Direct Synthesis of *N*-Hydroxy β-Amino Acid Esters from Carboxylic Esters and Nitrones

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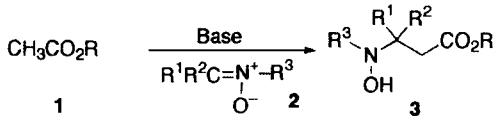
The direct synthesis of the title amino acid derivatives from carboxylic esters and nitrones can be achieved in fair to good yields when lithium or magnesium ester enolates were treated with nitrones in THF at −78 °C or in Et_2O at −20 to 0 °C, respectively. The products from the reaction of *t*-butyl acetate with 3,4-dihydroisoquinoline *N*-oxide or 5,5-dimethylpyrroline 1-oxide were transformed into (1,2,3,4-tetrahydroisoquinolin-1-ylidene)acetate or (pyrrolidin-2-ylidene)acetate derivatives in the presence of triphenylphosphine, carbon tetrachloride, and triethylamine in refluxing dichloromethane.

An efficient method for the preparation of protected *N*-hydroxy β-amino acid esters from ketene silyl acetals and nitrones has been reported by Tomoda et al.[1] Later, this method has been elegantly applied to the asymmetric synthesis of useful natural products by Kita et al.[2] Most recently, Murahashi et al. reported an efficient method for the asymmetric synthesis of α-substituted β-amino acids by utilizing the reaction of chiral enolates with nitrones via *N*-acyloxyiminium intermediates.[3] We investigated the possibility to obtain *N*-hydroxy β-amino acid esters directly from carboxylic esters and unprotected nitrones. In this paper, we wish to describe the results of our investigation, which show that *N*-hydroxy β-amino acid esters **3** and **7** are directly prepared from lithium or magnesium enolates of carboxylic esters **1** and **6**, and nitrones **2**. Previous reports have indicated that lithium,[4] sodium,[4] or zinc[5] enolate of carboxylic acid esters (even when *t*-butyl esters were used)[5] reacted with nitrones to give isooxazolidinone derivatives. *N*-Hydroxy β-amino acid derivatives can readily be converted β-amino acid derivatives,[6] which serve as useful precursor in the biologically important compounds, such as β-lactams[7] and β-peptides.[8] We also report a transformation of cyclic *N*-hydroxy β-amino carboxylates **3e** and **3f** into (1,2,3,4-tetrahydroisoquinolin-1-ylidene)acetate and (pyrrolidin-2-ylidene)-acetate derivatives **8** and **10**.

Results and Discussion

We first examined lithium enolate of *t*-butyl acetate (**1a**), which was generated by the standard method in THF at −78 °C. Addition of equimolar amounts of a range of nitrones **2** gave, after aqueous workup followed by distillation using Kugelrohr or preparative TLC on silica gel, *N*-hydroxy β-amino acid esters **3** (Scheme 1). The yields were good to high, as judged from ^{1}H NMR of the crude products after workup. Isolation of pure specimen of each product could be



Scheme 1.

performed by distillation using Kugelrohr or preparative TLC on silica gel, though the yields somewhat diminished. The isolated yields are summarized in Table 1. The yields were generally fair to good (Entries 1,3,7,9, and 10). Only one exception is the reaction using **2c**, in which the cyclization reaction occurred to give a cyclic compound, 2-isopropyl-3,3-dimethyl-1,2-oxazolidin-5-one (**4**) in 54% yield (Entry 5). We found that this direct preparation of *N*-hydroxy β-amino acid esters **3** could be carried out by using magnesium enolate[9] of **1a**, which was generated by the treatment of magnesium bis(diisopropylamide) (from diisopropylamine and EtMgBr in refluxing Et_2O) (MBDA); the reactions with nitrones **2a**, **2b**, and **2d** gave the corresponding hydroxy amino esters **3a**, **3b**, and **3d** in fair yields (Entries 2, 4, and 8). Although these results appeared to be inferior to those using lithium enolate, one of the advantages of using magnesium enolate is that the reaction can be conducted under milder reaction conditions (0 °C). The noticeable advantage was revealed by the isolation of *t*-butyl 3-[*N*-hydroxy-*N*-(1-methylethyl)amino]-3-methylbutanoate (**3c**) as the sole product from the reaction of **1a** and **2c** at −20 °C in moderate yield (Entry 6). The reactions using ethyl acetate (**1b**) produced results essentially analogous to those using *t*-butyl esters in terms of the relationship between LDA (lithium diisopropylamide) and MBDA. Thus, while the reaction of lithium enolate of **1b** with nitrone **2e** gave an inseparable mixture of the desired **3h** and 1,5,6,10b-tetrahydro-2*H*-isoquino[2,1-*b*][1,2]oxazol-2-one (**5**) (Entry 12), in the reaction using magnesium enolate at −20 °C compound **3h** was obtained

