Angewandte
Chemie

Alkene Hydrazination

Catalytic Hydrohydrazination of a Wide Range of Alkenes with a Simple Mn Complex**

*Jérôme Waser and Erick M. Carreira**

Heterofunctionalization reactions of olefins are highly desirable processes as they convert readily available starting materials into value-added building blocks for chemical synthesis.[1–4] In this respect, the best illustration is the role played by epoxides and diols in chemical synthesis which arises from the availability of a plethora of epoxidation reagents and catalysts[2,5,6] and advances in olefin dihydroxylation.[7] However, despite the numerous processes for the

---

[*] J. Waser, Prof. Dr. E. M. Carreira
Laboratorium für Organische Chemie
ETH Hönggerberg, HCI H335
8093 Zürich (Switzerland)
Fax: (+41) 1-632-1328
E-mail: carreira@org.chem.ethz.ch

[**] This research was supported by a Swiss National Science Foundation Grant.

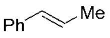
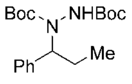
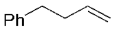
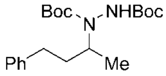
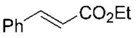
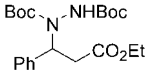
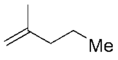
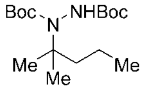
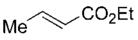
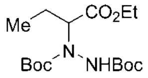
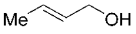
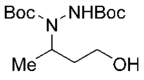
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

DOI: 10.1002/anie.200460811

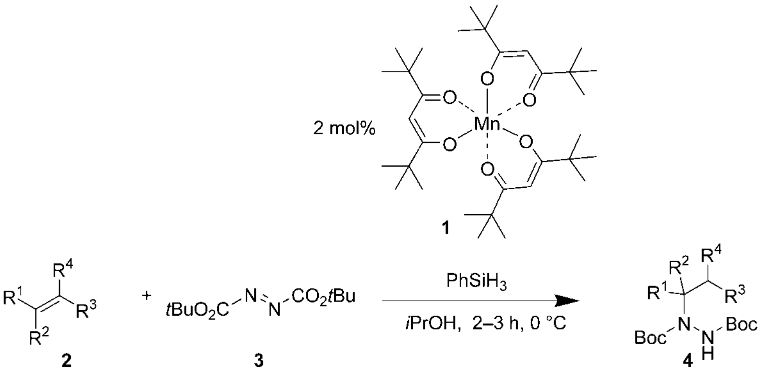
introduction of oxygen functions, there are relatively few methods available for the introduction of nitrogen-containing functional groups.[8–13] We have recently reported a Co complex[14] that mediates the conversion of simple olefins into the corresponding hydrazides with azodicarboxylates as the nitrogen source.[15] The hydrohydrazination reaction complements existing methods that involve azodicarboxylates to access hydrazine derivatives,[16–24] which are useful building blocks and precursors to free amines.[25,26] In our continuing interest in discovery and development of additional new catalysts for such a process we have identified a simple Mn^{III} complex, namely $[\mathrm{Mn(dpm)_3}]$ (**1**),[27,28] which catalyzes the reaction of azodicarboxylates and alkenes [Eq. (1)] (Boc = *tert*-butoxycarbonyl) with much higher activity and larger scope than the known Co catalysts we had previously studied. The introduction of a new catalytic system that differs both in metal and ligand to carry out the hydrohydrazination reaction sets the stage for further investigations of the process, including the development of its stereoselective counterpart.

In the earlier study involving the use of a Co catalyst for olefin hydrohydrazination we noted that substrates such as cyclohexene, crotyl alcohol, and tetrasubstituted alkenes were not sufficiently reactive to lead to product formation in useful yields; moreover, full conversion of the starting material was observed only with PhSiH$_3$ as reductant, even with the most reactive substrates. We subsequently focused our efforts in identifying improved conditions and catalysts, with particular attention on enhanced reactivity in order to expand the scope.

Table 1: Hydrohydrazination reactions of simple alkenes with $[\mathrm{Mn(dpm)_3}]$ (**1**).

