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Enantiospecific Total Synthesis of (+)-Tanikolide via a Key [2,3]-Meisenheimer Rearrangement with an Allylic Amine *N*-Oxide-Directed Epoxidation and a One-Pot Trichloroisocyanuric Acid *N*-Debenzylation and *N*-Chlorination

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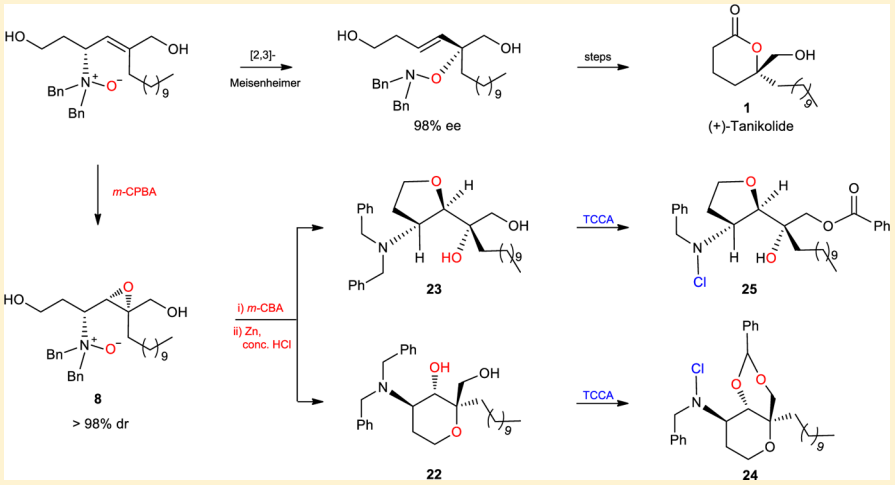
Supporting Information



ABSTRACT: The enantiospecific total synthesis of the δ-lactonic marine natural product (+)-tanikolide (**1**), isolated from *Lyngbya majuscula*, was achieved using a [2,3]-Meisenheimer rearrangement as the key reaction. During this rearrangement, we discovered that the allylic amine *N*-oxide could direct the *m*-CPBA double-bond epoxidation to the syn position. The resulting *syn* product **8** underwent epoxide ring opening under the *m*-CBA conditions to give the five- and six-membered cyclic ether amine *N*-oxides, which we further treated with Zn and conc. HCl to obtain the reduced bisbenzyl tertiary amines **23** and **22**, respectively. When **23** and **22** were treated with trichloroisocyanuric acid (TCCA) in dichloromethane, oxidation at the benzyl position occurred, forming iminium ions. These intermediates were trapped by intramolecular reaction with the hydroxyls, and the resulting intermediates were then oxidized or shifted to afford **25** and **24**, respectively. The entire one-pot process involves *N*-debenzylation, *N*-chlorination, and hemiacetal oxidation. The amine *N*-oxide-directed epoxidation complements Davies' ammonium-directed epoxidation. Thus, TCCA *N*-debenzylation is described for the first time and might be a useful *N*-debenzylation technique.

INTRODUCTION

(+)-Tanikolide (**1**) is a brine-shrimp toxin and antifungal marine metabolite isolated from the lipid extract of the cyanobacterium *Lyngbya majuscule* on Tanikely Island, Madagascar. When tested for toxicity, this compound displayed LD_{50} values of 3.6 μg/mL against brine shrimp and 9.0 μg/mL against snails.[1] Despite its potent biological activity, (+)-tanikolide **1** possesses a relatively simple molecular structure. It contains moderate functionalities (an α-hydroxymethyl group and a δ-lactone) around a synthetically challenging stereogenic quaternary carbon center. These structural features render (+)-tanikolide **1** an appropriate molecule for chemical researchers to rapidly evaluate synthetic methodologies for stereogenic tertiary alcohols.[2] Since the isolation and structural identification of this natural product in 1999, a total synthesis of (+)-tanikolide **1** has been reported every year except 2001 and 2009. Among the 16 synthetic routes reported, the use of the Sharpless asymmetric epoxidation (SAE) method on a trisubstituted alkene is exceptional for its convenient execution and its reliable production of the desired carbon chirality. SAE and subsequent ring opening with alkyl[3a,b] or vinyl[3c] Grignard cuprate reagents or by $LiEt_3BH$ reduction[3d,e] have been demonstrated as efficient strategies for constructing chiral tertiary alcohol moieties. Other important enantioselective methodologies utilized in these 16 synthetic routes include (a) trisimidazoline-catalyzed enantioselective bromolactonization of

