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Direct Chemical Method for Preparing 2,3-Epoxyamides Using Sodium Chlorite

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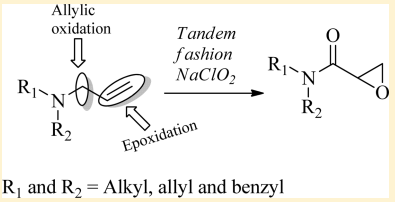
Supporting Information

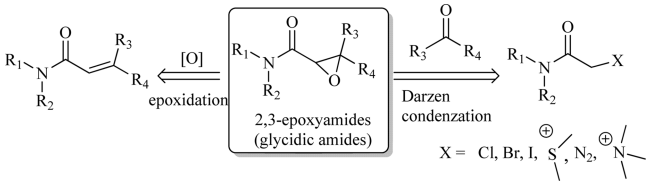
ABSTRACT: A direct method for preparing 2,3-epoxyamides from tertiary allylamines via a tandem C−H oxidation/double bond epoxidation using sodium chlorite is reported. Apparently, the reaction course consists of two steps: (i) allylic oxidation of the starting allylamine to corresponding unsaturated allylamide with sodium chlorite followed by (ii) epoxidation of the allylamide to the 2,3-epoxyamide mediated by hypochlorite ion, which is formed in situ by reduction of sodium chlorite. The reaction conditions tolerate the presence of free hydroxyl groups and typical functional groups such as TBS, aryl, alkyl, allyl, acetyl, and benzyl groups; however, when an activated aromatic ring (e.g., sesamol) is present in the substrate, the use of a scavenger is necessary.



INTRODUCTION

2,3-Epoxyamides (also known as glycidic amides) are very important organic compounds that are found in nature[1] or prepared in the laboratory for eventually being used as versatile and useful building blocks in organic synthesis.[2] In spite of the importance of these compounds, there still are no direct synthetic methods for their preparation. Generally, 2,3-epoxyamides are synthetized either by Darzen condensation of α-haloacetamides,[3] α-sulphoniumacetamides,[4] α-diazoacetamides[5] ammoniumacetamides[6] with carbonyl compounds, or by means of epoxidation of α,β-unsaturated amides.[7] In both procedures, the amide group is first prepared, then the epoxide group (Scheme 1).

Scheme 1. Known Strategies for the Synthesis of 2,3-Epoxyamides

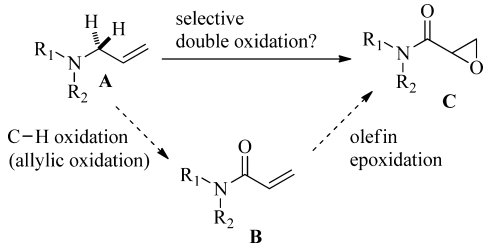


To overcome this backlog, we considered it necessary to introduce into the organic chemistry scenario a more direct method for the preparation of glycidic amides from simple substrates and chemical reagents.

RESULTS AND DISCUSSION

For this purpose, we wondered about the possibility of developing a selective double oxidation process of allylamines to 2,3-epoxyamides via C−H oxidation of **A** followed by epoxidation of the double bond in intermediate **B**. If both reactions could be performed in a sequential or "one-pot" fashion, then a more direct chemical method for preparing 2,3-epoxyamides (**C**) will be achieved (Scheme 2).

Scheme 2. Sequential Double Oxidation Strategy of Allylamines to 2,3-Epoxyamides



In order to prove our strategy and with the expectation to obtain optically pure epoxyamides, we chose chiral (*S*)-diallylamine **1** as model of study. Although there is a number of methods for the C−H oxidation of amines to their corresponding amides, most of them operate in the presence of transition metals and represent therefore a nonenvironmental process.[8]

Searching in the literature, mild chemical methods for allylic oxidation of olefins can be found,[9] such as the oxidation of steroid **2** to the corresponding α,β-unsaturated ketone **3** with sodium chlorite, which was reported by Salvador and

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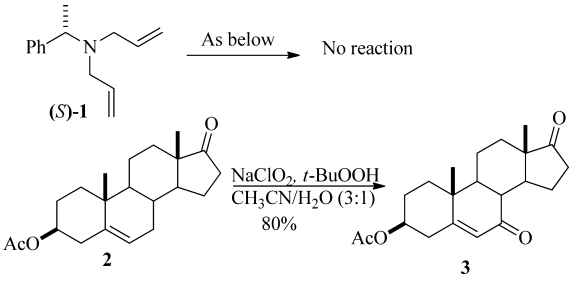
Silvestre.[9a] Unfortunately, the allylic oxidation of the model compound (*S*)-**1** did not proceed under these reaction conditions (Scheme 3).

Scheme 3. Allylic Oxidation with $NaClO_2$ (2 → 3) Tested for Chiral Diallylamine (*S*)-1

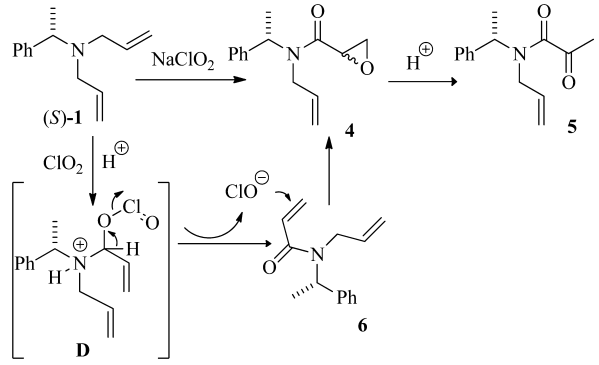


Having in mind that the use of $NaClO_2$ as oxidizing agent is a good choice (especially for being an environmentally friendly reagent), we explored variation in the reaction conditions. It is well-known that the effectiveness of sodium chlorite as oxidative agent in the transformation of aldehydes to carboxylic acids is improved in slightly acidic solutions (pH within 3−6).[10,11] Therefore, monosodium phosphate, hydrochloric acid, or acetic acid were employed, in the presence or absence of a chlorine scavenger agent such as 2-methyl-2-butene.[10] Further details for the condition reactions are listed in Table 1.

As expected, screening investigation showed that allylamine (*S*)-**1** underwent allylic oxidation under acidic conditions (compounds **4**−**6**, see all the entries in Table 1). Furthermore, an unexpected and gratifying result was observed: the epoxidation step proceeded in a tandem fashion to give epoxyamide (*S*/*R*)-**4** (see Table 1, entries 1−6). 2,3-Epoxyamide (*S*,*R*/*S*)-**4** (as an inseparable mixture of diastereoisomers) and ketoamide (*S*)-**5** were obtained in almost equimolar amounts (Table 1, entries 1−6). The formation of ketoamide (*S*)-**5** can be explained by the well-known isomerization process of epoxides to keto or aldehyde compounds under acidic conditions.[12]

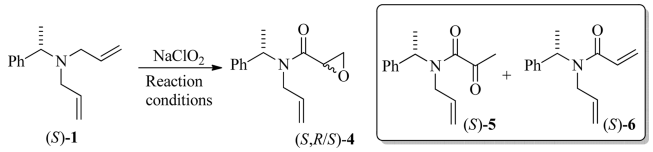
The fact that epoxyamide **4** is not formed when stronger acids are used proves this assumption to be correct (Table 1, entries 7−10). Another interesting result is that only one allyl group was oxidized, which suggests that the allylamines and not the allylamides undergo C−H oxidation with $NaClO_2$ in acidic media. To prove this, the allylamide (*S*)-**6** was treated under the same conditions as amine (*S*)-**1**, and there was no evidence for the formation of an oxidation product within 20 h; the starting material remained unchanged. Further, the lack of reactivity of amide (*S*)-**6** offers insights in the reaction course. Apparently, the amine functionality is needed for the C−H oxidation, and the epoxidation of the deactivated double bond does not proceed with $NaClO_2$. A rational reaction course might be as follows: first, C−H oxidation of the allylamine (*S*)-**1** by sodium chlorite to the unsaturated allylamide (*S*)-**6**, via the formation of intermediate **D**, which might be initiated by ClO_2 radical;[9a,13] second, epoxidation of the deactivated double bond of (*S*)-**6** by hypochlorite ion, which is formed in situ by the reduction of sodium chlorite,[14] to give 2,3-epoxyamide (*S*/*R*)-**4**; and finally, ketoamide (*S*)-**5** formed through acid-catalyzed isomerization of epoxyamide (*S*/*R*)-**4** (Scheme 4). The conversion of **6** to **4** was corroborated using hypochlorite from Clorox.

Scheme 4. Proposed Reaction Course for the Tandem Synthesis of Epoxyamide (*S*)-4, Ketoamide (*S*)-5 and Amide (*S*)-6 from Allylamine (*S*)-1



Under this scenario, this tandem oxidation reaction does not require the use of a scavenger, because most of the hypochlorite

Table 1. Developing the Selective Oxidation of Allylamine (*S*)-1[a,b]



entry	$NaClO_2$ (equiv)	acid (equiv/mL)	solvents scavenger	temp (°C)	*t* (h)	**4** (%)	**5** (%)	**6** (%)
1	10	NaH_2PO_4	*t*-BuOH/H_2O/THF (7:3:3) 2-methyl-2-butene (100 equiv)	20	12	42	40	5
2	21	NaH_2PO_4	*t*-BuOH/H_2O/THF (7:3:3) 2-methyl-2-butene (100 equiv)	21	21	38	39	traces
3	10	NaH_2PO_4	*t*-BuOH/H_2O/THF (7:3:3) 2-methyl-2-butene (100 equiv)	0	12	42	38	7
4[c]	5	NaH_2PO_4	*t*-BuOH/H_2O/THF (7:3:3) 2-methyl-2-butene (100 equiv)	20	12	10	12	
5[c]	5	NaH_2PO_4	*t*-BuOH/H_2O/THF (7:3:3) none	0	29	29	29	
6	10	NaH_2PO_4	*t*-BuOH/H_2O/THF (7:3:3) none	20	5	30	28	traces
7	10	HC1 IN (0.6)	*t*-BuOH/THF (7:3) 2-methyl-2-butene (100 equiv)	20	1		34	8
8	10	HC1 IN (0.3)	*t*-BuOH/THF (7:3) none	0	1		40	9
9	40	CH_3COOH (0.6)	*t*-BuOH/THF (7:3) none	0	1		40	8
10	10	CH_3COOH (0.3)	*t*-BuOH/THF (7:3) none	0	3		45	8

[a]Substrate concentration was 0.1 M in each case. [b]Yields after purification by column chromatography. [c]Approximately 50% of the starting material remained unchanged.

