

Allyltrimethoxysilane Addition to *N*-Acylhydrazones: Two Catalytic Methods Employing CuCl and Fluoride

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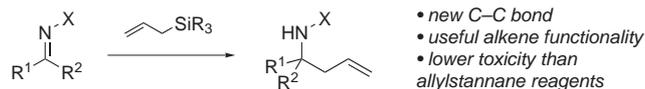
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Abstract: Two alternative reaction conditions developed for allyltrimethoxysilane addition to *N*-benzoylhydrazones enable efficient and versatile access to homoallylic α -branched amines. Aldehyde hydrazones, both aromatic and aliphatic, and ketone hydrazones all give good yields. One set of conditions employs catalytic amounts of CuCl and tetrabutylammonium triphenyldifluorosilicate (TBAT); improved yields and reaction times are obtained at 80 °C in the presence of bis(diphenylphosphino)ethane (dppe) and *t*-BuOH as additives. The second set of conditions employs 20 mol% TBAT as a fluoride source in a metal-free catalytic system; here *t*-BuOH offers only modest improvement, and ambient temperatures are optimal. For example, under this second set of conditions, the *N*-benzoylhydrazone from ethyl pyruvate affords the homoallylic *tert*-alkyl amine adduct in 78% yield.

Key words: addition reactions, allylation, catalysis, hydrazones, silicon

Allyl group addition to the C=N bond of imino compounds using organometallic nucleophiles is an important synthetic transformation, as it can generate a carbon-carbon bond and a new stereocenter while retaining the useful alkene functionality for subsequent elaboration (Scheme 1).¹ Allylsilanes have traditionally been considered insufficiently reactive to undergo addition to neutral imino compounds, but interest in this addition process has been renewed following the emergence of allylsilanes as competent nucleophiles for this transformation.²

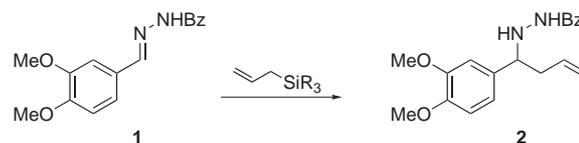


Scheme 1 Synthetic importance of allylsilane addition to imino compounds.

Our earlier efforts uncovered a novel dual activation method, whereby an allylsilane and a chiral *N*-acylhydrazone could be separately activated by tetrabutylammonium triphenyldifluorosilicate (TBAT) and In(OTf)₃, respectively, resulting in mild conditions for highly stereoselective amine synthesis.³ Several other impressive studies have introduced chiral sulfoxides as stoichiometric organocatalysts for allyltrichlorosilane addition to benzoylhydrazones,⁴ a chiral chlorosilane reagent for

asymmetric allyl or crotyl addition to *N*-benzoylhydrazones,⁵ and a CuCl–TBAT-catalyzed addition of allyltrimethoxysilane to *N*-benzylimines.⁶ A very promising recent report disclosed that a combination of ZnF₂ and chiral diamine catalyzes allyltrimethoxysilane addition to α -hydrazone esters with ee up to 86%,⁷ while elegant studies of Pd-catalyzed allylsilane addition have led to highly enantioselective allyl additions to aromatic imines.⁸ Still, a general and versatile asymmetric catalysis of this transformation remains a timely and challenging objective.

In connection with ongoing alkaloid synthesis objectives, we required homoallylic amine **2**, which we expected would arise from allyl addition to the C=N bond of an imino derivative of 3,4-dimethoxybenzaldehyde (Scheme 2). In attempting to apply allyltrichlorosilane addition^{2c} with **1**, we found reproducibly disappointing yields. We sought alternative conditions for this allylsilane addition to enable efficient access to **2**.



Scheme 2

In approaching the development of improved procedures for allylsilane addition, we hypothesized that CuCl–TBAT-mediated allyltrimethoxysilane addition might offer a new opportunity for asymmetric catalysis. Shibasaki demonstrated the potential of this approach in asymmetric allyl addition to aldehydes, wherein the CuCl–TBAT system was modified by the chiral phosphine BINAP.⁶ We hoped to test the potential of this method by extending it to *N*-acylhydrazones, and by modifying the CuCl with chiral ligands. Here we report two useful conditions for promoting allyltrimethoxysilane addition to *N*-acylhydrazones, including hydrazones derived from aliphatic aldehydes and ketones.