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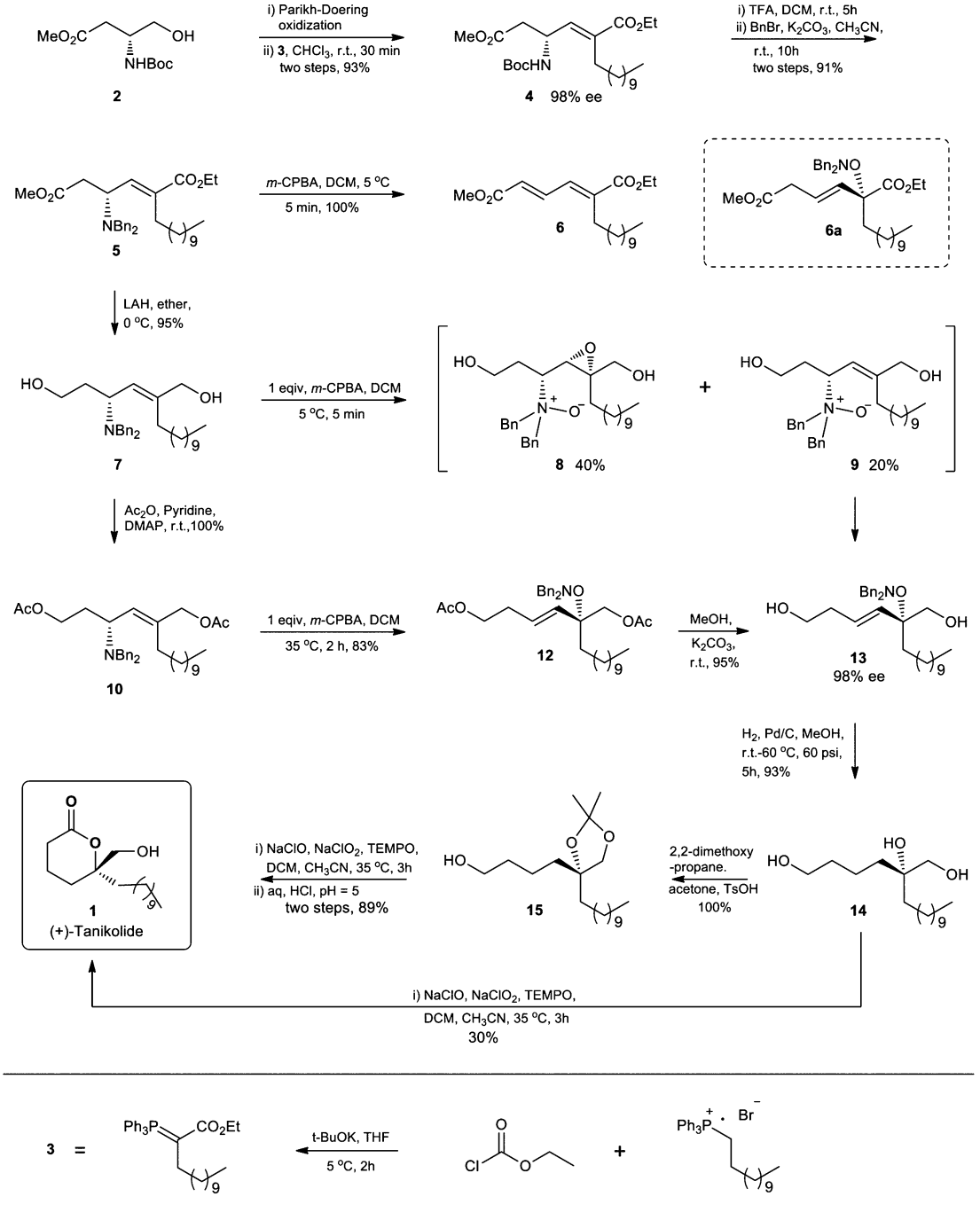
Scheme 1. Enantiospecific Total Synthesis of (+)-Tanikolide 1



internal alkenoic acids,[3f] (b) catalytic asymmetric dihydroxylation of enamides,[3g] (c) cinchona alkaloid-catalyzed asymmetric addition of a β-keto ester to an acrolein[3h] with subsequent Baeyer–Villiger oxidation of the α-chiral quaternary carbon ketone, (d) catalytic asymmetric hydrogen transfer reaction and subsequent Baeyer–Villiger oxidation of the α-chiral quaternary carbon ketone,[3i] and (e) lipase-catalyzed kinetic resolution of a racemic diol and subsequent Baeyer–Villiger oxidation of the α-stereogenic quaternary carbon ketone.[3j] Finally, chirality induction methodologies used in these 16 synthetic routes include (a) Barbier or Grignard reactions of D-glyceraldehyde[3k] and L-erythrulose[3l] derivatives, (b) a D-erythrose[3m] derivative-induced asymmetric Aldol reaction, (c) asymmetric Grignard reactions with (*S*)-2-(anilinomethyl)pyrrolidine chiral auxiliaries,[3n] and (d) intramolecular chiral hydroxyl-induced asymmetric epoxidation[3o] and subsequent hypervalent iodine(III)-mediated oxidative rearrangement. In addition to the above methodologies, the direct utilization of a chiral tertiary alcohol in (−)-quinic acid[3p] or the stereospecific insertion reaction of dichlorocarbene into a C–H bond of a chiral secondary alcohol[3q] have also been utilized.