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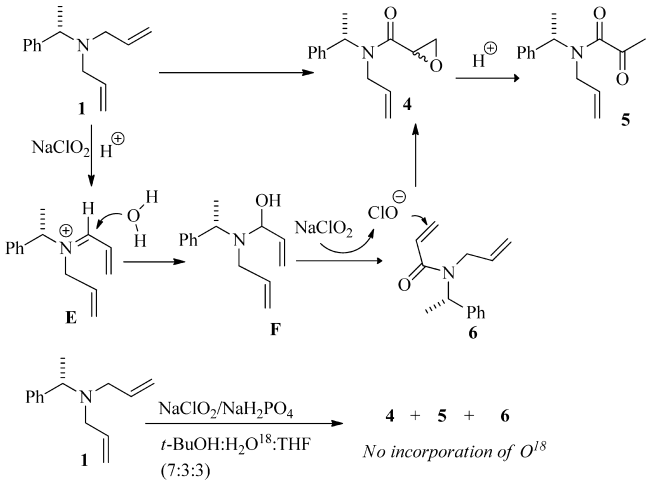
formed, which is normally considered an unwanted byproduct in other oxidation reactions,[10,11] is consumed during the epoxidation reaction.[15] Therefore, in this case the hypochlorite represents a key side-product for the success of the reaction. Furthermore, an alternative mechanistic course for the reaction might involve the iminium intermediate **E**, as in the case for α-oxidations of amines with transition metals,[16] then nucleophilic attack by water would provide carbinolamine **F**, which undergoes oxidation to amide **6**, followed by the above-described oxidation of double bond with hypochlorite to give epoxyamide **4** (Scheme 5). This alternative proposal forced us

Scheme 5. Alternative Proposed Reaction Course and ^{18}O-Labeling Experiment



to carry out a ^{18}O-labeling experiment using ^{18}O-enriched water (98% purity) in order to examine whether the amide oxygen atom is provided from water[16a,b] or if $NaClO_2$ is the source of all oxygen atoms. The mass spectra of compounds **4**–**6** evidenced that no incorporation of ^{18}O occurred in any of the products **4**–**6**, revealing thus that the mechanistic pathway given in Scheme 4 is more likely.

In order to extend the scope of this new reaction, we prepared a series of allylamines [(*S*)-**7**–(*S*)-**11**)]. Diallylic amine (*S*)-**7**, which is structurally related to amine (*S*)-**1**, was prepared to confirm that the oxidation occurs selectively only on one of the allyl groups. Additionally, a series of allylpiperidines (*S*)-**8**–(*S*)-**11** was designed, not only for examining the stability of the N-heterocyclic ring and the compatibility of common functional groups under this oxidizing condition reactions, but also for preparing advanced chiral intermediaries that can eventually be utilized for the synthesis of alkaloids (Scheme 6).

Chiral diallylamine (*S*)-**7** was prepared from amine (*S*)-**12** in the presence of 3,3-dimethylallyl bromide and Na_2CO_3 in dry acetonitrile at room temperature. Under the same reaction conditions, but using 2-(2-bromoethyl)-1,3-dioxolane instead 3,3-dimethylallyl bromide, the piperidine precursor (*S*)-**13** was also obtained in good yield. Treatment of (*S*)-**13** with aqueous HCl (5 N) gave aldehyde (*S*)-**11** in quantitative yield via hydrolysis followed by intramolecular aldol closure. Allylpiperidine (*S*)-**8** bearing a free hydroxyl group was prepared by treating (*S*)-**11** with $NaBH_4$ in ethanol. Allylpiperidines bearing a OTBS group (*S*)-**9** and a highly electron-donating aryl group (*S*)-**10** were obtained using TBSCl/imidazole and sesamol under Mitsunobu conditions,[17] respectively (Scheme 6).

Happily, we found that all the allylamines (*S*)-**7**–(*S*)-**11** were converted exclusively into their corresponding 2,3-epoxyamides [(*S*,*R*/*S*)-**12**, (*S*)-**13a** and (*S*)-**13b**, (*S*)-**14a** and (*S*)-**14b**, (*S*)-**15a** and (*S*)-**15b**, (*S*)-**16a** and (*S*)-**16b**, (*S*)-**17a** and (*S*)-**17b**] in modest to high yields (Table 2, entries 1–10), even when reducing the quantity of $NaClO_2$ from 10 to 8 equiv and in the absence of 2-methyl-2-butene. Despite the fact that diallylamine (*S*)-**7** gave a modest yield of epoxyamide (*S*,*R*/*S*)-**12** (as an inseparable mixture of diastereoisomer), again only one allyl group was oxidized (Table 2, entry 1), even in the absence of a scavenger (Table 2, entry 2).

Interestingly, allylpiperidine (*S*)-**8**, which contains a free hydroxyl group that could be oxidized, afforded 2,3-epoxyamides (*S*)-**13a** and (*S*)-**13b** in high yield with a ratio of 38:62, respectively (Table 2, entries 3 and 4). A similar result was observed for allylpiperidine (*S*)-**9**, which gave the cyclic

Scheme 6. Preparation of Diallylamine (*S*)-7 and Allylpiperidines (*S*)-8–(*S*)-11

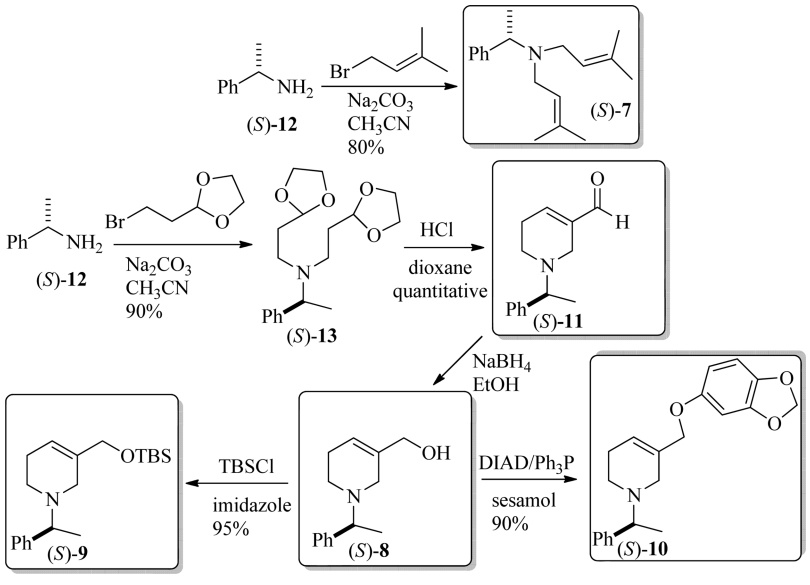


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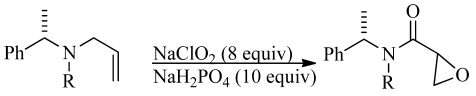
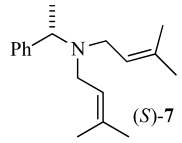
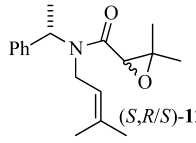
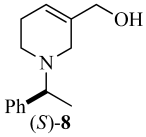
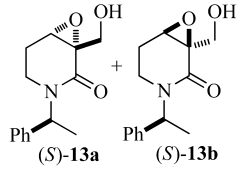
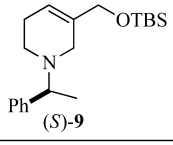
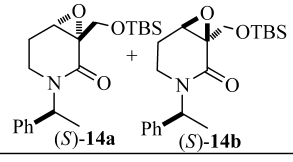
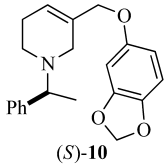
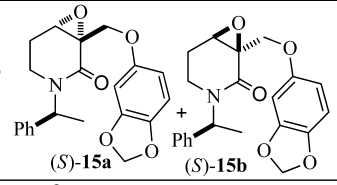
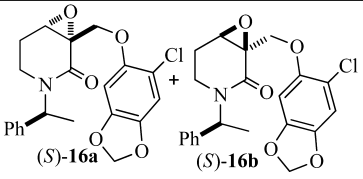
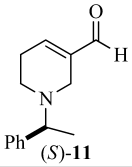
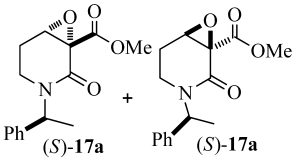
Table 2. Developing the First Direct Synthesis of 2,3-Epoxyamides[a,b]



