Chemoselectivity in Catalytic Transfer Hydrogenation – Reduction of Alkenes and Alkynes with the $H_2PO_2^-NH_4^+ \cdot H_2O$/Pd-C System

Bui The Khai* and Antionio Arcelli

Dipartimento di Chimica "G. Ciamician", Università degli Studi,
Via Selmi 2, 40126 Bologna, Italy

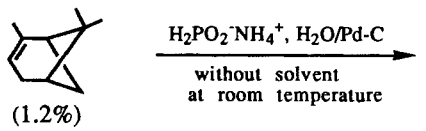
Received February 8, 1993

Key Words: Chemoselectivity / Protonolysis / Transfer hydrogenation / Alkenes, reduction of / Alkynes, reduction of

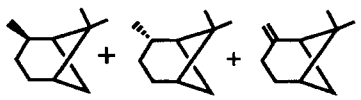
The $H_2PO_2^-NH_4^+ \cdot H_2O$/Pd-C system acts as an unusually powerful reducing agent, which is able to reduce cyclooctene to cyclooctane, $\Delta^{9,10}$-octalin to decalins, α- and β-pinenes to pinanes at room temperature in high yield without the formation of byproducts. This system selectively reduces each of these compounds or partly (alkynes to alkenes), depending on the competition between the transfer hydrogenation to give alkanes and the protonolysis to give hydrogen gas on the palladium catalyst.

Molecular hydrogen is easily ignited. This disadvantage is one of the stumbling blocks to the wide use of hydrogen as a fuel. In organic synthesis, hydrogenation with hydrogen gas also has some disadvantages, particularly large-scale application presents hazards, which can be overcome when hydrogen gas is replaced by hydrogen donors[1,2a]. In an open vessel, catalytic transfer hydrogenation offers a useful and safe method of reducing active alkenes such as terminal alkenes and α, β-unsaturated carbonyl compounds[2]. But this method is often sluggish or fails completely with tri- and tetrasubstituted olefins[2,3,4].

Recently, it has been reported that the system $NaBH_4$ or $LiAlH_4$/metal halide acts as a powerful reducing agent of alkenes, but a large amount of the metal halide is required[3,4]. Furthermore, a highly sterically hindered alkene such as α-pinene remains unchanged[4].

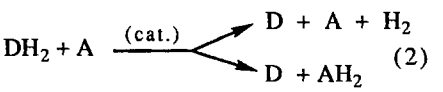


(1)



Now we have found that when ammonium hypophosphite monohydrate is used as an hydrogen donor, Pd-C displays a high activity, catalyzing the transfer hydrogenation without a solvent at room temperature. In an open vessel highly sterically hindered alkenes such as $\Delta^{9,10}$-octalin, α- and β-pinenes are reduced to decalins and pinanes, respectively, in high yield. To our knowledge, this is the first example of catalytic transfer hydrogenation which is able to reduce sterically hindered alkenes at room temperature in high yield without the formation of byproducts[5].

In the course of our investigation using ammonium salts as the hydrogen donor, we have found that there is a competition between the transfer hydrogenation and the desorption of hydrogen to give hydrogen gas on a metal catalyst as in equation (2)[1,2d].

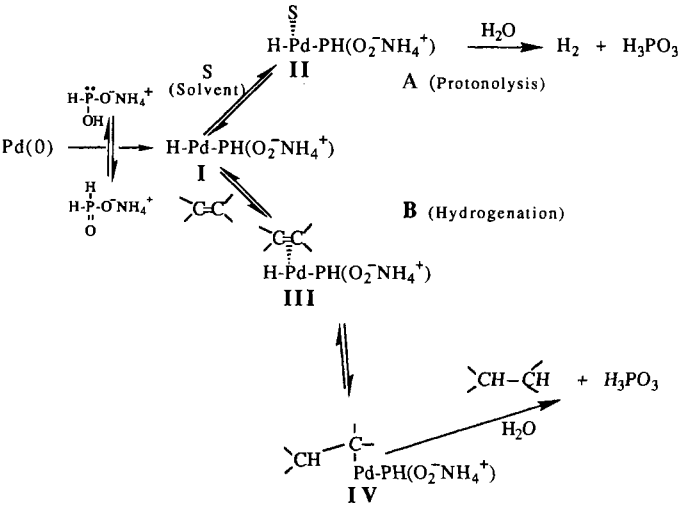


(2)

