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One-Carbon Chain Extension of Esters to α-Chloroketones: A Safer Route without Diazomethane

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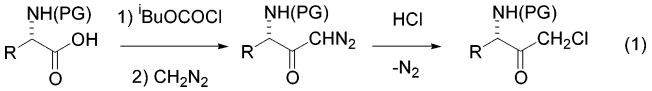
The reaction of a variety of methyl esters with dimethylsulfoxonium methylide at 0−25 °C affords the chain-extended *β*-keto dimethylsulfoxonium ylides. Subsequent treatment with hydrogen chloride in THF proceeds with loss of DMSO to afford the corresponding α-chloroketones. This sequence has been utilized to convert the methyl esters of CBZ-protected alanine and valine to the anti *N*-protected α-amino epoxides, which are important pharmaceutical intermediates. When the same protocol is applied to BOC-protected phenylalanine methyl ester, epimerization occurs so that the use of a more reactive aryl ester is required. This chemistry provides a practical route to α-chloroketones that avoids the use of toxic and explosive diazomethane.

Introduction

Organic chemists have a love/hate relationship with diazomethane—and for good reason. On one hand, diazomethane has proven to be a uniquely useful reagent.[1] For example, it has been widely utilized for the chain extension of carboxylic acids (via the mixed anhydrides) to the corresponding α-chloroketones, including the important amino acid-derived chloroketones[2,3] exemplified in eq 1. The products from eq 1 are readily converted



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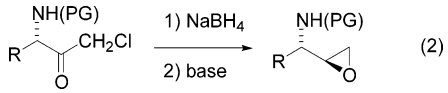
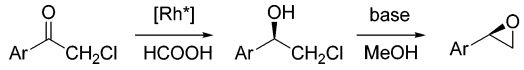
to *N*-protected α-amino epoxides (eq 2), which are ideal



(2)

precursors for the hydroxyethylamine class of protease inhibitors. Consequently, these building blocks are of interest in the fields of both antihypertensives[4] and HIV protease inhibitors such as saquinavir,[5] amprenavir,[6] and nelfinavir.[7] Moreover, even achiral α-chloroketones are of increasing interest as pharmaceutical building blocks. Ikariya, Noyori, and co-workers recently reported[8] that these compounds undergo highly catalytic asymmetric transfer hydrogenation to the *β*-chlorohydrins (eq 3), opening an efficient route to enantiopure styrene oxides.



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Balanced against the utility of diazomethane are the unique hazards associated with its use. This gaseous reagent is highly toxic, shock-sensitive, and explosive.[9] For intermediate-scale manufacturing, engineering solutions can be applied which limit the steady-state amount of CH_2N_2 in a reaction vessel and make these hazards manageable.[10] However, when faced with the need for a large-scale manufacturing process for *N*-protected α′-amino-α-chloroketones, we felt an urgent obligation to develop a safer alternative to eq 1.

In this regard, we were attracted to a 1987 report of Elkik and Imbeaux-Oudotte.[11] Building on earlier observations by others,[12,13] these researchers demonstrated a

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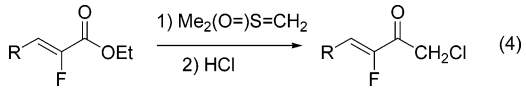
novel two-step conversion of several fluorine-containing α,β-unsaturated esters to the corresponding α-chloroketones (eq 4). This sequence involved treatment of the

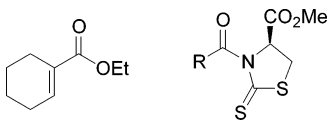


(4)

ester with dimethylsulfoxonium methylide to afford an intermediate β-keto sulfur ylide followed by protonation with HCl and thermolysis of the resultant salt.

If this transformation could be extended to *N*-protected α-amino esters, it would provide an attractive alternative to eq 1. However, two significant issues needed to be addressed. Would the *N*-protected α-amino esters survive exposure to the basic sulfur ylide without significant epimerization? Beyond that, would the addition of dimethylsulfoxonium methylide to an ester occur in the absence of a strongly activating fluorine substituent?

The latter question was of especial concern in light of two literature reports. Corey and Chaykovsky[14] examined the reaction of dimethylsulfoxonium methylide with ester **1**, which lacks the fluorine substituent of eq 4. They



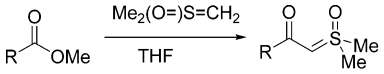
1 **2**

demonstrated that **1** undergoes Michael addition to the C=C bond while the ester group is recovered unchanged. Moreover, Nagao and co-workers[15] treated a series of methyl esters of structure **2** with dimethylsulfoxonium methylide and observed cleavage of the C−N bond rather than attack at the ester moiety.