Entry		Reaction conditions	Epoxiamide	Yield (Ratio)
1	 (*S*)-**7**	*t*-BuOH:H_2O:THF (7:3:3) 2-methyl-2-butene (100 equiv) 0 °C, 12 h	 (*S*,*R*/*S*)-**12**	54% (50:50)[c]
2	**7**	same as entry 1 but without scavenger	**12**	51% (50:50)[c]
3	 (*S*)-**8**	*t*-BuOH:H_2O:THF (7:3:3) 2-methyl-2-butene (100 equiv) 0 °C, 10 h	 (*S*)-**13a** + (*S*)-**13b**	80% (**13a**:**13b** = 38:60)
4	(*S*)-**8**	same as entry 3 but without scavenger	(*S*)-**13a** + (*S*)-**13b**	78% (**13a**:**13b** = 38:62)
5	 (*S*)-**9**	*t*-BuOH:H_2O:THF (7:3:1) 2-methyl-2-butene (100 equiv) 0 °C, 10 h	 (*S*)-**14a** (*S*)-**14b**	83% (**14a**:**14b** = 40:60)
6	(*S*)-**9**	same as entry 5 but without scavenger	(*S*)-**14a** + (*S*)-**14b**	79% (**14a**:**14b** = 40:60)
7	 (*S*)-**10**	*t*-BuOH:H_2O:THF (7:3:3) 2-methyl-2-butene (100 equiv) 0 °C, 16 h	 (*S*)-**15a** (*S*)-**15b**	84% (**15a**:**15b** = 40:60)
8	(*S*)-**10**	same as entry 7 but without scavenger 1.5 h	 (*S*)-**16a** (*S*)-**16b**	62% (**16a**:**16b** = 40:60)
9	 (*S*)-**11**	*t*-BuOH:H_2O:THF (7:3:3) 2-methyl-2-butene (100 equiv) 0 °C, 12 h then, TMS-CHN_2	 (*S*)-**17a** (*S*)-**17a**	60% (**17a**:**17b** = 40:60)
10	(*S*)-**11**	same as entry 9 but without scavenger	(*S*)-**17a** + (*S*)-**17b**	55% (**13a**:**13b** = 40:60)

[a]Substrate concentration was 0.1 M in each case. [b]Yields after purification by column chromatography. [c]As an inseparable mixture of diastereoisomers.

2,3-epoxyamides (*S*)-**14a** and (*S*)-**14b** in 83% yield and 40:60 ratio, respectively (Table 2, entries 5 and 6). Interestingly, but not surprisingly, 2,3-epoxyamides (*S*)-**15a** and (*S*)-**15b** were obtained in high yield when a scavenger was used (Table 2, entry 7); however, in its absence, chlorination on the sesamol moiety was observed (epoxyamides (*S*)-**16a** and (*S*)-**16b**; Table 2, entry 8). Allylpiperidine (*S*)-**11** was the most challenging case for this new tandem oxidation reaction because it was quite expectable that the aldehyde group might inhibit the tandem oxidation under this reaction condition because of oxidation to the corresponding carboxylic acid.[10,11] However, not only was the 2,3-epoxyamide moiety formed successfully, but also the aldehyde group was oxidized to the carboxylic acid group, which was isolated in form of the corresponding ester by adding TMS-CHN_2 (Table 2, entries 9 and 10). It is important to note that, with exception of the epoxyamides (*S*,*R*/*S*)-**4** and (*S*,*R*/*S*)-**12**, all of the epoxyamides [(*S*)-**13a** and (*S*)-**13b**, (*S*)-**14a** and (*S*)-**14b**, (*S*)-**15a** and (*S*)-**15b**, (*S*)-**16a** and (*S*)-**16b**,

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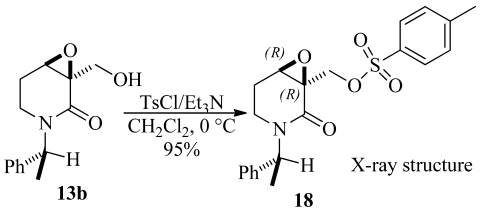
(*S*)-**17a** and (*S*)-**17b**] were separated by column chromatography.

In order to determine the absolute configuration of the two chiral centers formed for the epoxyamides, X-ray crystallographic study was performed for representative epoxyamide. To this end, epoxyamide (*S*)-**13b** was converted to its tosylate derivative (1′*S*,3*R*,4*R*)-**18**, which provided single crystals suitable for X-ray diffraction analysis (Scheme 7).[18]

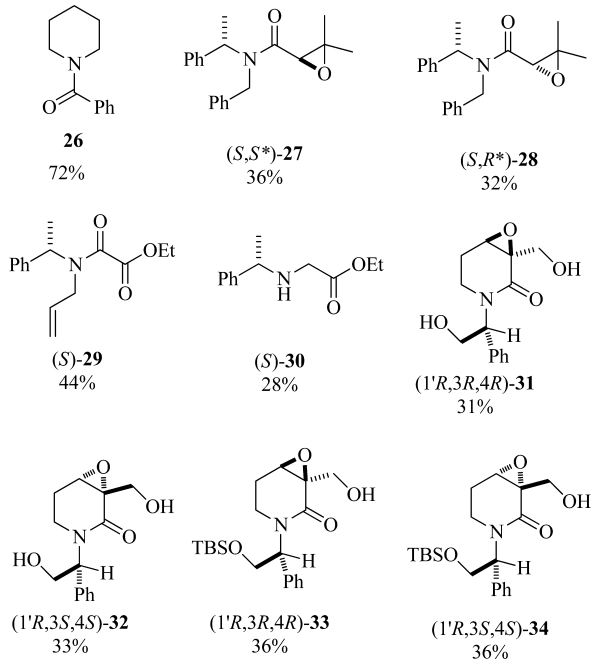
Scheme 7. Derivatization of Epoxyamide (*S*)-13b to (1′*S*,3*R*,4*R*)-18 for X-ray Crystallographic Diffraction Analysis[18]



In order to extend even more the scope of this unprecedented reaction, we considered it necessary to examine different functional groups looking for diversity, stereoselectivity, and mechanistic insights. To this end, tertiary amines (**19**−**23**) were prepared according to Scheme 8 (which is similar to Scheme 6). Piperidine benzylated **19** was selected to test benzylic C−H oxidation; allylbenzylamine (*S*)-**20** was prepared to examine the reactivity of both groups, allyl versus benzyl; similarly, with the allylamine (*S*)-**21** we wish to compare the reactivity between C−H acidic protons and allylic C−H hydrogen atoms. Finally, chiral piperidines (*R*)-**22** and (*R*)-**23** derived from (*R*)-2-phenylglycinol **24** were prepared to increase the stereoselectivity in the epoxidation step.

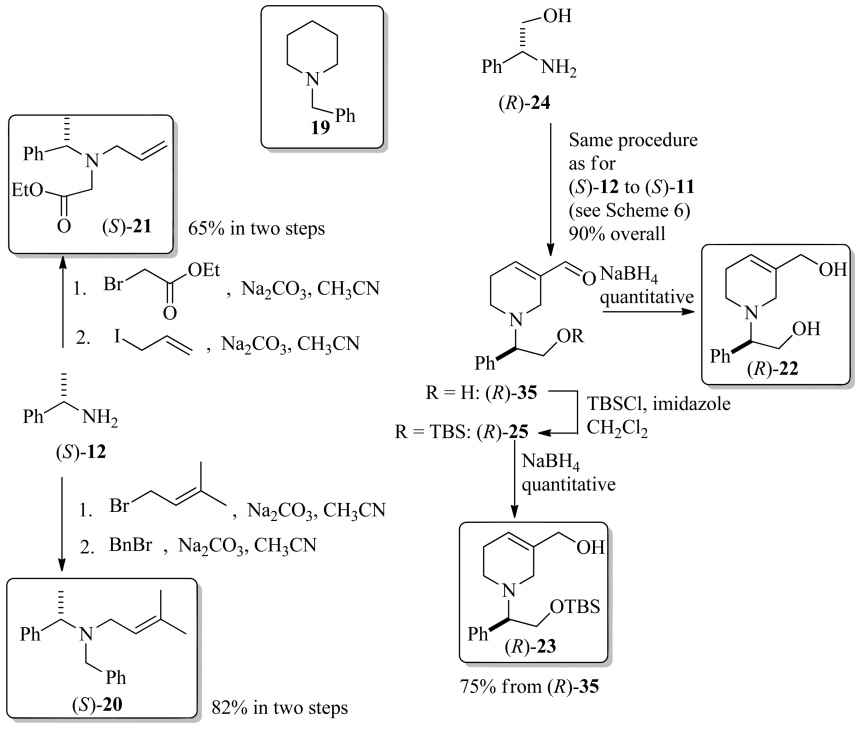
Treatment of piperidine **19** under reaction conditions shown in Table 2 (either in presence or absence of a scavenger) afforded amide **26**[19] in good yield, indicating that the benzyl group acts similar to the allyl group; however, when allylbenzylamine (*S*)-**20** was submitted to the same reaction conditions, epoxyamides (*S*,*S**)-**27** and (*S*,*R**)-**28** were obtained in modest yield (Chart 1). This establishes that allylic

Chart 1. Further Oxidation Products[a]



[a]Yields after purification by column chromatography *Absolute stereochemistry was not determined.