Entry	Alkene	Product[a]	Regioselectivity[b]	Yield [%][c]
1			> 20:1	94
2			5.5:1	94
3			9:1	87
4			> 20:1	86
5			> 20:1	88
6			1.8:1	90

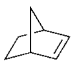
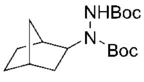
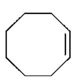
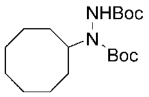
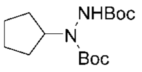
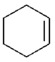
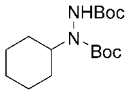
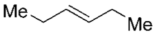
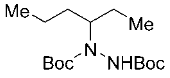
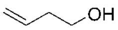
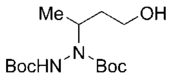
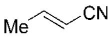
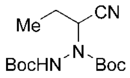
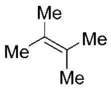
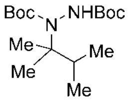
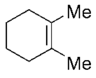
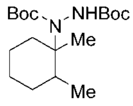
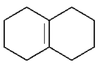
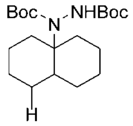
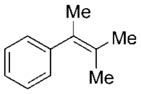
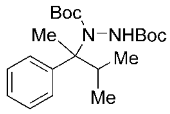
[a] Major product shown. [b] With the Co catalyst, the regioselectivity was generally higher than 20:1, except for entry 6 (3:1). [c] Standard conditions: alkene (0.5 mmol), PhSiH$_3$ (0.5 mmol), **3** (0.75 mmol), catalyst **1** (2 mol%), 2-propanol (2.5 mL), N$_2$, 0 °C.



A broad-based study of numerous metal salts and complexes led us to examine $[\mathrm{Mn(dpm)_3}]$ (**1**).[29] This complex has been studied in the hydration of α,β-unsaturated ketones and esters to give α-hydroxyketones and -esters, respectively,[27,28,30] as well as for epoxidation of alkenes,[31] reduction of ketones,[32] and conjugate reduction of α,β-unsaturated ketones.[33] Based on our speculations regarding the similarities between the metal-catalyzed functionalization of alkenes using oxygen and phenylsilane[27,28,34] and the hydrohydrazination reaction, we hypothesized that this complex could also catalyze the reaction of alkenes and azodicarboxylates. Indeed, as shown in Table 1, a selection of olefins that serve well in the Co-catalyzed reactions (catalyst (5 mol%), PhSiH$_3$ (1.0 equiv), di-*tert*-butyl azodicarboxylate (1.5 equiv), ethanol, 23 °C) also afford hydrazide adducts when $[\mathrm{Mn(dpm)_3}]$ (2 mol%) together with PhSiH$_3$ (1.0 equiv) and di-*tert*-butyl azodicarboxylate (**3**; 1.5 equiv) are employed at 0 °C in 2-propanol.[35] The adducts are obtained for 1,2- along with 1,1-disubstituted alkenes and α,β-unsaturated esters in 86–94% yield (Table 1, entries 1–5), which is comparable with the Co system (66–92%) but with shorter reaction times (2–3 h at 0 °C instead of 5–20 h at 23 °C). Interestingly, crotyl alcohol (Table 1, entry 6), which had proven to be a rather poor substrate with the Co system (25% yield, 3:1 mixture of regioisomers) furnished a 1.8:1 mixture of the bis-*N*-Boc-protected 3- and 2-hydrazinobutan-1-ol in 90% combined yield.

The initial set of reactions described above proved revealing in a number of important ways: 1) wider scope; 2) higher yields; and, perhaps most importantly, 3) the rate of product formation with 5 mol% of $[\mathrm{Mn(dpm)_3}]$ (**1**) was considerably higher (5 min, 23 °C)[35] than that observed for the Co catalyst (5 mol%, 6–20 h, 23 °C) under otherwise identical conditions. These observations led us to reexamine specifically other olefins that furnished lower yields in the earlier study. Table 2 illustrates the hydrohydrazination reaction of additional substrates for the Mn-catalyzed reaction along with a head-to-head comparison with the results for the Co-catalyzed reaction. Interestingly, for those cases that had given products in 62–74% yield with the Co catalyst (cyclopentene, norbornene, cyclooctene), the hydrazides could now be isolated in > 94% yield and it was never necessary to use more than 1.5 equivalents of di-*tert*-butyl

Table 2: Hydrohydrazination reactions of more-challenging alkenes.