Given these concerns, we elected to first delineate the scope of the reaction of achiral methyl esters with dimethylsulfoxonium methylide.

Results and Discussion

Synthesis of Achiral α-Chloroketones. A series of four diverse methyl esters, **3a**−**d**, was selected for study. Dimethylsulfoxonium methylide[16] was generated by treatment of trimethylsulfoxonium chloride with potassium *tert*-butoxide in refluxing THF. Treatment of **3a** or **3c** with 3 equiv of the resulting solution at room temperature overnight resulted in complete conversion to the corresponding β-keto sulfur ylide according to eq 5. In the case of **3b**, 5 equiv of the reagent and a longer reaction time (48 h) were required for complete conversion. (When dimethylsulfoxonium methylide was generated from trimethylsulfoxonium iodide, the reaction was not as clean and yields were diminished by 10−15%.)



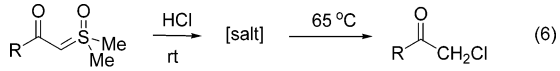
(5)

3a R = phenoxymethyl **4a**
3b R = 4-chlorophenyl **4b**
3c R = 2-furanyl **4c**
3d R = n-heptyl **4d**

While **4a**−**c** could be isolated in high yield (typically >80%) by flash chromatography, it is generally more convenient to crystallize the crude products from hot ethyl acetate. After drying, the β-keto sulfur ylides are obtained as analytically pure, white crystalline solids. Yields for compounds **4a**−**c** were 65%, 53%, and 80%, respectively. In the case of completely unactivated methyl caprylate, **3d**, the reaction was significantly slower. Even with 5 equiv of reagent and increasing the reaction time to 72 h, **4d** was isolated after chromatography in only 25% yield.

Attempts to replace the excess sulfur ylide in eq 5 with other bases were generally unsuccessful. These experiments are discussed in the Supporting Information.

We then examined the cleavage reaction of **4a** and **4b** with anhydrous hydrogen chloride. In both cases, treatment of a THF solution of the β-keto sulfur ylide at room temperature results in formation of a sparingly soluble salt (eq 6). Heating the resultant suspension at 65 °C



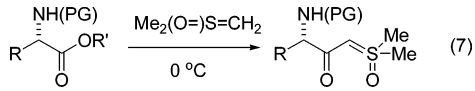
(6)

5a, R = phenoxymethyl
5b, R = 4-chlorophenyl

for 2 (for **4a**) or 16 h (for **4b**) results in clean conversion to the α-chloroketone. Extractive workup affords **5a** and **5b** in 97% and 92% yield, respectively.

Rhodium-catalyzed transfer hydrogenation of **5b** affords the β-chlorohydrin in 90% yield and 92% ee.[8a] Chloroketone **5a** has been reduced enzymatically.[17]

Chain Extension of α-Amino Esters. Encouraged by the preceding results, we turned our attention to the more sensitive *N*-protected methyl esters derived from alanine, valine, and phenylalanine (**6a**−**c**, R′ = methyl). In each case, treatment with dimethylsulfoxonium methylide, generated as above, resulted in conversion to the corresponding β-keto sulfur ylide (eq 7). Results are



(7)

6a R = Me, PG = CBZ **7a**
6b R = iPr, PG = CBZ **7b**
6c R = Bn, PG = BOC **7c**

summarized in Table 1. Again generating the methylide from trimethylsulfoxonium iodide rather than the chloride resulted in a lower yield, although the reduction in yield was not as severe in the absence of visible light.[18] Nominal yields in Table 1 are for crude products which were 85−95% pure by NMR. The remaining material appears to be oligomeric sulfur compounds as indicated by broad singlets at δ 0.85 and 1.25 in the ^{1}H NMR.

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(18) We thank Prof. Barry M. Trost for this suggestion.