Scheme 8. Preparation of Tertiary Amines 19, (*S*)-21, (*S*)-22, (*R*)-22 and (*R*)-23



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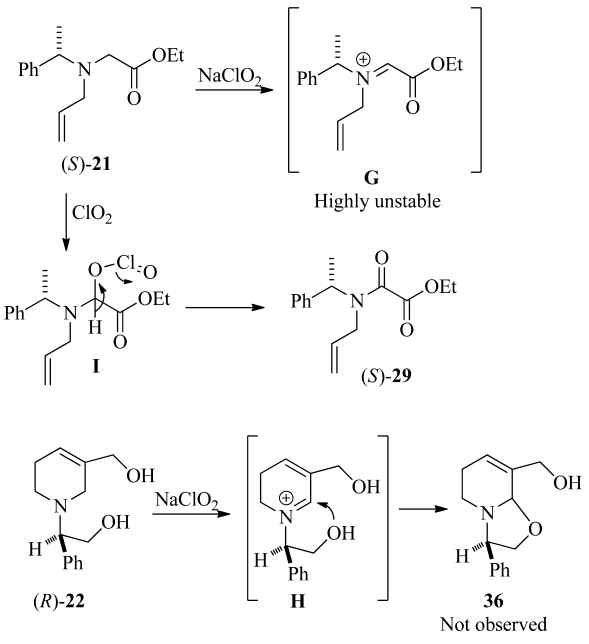
C−H bond is more reactive than benzylic C−H bond. On the other hand, amino ester (*S*)-**21** did not afford the expected epoxyamide (not shown), but an amide ester (*S*)-**29** was obtained in moderated yield, and deallylated product (*S*)-**30** as byproduct.[20] Therefore, it can be established that sodium chlorite selectively oxidizes C−H bond in the following order: $RNCH_2CO_2R$ > $RNCH_2C{=}CHR$ > $RNCH_2Ph$.

Piperidines derived from (*R*)-2-phenylglycinol, (*R*)-**22** and (*R*)-**23**, which were designed to improve the stereoselectivity for the epoxidation step, did not provide the expected results; actually, this chiral auxiliary resulted to be less effective than the (*S*)-(−)-α-methylbenzylamine (*S*)-**12**. In this case, the diastereomer ratio of epoxyamides (1′*R*,3*R*,4*R*)-**31**/(1′*R*,3*S*,4*S*)-**32** and (1′*R*,3*R*,4*R*)-**33**/(1′*R*,3*S*,4*S*)-**34** is 50:50 (Chart 1); however, each one of the epoxyamides could be separated by column chromatography. Although there are examples of asymmetric epoxidation of unsaturated amides with good enantiomeric excess,[21] the use of both chiral auxiliary (*S*)-**12** and (*R*)-**24** allows the easy separation of each of the epoxyamides (piperidine derivatives) by column chromatography and therefore enables the preparation of epoxyamides in enantiomerically pure form.

It is noteworthy to mention that C−H oxidation of compound (*S*)-**21** to amide ester (*S*)-**29** excludes the formation of iminium intermediate **G** (which is similar to intermediate **E** shown in Scheme 5), because of instability caused by the electron-withdrawing substituent (carbonyl group). Additionally, the oxidation of piperidine (*R*)-**22** would afford bicyclic compound **36** by nucleophilic addition of free hydroxyl group to iminium intermediate **H**; however, after detailed NMR analysis and exhaustive purification process, this putative compound (**35**) was not observed (Scheme 9).

Therefore, the mechanistic course for (*S*)-**21** to amide ester (*S*)-**29** occurs via the formation of intermediate **I**, which is similar to intermediate **D** shown in Scheme 4.

Scheme 9. Experimental Evidence against the Formation of an Iminium Intermediate



CONCLUSIONS

In summary, we have developed a direct protocol for the synthesis of 2,3-epoxyamides (glycidic amides) from tertiary allylamines under mild, nonexpensive, and environmentally friendly conditions. Further accounts describing the epoxidation step in a stereoselective fashion, mechanistic studies for the C−H oxidation step, and applications of this tandem oxidation in total synthesis of biologically important alkaloids will be reported in due course.

EXPERIMENTAL SECTION

General Information. All reagents purchased commercially were used without purification. The solvents were used as technical grade and freshly distilled prior use unless otherwise noted. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz spectrometers, respectively. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and are reported in ppm relative to tetramethylsilane (TMS). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), and integration. Data for ^{13}C NMR are reported in terms of chemical shift. Optical rotations, $[\alpha]_D$ values, are reported in 10^{-1} dg cm^2 g^{-1}; concentration (*c*) is in g/100 mL.

Procedure for *N*-Alkylation of (*S*)-(−)-α-Methylbenzylamine and (*R*)-2-Phenylglycinol. To a stirred suspension of Na_2CO_3 (3.14 g, 29.7 mmol) in 40 mL of CH_3CN at room temperature was added (*S*)-(−)-α-methylbenzylamine (1.5 g, 12.3 mmol); the reaction mixture was stirred for 15 min before the corresponding alkyl halide (29.7 mmol) dissolved in 5 mL of acetonitrile was added. The reaction mixture was stirred at room temperature until the starting materials were completely consumed. Then, the mixture was filtered off, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel to give the corresponding product.

(*S*)-*N*-Allyl-*N*-(1-phenylethyl)prop-2-en-1-amine-1.[22] Obtained 2.2 g (90%) as a yellow pale oil: $[\alpha]_D^{20}$ = −43.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (d, *J* = 6.8 Hz, 3H), 3.02 (dd, *J* = 14.4, 6.4 Hz, 2H), 3.14 (dd, *J* = 14.4, 6.4 Hz, 2H), 3.89 (q, *J* = 6.8, 1H), 5.13 (m, 4H); 5.84 (ddt, *J* = 17.2, 10.4, 6.4 Hz, 2H), 7.20 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.0, 52.5, 58.2, 116.8, 126.6, 127.6, 128.0, 136.5, 143.9.

(*S*)-3-Methyl-*N*-(3-methylbut-2-enyl)-*N*-(1-phenylethyl)but-2-en-1-amine-7. Obtained 2.5 g (80%) as a yellow pale oil: $[\alpha]_D^{20}$ = −50.16 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (d, *J* = 6.8 Hz, 3H), 1.56 (s, 6H), 1.70 (s, 6H), 2.96 (dd, *J* = 14.4, 6.8 Hz, 2H), 3.09 (dd, *J* = 14.4, 6.8 Hz, 2H), 3.87 (q, *J* = 6.8 Hz, 1H), 5.26 (t, *J* = 6.8 Hz, 2H), 7.20 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3, 17.9, 25.9, 47.1, 58.5, 122.41, 122.5, 126.4, 127.7, 127.9, 133.7, 144.5; HRMS-FAB (*m*/*z*) [M + H]$^+$ 258.2245 (calcd. 258.2222 for $C_{18}H_{28}N$).

(*S*)-*N*-Benzyl-3-methyl-*N*-(1-phenylethyl)but-2-en-1-amine-20. Obtained 1.85 g (82%) as a colorless oil: $[\alpha]_D^{20}$ = −49.23 (*c* = 1.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (d, *J* = 6.8 Hz, 3H), 1.52 (s, 3H), 1.69 (s, 3H), 2.90 (dd, *J* = 14.4, 6.4 Hz, 1H), 3.12 (dd, *J* = 14.4, 6.8 Hz, 1H), 3.46 (d, *J* = 14.0 Hz, 1H), 3.55 (d, *J* = 14.0 Hz, 1H), 3.93 (q, *J* = 6.8 Hz, 1H), 5.28 (m, 1H), 7.30 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 18.0, 25.9, 46.9, 53.7, 57.5, 122.4, 126.4, 126.5, 127.8, 127.9, 128.0, 128.5, 134.1, 140.9, 144.1; HRMS-FAB *m*/*z* [M + H]$^+$ 280.2073 (calcd. 280.2065 for $C_{20}H_{26}N$).

(*S*)-Ethyl 2-(Allyl(1-phenylethyl)amino)ethanoate-21. Obtained 1.31 g (65%) as a colorless oil: $[\alpha]_D^{20}$ = −115.22, (*c* = 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.2 Hz, 3H), 1.36 (d, *J* = 6.8 Hz, 3H), 3.22 (d, *J* = 6.8 Hz, 2H), 3.28 (d, *J* = 17.2 Hz, 1H), 3.44 (d, *J* = 17.2 Hz, 1H), 4.06 (q, *J* = 6.8 Hz, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 5.15 (m, 2H), 5.82 (ddt, *J* = 17.2 10.4, 6.4 Hz, 1H), 7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 19.4, 50.9, 54.2, 60.1, 117.4, 126.9, 127.5, 128.2, 136.1, 144.3, 172.1; HRMS-FAB *m*/*z* [M + H]$^+$ 248.1659 (calcd. 248.1651 for $C_{15}H_{22}NO_2$).

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(*S*)-*N*,*N*-Bis(2-(1,3-dioxolan-2-yl)ethyl)-1-phenylethanamine-13. To a stirred suspension of K_2CO_3 (8.55 g, 61.9 mmol) in 20 mL of CH_3CN at room temperature were added (*S*)-(−)-α-methylbenzylamine (3.0 g, 24.8 mmol) and 2-(2-bromoethyl)-[1.3]dioxolane (11.2 g, 61.9 mmol). The resulting mixture was refluxed for 12 h, and then the reaction mixture was cooled to room temperature. The solids were filtered off, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (SiO_2, hexanes/EtOAc, 4:1) yielding 7.14 g (90%) of **13** as a colorless oil: $[\alpha]_D^{20}$ = 3.86 (*c* = 1.53, CH_3Cl); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (d, *J* = 6.8, 3H), 1. 78 (td, *J* = 7.6, 4.8 Hz, 4H), 2.52 (m, 2H), 2.64 (m, 2H), 3.78 (m, 4H), 3.82 (q, *J* = 7.2 Hz, 1H), 3.90 (m, 4H), 4.82 (t, *J* = 5.2 Hz, 2H), 7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.6, 32.1, 45.0, 59.1, 64.5, 64.6, 103.3, 126.4, 127.5, 127.8, 143.9; HRMS-FAB (*m*/*z*) [M + H]$^+$ 322.2006 (calcd. 322.2018 for $C_{18}H_{28}NO_4$).

