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Hydrazines and Azides via the Metal-Catalyzed Hydrohydrazination and Hydroazidation of Olefins

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Abstract: The discovery, study, and implementation of the Co- and Mn-catalyzed hydrohydrazination and hydroazidation reactions of olefins are reported. These reactions are equivalent to direct hydroaminations of C−C double bonds with protected hydrazines or hydrazoic acid but are based on a different concept in which the H and the N atoms come from two different reagents, a silane and an oxidizing nitrogen source (azodicarboxylate or sulfonyl azide). The hydrohydrazination reaction using di-*tert*-butyl azodicarboxylate is characterized by its ease of use, large functional group tolerance, and broad scope, including mono-, di-, tri-, and tetrasubstituted olefins. Key to the development of the hydroazidation reaction was the use of sulfonyl azides as nitrogen sources and the activating effect of *tert*-butyl hydroperoxide. The reaction was found to be efficient for the functionalization of mono-, di-, and trisubstituted olefins, and only a few functional groups are not tolerated. The alkyl azides obtained are versatile intermediates and can be transformed to the free amines or triazoles without isolation of the azides. Preliminary mechanistic investigations suggest a rate-limiting hydrocobaltation of the alkene, followed by an amination reaction. Radical intermediates cannot be ruled out and may be involved.

Introduction

Olefins are inexpensive and readily available starting materials for organic synthesis. For this reason, the direct heterofunctionalization of the C−C double bond has been the focus of research for many years.[1] Most of the early methods were based on the use of stoichiometric reagents. The advances of catalysis in the past decades have allowed the development of economically and environmentally improved processes,[2] with particular success in the introduction of oxygen functionalities on alkenes, as examplified by Sharpless' epoxidation[3] and dihydroxylation[4] reactions. Progress in the amination of olefins has been much slower, and, thus, this transformation is much less selective and efficient than the corresponding oxyfunctionalization reactions.[1b] Because of the ubiquity of amine-derived functional groups in natural products and pharmaceuticals,[5] a fast and general access to amines would be highly desirable.

The olefin-hydroamination reaction, the direct addition of amines across C−C double bonds, represents a seemingly straightforward process to access amines.[6] Although the addition of amines to alkenes is thermodynamically neutral or exothermic, this reaction typically displays a relatively high activation barrier,[6e] and only the reaction with certain electron deficient olefins occurs spontaneously.[7] Whereas heterogeneous catalysts are used in industrial processes,[6b] the extreme conditions needed (>100 bar ammonia, >200 °C) demand special equipment. Furthermore, any effective hydroamination method must deal with the problem of regio- and stereoselectivity.[8] Given these limitations, the majority of academic research has focused on well-defined homogeneous systems. The first report on a hydroamination reaction of olefins was published in 1932 by Hickinbottom, who described the direct reaction of arylamines with cyclohexene, styrene, and certain dienes at high temperature (250−300 °C) in very low yields (<20%).[9] Later, strong bases were found to catalyze the hydroamination reaction.[10] The first transition-metal-catalyzed olefin hydroamination was reported in 1971 by Coulson using Rh salts.[11] Since this initial report,

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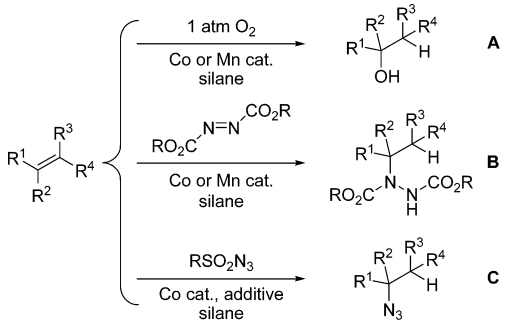
(10) For a review, see: (a) Seayad, J.; Tillack, A.; Hartung, C. G.; Beller, M. *Adv. Synth. Catal.* **2002**, *344*, 795. For a recent example of an application of base-promoted hydroamination in total synthesis, see: (b) Trost, B. M.; Tang, W. P. *J. Am. Chem. Soc.* **2002**, *124*, 14542.
(11) Coulson, D. R. *Tetrahedron Lett.* **1971**, *12*, 429.

two catalyst classes have proven efficient in the hydroamination reaction: lanthanide and early metal-based catalysts are typically used for *intra*molecular hydroaminations,[12] whereas for late transition metals, the preferred substrates are Michael acceptors,[13] olefins activated via conjugation (vinylarenes and dienes) or ring-strain (norbornene) for *inter*molecular hydroaminations.[14] Despite encouraging recent progress,[15] the search for a truly general method for the hydroamination of olefins is still ongoing.

To avoid the difficulties inherent to the hydroamination approach, more active electrophilic amination reagents had been devised, which allow the functionalization of simple carbon nucleophiles under mild conditions.[16] Among these reagents, nitroso compounds,[17] azides,[18] and especially azodicarboxylates[16,19] have emerged as useful nitrogen sources. However, with the exception of Diels−Alder[20a−d] and ene reactions,[20e−g] such reagents cannot be used for the direct functionalization of nonnucleophilic C−C double bonds.

The hydration of olefins[21] is the oxygen analogue of the hydroamination reaction and could as such serve as a source of inspiration for the development of new hydroamination methods.

Scheme 1. Hydration, Hydrohydrazination, and Hydroazidation of Olefins



However, there are no really general methods for the direct addition of an O−H bond onto a C−C double bond.[21] In 1989, Mukaiyama and Isayama developed a new concept for the hydration of olefins: instead of activating a single O−H bond for addition, they decided to use simultaneously a hydride source and an oxygen source.[22] This stepwise approach allows the use of much more reactive reagents, with the hope of overriding the kinetic barrier to the functionalization of nonactivated alkenes. However, this gain goes together with formidable challenges for the development of an efficient process. Three undesired pathways must be taken into account: overoxidation to ketone, over-reduction to the alkane, and direct reaction of the oxidant with the reductant. With the choice of silanes or alcohols as reductants, molecular oxygen as oxidant, and Co or Mn as catalyst, Mukaiyama and Isayama were able to manage these difficulties (Scheme 1**A**).

Upon examination of Mukaiyama's work, a question arises: would it be possible to combine the metal-mediated activation of otherwise nonactivated olefins with an electrophilic/oxidizing nitrogen source, while avoiding direct reduction of the nitrogen-transfer reagent?[23] Indeed, we have developed such an approach both successful with azodicarboxylates and sulfonyl azides as nitrogen sources, allowing the development of the hydrohydrazination[24] (Scheme 1**B**) and hydroazidation[25] (Scheme 1**C**) of olefins. Herein, we provide a full account of our work, including effect of catalyst structure, reaction conditions, process optimization, and expanded scope. Furthermore, investigations on the reaction mechanism are described.

Results and Discussion

Co-Catalyzed Hydrohydrazination Reaction. Alkyl hydrazines are useful precursors to amines in the assembly of synthetic building blocks and have been broadly used for the elaboration of heterocycles omnipresent in pharmaceuticals.[26] The substitu-

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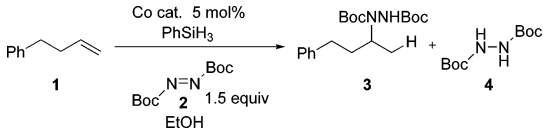
Table 1. Simple Co Complexes Tested in the Hydrohydrazination of 4-Phenylbutene **1**



entry	complex	time[a]	yield of **3**[b]
1	none	48 h	0%
2	$CoCl_2 \cdot 6H_2O$	4 h	3%
3	$Co(OAc)_2$	2 h	<5%
4	$Co(NO_3)_2 \cdot 6H_2O$	8 h	<5%
5	$Co(acac)_2$	8 h	5%
6	$Co(modp)_2$	48 h	<5%
7	$Co(dpm)_2$	4 h	<5%

[a] The reaction was stopped when all di-*tert*-butylazodicarboxylate (**2**) was consumed. [b] Standard conditions: 0.50 mmol 4-phenylbutene **1**, 0.50 mmol $PhSiH_3$, 0.75 mmol di-*tert*-butylazodicarboxylate (**2**), 5 mol % catalyst, and 2.5 mL of EtOH at 23 °C under argon.

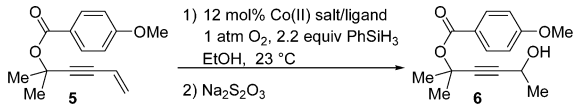
tion of alkyl halides with hydrazine has been used for a long time for the synthesis of alkylated hydrazines.[26] More recently, other approaches, including asymmetric variations such as nucleophilic additions to hydrazones[27] or azodicarboxylates[16] and conjugate additions of hydrazines to Michael acceptors have been developed. However, the formation of hydrazines from nonactivated olefins have been limited to cycloaddition or ene reactions with azodicarboxylates,[20e−f] and the synthesis of *N*-alkyl hydrazides by direct functionalization of the C−C double bond of unactivated olefins was unprecedented prior to this work.

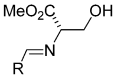
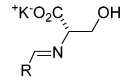
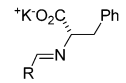
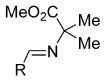
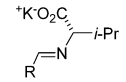
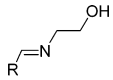
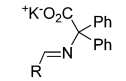
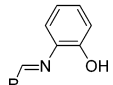
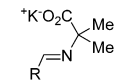
At the beginning of our studies, we decided to examine the functionalization of 4-phenylbutene (**1**) as a prototype for monosubstituted unactivated olefins, as the presence of the phenyl group in a remote position was expected to show no significant effect on the reaction but confers UV activity and a lower volatility to this substrate. Moreover, **1** was known to be a good substrate in Mukaiyama's hydration reaction.[22] One of the major hurdles in the development of an efficient hydrohydrazination reaction becomes apparent when considering the effect of simple Co salts in the hydrohydrazination of 4-phenylbutene **1** with di-*tert*-butyl azodicarboxylate (**2**; Table 1). In the absence of catalyst, no reaction occurs (entry 1), but simple Co salts all promote the direct reduction of azodicarboxylate **2** to hydrazine **4** instead of the desired hydrohydrazination reaction (entries 2−4). Moreover, $Co(acac)_2$, $Co(modp)_2$, and $Co(dpm)_2$,[28] which are efficient catalysts for the related hydration reaction,[22] also favor the formation of **4** (entries 5−7). Traces (5%) of the desired hydrohydrazination product **3** could be isolated only in the case of $Co(acac)_2$ (entry 5). Thus, despite the seeming similarity between the hydrohydrazination and Mukaiyama hydration, the parallels are limited.

From these results, it became clear that the acetylacetonate ligand scaffold was not well-suited for the hydrohydrazination reaction. In ongoing investigations of the Mukaiyama hydration of enynes, we had found that Schiff-base ligands were also efficient catalysts (Table 2). The Co(II) complex derived from ligand **7** had been introduced by Iqbal and co-workers to promote the epoxidation and allylic oxidation of olefins with oxygen[29] and is easily obtained by simply mixing ligand **7** and $CoCl_2$ in CH_3CN. This complex had proven efficient in the hydration reaction but was unstable under the reactions requiring high catalyst loadings (>10%) to achieve full conversion. Subsequent systematic variation of the amine moiety of the ligand showed a strong effect on the outcome of the reaction (Table 2). Modification of the side chain of the amino acid (entries 2 and 3) or removal of the ester group (entries 4 and 5) did not lead to more active or stable catalysts, but ligands **12**−**16**, bearing a free carboxylate group, were stable under the reaction conditions (entries 6−10). Among those, the use of Schiff-base ligand **16** led to unique reactivity, allowing full conversion of enyne **5** to alcohol **6** in 30 min.

The behavior of the Co system derived from **16** was peculiar: all the Co(II) complexes synthesized from ligands **7**−**11** were green. In contrast, the solution of **16** and $Co(NO_3)_2 \cdot 6H_2O$ turned partially dark-red during its synthesis. We hypothesized that this change of color was an indication of a change in the oxidation state of Co from +II to +III, thus, the synthetic protocol was altered to obtain the Co(III) mixture

Table 2. Influence of Ligand Structure in the Hydration of **5**[31]



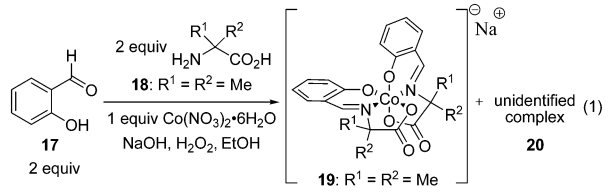
entry	ligand[a,b]	conversion time[c]	entry	ligand	conversion time
1	 **7**	>95% 2 h	**6**	 **12**	>95% 5 h
2	 **8**	>95% 5 h	**7**	 **13**	20% 24 h
3	 **9**	20% 24 h	**8**	 **14**	20% 24 h
4	 **10**	50% 24 h	**9**	 **15**	>95% 4 h
5	 **11**	>95% 2 h	**10**	 **16**	>95% 30 min

[a] Two equiv of ligands **7**−**11** and **16** were mixed with 1 equiv of $CoCl_2$ in acetonitrile for 20 h, followed by solvent removal. Ligands **12**−**16** were formed in situ from the amino acid, salicylaldehyde, and KOH in EtOH; addition of 0.50 equiv of $Co(NO_3)_2 \cdot 6H_2O$, oxidation with H_2O_2, and solvent removal gave the Co catalyst. [b] R = 2-hydroxyphenyl. [c] Standard conditions: 0.04 mmol enyne **5**, 0.12 mmol $PhSiH_3$, 12 mol % catalyst, 1 atm O_2, and 0.7 mL of EtOH at 23 °C.

(26) Ragnarsson, U. *Chem. Soc. Rev.* **2001**, *30*, 205.
(27) (a) Kobayashi, S.; Ishitani, H. *Chem. Rev.* **1999**, *99*, 1069. (b) Sugiura, M.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 5176.
(28) acac = acetylacetonato, dpm = dipivaloylmethanato, modp = 1-morpholinocarbamoyl-4,4-dimethyl-1,3-pentanedionato.
(29) Punniyamurthy, T.; Bhatia, B.; Reddy, M. M.; Maikap, G. C.; Iqbal, J. *Tetrahedron* **1997**, *53*, 7649.
(30) Burrows, R. C.; Bailar, J. C. *J. Am. Chem. Soc.* **1966**, *88*, 4150.
(31) The choice of a *para*-methoxybenzoyl protecting group was motivated by its favorable properties for monitoring the reaction (high UV activity, low volatility).

directly. The first protocol we examined to effect the synthesis of the Co(III) complexes was based on a reported procedure of Bailar and Burrows for the synthesis of Co(III) coordination complexes with ligands derived from salicylaldehyde (**17**) and amino acids.[30] In the Bailar one-pot procedure, the template condensation of salicylaldehyde **17** and an α-monosubstituted amino acid (in eq 1, $R^1 = H$ and $R^2 =$ alkyl) in the presence of Co(II) salts, base, and hydrogen peroxide led to the formation of the coordinatively saturated cobaltate complexes (eq 1). It was not, however, clear if this procedure could be extended to the system of interest in our study involving the more sterically hindered α,α-dimethyl-substituted amino acid **18** in order to synthesize the targeted complex **19**.

