32 (dd, J_1 = J_2 = 5 Hz, 1 H), 7.25 (ABq, J_{AB} = 8 Hz, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.92, 21.64, 36.9, 38.42, 112.40, 128.70, 129.58, 133.35, 140.59 ppm. MSEI: *m*/*z* (%) = 218/220 (5) [$M^{+\cdot}$], 139/141 (100) [$ClC_6H_4CHCH_3^+$], 103 (31) [$C_8H_7^+$], 77 (29) [$C_6H_5^+$], 65 (5) [$C_3HN_2^+$]. $C_{12}H_{11}ClN_2$ (218.676): calcd. C 65.91, H 5.07, N 12.81; found C 65.93, H 5.23, N 12.42.

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[2-(4-Methoxyphenylpropyl)]propanedinitrile (**5**, $R^1 = OCH_3$, $R^2 = R^3 = CN$) was obtained in 57% yield as a pale yellow viscous oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (d, J = 7 Hz, 3 H), 2.14 (m, 1 H), 2.36 (m, 1 H), 2.98 (m, 1 H), 3.30 (dd, $J_1 = J_2$ = 5 Hz, 1 H), 3.80 (s, 3 H), 7.01 (ABq, J_{AB} = 9 Hz, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.91, 21.90, 36.72, 39.00, 55.23, 112.49, 114.60, 127.82, 128.98, 159.01 ppm. MSEI: *m*/*z* (%) = 214 (8) [$M^{+\cdot}$], 135 (100) [$CH_3OC_6H_4CHCH_3^+$], 121 (4) [$C_8H_9O^+$], 107 (9) [$C_7H_7O^+$], 91 (14) [$C_7H_7^+$], 77 (8) [$C_6H_5^+$], 65 (6) [$C_3HN_2^+$]. $C_{13}H_{14}N_2O$ (214.263): calcd. C 72.87, H 6.58, N 13.07; found C 72.67, H 6.54, N 12.85.

Acknowledgments

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[1] a) J. Blum, D. Avnir, H. Schumann, *Chemtech* **1999**, *29*, 32–38; b) J. Blum, D. Avnir in *Handbook of Sol–Gel Science and Technology* (Ed.: S. Sakka), Kluwer Academic Pub., Boston, **2005**, vol. 3, ch. 24.

[2] a) F. Gelman, J. Blum, D. Avnir, *J. Am. Chem. Soc.* **2000**, *122*, 11999–12000; b) F. Gelman, J. Blum, D. Avnir, *Angew. Chem. Int. Ed.* **2001**, *40*, 3647–3649; c) F. Gelman, J. Blum, D. Avnir, *J. Am. Chem. Soc.* **2002**, *124*, 14460–14463; d) F. Gelman, J. Blum, D. Avnir, *J. Sol–Gel Sci. Technol.* **2003**, *26*, 43–46; e) F. Gelman, J. Blum, D. Avnir, *New J. Chem.* **2003**, *27*, 205–207; f) Y. Levin, K. Hamza, R. Abu-Reziq, J. Blum, *Eur. J. Org. Chem.* **2006**, 1396–1399; g) K. Hamza, J. Blum, *Tetrahedron Lett.* **2007**, *48*, 293–295.

[3] For further examples of one-pot, multistep reactions conducted in other laboratories, see: S. J. Broadwater, S. L. Roth, K. E. Price, M. Kobaslija, D. T. McQuade, *Org. Biomol. Chem.* **2005**, *3*, 2899–2906 and references cited therein.

[4] K. Hamza, J. Blum, *Eur. J. Org. Chem.* **2007**, 4706–4710.

[5] M. Ohashi, K. Nakatani, H. Maeda, K. Mizuno, *Org. Lett.* **2008**, *10*, 2741–2743.

[6] D. Kruger, A. E. Sopchik, C. A. Kingsbury, *J. Org. Chem.* **1984**, *49*, 778–788.

[7] U. Holzgrabe, J. Reinhardt, G. Zlotos, *Arch. Pharm.* **1994**, *327*, 515–523.

[8] K. Yamashita, T. Tanaka, M. Hayashi, *Tetrahedron* **2005**, *61*, 7981–7985.

[9] See e.g. *Carbonylation: Direct Synthesis of Carbonyl Compounds* (Eds.: H. M. Colquhoun, D. J. Thompson, N. V. Twigg), Plenum Press, New York, **1991**.

[10] V. César, S. Bellemin-Loponnazi, L. H. Gade, *Chem. Soc. Rev.* **2004**, *33*, 619–636.

[11] a) A. C. Chen, L. Ren, a. Decken, C. M. Crudden, *Organometallics* **2000**, *19*, 3459–3461; b) M. Haumann, A. Riisager, *Chem. Rev.* **2008**, *108*, 1474–1497.

[12] a) Y. V. Subba Rao, D. E. De Vos, P. A. Jacobs, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2661–2663; b) N. Hüsing, U. Schubert, R. Mezei, P. Fratzl, B. Riegal, W. Kiefer, D. Kohler, W. Moder, *Chem. Mater.* **1999**, *11*, 451–457.

[13] F. Wen, H. Bönnemann, J. Jiang, D. Lu, Y. Wang, Z. Jin, *Appl. Organomet. Chem.* **2005**, *19*, 81–89.

[14] A. J. Bruss, M. A. Gelesky, G. Machado, J. Dupont, *J. Mol. Catal. A* **2006**, *252*, 212–218.

[15] See e.g. A. Roucous, A. Nowicki, K. Philippot in *Nanoparticles and Catalysis* (Ed.: D. Astruc), Wiley-VCH, Weinheim, **2008**, pp. 349–388.

[16] G. Giordano, R. H. Crabtree, *Inorg. Synth.* **1990**, *28*, 88–90.

[17] S. Arland, J. Chatt, N. R. Davis, A. A. Williams, *J. Chem. Soc.* **1958**, 276–288.

[18] T. Mizagaki, Y. Miyauchi, M. Murata, K. Ebitani, K. Kaneda, *Chem. Lett.* **2005**, *34*, 286–287.

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