(*R*)-2-(Bis(2-(1,3-dioxolan-2-yl)ethyl)amino)-2-phenylethanol. Obtained 6.6 g (90%) as a colorless oil: $[\alpha]_D^{20}$ = −37.7 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.81 (m, 2H), 1.92 (m, 2H), 2.36 (m, 2H), 2.83 (dt, *J* = 13.2, 7.6 Hz, 2H), 3.60 (dd, *J* = 10.4, 4.4 Hz, 1H), 3.92 (m, 11H), 4.93 (t, *J* = 4.8 Hz, 2H), 7.26 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.1, 44.6, 60.8, 64.7, 64.8, 64.9, 103.4, 127.6, 128.2, 128.8, 136.2; HRMS-FAB *m*/*z* [M + H]$^+$ 338.1970 (calcd. 338.1967 for $C_{18}H_{28}NO_5$).

(*S*)-1-(1-Phenylethyl)-1,2,5,6-tetrahydropyridine-3-carbaldehyde-11. To a flask containing a solution of **13** (1.0 g, 3.31 mmol) in 1,4-dioxane (1.0 mL) was added 1 mL of HCl (5 M solution in water) at room temperature. The resulting mixture was stirred under reflux until the total consumption of starting materials. The reaction was quenched with the addition of NaOH until reaching a pH = 8. The biphasic mixture was extracted with EtOAc (3 × 15 mL) and dried with Na_2SO_4. The solvent was evaporated under reduced pressure. The desired product was obtained in quantitative yield as brown oil: $[\alpha]_D^{20}$ = 30.13 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (d, *J* = 6.8 Hz, 3H), 2.40 (m, 3H), 2.66 (m, 1H), 3.05 (d, *J* = 16.0 Hz, 1H), 3.46 (d, 16.0 Hz, 1H), 3.57 (q, *J* = 6.8 Hz, 1H), 6.84 (s, 1H), 7.3 (m, 5H), 9.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 27.6, 46.5, 46.6, 64.4, 127.1, 127.5, 128.3, 140.3, 143.0, 148.9, 192.5; HRMS-EI (*m*/*z*) 215.1297 (calcd. 215.1310 for $C_{14}H_{17}NO$).

(*R*)-1-(2-Hydroxy-1-phenylethyl)-1,2,5,6-tetrahydropyridine-3-carbaldehyde-35. Obtained in quantitative yield as an orange oil: $[\alpha]_D^{20}$ = −17.7 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (m, 1H), 2.48 (m, 2H), 2.82 (dt, *J* = 10.4, 4.8 Hz, 1H), 2.92 (br, 1H), 3.24 (m, 2H) 3.73 (dd, *J* = 10.4, 5.2 Hz, 1H), 3.81 (dd, *J* = 10.4, 5.2 Hz, 1H), 4.06 (t, *J* = 9.2 Hz 1H), 6.81 (s, 1H), 7.3 (m, 5H), 9.38 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5, 45.4, 60.6, 69.6, 128.0, 128.3, 128.8, 135.3, 140.1, 148.3, 192.1; HRMS-FAB (*m*/*z*) [M + H]$^+$ 232.1318 (calcd. 232.1338 for $C_{14}H_{18}NO_2$).

(*S*)-(1-(1-Phenylethyl)-1,2,5,6-tetrahydropyridin-3-yl)-methanol-8. To a solution of **11** (1.0 g, 4.64 mmol) in 25 mL of MeOH at 0 °C was added dropwise a solution of $NaBH_4$ (0.263 g, 6.95 mmol) in MeOH (5 mL). The reaction mixture was stirred for 30 min at room temperature before 15 mL of water was added. The biphasic mixture was evaporated under reduced pressure, and then the aqueous mixture was extracted with EtOAc (3 × 15 mL). The organic phase was dried over Na_2SO_4, and the solvent was evaporated under reduced pressure to give quantitatively **8** as pale yellow oil: $[\alpha]_D^{20}$ = 7.39 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (d, *J* = 6.8 Hz, 3H), 2.12 (m, 2H), 2.34 (ddd, *J* = 11.2, 7.6, 5.2 Hz, 1H), 2.60 (dt, *J* = 11.2, 5.2 Hz, 1H), 2.89 (d, *J* = 16 Hz, 1H), 3.21 (d, *J* = 16 Hz, 1H), 3.49 (q, *J* = 6.8 Hz, 1H), 3.96 (s, 2H), 5.71 (m, 1H), 7.3 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 25.7, 47.2, 50.5, 64.4, 65.09, 120.9, 126.9, 127.6, 128.1, 136.5, 143.0; HRMS-FAB (*m*/*z*) [M + H]$^+$ 218.1541 (calcd. 218.1545 for $C_{14}H_{20}NO$).

(*R*)-2-(3-(Hydroxymethyl)-5,6-dihydropyridin-1(2*H*)-yl)-2-phenylethanol-22. Obtained 0.620 g (90%) as a yellow oil: $[\alpha]_D^{20}$ = −8.97 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (m, 2H), 2.31 (dt, *J* = 11.2, 5.6 Hz, 1H), 2.74 (dt, *J* = 11.2, 5.6 Hz, 1H), 2.92 (br, 2H), 3.06 (m, 2H), 3.74 (m, 2H), 3.96 (s, 2H), 4.04 (m, 1H), 5.67 (s, 1H), 7.3 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 45.9, 49.3, 60.9, 65.2, 69.8, 121.3, 127.9, 128.2, 128.9, 135.9, 136.4; HRMS-FAB *m*/*z* [M + H]$^+$ 234.1505 (calcd for 234.1494 for $C_{14}H_{20}NO_2$).

(*S*)-5-((*t*-Butyldimethylsilyloxy)methyl)-1-(1-phenylethyl)-1,2,3,6-tetrahydropyridine-9. To a flask containing a solution of **8** (0.660 g, 3.04 mmol) and imidazole (0.414 g, 6.08 mmol) in 20 mL of CH_2Cl_2 at 0 °C was added dropwise *t*-Bu$(CH_3)_2$SiCl (0.686 g, 4.54 mmol) dissolved in 4 mL of CH_2Cl_2. The reaction was stirred for 1.5 h, and then water (4 mL) was added. The phases were separated, and the aqueous phase was extracted with EtOAc (2 × 15 mL). The combined organic phases were dried over Na_2SO_4, and the solvent was removed under reduced pressure. Flash chromatography on silica gel gave 0.96 g (95%) of desired product **9** as a yellow oil: $[\alpha]_D^{20}$ = −0.83 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.90 (s, 9H), 1.43 (d, *J* = 6.8 Hz, 3H), 2.12 (m, 2H), 2.40 (ddd, *J* = 12.8, 7.6, 5.2 Hz, 1H), 2.58 (dt, *J* = 10.8, 5.2 Hz, 1H), 2.85 (d, *J* = 16.0 Hz, 1H), 3.10 (d, *J* = 16.0 Hz, 1H), 3.45 (q, *J* = 6.8 Hz, 1H), 4.03 (apparent s, 2H), 5.70 (apparent s, 1H) 7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.4, 18.3, 20.2, 25.8, 25.8, 47.4, 50.7, 64.8, 65.6, 119.8, 126.8, 127.5, 128.1, 136.1, 144.1; HRMS-FAB (*m*/*z*) [M + H]$^+$ 332.2431 (calcd 332.2410 for $C_{20}H_{34}NOSi$).

(*R*)-(1-(2-(*t*-Butyldimethylsilyloxy)-1-phenylethyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol-23. To a flask containing a solution of **25** (0.685 g, 2.96 mmol) and imidazole (0.403 g, 5.92 mmol) in 20 mL of CH_2Cl_2 at 0 °C was added dropwise *t*-Bu$(CH_3)_2$SiCl (0.892 g, 2.27 mmol) dissolved in 5 mL of CH_2Cl_2. The reaction was stirred for 2.0 h, and then water (5 mL) was added. The phases were separated, and the aqueous phase was extracted with EtOAc (2 × 10 mL) and dried over Na_2SO_4, and the solvent was removed under reduced pressure at 0 °C. The residue was dissolved in MeOH (20 mL) and a solution of $NaBH_4$ (0.168 g, 4.44 mmol) in MeOH (5 mL) was added dropwise. After it was stirred at room temperature for 30 min, water (15 mL) was added. The mixture was evaporated under reduced pressure, and then the aqueous mixture was extracted with EtOAc (3 × 15 mL). The organic layer was dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. Flash chromatography on silica gel gave the desired product **23** as yellow oil (0.770 g, 75% yield): $[\alpha]_D^{20}$ = 5.05 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.09 (s, 3H), −0.04 (s, 3H), 0.82 (s, 9H), 2.12 (m, 2H), 2.50 (ddd, *J* = 11.4, 7.2, 4.8 Hz, 1H), 2.66 (dt, *J* = 10.8, 5.2 Hz, 1H), 3.02 (d, *J* = 16.0 Hz, 1H), 3.27 (d, *J* = 16.0 Hz, 1H), 3.49 (t, *J* = 5.6 Hz, 1H), 3.87 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.96 (s, 2H), 4.11 (dd, *J* = 10.4, 6.0 Hz, 1H), 5.70 (s, 1H) 7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ - 5.6, −5.6, 18.1, 25.67 48.0, 51.6, 65.4, 65.7, 71.8, 121.2, 127.1, 128.0, 128.6, 136.6, 140.4; HRMS-FAB *m*/*z* [M + H]$^+$ 348.2359 (calcd. 348.2359 for $C_{20}H_{34}NO_2Si$).