During the enantiospecific synthesis of the homoharringtonine and harringtonine side-chain acids, we demonstrated the potential of the [2,3]-Meisenheimer rearrangement as a general strategy for constructing chiral tertiary alcohols.[4] In this strategy, the α-amino acid chirality is completely transferred to the tertiary

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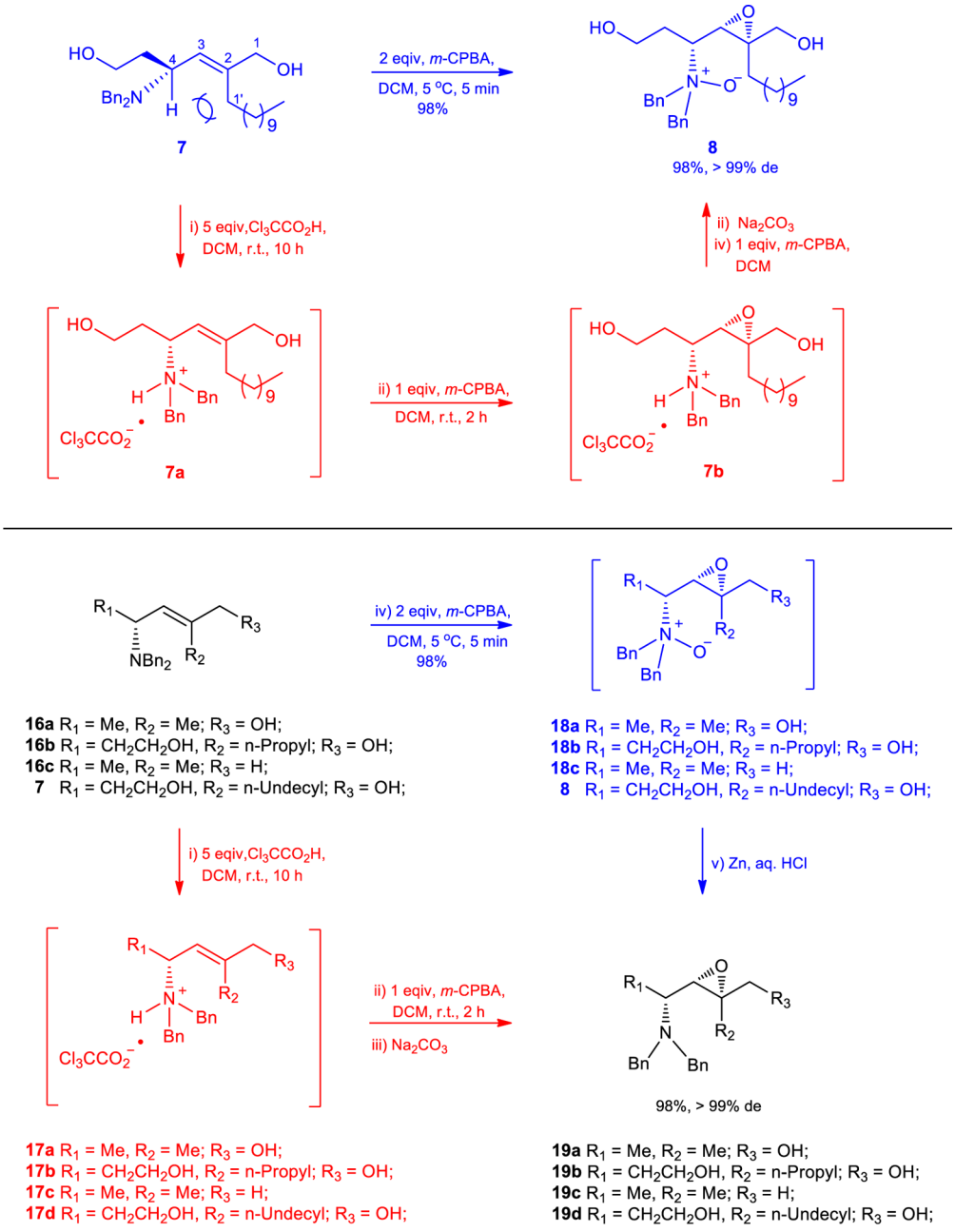
Scheme 2. Stereospecific and *N*-Oxide-Directed Epoxidation of Allylamines



alcohol. The striking features of our methodology are the predictability of the chiral carbon configuration and convenient operation at every synthetic step. For the enantioselective synthesis of the homoharringtonine and harringtonine side-chain acids, the substrate was limited to α,β-unsaturated esters.

RESULTS AND DISCUSSION

In our initial synthetic plan for (+)-tanikolide **1**, α,β-unsaturated ester **5** was utilized (Scheme 1). Compound **5** was prepared according to our previous procedure.[4] We were frustrated by the competitive Cope elimination, which provided conjugated diene **6** instead of the desired product **6a**. This result was identical to the results reported by Davies and co-workers.[5] If **6a** had been obtained, it could have been transformed into (+)-tanikolide **1** within two steps. Therefore, we reduced α,β-unsaturated ester **5** with LAH to obtain allylic alcohol **7**.[5] To our delight, the [2,3]-Meisenheimer rearrangement proceeded with the isolated olefin **7**. This successful result broadened our technique's substrate availability to isolated olefins and further demonstrated the general applicability of our chiral quaternary carbon synthetic methodology.