Cu-Dependent Conditions

Although *N*-acylhydrazones are electronically somewhat different from the *N*-benzylimines, the CuCl–TBAT-mediated conditions employed by Shibasaki for the latter substrates seemed to offer some potential for new catalyt-

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ic methods with *N*-acylhydrazones. We began by screening some modified reaction conditions for the addition to **1** (Scheme 2). Using CuCl and TBAT (each at 20 mol% loading) with allyltrimethoxysilane (2 equiv) in DMF at ambient temperature, no addition occurred in the absence of additives (Table 1, entry 1). When *t*-BuOH or MeOH was included as a proton source, the reaction was facilitated to a small extent (entries 2 and 3), but much unreacted hydrazone remained. Triphenylphosphine, bis(diphenylphosphino)ethane (dppe), and bis(diphenylphosphino)ferrocene (dppf) proved to be effective promoters of the CuCl-mediated addition to hydrazone **1** (entries 4–6). To test the potential for asymmetric catalysis, we began to explore the effects of various chiral ligands for this reaction (Table 1). Chiral bisphosphines were among the best promoters as judged by yields, but unfortunately, they transmitted stereochemical information with barely detectable selectivity (entries 8–10). Chiral phenolic and oxazoline ligands were also screened (entries 11–13); measurable enantioselectivity (9.7% ee) was observed with the *tert*-butylbisoxazoline (entry 12).^{9,10} Low enantioselectivity notwithstanding, these experiments suggested some good synthetic utility.

Some subsequent experiments showed that the effectiveness of dppe, used as the sole additive, was limited when the reaction conditions were extended to a variety of hydrazones **5a–5d** (Scheme 3). Yields were modest, reac-

Table 1 Effects of Additives on CuCl–TBAT-Catalyzed Allyltrimethoxysilane Addition to **1** (Scheme 2).

Entry	Additive (2 equiv)	Yield of 2 , (%) [recovered 1 , (%)]
1	none	< 5
2	<i>t</i> -BuOH	27 [38]
3	MeOH	20 [44]
4	PPh ₃	80
5	PBu ₃	29
6	Ph ₂ PCH ₂ CH ₂ PPh ₂ (dppe)	67
7	dppf ^d	81
8	(<i>S</i>)-BINAP ^d	74 ^a
9	(<i>R,R</i>)-CHIRAPHOS ^d	80 ^b
10	(<i>R,R</i>)-DUPHOS ^d	84 ^a
11	(<i>S</i>)-BINOL ^d	51 ^a
12	(<i>S,S</i>)- <i>t</i> -BuBOX (3) ^d	40 ^c
13	4 ^d	63 ^a

Reaction conditions: *N*-benzoylhydrazone (0.2 mmol) was added to a mixture of allyltrimethoxysilane (0.4 mmol), CuCl (0.04 mmol), TBAT (0.04 mmol) and additive (0.4 mmol) in DMF (2.6 mL).

^a Less than 2% ee.

^b 3.8% ee.

^c 9.7% ee.

^d See Figure 1 for structure.

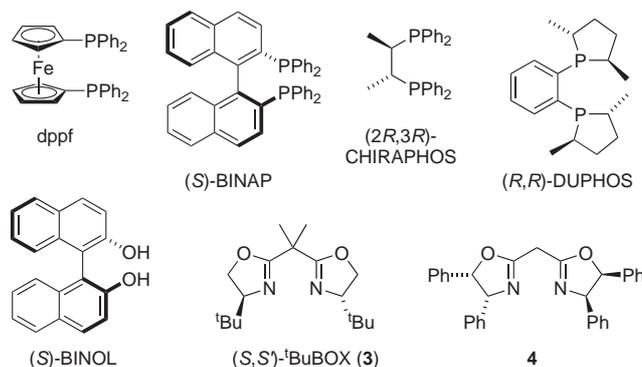


Figure 1 Structures of phosphines and chiral ligands used as additives in CuCl-mediated allyltrimethoxysilane addition to *N*-acylhydrazone **1**.



Scheme 3

tion times were long, and the reaction did not occur at all with electron-deficient *p*-nitrobenzaldehyde hydrazone **5d**.