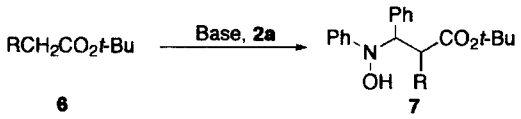
Table 1. Preparation of β-(*N*-Hydroxyamnio)carboxylates **3** from Acetates **1** and Various Nitrones **2**

Entry	1	2	Base	Temp/ °C	Product(s) (Yield/%)[a]
1	**1a** (R = *t*-Bu)	**2a** ($R^1 = R^3 = Ph$, $R^2 = H$)	LDA	−78	**3a** (71)
2	**1a**	**2a**	MBDA	0	**3a** (61)
3	**1a**	**2b** ($R^1 = Me$, $R^2 = H$, $R^3 = Et$)	LDA	−78	**3b** (79)
4	**1a**	**2b**	MBDA	0	**3b** (65)
5	**1a**	**2c** ($R^1 = R^2 = Me$, $R^3 = i$-Pr)	LDA	−78	**4**[b] (54)
6	**1a**	**2c**	MBDA	−20	**3c** (40)
7	**1a**	**2d** [R^1—$R^3 = (CH_2)_3$, $R^2 = H$]	LDA	−78	**3d** (70)
8	**1a**	**2d**	MBDA	0	**3d** (53)
9	**1a**	**2e** [R^1—$R^3 = o$-$C_6H_4(CH_2)_2$, $R^2 = H$]	LDA	−78	**3e** (91)
10	**1a**	**2f** [R^1—$R^3 = (CH_2)_2CMe_2$, $R^2 = H$]	LDA	−78	**3f** (77)
11	**1b** (R = Et)	**2d**	LDA	−78	**3g** (53)
12	**1b**	**2e**	LDA	−78	**3h** (46),[c] **5** (16)[c),d]
13	**1b**	**2e**	MBDA	−20	**3h** (44)

a) Isolated yields. b) 2-Isopropyl-3,3-dimethyl-1,2-oxazolidin-5-one. c) Inseparable from each other. d) 1,5,6,10b-Tetrahydro-2*H*-isoquino[2,1-*b*][1,2]oxazol-2-one.

as the sole product in moderate yield (Entry 13). Attempts to obtain **3c** or **3h** uncontaminated with **4** or **5**, respectively, at 0 °C have been unsuccessful. It can be assumed that the divalent magnesium ion, which probably stabilizes the aminooxide ion intermediate, is responsible for the success of the isolation of *N*-hydroxy β-amino acid derivatives **3b** and **3h**.

Next, the reactions of *t*-butyl propanoate (**6a**) or *t*-butyl (phenylthio)acetate (**6b**) with nitrone **2a** were carried out under similar conditions, as depicted in Scheme 2. Each reaction gave a mixture of diastereomers as shown in Table 2, which were readily separated by preparative TLC on silica gel. The stereochemical outcomes of these reactions were in accord with the Tomoda's results[1] and the stereochemistry of each product **7** was established by a detailed comparison of the spectrum data with those reported by Tomoda[1] (See experimental).



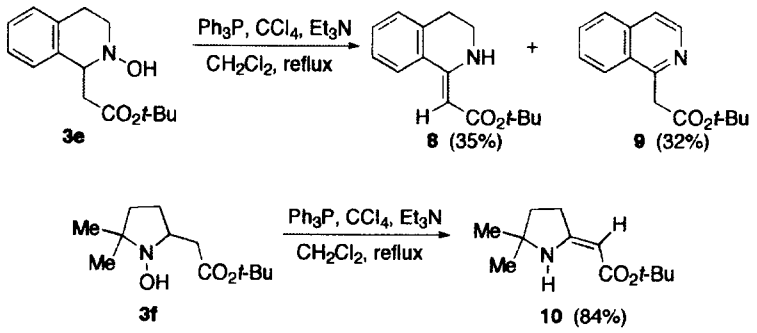
Scheme 2.

