Use of Acylhydrazones as Stable Surrogates of Unstable Imines in Allylation, Mannich-Type, and Cyanide Addition Reactions

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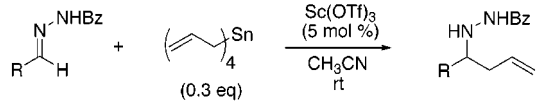
Imines are versatile intermediates for the synthesis of nitrogen-containing compounds. Although some imines are easily prepared from carbonyl compounds and amines, most of them necessitate dehydrative preparation by azeotropic distillation or with dehydrating agents. In addition, imines are generally difficult to purify by distillation or column chromatography and unstable when stored for long periods. Recently, we have focused our attention on the use of hydrazones as imine equivalents because they are much more stable than imines and are often isolated as stable crystals. A drawback of using hydrazones as electrophiles is their low reactivity. In fact, there have been many fewer reports on the reactions of hydrazones with nucleophiles than those of imines.[1−7] However, we have recently found that acylhydrazones derived from simple aldehydes reacted smoothly with silyl enolates in the presence of a catalytic amount of a Lewis acid such as scandium triflate ($Sc(OTf)_3$) to afford *β-N′*-benzoylhydrazinocarbonyl compounds, which are readily converted to *β*-aminocarbonyl compounds such as *β*-lactams, pyrazolones, and pyrazolidinones.[8−10] Furthermore, unfunctionalized benzoylhydrazones have been successfully used for $Sc(OTf)_3$-catalyzed allylation using tetraallyltin to give the corresponding homoallylic hydrazines.[11] In addition, most acylhydrazones including those derived from aromatic, α,*β*-unsaturated, and even aliphatic aldehydes can be purified by recrystallization and are easy to handle at room temperature under air.

In the course of our investigations to develop useful reactions using acylhydrazones as stable surrogates of unstable imines, we planned to use acylhydrazones derived from functionalized or unstable aldehydes for various types of reactions with nucleophiles. In this paper, we report the use of benzoylhydrazones derived from α-functionalized aldehydes and formaldehyde as electrophiles in Lewis acid-catalyzed allylation, Mannich-type, and cyanide addition reactions.

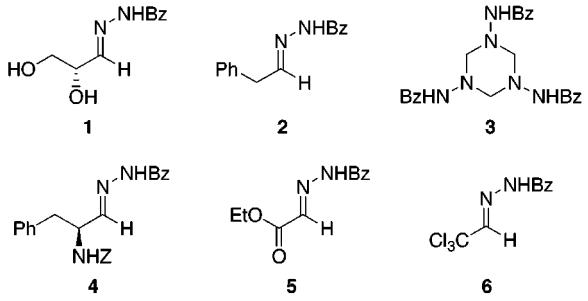
Table 1. Allylation Reactions of the Benzoylhydrazones



entry	benzoylhydrazone	time/h	yield/% (dr[a])
1[b]	**1**	40	70[c] (83/17)
2	**2**	2	79
3[d]	**3**	2	86
4	**4**	2	>99 (56/44)
5	**5**	1	91
6	**6**	2	85

[a] Diastereomer ratio. Relative stereochemical assignment was not made. [b] $Sc(OTf)_3$ (10 mol %). [c] NMR yield. [d] $Sc(OTf)_3$ was added after addition of tetraallyltin.

The acylhydrazones (**1**−**6**) were readily prepared from the corresponding aldehydes and benzoylhydrazine. While both the aldehydes and the corresponding imines are unstable and difficult to handle due to polymerization and/or decomposition, all these α-functionalized hydrazones and the hydrazone trimer are stable crystalline compounds and are easily stored and handled at room temperature.



First, we carried out allylation reactions of these hydrazones with tetraallyltin in the presence of a catalytic amount of scandium triflate ($Sc(OTf)_3$).[11] The reactions proceeded smoothly at room temperature to afford the corresponding homoallylhydrazines in high yields (Table 1). The following features are noteworthy in these reactions. (1) No decomposition of the hydrazones occurred under the reaction conditions and the hydrazones were effectively activated by the Lewis acid. (2) Protection of the hydroxy groups in hydrazone **1** was not needed for either the preparation of the hydrazone or for the allylation reaction. (3) Even in the reaction of the hydrazone (**2**) derived from phenylacetaldehyde, which easily polymerizes through self-condensation, the desired product was produced in a high yield. (4) Hydrazone trimer **3** also reacted with tetraallyltin to give *N*-benzoyl-*N′*-3-butenylhydrazine, although a small amount (∼6%) of a diallylated compound ($BzNHN(CH_2CH_2CH{=}CH_2)_2$) was obtained as a byproduct.