Unfortunately, a yield of only approximately 20% of the [2,3]-Meisenheimer rearrangement precursor **9** was formed, which underwent rearrangement into **13** when refluxed in dichloromethane for 2 h. When the molar ratio of *m*-CPBA to **7** was increased, the ratio of **8** to **9** also increased. When 2 equiv of *m*-CPBA was employed, **7** was transformed into **8** in 100% yield. We assumed that the undesired **8** was produced because intramolecular hydrogen bonding of the non-allyl hydroxyl with the amine *N*-oxide caused the [2,3]-Meisenheimer rearrangement to be slow. Similar intramolecular hydrogen bonding was suggested in studies by Guarna et al.[6] and Davies and Smyth.[7]

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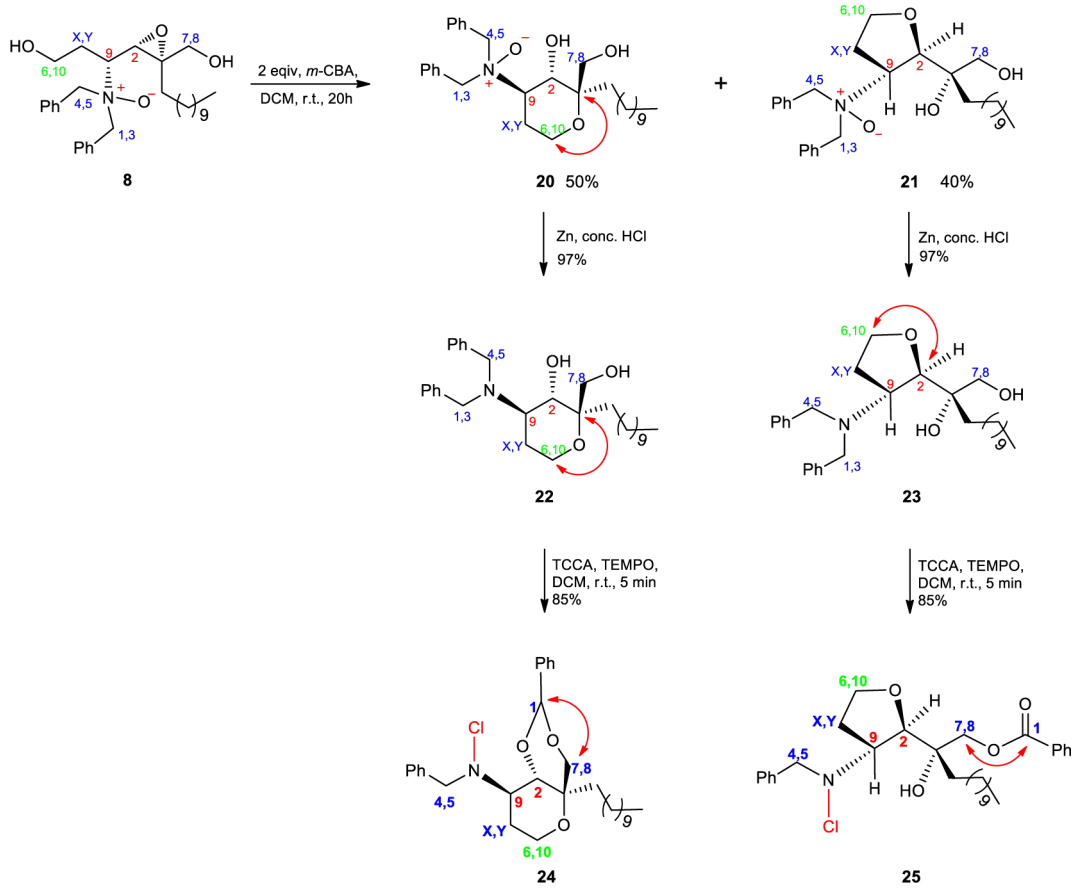
Scheme 3. Epoxide Ring Opening and One-Pot Debenzylation and Nitrogen Chlorination by TCCA



Treatment of **7** with acetic anhydride afforded acetoxy-protected **10** in quantitative yield. Under the *m*-CPBA conditions, **10** smoothly rearranged to give **12** in 83% yield. The stable compound **12** was purified by column chromatography,[4] and transesterification of **12** with MeOH provided diol **13** in 95% yield. Double-bond saturation and N−O bond cleavage using Pd/C-catalyzed hydrogenation afforded triol **14** in 93% yield. **14** could be directly oxidized to (+)-tanikolide **1** in 30% yield under $NaClO/NaClO_2$/TEMPO conditions.[4] The lower yield was observed because the primary hydroxyl group closest to the quaternary carbon side was also oxidized to a carboxyl group. Therefore, the vicinal diol in **14** was protected as acetonide **15**. After oxidation with $NaClO/NaClO_2$/TEMPO, a one-pot deprotection of acetonide with aq. HCl led to (+)-tanikolide **1** in 89% yield. The NMR, specific rotation, EIMS, and IR data were completely consistent with the literature data.[1] The ee values for compounds **4** and **13** were determined by HPLC to be 98%, which confirmed the complete transfer of chirality from **10** to **12**. Moreover, the ee results supported our proposed transition state, which is characterized by allylic 1,3-strain.[4] In summary, our chiral tertiary alcohol synthetic methodology using a [2,3]-Meisenheimer rearrangement was expanded to trisubstituted isolated olefins and was applied to the enantiospecific total synthesis of (+)-tanikolide **1**. The total yield was 52.5% over nine linear steps, which is currently the highest yield of the reported synthetic routes.[3]