Finally, transformation of some of the *N*-hydroxy β-amino esters prepared was carried out as shown in Scheme 3. Compound **3e** was treated with Ph_3P/CCl_4 in the presence of Et_3N in refluxing CH_2Cl_2. This combination of reagents has been successfully used to convert oximes to the corresponding nitriles.[10] The reaction was found to afford (*Z*)-(1,2,3,4-tetrahydroisoquinolin-1-ylidene)acetate (**8**) and (isoquinolin-1-yl)acetate (**9**) in fair combined yield. The formation of **9** may be explained by dehydration of **3e** to give (1,4-dihydro-

Table 2. Preparation of β-(*N*-Hydroxyamnio)carboxylates **7** from *t*-Butyl Propanoate (**6a**) and (Phenylthio)acetate (**6b**)

Entry	6	Base	Temp/°C	7 (Yield/%;[a] *threo* : *erythro*[b])
1	**6a** (R = Me)	LDA	−78	**7a** (73; 23 : 77)
2	**6a**	MBDA	0	**7a** (58; 41 : 59)
3	**6b** (R = PhS)	LDA	−78	**7b** (74; 37 : 63)
4	**6b**	MBDA	0	**7b** (62; 40 : 60)

a) Isolated yields. b) Determined by ^1H NMR spectra. See. Ref. 1.



Scheme 3.

isoquinolin-1-yl)acetate. This was oxidized probably with air to give rise to **9**. The Z stereochemistry of **8** was determined by NOE experiments. Irradiation of the signal due to the vinyl proton appeared at δ 5.11, caused a strong enhancement of the signal due to H-8 at δ 8.46. Similar treatment of compound **3f** with Ph_3P/CCl_4 resulted in the formation of (*Z*)-(5,5-dimethylpyrrolidin-2-ylidene)acetate (**10**) in good yield.[11] The determination of the stereochemistry of compound **10** was performed on the basis of spectral analyses (see Experimental). We have previously provided the characterization of both the *E* and *Z* isomers of (pyrrolidinylidene)acetates.[12] Several studies on the stereochemistry of (pyrrolidinylidene)acetates by other groups have also point out that the stereochemistry of **10** should be *Z*.[13] NOE experiments were undertaken to established unambiguously this stereochemical assignment. Thus, upon irradiation of the signal due to H-3 at d 2.62, large NOE's were recorded for the signals due to the vinyl proton at δ 4.37 as well as H-3 at δ 1.76.

The results described in the forgoing section disclosed that *N*-hydroxy β-amino carboxylates can be formed in reasonable yields directly from the reactions of lithium or magnesium enolates of carboxylic esters with nitrones. Cyclic *N*-hydroxy β-amino carboxylates could be transformed into (isoquinolinylidene)acetate or (pyrrolidinylidene)acetate derivatives, which have been used as intermediates for the synthesis of useful organic compounds including natural products.[14]

Experimental

General. All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were determined with a Perkin-Elmer 1600 Series FT IR spectrometer. The ^{1}H NMR spectra were determined in $CDCl_3$ with either a JEOL JNM-GX270 FT NMR spectrometer operating at 270 MHz. Chemical shifts were referenced relative to tetramethylsilane as an internal standard. Low- resolution MS analyses were performed on a JEOL AUTOMASS 20 spectrometer (Center for Joint Research and Development, this University). High-resolution MS analyses were performed a JEOL JMS-AX505 HA spectrometer (Faculty of Agriculture, this University). TLC was carried out on a Merck Kieselgel 60 PF_{254}. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use. All reactions were carried out under argon.

Starting Materials. *N*-Benzylideneaniline *N*-oxide (**2a**)[15] and 5,5-dimethyl-1-pyrroline 1-oxide (**2f**)[16] were prepared following the appropriate reported procedures. All other nitrones were prepared following the procedures reported by Murahashi et al.[17] *t*-Butyl (phenylthio)acetate (**6b**) was prepared following the procedure reported by Babin et al.[18] All of the other chemicals used in this study were commercially available.