In the experiment, we indeed isolated a dark red-brown solid, which when employed in the hydration reaction afforded complete conversion. However, the isolated solid did not consist exclusively of **19**, although its presence in the mixture was confirmed by mass spectrometry. The NMR data were indeterminate due to the presence of remaining Co(II) impurities but suggested the presence of another unidentified complex (referred to as **20**). Importantly, the red-brown solid proved uniquely able to promote the hydrohydrazination of 4-phenylbutene **1**, and hydrohydrazination product **3** was obtained in 85% yield in 4 h on a 0.50 mmol scale (eq 2).



At this stage of development, the enhanced reactivity displayed by the red-brown mixture of Co complexes **19** and **20** was puzzling for us, as we had assumed that complex **19** was the active catalyst and there were no reasons to expect higher reactivity for **19**, especially when considering that **19** is coordinatively saturated. As the results obtained using the mixture of **19** and **20** were consistent from batch to batch, this had no practical consequences of our studies on the hydrohydrazination of alkenes.[24a] However, a deeper knowledge of the catalyst structure was deemed essential for further improvements. Subsequently, after examination of the scope of the hydrohydrazination reaction, we made use of another procedure reported by Bailar and Burrows and were finally able to obtain clean samples of **19** starting directly with $Co(OH)_3$.[30] The structure of **19** could be then further confirmed via ^1H and ^{13}C NMR, IR, and high-resolution mass spectrometry. To our dismay, however, complex **19** was not an effective catalyst for hydration and hydrohydrazination, showing only a few conversions (<20%) after 2 days for the hydrohydrazination of 4-phenylbutene **1**. At this point, it was clear the active catalyst was not **19**, but most probably the nonidentified complex **20**.

Consequently, we intensified our efforts toward the purification of the mixture obtained using our previous procedure (eq 1). After several thwarted attempts at recrystallization, we were pleasantly surprised to find out that the major component of

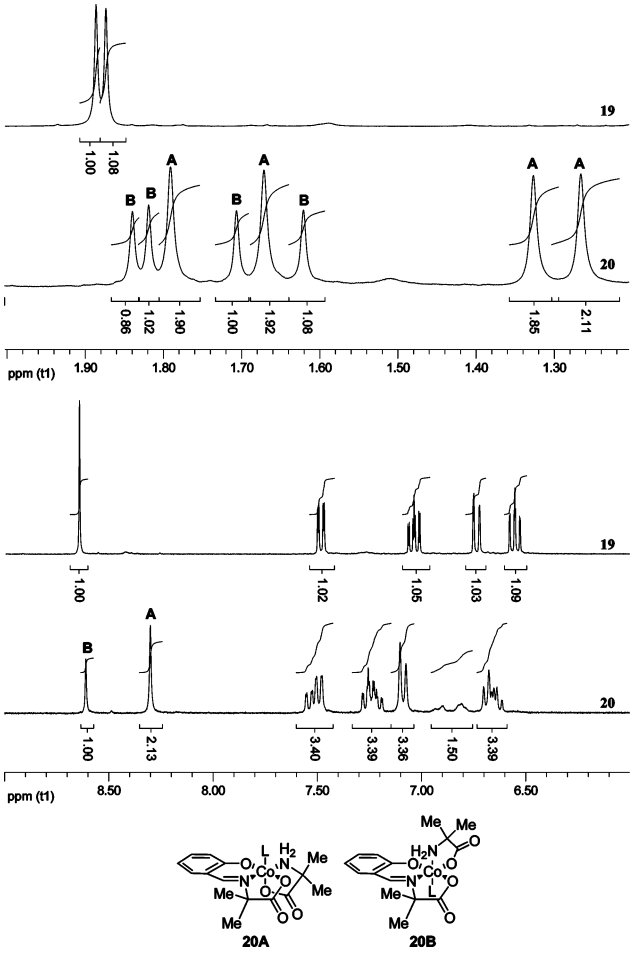


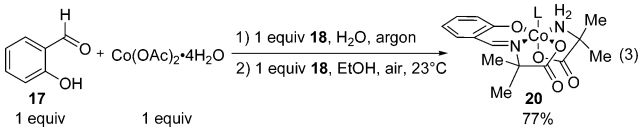
Figure 1. Proposed structure and ^1H NMR spectrum of complex **20** in comparison with **19** (the assignment of **A** and **B** is arbitrary).

this mixture could be purified by simple column chromatography on silica gel using $MeOH/CH_2Cl_2$ solvent mixtures without decomposition. This new complex accounted in fact for about 60−80% of the crude mass and was pure enough to allow us to provide spectra displaying well-defined sharp signals. Careful comparison of the ^1H NMR spectra of **19** and the new complex **20** allowed us to propose a possible structure for **20** (Figure 1). The highly symmetrical complex **19** displays a single peak for the imino H at 8.65 ppm and only two signals for the methyl groups; the ratio of aromatic/aliphatic H is 2/3, as expected. In the spectrum of **20**, a ratio of aromatic/aliphatic H of 1/2.8 is found (expected: 1/3). The appearance of a doubling of all peaks suggests the presence of two structural isomers **A** and **B** in a ratio of 2 to 1. Clearly, two sets of four nonequivalent methyl groups are present in the molecule (**A** and **B**) between 1 and 2 ppm (Figure 1). This is consistent with structure **20**, if the fact that two different structural isomers **A** and **B** are possible is taken into account. For the sake of simplicity, only one of the isomers will be portrayed in this work, as no attempt was made to determine which structure was the major and which was the minor isomer. Apart from the tridentate Schiff-base ligand **16** and 2-amino-isobutyric acid **18**, the ligand sphere of the complex is further completed by a solvent molecule. The presence of this potentially free-binding site on complex **20** could be the reason of its enhanced reactivity.

A confirmation of the structure of **20** could be obtained via high-resolution mass spectrometry. Initially, as we were target-

ing the anionic complex **19**, we had only detected negative mass in our measurements. However, under these conditions, the neutral complex **20** could not be detected. With our new structure proposal, we extended our measurements to include positive mass signals. Indeed, high-resolution mass peaks were obtained for both $[M + H]^+$ and $[M + Na]^+$ in the case of neutral complex **20**.

With a new structure proposal for the active catalyst, we designed a two-step synthesis for complex **20** that gives higher yield and purity (eq 3). A mixture of salicylaldehyde **17**, amino acid **18**, and $Co(OAc)_2 \cdot H_2O$ provides Co(II) complex as a yellow-orange precipitate. After filtration, suspension of this precipitate in ethanol and stirring in air in the presence of amino acid **18** provides the dark red complex **20**. The fact that complex **20** is obtained in higher yield and purity when introducing the tridentate and the bidentate ligands in a two-steps procedure suggests that the proposed structure is indeed correct.

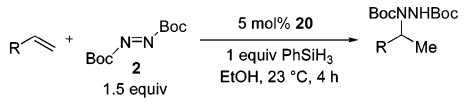


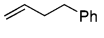
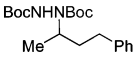
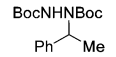
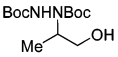
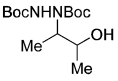
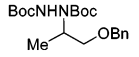
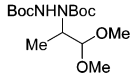
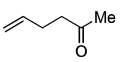
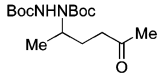
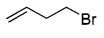
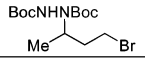
Without doubt, the discovery of catalyst **20** was the key for the development of an efficient hydrohydrazination reaction. Nevertheless, other reaction parameters also play an important role in the hydrohydrazination of 4-phenylbutene **1** as test substrate. For example, the use of diethyl azodicarboxylate (DEAD) afforded the corresponding hydrazine in only 34% yield, probably because DEAD lacks the steric hindrance of **2**, allowing a faster competitive reduction of the N−N double bond. On the other hand, hydrohydrazination product **3** could be obtained in 72% yield using only 1 equiv of azodicarboxylate **2**. In contrast to Mukaiyama hydration reaction, the hydrohydrazination reaction displayed a strong solvent effect: alcoholic solvents (methanol, ethanol, 2-propanol) proceeded equally well, whereas acetonitrile gave low yields of hydrohydrazination product and less-polar solvents (CH_2Cl_2, THF) lead to no conversion at all.

Next, several other hydride sources were tested in the reaction. Trialkylsilanes, sodium borohydride, or hydrogen gas could not be used, as they led either to no conversion (hydrogen gas, trialkylsilanes) or favored the direct reduction of azodicarboxylate **2** (sodium borohydride), but poly(methylhydrosiloxane) (PMHS) and tetramethylhydrosiloxane (TMDSO) led to the formation of hydrazine **3**. In the case of PMHS, conversion and reaction rate were too low to be useful (20% over 24 h), but TMDSO was as efficient as phenylsilane, affording **3** in 86% in 4 h. As this silane is inexpensive and widely available, this constitutes an improvement when compared to phenysilane.[32] Finally, it was established that the reaction can be run on a larger scale by scaling it up 10-fold (5 mmol). Using only 2.5 mol % catalyst **20**, the hydrohydrazination product **3** was obtained from 4-phenylbutene **1** in 94% yield (1.75 g, starting from 0.67 g of **1**).

The scope of the Co-catalyzed hydrohydrazination reaction with monosubstituted olefins was then examined (Table 3). Importantly, the use of thoroughly purified complex **20** was not

Table 3. Co-Catalyzed Hydrohydrazination of Monosubstituted Olefins



entry	alkene	product	yield[a]
1			85%
2			86%[b]
3			78%
4			73% (d.r. 1:1)
5			76%
6			70%
7			76%
8			90%

[a] Standard conditions: 0.50 mmol alkene, 0.50 mmol $PhSiH_3$, 0.75 mmol **2**, 5 mol % catalyst **20**, and 2.5 mL of ethanol at 23 °C under argon. [b] Alkene (0.50 mmol) was added as a solution in 1 mL of CH_2Cl_2, using 1.5 mol % catalyst **20**.

necessary: although the reaction time was indeed shortened (1.5×), no difference in yield was observed compared to that of the mixture obtained using our previously published procedure.[24a] Key features of the Co-catalyzed hydrohydrazination of monosubstituted olefins are the following: (1) high Markovnikov selectivity with nearly exclusive formation of the secondary hydrazine product; (2) a strong activating and α-directing effect of a phenyl group (entry 2), in this case, slow substrate addition and low catalyst loadings were needed to prevent competitive polymerization (for acrylate derivatives, no product could be isolated due to extensive polymerization); and (3) broad functional group tolerance, including free alcohols (entries 3 and 4), an ether (entry 5), an acetal (entry 6), a ketone (entry 7) and a bromide (entry 8).

The large functional group tolerance observed is one of the major advantages of the hydrohydrazination reaction. To further extend the scope of the reaction, we decided to examine the functionalization of vinyl-substituted heterocycles. Heterocycles are ubiquitous in organic chemistry: in 2003, from more than 20 million compounds registered, about one-half featured heterocycles.[33] They have found applications in chemistry, biology, agriculture, and material science and are the constituents of many natural products, pharmaceuticals, herbicides, dyes, and other products of technical importance.[33,34] For these reasons, the synthesis, elaboration, and functionalization of heterocycles

(32) Typical prices for laboratory-scale quantities: phenylsilane, 7.50 CHF/g, 271 CHF/mol(H); PMHS, 0.20 CHF/g, 12 CHF/mol(H); TMDSO, 1.3 CHF/g, 87 CHF/mol(H).

(33) Eicher, T.; Siegfried, H. *The Chemistry of Heterocycles: Structure, Reactions, Syntheses, and Applications*; Wiley−VCH: Weinheim, Germany, 2003.

(34) Pozharskii, A. F.; Soldatenkov, A. T.; Katritzky, A. R. *Heterocycles in Life and Society: An Introduction to Heterocyclic Chemistry and Biochemistry and the Role of Heterocycles in Science, Technology, Medicine and Agriculture*; John Wiley & Sons, Ltd.: Chichester, 1997.

is an intense field of research in organic chemistry. However, when dealing with heterocycles, any catalytic process faces a great challenge. Many heterocycles are also good ligands for transition metals and can poison the catalyst. Some basic heterocycles preclude the use of Brønsted or Lewis acids as catalysts. Consequently, high catalytic loadings and harsh reaction conditions are often needed for catalytic methods if heterocycles are present.

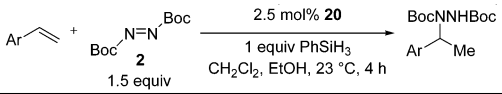
In this context, the hydroamination of vinyl-substituted heterocycles would be an interesting method to access densely functionalized building blocks. To the best of our knowledge, the full potential of this class of compounds has not been examined for the hydroamination reaction. Marks reported that pyridines were not compatible with lanthanide catalysts.[12] Beller introduced Rh-based catalysts for the anti-Markovnikov hydroamination of vinylpyridines,[35] but no other heterocyclic substrates were reported. Hartwig documented the use of amino pyridine for the hydroamination of cyclohexadienes at elevated temperature.[14j]

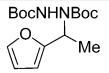
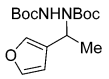
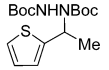
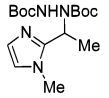
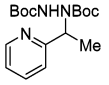
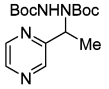
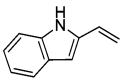
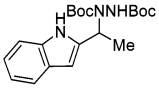
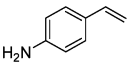
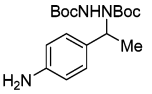
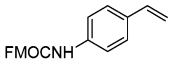
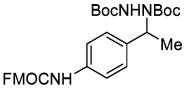
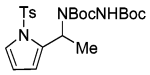
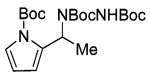
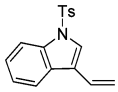
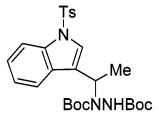
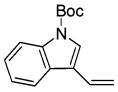
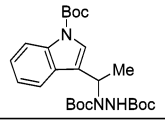
We began our studies with the examination of simple unprotected vinyl- substituted heterocycles (Table 4, entries 1−8). Both 2- and 3-vinylfurans could be aminated in useful yields (entries 1 and 2). This result is noteworthy, as vinylfurans are otherwise prone to polymerization. The higher yields observed for 2-vinylthiophene (entry 3) reflect the higher stability of this compound. Among nitrogen heterocycles, 2-vinylpyrrole (entry 4) did not give the desired product, as we were not able to suppress polymerization. However, *N*-methyl-2-vinylimidazole could be functionalized in moderate yields (entry 5). The fact that our reaction is compatible with the relatively high basicity of *N*-methyl-2-vinylimidazole (pK_a = 7) is interesting. Six-membered ring nitrogen heterocycles could also be functionalized in useful yields, for example, 2-vinylpyridine (entry 6) or the electron-poor 2-vinylpyrazine (entry 7). Finally, in contrast to 2-vinyl-pyrrole, 2-vinylindole (entry 8) gives the desired amination product in good yield. However, the corresponding 3-vinylindole (not shown) polymerized before a reaction could take place. The successful functionalization of 2-vinylindole showed the tolerance of the reaction toward a free indole N−H bond. In this context, 4-vinyl aniline (entry 9) was examined. The yields were moderate in this case. However, simple protection of the aniline nitrogen was sufficient to afford quantitative yield of the hydrohydrazination product (entry 10). The FMOC protecting group appeared particularly well-suited, as protection and subsequent deprotection were easy and high yielding, finally furnishing the hydrohydrazination product with a free amino group in 83% yield over four steps.