The diastereoselective formation of *syn*-epoxide **8** was confirmed by the method of Davies.[8,9] This method involves protonation of **7** with 5 equiv of Cl_3CCO_2H to give ammonium species **7a** and subsequent epoxidation with 1 equiv of *m*-CPBA to afford ammonium epoxide **7b**. After deprotonation with Na_2CO_3, the dibenzylamine epoxide is oxidized again with 1 equiv of *m*-CPBA to provide **8** with >99% diastereoselectivity (Scheme 2). The ^1H and ^{13}C NMR spectra of **8** produced by the two methods were completely identical. Because Davies and co-workers have shown their method to be >99% diastereoselective for the *syn*-epoxide, our method should also be >99% diastereoselective. Presumably, the diastereoselectivity results from the most stable conformation of **7**, in which the allylic C−H bond (i.e., C-4−H) is coplanar with the olefinic C−C bond (i.e., C-2−C-1′) to minimize allylic 1,3-strain.[9] Upon treatment of **7** with *m*-CPBA, the allylamine *N*-oxide formed quickly. Through electrostatic interactions or hydrogen bonding, the *N*-oxide directed the second *m*-CPBA molecule to the double bond on the same face as the *N*-oxide, leading to epoxidation rather than the [2,3]-Meisenheimer rearrangement. By surveying the literature, we discovered that Davies and co-workers reported the only *N*-oxide-directed epoxidation (using a cyclohexenyl amine oxide), and their diastereoselectivity was a mere 46%.[10] The 46% de obtained by Davies and co-workers was in favor of the *anti*-epoxide product, and superior *anti* diastereoselectivity (97% de) was observed in the presence of Cl_3CCO_2H. Here, we report the first aliphatic acyclic allylamine *N*-oxide-directed epoxidation with superior *syn* diastereoselectivity (>99% de) in excellent yield. We have demonstrated the generality of our method by synthesizing **19a**, **19b**, **19c**, and **19d**. The two routes (**16a**, **16b**, **16c**, **7** → **17a**, **17b**, **17c**, **17d** → **19a**, **19b**, **19c**, **19d** and **16a**, **16b**, **16c**, **7** → **18a**, **18b**, **18c**, **8** → **19a**, **19b**, **19c**, **19d**) afforded equally good yields and diastereoselectivities (98% yield and >99% *syn* diastereoselectivity). Our method is comple-

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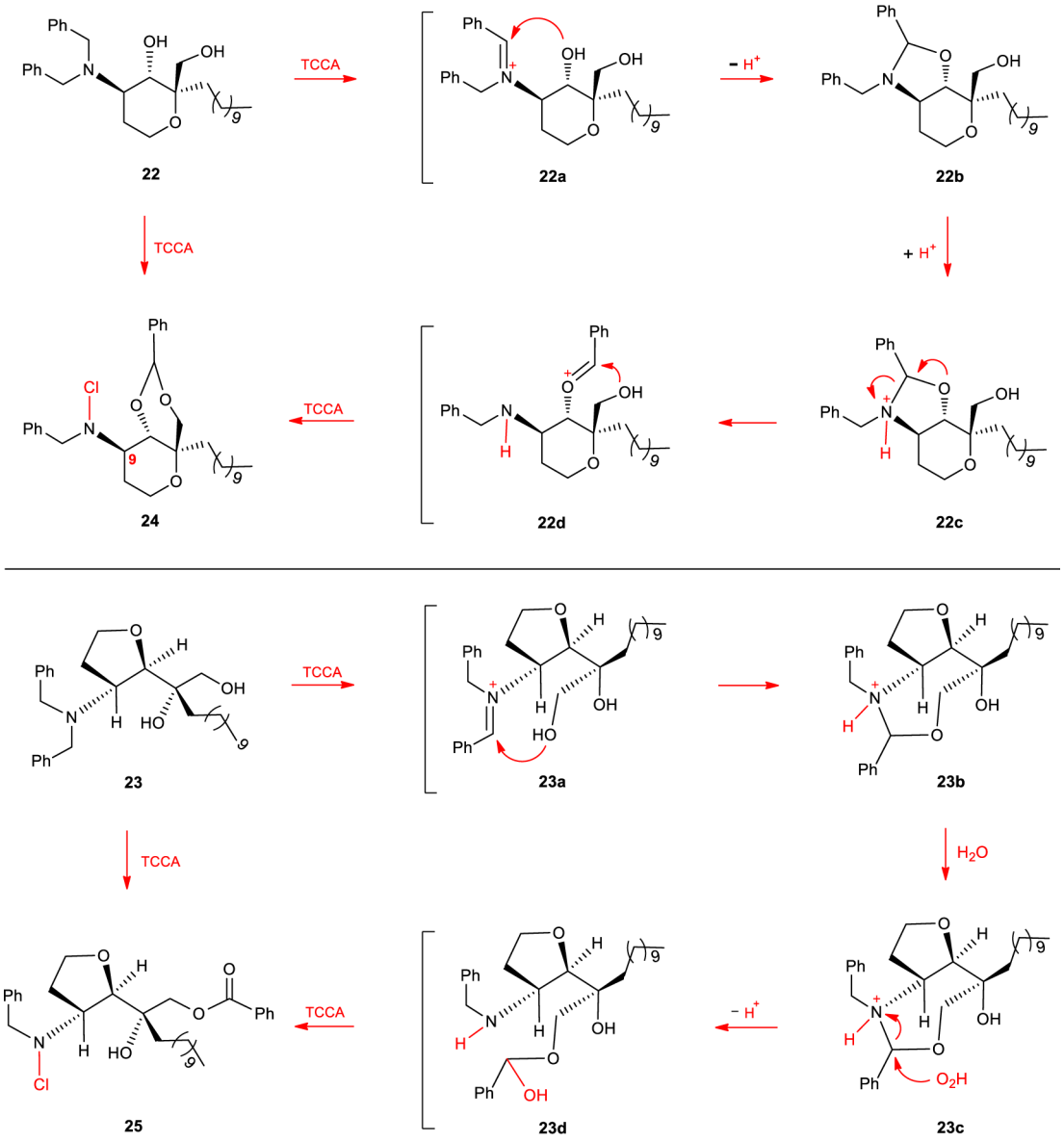
Scheme 4. Proposed Mechanisms for 22 → 24 and 23 → 25