***t*-Butyl 3-(*N*-Hydroxy-*N*-phenylamino)-3-phenylpropanoate (3a). Reaction of Lithium Enolate of *t*-Butyl Acetate (1a) with *N*-Benzylideneaniline *N*-oxide (2a).** To a stirred solution of LDA, generated in situ from *i*-Pr_2NH (1.0 mmol, 0.10 g) and *n*-BuLi (1.7 M in hexane, 1 M = 1 mol dm^{-3}, 1.0 mmol) by the standard method, in THF (5 ml) at -78 °C was added **1a** (1.0 mmol, 0.12 g). After 15 min, a THF (3 ml) solution of **2a** (1 mmol, 0.20 g) was added to the solution of lithium enolate. The mixture was stirred for 50 min at the same temperature before saturated aqueous NH_4Cl was added to it. The resulting mixture was extracted with Et_2O, dried over anhydrous Na_2SO_4, and evaporated. The crude product was purified by preparative TLC on SiO_2 to give **3a** (0.22 g, 71%): mp 107—108 °C (hexane–AcOEt); IR (KBr disk) 3395 and 1728 cm^{-1}; ^{1}H NMR δ = 1.37 (9H, s), 2.89 (1H, dd, *J* = 14.6 and 7.4 Hz), 3.05 (1H, dd, *J* = 14.6 and 7.9 Hz), 4.98 (1H, dd, *J* = 7.9 and 7.4 Hz), 5.70 (1H, br. s), 6.93 (1H, t, *J* = 7.4 Hz), 7.08 (2H, d, *J* = 7.9 Hz), and 7.2—7.3 (7H, m); MS *m/z* (%) 297 [$(M-O)^+$, 4.3], 241 (8.7), and 182 (100). Found: C, 72.79; H, 7.38; N, 4.47%. Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47%.

Reaction of Magnesium Enolate of 1a with 2a. To a stirred turbid solution (0 °C) of a magnesium amide, generated in situ by refluxing *i*-Pr_2NH (2.5 mmol, 0.26 g) and EtMgBr (1.3 mmol) in Et_2O (4 ml) for 1 h, was added **1a** (0.63 mmol, 73 mg). After 5 min a solution of **2a** (0.63 mmol, 0.12 g) in Et_2O (5 ml) was added to the solution of magnesium enolate. The mixture was stirred for 2.5 h at the same temperature and then worked up in a manner similar to that described above. Purification of the crude product by preparative TLC gave **3a** (0.12 g, 61%).

***t*-Butyl 3-(*N*-Ethyl-*N*-hydroxyamino)butanoate (3b):** prepared from the reaction of lithium or magnesium enolate of **1a** with nitrone **2b**: bp 180 °C (bath temp)/93 Pa; IR (neat) 3403, 1730, and 1160 cm^{-1}; ^{1}H NMR δ = 1.10 and 1.12 (combined 6H, d and t, *J* = 6.9 and 7.4 Hz, respectively), 1.45 (9H, s), 2.27 (1H, dd, *J* = 14.2 and 6.9 Hz), 2.5—2.7 (2H, m), 2.79 (1H, dq, *J* = 12.6 and 7.4 Hz), 3.25 (1H, sept, *J* = 6.9 Hz), and 5.01 (1H, br. s); MS *m/z* (%) 203 (M^+, 1.5), 202 (14), and 146 (100). Found: C, 59.07; H, 10.52; N, 7.00%. Calcd for $C_{10}H_{21}NO_3$: C, 59.08; H, 10.41; N, 6.89%.

3,3-Dimethyl-2-(1-methylethyl)-1,2-oxazolidin-5-one (4): prepared from the reaction of lithium enolate of **1a** with nitrone **2c**: R_f 0.24 (3 : 1 hexane–EtOAc); IR (neat) 1783 and 1771 cm^{-1}; ^{1}H NMR δ = 1.19 (6H, d, *J* = 6.3 Hz), 1.35 (6H, s), 2.62 (2H, s), 3.25 (1H, sept, *J* = 6.3 Hz); MS *m/z* (%) 157 (M^+, 42), 142 (99), 100 (99), and 83 (100). Found: *m/z* 157.1113. Calcd for $C_8H_{15}NO_2$: M, 157.1104.