In order to increase the yield and generality of the allyltrimethoxysilane addition, the effects of temperature and proton source (*t*-BuOH) were examined next (Table 2). Upon increasing the reaction temperature, the increase in rate was unfortunately accompanied by decreased yield when dppe was the sole additive (entries 1–3). In the presence of both dppe and *t*-BuOH, there was only a slight change in the time to completion (compare entries 1–3 with 4–6). However, *t*-BuOH dramatically improved the yield in reactions at 80 °C and 150 °C (entries 5 and 6), consistent with qualitative TLC observations, which showed much cleaner conversion.

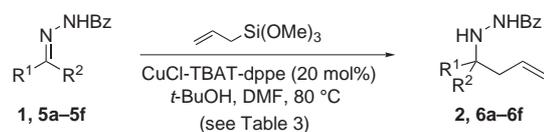
The combination of dppe and *t*-BuOH also resulted in improved versatility. Reaction of allyltrimethoxysilane in the presence of CuCl–TBAT at 80 °C with dppe and *t*-

Table 2 Temperature Effect on CuCl–TBAT-Catalyzed Allyl Addition to **5a** in the Presence of dppe and *t*-BuOH.

Entry	Temp (°C)	Additives	Time (h)	Yield of 6a (%)
1	20	dppe	60	66
2	80	dppe	1	60
3	150	dppe	0.5	57
4	20	dppe, <i>t</i> -BuOH	40	73
5	80	dppe, <i>t</i> -BuOH	1	84
6	150	dppe, <i>t</i> -BuOH	0.5	81

Reaction conditions: See Table 1.

BuOH as additives gave dramatically improved yields and brief reaction times across a series of hydrazones (Scheme 4, Table 3). Even the electron-deficient *p*-nitrobenzaldehyde hydrazone **5d** and the ketohydrazone **5e** reacted under these conditions, though with moderate yield.



Scheme 4

Table 3 Versatility of CuCl–TBAT–Catalyzed Addition to *N*-Benzoylhydrazones

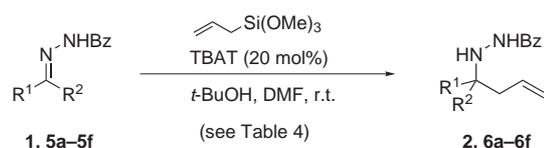
Entry	Hydrazone	R ¹ , R ²	Time (h)	Product yield (%)
1	5a	Ph, H	1	84
2	5b	<i>n</i> -pentyl, H	2	71
3	5c	(<i>E</i>)-PhCH=CH, H	1	75
4	5d	<i>p</i> -nitrophenyl, H	1	60
5	5e	Me, Me	1	48
6	1	3,4-dimethoxyphenyl, H	1	75

Reaction conditions: Table 2, entry 5 (for details, see experimental section).

Metal-Free Conditions

Considering the effect of the phosphines on reactivity, and the observable enantioselectivity in the presence of chiral ligands expected to associate with Cu(I), it was surprising to find that fluoride catalyzed the allyltrimethoxysilane addition to **1** (Scheme 5) in the absence of CuCl! In spite of precedent⁶ and control experiments¹⁰ which demonstrated an important role for CuCl, the reaction proceeded without CuCl at 80 °C (1 h, 72% yield) or room temperature (48 h, 67% yield).¹¹ Apparently, allyltrimethoxysilane reacts with *N*-acylhydrazones through distinctly different mechanisms depending on the presence or absence of CuCl. Interestingly, if the CuCl is mixed with the hydrazone prior to addition of allyltrimethoxysilane and TBAT, no reaction occurs, suggesting that the two mechanisms are both inhibited in some way by the presence of some inactive form of the Cu(I).^{10,12}

The metal-free catalysis conditions (Scheme 5) were quite effective across a series of aldehyde and ketone hydra-



Scheme 5

Table 4 Versatility of TBAT–Catalyzed Addition to *N*-Benzoylhydrazones

Entry	Hydrazone	R ¹ , R ²	Time (h)	Product yield (%)
1	5a	Ph, H	24	81
2	5b	<i>n</i> -pentyl, H	48	77
3	5c	(<i>E</i>)-PhCH=CH, H	22	85
4	5d	<i>p</i> -nitrophenyl, H	29	74
5	5e	Me, Me	72	55
6	5f	Me, CO ₂ Et	17	78
7 ^a	1	3,4-dimethoxyphenyl, H	44	89

Reaction conditions: *N*-benzoylhydrazone (0.1 mmol) and *t*-BuOH (0.2 mmol) were added to a mixture of allyltrimethoxysilane (0.2 mmol) and TBAT (0.02 mmol) in DMF (1.3 mL). See experimental section.