mentary to the method of Davies and co-workers, particularly for substrates that could not withstand the strongly acidic conditions produced by 5 equiv of Cl_3CCO_2H.[8] Moreover, the *m*-CPBA oxidation and Zn/conc. HCl reduction is convenient and efficient. Both reactions can be completed within 20 min, whereas ammonium-directed epoxidations generally require longer reaction times.[9]

When **8** was formed in the *m*-CPBA reaction, its epoxy ring slowly opened at either side, producing a mixture of six-membered cyclic ether **20** and five-membered cyclic ether **21** in an approximate 5 to 4 molar ratio as determined by ^{1}H NMR analysis (Scheme 3).[11] We obtained pure **20** by recrystallizing it from acetone. Reduction of **20** with Zn/conc. HCl furnished **22** in almost quantitative yield. Compound **21** could not be separated from **20**; however, reduction of the mixture of **20** and **21** with Zn/conc. HCl resulted in separable compounds **22** and **23**, respectively. The structures of **20**, **22**, and **23** were established by ^{1}H−^{1}H COSY, HSQC, and HMBC experiments, as shown in Scheme 3.[12] The δ 3.75 methylene proton (H-6) of **20** exhibited key HMBC correlations with the δ 79.1 quaternary carbon, whereas the δ 3.79 methylene proton (H-6) of **22** exhibited key HMBC correlations with the δ 78.4 quaternary carbon. The δ 3.98−3.94 methylene proton (H-6 or H-10) of **23** showed key HMBC correlations with the δ 80.9 methine carbon (C-2) instead of the δ 74.8 quaternary carbon. To further support these assignments, we attempted to oxidize the secondary hydroxyl to the ketone carbonyl and the primary hydroxyl to the aldehyde carbonyl in **22**. We also attempted to oxidize the primary hydroxyl to the aldehyde carbonyl in **23**. After surveying a large number of reported oxidation methods, we chose a mild oxidation method reported by Giacomelli and co-workers that uses trichloroisocyanuric acid (TCCA) as a terminal oxidant.[13] Treatment of **22** and **23** with a 2-fold excess of TCCA led to the unexpected products **24** and **25**, respectively. The structure of **24** was established by HMBC correlations of the δ 5.75 hemiacetal proton (H-1) with the δ 72.6 methlyene carbon (C-7,8). The structure of **25** was established by HMBC correlations of the δ 4.37 and δ 4.31 methylene protons (H-7 and H-8, respectively) with the δ 166.4 ester carbonyl carbon (C-1). In contrast to its analogues NCS and NBS, the chemical properties of TCCA have

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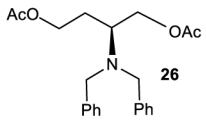
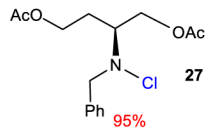
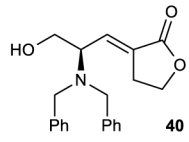
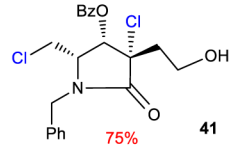
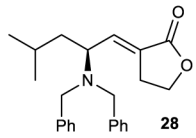
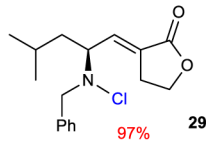
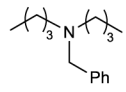
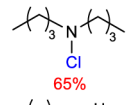
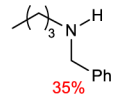
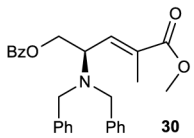
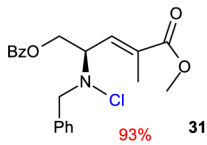
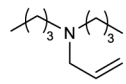
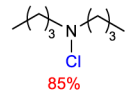
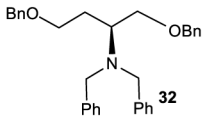
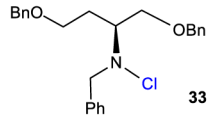
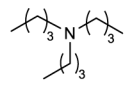
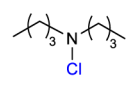
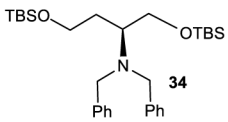
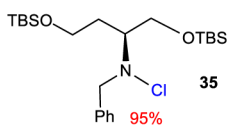
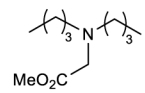
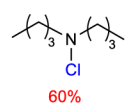
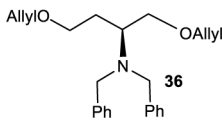
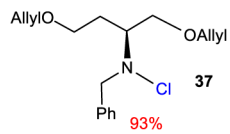
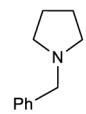
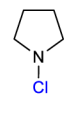
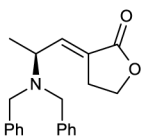
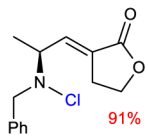
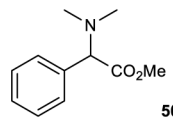
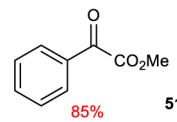
Table 1. Methodological Studies of One-Pot *N*-Debenzylation and *N*-Chlorination by TCCA