DH_2: hydrogen donor; A: hydrogen acceptor

This competition can play an important role in the chemoselective reduction with the system $H_2PO_2^-NH^+{}_4 \cdot H_2O$/Pd-C. This system acts as a powerful reducing agent, which is able to reduce cyclooctene, octalin, α- and β-pinenes, and alkynes to alkanes in high yield. It selectively reduces cyclooctene to cyclooctane in the presence of $\Delta^{9,10}$-octalin and alkynes to alkenes, depending on the competition between

Scheme 1



the transfer hydrogenation to give alkanes, and the protonolysis to give hydrogen gas on the metal catalyst.

Based on other reports[2a,6] we propose the mechanism in Scheme 1 for this reaction.

We have found that in the presence of the solvents benzene, ethanol and THF (Table 1, method A) or in the two-phase system benzene/H_2O (Table 1, method B) the less hindered alkenes are reduced selectively: in the mixture of cyclooctene and $\Delta^{9,10}$-octalin, or each of them alone, only cyclooctene is reduced to cyclooctane (100%) while $\Delta^{9,10}$-octalin remains unchanged (100%) (Table 1, entries 6, 7).

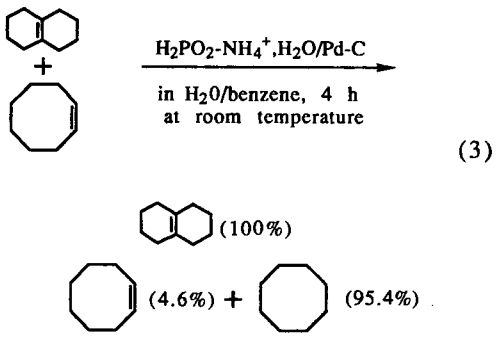
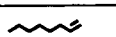
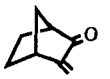
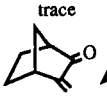
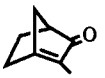
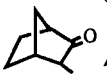
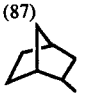
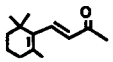
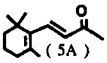
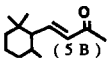
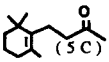
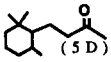
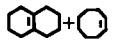


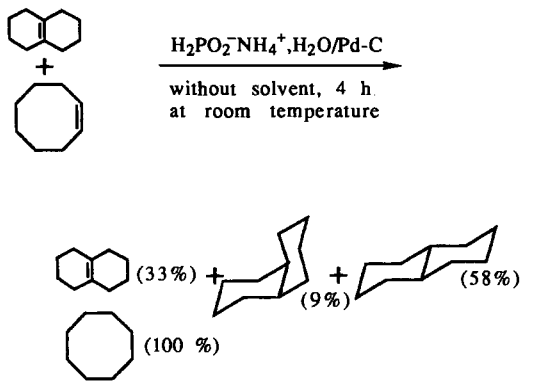
Table 1. Reduction of alkenes with the system $H_2PO_2^-NH_4^+ \cdot H_2O$/Pd-C

No	Substrate	Method	Time h	Product (Yield %)[a]					
1		A	1	3	4.7	92.3			
			2	0	0	100 (92)			
2		A	1	0	18.7	81.3			
			2	0	trace	100 (91)			
3									
		A	1	3.7	79.5	16.8			
			3	trace	trace	100 (87)			
4									
		A	2.5	0	0	92 (87)	8		
5				 (5A)	 (5B)	 (5C)	 (5D)		
		C	4	0	31	12	57		
			12	trace	trace	trace	100 (82)		
6									
		B	4	100	0	0	0		
		C	12	3	0	92 (84)	5		
7		B	4	100	0	0	0	4.6	95.4
		C	4	33	0	58	9	0	100
				α-Pinene	β-Pinene	cis-Pinane	trans-Pinane		
8	β-Pinene	B	0.5	99.09	0.6	0.3	trace		
9	α-Pinene	C	3.5	1.2	trace	68.5	30.3		
10	β-Pinene	C	3.5	1.1	0	66.9	32		