The heterocycles that we were unable to hydroaminate, 2-vinylpyrrole and 3-vinylindole, are among the more frequently used heterocycles. The instability of these compounds is due mostly to the high donor ability of the nitrogen atom. For this reason, we subsequently protected the nitrogen atom to diminish the electron-density of the heterocycles. We were pleased to find that both Boc- and tosyl-protected 2-vinylpyrroles (entries 11 and 12) and 3-vinylindoles (entries 13 and 14) react with useful yields in the hydrohydrazination reaction.

Next, we examined the hydrohydrazination reaction of di- and trisubstituted olefins (Table 5). Again, a strong activating and directing effect of a phenyl group was observed, allowing the functionalization of di- and trisubstituted styrene derivatives in high yield, with exclusive formation of the hydrazine product at the benzylic position (entries 1−5). In the case of heterocyles, both α- and *β*-methylvinylpyridines react in the hydrohydrazination reaction with moderate yields (entries 6 and 7). α-Methyl vinylthiophene (entry 8) could also be functionalized,

Table 4. Hydrohydrazination of Vinyl-Substituted Heterocycles

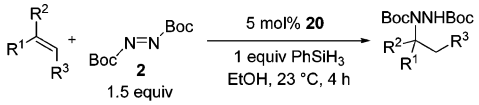


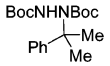
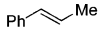
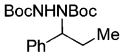
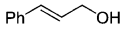
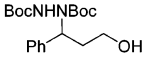
entry	heterocyclic substrates	product	yield[a]
1			68%
2			75%
3			84%
4			<5%
5			60%
6			77%
7			63%
8			82%
9			20-40%[b]
10			98%
11			74%
12			67%
13			85%
14			76%

[a] General procedure: 0.50 mmol alkene was added as a solution in 1.0 mL of CH_2Cl_2 and 1.0 mL of ethanol to a solution of 0.50 mmol $PhSiH_3$, 0.75 mmol di-*tert*-butyl azodicarboxylate (**2**), 2.5 mol % catalyst **20**, and 2.5 mL of ethanol at 23 °C under argon. [b] The desired product could not be separated from nonidentified impurities.

(35) Beller, M.; Trauthwein, H.; Eichberger, M.; Breindl, C.; Müller, T. E. *Eur. J. Inorg. Chem.* **1999**, 1121.

Table 5. Hydrohydrazination of Di- and Trisubstituted Olefins



entry	alkene	product	yield[a]
1			88%[b]
2			88%
3			91%
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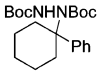
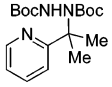
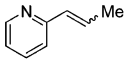
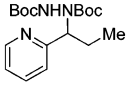
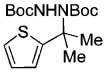
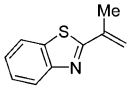
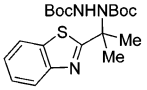
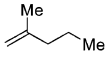
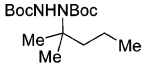
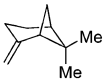
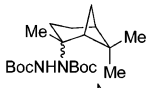
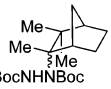
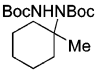
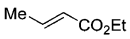
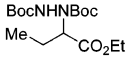
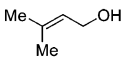
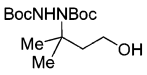
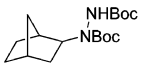
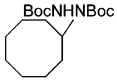
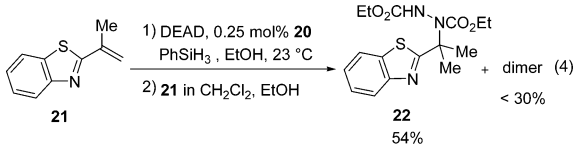
5			80%[c]
6			60%[b]
7			54%[b]
8			58%[b]
9			<14%[d]
10			88%[c]
11			84% dr 2:1-3:1
12			69% dr>5:1
13			90%
14			66%[c]
15			70%
16			66%
17			62%[c]
18			74%[c]

[a] Standard conditions: 0.50 mmol alkene, 0.50 mmol $PhSiH_3$, 0.75 mmol **2**, 5 mol % catalyst **20**, and 2.5 mL of ethanol at 23 °C under argon. [b] Alkene (0.50 mmol) was added as a solution in 1 mL of CH_2Cl_2 using 2.5 mol % catalyst **20**. [c] Alkene (0.50 mmol), 0.75 mmol $PhSiH_3$, and 1.0 mmol **2** were used. [d] Dimerization at the tertiary center was observed.

but α-methyl 2-vinylbenzothiazole (entry 9) gives only very low yield.

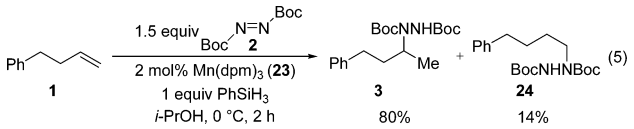
For the α-substituted heterocycles, the lower yields observed in comparison with unsubstituted substrates are partially due to dimerization of the starting material. In the case of α-methyl 2-vinylbenzothiazole (entry 9), this becomes the main pathway. To override the tendency of α-methyl 2-vinylbenzothiazole to dimerize, we ran the reaction with a large excess of the more reactive DEAD and at a lower catalyst loading (eq 4). Under these conditions, it was possible to obtain the desired amination product in moderate yields, but the dimerization of the starting material could not be suppressed completely.



When no aromatic activating group was present, an important difference in reactivity became apparent: α,α-disubstituted olefins were good substrates, giving the tertiary hydrazine products exclusively in good yields (Table 5, entries 10−13), but α,*β*-disubstituted olefins react only in low yields (<50%) in the hydrohydrazination reaction. Useful yields could be obtained only in the case of an α,*β*-unsaturated ester (entry 14) and some endocyclic alkenes (entries 16−18), using a larger excess of azodicarboxylate **2** (2 equiv). For this class of substrates, the hydrohydrazination reaction is much slower, and hydrazine **3** resulting from the direct reduction of **2** becomes the major product. The examination of a trisubstituted alkene revealed an intermediate reactivity between α,*β*-disubstituted and α,α-disusbstituted olefins, allowing useful yields (entry 15).

Mn-Catalyzed Hydrohydrazination Reaction. Though highly active for most substrates, Co catalyst **20** was not able to make hydrohydrazination competitive with azodicarboxylate reduction in the case of sterically hindered substrates. No Co complex tested proved more active than **20**. Therefore, we decided to expand our study to other metals. Mukaiyama has reported the hydration of olefins using $Mn(dpm)_2$.[36] Indeed, a first attempt for the hydrohydrazination of 4-phenylbutene **1** with $Mn(dpm)_2$ was promising: the amination of **1** was quantitative in 5 min instead of the 4 h required by catalyst **20**. However, this increase in reactivity comes at the cost of the selectivity: the ratio of Markovnikov/anti-Markovnikov was only 3:1. Another convenient feature of the Mn catalyst is that the progress of the reaction can be monitored by the color of the reaction mixture: as long as azodicarboxylate **2** is present, the reaction mixture is brown-green. When **2** is consumed, the color changes to light yellow. To improve upon this initial result, we first changed the catalyst to the Mn(III) complex $Mn(dpm)_3$ (**23**). The activity of the Mn(II) complex $Mn(dpm)_2$ and **23** is identical, but $Mn(dpm)_2$ is unstable in air and slowly oxidizes to give a mixture of Mn(II) and Mn(III) compounds.[37] On the other hand, Mn(III) complex **23** is bench-stable and requires no special care in storage. Diminishing the catalyst loading to 2 mol % and the temperature to 0 °C finally allowed us to increase the Markovnikov/anti-Markovnikov selectivity to 5.5:1 (eq 5).

(36) Inoki, S.; Kato, K.; Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1990**, 1869.
(37) Cotton, F. A.; Soderberg, R. H. *Inorg. Chem.* **1964**, *3*, 1.



Next, substrates which gave low yields with Co catalyst **20** were examined (Table 6). Homoallyllic alcohol could be aminated in much better yield (72%, 22% with Co catalyst **20**; entry 1). α,β-Disubstituted acyclic olefins (entries 2−5) give good yields with catalyst **20**, except for crotonyl nitrile (entry 4). However, the regioselectivity was low (entry 2). Cyclic substrates are particularly well-suited for the new Mn-catalyzed protocol (entries 6−10), showing increased yields for all substrates compared with **20**. A cyclic ether was also well tolerated (entry 10).

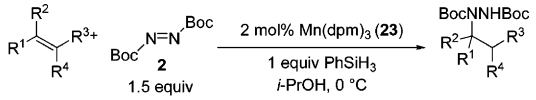
Mn catalyst **23** was also effective for the functionalization of vinyl-substituted heterocycles, giving yields comparable to those obtained with Co catalyst **20**. However, in the case of *N*-methyl-2-vinylimidazole (entry 11) and 4-vinylaniline (entry 12), a significant increase in yield was observed (83% vs 60% for *N*-methyl-2-vinylimidazole and 60−80% vs 20−40% for 4-vinylaniline). These results together with the improvement observed for homoallylic alcohol (entry 1) suggest that Mn catalyst **23** is more tolerant toward coordinating groups, which slow the reaction for Co catalyst **20**. Finally, we turned to the most challenging substrates for Co catalyst **20**: tetrasubstituted olefins (entries 13−16). Although the yields were very low with **20** (<20%), useful yields were obtained with Mn catalyst **23** (51−79%).

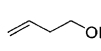
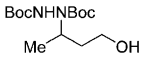
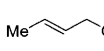
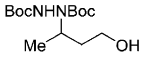
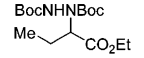
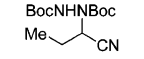
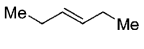
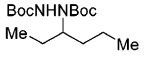
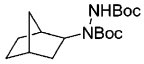
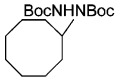
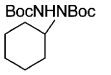
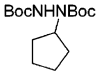
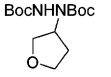
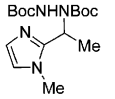
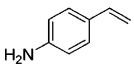
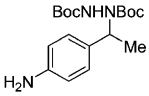
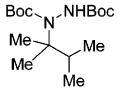
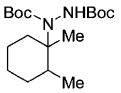
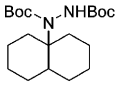
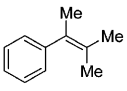
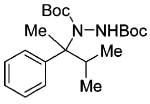
To get more detailed information concerning the relative activity of the two catalytic systems, reactions with low catalytic loadings (0.1 mol %) were run with 4-phenylbutene **1** and tetramethylethylene. In the case of olefin **1**, a 10-fold increase of turnover number[38] was observed with **23** in comparison with **20** (430 vs 44). For tetramethylethylene, this difference even rises to 80 (240 vs 3).

The increased reactivity of Mn catalyst **23** also makes the use of other silanes as a reductant viable. Diphenylsilane was found to be an efficient hydride source. More interestingly, PMHS could be used in the hydrohydrazination of 4-phenylbutene **1**. Hydrazine **3** was obtained in 88% yield, although the reaction must be run at room temperature and was slower (15 h). The result with TMDSO (full conversion in 24 h at 23 °C) is intriguing: in the case of Mn catalyst **23**, the reaction with this silane was even slower than with PMHS, in contrast with what was observed with Co catalyst **23**, where it displays reaction rates comparable to phenylsilane. Other silanes or sodium borohydride could not be used as hydride sources, as they led either to no conversion (trialkylsilanes) or favored the direct reduction of azodicarboxylate **2** (sodium borohydride). PMHS could also be used in the case of more challenging substrates such as 4-butenol or tetramethylethylene, and the desired product was obtained in useful yields (60% and 60%, respectively), although the yields were consistently lower than those obtained with the use of phenylsilane (entries 1 and 11, Table 6).

(38) The "turnover numbers" obtained this way are not really accurate because they reflect the activity of the catalysts for two reactions at least (hydrohydrazination reaction and reduction of azodicarboxylate). In the case of **1**, moreover, some side products resulting from a direct ene reaction were also isolated. Nevertheless, these numbers allow a good comparison for practical purposes.

Table 6. Mn-Catalyzed Hydrohydrazination of Olefins



entry	alkene	product	yield Mn[a]
1			72%
2			90% (1.8:1)[b]
3			88%
4			45%
5			66%
6			98%
7			95%
8			90%
9			94%
10			81%
11			83%
12			60-80%[c]
13			78%
14			79%
15			74%
16			51%

[a] General procedure: 0.50 mmol alkene, 0.50 mmol $PhSiH_3$, 0.75 mmol di-*tert*-butyl azodicarboxylate (**2**), 2 mol % catalyst **23**, and 2.5 mL of *i*-PrOH at 0 °C under argon. [b] Major product drawn, the minor compound results from the hydrohydrazination next to the hydroxy group. [c] The desired product could not be separated from nonidentified impurities.

Chiral esters and imide substrates were examined to find out if diastereoselective reactions were possible with Co catalyst **20** or Mn catalyst **23**. Whereas menthyl and oxazolidinone auxiliaries did not show any significant diastereoselectivity, crotyl ester **25** derived from pantolactone showed asymmetric

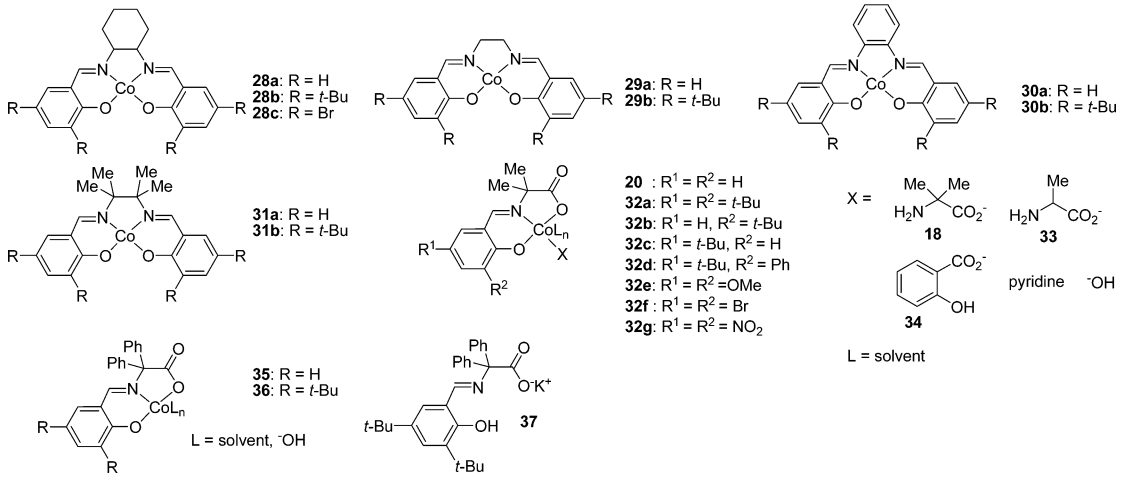
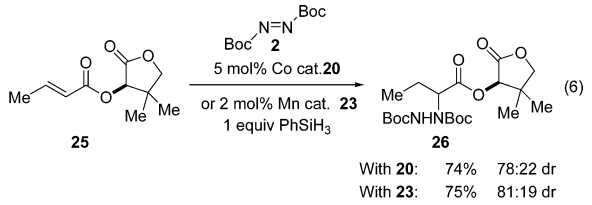


Figure 2. Complexes and ligands tested for the hydroazidation of 4-phenylbutene **1**.