As shown in Table 2, $Sc(OTf)_3$-catalyzed Mannich-type reactions[8,9] of the hydrazones with ketene silyl acetal **7** also proceeded readily to afford the corresponding *β-N′*-benzoylhydrazinocarbonyl compounds. In the case of **1**, five-membered lactone **8**, whose stereochemistry was

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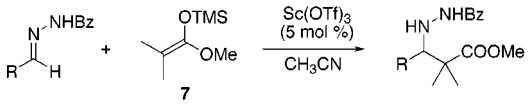
Table 2. Mannich-Type Reactions of the Benzoylhydrazones



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entry	benzoylhydrazone	time/h	temp/°C	yield/% (dr[a])
1[b]	**1**	2	rt	86[c]
2	**2**	1	0	95
3	**3**	15	rt	71
4[b]	**4**	24	0	60 (88/12)
5	**5**	17	0	75

[a] Diastereomer ratio. Relative stereochemical assignment was not made. [b] **7** (3.5 eq). [c] The product was lactone **8**.

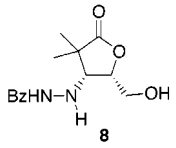

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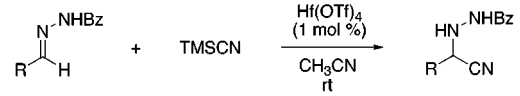
Table 3. Cyanide Addition Reactions of the Benzoylhydrazones



entry	benzoylhydrazone	TMSCN/eq.	time/h	yield/% (dr[a])
1	**1**	3.5	4	79 (73/27)
2	**2**	3.0	16	81
3	**3**	2.5	17	88
4	**4**	5.0	17	99 (63/37)

[a] Diastereomer ratio. Relative stereochemical assignment was not made.

determined by NOE experiments, was obtained in a high yield as a single isomer after treatment with an acid. Unfortunately, the reaction of chloral-derived hydrazone **6** did not proceed under these conditions.

α-Amino nitriles are useful intermediates for the synthesis of amino acids and other nitrogen-containing compounds.[12] Lewis acid-catalyzed addition of a cyanide anion to imines constitutes one of the most efficient methods to prepare α-amino nitriles.[13] We planned to use acylhydrazones as imine equivalents in the cyanide addition reaction. We found that trimethylsilyl cyanide reacted smoothly with acylhydrazones in the presence of hafnium triflate ($Hf(OTf)_4$),[14] which was found to be superior to $Sc(OTf)_3$ under the conditions used (Table 3). Note that only 1 mol % of $Hf(OTf)_4$ is sufficient to catalyze the reactions. To the best of our knowledge, this is the first example of Lewis acid-catalyzed cyanide addition to hydrazones.[15]

In summary, benzoylhydrazones derived from α-functionalized aldehydes and formaldehyde were successfully utilized as electrophiles in Lewis acid-catalyzed allylation, Mannich-type, and cyanide addition reactions. Since the N−N bond of acylhydrazines can be readily cleaved,[7] the reactions described in the present paper provide useful intermediates for the synthesis of functionalized amines. It is noted that the hydrazones used in the present work can be stored and handled at room temperature even under air. Further studies to use acylhydrazones in other synthetic reactions as well as to develop catalytic asymmetric reactions are currently under way.

Experimental Section

General Procedure for Preparation of Benzoylhydrazones. A solution of benzoylhydrazine (20 mmol) in MeOH (7 mL) and then AcOH (ca. 1.5 mL) was added to a solution of an aldehyde (20 mmol) in MeOH (5 mL) at room temperature, and the whole was stirred overnight. The resulting precipitate was collected and dried to give the corresponding hydrazone.

Benzoylhydrazones **2**,[16] **3**,[17] **5**,[8,18] and **6**[19] are known compounds.