Entry	Alkene	Product	Yield [%] Co[a]	Yield [%] Mn[b]
1			66	98
2			62	95
3			74	94
4			24	90
5			16	66
6			22[c]	72[c]
7			44[c]	45[c]
8			16	78
9			18	79
10			10	74
11			13[c]	51[c]

[a] Standard conditions: alkene (0.5 mmol), $PhSiH_3$ (0.5 mmol), **3** (0.75 mmol), Co catalyst[14] (5 mol%), ethanol (2.5 mL), N_2, 23 °C. [b] Standard conditions: alkene (0.5 mmol), $PhSiH_3$ (0.5 mmol), **3** (0.75 mmol), catalyst **1** (2 mol%), 2-propanol (2.5 mL), N_2, 0 °C. [c] Only one regioisomer was observed.

azodicarboxylate (**3**) as was the case of cobalt (Table 2, entries 1–3). The advantages of the Mn-catalyzed process are best appreciated, however, upon comparing substrates such as cyclohexene, 3-hexene, and buten-3-ol (Table 2, entries 4–6), which had previously afforded products in only 16–24 % yield with the Co catalyst. Under catalysis with [Mn(dpm)$_3$] (**1**) the corresponding adducts can now be isolated in much higher yields (72–90 %). Only acrylonitrile proved recalcitrant to improvement (44 % with Co and 45 % with Mn) (Table 2, entry 7). Given the promising results, we decided to examine the sterically most challenging substrates for heterofunctionalization, namely tetrasubstituted olefins, which under Co catalysis afford products in 10–16 % yield. Remarkably, for the tetrasubstituted alkenes examined (2,3-dimethyl-2-butene, 1,2-dimethylcyclohexene, 9,10-dehydrodecalin, and 3-methyl-2-phenyl-2-butene) the highly substituted hydrohydrazination adducts could be isolated in useful yields (51–79 %; Table 2, entries 8–11).

In the studies conducted to date, we have examined the use of $PhSiH_3$ as the reductant, because it had proven most convenient and effective in the Co-catalyzed process. Given the observation of unique reactivity for the Mn complex, we proceeded to investigate whether this catalyst would permit the use of other silanes. We were pleased to note that in the hydrohydrazination reaction of 4-phenylbutene with [Mn(dpm)$_3$] (2 mol %) the hydrazide adduct is obtained when using PMHS (poly(methylhydrosiloxane)), a considerably less-expensive and more-stable silane, in 88 % yield in 12 h at 23 °C, whereas the Co system showed less than 20 % conversion after 24 h when using this silane.

In summary, with [Mn(dpm)$_3$] (**1**) we have identified a new catalyst class for the hydrohydrazination reaction of alkenes. The salient features of this catalyst system are the broad substrate scope of the process (to include tetrasubstituted alkenes), faster reaction rates (minutes), higher yields, and the compatibility with the less-expensive PMHS reductant. In this expanded scope, the hydrohydrazination process allows access to a wider range of structurally diverse building blocks, which should find use for drug synthesis. The availability of another class of complexes that catalyzes this process also offers several new avenues for the development of versatile and improved transformations that may be amenable to development into the corresponding asymmetric transformations. Studies in this respect are ongoing and their results will be reported as they become available.

Received: May 27, 2004 [Z460811]

Keywords: alkenes · homogeneous catalysis · hydrazination · manganese · silanes

---

[1] S. Patai, Z. Rappoport, *The Chemistry of Double-Bonded Chemical Groups*, Wiley, New York, **1997**.

[2] A. S. Rao, R. A. Johnson, K. B. Sharpless, A. H. Haines, J. Tsuji, J. E. G. Kemp, K. A. Swiss, D. C. Liotta, S. Torii, T. Inokuchi, D. G. Lee, T. Chen in *Comprehensive Organic Synthesis*, *Vol. 7* (Eds.: B. M. Trost, I. Fleming, S. V. Ley), Pergamon, Oxford, **1991**, p. 357.

[3] A. Togni, H. Grützmacher, *Catalytic Heterofunctionalization. From Hydroamination to Hydrozirconation*, Wiley-VCH, Weinheim, **2001**.

[4] *Comprehensive Organic Synthesis*, *Vol. 4* (Eds.: B. M. Trost, I. Fleming, M. F. Semmelhack), Pergamon, Oxford, **1991**.