(*S*)-5-((Benzo[*d*][1,3]dioxol-5-yloxy)methyl)-1-(1-phenylethyl)-1,2,3,6-tetrahydropyridine-10. To a flask containing **9** (1.26 g, 5.8 mmol), PPh_3 (3.04 g, 11.6 mmol), and sesamol (1.04 g, 7.53 mmol) in 40 mL of dry benzene at 0 °C was added dropwise DIAD (2.11 g, 10.4 mmol). The reaction mixture was allowed to stir vigorously for 3 h and then concentrated under reduced pressure. Flash chromatography on silica gel (hexanes/EtOAc 4:1) gave 1.76 g of **10** as a yellow oil (90%): $[\alpha]_D^{20}$ = 3.39, (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (d, *J* = 6.8 Hz, 3H), 2.15 (m, 2H), 2.36 (ddd, *J* = 12.0, 7.2, 5.2 Hz, 1H), 2.62 (dt, *J* = 11.2, 5.2 Hz, 1H), 2.94 (d, *J* = 15.6 Hz, 1H), 3.24 (d, *J* = 15.6 Hz, 1H), 3.48 (q, *J* = 6.8 Hz, 1H), 4.29 (s, 2H), 5.83 (s, 1H), 5.87 (s, 2H), 6.30 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.48 (d, *J* = 5.6 Hz, 1H), 6.67 (d, *J* = 8.4 Hz, 1H), 7.27 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 25.8, 46.8, 50.8, 64.5, 71.6, 98.2, 100.9, 105.7, 107.7, 124.1, 126.9, 127.5, 128.1, 132.5, 141.5, 143.7, 148.0, 154.2; HRMS-FAB (*m*/*z*) [M + H]$^+$ 338.1731 (calcd. 338.1756 for $C_{21}H_{24}NO_3$).

General Procedure for Tandem Oxidation. Allylamine (1.0 mmol) and NaH_2PO_4 (1.37 g, 10 mmol) were dissolved in 13 mL of a mixture of *t*-BuOH/THF/H_2O (7:3:3), and the reaction mixture was vigorously stirred at room temperature for 15 min. Then, the reaction mixture was cooled to 0 °C followed by addition of 2-methyl-2-butene (optional) and sequential addition of $NaClO_2$ (0.722 g, 8.0 mmol) dissolved in 1.5 mL of H_2O. The reaction mixture was stirred until the starting material was consumed (see Table 1 in manuscript for selected

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entry). The phases were separated, and the aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic phases were dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel to give the corresponding product.

(*S*)-*N*-Allyl-*N*-(1-phenylethyl)oxirane-2-carboxamide-4. Obtained 0.096 g (42%) as a colorless oil: NMR data are reported for the mixture of diastereoisomers and *E*/*Z* rotamers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51 (d, J = 7.2 Hz), 1.52 (d, J = 7.2 Hz), 1.69 (d, J = 7.2 Hz), 2.90 (m), 3.03 (m), 3.57 (m), 3.83 (m), 5.02 (m), 5.14 (m), 5.43 (q, J = 6.8 Hz), 5.67 (m), 6.00 (m), 6.06 (q, J = 7.2 Hz), 6.07 (q, J = 7.2 Hz), 7.3 (m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 45.1, 45.3, 46.5, 46.7, 47.3, 47.5, 51.7, 116.7, 116.9, 127.5, 127.6, 127.6, 128.4, 128.7, 134.0, 134.6, 134.8, 139.9, 140.0, 168.2; HRMS-FAB (m/z) [M + H]$^+$ 232.1341 (calcd. 232.1338 for $C_{14}H_{18}NO_2$).

(*S*)-*N*-Allyl-2-oxo-*N*-(1-phenylethyl)propanamide-5. Obtained 0.09 g (40%) as a colorless oil: $[\alpha]_D^{20}$ = −130.68 (c = 1.0, CH_3Cl); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58 (d, J = 6.8 Hz, 3H), 1.65 (d, 6.8 Hz, 3H), 2.35 (s, 3H), 2.39 (s, 3H), 3.52 (dd, J = 15.6, 6.4 Hz, 1H), 3.64 (dd, J = 16.8, 6.0 Hz, 1H), 3.84 (dd, J = 16.8, 6.0 Hz, 1H), 4.04 (dd, J = 15.6, 5.2 Hz, 1H), 4.95 (m, 1H), 4.99 (m, 1H), 5.05 (m, 1H), 5.07 (m, 2H), 5.54 (ddt, J = 17.2, 10.0, 6.0 Hz, 1H), 5.72 (dddd, J = 17.2, 10.4, 5.6, 5.2 Hz, 1H), 5.92 (q, J = 6.8 Hz, 1H), 7.3 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 18.2, 27.4, 27.6, 44.8, 45.6, 51.3, 55.7, 117.2, 118.0, 127.3, 127.5, 127.7, 127.9, 128.5, 128.6, 133.2, 134.8, 139.2, 139.4, 167.4, 167.5, 198.3, 198.8; HRMS-FAB (m/z) [M + H]$^+$ 232.1337 (calcd. 232.1338 for $C_{14}H_{18}NO_2$).

(*S*)-*N*-Allyl-*N*-(1-phenylethyl)prop-2-enamide-6. Obtained 0.019 g (9%) as a colorless oil: $[\alpha]_D^{20}$ = −198.12 (c = 1.0, $CHCl_3$); NMR data are reported for the mixture of *E*/*Z* rotamers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52 (d, J = 7.2 Hz), 1.64 (d, J = 6.8 Hz), 3.64 (d, J = 17.2 Hz), 3.80 (d, J = 17.2 Hz), 5.08 (m), 5.24 (m), 5.61 (m), 5.70 (m), 5.8 (m), 6.16 (q, J = 7.2 Hz), 6.5 (m), 6.64 (m), 7.3 (m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 18.7, 45.6, 45.7, 51.1, 51.2, 116.4, 116.6, 126.5, 126.6, 127.6, 127.3, 127.4, 127.4, 127.9, 128.3, 128.5, 131.0, 134.5, 134.9, 140.4, 140.5, 160.7; HRMS-FAB (m/z) [M + H]$^+$ 216.1387 (calcd. 216.1388 for $C_{14}H_{18}NO_2$).

(*S*)-3,3-Dimethyl-*N*-(3-methylbut-2-enyl)-*N*-(1-phenylethyl)-oxirane-2-carboxamide-12. Obtained 0.17 g (54%) as a pale yellow oil: NMR data is reported as a mixture of diastereoisomers and *E*/*Z* rotamers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32−1.72 (m), 3.38 (s, 1H), 3.03 (m), 3.16 (m), 3.31−3.72 (m), 3.89 (m), 4.03 (dd, J = 14.8, 6.8 Hz), 4.10 (dd, J = 14.8, 6.8 Hz), 4.84 (m), 4.96 (m), 5.50 (m), 5.16 (m), 5.28 (q, J = 7.2 Hz), 5.38 (q, J = 7.2 Hz), 6.03 (q, J = 7.2 Hz), 6.10 (q, J = 7.2 Hz), 7.29 (m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 16.5, 17.6, 17.7, 17.9, 18.6, 23.9, 24.0, 25.6, 25.9, 41.0, 41.1, 47.1, 50.8, 51.3, 54.2, 54.8, 59.6, 59.9, 60.9, 61.3, 121.2, 122.0, 122.2, 126.7, 126.8, 127.4, 127.5, 127.6, 127.8, 128.3, 128.6, 128.7, 133.6, 133.9, 140.1, 140.5, 167.3, 167.4; HRMS-FAB (m/z) [M + H]$^+$ 288.1976 (calcd. 288.1964 for $C_{18}H_{26}NO_2$).

2,3-Epoxyamide (1′*S*,3*S*,4*S*)-13a. Obtained 0.079 g (31%) as a pale yellow oil: $[\alpha]_D^{20}$ = −118.6 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (d, J = 7.2 Hz, 3H), 1.94 (m, 1H), 2.21 (apparent dq, J = 14.4, 2.8, Hz, 1H), 2.81 (dd, J = 9.6, 2.8 Hz, 2H), 3.27 (br, 1H), 3.54 (d, J = 2.8 Hz, 1H), 3.96 (s, 2H), 5.93 (q, J = 7.2 Hz, 1H), 7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 24.0, 35.9, 50.5, 56.7, 56.8, 62.2, 127.1, 127.4, 128.4, 138.9, 167.4; HRMS-FAB (m/z) [M + H]$^+$ 248.1281 (calcd. 248.1287 for $C_{14}H_{18}NO_3$).

2,3-Epoxyamide (1′*S*,3*R*,4*R*)-13b. Obtained 0.120 g (49%) as a pale yellow oil: $[\alpha]_D^{20}$= −113.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (d, J = 7.2 Hz, 3H), 1.71 (ddd, J = 14.4, 12.8, 6.0 Hz, 1H), 2.17 (d, J = 14.4 Hz, 1H), 2.76 (dd, J = 12.4, 5.6 Hz, 1H), 3.22 (td, J = 12.8, 4.4 Hz, 1H), 3.54 (d, J = 3.2 Hz, 1H), 3.99 (s, 2H), 5.99 (q, J = 7.2 Hz, 1H), 7.3 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 23.8, 34.9, 50.4, 56.6, 56.8, 62.6, 126.9, 127.5, 128.4, 139.6, 167.6; HRMS-FAB (m/z) [M + H]$^+$ 248.1295 (calcd 248.1287 for $C_{14}H_{18}NO_3$).

2,3-Epoxyamide (1′*S*,3*S*,4*S*)-14a. Obtained 0.120 g (33%) as a yellow solid: mp 73−75 °C; $[\alpha]_D^{20}$ = −91.17 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.90 (s, 9H), 1.47 (d, J = 7.2 Hz, 3H), 1.88 (m, 1H), 2.22 (apparent dq, J = 14.4, 2.8 Hz, 1H), 2.80 (m, 1H), 3.13 (m, 1H), 3.72 (d, J = 3.2 Hz, 1H), 4.20 (d, J = 12.8 Hz, 1H), 4.33 (d, J = 12.8 Hz, 1H), 5.95 (q, J = 7.2 Hz, 1H), 7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.5, 5.4, 15.4, 18.3, 23.9, 25.8, 36.0, 50.2, 54.3, 57.5, 58.6, 127.2, 127.3, 128.4, 139.4, 167.1; HRMS-FAB (m/z) [M + H]$^+$ 362.2180 (calcd. 362.2151 for $C_{20}H_{32}NO_3Si$).