D-Glycelaldehyde Benzoylhydrazone (1). Colorless prisms; mp 112.5−114 °C; $[\alpha]^{24}_D$ −3.83 (*c* 0.932, MeOH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.41−3.50 (2H, m), 4.06−4.09 (1H, m), 4.77 (1H, t, *J* = 5.0 Hz, OH), 5.30 (1H, d, *J* = 4.2 Hz, OH), 7.49−7.56 (3H, m), 7.65 (1H, d, *J* = 5.5 Hz), 7.84 (2H, d, *J* = 7.0 Hz), 11.56 (1H, s, NH); ^{13}C NMR (75 MHz, DMSO-d_6) δ 64.07, 71.66, 127.56, 128.47, 131.70, 133.41, 152.49, 163.13; IR (KBr) 3375, 3226, 1654, 1553, 1284 cm^{-1}; HRMS calcd for $C_{10}H_{12}N_2O_3$, 208.0848; found, 208.0870.

(*S*)-2-(Benzyloxycarbonyl)amino-3-phenylpropanal Benzoylhydrazone (4). Colorless needles; mp 93 °C; $[\alpha]^{24}_D$ −37.2 (*c* 0.826, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.86 (1H, dd, *J* = 13.7, 10.4 Hz), 3.03 (1H, dd, *J* = 13.7, 5.0 Hz), 4.37−4.47 (1H, m), 4.97 (2H, s), 7.19−7.36 (10H, m), 7.47−7.59 (3H, m), 7.69 (1H, d, *J* = 8.6 Hz), 7.78 (1H, d, *J* = 4.6 Hz), 7.85 (2H, d, *J* = 7.1 Hz), 11.61 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.63, 53.93, 65.26, 126.34, 127.54, 127.60, 127.76, 128.24, 128.39, 128.51, 129.39, 131.78, 133.36, 137.10, 137.93, 150.89, 155.63, 163.14; IR (KBr) 3313, 3228, 1685, 1651, 1527 cm^{-1}; MS *m*/*z* 401 (M+). Anal. Calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47. Found: C, 71.57; H, 5.87; N, 10.46.

General Procedure for Allylation Reactions. To a solution of $Sc(OTf)_3$ (0.020 mmol) and a hydrazone (0.40 mmol) in acetonitrile (2.4 mL) was added tetraallyltin (0.12 mmol) in acetonitrile (0.8 mL) at room temperature. After stirring at the same temperature, the reaction was quenched with saturated aqueous $NaHCO_3$ solution and the aqueous layer was extracted with CH_2Cl_2. After a usual workup, the crude product was purified by silica gel chromatography to give the desired homoallylic hydrazine.

***N′*-(1,2-Dihydroxy-5-hexen-3-yl)benzohydrazide.** A mixture of two diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.21−2.51 (2H, m), 3.03 (1H, br), 3.62−3.91 (3H, m), 4.66 (2H, br), 5.09 (1H, d, *J* = 8.6 Hz), 5.13 (1H, d, *J* = 14.6 Hz), 5.78−5.93 (1H, m), 7.32−7.39 (2H, m), 7.42−7.49 (1H, m), 7.71−7.79 (2H, m), 8.83 (0.83H, br), 9.32 (0.17H, br); ^{13}C NMR (75 MHz, $CDCl_3$) for major isomer: δ 34.58, 62.01, 64.37, 72.10, 117.90, 126.94, 128.69, 132.00, 132.25, 134.94, 167.51; for minor isomer: δ 33.41, 62.49, 63.48, 71.44, 118.09, 127.04, 127.30, 128.62, 128.76, 133.94, 168.34; IR (neat) 3296, 1644 cm^{-1}; HRMS calcd for $C_{13}H_{18}N_2O_3$, 250.1317; found, 250.1307.

***N′*-(1-Phenyl-4-penten-2-yl)benzohydrazide.** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.15−2.33 (2H, m), 2.76 (2H, d, *J* = 7.0 Hz), 3.34 (1H, brs), 5.0 (1H, br), 5.15 (1H, d, *J* = 10.3 Hz), 5.16 (1H, d, *J* = 17.0 Hz), 5.91 (1H, ddt, *J* = 17.0, 10.3, 6.6 Hz), 7.19−7.32 (5H, m), 7.36 (2H, t, *J* = 7.8 Hz), 7.46 (1H, t, *J* = 7.8 Hz), 7.55 (2H, dd, *J* = 7.8, 1.3 Hz), 7.72 (1H, brs); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.64, 40.35, 60.83, 117.89, 126.36, 126.83, 128.52, 128.60, 129.27, 131.73, 132.70, 135.03, 139.12, 166.92; IR (neat) 3279, 1637, 1458 cm^{-1}; HRMS calcd for $C_{18}H_{20}N_2O$, 280.1576; found, 280.1586.