***t*-Butyl 3-[*N*-Hydroxy-*N*-(1-methylethyl)amino]-3-methylbutanoate (3c):** prepared from the reaction of magnesium enolate of **1a** with nitrone **2c** at -20 °C: a colorless liquid; bp 150 °C (bath temp)/77 Pa; IR (neat) 1724 cm^{-1}; ^{1}H NMR δ = 1.08 (6H, d, *J* = 6.3 Hz), 1.22 (6H, s), 1.46 (9H, s), 2.35 (2H, s), 3.23 (1H, sept, *J* = 6.3 Hz), 5.05 (1H, br. s); MS *m/z* (%) 231 (M^+, 2.9), 230 (14), 174 (16), 133 (28), 118 (28), and 57 (100). Found: *m/z* 231.1851. Calcd for $C_{15}H_{25}NO_3$: M, 231.1836.

***t*-Butyl (1-Hydroxypyrrolidin-2-yl)acetate (3d):** prepared from the reaction of lithium or magnesium enolate of **1a** with nitrone **2d**; bp 120 °C (bath temp)/39 Pa; IR (neat): 3192 and 1730 cm^{-1}; ^{1}H NMR δ = 1.35—1.55 (10H, m including s at 1.45), 1.65—1.85 (2H, m), 1.95—2.2 (1H, m), 2.32 (1H, dd, *J* = 7.4 and 14.78 Hz), 2.66 (1H, dd, *J* = 5.8 and 14.8 Hz), 2.75—2.9 (1H, m), 3.0—3.18 (1H, m), 3.23—3.31 (1H, m), and 5.42 (1H, bs); MS *m/z* (%) 201 (M^+, 0.04), 143 (50), and 126 (100). Found: *m/z* 201.1363. Calcd for $C_{10}H_{19}NO_3$: M, 201.1366.

***t*-Butyl (2-Hydroxy-1,2,3,4-tetrahydroisoquinolin-1-yl)-acetate (3e):** prepared from the reaction of lithium enolate of **1a** with nitrone **2e**; bp 220 °C (bath temp)/24 Pa; IR (neat) 3220 and 1727 cm^{-1}; ^{1}H NMR δ = 1.43 (9H, s), 2.81 (2H, d, *J* = 5.8 Hz), 2.85—2.95 (2H, m), 3.0—3.2 (1H, m), 3.41 (1H, dt, *J* = 11.1 and 4.8 Hz), 4.42 (1H, t, *J* = 5.8 Hz), 5.75 (1H, br. s), and 7.05—7.2 (4H, m); MS *m/z* (%) 263 (M^+, 0.42), 205 (79), and 188 (100). Found: *m/z* 263.1518. Calcd for $C_{15}H_{21}NO_3$: M, 263.1522.

***t*-Butyl (1-Hydroxy-5,5-dimethylpyrrolidin-2-yl)acetate (3f):** prepared from the reaction of lithium enolate of **1a** with nitrone **2f**; bp 180 °C (bath temp)/110 Pa; IR (neat) 3435 and 1729 cm^{-1}; ^1HNMR δ = 1.04 (3H, s), 1.17 (3H, s), 1.45 (9H, s), 1.5—1.6 (3H, m), 1.9—2.05 (1H, m), 2.31 (1H, dd, J = 14.6 and 7.7 Hz), 2.62 (1H, dd, J = 14.6 and 5.2 Hz), 3.35 (1H, m), and 4.53 (1H, br. s); MS *m/z* (%) 212 [$(M-OH)^+$, 8.0], 156 (65), and 70 (100). Found: C, 62.55; H, 10.34; N, 6.02%. Calcd for $C_{12}H_{23}NO_3$: C, 62.85; H, 10.11; N, 6.11%.