Entry	Substrate	Product	Entry	Substrate	Product
1	 **26**	 **27** 95%	8	 **40**	 **41** 75%
2	 **28**	 **29** 97%	9	 **42**	 **43**[a] 65%  **44** 35%
3	 **30**	 **31** 93%	10	 **45**	 85% **43**[b]
4	 **32**	 **33** 95%	11	 **46**	 80% **43**
5	 **34**	 **35** 95%	12	 **47**	 60% **43**
6	 **36**	 **37** 93%	13	 **48**	 **49**[b] > 80%
7	 **38**	 **39** 91%	14	 **50**	 85% **51**

[a]Compound **43** was prone to polymerize to form white floe after column chromatography purification at room temperature. [b]Compound **49** was prone to explosion and decomposition above 10 °C. It was identified in contrast to a sample prepared according to a standard procedure. For this, see ref 26. The yield was estimated to be more than 80% according to TLC.

not been fully understood since its discovery in 1902.[14] Over the past 11 years, some important applications of TCCA in organic synthesis have been reported. The following are selected examples: (a) mild and chemoselective oxidation of alcohols to aldehydes or ketones as an alternative to Swern oxidation,[13] (b) enone epoxidation,[15] (c) dehydrogenation of nitrogen-containing compounds,[16] (d) efficient oxidation of primary alcohols to carboxylic acids or esters,[17] (e) oxidation of primary amines to nitriles or *N*-dichloride compounds,[18] (f) monochlorination of amides or secondary amines,[18,19] (g) mild and efficient deprotection of the amine-protecting *p*-methoxyphenyl (PMP) group,[20] and (h) other reactions.[14] To the best of our knowledge, although the reactions of primary amines, secondary amines, and amides with TCCA have been well-studied, there is only one literature example of the reaction of an aliphatic tertiary amine with TCCA.[20] The transformations **22** → **24** and **23** → **25** were the second example; however, the reaction models are completely different. These reactions represent the first one-pot debenzylation and nitrogen chlorination of aliphatic tertiary amines using TCCA. A plausible mechanism for **22** → **24** and **23** → **25** (Scheme 4) involves iminium ion formation (**22a**, **23a**), intramolecular capture by the adjacent hydroxyl to form unstable N−O acetals (**22b**, **23b**), acid-catalyzed ring opening (**22d**, **23d**),[21] and further chlorination or chlorination plus TCCA

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oxidation to form chloroamine acetal **24** and chloroamine benzoate **25**, respectively.[22,23]

To investigate the proposed mechanism, one-pot debenzylation and nitrogen chlorination methodological studies with TCCA were performed (Table 1). In each case, 0.75 equiv of TCCA was sufficient to achieve a good to excellent yield in a short time (5−30 min) at room temperature in dichloromethane. For entries 1−7, 9, and 13, benzaldehyde was obtained in addition to the listed *N*-debenzylation and *N*-chlorination products **27**, **29**, **31**, **33**, **35**, **37**, **43**, and **49**. Common functional groups such as esters (entries 1 and 3), lactones (entries 7 and 8), double bonds (entries 6 and 10), and TBS (entry 5) survived the TCCA conditions. Moreover, the *N*-debenzylation and *N*-chlorination reaction rate was observed to be faster than the *O*-debenzylation rate (entry 4)[24] and the hydroxyl oxidation rate (entry 8 and for **22** → **24** and **23** → **25**).[13,25] *N*-Monobenzylated substrates afforded the *N*-debenzylated and *N*-chlorinated compounds as the major products (entries 9 and 13). When *N*-benzyl was substituted with *N*-allyl or *N*-alkyl, *N*-deallylated or *N*-dealkylated compounds were the major products (entries 10 and 11). The example of entry 12 demonstrates that an *N*-alkyl group with a more acidic α proton could be preferentially removed from the nitrogen atom. The example in entry 13 illustrates that *N*-dealkylation and *N*-chlorination occurred on one fragment, whereas oxidation occurred on another fragment. The relative configuration of the stereogenic center of compound **41** was determined by 2D NMR and NOESY, and the configuration was inconsistent with a concerted reaction mechanism.[27]