***N′*-(3-Butenyl)benzohydrazide.** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (2H, q, *J* = 7.0 Hz), 3.02 (2H, t, *J* = 7.0 Hz), 5.07 (1H, d, *J* = 10.3 Hz), 5.13 (1H, d, *J* = 17.2), 5.79−5.93 (1H, m), 7.43

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(2H, t, J = 7.1 Hz), 7.51 (1H, t, J = 7.1 Hz), 7.77 (2H, d, J = 7.1 Hz), 8.15 (1H, br); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.42, 51.08, 116.34, 126.81, 128.52, 131.67, 132.78, 135.77, 167.12; IR (film) 3223, 1638, 1543 cm^{-1}; HRMS calcd for $C_{11}H_{13}N_2O$ ($M^+ - 1$), 189.1028; found, 189.1052.

***N′*-(2-(Benzyloxycarbonyl)amino-1-phenyl-5-hexen-3-yl)-benzohydrazide.** A mixture of two diastereomers: ^{1}H NMR for one isomer (400 MHz, $CDCl_3$) δ 2.08 (1H, dt, J = 13.9, 9.5 Hz), 2.39 (1H, brd, J = 13.9 Hz), 2.70 (1H, dd, J = 14.4, 9.8 Hz), 2.75 (1H, dd, J = 14.4, 5.4 Hz), 3.12 (1H, dt, J = 9.8, 2.9 Hz), 4.33−4.36 (1H, m), 5.02 (1H, d, J = 12.5 Hz), 5.03 (1H, d, J = 9.5 Hz), 5.12 (1H, d, J = 12.5 Hz), 5.24 (1H, d, J = 12.0 Hz), 5.28 (1H, d, J = 19.0 Hz), 5.90−6.00 (1H, m), 7.14−7.31 (10H, m), 7.42 (2H, t, J = 7.3 Hz), 7.49 (1H, t, J = 7.3 Hz), 7.83 (2H, d, J = 7.3 Hz), 8.98 (1H, s); for the another isomer (300 MHz, DMSO-d_6) δ 2.05−2.15 (1H, m), 2.33−2.38 (1H, m), 2.60 (1H, t, J = 12.6 Hz), 2.96 (1H, brs), 3.10 (1H, d, J = 12.6 Hz), 3.95 (1H, t, J = 9.5 Hz), 4.90 (1H, d, J = 12.8 Hz), 4.93 (1H, d, J = 12.8 Hz), 5.07 (1H, d, J = 10.4 Hz), 5.14 (1H, d, J = 17.2 Hz), 5.85−5.98 (1H, m), 7.16−7.32 (11H, m), 7.43−7.54 (3H, m), 7.85 (2H, d, J = 7.3 Hz), 10.12 (1H, s); ^{13}C NMR for one isomer (100 MHz, $CDCl_3$) δ 31.69, 37.26, 52.34, 60.41, 66.79, 118.83, 126.55, 126.82, 127.53, 127.96, 128.42, 128.54, 128.56, 128.58, 131.62, 132.51, 134.09, 136.24, 137.63, 157.56, 166.26; for the another isomer (75 MHz, DMSO-d_6) δ 32.81, 34.90, 53.26, 62.35, 64.83, 117.04, 125.80, 127.15, 127.19, 127.55, 127.94, 128.26, 128.37, 129.26, 131.31, 133.32, 136.15, 137.34, 139.76, 155.69, 165.94; IR (film) 3297, 1703, 1535 cm^{-1}; HRMS calcd for $C_{27}H_{29}N_3O_3$, 443.2209; found, 443.2194.