^a The reaction was carried out in the absence of *t*-BuOH.

zones (Table 4). Inclusion of *t*-BuOH generally halved the time required to reach complete conversion. With reaction times of 1–2 days at ambient temperature, yields ranged from 74–85% for various simple aromatic and aliphatic aldehyde hydrazones (entries 1–4). In contrast to the Cu-dependent reactions, the electron-withdrawing nitro substituent of **5d** did not impede the allyl addition, even at ambient temperature. Additions to imino derivatives of ketones offer the opportunity to access valuable tertiary alkyl amines. With the metal-free catalysis conditions, acetone hydrazone **5e** gave a moderate, but synthetically useful, yield of allyl adduct (Table 4, entry 5). An activating effect of an adjacent ethoxycarbonyl group was observed in hydrazone **5f**, derived from ethyl pyruvate (entry 6). Here the allyl addition occurred in 78% yield, generating a highly functionalized quaternary center bearing nitrogen and differentially functionalized carbon substituents. In comparison with existing methods for allylsilane addition, these conditions are an attractive and versatile complement, considering the superior yields obtained with electron-rich aromatic substrate **1** and electron-deficient substrates **5d** and **5f**.

There are significant qualitative differences, uncovered through control experiments (Table 5), which distinguish the metal-free reactions from Cu-dependent reactions. First, the metal-free catalysis can function in the absence of *t*-BuOH without decreased yield (entry 1). A high yield of **6a** was obtained using allyltrimethoxysilane and TBAT (20 mol%) as the only reagents, although it required 48 hours to reach complete conversion. Second, phosphine additive (dppe) had no effect on this reaction (entry 2). Third, increased reaction temperature resulted in significantly lower yield (entries 3 and 4); at 80 °C complete conversion was reached within 90 min, but **6a** was accompanied by a complex mixture of byproducts which were not readily identified. Unlike the CuCl-mediated reac-

tions, the addition of *t*-BuOH to the mixture did not improve the results at 80 °C.

Table 5 Control Experiments in TBAT-Catalyzed Addition to *N*-Benzoylhydrazones

Entry	Hydrazone	R ¹ , R ²	Additive	Time (h)	Product yield (%)
1	5a	Ph, H	none	48	6a (83)
2	5a	Ph, H	dppe	48	6a (83)
3 ^a	5a	Ph, H	none	1.5	6a (56)
4 ^a	5a	Ph, H	<i>t</i> -BuOH	1.5	6a (53)
5	5a	Ph, H	<i>t</i> -BuOH	24	6a (81)
6	5b	<i>n</i> -pentyl, H	<i>t</i> -BuOH	48	6b (77)
7 ^b	5b	<i>n</i> -pentyl, H	<i>t</i> -BuOH	7	6b (77)
8	1	3,4-dimethoxyphenyl, H	none	44	2 (89)
9	1	3,4-dimethoxyphenyl, H	<i>t</i> -BuOH	48	2 (67)

^a The reaction temperature was 80 °C.

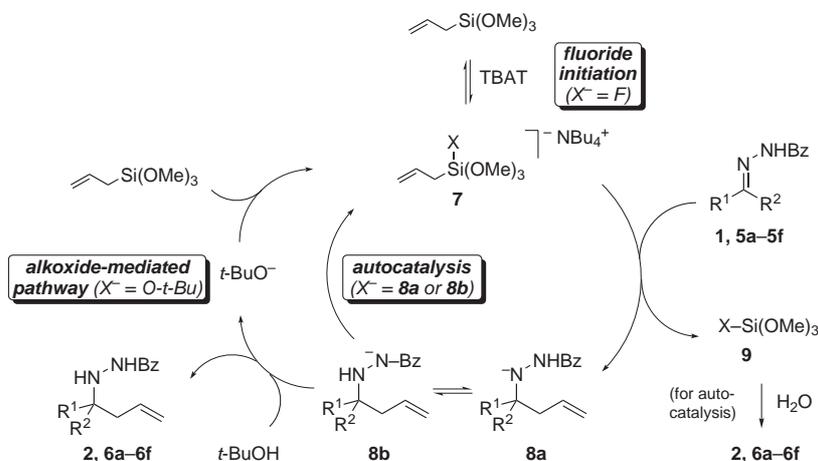
^b The solvent was CH₂Cl₂.