[a] Determined by GC-MS, yields of isolated products in parentheses. – A: Solvent benzene, alkene (12.6 mmol) in 20 ml of benzene, $H_2PO_2^-NH_4^+ \cdot H_2O$ (31.8 mmol), Pd-C 10% (0.19 mmol) was stirred at room temp. – B: Solvent benzene/water, alkene (12.6 mmol) in 20 ml of benzene, $H_2PO_2^-NH_4^+ \cdot H_2O$ (36.4 mmol) in 30 ml of water, Pd-C 10% (0.19 mmol) at room temp. – C: Without a solvent; alkene (12.6 mmol), $H_2PO_2^-NH_4^+ \cdot H_2O$ (31.8 mmol) and Pd-C 10% (0.19 mmol) at room temp.

This fact can be explained by assuming that there is a competition between the coordination of the substrate and of the solvent on the vacant coordination site of the palladium atom (the benzene in this case acts as a competitive inhibitor in the reduction of sterically hindered olefins[7]). The olefin coordination step is reversible (**I**⇌**III**): $\Delta^{9,10}$-Octalin displays high steric hindrance and is thus a weaker coordinator, so that the equilibrium is strongly shifted to stage **I**, then to **II** (Scheme 1). Therefore, the protonolysis is a dominant reaction, and all the hypophosphorous acid is converted to free H_2 and H_3PO_3, while $\Delta^{9,10}$-octalin remains unchanged. Since cyclooctene, representing a less sterically hindrered compound, exhibits a higher coordinating power than that of benzene, the complexes **III** and **IV** are the dominant species in solution, so that cyclooctene is reduced to cyclooctane (95.4%) (Table 1, entry 7).

In the case of the reaction without a solvent, the highly sterically hindered alkenes are reduced; this fact can be explained by assuming that the equilibrium between **I** and **III** is strongly shifted to stage **III** (Scheme 1). The olefin complex **III** is a dominant species and thus $\Delta^{9,10}$-octalin and pinenes are reduced. Comparable to the results of hydrogenation under hydrogen pressure[8,9] with Pd-C: $\Delta^{9,10}$-octalin gives predominantly the more stable product isomer (92% *trans*- and 5% *cis*-decalin); α-pinene gives the less stable isomer (68.5% *cis*- and 30.3% *trans*-pinane) (Table 1, entries 6, 9).



For the same reason we can understand why the reduction rates of α-pinene and β-pinene have been found to be quite similar (Table 1, entries 9, 10), even though they differ widely when the $CoCl_2/NaBH_4$/THF system[4] is used.

We have studied the reaction conditions without a solvent for the reduction of $\Delta^{9,10}$-octalin, β-ionone, α- and β-pinene and have found that the formation of polymeric products is negligible, and the reduced products are isolated in about 80% yields. This fact may be explained by assuming that these alkenes are highly sterically hindered compounds, therefore a second alkene molecule hardly coordinates to the palladium atom, and probably the reductive elimination step (alkylpalladium **IV** to alkane) is easier and faster with $H_2PO_2^-NH_4^+ \cdot H_2O$ than that with formic acid[10].

It has been reported that alkynes are selectively reduced to alkenes with NaH_2PO_2/Pd-C, but Pd-C must be modified with lead or mercury[11]. Now we find that we can use commercial Pd-C without modifications. The system H_2PO^-