Ethyl 2-(*N′*-Benzoylhydrazino)-4-pentenoate. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (3H, t, J = 7.1 Hz), 2.42−2.52 (1H, m), 2.58−2.66 (1H, m), 3.85 (1H, t, J = 5.9 Hz), 4.08−4.28 (2H, m), 5.16 (1H, d, J = 8.6 Hz), 5.20 (1H, d, J = 15.4 Hz), 5.80−5.94 (1H, m), 7.42 (2H, t, J = 7.1 Hz), 7.51 (1H, t, J = 7.1 Hz), 7.77 (2H, d, J = 7.1 Hz), 8.41 (1H, br); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.21, 35.24, 61.14, 62.13, 118.85, 127.03, 128.62, 131.90, 132.59, 132.93, 167.09, 172.68; IR (neat) 3290, 1736, 1647, 1465, 1200 cm^{-1}; HRMS calcd for $C_{14}H_{18}N_2O_3$, 262.1317; found, 262.1281.

***N′*-(1,1,1-Trichloro-4-penten-2-yl)benzohydrazide.** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (1H, dt, J = 15.0, 9.7 Hz), 2.94−3.00 (1H, m), 3.71 (1H, dd, J = 9.7, 2.9 Hz), 5.19 (1H, br), 5.31 (1H, d, J = 12.3 Hz), 5.31 (1H, d, J = 13.9 Hz), 6.13−6.26 (1H, m), 7.44 (2H, t, J = 7.7 Hz), 7.59 (1H, t, J = 7.7 Hz), 7.74 (2H, d, J = 7.7 Hz), 7.97 (1H, brs); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.47, 74.70, 103.85, 119.43, 126.86, 128.77, 132.15, 132.24, 133.37, 166.96; IR (film) 3294, 1643, 1528, 1469 cm^{-1}; HRMS calcd for $C_{12}H_{13}Cl_3N_2O$, 306.0093; found, 306.0067.

General Procedure for Mannich-Type Reactions. To a solution of $Sc(OTf)_3$ (0.020 mmol) and a hydrazone (0.40 mmol) in acetonitrile (2.4 mL) was added a ketene silyl acetal (0.60 mmol) in acetonitrile (0.8 mL) at room temperature. After stirring at the same temperature, the reaction was quenched with saturated aqueous $NaHCO_3$ solution, and the aqueous layer was extracted with CH_2Cl_2. After a usual workup, the crude product was purified by silica gel chromatography to give the desired product.

(3*R*,4*S*)-3-(*N′*-Benzoylhydrazino)-4-hydroxymethyl-2,2-dimethyl-4-butanolide (8). Colorless plates; mp 151.5−153.0 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 1.25 (3H, s), 1.29 (3H, s), 3.62 (1H, d, J = 6.2 Hz), 3.92 (1H, dd, J = 12.3, 5.9 Hz), 3.98 (1H, dd, J = 12.3, 4.6 Hz), 4.62 (1H, ddd, J = 6.2, 5.9, 4.6 Hz), 7.34−7.40 (2H, m), 7.43−7.49 (1H, m), 7.67−7.72 (2H, m); ^{13}C NMR (75 MHz, CD_3OD) δ 19.53, 25.56, 44.67, 61.28, 67.79, 81.48, 128.21, 129.62, 132.97, 134.02, 169.50, 183.14; IR (KBr) 3334, 1750, 1646, 1352, 1139, 1053 cm^{-1}; MS m/z 278 (M+); Anal. Calcd for $C_{14}H_{18}N_2O_4$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.19; H, 6.67; N, 9.95.

Methyl 3-(*N′*-benzoylhydrazino)-2,2-dimethyl-4-phenylbutanoate. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (3H, s), 1.37 (3H, s), 2.64 (1H, dd, J = 13.9, 9.9 Hz), 2.92 (1H, dd, J = 13.9, 3.1 Hz), 3.56 (3H, s), 3.62 (1H, dd, J = 9.9, 3.1 Hz), 7.19−7.32 (8H, m), 7.38−7.44 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.75, 22.65, 36.46, 45.79, 51.89, 67.11, 126.34, 126.60, 128.23, 128.60, 129.01, 131.44, 132.28, 139.38, 165.98, 177.82; IR (KBr) 3275, 31.93, 3076, 2983, 1735, 1629, 1605, 1570 cm^{-1}; HRMS calcd for $C_{20}H_{24}N_2O_3$, 340.1787; found, 340.1740.

Methyl 3-(*N′*-benzoylhydrazino)-2,2-dimethylpropanoate. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (6H, s), 3.10 (2H, brs), 3.67 (3H, s), 5.04 (1H, br), 7.40−7.45 (2H, m), 7.48−7.54 (2H, m), 7.73−7.77 (2H, m), 7.94 (1H, brs); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.63, 42.93, 52.02, 60.73, 126.82, 128.68, 131.84, 132.67, 167.06, 177.86; IR (neat) 3300, 2974, 1729, 1646, 1469, 1151 cm^{-1}; HRMS calcd for $C_{13}H_{18}N_2O_3$, 250.1317; found, 250.1330.