The metal-free catalysis raises mechanistically interesting questions regarding nucleophilic activation of the allyltrimethoxysilane.¹³ A working mechanistic model consistent with the results reported herein can be tentatively proposed (Scheme 6), although the nature of the allylation transition state and other precise details require further elucidation. Reaction of fluoride ion with allyltrimethoxysilane would generate hypervalent allylsilicate **7**, initiating the catalytic cycle. True catalysis by fluoride is unlikely because turnover would require breaking a strong Si–F bond, and this type of fluoride turnover has not yet been demonstrated in the absence of transition metal catalysts.¹² Therefore, other nucleophilic activators must be considered. DMF is merely important for solubility reasons, and is not involved in this activation process. Evi-

dence for this is seen in reactions of aliphatic hydrazone **5b**, which is soluble in CH₂Cl₂; allyl addition occurred even more rapidly in this medium (Table 5, compare entries 6 and 7). At ambient temperature, *t*-BuOH did appear to facilitate the reaction of **5a**. The role of *t*-BuOH may be two-fold: it can serve as proton source after allyl addition, and the resulting *t*-BuO[−] can also serve as the nucleophilic activator of the allyltrimethoxysilane (alkoxide-mediated pathway, Scheme 6).

In the absence of a proton source, an autocatalytic mechanism^{1b} may be proposed, wherein the allyl adduct **8a** or **8b**¹⁴ activates the allyltrimethoxysilane (autocatalysis pathway, Scheme 6). The effectiveness of *t*-BuOH in facilitating the reaction appears to be dependent on the electronic properties of the hydrazone. With benzaldehyde hydrazone **5a** reaction time is halved by use of *t*-BuOH in the reaction (Table 5, entries 1 and 5), but there is no such decrease in the reaction rate with electron-rich hydrazone **1** (entries 8 and 9). This is consistent with an autocatalysis mechanism because the adduct derived from **5a** (**8a/8b**; R¹, R² = Ph, H) would be expected to be less nucleophilic (compared to the corresponding adduct derived from electron-rich **1**), a less effective activator of allyltrimethoxysilane, and hence more likely to benefit from the *t*-BuOH additive. In the absence of *t*-BuOH, the N–H proton may come from hydrolysis of **9** (X[−] = **8a** or **8b**) on silica gel or upon aqueous workup. Further mechanistic studies are needed to test these hypotheses, and to examine the extent to which the autocatalysis pathway contributes.

In conclusion, two types of mild reaction conditions were identified for allyltrimethoxysilane addition to *N*-benzoylhydrazones. Both methods derive some practical advantages by avoiding corrosive and moisture sensitive allylchlorosilanes in favor of conveniently handled allyltrimethoxysilane. Reaction in the presence of CuCl–TBAT showed some interesting effects of additives, leading to discovery of synthetically useful conditions. Alternatively, metal-free reactions in the presence of TBAT offer a simple, efficient, and versatile complement to existing allylsilane additions, indeed affording superior



Scheme 6

yields for allylsilane addition to certain electron-rich and electron-deficient substrates. Both allyl addition methods succeed with hydrazones derived from aliphatic carbonyl compounds, including ketones, which give access to *tert*-alkyl amines.