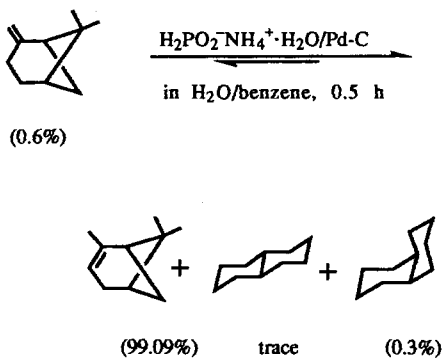
$NH_4^- \cdot 4H_2O$/Pd-C/H_2O-benzene selectively reduces alkynes to alkenes at room temperature with a high stereoselectivity (Table 2). Thus 89.2% of stilbenes (83.5% *cis* and 5.7% *trans*) have been obtained from tolan after 2 hours. Similarly 4-phenyl-3-butyn-2-one is converted in 91% yield to 4-phenyl-3-buten-2-one (81.5% *cis* and 9.5% *trans*), and ethyl phenylpropiolate in 90% yield to cinnamate (83% *cis* and 7% *trans*). In this case benzene acts as a competitive inhibitor of olefin hydrogenation by blocking active catalyst sites[7]. Instead of the selective reduction with NaH_2PO_2/Pd-C (Hg)[11], mercury acts to rearrange the surface structure of the catalyst[12]. It should be noted that overreduction of alkenes can occur when the reaction time is prolonged (after 6 hours tolan has been converted in 65.7% yield to stilbenes and in 34.3% yield to 1,2-diphenylethane under the same condition B, Table 2). But in the presence of quinoline, the reduction can be stopped at the stage of the olefin (Condition B_3). This process offers a convenient method for reducing selectively alkynes to alkenes. Thus, we can use an excess of hydrogen donor and a long reaction time in order to achieve a complete conversion of alkynes to alkenes. The formation of byproducts (alkanes) is negligible. We have studied, as an example, the reduction of tolan: after 12 hours only 0.5% of 1,2-diphenylethane have been detected (Table 2, entry 3). This fact can be explained by assuming that stilbene displays a weak coordination capability so that the equilibrium is strongly shifted to **I**, then toward **II** (Scheme 1). The protonolysis is the dominant reaction, and the excess hydrogen donor ($H_2PO_2^-NH_4^+ \cdot H_2O$) is converted to free H_2, while stilbene remains unchanged.

Table 2. Semihydrogenation of alkynes with the system $H_2PO_2^-NH_4^+ \cdot H_2O$/Pd-C at room temperature

No	Substrate[a]	Method	Time h	Product (Yield %)[b]			
1	$R_1-\equiv-R_1$			Tolan	Z-Stilbene	E-Stilbene	$Ph(CH_2)_2Ph$
		B	2	2.8	83.5	5.7	8
			6	0	46.2	19.5	34.3
2	$R_1-\equiv-R_1$	B_2	2	0	0	0	100 (94)
3	$R_1-\equiv-R_1$	B_3	12	0	91	8.5	0.5
4	$R_1-\equiv-R_2$			$R_1-\equiv-R_2$	$Z\text{-}R_1CH{=}CHR_2$	$E\text{-}R_1CH{=}CHR_2$	$R_1(CH_2)_2R_2$
		B	2	2	81.5	9.5	7
		B_3	3	3	86	7.5	3.5
5	$R_1-\equiv-R_3$			$R_1-\equiv-R_3$	$Z\text{-}R_1CH{=}CHR_3$	$E\text{-}R_1CH{=}CHR_3$	$R_1(CH_2)_2R_3$
		B	2	1	83	7	9
		B_3	3	0	90	5.5	4.5

[a] $R_1 = Ph$; $R_2 = COCH_3$; $R_3 = CO_2Et$. — [b] Determined by GC-MS, yields of isolated products in parentheses. — B: $H_2PO_2^-NH_4^+ \cdot H_2O$ (36.4 mmol) in 30 ml of H_2O, alkyne (12.64 mmol) in 20 ml of benzene, Pd-C 10% (0.19 mmol) at 23°C. — B_2: The same procedure as B, but H_2O replaced by aqueous ammonia (30%). — B_3: The same procedure as B, but quinoline (0.42 mmol) was added.