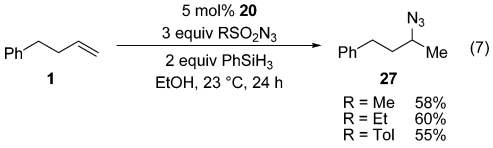
induction (eq 6). In 2005, Yamada reported high diastereoselectivity in the hydrohydrazination reaction using Oppolzer sultam auxiliary.[39]



At this stage of development, the properties of the Co and the Mn catalysts are complementary, **20** being more selective and **23** more reactive. For example, the lower reactivity and higher selectivity of **20** has allowed the development of an efficient method to convert conjugated dienes and enynes to allylic and propargylic hydrazines.[24c]

Hydroazidation Reaction. Azides occupy a privileged role in organic chemistry as precursor of amines.[40] More recently, their use in cycloaddition reactions has been thoroughly investigated for the synthesis of pharmaceutically relevant heterocycles.[41] Azides usually do not occur in natural systems, yet they can display stability under physiological conditions: these properties have led to increased interest for their use in biochemistry, especially for bioconjugation via Staudinger ligation[42] or click chemistry.[43] Azides are typically prepared from the substitution of alkyl halides with sodium azide, but this approach requires the prior synthesis of the alkyl halides and is less successful for the synthesis of tertiary azides.[44] The hydroazidation of olefins from alkenes represents a more direct access to these interesting compounds. However, such an approach has been limited to alkenes, which give rise to stabilized carbocations and require excess HN_3,[45a] $TMSN_3$,[45b] or zeolite-supported NaN_3.[45c] Simple hydroazidation of unactivated, monosubstituted olefins have not been reported so far, although several multifunctionalization methods have been developed.[45] Herein, a full report on the discovery and development of the Co-catalyzed hydroazidation of olefins with sulfonyl azide and silanes is presented.[46]

After the successful development of the hydrohydrazination reaction, we first turned to the examination of other acceptors for olefin heterofunctionalization. We were interested in new nitrogen sources, as the transformation of the hydrazine derivatives obtained in the hydrohydrazination reaction can be troublesome in some cases. We were pleased to see that alkyl- and arylsulfonyl azides were uniquely able to act as azide sources in the amination of 4-phenylbutene with Co catalyst **20**, giving the product **27** derived from the formal Markovnikov addition of hydrazoic acid onto the C−C double bond exclusively, albeit in moderate yields (40−60%; eq 7). Surprisingly, no reaction was observed with Mn catalyst **23**. This underscores the differences between the hydrohydrazination and the hydroazidation reactions. With this lead result in hand, we proceeded to the optimization of the hydroazidation reaction.



We first examined simple variations of the reaction conditions (stoichiometry of reagents, concentration, order of addition), but no effects on yield or rate were observed. Increasing the

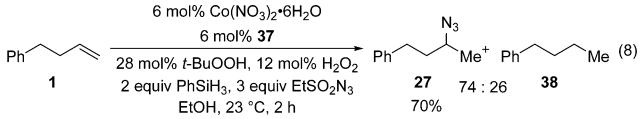
(39) Sato, M.; Gunji, Y.; Ikeno, T.; Yamada, T. *Chem. Lett.* **2005**, *34*, 316.
(40) (a) Rao, H. S. P.; Siva, P. *Synth. Commun.* **1994**, *24*, 549. (b) Corey, E. J.; Nicolaou, K. C.; Balanson, R. D.; Machida, Y. *Synthesis* **1975**, 590.
(41) (a) Huisgen, R.; Knorr, R.; Mobius, L.; Szeimies, G. *Chem. Ber.* **1965**, *98*, 4014. (b) Demko, Z. P.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2110. (c) Demko, Z. P.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2113. (d) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596.
(42) Kohn, M.; Breinbauer, R. *Angew. Chem., Int. Ed.* **2004**, *43*, 3106.
(43) Kolb, H. C.; Sharpless, K. B. *Drug Discovery Today* **2003**, *8*, 1128.
(44) For general reviews on azides, see: (a) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297. (b) Bräse, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188.
(45) (a) Hassner, A.; Fibiger, R.; Andisik, D. *J. Org. Chem.* **1984**, *49*, 4237. (b) Breton, G. W.; Daus, K. A.; Kropp, P. J. *J. Org. Chem.* **1992**, *57*, 6646. (c) Sreekumar, R.; Padmakumar, R.; Rugmini, P. *Chem. Commun.* **1997**, 1133. For silyl enolate azidation, see: (d) Magnus, P.; Lacour, J.; Evans, P. A.; Roe, M. B.; Hulme, C. *J. Am. Chem. Soc.* **1996**, *118*, 3406. For olefin iodoazidation, see: (e) Hassner, A.; Levy, L. A. *J. Am. Chem. Soc.* **1965**, *87*, 4203. For diazidation, see: (f) Fristad, W. E.; Brandvold, T. A.; Peterson, J. R.; Thompson, S. R. *J. Org. Chem.* **1985**, *50*, 3647. (g) Snider, B. B.; Lin, H. *Synth. Commun.* **1998**, *28*, 1913. For olefin selenoazidation, see (h) Tiecco, M.; Testaferri, L.; Sand, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3131. For conjugate addition to unsaturated carbonyl compounds, see: (i) Myers, J. K.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1999**, *121*, 38, 8959. (j) Horstmann, T. E.; Guerin, D. J.; Miller, S. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 3635. For olefin aziridination using azides, see: (k) Mahoney, J. M.; Smith, C. R.; Johnston, J. N. *J. Am. Chem. Soc.* **2005**, *127*, 1354.
(46) Part of this work has been published in a previous communication.[25]

temperature led to a higher reaction rate, but the yield or conversion were not improved. At this point, we re-examined several Co-derived catalysts (Figure 2) for the hydroazidation of 4-phenylbutene **1**. Interestingly, simple Co catalysts **28**−**31** were also able to catalyze the hydroazidation reaction, although the yields were lower (typically <40%). For these complexes, the presence of a *tert*-butyl group on the aromatic ring was necessary to have active catalysts. The best salen catalyst is complex **28b**, which afforded 45% yield of the desired azide.[47] However, the reaction was not as clean compared to **20**, and the formation of several side products could not be suppressed.

The synthesis of catalyst **20** is well-suited for modifications, and the influence of substituents on the aromatic ring were first studied. However, none of the complexes **32a**−**g** displayed enhanced rate or conversion. Interestingly, the second ligand on Co (X in **32**, Figure 2) did not have any influence on the reaction, and 2-amino-isobutyric acid (**18**) could be replaced by other amino acids, acid **34** or pyridine. Furthermore, even the Co(II) precursor obtained from the reaction of Co(II) salts with amino acids and salicylaldehyde was an equally active catalyst, although the catalyst was not soluble under the reaction conditions. However, these catalysts did not offer the advantage of purification and stability on the storage characteristic of **20**.

We then turned to complexes **35** and **36** derived from α,α-diphenylglycine.[48] Complex **36** was the first to display increased reactivity when compared to standard catalyst **20**, and, in a first run, azide **27** was obtained in 8 h in 58% yield with ethanesulfonyl azide from 4-phenylbutene **1**. The structural features of **36** are noteworthy; even in the presence of an excess of amino acid, only the 1:1 complex from **37** and Co was detected by NMR and mass spectroscopy in sharp contrast to complex **20**. This is probably due to the steric bulk of the corresponding Schiff-base ligand **37** and could explain its increased reactivity and lower stability. Unfortunately, we were unable to obtain reproducible results using complex **36**, as yields (40−70%) and reaction times (8−48 h) showed a considerable batch dependence. In many cases, a long initiation time was observed before the reaction started. The reasons for the particular behavior of **36** are not clear, but the fact that we were able to obtain clean NMR spectra of **36** only in DMSO could suggest that this complex forms aggregates in other solvents, and the difference in reactivity observed could be the result of different aggregation states. The problem of slow initiation when using Co catalysts had already been encountered by Mukaiyama and co-workers for the hydration of certain olefins. In this case, the addition of *tert*-butyl hydroperoxide as cocatalyst accelerated the reaction. We were pleased to see a similar effect in the hydroazidation reaction: when using catalyst **36** with ethanesulfonyl azide for the hydoazidation of 4-phenylbutene **1**, complete conversion was observed after 2−8 h. Finally, we found that in situ formation of complex **36** in the reaction mixture leads to reproducible reaction times (2 h) and yield (70%).

To further optimize the reaction conditions, we then turned to gas chromatography for analysis of the reaction mixture. This allowed us to identify 4-phenylbutane (**38**) as the main side product (eq 8). The ratio of azidation versus reduction was determined to be 74:26, while the conversion was higher than 95%. Combined with the isolated yield of 70% for azide **27**, this means that alkane **38** is the only side product of the reaction present in significant amounts, and improving the azide/alkane ratio was paramount to improving the efficiency of the process.



We began our studies toward this goal by careful examination of the conditions for catalyst formation and the effect of the *tert*-butyl hydroperoxide additive in the hydroazidation reaction of 4-phenylbutene **1** with phenylsilane and ethanesulfonyl azide (Table 7). From these studies, it was concluded that: (1) *tert*-butyl hydroperoxide (30 mol %) was necessary to obtain useful reaction rates (runs 1−3, 8, and 11), (2) in situ formation of the catalyst allowed suppression of the batch dependency observed with the isolated catalyst; the most convenient Co salt for complex formation was $Co(BF_4)_2 \cdot 6H_2O$, as it allowed nearly instantaneous catalyst formation (runs 4−6 and 12), (3) the ratio of ligand to Co had nearly no influence on the reaction (runs 9 and 10), and (4) other catalysts tested to assess the generality of the activating effect of *tert*-butyl hydroperoxide gave inferior results (runs 13−16).

The examination of the catalytic system allowed us to develop a more practical and reproducible procedure for the hydroazidation reaction, but we could not solve the problem of chemoselectivity (olefin azidation vs reduction). To solve this problem, we further examined the variation of the solvent and sulfonyl azide (Table 8). In these studies, no solvents proved to be superior to ethanol (runs 1−4). In contrast to these results, modification of the sulfonyl azide was crucial to favor the desired hydroazidation reaction against double-bond reduction. Phenyl and toluenesulfonyl aides were optimal (runs 5−9).

Table 7. Influence of Catalytic System on the Hydroazidation of 4-Phenylbutene **1** (Eq 8)

run	catalyst	conditions	conversion;[a] time	**27**:**38**[b]
1	**36**	*t*-BuOOH; 30%	>98%; 2 h	67:33
2	**36**	*t*-BuOOH; 60%	>98%; 1.5 h	65:35
3	**36**	*t*-BuOOH; 15%	>98%; 6 h	71:29
4	$Co(NO_3)_2 \cdot 6H_2O$/**37**/H_2O_2		74%; 18 h	75:25
5	$Co(NO_3)_2 \cdot 6H_2O$/**37**/H_2O_2	*t*-BuOOH; 30%	>98%; 2 h	74:26
6	$Co(OAc)_2$/**37**/H_2O_2	*t*-BuOOH; 30%	>98%; 2 h	71:29
7	$CoCl_2$/**37**/H_2O_2	*t*-BuOOH; 30%	50%; 24 h	nd[c]
8	$Co(NO_3)_2 \cdot 6H_2O$/**37**	*t*-BuOOH; 30%	>98%; 2 h	72:28
9	$Co(NO_3)_2 \cdot 6H_2O$/**37** (1:2)	*t*-BuOOH; 30%	>98%; 2 h	68:32
10	$Co(NO_3)_2 \cdot 6H_2O$/**37** (2:1)	*t*-BuOOH; 30%	>98%; 2 h	72:28
11	$Co(NO_3)_2 \cdot 6H_2O$/**37**		>98%; 18 h	70:30
12	$Co(BF_4)_2 \cdot 6H_2O$/**37**	*t*-BuOOH; 30%	>98%; 2 h	77:23
13	**20**	*t*-BuOOH; 30%	78%; 2.5 h	58:42
14	$Co(acac)_2$	*t*-BuOOH; 30%	50%; 12 h	nd[c]
15	$Mn(dpm)_3$ (**23**)	*t*-BuOOH; 30%	<10%; 24 h	nd[c]
16	$Mn(OAc)_2 \cdot 4H_2O$/**37**	*t*-BuOOH; 30%	61%; 18 h	72:28

[a] Standard conditions: 0.10 mmol 4-phenylbutene **1**, 0.16 mmol phenylsilane, 0.30 mmol ethanesulfonyl azide, and 6 mol % catalyst in 0.50 mL of ethanol at 23 °C under argon. [b] Determined by gas chromatography. [c] Not determined.

(47) As **28b** is chiral, the enantiomeric excess of the obtained azide **27** was determined. However, **27** was racemic.

(48) Sterically hindered complex **36** could not be synthesized following the same procedure as **20**, as the in situ condensation to form the Schiff-base ligand did not occur. However, preformation of the Schiff-base ligand **37**, followed by complex formation with Co(II) salts and subsequent oxidation with hydrogen peroxide, afforded **36**.

Table 8. Influence of Solvents and Sulfonyl Azide on the Hydroazidation of 4-Phenylbutene **1** (Eq 8)

run	azide solvent	catalyst ligand	conversion;[a] time	**27**:**38**[b]
1	$EtSO_2N_3$ EtOH	$Co(BF_4)_2{\cdot}6H_2O$ **37**	>98%; 2 h	77:23
2	$EtSO_2N_3$ EtOH[c]	$Co(NO_3)_2{\cdot}6H_2O$ **37**	>98%; 2 h	71:29
3	$EtSO_2N_3$ MeOH	$Co(NO_3)_2{\cdot}6H_2O$ **37**	>98%; 18 h	50:50
4	$EtSO_2N_3$ *i*-PrOH	$Co(NO_3)_2{\cdot}6H_2O$ **37**	>98%; 2 h	72:28
5	$MeSO_2N_3$ EtOH	$Co(NO_3)_2{\cdot}6H_2O$ **37**	>98%; 2 h	77:23
6	$TolSO_2N_3$ EtOH	$Co(NO_3)_2{\cdot}6H_2O$ **37**	>98%; 4 h	89:11
7	$MesSO_2N_3$ EtOH	$Co(NO_3)_2{\cdot}6H_2O$ **37**	>98%; 18 h	89:11
8	NsN_3 EtOH	$Co(NO_3)_2{\cdot}6H_2O$ **37**	<10%; 24 h	nd[d]
9	$PhSO_2N_3$ EtOH	$Co(BF_4)_2{\cdot}6H_2O$ **37**	>98%; 4 h	90:10
10	$TolSO_2N_3$ EtOH	**20**	97%; 16 h	90:10

[a] Standard conditions: 0.10 mmol 4-phenylbutene **1**, 0.16 mmol phenylsilane, 0.30 mmol sulfonyl azide, 30 mol % *t*-BuOOH, and 6 mol % catalyst in 0.50 mL of solvent at 23 °C under argon. [b] Determined by gas chromatography. [c] Ethanol was distilled over CaH_2 and degassed before use. [d] Not determined.