Methyl 3-(*N′*-Benzoylhydrazino)-4-benzyloxycarbonylamino-2,2-dimethyl-5-phenylpentanoate. A mixture of two diastereomers, ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.11 (2.64H, s), 1.14 (2.64H, s), 1.40 (0.36H, s), 1.44 (0.36H, s), 2.77−3.05 (2H, m), 3.21 (0.88H, brs), 3.31 (0.12H, d, J = 4.0 Hz), 3.58 (2.64H, s), 3.65 (0.36H, s), 4.17−4.30 (1H, m), 4.88−5.09 (2H, m), 5.14 (1H, br), 6.47 (0.12H, brd, J = 10.0 Hz), 6.73 (0.88H, d, J = 10.0 Hz), 7.14−7.31 (10H, m), 7.41−7.56 (3H, m), 7.74−7.79 (2H, m), 8.07 (0.88H, brs), 8.34 (0.12H, br); ^{13}C NMR (75 MHz, $CDCl_3$) for major isomer δ 19.68, 23.60, 42.55, 46.78, 51.18, 52.01, 66.41, 66.69, 126.43, 126.84, 127.80, 127.86, 128.32, 128.37, 128.80, 129.40, 132.10, 132.22, 136.77, 137.84, 156.06, 167.55, 177.93; IR (neat) 3317, 2951, 1720, 1641 cm^{-1}; HRMS calcd for $C_{29}H_{33}N_3O_5$, 503.2420; found, 503.2390.

1-Methyl Ethyl 3-(*N′*-benzoylhydrazino)-2,2-dimethylsuccinate. Colorless prisms; mp 101−103 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (3H, s), 1.25 (3H, t, J = 7.1 Hz), 1.36 (3H, s), 3.72 (3H, s), 3.95 (1H, d, J = 5.1 Hz), 4.12−4.28 (2H, m), 5.44 (1H, t, J = 5.1 Hz), 7.41 (2H, t, J = 7.1 Hz), 7.51 (1H, t, J = 7.1 Hz), 7.74 (2H, d, J = 7.1 Hz), 8.15 (1H, d, J = 5.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.10, 21.66, 21.99, 45.69, 52.19, 61.37, 69.37, 126.98, 128.61, 131.85, 132.59, 167.12, 171.38, 176.24; IR (KBr) 3304, 1740, 1640, 1510, 1211 cm^{-1}; MS m/z 322 (M^+); Anal. Calcd for $C_{16}H_{22}N_2O_5$: C,59.62; H, 6.88; N, 8.69. Found: C, 59.50; H, 6.74; N, 8.45.

General Procedure for Cyanide Addition Reactions. To a solution of a hydrazone (0.40 mmol) in acetonitrile (2.4 mL) was added trimethylsilyl cyanide (1.2 mmol) in acetonitrile (0.8 mL) at room temperature. After stirring for 5 min, 0.04 M $Hf(OTf)_4$ (0.020 mmol) in acetonitrile was added and the whole was stirred at the same temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ solution, and the aqueous layer was extracted with CH_2Cl_2. After a usual workup, the crude product was purified by silica gel chromatography to give the desired product.

***N′*-(1-Cyano-2,3-dihyrdoxypropyl)benzohydrazide.** A mixture of two diastereomers, ^{1}H NMR (300 MHz, acetone-d_6) δ 3.71−4.25 (5H, m), 4.91 (0.27H, d, J = 5.3 Hz, secondary OH), 5.17 (0.73H, d, J = 4.6 Hz, secondary OH), 5.88 (0.73H, t, J = 5.5 Hz, NH), 5.96 (0.27H, t, J = 7.5 Hz, NH), 7.45−7.57 (3H, m), 7.89−7.94 (2H, m), 9.64 (1H, brs, CONH); ^{13}C NMR (75 MHz, acetone-d_6) for major isomer δ 55.28, 63.18, 71.25, 118.59, 127.82, 129.01, 132.40, 133.09, 168.02; for minor isomer δ 56.42, 63.48, 70.87, 117.96, 127.73, 129.01, 132.30, 133.19, 167.43; IR (KBr) 3511, 3276, 2238, 1635 cm^{-1}; HRMS calcd for $C_{11}H_{13}N_3O_3$, 235.0957; found, 235.0939.