TABLE 1. Reaction of *N*-Protected α-Amino Esters with Dimethylsulfoxonium Methylide According to Eq 7[a]

ester	R′	X	yield[b]	ee[c]
6a	Me	Cl	97	99
6b	Me	Cl	98[d]	90
6c	Me	Cl	87	<2
6c	Me	I	59[e]	<2
6a	Np[f]	I	67	>99
6b	Np[f]	I	100	>99
6c	Np[f]	I	99	>99

[a] Reactions were 0.1 M in THF at 0 °C, using 3 equiv of sulfur ylide; see the Experimental Section. [b] Nominal yield of crude product after extractive workup and vacuum drying. [c] Determined by HPLC after conversion to α-chloroketone. [d] 5 equiv of sulfur ylide was used. [e] Reaction run with exclusion of light. [f] Np = 4-nitrophenyl.

TABLE 2. Conversion of Sulfur Ylides to Chloroketones According to Eq 8[a]

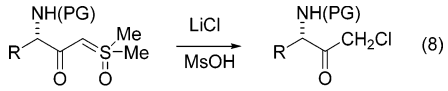
R′	PG	product	yield (%)[b]	ee (%)
Me	CBZ	**8a**	70	>99
^{i}Pr	CBZ	**8b**	75[c,d]	>99
Bn	BOC	**8c**	81	>99

[a] Conditions: substrate/MsOH/LiCl = 1.0:1.1:1.2 in solvent THF, 65 °C, 4 h; see the Experimental Section. [b] Isolated yield of chloroketone after crystallization. [c] Reaction time 48 h. [d] Yield after flash chromatography.

Determination of the ee of the products from eq 7 was most readily accomplished by supercritical fluid chromatography after conversion to the corresponding α-chloroketones. As shown in Table 1, the optical purity for **7a** was excellent and remained in the synthetically useful range for **7b**. However, for the phenylalanine-derived **7c** we observed essentially complete racemization.

To address this problem, we examined the use of 4-nitrophenyl (Np) esters in place of the methyl esters as starting materials. The requisite Np esters are readily available and the 4-nitrophenoxide group functions as an excellent nucleofuge. With these alternative substrates, we observed clean conversion to the *β*-keto sulfur ylides without detectable epimerization even when using trimethylsulfoxonium iodide as precursor to the methylide (Table 1). This is, of course, advantageous since the iodide is the inexpensive reaction product of methyl iodide with DMSO.

Conversion of the *β*-keto sulfur ylides to the α-chloroketones (eq 8) proved straightforward in all cases. The results shown in Table 2 are for the *β*-keto sulfur ylides prepared from the Np esters. Chloroketones **8a** and **8c**



(8)

7a R = Me, PG = CBZ **8a**
7b R = ^{i}Pr, PG = CBZ **8b**
7c R = Bn, PG = BOC **8c**

were crystallized from 80:20 hexanes/ethyl acetate. Chloroketone **8b** was an oil, which was purified by flash chromatography. The lower yields in Table 2 versus those for cleavage of **4a** and **4b** reflect, at least in part, the use of crude (uncrystallized) *β*-keto sulfur ylides as starting materials.

As a practical source of HCl, the combination of lithium chloride and methanesulfonic acid provided the cleanest

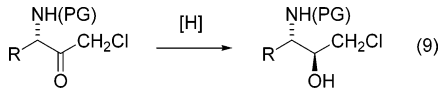
TABLE 3. Reduction of Alanine-Derived Chloroketone 8a According to Eq 9[a]

reductant	temp (°C)	t (h)	dr[b]
$NaBH_4$/EtOH	0	0.5	2.3/1
$NaBH_4$/EtOH	−70	1[c]	2.9/1
(*R*)−(BINAP)$RuCl_2/H_2$	50	24	23/1
(*S*)-BINAP)$RuCl_2/H_2$	50	48	1/2.2

[a] Catalytic hydrogenations were carried out in methanol under 65 psi of hydrogen at substrate/catalyst = 100:1; see the Experimental Section. [b] Diastereomer ratio of anti to syn chlorohydrins by HPLC. [c] 15% of unreacted chloroketone remained after HOAc quench.

reaction. With alternative HCl sources (tetrabutylammonium chloride/MsOH or concentrated aqueous HCl), cleavage of the methyl C−S bond became a significant competing pathway (up to 37% in polar solvents such as DMSO).

***anti*-α-*N*-Protected Amino Epoxides.** Although it is not the principal focus of this paper, we wish to record several observations regarding the reduction of chloroketones **8a**−**c** to the corresponding *β*-chlorohydrins (eq 9)



(9)

8a R = Me, PG = CBZ **9a**
8b R = iPr, PG = CBZ **9b**
8c R = Bn, PG = BOC **9c**

and their subsequent cyclization to the epoxides. Both of these steps have been studied in some detail by others.[19] When sodium borohydride is used as reducing agent for eq 9, the anti diastereoselectivity of the reduction is sensitive to the steric bulk of the R group and decreases along the series R = ^{i}Pr > Bn > Me.