Table 9. Influence of Silane on the Hydroazidation of 4-Phenylbutene **1** (Eq 8)

run	sulfonyl azide	silane	conversion;[a] time	**27**:**38**[b]
1	$EtSO_2N_3$	$PhSiH_3$, 1.6 equiv	>98%; 1.5 h	77:23
2	$TolSO_2N_3$	$PhSiH_3$, 1.6 equiv	>98%; 2 h	89:11
3	$EtSO_2N_3$	TMDSO, 2 equiv	>98%; 2 h	84:16
4	$EtSO_2N_3$	PMHS, 4H equiv	20%; 24 h	nd[c]
5	$EtSO_2N_3$	PMHS, 4H equiv $PhSiH_3$, 0.2 equiv	81%; 18 h 81%; 18 h	90:10
6	$EtSO_2N_3$	Et_3SiH, 4 equiv	<10%; 24 h	nd[c]
7	$EtSO_2N_3$	$(EtO)_3SiH$, 4 equiv	<10%; 24 h	nd[c]
8	$TolSO_2N_3$	TMDSO, 2 equiv	>98%; 3 h	96:4

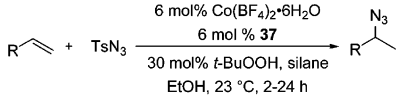
[a] Standard conditions: 0.10 mmol 4-phenylbutene **1**, 0.30 mmol sulfonyl azide, 30 mol % *t*-BuOOH, 6 mol % $Co(BF_4)_2{\cdot}6H_2O$, and 6 mol % ligand **37** in 0.50 mL of ethanol at 23 °C under argon. [b] Determined by gas chromatography. [c] Not determined.

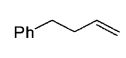
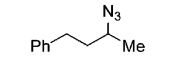
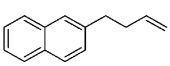
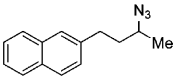
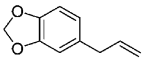
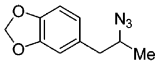
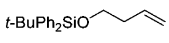
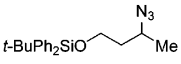
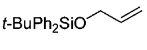
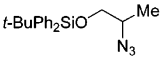
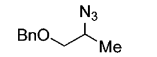
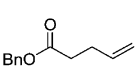
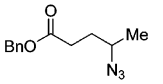
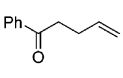
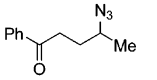
Interestingly, the hydrohydrazination catalyst **20** could also be used with tosyl azide (run 10) with good selectivity, although the reaction was slower.

Finally, we examined the effect of varying the silane structure on reaction rate and selectivity for the hydroazidation of 4-phenylbutene with $Co(BF_4)_2{\cdot}6H_2O$ and ligand **37** as catalyst (Table 9). It was found that TMDSO offers the best compromise between selectivity and reactivity, and combining tosyl azide and TMDSO gave full conversion of 4-phenylbutene **1** in 3 h, with an improved azide/alkane ratio of 96:4 (run 8). Using the conditions of runs 2 and 8 for preparative scale (0.50 mmol) hydroazidation of 4-phenylbutene **1**, the desired azide **27** was obtained in 90 and 86% isolated yield, respectively.

Next, we proceeded to examine the scope of the hydroazidation reaction for monosubstituted olefins, both with phenylsilane and TMDSO (general procedure **A** and **B**, Table 10). The reaction displayed very good Markovnikov selectivity, and only the secondary azides were isolated. The yields with phenylsilane or TMDSO are comparable, except in the case for which the competitive reduction is more pronounced (entries 4 and 5). Apart from 4-phenylbutene **1** (entry 1), 4-naphthylbutene (entry 2) and safrole (entry 3) also give the desired azide in useful

Table 10. Hydroazidation of Monosubstituted Olefins



entry	alkene	product	yield[a] with $PhSiH_3$	yield[b] with TMDSO
1			90%	86%
2			72%	69%
3			65%	62%
4			73%	85%[c]
5			55%	67%
6			35%	39%[c]
7			75%	77%
8			49%[d]	46%[d]

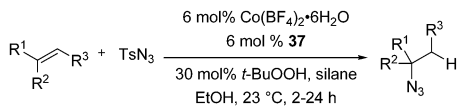
[a] General procedure **A**: 0.5 mmol alkene, 0.8 mmol $PhSiH_3$, 1.5 mmol TsN_3, 30 mol % *t*-BuOOH, 6 mol % ligand **37**, 6 mol % $Co(BF_4)_2{\cdot}6H_2O$, and 2.5 mL of ethanol at 23 °C under argon. [b] General procedure **B**: 1.0 mmol TMDSO was used instead of $PhSiH_3$. [c] 2.0 mmol TMDSO was used. [d] Starting material was partially recovered (see Supporting Information for further details).

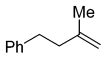
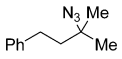
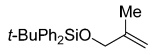
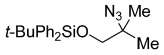
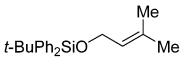
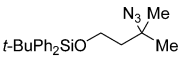
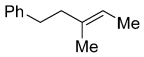
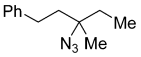
yields. Surprisingly, styrene derivatives (not shown) were not reactive, although they had proven to be excellent substrates for the hydrohydrazination reaction. The functionalization of safrole (entry 3) is of special interest, as safrole is widely available in bulk quantities and the amines derived from the obtained azide are a class of biologically active compounds well-known for their psychopharmacological activity.[49] The hydroazidation of unprotected allylic and homoallylic alcohols was not successful, but the introduction of a bulky silyl protecting group allowed the conversion of these substrates (entries 4 and 5). A benzyl protecting group was less successful (entry 6). An ester (entry 7) and a ketone (entry 8) were tolerated with excellent chemoselectivity, as no C=O reduction was observed.

Di- and trisubstituted olefins also undergo reaction in the hydroazidation reaction (Table 11). α,α-Disubstituted olefins (entries 1−3) give good yields of the tertiary azides, which are difficult to synthesize via substitution of halides. For these substrates, competitive reduction of the alkene was less pronounced and, thus, the more reactive phenylsilane gives higher yields. Cyclooctene also reacts, but the yield is moderate (entry 4). Finally, trisubstituted olefins (entries 5 and 6) were examined. In these cases, full conversion of the starting material could not be achieved. Nevertheless, useful yields could be obtained with phenylsilane as reductant.

(49) Nichols, D. E.; Hoffman, A. J.; Oberlender, R. A.; Jacob, P.; Shulgin, A. T. *J. Med. Chem.* **1986**, *29*, 2009.

Table 11. Hydroazidation of Di- and Trisubstituted Olefins



entry	alkene	product	yield[a] with $PhSiH_3$	yield[b] with TMDSO
1			86%	90%
2			89% dr: 4:1	76%[c] dr: 4:1
3			73%[d]	58%[c,d]
4			56%	
5			63%[d]	48%[c,d]
6			66%	48%[c,d]

[a] General procedure **A**: 0.5 mmol alkene, 0.8 mmol $PhSiH_3$, 1.5 mmol TsN_3, 30 mol % *t*-BuOOH, 6 mol % ligand **37**, 6 mol % $Co(BF_4)_2 \cdot 6H_2O$, and 2.5 mL of ethanol at 23 °C under argon. [b] General procedure **B**: 1.0 mmol TMDSO was used instead of $PhSiH_3$. [c] 2.0 mmol TMDSO was used. [d] Starting material was partially recovered (see Supporting Information for further details).

When considering the scope of the hydroazidation reaction, two major limitations are apparent: substrates bearing a stabilizing group (ester, phenyl, alkyne) in conjugation with the olefin do not react, and full conversion could not be obtained with sterically more-hindered substrates (di- and trisubstituted olefins). Even for monosubstituted olefins, a large excess (3 equiv) of sulfonyl azides is needed to achieve full conversion. Careful monitoring of the reaction with tosyl azide showed that in the case of sterically hindered substrates the problem does not reside in activity but in the stability of the catalyst. After about a 2−5 h reaction, precipitation of the catalyst occurs and no further conversion is observed. Unfortunately, the exact identity of the precipitate could not be assigned, but one explanation would be the formation of insoluble oligomeric Co−sulfinate salts.

The reaction conditions are similar to those for the hydrohydrazination reaction, and we hypothesize that the same active Co−alkyl intermediates should be generated in the two reactions. Consequently, the solution to the limitations of the hydroazidation reaction resides in the modification of the azide source to obtain a more active nitrogen-transfer reagent, less prone to deactivate the catalyst. For this reason, several other potential azide sources were examined for the hydroazidation of 4-phenylbutene **1** (Figure 3).

Phosphorus-based azide reagents **39** and **40** could not be used as azide sources. The chiral sulfonyl azide **41** also showed no conversion. Electron-rich sulfonyl azide **42** and commercially available sulfonyl azide **43** react in the hydroazidation reaction of 4-phenylbutene **1**, but full conversion was not observed, as precipitation of the catalyst occurs already after 1 h. To study potential favorable interactions between the sulfonyl azide and the Co catalyst, we examined arylsulfonyl azides functionalized at the ortho position (Figure 3, compounds **44**−**47**). The first result obtained with azide **44** bearing a free OH group was encouraging, as full conversion was observed after 2 h. More importantly, no precipitation of the catalyst occurred. The synthesis of **44** was not optimal, however, mainly because the intermediate sulfonyl chloride is very unstable and could not be purified. Unfortunately, these impurities could not be removed from azide **44**. Azide **45** could be synthesized with high purity, but it gives only low conversion in the hydroazidation reaction of 4-phenylbutene **1**. We then turned to azide **46** bearing a methoxy group instead of the free OH. We were pleased to see that this azide is also a good azide source, giving full conversion in 4 h without precipitation of the catalyst. Azide **46** is an easy to handle solid and is obtained in two steps from 4-methoxy toluene without the need of chromatography.[50] To rule out a simple electron-donating effect of the methoxy group, azide **47** bearing an electron-withdrawing ester group was next examined. Azide **47** gives nearly identical results to **46**, although the addition of methylene chloride as cosolvent for the hydroazidation reaction was necessary due to the low solubility of this reagent in ethanol. We have no experimental-based explanation for the success of **46** and **47** in stabilizing the catalytic system, and further studies are needed to better understand this effect. Interestingly, the reaction mixture in the hydroazidation reaction of 4-phenylbutene **1** with TMDSO and azides **46** and **47** had a different color than that observed for tosyl azide (from brown-green to dark green). That could suggest that indeed an interaction between the sulfonyl azide and the Co catalyst is occurring during the reaction.

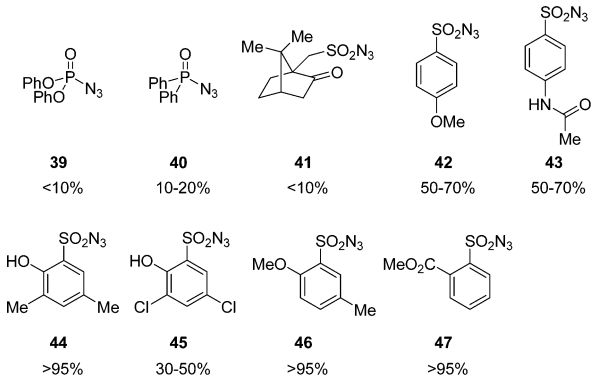
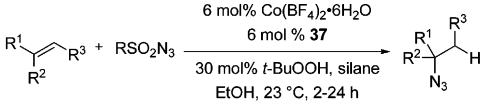


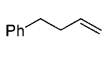
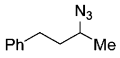
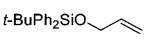
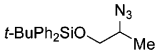
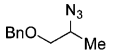
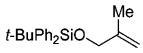
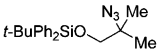
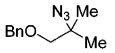
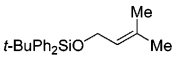
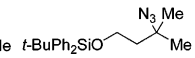
Figure 3. Azides tested as nitrogen sources for the hydroazidation of 4-phenylbutene **1**.[51]

Substrates that could be functionalized only in moderate yields with tosyl azide were examined next (Table 12). For 4-phenylbutene **1**, it was possible to use only 1.5 equiv of azide **46** or **47** to obtain more than 90% yield of the desired azide **27** (entry 1). When the reaction was performed with only 1.5 equiv of tosyl azide, **27** was obtained in 70% yield only, and the reaction failed to go to full conversion. The use of **46** or **47** gave no improvement for the hydroazidation of monosubstituted ethers (entries 2 and 3), but the yields were significantly improved for α-methyl disubstituted allylic ether (entries 4 and 5), leading to nearly complete conversion with half as much sulfonyl azide. Finally, a trisubstituted olefin could also be functionalized in good yield (entry 6).

(50) Chlorosulfonylation, followed by reaction with sodium azide, see Supporting Information for further details.

Table 12. Comparison of TsN_3, Azide **46**, and Azide **47** in the Hydroazidation Reaction



entry	alkene	product	Yield[a] with TsN_3	Yield[b] with **46**	Yield[c] with **47**
1			86%	94%	91%
2			67%	19%	44%
3			39%	<20%	28%
4			58%	89%	91%
5			40%	64%	76%
6			48%	83%	79%

[a] Standard conditions: 0.50 mmol 4-phenylbutene **1**, 1.5 mmol TsN_3, 1.0 mmol TMDSO, 30 mol % *t*-BuOOH, 6 mol % $Co(BF_4)_2 \cdot 6H_2O$, and 6 mol % ligand **37** in 2.5 mL of ethanol at 23 °C under argon. [b] Sulfonyl azide **46** (0.75 mmol) and 0.75 mmol TMDSO were used. [c] Sulfonyl **47** (0.75 mmol) and 0.75 mmol TMDSO were used and 1.0 mL of methylene chloride was added as cosolvent.

Substrates with the C−C double bond in conjugation with stabilizing groups, such as an ester, a phenyl, or an alkyne, still showed no conversion to the desired azides under the improved reaction conditions. This shows the possibility and limitations of the newly introduced azide sources **46** and **47**: these reagents give much better yield for substrates that react slowly but cleanly in the hydroazidation reaction (especially geminally disubstituted and trisubstituted alkenes), but they are not well-suited for substrates prone to a side reaction (such as monosubstituted allylic ethers) or olefins that have shown no conversion at all when using tosyl azide.

Mechanistic Investigations. To further develop the hydrohydrazination and hydroazidation reactions, a better understanding of the reaction mechanism is needed. When compared with the classical hydroamination reaction, the mechanistic studies of these reactions are complicated by the presence of both an oxidizing nitrogen source and a reducing hydride source. In the case of the hydroazidation, the *tert*-butyl hydroperoxide additive adds a level of complexity to the problem. Consequently, the primary goal of our investigations was a qualitative understanding of the catalytic cycle, focusing mostly on the hydrohydrazination reaction. This will facilitate the design of further experiments.