Ethyl (1-Hydroxypyrrolidin-2-yl)acetate (3g): prepared from the reaction of lithium enolate of **1b** with nitrone **2d**: bp 150 °C (bath temp)/53 Pa; IR (neat) 3246 and 1735 cm^{-1}; ^1HNMR δ = 1.26 (3H, t, J = 7.4 Hz), 1.2—1.3 (1H, m), 1.45—1.55 (2H, m), 1.95—2.05 (1H, m), 2.42 (1H, dd, J = 6.7 and 15.0 Hz), 2.72 (1H, dd, J = 5.8 and 15.0 Hz), 2.75—2.9 (1H, m), 3.05—3.35 (3H, m), and 4.15 (2H, q, J = 7.4 Hz); MS *m/z* (%)173 (M^+, 0.43), 172 (3), 171 (19), 125 (53), and 80 (100). Found: *m/z* 173.1053. Calcd for $C_8H_{15}NO_3$: M, 173.1053.

Ethyl (2-Hydroxy-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3h): prepared from the reaction of lithium or magnesium enolate of **1b** with nitrone **2e**; R_f 0.54 (1 : 1 hexane–EtOAc); IR (neat) 3227 and 1732 cm^{-1}; ^1HNMR δ = 1.24 (3H, t, J = 7.4 Hz), 2.87 (2H, d, J = 6.3 Hz), 2.9—3.0 (2H, m), 3.1—3.25 (1H, m), 3.40 (1H, dt, J = 11.1 and 5.3 Hz), 4.17 (2H, q, J = 7.4 Hz), 4.50 (1H, t, J = 6.3 Hz), 5.67 (1H, br. s), and 7.05—7.2 (4H, m); MS *m/z* (%) 235 (M^+, 8.0), 205 (84), and 188 (100). Found: C, 66.25; H, 7.30; N, 6.00%. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95%.

1,5,6,10b-Tetrahydro-2*H*-isoquino[2,1-*b*][1,2]oxazol-2-one (5):[19] obtained along with **3h** from the reaction of lithium enolate of **1b** with nitrone **2e**; R_f 0.65 (2 : 1 hexane–EtOAc); IR (neat) 1786 cm^{-1}; ^1HNMR δ = 2.75—2.95(2H, m), 3.08 (1H, ddd, J = 17.0, 8.9, and 5.4 Hz), 3.27 (1H, dd, J = 18.9 and 7.8 Hz), 3.39 (1H, ddd, J = 12.3, 8.9, and 4.9 Hz), 3.64 (1H, ddd, J = 12.3, 10.5, and 4.6 Hz), 5.08 (1H, br. t, J = 7.0 Hz), 7.05 (1H, dd, J = 8.9 and 2.4 Hz), 7.15 (1H, dd, J = 8.4 and 2.7 Hz), and 7.2—7.3 (2H, m); MS *m/z* (%) 189 (M^+, 73) and 147 (100).

***t*-Butyl *erythro* and *threo*-3-(*N*-Hydroxy-*N*-phenylamino)-2-methyl-3-phenylpropanoate (7a):** prepared from the reaction of lithium or magnesium enolate of **6a** with nitrone **2a**. ***erythro*-7a**: mp 134—137 °C (hexane–AcOEt); IR (KBr disk) 3390 and 1698 cm^{-1}; ^1HNMR δ = 1.14 (9H, s), 1.54 (3H, d, J = 6.8 Hz), 3.43 (1H, m), 4.51 (1H, d, J = 10.7 Hz), 4.76 (1H, br. s), and 6.85—7.25 (10H, m); MS *m/z* (%) 311 [$(M-O)^+$, 5.2] and 182 (100). Found: C, 73.12; H, 7.69; N, 4.35%. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28%. ***threo*-7a**: mp 139—142 °C (hexane); IR (KBr disk) 3514 and 1705 cm^{-1}; ^1HNMR δ = 1.00 (3H, d, J = 6.9 Hz), 1.52 (9H, s), 3.39 (1H, m), 4.45 (1H, d, J = 11.1 Hz), 5.48 (1H, s), and 6.8—7.25 (10H, m); MS *m/z* (%) 311 [$(M-O)^+$, 2.0] and 182 (100). Found: C, 73.11; H, 7.78; N, 4.30%. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28%.