TBAT (Aldrich) was recrystallized from EtOAc before use. All other reagents were obtained from commercial sources and used without further purification. Reactions employed oven- or flame-dried glassware under Ar unless otherwise noted. TLC employed glass 0.25 mm silica gel plates with UV indicator. Flash chromatography columns were packed with 230–400 mesh silica gel and eluted with hexane–EtOAc (2:1). Melting points were determined on a Melt-emp apparatus and are uncorrected. ¹H and ¹³C NMR data were obtained with a Bruker ARX 500 spectrometer. IR spectra were recorded with a Perkin-Elmer 2000 FT-IR spectrophotometer. Low-resolution mass spectra were obtained with a Voyager MALDI-TOF mass spectrometer. Combustion analyses were performed by Atlantic Microlab (Norcross, GA, USA). Enantiomeric ratio of **2** was determined by HPLC using a Chiralpak OJ column eluted with hexane–*i*-PrOH (95:5); retention times were 26.4 min and 34.9 min.

Preparation of *N*-Benzoylhydrazones; General Procedure

Known *N*-Benzoylhydrazones **1** and **5a**, **5b**, **5c**, **5d**, **5e**, and **5f** were prepared by condensation of benzoic hydrazide with the corresponding carbonyl compounds according to standard procedures.^{2e,15–17}

Veratraldehyde *N*-Benzoylhydrazone (**1**)

Colorless solid; mp 178–180 °C (lit. 176 °C,¹⁸ 181 °C¹⁹).

IR (film): 3197, 3072, 2897, 2833, 1641, 1597, 1547, 1502, 1422, 1260, 1166, 1024, 973 cm⁻¹.

¹H NMR (500 MHz, DMSO-*d*₆): δ = 11.72 (s, 1 H), 8.43 (s, 1 H), 7.94 (d, *J* = 7.3 Hz, 2 H), 7.60–7.51 (m, 3 H), 7.38 (s, 1 H), 7.22 (d, *J* = 7.6 Hz, 1 H), 7.03 (d, *J* = 8.3 Hz, 1 H), 3.83 (s, 3 H), 3.82 (s, 3 H).

¹³C NMR (125 MHz, DMSO-*d*₆): δ = 162.9, 150.8, 149.1, 148.1, 133.6, 131.4, 128.3, 127.4, 127.0, 121.7, 111.5, 108.4, 55.5, 55.4.

MS (MALDI): *m/z* (% relative intensity): 285 (42) [M + 1]⁺.

Anal. Calcd for C₁₆H₁₆N₂O₃: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.67; H, 5.64; N, 9.79.

p-Nitrobenzaldehyde *N*-Benzoylhydrazone (**5d**)

Colorless solid; mp 247–248 °C (lit. 243 °C,²⁰ 240 °C,²¹ 247 °C²²).

IR (film): 3185, 3014, 1642, 1556, 1513, 1338, 1291, 1146, 1074, 837 cm⁻¹.

¹H NMR (500 MHz, DMSO-*d*₆): δ = 12.09 (s, 1 H), 8.57 (s, 1 H), 8.30 (d, *J* = 8.0 Hz, 2 H), 8.05–7.93 (m, 4 H), 7.70–7.53 (m, 3 H).

¹³C NMR (125 MHz, DMSO-*d*₆): δ = 163.4, 147.8, 145.4, 140.7, 133.1, 131.9, 128.3, 127.8, 127.6, 123.9.

MS (MALDI): *m/z* (% relative intensity) = 270 (16) [M + 1]⁺.

Anal. Calcd for C₁₄H₁₁N₃O₃: C, 62.45; H, 4.12; N, 15.61. Found: C, 62.45; H, 4.13; N, 15.53.

Ethyl pyruvate *N*-Benzoylhydrazone [(*Z*)-**5f**]

Colorless solid; mp 168–169 °C (lit. 155 °C²³).

IR (film): 3283, 2978, 1709, 1667, 1434, 1263, 1132, 1019, 914 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 13.3 (s, 1 H), 7.90–7.45 (m, 5 H), 4.33 (q, *J* = 7.2 Hz, 2 H), 2.28 (s, 3 H), 1.36 (t, *J* = 15.0 Hz, 3 H).

¹³C NMR (125 MHz, CDCl₃): δ = 163.9, 163.0, 137.7, 132.6, 132.3, 128.7, 127.5, 61.9, 20.1, 13.9.

MS (MALDI): *m/z* (% relative intensity) = 235 (42) [M + 1]⁺.

Anal. Calcd for C₁₂H₁₄N₂O₃: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.58; H, 6.06; N, 11.94.