Consistent with this, treatment of valine-derived chloroketone **8b** with sodium borohydride in ethanol at 0 °C proceeded in 92:8 dr and the anti *β*-chlorohydrin could be isolated by crystallization in 84% yield. In contrast, sodium borohydride reduction of phenylalanine-derived **8c** proceeded with only 4:1 selectivity for the anti *β*-chlorohydrin. Nevertheless, crystallization of the crude product from hot ethyl acetate afforded the pure (*S*,*S*)-chlorohydrin in 50% yield without the need for chromatography.

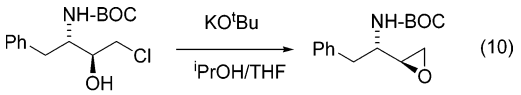
Reduction of the sterically small alanine-derived chloroketone **8a** represents a particular challenge and results are summarized in Table 3. Reduction with sodium borohydride proceeded in 2.3:1 diastereoselectivity at 0 °C and this improved to only 2.9:1 at −70 °C. It occurred to us that higher diastereoselectivity might be achieved by hydrogenation with an asymmetric homogeneous catalyst. Entries 3 and 4 of Table 3 provide evidence for "matched versus mismatched" interaction between (BINAP)$RuCl_2$ as catalyst[20] and the chloroketone substrate. With use of (*R*)-BINAP as the ligand and the chloroketone derived from natural L-alanine as substrate, 23:1 anti/syn diastereoselectivity could be achieved. Formation of the desired *anti*-(*S*,*S*)-isomer was confirmed by conver-

(19) Rotella, D. P. *Tetrahedron Lett.* **1995**, *36*, 5453 and references therein.

(20) For the asymmetric hydrogenation of an achiral α-chloroketone with (BINAP)$RuCl_2$, see: (a) Kitamura, M.; Ohkuma, T.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1988**, *29*, 1555. (b) Davies, S. G.; Ichihara, O. *Tetrahedron*: *Asymmetry* **1996**, *7*, 1919.

sion to the corresponding epoxide and comparison with an authentic sample.

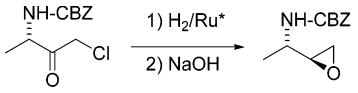
Ring-closure of the *N*-protected *β*-chlorohydrins is again well precedented in the literature[21] and proceeded uneventfully. For example, epoxide **10** was formed in 96% yield and >99% ee upon treatment with potassium *tert*-butoxide in a 2-propanol/THF mixed solvent system (eq 10).



(10)

9c **10**

Although our primary interest was in the large-scale manufacturing of α-amino epoxides, this chemistry works quite well on a laboratory scale. As a demonstration of this, we have carried out the (*R*)-(BINAP)$RuCl_2$ reduction/cyclization sequence on a 30-g scale (eq 11). The



(11)

8a **11**

methanolic solution of *β*-chlorohydrin obtained from the hydrogenation was filtered through Celite and treated with a 10% excess of 1 M sodium hydroxide overnight. The overall yield of crystalline **11** (>99% ee) for this two-step sequence was 67%.

Conclusion

We have demonstrated a straightforward two-step chain extension of esters to α-chloroketones, which avoids the use of diazomethane. We have found that even modestly activated methyl esters will react with dimethylsulfoxonium methylide to afford the chain-extended *β*-keto sulfur ylides in synthetically useful yields. Where applicable, this is advantageous since methyl esters can generally be prepared without the intermediacy of a moisture-sensitive acid chloride. Nevertheless, for unactivated or base-sensitive substrates, the use of the more reactive aryl esters (such as the 4-nitrophenyl esters) may be required.

As one application of this methodology, we have demonstrated a novel and practical route to anti *N*-protected α-amino epoxides. It should be noted that the same chloroketones **8a**−**c** can also be reduced enzymatically[22] to the corresponding syn chlorohydrins so that our route can be used to access both sets of diastereomeric epoxides. An attractive feature of this chemistry as a practical route[23] to the anti epoxides is that, with the exception of compound **8b**, all of the intermediates are crystalline solids and hence no chromatographic purification is required.