Our first attempt to get further information about potential intermediates in the reaction was to perform the hydrohydrazination reaction with a stoichiometric amount of Co complex **20**, with the hope of detecting some intermediate complexes during the course of the reaction (Figure 4). Addition of a stoichiometric amount of 4-phenylbutene **1** or azodicarboxylate **2** to a solution of complex **20** in methanol-d_4 resulted in no

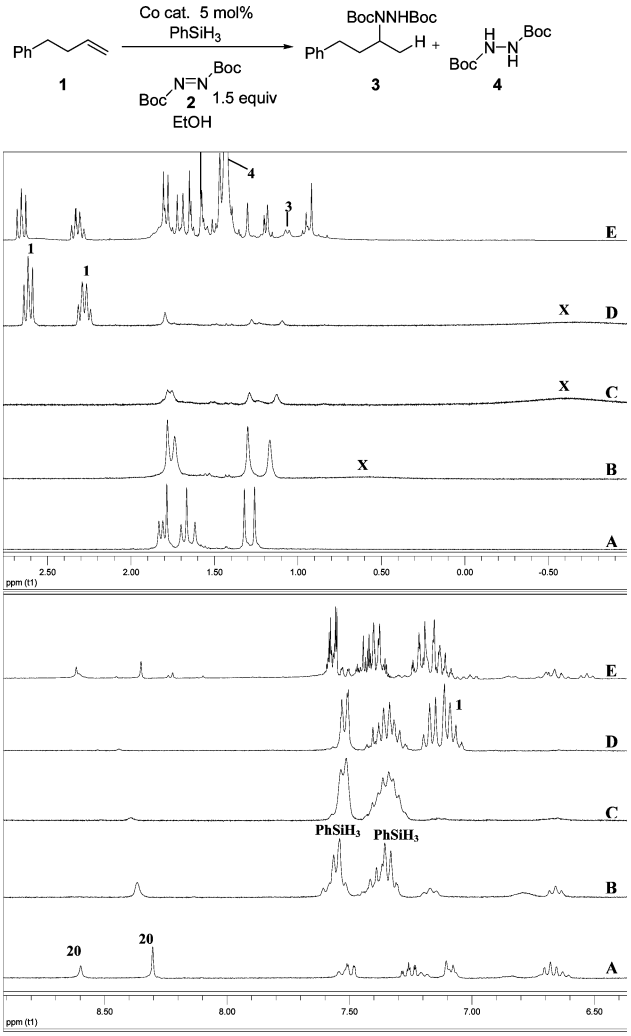
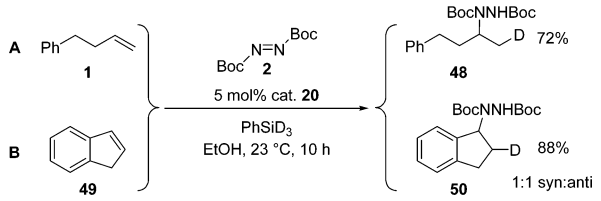


Figure 4. ^{1}H NMR monitoring of the hydrohydrazination reaction using a stoichiometric amount of Co catalyst **20**. **A**: Only catalyst **20**. **B**: Immediately after addition of $PhSiH_3$. **C**: After warming to 40 °C over 20 min. **D**: Back to 23 °C, 2 min after addition of alkene **1**. **E**: 30 min after addition of **2**.

visible changes in the signals of **20** when the reaction was monitored by ^{1}H NMR spectroscopy. However, when a stoichiometric amount of phenylsilane was added to **20**, the observed ^{1}H NMR spectrum changed completely and a new complex was detected (**B**, Figure 4). Unfortunately, this was accompanied by a broadening of all signals, precluding any precise structure assignment. This is likely due to a partial reduction of Co(III) to Co(II). Interestingly, a new broad signal appeared between −0.5 and 1 ppm (**X** in Figure 4). This signal was first thought to indicate the presence of a Co hydride complex. With the hope of obtaining better-resolved signals, the reaction mixture was heated slowly to 40 °C (**C**, Figure 4). Under these conditions, signal **X** was shifted to about −0.5 ppm and was sharper, but this was accompanied by a broadening of all other signals. Furthermore, a control experiment using phenylsilane-d_3 showed no change in shape or intensity for signal **X**, and this peak most probably results from a paramagnetic Co(II) complex and not from a hydride signal. No changes were observed when 4-phenylbutene **1** was added (**D**, Figure 4). The addition of azodicarboxylate **2** resulted in a fast conversion of **2** into hydrohydrazination product **3** and hydrazine **4**. In contrast to the reaction with catalytic amount of **20**,

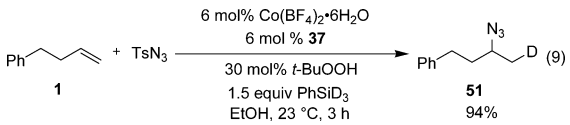
Scheme 2. Hydrohydrazination of 4-Phenylbutene **1** and Indene **49** with $PhSiD_3$ and Azodicarboxylate **2**



hydrazine **4** was the major product (**4**:**3** = 4:1). The reaction was accompanied by a shift of the signals corresponding to the Co complex, and after 30 min, several sets of sharp peaks similar to the starting complex **20** were observed, showing again the presence of Co(III) complexes (**E**, Figure 4).

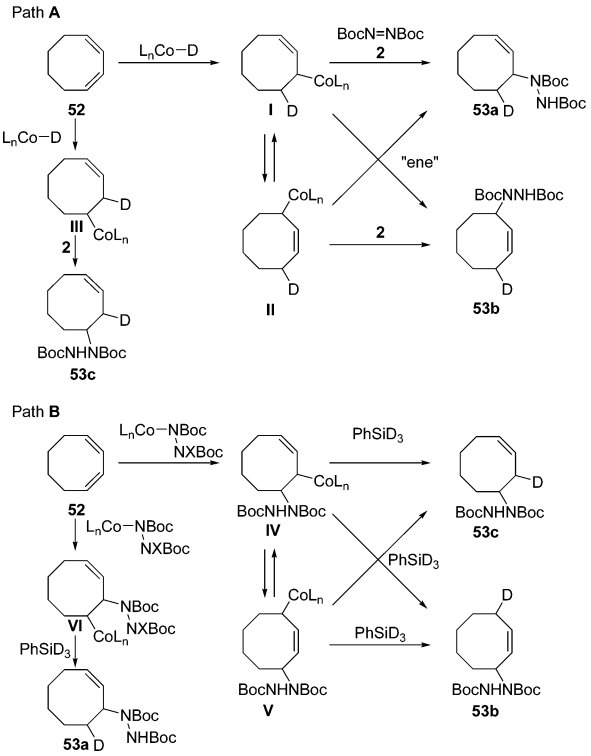
As we were not successful in identifying reaction intermediates via ^1H NMR spectroscopy, we turned to deuterium-labeling experiments. As a first experiment, the hydrohydrazination of 4-phenylbutene **1** was run under standard conditions, but using $PhSiD_3$ instead of $PhSiH_3$ (Scheme 2, **A**). The reaction displayed clean and complete deuterium incorporation at the primary position, as shown by ^1H and ^{13}C NMR spectroscopy. This suggests that the silane acts as a hydride source in these reactions, such that a pathway involving protonolysis of a Co−alkyl complex with ethanol is unlikely. Finally, a kinetic isotope effect on the reaction rate of 2.2(3) ± 0.5 was observed. This moderate primary isotope effect suggests that the formation of the C−H bond in the product is rate-determining. Next, the hydrohydrazination reaction of indene (**49**) using $PhSiD_3$ was examined to see if the formation of the product was stereospecific (Scheme 2, **B**). This proved not to be the case, as the product was obtained as a 1:1 mixture of diastereoisomers, as shown by ^1H NMR spectroscopy. This result is expected if the formed Co−alkyl complex is not stable and undergoes epimerization prior to reaction with azodicarboxylate **2**, if the reaction proceeds from a dissociated free radical, or if the amination is not stereospecific.

As in the case of the hydrohydrazination reaction, the hydroazidation of 4-phenylbutene with phenylsilane-d_3 resulted in the exclusive formation of azide **51** bearing a deuterium atom at the primary position (eq 9). Interestingly, the kinetic isotope effect displayed by the hydroazidation reaction (1.65(15) ± 0.32) is smaller than that for the hydrohydrazination reaction (2.2(3) ± 0.5).



From these first labeling experiments, it was clear that an insertion of the double bond in a Co−D complex with the Co atom ending at the primary or homobenzylic position cannot account for the reaction outcome, whereas an insertion placing the Co atom at the secondary or benzylic position and subsequent reaction with **2** leads to the observed products. However, another alternative cannot be excluded: insertion of the double bond in the C−N bond of a Co−hydrazido complex, placing the Co atom at the primary position, followed by reductive elimination. To gain more information about this step of the reaction, we decided to examine the hydrohydrazination of cyclooctadiene using $PhSiD_3$ (Scheme 3). Depending on the

Scheme 3. Possible Pathways for the Hydrohydrazination of Cyclooctadiene (**52**)

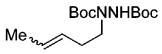
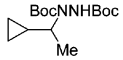
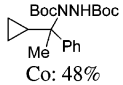
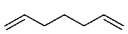
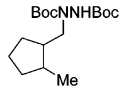
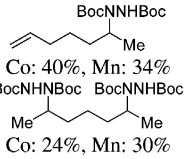
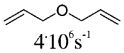
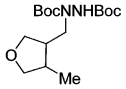
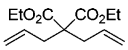
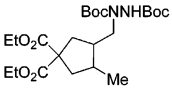


mechanism, products **53a**, **53b**, **53c**, or a mixture thereof are expected. In path **A**, a Co−D complex is first formed, and insertion of one of the double bonds of cyclooctadiene (**52**) gives the regioisomeric Co-allyl intermediates **I** or **III**. From **I**, direct addition to azodicarboxylate **2** gives product **53a**, whereas reaction via an ene pathway gives product **53b**.[52] Alternatively, complex **I** could be in fast equilibrium with the isomeric complex **II**. Intermediate **II** could also react directly to give **53b** or via ene reaction to give **53a**. Co intermediate **III** would be expected to lead to the exclusive formation of homoallylic hydrazine **53c**. In path **B**, a Co−hydrazido complex formed from azodicarboxylate **2**, and $PhSiD_3$ reacts via insertion in the C−N bond to give regioisomeric intermediates **IV** or **VI**. Subsequent reaction of complex **IV** with $PhSiD_3$ is expected to lead to homoallylic hydrazine **53c** or to allylic hydrazine **53b**. Once again, a fast equilibrium between complex **IV** and **V** can be envisaged, **V** can then further react to give **53b** or **53c**. Intermediate **VI** is anticipated to lead to **53a** through reaction with $PhSiD_3$, and no other products are expected.

When the hydrohydrazination reaction of **52** was run under standard conditions with $PhSiD_3$, a 1:1 mixture of products **53a** and **53b** was obtained in 52% combined yield. Homoallylic hydrazine **53c** was never observed so that the pathways leading to this compound are not operative. Path **B** is unlikely, as in this case formation of hydrazines **53a**, **53b**, or **53c** only, or a mixture of **53b** and **53c**, are the most likely results.[53] However, a 1:1 mixture of **53a** and **53b** is consistent with the operation of path **A**, in the case of a fast equilibrium of the two allyl

(51) The conversions using 2 equiv of azide are given.
(52) Alternatively, dissociation of a free radical from the Co complex prior to amination can be envisaged.
(53) In fact, the only possibility to obtain the observed mixture via pathway **B** would be a nonregioselective insertion of **30** in the Co−N bond and the exclusive formation of **31b** from either **IV** or **V**.

Table 13. Radical Clocks Examined in the Hydrohydrazination Reaction

entry	alkene rearrangement rate	"radical" product yield	other products yield
1	 $4\cdot10^7\ s^{-1}$	 Co: 59%[a]	 Co: <5%
2	 $4\cdot10^5\ s^{-1}$	mixture Co: 20-30% Mn: 20%[b]	 Co: 48% Mn: 60%
3	 cis: $1\cdot10^5\ s^{-1}$ trans: $3\cdot10^4\ s^{-1}$	 Co: 8%, dr: 1.4:1 Mn: 6%, dr: 5:1	 Co: 40%, Mn: 34% Co: 24%, Mn: 30%
4	 $4\cdot10^6\ s^{-1}$	 Co: 68%, dr: 1.6:1 Mn: 88%, dr: 2.5:1	<5%
5		 Co: 62%, dr: 7:1 Mn: 93%, dr: 9:1	<5%

[a] Standard conditions: 0.50 mmol alkene, 0.50 mmol $PhSiH_3$, 0.75 mmol di-*tert*-butyl azodicarboxylate (**2**), 5 mol % catalyst **20**, and 2.5 mL of ethanol at 23 °C under argon. [b] Standard conditions: 0.50 mmol alkene, 0.50 mmol $PhSiH_3$, 0.75 mmol di-*tert*-butyl azodicarboxylate (**2**), 2 mol % catalyst **23**, and 2.5 mL of *i*-PrOH at 0 °C under argon.

complexes **I** and **II**, followed by reaction via either ene or direct pathway. The same result would be obtained if **I** reacts via ene and direct pathways at the same rate.

Deuterium-labeling experiments have allowed us to better understand the transfer of the H atom to the double bond, but nearly no information on the crucial amination step was obtained. One commonly proposed mechanism for the Co-catalyzed *Mukaiyama* hydration reaction involves carbon radicals.[54] To test the presence of radical intermediates, we made use of radical clocks based on cyclopropane ring opening or cyclization.[55]

We first tested vinylcyclopropane itself (entry 1, Table 13). The secondary carbinyl cyclopropyl radical is known to undergo rearrangement with a rate of $4 \times 10^7\ s^{-1}$.[55c] Usually, competition experiments are run with a large excess of the radical trap, but it was difficult in our case due to the limited solubility of azodicarboxylate **2**. For these reasons, we preferred to use our standard reaction conditions, as the obtained rates can be mathematically corrected.[55c] Vinylcyclopropane gave hydrazine derivative resulting from the opening of the cyclopropane ring as the only isolated product and, as such, set a higher limit for the reaction rate of the intermolecular amination reaction (entry 1). We then turned to α-phenyl vinylcyclopropane, as the stabilizing effect of the phenyl group slows down the rearrangement for this compound ($4 \times 10^5\ s^{-1}$; entry 2).[56] In fact, the major product was the nonrearranged hydrohydrazination product for both Co and Mn catalysts. Ring-opening products were also obtained, but, due to multiamination, several products were formed, and they could not be separated. Nevertheless, the ratio of rearranged/unrearranged products can be estimated roughly to be 1:2−1:3. This leads to a reaction rate of about $1.5-2.5 \times 10^8\ s^{-1}\ mol^{-1}$ for the amination step, with no significant difference between the Co and the Mn catalysts.