Allylsilane Addition Reactions; General Procedure

General Procedure A; CuCl-Dependent Conditions, 80 °C (Table 3): A mixture of CuCl (4 mg, 0.04 mmol), TBAT (16 mg, 0.04 mmol) and dppe (17 mg, 0.04 mmol) in DMF (2 mL) was stirred at r.t. for 1 h. To the resulting white suspension was added allyltrimethoxysilane (72 μL, 0.4 mmol) via microsyringe. After 5 min, a solution of the *N*-benzoylhydrazone (0.2 mmol) in DMF (0.6 mL) was added to the above mixture via syringe. This was followed by addition of *t*-BuOH (40 μL, 0.4 mmol) via microsyringe. The yellow-greenish suspension was heated to 80 °C, and it turned to an orange solution after about 15 min. The reaction was monitored by TLC until complete (typically 1–2 h). After cooling to r.t., the reaction was quenched by addition of 2 M HCl (0.4 mL). The mixture was diluted with water (15 mL) and extracted with CH₂Cl₂ (3 × 15 mL). The organic phase was washed with water and brine, dried (MgSO₄), concentrated, and purified by flash chromatography (hexane–EtOAc) to give the allyl adduct.

General Procedure B; Metal-Free Conditions (Table 4): To a solution of TBAT (8 mg, 0.02 mmol) in DMF (1.3 mL) was added allyltrimethoxysilane (36 μL, 0.2 mmol) via microsyringe. After 5 min, *N*-benzoylhydrazone (0.1 mmol) was added in one portion, followed by addition of *t*-BuOH (20 μL, 0.2 mmol) via microsyringe, resulting in a yellow solution. The reaction was monitored by TLC until complete (typically 1–2 d). The reaction was quenched by addition of 2 M HCl (0.2 mL). The mixture was diluted with water (10 mL) and extracted with CH₂Cl₂ (3 × 15 mL). The combined organic phases were washed with water, brine and dried (MgSO₄). The solvent was evaporated and the crude product was purified by flash chromatography (hexane–EtOAc) to give the allyl adduct.

Known allyl addition products **6a–6c** and **6e** obtained by the General Procedures A and B had spectroscopic properties consistent with data reported in the literature.^{2e}

Benzoic Acid *N'*-[1-(3',4'-Dimethoxyphenyl)-3-butenyl]hydrazide (**2**)

Colorless solid; mp 139–140 °C.

IR (film): 3283, 3066, 2934, 2843, 1638, 1515, 1460, 1263, 1140, 1028, 916, 802 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.58 (d, *J* = 7.5 Hz, 2 H), 7.46 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.37 (dd, *J* = 7.5, 7.5 Hz, 2 H), 7.30 (d, *J* = 7.0 Hz, 1 H), 6.93 (s, 1 H), 6.89 (d, *J* = 8.0 Hz, 1 H), 6.82 (d, *J* = 8.0 Hz, 1 H), 5.72 (dddd, *J* = 17, 10, 8.0, 6.0 Hz, 1 H), 5.24 (dd, *J* = 7.0, 2.0 Hz, 1 H), 5.18 (dd, *J* = 17.1, 1.4 Hz, 1 H), 5.12 (d, *J* = 10.2 Hz, 1 H), 4.10 (t, *J* = 7.1 Hz, 1 H), 3.87 (s, 3 H), 3.86 (s, 3 H), 2.78–2.72 (m, 2 H).

¹³C NMR (125 MHz, CDCl₃): δ = 167.2, 149.7, 148.5, 134.6, 134.2, 132.9, 131.7, 128.5, 126.9, 111.1, 110.6, 63.7, 55.8 (2 × C), 40.3.

MS (MALDI): *m/z* (% relative intensity) = 327 (0.4) [M + 1]⁺.

Anal. Calcd for C₁₉H₂₂N₂O₃: C, 69.92; H, 6.79; N, 8.58. Found: C, 69.98; H, 6.79; N, 8.55.

Benzoic Acid *N'*-[1-(4'-Nitrophenyl)-3-butenyl]hydrazide (**6d**)

Colorless solid; mp 120–121 °C (from Et₂O).