2,3-Epoxyamide (1′*S*,3*R*,4*R*)-14b. Obtained 0.179 g (50%) as a yellow oil: $[\alpha]_D^{20}$ = −86.17 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 3H), 0.09 (s, 3H), 0.89 (s, 9H), 1.48 (d, J = 6.8 Hz, 3H), 1.66 (ddd, J = 14.8, 12.8, 6.0 Hz, 1H), 2.16 (d, J = 14.8 Hz, 1H), 2.72 (dd, J = 12.4, 5.6 Hz, 1H), 3.22 (td, J = 12.8, 4.4 Hz, 1H), 3.70 (d, J = 3.2 Hz, 1H), 4.19 (d, J = 12.8 Hz, 1H), 4.36 (d, J = 13.2 Hz, 1H), 5.98 (q, J = 6.8 Hz, 1H), 7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.4, −5.3, 15.5, 18.3, 23.6, 25.8, 35.0, 50.1, 54.2, 57.4, 58.6, 127.0, 127.3, 128.4, 140.1, 167.2; HRMS-FAB (m/z) [M + H]$^+$ 362.2180 (calcd. 362.2151 for $C_{20}H_{32}NO_3Si$).

2,3-Epoxyamide (1′*S*,3*S*,4*S*)-15a. Obtained 0.123 g (33.5%) as a pale yellow solid: mp 105−107 °C; $[\alpha]_D^{20}$ = −88.3 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (d, J = 7.2 Hz, 3H), 1.87 (m, 1H), 2.25 (dq, J = 14.4, 2.8 Hz, 1H), 2.83 (dd, J = 9.6, 2.8 Hz, 2H), 3.83 (d, J = 2.8 Hz, 1H), 4.41 (d, J = 12.0 Hz, 1H), 4.69 (d, J = 12.0 Hz, 1H), 5.89 (s, 2H), 5.98 (q, J = 7.2 Hz, 1H), 6.39 (dd, J = 8.4, 2.4 Hz, 1H), 6.54 (d, J = 2.4 Hz, 1H), 6.69 (d, J = 8.4 Hz, 1H), 7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 23.9, 35.9, 50.5, 55.6, 56.2, 65.2, 98.4, 101.1, 106.0, 107.8, 127.2, 127.4, 128.4, 139.1, 141.8, 148.0, 153.9, 166.2; HRMS-EI (m/z) 367.1389 (calcd. 367.1420 for $C_{21}H_{21}NO_5$).

2,3-Epoxyamide (1′*S*,3*R*,4*R*)-15b. Obtained 0.185 g (50.5%) as a pale yellow oil: $[\alpha]_D^{20}$= −85.1 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (d, J = 7.2 Hz, 3H), 1.72 (ddd, J = 14.4, 12.8, 6.0 Hz, 1H), 2.19 (d, J = 13.6 Hz, 1H), 2.76 (dd, J = 12.4 Hz, 5.6, 1H), 3.25 (td, J = 12.8, 4.4 Hz, 1H), 3.83 (d, J = 2.5 Hz, 1H), 4.44 (d, J = 12.0 Hz, 1H), 4.69 (d, J = 12.0 Hz, 1H), 5.90 (s, 2H), 6.01 (q, J = 7.2 Hz, 1H), 6.40 (dd, J = 8.4, 2.4 Hz, 1H), 6.54 (d, J = 2.4 Hz, 1H), 6.69 (d, J = 8.4 Hz, 1H), 7.3 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 23.7, 35.0, 50.5, 55.6, 56.1, 65.2, 98.4, 101.1, 106.1,107.8, 127.0, 127.5, 128.5, 139.9, 1419, 148.1, 154.0, 166.4; HRMS-EI (m/z) 367.1411 (calcd. 367.1420 for $C_{21}H_{21}NO_5$).

2,3-Epoxyamide (1′*S*,3*S*,4*S*)-16a. Obtained 0.10 g (27%) as a pale yellow oil: $[\alpha]_D^{20}$= −36.6 (c = 0.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (d, J = 7.2 Hz, 3H), 1.97 (m, 1H), 2.29 (apparent dq, J = 10.4, 3.2 Hz, 1H), 2.81 (dd, J = 10.4, 3.2 Hz, 2H), 4.01 (d, J = 2.8 Hz, 1H), 4.48 (d, J = 12.0 Hz, 1H), 4.78 (d, J = 12.0 Hz, 1H), 5.94 (s, 2H), 5.99 (q, J = 7.2 Hz, 1H), 6.71 (s, 1H), 6.81 (s, 1H), 7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 24.1, 36.0, 50.6, 55.7, 56.3, 66.6, 94.4, 98.4, 101.8, 109.8, 114.7, 127.3, 127.5, 128.6, 139.3, 142.2, 146.9, 149.2, 166.3; HRMS-FAB m/z [M + H]$^+$ 402.1117 (calcd. 402.1108 for $C_{21}H_{21}NO_5Cl$).

2,3-Epoxyamide (1′*S*,3*R*,4*R*)-16b. Obtained 0.16 g (41%) as a pale yellow oil: $[\alpha]_D^{20}$= −70.87 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (d, J = 7.2 Hz, 3H), 1.74 (ddd, J = 14.4, 12.8, 6.0 Hz, 1H), 2.20 (d, J = 14.8 Hz, 1H), 2.76 (dd, J = 12.4, 6.0 Hz, 1H), 3.25 (td, J = 12.4, 4.0 Hz, 1H), 3.99 (d, J = 2.8 Hz, 1H), 4.49 (d, J = 12.0 Hz, 1H), 4.78 (d, J = 12.0 Hz, 1H), 5.93 (s, 2H), 6.00 (q, J = 7.2 Hz, 1H), 6.71 (s, 1H), 6.80 (s, 1H), 7.31 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 20.2, 23.6, 34.9, 50.4, 55.5, 56.1, 66.3, 98.2, 101.7, 109.7, 114.5, 127.0, 127.4, 128.4, 139.8, 142.0, 146.8, 149.1, 166.3; HRMS-FAB (m/z) [M + H]$^+$ 402.1110 (calcd. 402.1108 for $C_{21}H_{21}NO_5Cl$).

2,3-Epoxyamide (1′*S*,3*S*,4*S*)-17a. Obtained 0.067 g (24%) as a pale yellow oil: $[\alpha]_D^{20}$= −113.1 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (d, J = 7.2 Hz, 3H), 2.05 (ddd J = 14.8, 12.4, 6.0 Hz, 1H), 2.27 (m, 1H), 2.76 (td, J = 12.8, 4.0 Hz, 1H), 2.88 (dd, J = 12.8, 6.0 Hz, 1H), 3.73 (d, J = 2.5 Hz, 1H), 3.88 (s, 3H), 5.99 (q, J = 7.2 Hz, 1H), 7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 23.8, 35.6, 50.7, 52.8, 56.9, 57.6, 127.2, 127.5, 128.5, 138.8, 162.9, 166.0; HRMS-FAB (m/z) [M + H]$^+$ 276.1265 (calcd. 276.1236 for $C_{15}H_{18}NO_4$).

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2,3-Epoxyamide (1′*S*,3*R*,4*R*)-17b. Obtained 0.10 g (36%) as a pale yellow solid: mp 97−100 °C; $[\alpha]_D^{20}$= −128.30 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (d, *J* = 7.2 Hz, 3H), 1.82 (ddd, *J* = 14.8, 12.4, 6.0 Hz, 1H), 2.20 (m, 1H), 2.77 (dd, *J* = 12.4, 6.0 Hz, 1H), 3.18 (td, *J* = 12.4, 4.4 Hz, 1H), 3.71 (d, *J* = 2.1 Hz, 1H), 3.89 (s, 3H), 5.98 (q, *J* = 7.2 Hz, 1H), 7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 23.6, 34.7, 50.9, 52.8, 56.9, 57.5, 127.2, 127.6, 128.5, 139.4, 163.1, 166.1. HRMS-FAB (*m*/*z*) [M + H]$^+$ 276.1211 (calcd. 276.1236 for $C_{15}H_{18}NO_4$).

2,3-Epoxyamide (1′*S*,3*R*,4*R*)-18. To a flask containing a solution of **8** (0.070 g, 0.28 mmol) and TsCl (0.064 g, 0.34 mmol) in 5 mL of CH_2Cl_2 was added NEt_3 (0.057 g, 0.568 mmol). The reaction was stirred for 3 h, and then water (2 mL) was added. The phases were separated, and the aqueous phase was extracted with EtOAc (2 × 10 mL). The combined organic phases were dried over Na_2SO_4, and the solvent was removed under reduced pressure. Flash chromatography on silica gel gave 0.107 g (95%) of the desired product **18** as a white solid: mp 133−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (d, *J* = 7.2 Hz, 3H), 1.68 (ddd, *J* = 14.4, 12.8, 6.0 Hz, 1H), 2.15 (d, *J* = 14.8 Hz, 1H), 2.45 (s, 3H), 2.72 (dd, *J* = 12.4 Hz, 5.6, 1H), 3.17 (td, *J* = 12.4, 4.4 Hz, 1H), 3.75 (d, *J* = 3.2 Hz, 1H), 4.38 (d, *J* = 12.0 Hz, 1H), 4.83(d, *J* = 12.0 Hz, 1H), 5.92 (q, *J* = 7.2 Hz, 1H), 7.30 (m, 7H), 7.82 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 15.5, 21.6, 23.5, 34.8, 50.6, 55.0, 66.2, 127.0, 127.6, 128.0, 128.5, 129.9, 132.4, 139.6, 145.0, 167.3.