***t*-Butyl *erythro* and *threo*-3-(*N*-Hydroxy-*N*-phenylamino)-3-phenyl-3-(phenylthio)propanoate (7b):** prepared from the reaction of lithium or magnesium enolate of **6b** with nitrone **2a**. ***erythro*-7b**: mp 142—145 °C (hexane); IR (KBr disk) 3537 and 1720 cm^{-1}; ^1HNMR δ = 1.46 (9H, s), 4.52 (1H, d, J = 11.1 Hz), 4.76 (1H, d, J = 11.1 Hz), 5.20 (1H, s),and 6.85—7.0 (3H, m), and 7.1—7.3 (12H, m); MS *m/z* (%) 421 (M^+, 0.71) and 403 (100). Found: C, 71.15; H, 6.41; N, 3.09%. Calcd for $C_{25}H_{27}NO_3S$: C, 71.23; H, 6.46; N, 3.32%. ***threo*-7b**: mp 164—169 °C (hexane–AcOEt); IR (KBr disk) 3528 and 1723 cm^{-1}; ^1HNMR δ = 1.02 (9H, s), 4.60 (1H, d, J = 11.1 Hz), 4.77 (1H, d, J = 11.1 Hz), 5.15 (1H, s), 6.86 (1H, t, J = 7.8 Hz), 6.98 (2H, d, J = 7.8 Hz), 7.15—7.25 (7H, m), 7.3—7.35 (3H, m), and 7.6—7.7 (2H, m); MS *m/z* (%) 421 (M^+, 0.29) and 403 (100). Found: C, 71.01; H, 6.48; N, 3.12%. Calcd for $C_{25}H_{27}NO_3S$: C, 71.23; H, 6.46; N, 3.32%.

***t*-Butyl (1,2,3,4-Tetrahydroisoquinolin-1-ylidene)acetate (8) and *t*-Butyl (Isoquinolin-1-yl)acetate (9).** A solution of **3e** (1.0 mmol, 0.26 g) in CH_2Cl_2 (5 ml) containing Ph_3P (1.5 mmol, 0.39 g), Et_3N (1.5 mmol, 0.15 g), and CCl_4 (1.5 mmol, 0.23 g) was heated at reflux temperature for 30 min. The cooled mixture was filtered through a small pad of SiO_2 to remove Ph_3P=O. The filtrate was concentrated in vacuo, and the residue was purified by preparative TLC on SiO_2 to afford **8** (86 mg, 35%) and **9** (78 mg, 32%). **8**: R_f 0.57 (3 : 1 hexane–EtOAc); IR (neat) 3286, 1644, and 1602 cm^{-1}; ^1HNMR δ = 1.51 (9H, s), 2.89 (2H, t, J = 6.2 Hz), 3.35—3.45 (2H, m), 5.11 (1H, s), 7.17 (1H, d, J = 7.4 Hz), 7.24 (1H, td, J = 7.4 and 1.6 Hz), 7.33 (1H, td, J = 7.4 and 1.6 Hz), 7.64 (1H, d, J = 7.4 Hz), and 9.02 (1H, br. s); MS *m/z* (%) 245 (M^+, 76) and 189 (100). Found: C, 73.20; H, 7.90; N, 5.59%. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71%. **9**: R_f 0.32 (3 : 1 hexane–EtOAc); IR (neat) 1731 cm^{-1}; ^1HNMR δ = 1.41 (9H, s), 4.36 (2H, s), 7.55—7.7 (3H, m), 7.83 (1H, d, J = 8.2 Hz), 8.08 (1H, d, J = 8.2 Hz), and 8.46 (1H, d, J = 7.8 Hz); MS *m/z* (%) 243 (M^+, 7.6), 170 (15), 143 (65), and 57 (100). Found: *m/z* 243.1280. Calcd for $C_{15}H_{17}NO_2$: M, 243.1260.

***t*-Butyl (*Z*)-(5,5-Dimethylpyrrolidin-2-ylidene)acetate (10):** prepared from **3f** in a manner similar to that described above from **3e** to **8** and **9**; bp 150 °C/120 mmHg; IR (neat) 3349, 1657, and 1600 cm^{-1}; ^1HNMR δ = 1.28 (6H, s), 1.46 (9H, s), 1.76 (2H, t, J = 7.4 Hz), 2.62 (2H, t, J = 7.4 Hz), 4.37 (1H, s), and 7.73 (1H, br. s); MS *m/z* (%) 211 (M^+, 11), 155 (28), 140 (71), and 122 (100). Found: *m/z* 211.1555. Calcd for $C_{12}H_{21}NO_2$: M, 211.1573.

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