It should be noted that there is a competition with double bond migration in this system. This migration follows both Bredt's rule and thermodynamic control. Bredt's rule during the reduction of 3-methylene-2-norbornanone, the GC/mass spectral analysis reveals only the presence of 3-methyl- and 3-methylene-2-norbornanone, but byproducts of double bond migration have not been found (Table 1, entry 4). Concerning thermodynamic control, olefins seem to resist the reduction, and migration of the double bond leads to the thermodynamically more stable isomer. During the reduction of 1-octene, *cis*- and *trans*-2-octene are formed as byproducts, but in the reduction of 2-octene, 1-octene is not detected. Similarly, in the reduction of 3-phenyl-1-propene, 1-phenyl-1-propene is generated as a byproduct, but in the reduction of 1-phenyl-1-propene, a byproduct of double bond migration has not been detected. (−)-β-Pinene has been converted to pure (−)-α-pinene with $[\alpha]_D^{20} = -43.7$ as in equation (5).



(5)

Conclusion

The replacement of sodium by ammonium cation offers two advantages:

1. The hydrogen transfer reaction can be performed without using a solvent. Highly sterically hindered alkenes such as $\Delta^{9,10}$-octalin, α- and β-pinene are reduced with the system $H_2PO_2^-NH_4^+$/Pd-C in high yield at room temperature in an open vessel.

2. Ammonium (NH_4^+) acts as a proton donor. The competition between the protonolysis to give hydrogen gas and the transfer hydrogenation plays an important role in the chemoselective reduction.

Experimental

IR: Perkin Elmer 682. — MS: H.P. 5970 Mass Selective Detector, 70 eV, connected with a H.P. 5890 gas chromatograph. — GLC: Carlo Erba HRGC 5300 Mega Series.

Hypophosphorous acid (50 wt %, water) was purchased from Fluka. Other reagents were obtained commercially and used without further purification. Solvents were appropriately dried and purified.

$H_2PO_2^-NH_4^+ \cdot H_2O$: Ammonia gas was slowly passed into 100 ml of aqueous hypophosphorous acid (50%) until white crystals began to precipitate. The solution was then allowed to stand at 10−15°C for 5 h. The white precipitate was filtered and analyzed. Yield: 52 g (56% based on H_3PO_2). — $H_6NO_2P \cdot H_2O$ (101.0): calcd. H 7.98, N 13.86, P 30.65; found H 7.92, N 13.98, P 30.52.

$H_2PO_2^-NH_4^+ \cdot H_2O$ is slightly deliquescent in air after 3−4 months leading to a decrease of the reducing ability. The salt must

therefore be stored in a tightly closed flask. It is soluble in water, *N,N*-dimethylacetamide and slightly soluble in ethanol and methanol, insoluble in THF, ether, benzene.

Reduction of Methylenecyclohexane. Conditions A: $H_2PO_2^-NH_4^+ \cdot H_2O$ (3.21 g, 31.8 mmol) was added to a solution of methylenecyclohexane (1.52 ml, 12.6 mmol) in 20 ml of benzene. The suspension was stirred magnetically at room temp. in a stream of argon for 5 min. Subsequently Pd-C (10%, 0.202 g, 0.19 mmol) was added, and evolution of hydrogen was observed. The course of the reaction was monitored by GLC with a fused silica capillary Supelcowax column (30 m, 0.32 mm, 0.25 μm) by comparison with authentic samples of methylene- and methylcyclohexane and 1-methyl-1-cyclohexene. After 2.5 h, 20 ml of ether was added, the catalyst was filtered from the suspension, the filtrate was washed with water, dried with $MgSO_4$, and concentrated to give 1.08 g (87.3%) of methylcyclohexane, b.p. 99–101 °C.

Conversion of (−)-β-Pinene to (−)-α-Pinene. Conditions B: $H_2PO_2^-NH_4^+ \cdot H_2O$ (3.68 g, 36.4 mmol) in 30 ml of degassed distilled water was added to a solution of (−)-β-pinene (2 ml, 12.6 mmol) in 20 ml of benzene. The mixture was stirred with a magnetic bar at a constant rate of 390 rpm under argon for 5 min. Then Pd-C (10%, 0.202 g, 0.19 mmol) was added. Every 10 min a small amount of the benzene layer was extracted and analyzed by GC-MS (H.P.I. column = 12 m, 0.2 mm, 0.32 μm). After 30 min 20 ml of ether was added, the catalyst was filtered from the mixture, the combined organic layer was washed with water and dried with $MgSO_4$. Then the solvent was evaporated to give 1.69 g (98.4%) of (−)-α-pinene, $[\alpha]_D^{20} = -43.7$ (neat) (99.1% purity determined by GLC). – MS, *m/z* (%): 136 (2.3) [M^+], 121 (10) [$M^+ - CH_3$], 93 (100) [$M^+ - C_3H_7$].