In our opinion, this chemistry represents a useful advance in the manufacture of α-chloroketones as pharmaceutical intermediates. Given the simplicity of this approach and the hazards associated with diazomethane, we would certainly recommend that synthetic chemists also consider this methodology for the laboratory scale preparation of α-chloroketones.

Experimental Section

Dimethylsulfoxonium 2-Oxo-3-(phenoxy)propylide, 4a. A 100-mL flask was charged with trimethylsulfoxonium chloride (3.90 g, 30 mmol), tetrahydrofuran (30 mL), and 1.0 M potassium *tert*-butoxide in THF solution (31.5 mL, 31.5 mmol). The suspension was heated at reflux for 2 h then cooled to room temperature. Methyl phenoxyacetate (1.66 g, 10 mmol) was added dropwise over 10 min whereupon the mixture was stirred overnight at room temperature. After distillation of the solvent, water (10 mL) was added and the product was extracted into ethyl acetate (2 × 50 mL). The organic phase was washed with brine (2 × 10 mL), dried over sodium sulfate, and concentrated in a vacuum to afford the crude product (2.1 g). Recrystallization from ethyl acetate (10 mL) afforded the sulfur ylide (1.47 g, 65%) as a white crystalline solid. Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.38; H, 6.34. Found: C, 58.50; H, 6.10. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 3.40 (s, 6H), 4.38 (s, 2H), 4.90 (s, 1H), 6.83−6.96 (m, 3H), 7.24 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 41.8, 69.3, 70.3, 114.5, 121.0, 129.4, 158.0, 185.5.

1-Chloro-3-phenoxy-2-propanone, 5a. A glass tube was charged with **4a** (0.91 g, 4.0 mmol), THF (15 mL), and 4 M HCl in dioxane solution (1.15 mL, 4.6 mmol). The tube was sealed with a Teflon stopper and stirred at room temperature for 10 min then for 2 h in a 70 °C heated block at which time the mixture was homogeneous. After cooling, the solvent was removed at reduced pressure. The residue was added to water (15 mL) and extracted into methyl *tert*-butyl ether (2 × 10 mL). Removal of the solvent afforded **5a** as a colorless oil (0.72 g, 97%) which crystallized upon standing to a low melting solid. Anal. Calcd for $C_9H_9ClO_2$: C, 58.55; H, 4.91. Found: C, 58.57; H, 5.00. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 4.27 (s, 2H), 4.60 (s, 2H), 6.77 (d, *J* = 8.0 Hz, 2H), 6.90 (t, *J* = 7.4 Hz, 1H), 7.19 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 46.7, 71.3, 114.6, 121.6, 129.6, 157.1, 198.8.

Dimethylsulfoxonium (3*S*)-2-Oxo-3-(benzyloxycarbonylamino)butylide, 7a. A solution of 1.0 M potassium *tert*-butoxide in THF (60 mL, 60 mmol) was added at room temperature to a suspension of trimethylsulfoxonium chloride (7.72 g, 60 mmol) in THF (40 mL). The mixture was heated at reflux for 2 h and was then cooled to 0 °C. A solution of CBZ-alanine methyl ester (4.74 g, 20 mmol) in THF (10 mL) was added dropwise at 0 °C and the resultant solution was stirred for 4 h at 0 °C. The reaction was quenched with water (20 mL). The organic layer was separated and washed with brine (2 × 20 mL). The solvent was removed at reduced pressure to afford the crude sulfur ylide (5.76 g, 97%) as an off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 1.30 (d, *J* = 16.6 Hz, 3H), 3.34 (s, 3H), 3.36 (s, 3H), 4.16 (m, 1H), 4.61 (S, 1H), 5.08 (s, 2H), 5.81 (d, *J* = 7.0 Hz, 1H), 7.28 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 20.3, 42.0, 42.2, 53.2, 66.7, 68.7, 109.8, 128.2, 128.7, 136.9, 155.9, 188.7.