***N′*-(1-Cyano-2-phenylethyl)benzohydrazide.** Colorless plates; mp 138−139 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.99 (1H, dd, J = 13.7, 8.1 Hz), 3.10 (1H, dd, J = 13.7, 6.2 Hz), 4.32 (1H, dt, J = 8.1, 6.2 Hz), 6.08 (1H, t, J = 6.2 Hz), 7.14−7.32 (5H, m), 7.41 (2H, t, J = 7.1 Hz), 7.48 (1H, t, J = 7.1 Hz), 7.80 (2H, d, J = 7.1 Hz), 10.30 (1H, d, J = 6.2 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 36.64, 53.47, 119.65, 127.06, 127.36, 128.44, 128.49, 129.61, 131.77, 132.58, 136.12, 166.19; IR (KBr) 3283, 2249, 1637, 1517, 1471 cm^{-1}; MS m/z 265 (M^+). Anal. Calcd for $C_{16}H_{15}N_3O$: C, 72.43; H, 5.70; N, 15.84. Found: C, 72.22; H, 5.84; N, 15.57.

***N′*-(Cyanomethyl)benzohydrazide.** Colorless plates; mp 152−155 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.91 (2H, d, J = 5.1 Hz), 5.98 (1H, q, J = 5.1 Hz), 7.44−7.57 (3H, m), 7.84 (2H, dd, J = 8.3, 1.3 Hz), 10.31 (1H, d, J = 5.9 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 39.06, 118.53, 127.21, 128.46, 131.68, 132.60, 165.90; IR (KBr) 3286, 2246, 1639, 1563, 1308 cm^{-1}; MS m/z 175 (M^+). Anal. Calcd for $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.62; H, 5.24; N, 24.00.

***N′*-(2-Benzyloxycarbonylamino-1-cyano-3-phenyl)benzohydrazide.** For major isomer ^{1}H NMR (300 MHz, acetone-d_6) δ 3.01 (1H, dd, J = 13.7, 9.7 Hz), 3.27 (1H, dd, J = 13.7, 4.6 Hz), 4.31−4.46 (2H, m), 5.04 (2H, s), 5.95 (1H, t, J = 6.2 Hz), 6.90 (1H, d, J = 8.8 Hz), 7.19−7.36 (10H, m), 7.48 (2H, tt, J =

7.0, 1.5 Hz), 7.56 (1H, tt, J = 7.0, 1.5 Hz), 7.91 (2H, dd, J = 7.0, 1.5 Hz), 9.57 (1H, d, J = 6.2 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 37.55, 53.59, 57.51, 66.49, 117.98, 127.15, 127.84, 128.01, 128.25, 128.90, 128.97, 129.11, 129.92, 132.40, 133.40, 137.80, 138.32, 157.22, 167.27; IR (film) 3288, 1707, 1658, 1534, 1259 cm^{-1}; HRMS calcd for $C_{25}H_{24}N_4O_3$, 428.1848; found, 428.1852. For minor isomer ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.98 (1H, dd, J = 14.5, 7.5 Hz), 3.23 (1H, dd, J = 14.5, 4.2 Hz), 3.77 (1H, dd, J = 9.3, 2.7 Hz), 4.29−4.39 (1H, m), 5.07 (2H, s), 5.14 (1H, d, J = 9.3 Hz), 5.77−5.80 (1H, m), 7.22−7.37 (10H, m), 7.44 (2H, t, J = 7.3 Hz), 7.54 (1H, t, J = 7.3 Hz), 7.83 (2H, d, J = 7.3 Hz), 8.69 (1H, d, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 36.85, 52.01, 55.45, 67.35, 117.78, 127.20, 127.43, 127.93, 128.30, 128.56, 128.74, 129.07, 129.35, 131.65, 132.30, 135.24, 135.87, 157.21, 167.20; IR (film) 3289, 1707, 1658, 1531 cm^{-1}; HRMS calcd for $C_{25}H_{24}N_4O_3$, 428.1848; found, 428.1810.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for **1** and reaction products of allylation, Mannich-type, and cyanation reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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