Reduction of α-Pinene. Conditions C: A mixture of α-pinene (2 ml, 12.6 mmol), $H_2PO_2^-NH_4^+ \cdot H_2O$ (3.21 g, 31.8 mmol), and Pd-C (10%, 0.202 g, 0.19 mmol) was stirred at room temp. under argon. The progress of the reaction was monitored by GC-MS in comparison with authentic samples of α-pinene, β-pinene, *cis*- and *trans*-pinane. After 3.5 h the products were isolated as described above. Yield: 1.68 g (96.5%) of pinanes (68.47% *cis* and 30.34% *trans*). – MS, *m/z* (%): *cis*-Pinane 138 (1.6) [M^+], 123 (31) [$M^+ - CH_3$], 95 (100) [$M^+ - C_3H_7$], *trans*-pinane 138 (2.6) [M^+], 123 (41) [$M^+ - CH_3$], 95 (100) [$M^+ - C_3H_7$].

Reduction of β-Ionone. Conditions C: A mixture of β-ionone (**5A**) (2.56 ml, 12.6 mmol), $H_2PO_2^-NH_4^+ \cdot H_2O$ (3.21 g, 31.8 mmol) and Pd-C (10%, 0.202 g, 0.19 mmol) was stirred at room temp. under argon. The progress of reaction was monitored by GC-MS, and the products were isolated as described above. After 12 h, 2.03 g of tetrahydroionone was obtained [100% tetrahydroionone (**5D**) and traces of dihydroionones (**5B**, **5C**) as determined by GLC].

5B: MS, *m/z* (%): 194 (7) [M^+], 179 (9) [$M^+ - CH_3$], 109 (94) [$M^+ - C_5H_9O$], 95 (100) [$M^+ - C_6H_{11}O$]. – ^{1}H NMR ($CDCl_3$): δ = 6.04 (d, *J* = 15 Hz, 1 H, olefinic), 6.8 (dd, *J* = 12 Hz, 1 H, olefinic), 2.1 (s, 3H, $COCH_3$). – IR (nujol): $\tilde{\nu} = 1690$ cm^{-1} (C=O), 1615 (C=C).

5C: MS, *m/z* (%): 194 (4.5) [M^+], 179 (5.8) [$M^+ - CH_3$], 123 (28) [$M^+ - C_4H_7O$], 121 (13.7) [$M^+ - C_4H_9O$], 109 (84.5) [$M^+ - C_5H_9O$], 95 (100) [$M^+ - C_6H_{11}O$]. – ^{1}H NMR ($CDCl_3$): δ = 2.26 (t, *J* = 8.5 Hz, 2H, $-CH_2CO-$), 2.51 (t, *J* = 8.5 Hz, 2H, $-CH_2CH_2CO-$), 2.15 (s, 3H, $COCH_3$), 1.91 (t, *J* = 6.3, 2H), 1.56 (s, 3H, CH_3), 1.41 (m, 2H), 0.96 (s, 6H, 2 CH_3). – IR (nujol): $\tilde{\nu} = 1710$ cm^{-1} (C=O), 1620 (C=C).

5D: MS, *m/z* (%): 196 (12.6) [M^+], 181 (11) [$M^+ - CH_3$], 123 (100) [$M^+ - C_4H_9O$], 95 (86) [$M^+ - C_6H_{13}O$]. – IR (nujol): $\tilde{\nu} = 1710$ cm^{-1} (C=O).