Next, we decided to examine another type of radical clock based on the 5-*exo*-trig cyclization of dienes (entries 3 to 5).[55c] The hexenyl radical derived from heptadiene cyclizes quite slowly ($1 \times 10^5\ s^{-1}$ to the *cis* product and $3 \times 10^4\ s^{-1}$ to the *trans* product).[57] In accord with these reported data, the main products resulting from the hydrohydrazination reaction of heptadiene were not cyclized monoaminated and diaminated products, but small amounts of the cyclization product could be isolated. The rate for the amination step can be estimated again to be $1.5-2.0 \times 10^8\ s^{-1}\ mol^{-1}$ for the Co catalyst and $2.0-2.5 \times 10^8\ s^{-1}\ mol^{-1}$ for the Mn catalyst. Although the values obtained are only rough estimations,[58] the fact that two systems based on different mechanisms gave the same value is noteworthy. This enhances the probability that the reaction coud proceed via free radicals or at least Co−alkyl radical pairs. If another reactive intermediate was involved, the reaction rates would have not been expected to display exactly the same behavior as known for free radical reactions in two structurally distinct substrates. However, a rearrangement or cyclization "on Co" could still be envisaged.

Finally, in the case of dienes more prone to cyclization, preparatively useful yields of the tandem cyclization/hydrohydrazination reaction can be obtained (entries 4 and 5). For diallyl ether,[59] the two diastereisomers could be separated, and the major product was found to be the *cis*-isomer by NOE ^1H NMR (entry 4). Again, this is in accordance with the well-known preference of free radicals for the formation of *cis* products in the 5-*exo*-trig cyclization.[60] In these reactions, the Mn catalyst **23** usually displays higher yield and selectivity, especially in the case of diallyl malonate (entry 5), for which the cyclization/hydrohydrazination product was obtained in 94% yield and 9:1 diastereoselectivity.

Next, we proceeded to examine the kinetics of the hydrohydrazination and hydroazidation reactions. We decided to limit our kinetic investigations to the Co-catalyzed hydrohydrazination and hydroazidation of 4-phenylbutene **1**. The hydrohydrazination reaction could be monitored by ^1H NMR spectroscopy, as running the reaction in methanol-d_4 gave only minor differences in rate when compared with the standard conditions (ethanol). The hydroazidation reaction was monitored by gas chromatography.

We first examined the dependence of the reaction rate on the initial concentration of 4-phenylbutene **1**. When the concentration of **1** was systematically increased, the rate of the reaction also increased for both reactions. An approximation of the reaction order was obtained from a van't Hoff plot on the initial rate. In the case of the hydrohydrazination reaction,

(54) Tokuyasu, T.; Kunikawa, S.; Masuyama, A.; Nojima, M. *Org. Lett.* **2002**, *4*, 3595.
(55) (a) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317. (b) Nonhebel, D. C. *Chem. Soc. Rev.* **1993**, *22*, 347. (c) Newcomb, M. *Tetrahedron* **1993**, *49*, 1151.
(56) Bullock, R. M.; Samsel, E. G. *J. Am. Chem. Soc.* **1987**, *109*, 6542.
(57) Lusztyk, J.; Maillard, B.; Deycard, S.; Lindsay, D. A.; Ingold, K. U. *J. Org. Chem.* **1987**, *52*, 3509.
(58) For more exact values, more data would be needed, for example through a series of reactions at different concentrations.
(59) Burkhard, P.; Roduner, E.; Hochmann, J.; Fischer, H. *J. Phys. Chem.* **1984**, *88*, 773.
(60) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.

this gives an order of 0.98(16) ± 0.23, which means that the reaction is first order in the substrate and suggests that the alkene is involved in the rate-determining step of the reaction in accordance with the results of the deuterium-labeling studies. For the hydroazidation reaction, the calculated reaction order was only 0.45(3) ± 0.07, suggesting that several steps contribute equally to the reaction rate.

In the case of the nitrogen source, azodicarboxylate **2** or tosyl azide, the rate of the reactions was completely independent of the initial concentrations. The van't Hoff plot gives an order of −0.18(8) ± 0.12[61] and 0.06(4) ± 0.26, respectively, which correspond to a zero order for **2** or tosyl azide. This suggests that the amination step is faster than the rate-determining step and, as such, does not influence the apparent reaction rate.

For phenylsilane and the Co catalyst **20**, the situation is not so clear, and we obtained mixed-order results. The reaction rate shows only a very weak dependence from the initial concentration of silane when enough silane (>0.8 equiv) is present. However, at low concentration, the silane begins to play a more pronounced role on the reaction rate. As the high concentrations are more relevant to our standard conditions, the order of the reaction in phenylsilane was determined only for concentrations higher than 0.14 M (0.8 equiv), and we obtained an order of 0.22(11) ± 0.16 for the hydrohydrazination reaction and 0.33(3) ± 0.1 for the hydroazidation reaction. In the case of the hydrohydrazination with Co catalyst **20**, the data obtained were of lower quality and the order of 0.54(10) ± 0.22 is difficult to interpret. The influence of the catalyst was stronger in the case of the hydroazidation reaction (order of 0.82(5) ± 0.11 with a 1:1 ligand-to-Co ratio). Changing the ligand-to-Co ratio gives nearly no change in rate. In the case of the peroxide, we observed a good linearity for the van't Hoff plot in a concentration range of 0.014 to 0.2 M (7 to 100%) with a reaction order of 0.643(14) ± 0.020. This indicates that the peroxide is not only important as an initiator, but also during the reaction. Up to now, we have still no explanation for this very strong effect. The fact that the hydrohydrazination reaction needed no additive to attain a useful rate suggests that the effect of the peroxide occurs after hydrocobaltation of the double bond. This effect could be due to activation of the Co species such that it is more prone to react with the azide or by helping the regeneration of a Co−hydride complex at the end of the catalytic cycle. A (partially) rate-determining catalyst regeneration step would further be consistent with the lower kinetic isotope effect and the mixed order in alkene observed for the hydroazidation reaction.

As a result of the complexity of the reactions, including probably an initiation step for the generation of a Co−hydride complex, mixed orders are not unexpected. Furthermore, the kinetics are complicated by the presence of the direct reduction of azodicarboxylate in the case of the hydroydrazination reaction and the strong effect of the peroxide in the hydroazidation reaction. For these reasons, although the data obtained in these studies were statistically significant, their interpretation in terms of mechanistic relevance is difficult.

The temperature dependence of the reactions was examined next (Figure 5 and Figure 6). The Arrhenius plot for the reaction allowed us to determine the energy of activation for the

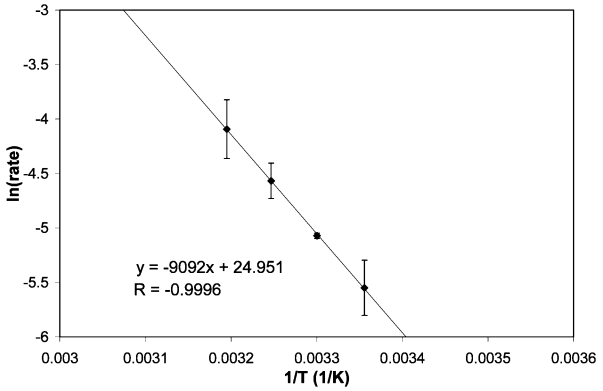


Figure 5. Arrhenius plot for the hydrohydrazination reaction.

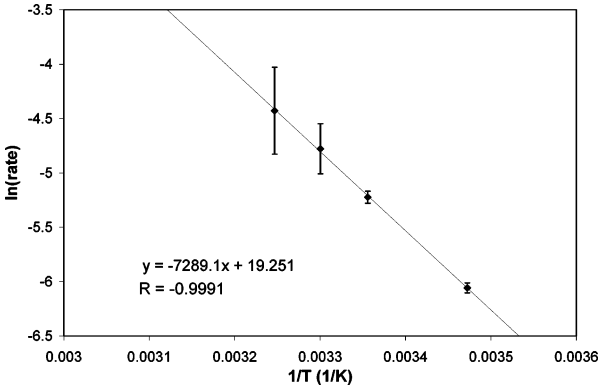
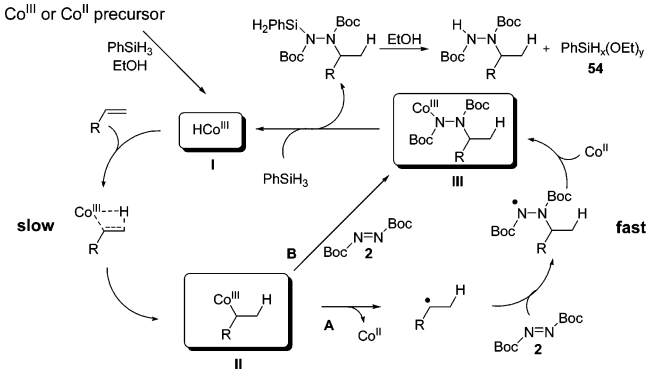


Figure 6. Arrhenius plot for the hydroazidation reaction.

Scheme 4. Working Model for the Mechanism of the Hydrohydrazination Reaction



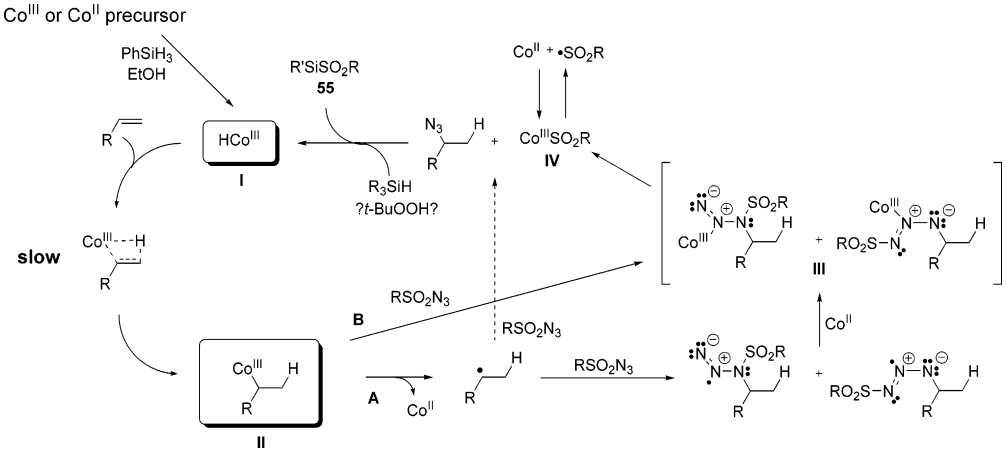
reactions: 76(7) ± 15 kJ·mol^{-1} for the hydrohydrazination and 60(3) ± 6 kJ·mol^{-1} for the hydroazidation reaction. Interestingly, these values are lower than the activation barrier calculated by Togni and co-workers for the direct hydroamination reaction via olefin activation using Ni catalysts (108 kJ·mol^{-1}), which was predicted to be the lowest of all the metals examined.[62]

The results of our preliminary mechanistic investigations led us to propose the working model shown in Scheme 4 for the mechanism of the hydrohydrazination reaction. The first step of the reaction is the initiation of the catalytic cycle via formation of active Co−hydride complex **I**. Already at this stage, there are a number of questions about the identity of **I**. As we were not successful in isolating or detecting a clean Co(III)−hydride complex, its presence in the catalytic cycle

(61) The low correlation ($R = -0.412$) observed for the data further confirms that the reaction rate is indeed independent of the concentration of **2**.

(62) Senn, H. M.; Blochl, P. E.; Togni, A. *J. Am. Chem. Soc.* **2000**, *122*, 4098.

Scheme 5. Working Model for the Mechanism of the Hydroazidation Reaction



remains speculative. In the case of the Co-catalyzed Mukaiyama peroxidation reaction, the generation of a hydride complex is thought to proceed via prior activation of Co(II) with oxygen.[54] In our case, the silane seems able to reduce at least partially the catalyst, as shown by our NMR experiments, but it is difficult to know if the catalyst is further activated by the azodicarboxylate. It would be interesting in the future to synthesize Co−hydrazido complexes to see if they are also active catalysts.

From **I**, hydrocobaltation of the double bond led to Co−alkyl complex **II**. The insertion of the double bond in the Co−H bond placing the Co atom at the secondary center is in accordance with our deuterium-labeling experiments. Furthermore, both the reaction order in alkene substrate and the significant kinetic isotope effect observed for the reaction suggest that this step is rate-determining, whereas the following amination step is fast. This explains why we were never able to observe Co−alkyl complex **II**. As adding the alkene to a stoichiometric mixture of Co complex **20** and $PhSiH_3$ leads to no reaction, two possibilities can be envisaged: either the insertion of the double bond is reversible and the equilibrium lies in the favor of **I**, or the azodicarboxylate is indeed needed to generate an active catalyst. However, we have never observed an isomerization of the C−C double bond in the olefins tested, making reversible olefin insertion less probable.

From **II**, the crucial amination step is difficult to examine, as it is very fast. The reaction of radical clocks, both via rearrangement and via cyclization strongly suggest the presence of free radicals. However, this is not a proof that the generated radical also adds on azodicarboxylate **2** (path **A**). One could envision that radical generation is an unproductive pathway, and the reaction in fact proceeds from the Co-bound intermediate (path **B**). In this aspect, it will be interesting in the future to generate free radicals via an independent method and test their addition on azodicarboxylate **2**.

After the reaction with **2**, the generated Co−hydrazido complex could react with the silane to regenerate an active Co−hydride complex **I**. We did not observe silylated hydrazine derivatives, but instead, product **54**, resulting from the ethanolysis of phenylsilane, was isolated. The strong effect of protic solvents on the reaction rate is probably effective in this step, and ethanol must play a role in the regeneration of complex **I** and not be simply limited to the alcoholysis of silylated hydrazines.

The scarce mechanistic information obtained so far for the hydroazidation reaction does not allow the proposal of a precise mechanism for the reaction. However, a speculative working model, which is in accordance with our observations, is presented in Scheme 5. We hypothesize a similar entry in the catalytic cycle via a Co−hydride complex **I**. For this step, the *tert*-butyl hydroperoxide additive could already play an important role. Hydrocobaltation would then give a Co−alkyl complex **II**. At this point, we can only speculate at what happens next. Again, two pathways can be envisaged: a free radical pathway (**A**) or direct reaction of Co−akyl complex **II** with sulfonyl azide (**B**). Free radicals have been reported to react with sulfonyl azide by Renaud and co-workers.[18b,c] However, this reaction was run at elevated temperature. The radical adduct formed in the addition to the sulfonyl azide (as a result of addition on the terminal or internal N═N bond of the sulfonyl azide) could either be recaptured by a Co(II) complex to give a new Co complex **III**, in analogy to the Co−hydrazido complex **III** proposed for the hydrohydrazination reaction, or collapse directly to the azide and a sulfonyl radical. A direct reaction of the Co−alkyl complex **II** with the sulfonyl azide would also give **III**. In contrast to the hydrohydrazination reaction, the amination step is much more substrate-dependent: if the R group on the alkene has a stabilizing effect (for example with phenyl, ester, or alkyne), no reaction is observed.