[5] R. A. Johnson, K. B. Sharpless, in *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), Wiley-VCH, Weinheim, **2000**, p. 231.

[6] T. Katsuki in *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), Wiley-VCH, Weinheim, **2000**, p. 287.

[7] R. A. Johnson, K. B. Sharpless in *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), Wiley-VCH, Weinheim, **2000**, p. 357.

[8] A. Ricci, *Modern Amination Methods*, Wiley-VCH, Weinheim, **2000**.

[9] B. R. Brown, *The Organic Chemistry of Aliphatic Nitrogen Compounds*, Oxford University Press, New York, **1994**.

[10] D. Enders, U. Reinhold, *Tetrahedron: Asymmetry* **1997**, *8*, 1895.

[11] S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069.

[12] P. W. Roesky, T. E. Müller, *Angew. Chem.* **2003**, *115*, 2812; *Angew. Chem. Int. Ed.* **2003**, *42*, 2708.

[13] M. Nobis, B. Drießen-Hölscher, *Angew. Chem.* **2001**, *113*, 4105; *Angew. Chem. Int. Ed.* **2001**, *40*, 3983.

[14] Sodium-bis-[*N*-salicylidene-2-amino-isobutyrato]-cobaltate(III).

[15] J. Waser, E. M. Carreira, *J. Am. Chem. Soc.* **2004**, *126*, 5676.

[16] P. S. Baran, C. A. Guerrero, E. J. Corey, *Org. Lett.* **2003**, *5*, 1999.

[17] M. A. Brimble, C. H. Heathcock, *J. Org. Chem.* **1993**, *58*, 5261.

[18] D. A. Evans, T. C. Britton, R. L. Dorow, J. F. Dellaria, *J. Am. Chem. Soc.* **1986**, *108*, 6395.

[19] D. A. Evans, T. C. Britton, R. L. Dorow, J. F. Dellaria, *Tetrahedron* **1988**, *44*, 5525.

[20] D. A. Evans, S. G. Nelson, *J. Am. Chem. Soc.* **1997**, *119*, 6452.

[21] D. A. Evans, D. S. Johnson, *Org. Lett.* **1999**, *1*, 595.

[22] C. Gennari, L. Colombo, G. Bertolini, *J. Am. Chem. Soc.* **1986**, *108*, 6394.

[23] L. A. Trimble, J. C. Vederas, *J. Am. Chem. Soc.* **1986**, *108*, 6397.

[24] B. List, *J. Am. Chem. Soc.* **2002**, *124*, 5656.

[25] E. W. Schmidt, *Hydrazine and Its Derivatives, Preparation, Properties, Applications*, 2nd ed., Wiley-Interscience, New York, **2001**.

[26] U. Ragnarsson, *Chem. Soc. Rev.* **2001**, *30*, 205.

[27] S. Inoki, K. Kato, S. Isayama, T. Mukaiyama, *Chem. Lett.* **1990**, 1869.

[28] P. Magnus, A. H. Payne, M. J. Waring, D. A. Scott, V. Lynch, *Tetrahedron Lett.* **2000**, *41*, 9725.

[29] dpm = dipivaloylmethanato. Both [Mn(dpm)$_2$] and [Mn(dpm)$_3$] proved equally active in the hydrohydrazination reaction, but as the former is very air sensitive, the more-stable [Mn(dpm)$_3$] complex was preferentially used.

[30] P. Magnus, D. A. Scott, M. R. Fielding, *Tetrahedron Lett.* **2001**, *42*, 4127.

[31] T. Yamada, K. Imagawa, T. Mukaiyama, *Chem. Lett.* **1992**, 2109.

[32] P. Magnus, M. R. Fielding, *Tetrahedron Lett.* **2001**, *42*, 6633.

[33] P. Magnus, M. J. Waring, D. A. Scott, *Tetrahedron Lett.* **2000**, *41*, 9731.

[34] S. Isayama, T. Mukaiyama, *Chem. Lett.* **1989**, 1071.

[35] Conducting the reaction with 5 mol% catalyst at 23 °C gave full conversion after 5 min, but the regioselectivity was lower in certain cases (e.g. 4-phenylbutene give a 3:1 mixture of secondary/primary hydrazide at 23 °C versus a 5.5:1 mixture at 0 °C).