Semihydrogenation of Tolan to cis-Stilbene. Condition B$_3$: A solution of $H_2PO_2^-NH_4^+ \cdot H_2O$ (3.68 g, 36.4 mmol) in 30 ml of degassed water was added to a solution of tolan (2.3 ml, 12.64 mmol) and quinoline (0.05 ml, 0.43 mmol) in 20 ml of benzene. The mixture was stirred in a stream of argon for 5 min, then Pd-C (10%, 0.19 mmol, 0.202 g) was added. The course of the reaction was monitored by GC-MS with (H.P.I. column = 12 m, 0.2 mm, 0.32 μm). After 12 h, *cis*-stilbene was isolated as described above. Yield: 2.2 g of stilbene (91% of *cis*-stilbene, 8.5% of *trans*-stilbene and 0.5% of 1,2-diphenylethane as determined by GLC). – MS, *m/z* (%): 1,2-Diphenylethane 182 (17) [M^+], 91 (100) [$M^+ - C_6H_5CH_2$], *cis*-stilbene 180 (93) [M^+], 179 (100) [$M^+ - H$], 102 (8) [$M^+ - C_6H_6$].

[1] B. Th. Khai, A. Arcelli, *J. Org. Chem.* **1989**, *54*, 949–953.
[2] [2a] R. A. W. Johnstone, A. H. Wilby, *Chem. Rev.* **1985**, *85*, 129–170. – [2b] G. Zassinovich, G. Mestroni, S. Gladiali, *Chem. Rev.* **1992**, *92*, 1051–1069. – [2c] H. Brunner, W. Leitner, *Angew. Chem.* **1988**, *100*, 1231; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1180–1181. – [2d] B. Th. Khai, A. Arcelli, *J. Organomet. Chem.* **1986**, *309*, C36. – [2e] J. M. Tour, Sh. L. Pendalwar, *Tetrahedron Lett.* **1990**, 4719–4722. – [2f] N. A. Cortese, R. F. Heck, *J. Org. Chem.* **1978**, *43*, 3985–3987.
[3] E. C. Ashby, J. J. Lin, *J. Org. Chem.* **1978**, *43*, 2567–2572.
[4] [4a] S. K. Chung, *J. Org. Chem.* **1979**, *44*, 1014–1015. – [4b] N. Satyanarayna, M. Periasamy, *Tetrahedron Lett.* **1984**, *25*, 2501–2504.
[5] We have not found an example of the reduction of α-pinene with hydrogen donors at room. temperature. Only one example has been reported (G. Brieger, T. J. Nestrick, Tz. H. Fu, *J. Org. Chem.* **1979**, *44*, 1876–1878), where special conditions are applied: with limone as a solvent at reflux temperature, α-pinene is converted to a mixture of products. This result can be explained as follows: [5a] The cyclobutane ring of pinene is easily cleaved to camphene, terpinolene, etc. (C. M. Williams and D. Whittaker, *J. Chem. Soc., Chem. Commun.* **1970**, 980–981). – [5b] There is a competition between desorption of hydrogen to give hydrogen gas and transfer hydrogenation as illustrated by equ. (2). These factors are responsible for the difficult reduction of α-pinene with hydrogen donors.
[6] R. N. Mehrotra, L. J. Kirschenbaum, *Inorg. Chem.* **1989**, *28*, 4327–4330.
[7] J. P. Collman, L. S. Hegedus, J. R. Norton, R. G. Finke, *Principles and Applications of Organotransition Metal Chemistry*, University Science Books, Mill Valley, **1987**, part II, p. 536.
[8] J. F. Sauvage, R. H. Baker, A. S. Hussey, *J. Am. Chem. Soc.* **1961**, *83*, 3874–3877.
[9] W. Cocker, P. V. R. Shannon, P. A. Staniland, *J. Chem. Soc. (C)*. **1966**, 41–47.
[10] J. P. Neilan, R. M. Laine, N. Cortese, R. F. Heck, *J. Org. Chem.* **1976**, *41*, 3455–3460.
[11] R. A. W. Johnstone, A. H. Wilby, *Tetrahedron* **1981**, *37*, 3667–3670.
[12] A. B. McEwen, M. J. Guttieri, W. F. Maier, R. M. Laine, Y. Shvo, *J. Org. Chem.* **1983**, *48*, 4438–4439.

[44/93]