IR (film): 3282, 3070, 2920, 1649, 1521, 1463, 1345, 1109, 923 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 8.14 (d, *J* = 8.0 Hz, 2 H), 7.58 (d, *J* = 8.0 Hz, 2 H), 7.53 (d, *J* = 8.5 Hz, 2 H), 7.46 (dd, *J* = 7.0, 7.0 Hz, 2 H), 7.35 (dd, *J* = 8.0, 8.0 Hz, 2 H), 5.82–5.76 (m, 1 H), 5.40–4.60

(br s, 1 H), 5.13 (dd, $J = 17.1, 1.5$ Hz, 1 H), 5.11 (d, $J = 9.5$ Hz, 1 H), 4.30 (dd, $J = 7.0, 7.0$ Hz, 1 H), 2.53–2.41 (m, 2 H).

^{13}C NMR (125 MHz, CDCl_3): $\delta = 167.7, 149.6, 147.5, 133.3, 132.4, 132.1, 128.7, 128.6, 126.9, 123.8, 118.9, 63.5, 40.4$.

MS (MALDI): m/z (% relative intensity) = 312 (48) [$\text{M} + 1$] $^+$.

Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_3$: C, 65.58; H, 5.50; N, 13.50. Found: C, 65.52; H, 5.60; N, 13.43.

Benzoic Acid *N'*-[1-Methyl-1-(1-ethoxycarbonyl)-3-but-2-enyl]hydrazide (6f)

Colorless oil.

IR (film): 3281, 3074, 2982, 2941, 1730, 1644, 1540, 1461, 1305, 1219, 1152, 1025, 920 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): $\delta = 7.90$ (br s, 1 H), 7.70 (d, $J = 7.1$ Hz, 2 H), 7.50–7.30 (m, 3 H), 5.81 (dddd, $J = 17.2, 9.5, 7.4, 7.4$ Hz, 1 H), 5.14 (dd, $J = 17.2, 1.3$ Hz, 1 H), 5.12 (d, $J = 10.1$ Hz, 1 H), 5.0–4.5 (br s, 1 H), 4.22–4.13 (m, 2 H), 2.55–2.45 (m, 2 H), 1.38 (s, 3 H), 1.27 (t, $J = 7.2$ Hz, 3 H).

^{13}C NMR (125 MHz, CDCl_3): $\delta = 174.8, 166.6, 133.1, 132.3, 131.7, 128.7, 126.9, 119.4, 64.9, 61.3, 41.5, 21.2, 14.2$.

MS (MALDI): m/z (% relative intensity) = 277 (68) [$\text{M} + 1$] $^+$.

Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_3$: C, 65.20; H, 7.30; N, 10.14. Found: C, 65.14; H, 7.30; N, 10.07.

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- In combination with *t*-BuOH as proton source, the yield with *t*-BuBOX improved to 51%, but the enantioselectivity decreased to only 1.8% ee.
- (a) Some control experiments were examined in order to obtain evidence about the roles of the reagents. First, hydrazone **1** was mixed with the CuCl and *t*-BuBOX ligand for 2 h, followed by addition of a mixture of allyltrimethoxysilane and TBAT; no reaction occurred. Under conditions otherwise identical to the first control experiment, additional CuCl was included in the silane mixture; still there was no reaction. On the other hand, including both CuCl and dppe in the silane mixture restored the reactivity, affording **2** in 67% yield. These experiments suggest that the main role of CuCl is in generating the active nucleophilic species, not as a Lewis acid activator of the benzoylhydrazone. The phosphine may serve as a stabilizing ligand within a Cu-containing allyl nucleophile; the exact identity of this nucleophile is unclear. Shibasaki has suggested an allylcopper or an allylsilicate–Cu $^+$ ion pair (ref.⁶). (b) The hydrazone N–H was changed to N–Me; benzaldehyde *N*-methyl-*N*-benzoylhydrazone gave no reaction, suggesting that deprotonation of the hydrazone N–H, or its involvement in a hydrogen bond, may be essential to the mechanism. Leighton has observed a similar requirement for the N–H bond (see ref.^{5b}).
- The availability of the Cu-free achiral pathway may contribute to the low enantioselectivity found in reactions employing chiral ligands. For related observations in Cu(II)-catalyzed Mannich-type additions to iminophosphonates, see: Kobayashi, S.; Kiyohara, H.; Nakamura, Y.; Matsubara, R. *J. Am. Chem. Soc.* **2004**, *126*, 6558.
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