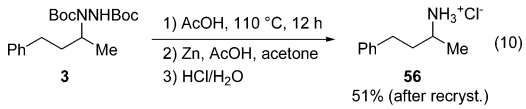
The fate of the catalyst after the azidation step is uncertain: A Co−sulfonato complex **IV** could be formed directly from **III** via elimination or after recombination with a Co(II) complex, but the formation of **IV** is speculative and Co−hydride complex **I** could also be regenerated from **III** directly. It is also possible that **IV** could be the inactive precipitate observed in the reaction (vide supra). As the order of the reaction in the sulfonyl azide was zero, a possible explanation for the strong additive effect of the peroxide is the acceleration of the conversion of **III** or **IV** to Co−hydride complex **I**, allowing useful turnovers. The end product resulting from the silane has yet to be identified, but silane derivatives of polymeric nature were often detected in the crude mixture. A possible structure would be a mixed silane/sulfonate such as **55**. Obviously, further efforts are needed to identify the inactive precipitate as well as the end products resulting from the silane and the sulfonyl azides.

The fact that Mn catalyst **23** was more active for the hydrohydrazination reaction but failed completely in the case of the hydroazidation reaction is also intriguing. It could be

envisaged that Mn−alkyl complexes similar to **II** are unable to react with the sulfonyl azide, but in this case, a common free-radical manifold for the two catalysts would be excluded. Another possibility is that catalyst **23** is too unstable under the reaction conditions, and deactivation occurs immediately after one turnover. In fact, we observed that Mn catalysts bearing the more robust tridentate ligand **37** indeed display some activity in the hydroazidation reaction.

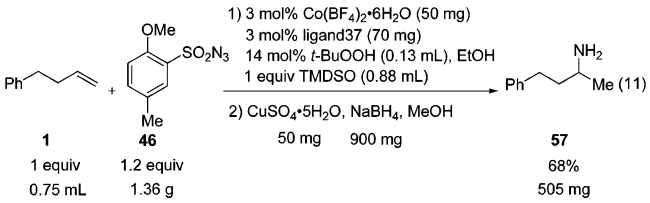
Transformation of Azide and Hydrazine Products. Hydrazines and azides are useful building blocks by themselves, but the final products in pharmaceutical and natural products seldom contain these functionalities.[63] A fast and convenient access to the free amine is highly desirable. At this stage of development, we focused on the transformation of a few chosen substrates to test and optimize known literature procedures.

There are several reports for the conversion of Boc-protected hydrazines to the free amines.[64] The most frequently used methods are hydrogenation reactions over metal catalysts. The procedure involving Raney Ni is inconvenient because it requires high pressure hydrogen (>20 bar).[64a] Pt-based catalysts are more active,[64c−e] but they also promoted the hydrogenation of aromatic rings of the substrates in our experience. For these reasons, we turned to the reduction of the N−N bond of the hydrazines using Zn dust.[65] This method is very mild but requires prior removal of the Boc protecting groups. One possibility is to perform this deprotection in trifluoroacetic acid (TFA), but as the Zn reduction did not work in TFA, removal of the highly corrosive TFA was needed. However, it was possible to devise a one-pot procedure for the transformation of hydrazine **3**, the product of the hydrohydrazination of 4-phenylbutene **1**, to the free amine hydrochloride **56** (eq 10). Deprotection occurred in acetic acid when refluxing for 12 h. Addition of acetone resulted in the formation of the hydrazone, which was subsequently reduced with Zn dust.[66] The crude amine was treated with aqueous HCl and water was removed, and pure amine hydrochloride **56** could be isolated in 51% yield after recrystallization. This represents a 43% overall yield for the formal addition of ammonia on the double bond of 4-phenylbutene **1**.



In the case of azides, the reduction to the free amine is possible under much milder conditions.[40] Furthermore, the cycloaddition reaction of azides with terminal alkynes increases the versatility of these compounds.[41] The mild conditions of the olefin hydroazidation reaction had allowed us to develop a one-pot conversion of olefins to amines using in situ reduction[40a] and to 1,4-disubstituted triazoles using Sharpless' procedure[41b] for 4-phenylbutene **1** in useful yields.[25]

However, the initially developed procedure using TsN_3 is not convenient for reactions conducted on a larger scale because a large excess of reagents (3 equiv of TsN_3 and 2 equiv of TMDSO) is needed to achieve full conversion. To limit the amount of waste, we made use of azide **46** for the reaction of 4-phenylbutene **1** on a 5 mmol scale (eq 11). We were pleased to see that in this case the use of only 1.2 equiv of **46** and 1 equiv of TMDSO were sufficient to afford the desired amine **57** in 68% overall yield.



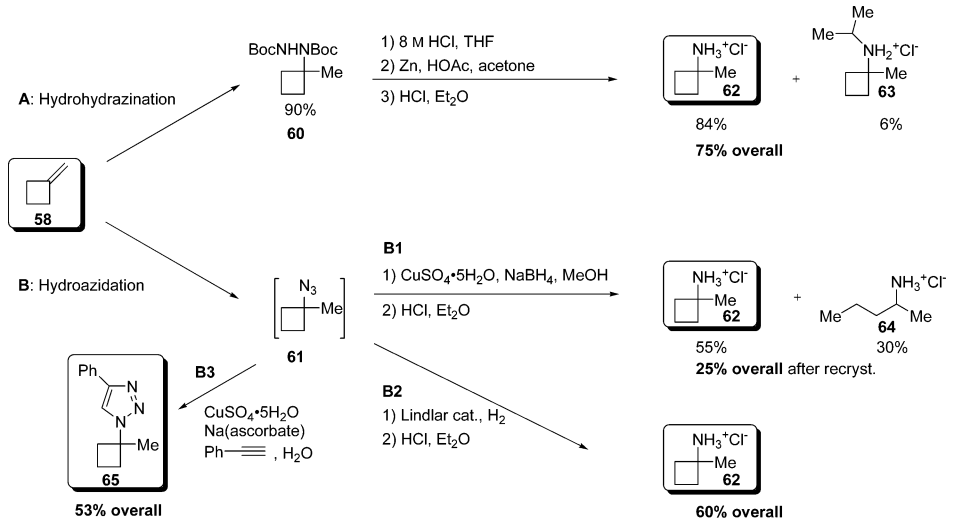
Small, geometrically constrained amines such as methylcyclobutylamine and methylcyclopropylamine are of interest as building blocks in medicinal chemistry in the optimization of the activity of pharmaceuticals.[67a−c] The influence of the ring structure on the basicity of the amine is also of theoretical interest.[67d] However, these compounds are not easy to prepare, and published procedures made use of multistep sequences based on the Ritter reaction[68] or the Hofmann rearrangement.[69] Our methods offer the possibility to access these compounds directly from commercially available methylenecyclobutane (**58**) and methylenecyclopropane (**59**). The amination of methylenecyclopropanes mediated by lanthanide catalysts has been reported, but opening of the cyclopropyl ring was observed in this reaction.[12b] We decided to further demonstrate the strengths and limitations of the hydrohydrazination and hydroazidation reactions in the synthesis of these interesting amines.

We first examined the reaction of methylenecyclobutane (**58**; Scheme 6). The Co-catalyzed hydrohydrazination reaction of **58** gives 90% yield of the desired tertiary hydrazine derivative **60** after column chromatography (path **A**, Scheme 6). The Mn-catalyzed hydrohydrazination reaction could also be used, but in this case, a small amount of the primary hydrazine derivative was also obtained and could not be separated from the main product. At this point, removal of the Boc group of **60** in boiling acetic acid did not proceed in good yield. Clean removal of the Boc groups was achieved in a 1:1 mixture of 8 M HCl and THF in 1 h at room temperature. After subsequent reduction with Zn dust in acetone/acetic acid, formation of the amine hydrochloride salt and recrystallization, **62** was obtained in 84% yield together with a small amount of **63** resulting from a reductive amination of **62** with acetone. Unfortunately, **62** and **63** were difficult to separate via recrystallization, and higher purity of **62** could be obtained only with great substance loss. Nevertheless, this reaction sequence represents a formal addition of ammonia on methylenecyclobutane **58** with 75% overall yield.

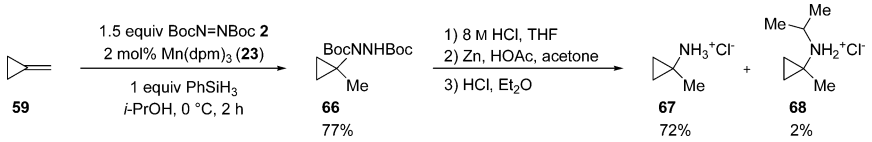
The hydroazidation reaction of **58** was examined next (path **B**, Scheme 6). Hydroazidation of **58** gives the volatile and

(63) The wide-spread use of AZT in the treatment of AIDS constitutes a noteworthy exception.
(64) (a) Evans, D. A.; Britton, T. C.; Dorow, R. L.; Dellaria, J. F. *J. Am. Chem. Soc.* **1986**, *108*, 6395. (b) Evans, D. A.; Britton, T. C.; Dorow, R. L.; Dellaria, J. F. *Tetrahedron* **1988**, *44*, 5525. (c) Gennari, C.; Colombo, L.; Bertolini, G. *J. Am. Chem. Soc.* **1986**, *108*, 6394. (d) Oppolzer, W.; Moretti, R. *Helv. Chim. Acta* **1986**, *69*, 1923. (e) Oppolzer, W.; Moretti, R. *Tetrahedron* **1988**, *44*, 5541. (f) Trimble, L. A.; Vederas, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 6397.
(65) Leblanc, Y.; Fitzsimmons, B. J. *Tetrahedron Lett.* **1989**, *30*, 2889.
(66) It is important to use a good quality of freshly activated (over diluted HCl) Zn dust to obtain good yields.
(67) (a) Castagnoli, N.; Rimoldi, J. M.; Bloomquist, J.; Castagnoli, K. P. *Chem. Res. Toxicol.* **1997**, *10*, 924. (b) Burgess, K.; Ke, C. Y. *J. Org. Chem.* **1996**, *61*, 8627. (c) Jimenez, A. I.; Cativiela, C.; Aubry, A.; Marraud, M. *J. Am. Chem. Soc.* **1998**, *120*, 9452. (d) McDonald, R. N.; Reitz, R. R. *J. Am. Chem. Soc.* **1976**, *98*, 8144.
(68) Cox, E. F.; Silver, M. S.; Roberts, J. D.; Caserio, M. C. *J. Am. Chem. Soc.* **1961**, *83*, 2719.
(69) Vaidyanathan, G.; Wilson, J. W. *J. Org. Chem.* **1989**, *54*, 1815.

Scheme 6. Comparison of the Hydrohydrazination and Hydroazidation Reaction for the Amination of Methylenecyclobutane (**58**)



Scheme 7. Hydrohydrazination Reaction for the Amination of Methylenecyclopropane (**59**)



potentially explosive azide **61**, which was directly reduced in situ. When we used the standard reduction conditions with sodium borohydride and a Cu catalyst, a significant amount of ring-opening product **64** was also obtained (path **B1**). Fortunately, this problem could be circumvented by changing to the Lindlar catalyst using hydrogen as reductant (path **B2**).[40b] In this case, the methylcyclobutylamine hydrochloride **62** was obtained in 60% overall yield with high purity after recrystallization. The overall yield is slightly lower for the hydroazidation reaction when compared with the hydrohydrazination reaction, but amine hydrochloride **62** was obtained in higher purity, and all reactions of the sequence were run in one pot without the need of column chromatography for product purification. Finally, the combination of the hydroazidation reaction with Sharpless' click chemistry was also successful and gives the triazole **65** in 53% overall yield after column chromatography (path **B3**).

In the case of methylenecyclopropane (**59**), the compound is too volatile to run the reaction at room temperature (bp = 9 °C). In this case, the Mn-catalyzed hydrohydrazination reaction proved to be the best procedure, as this reaction readily proceeds at 0 °C to give the desired hydrazine product **66** in 77% yield after column chromatography (Scheme 7). Deprotection with HCl followed by reduction with Zn dust and isolation as amine hydrochloride proceeded smoothly to give **67** in 72% yield after recrystallization. In this case, the reductive amination with acetone occurred in 2% yield only, and pure **67** could be obtained after a second recrystallization. Overall, the formal Markovnikov amination of methylenecyclopropane with ammonia has been achieved in 55% yield. Importantly, no products resulting from ring opening have been detected.

Conclusion

We have described the development of the Co- and Mn-catalyzed hydrohydrazination reaction of olefins. This reaction corresponds to a direct hydroamination of C−C double bonds with protected hydrazines but is based on a fundamentally different concept in which the H and the N atoms come from two different reagents, a silane and an azodicarboxylate. The reaction is characterized by its ease of use: commercially available silanes and azodicarboxylates as reagents, easily synthesized and bench-stable Co and Mn catalysts **20** and **23**, alcohol solvents of commercially available purity, and operationaly simple procedures. Moreover, in contrast to many classical hydroamination methods, the reaction readily proceeds at room temperature under neutral conditions. The scope of the reaction is very broad for an amination reaction, including mono-, di-, tri-, and tetrasubstituted olefins, activated and nonactivated olefins, dienes, enynes, and heterocycles.

Based on the same principles, we then described the development of the Co-catalyzed hydroazidation of olefins. This reaction allows a direct access to secondary and tertiary alkyl azides, complementing existing methods using substitution or hydrazoic acid addition. Alkyl azides are versatile intermediates, easy to reduce to the free amine or to convert to triazoles and tetrazoles via cycloaddition reactions. Key to the successful development of the hydroazidation reaction was the use of sulfonyl azides as nitrogen sources and the discovery of the activating effect of *tert*-butyl hydroperoxide. After careful optimization, the reaction was found to be efficient for the functionalization of mono-, di-, and trisubstituted olefins. The scope is more limited than that of the hydrohydrazination reaction, however, as several functional groups were not well-tolerated and no azide products were isolated for olefins in conjugation with a stabilizing group (phenyl, ester, or alkyne).

The conversion of the hydrazine and azide products obtained into the free amines was further demonstrated. In the case of the hydrohydrazination reaction, this transformation was achieved via acid-promoted deprotection and reduction with Zn dust. For the hydroazidation reaction, it was possible to develop a one-

pot hydroazidation/reduction protocol to obtain directly the free amine. This corresponds formally to the direct hydroamination of olefins with ammonia. Alternatively, a one-pot procedure allowing direct access to triazoles was also disclosed.

Finally, our preliminary mechanistic investigations have been presented. On the basis of NMR, deuterium-labeling studies, radical clocks, and kinetic measurements, a first speculative image of the catalytic cycle was proposed. However, many important questions remain to be elucidated.

In summary, we have reported the first successful use of an "oxido-reductive" approach for the hydroamination of unactivated olefins. This allows a new direct access to hydrazines and azides from olefins in high yields under operationally simple reaction conditions. The methodology is still in its infancy, and future work will be dedicated to overcome the limitations of the scope observed for the hydroazidation reaction, to the functionalization of more complex substrates en route to natural products, bioconjugates, or pharmaceuticals, and to the identification of more convenient nitrogen sources, which do not have the safety concern associated with azodicarboxylates and sulfonyl azides. Finally, the development of asymmetric hydrohydrazination and hydroazidation reactions will be pursued, as the access to chiral amines is highly desirable.

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Supporting Information Available: Experimental procedures, kinetics, and spectral data for all products (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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