(R*)-*N*-Benzyl-3,3-dimethyl-*N*-((*S*)-1-phenylethyl)oxirane-2-carboxamide-27.** Obtained 0.057 g (36%) as a white solid: mp 104−107 °C; $[\alpha]_D^{20}$ = −32.21 (*c* = 0.81, CH_2Cl_2); NMR data is reported as a mixture of *E*/*Z* rotamers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (s, 3H), 1.23 (s, 3H), 1.33 (s, 3H), 1.39 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H), 1.60 (d, *J* = 7.2 Hz, 3H), 3.21 (s, 1H), 3.56 (s, 1H), 4.00 (d, *J* = 15.2 Hz, 1H), 4.27 (d, *J* = 17.6 Hz, 1H), 4.46 (d, *J* = 17.6 Hz, 1H), 4.92 (d, *J* = 15.2 Hz, 1H), 5.47 (q, *J* = 7.2 Hz, 1H), 6.17 (q, *J* = 7.2 Hz, 1H), 7.27 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.8, 18.3, 19.1, 19.6, 23.6, 24.0, 46.2, 47.0, 52.0, 55.5, 60.5, 61.0, 61.4, 126.1, 126.8, 126.8, 127.4, 127.5, 127.6, 127.7, 128.2, 128.5, 128.5, 128.7, 128.8, 138.3, 140.3, 168.0, 168.2; HRMS-FAB *m*/*z* [M + H]$^+$ 310.1820 (calcd. 310.1807 for $C_{20}H_{24}NO_2$).

(S*)-*N*-Benzyl-3,3-dimethyl-*N*-((*S*)-1-phenylethyl)oxirane-2-carboxamide-28.** Obtained 0.051 g (32%) as a white solid: mp 131−134 °C; $[\alpha]_D^{20}$ = −115.27 (*c* = 0.5, CH_2Cl_2); NMR data is reported as a mixture of *E*/*Z* rotamers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (s, 3H), 1.24 (s, 3H), 1.33 (s, 3H), 1.39 (s, 3H), 1.46 (d, *J* = 7.2 Hz, 3H), 1.52 (d, *J* = 7.2 Hz, 3H), 3.24 (s, 1H), 3.48 (s, 1H), 4.06 (d, *J* = 15.6 Hz, 1H), 4.29 (d, *J* = 17.6 Hz, 1H), 4.43 (d, *J* = 17.6 Hz, 1H), 4.94 (d, *J* = 15.6 Hz, 1H), 5.36 (q, *J* = 7.2 Hz, 1H), 6.24 (q, *J* = 7.2 Hz, 1H), 7.23 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.7, 18.4, 19.2, 19.4, 23.7, 23.8, 46.4, 46.6, 51.6, 54.9, 59.9, 61.0, 61.3, 126.1, 126.8, 126.9, 127.4, 127.7, 127.8, 128.2, 128.5, 128.6, 128.7, 128.8, 137.7, 138.8, 140.4, 168.2; HRMS-FAB *m*/*z* [M + H]$^+$ 310.1825 (calcd. 310.1807 for $C_{20}H_{24}NO_2$).

(*S*)-Ethyl 2-(Allyl(1-phenylethyl)amino)-2-oxoacetate-29. Obtained 0.046 g (44%) as a colorless oil: $[\alpha]_D^{20}$ = −115.21 (*c* = 1.0, CH_2Cl_2); NMR data is reported as a mixture of *E*/*Z* rotamers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (t, *J* = 7.6 Hz, 3H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.57 (d, *J* = 7.2, 3H), 1.65 (d, *J* = 7.2 Hz, 3H), 3.44 (dd, *J* = 15.2, 6.4 Hz, 1H), 3.63 (dd, *J* = 16.8, 6.4 Hz, 1H), 3.79 (dd, *J* = 16.8, 5.2 Hz, 1H), 3.94 (dd, *J* = 15.6, 5.2 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 4.95 (q, *J* = 7.2 Hz, 1H), 5. 02 (m, 4H), 5.63 (m, 2H), 5.89 (q, *J* = 7.2 Hz, 1H), 7.3 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.0, 16.5, 17.8, 44.1, 46.4, 51.4, 56.4, 61.9, 62.1, 117.1, 117.6, 127.3, 127.7, 127.8, 128.1, 128.5, 128.6, 133.0, 134.5, 138.5, 139.1, 162.0, 162.3, 162.9, 163.4; HRMS-FAB *m*/*z* [M + H]$^+$ 262.1468 (calcd. 262.1443 for $C_{15}H_{20}NO_3$).

(*S*)-Ethyl 2-(1-Phenylethylamino)acetate-30. Obtained 0.033 g (28%) as a colorless oil: $[\alpha]_D^{20}$ = −68.80 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.6 Hz, 3H), 1.38 (d, *J* = 6.8 Hz, 3H), 2.01 (br, 1H), 3.22 (d, *J* = 17.6 Hz, 1H), 3.29 (d, *J* = 17.6 Hz, 1H), 3.79 (q, *J* = 6.8 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 7.3 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 24.2, 48.8, 57.7, 60.7, 126.7, 127.1, 128.5, 144.5, 172.5; HRMS-FAB *m*/*z* [M + H]$^+$ 208.1346 (calcd. 208.1338 for $C_{12}H_{18}NO_2$).

2,3-Epoxyamide (1′*R*,3*R*,4*R*)-31. Obtained 0.07 g (31%) as a white solid: mp 124−127 °C; $[\alpha]_D^{20}$ = −94.65 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.77 (ddd, *J* = 14.4, 12.8, 6.0 Hz, 1H), 2.20 (d, *J* = 14.8 Hz, 1H), 2.90 (dd, *J* = 12.4, 5.2 Hz, 1H), 3.34 (td, *J* = 12.8, 4.4 Hz, 1H), 3.59 (d, *J* = 2.8 Hz, 1H), 3.94 (d, *J* = 12.4 Hz, 1H), 4.03 (d, *J* = 12.4 Hz, 1H), 4.14 (dd, *J* = 11.6, 5.6 Hz, 1H), 5.80 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 36.4, 56.7, 56.9, 58.1, 61.1, 62.2, 127.4, 127.9, 128.7, 136.4, 168.9; HRMS-FAB *m*/*z* [M + H]$^+$ 264.1237 (calcd. 264.1236 for $C_{14}H_{18}NO_4$).

2,3-Epoxyamide (1′*R*,3*S*,4*S*)-32. Obtained 0.050 g (22%) as a yellow pale oil: $[\alpha]_D^{20}$ = −57.1 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.10 (m, 1H), 2.21 (apparent dq, *J* = 14.8, 2.8 Hz, 1H), 2.96 (m, 2H), 3.23 (br, 1H), 3.60 (d, *J* = 2.8 Hz, 1H), 3.90 (d, *J* = 12.6 Hz, 1H), 4.05 (d, *J* = 12.6 Hz, 1H), 4.15 (m, 2H), 5.74 (dd, *J* = 8.8, 4.8 Hz, 1H), 7.33 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.9, 37.9, 57.1, 57.3, 58.7, 61.2, 62.6, 127.7, 128.1, 128.8, 135.8, 169.4; HRMS-FAB *m*/*z* [M + H]$^+$ 264.1233 (calcd. 264.1236 for $C_{14}H_{18}NO_4$).

2,3-Epoxyamide (1′*R*,3*R*,4*R*)-33. Obtained 0.048 g (36%) as a colorless oil: $[\alpha]_D^{20}$ = −62.13 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 6H), 0.89 (s, 9H), 1.78 (ddd, *J* = 14.4, 12.8, 6.0 Hz, 1H), 2.19 (d, *J* = 14.8 Hz, 1H), 2.93 (dd, *J* = 12.4, 5.6 Hz, 1H), 3. 08 (br, 1H), 3.34 (td, J = 12.4, 4.0 Hz, 1H), 3.55 (d, *J* = 2.4 Hz, 1H), 3. 96 (s, 2H), 4.04 (dd, *J* = 10.8, 7.6 Hz, 1H), 4.10 (dd, *J* = 10.8, 5.6 Hz, 1H), 5.81 (apparent t, *J* = 5.6 Hz, 1H), 7.31 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ-5.6, −5.5, 18.0, 24.1, 25.7, 36.5, 56.7, 56.8, 57.0, 61.7, 62.9, 127.6, 127.7, 128.6, 137.1, 168.5; HRMS-FAB *m*/*z* [M + H]$^+$ 378.2103 (calcd. 378.2101 for $C_{20}H_{32}NO_4Si$).

2,3-Epoxyamide (1′*R*,3*S*,4*S*)-34. Obtained 0.048 g (36%) as a colorless oil: $[\alpha]_D^{20}$ = −28.9 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 3H), 0.10 (s, 3H), 0.89 (s, 9H), 2.03 (ddd, *J* = 14. 4, 12.8, 6.0 Hz, 1H), 2.23 (d, *J* = 14.4 Hz, 1H), 3.02 (td, *J* = 12.8, 4.0 Hz, 1H), 3.14 (dd, *J* = 12.8, 6.0 Hz, 1H), 3.58 (d, *J* = 2.8 Hz, 1H), 3.95 (s, 2H), 4.04 (dd, *J* = 10.8, 5.2 Hz, 1H), 4.11(dd, *J* = 10.8, 6.8 Hz, 1H), 5.70 (apparent t, *J* = 6.0 Hz, 1H), 7.3 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.6, −5.4, 18.0, 24.1, 25.7, 38.1, 57.1, 57.1, 57.4, 61.8, 62.9, 127.7, 127.9, 128.5, 136.8, 168.3; HRMS-FAB *m*/*z* [M + H]$^+$ 378.2100 (calcd. 378.2101 for $C_{20}H_{32}NO_4Si$).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra and CIF file for epoxyamide (1′*S*,3*R*,4*R*)-**18**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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