(3*S*)-1-Chloro-3-(benzyloxycarbonylamino)-2-butanone, 8a. Crude **7a** (6.18 g, 22.0 mmol) was dissolved in THF (100 mL) and the solution was cooled to 0 °C. Lithium chloride (1.6 g, 25 mmol) and methanesulfonic acid (1.6 mL, 24 mmol) were added. The temperature was slowly raised to 70 °C and stirring was continued at that temperature for 2 h. After cooling, the reaction was quenched by addition of water (100 mL). The phases were separated and 2:1 heptane/ethyl acetate (100 mL) was added. To remove DMSO, the organic layer was washed with saturated $NaHCO_3$ (20 mL), water (2 × 20 mL), and brine (20 mL) and dried over Na_2SO_4. Removal of solvent afforded the crude chloroketone (5.0 g). The enantiomeric excess was determined to be >99% by supercritical fluid chromatography (Chiralpak AD-H, 150 × 4.6 mm, 5 *μ* particle

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size, 15% methanol in CO_2 mobile phase, 40 °C, 2 mL/min, 150 bar). Retention times for the enantiomers were assigned by using an authentic racemate as 3.00 and 3.18 min. Crystallization of the product from hot 5:1 heptane/ethyl acetate (50 mL) afforded pure **8a** (2.9 g, 70%) as a snow-white solid. Anal. Calcd for $C_{12}H_{14}ClNO_3$: C, 56.37; H, 5.52; N, 5.48. Found: C, 56.47; H, 5.30; N, 5.35. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (d, J = 7.1 Hz, 3H), 4.32 (s, 2H), 4.64 (m, 1H), 5.12 (s, 2H), 5.48 (br s, 1H), 7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.8, 46.2, 53.7, 67.4, 128.4, 128.5, 128.8, 136.2, 155.9, 201.8.

(2*S*,3*S*)-1-Chloro-3-(benzyloxycarbonylamino)-2-butanol, 9a. Chloroketone **8a** (30.0 g, 117 mmol) was dissolved in methanol (300 mL). The solution was purged with N_2. Hydrochloric acid in isopropyl alcohol 5−6 N solution (2.4 mL) and [(*R*)-BINAP]$RuCl_2$ (2.6 g, 3.3 mmol) was then added and the mixture was purged with N_2 and H_2. The mixture was heated to 40 °C and hydrogenation was performed at 2.6 bar of pressure. After reaction was complete (2.64 L of H_2 absorbed), the mixture was allowed to cool to 25 °C and was filtered through Celite. The anti/syn ratio was determined to be 23:1 with a 250 mm Zorbax EclipseXDB-C18 column (1.5 mL/min, 25-min runs), using a solvent gradient as follows. Solvent 1 = 0.1% trifluoroacetic acid in water, solvent 2 = 0.1% trifluoroacetic acid in acetonitrile; the initial ratio water/acetonitrile was 95:5 and this was ramped to 5:95 over the course of 23 min. A small analytical sample of the product was prepared by crystallization from hot hexane/ethyl acetate. Anal. Calcd for $C_{12}H_{16}ClNO_3$: C, 55.93; H, 6.26; N, 5.44. Found: C, 55.83; H, 6.07; N, 5.63. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (d, J = 6.6 Hz, 3H), 3.29 (d, J = 4.3 Hz, 1H), 3.48 (dd, J = 11.2, 7.3 Hz, 1H), 3.50 (dd, J = 11.2, 3.8 Hz, 1H), 3.84 (m, 1H), 3.90 (m, 1H), 5.09 (m, 2H), 5.25 (d, J = 8.1 Hz, 1H), 7.30 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 46.0, 48.2, 66.0, 73.2, 127.1, 127.2, 127.6, 135.2, 155.0.

[(1*S*)-1-(2*S*)-Oxiranylethyl]carbamic Acid Benzyl Ester, 11. The remainder of the filtered solution of **9a** from the preceding example was treated with 1 M aqueous NaOH solution (130 mL, 0.13 mol) and stirred at room temperature overnight. The solution was concentrated under vacuum and toluene (225 mL), *tert*-butyl methyl ether (75 mL), and water (30 mL) were added. Layers were separated. The aqueous phase was twice extracted with a mixture of *tert*-butyl methyl ether (150 mL) and toluene (75 mL). All organic layers were combined and washed twice with water (100 mL), and then concentrated to an oil. The oil was dissolved in isopropyl acetate (120 mL) and purified by filtration through a silica gel column and crystallization obtaining 17.0 g of epoxide **11** (67% overall yield). Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.19; H, 6.71; N, 6.42. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (d, J = 6.9 Hz, 3H), 2.70 (br d, 2H), 2.90 (br s, 1H), 3.72 (m, 1H), 4.9−5.1 (m, 3H), 7.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.6, 46.3, 48.1, 54.6, 67.0, 128.3, 128.4, 128.8, 136.5, 156.0.

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Supporting Information Available: Additional experimental details and a summary of preliminary mechanistic studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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