■ CONCLUSIONS

The enantiospecific total synthesis of (+)-tanikolide was successfully completed over nine linear steps in 52.5% overall yield. This efficient and convenient synthesis further demonstrates the reliability and practicality of our chiral tertiary alcohol methodology using the [2,3]-Meisenheimer rearrangement. The substrate scope for these [2,3]-Meisenheimer rearrangements was expanded to nonconjugated olefins with high diastereoselectivity, and *N*-oxide-directed epoxidations using aliphatic acyclic compounds were discovered for the first time. This discovery enabled the rapid synthesis of a large number of branched-chain amino sugars with chiral tertiary alcohol moieties.[28] For example, (+)-lycoperdic acid was conveniently synthesized using our methodology, and we will soon report the results.[29] In addition to the *N*-oxide-directed epoxidations, one-pot *N*-debenzylation and *N*-chlorination in combination with reported *N*-dechlorination[30,31] would be a mild *N*-debenzylation methodology[32] that would be a beneficial complement to currently available methods.[33] The substrate scope and reaction capabilities for these one-pot *N*-debenzylations and *N*-chlorinations are being investigated in detail; the experimental results will be reported shortly. The one-pot *N*-debenzylation and *N*-chlorination also constitutes an aliphatic tertiary amine oxidation, and the dealkylated product could be oxidized to an aldehyde or ketone. Currently, we are attempting to oxidize primary amines[34] to aldehydes or ketones using TCCA, and our results will be reported in due course.

■ EXPERIMENTAL SECTION

General Methods. For general methods, see our previous paper (i.e., ref 4).

General Procedure for Allylic Amine *N*-Oxide-Directed Epoxidation: The Preparation of Compounds 8, 18a, 18b, and 18c. To a solution of allylic amine **7** (or **16a**, **16b**, or **16c**) (1 mmol) in dry CH_2Cl_2 (6 mL) was added *m*-CPBA (2 mmol) at 5 °C. The reaction mixture was stirred for 5 min. CH_2Cl_2 was removed under reduced pressure at 35 °C. The residue was purified by column chromatography on basic alumina (gradient elution, EtOAc at first, then acetone or methanol) to give pure **8** (or **18a**, **18b**, or **18c**) in almost quantative yield.

General Procedure for Amine *N*-Oxide Reduction To Give Tertiary Amines with Zn/Conc. HCl: The Preparation of Compounds 19a, 19b, 19c, 19d, 22, and 23. To a solution of epoxy amine *N*-oxide **18a** (or **18b**, **18c**, **8**, **20**, or **21**) (1 mmol) in MeOH (20 mL) were added Zn powder (5 mmol) and conc. HCl (0.42 mL, 5 mmol) with vigorous stirring. The reaction mixture was stirred for 3 min, and conc. $NH_3{\cdot}H_2O$ was added to adjust the pH to 7 at 5 °C; the mixture was then extracted with EtOAc (3 × 40 mL). The combined organic phases were washed with saturated Na_2CO_3, dried (magnesium sulfate), filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc) to give pure **19a** (or **19b**, **19c**, **19d**, **22**, or **23**) in almost quantative yield.

General Procedure for One-Pot *N*-Debenzylation and *N*-Chlorination with TCCA: The Preparation of Compounds 24, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, and 49. To a solution of benzylamine compound (1 mmol) in CH_2Cl_2 (6 mL) was added TCCA (0.75 mmol) at 5 °C. The reaction mixture was stirred for 3−30 min, diluted with CH_2Cl_2 (30 mL), and then filtered through basic alumina. After concentration, the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc) to give the pure *N*-debenzylation and *N*-chlorination product **24**, **25**, **27**, **29**, **31**, **33**, **35**, **37**, **39**, **41**, **43**, or **49**.

Ethyl 2-(Triphenylphosphoranylidene)tridecanoate (3).[35] A solution of 1-bromododecane (11.87 g, 47.78 mmol) and triphenylphosphane (12.86 g, 50.17 mmol) in toluene was refluxed for 3 days. The resulting white triphenylphosphine Wittig salt (24.42 g, 47.7 mmol, 99%) was filtered and dried overnight in a vacuum desiccator. To a solution of *n*-dodecylphosphonium bromide (24.4 g) in dry THF (175 mL) was added ^{t}BuOK (5.36 g, 47.78 mmol) rapidly at 5 °C under N_2. The reaction mixture was stirred at this temperature for 2 h, and the colorless transparent solution gradually became turbid orange-red. To this was added a solution of ethyl chloroformate (2.26 mL, 23.8 mmol) in dry THF (40 mL) dropwise at 5 °C under N_2. The reaction mixture was stirred continually at this temperature for 2 h, and the turbid orange-red solution became light yellow. The suspension was filtered, and the filtrate was concentrated under reduced pressure to give a deep-orange-red oil, which was used for next step without further purification.

(*R*,*E*)-Dimethyl 4-((*tert*-Butoxycarbonyl)amino)-2-propylhex-2-enedioate (4). To a solution of **2** (3.19 g, 13.7 mmol) and TEA (11.4 mL, 82.1 mmol) in dry CH_2Cl_2 (30 mL) was added Py·SO_3 (13.1 g, 82.1 mmol) in dry DMSO (30 mL) at 5 °C.[36] The reaction mixture was allowed to warm to room temperature. The reaction mixture was then stirred at room temperature for 35 min (longer times were used on larger scales, monitored by TLC), and the reaction was quenched with water/ice (120 mL). The mixture was extracted with CH_2Cl_2 (3 × 200 mL). The organics were washed successively with 10% citric acid (3 × 40 mL), H_2O (3 × 40 mL), saturated $NaHCO_3$ (30 mL), and brine (30 mL). After drying over $MgSO_4$, the organics were concentrated under reduced pressure, yielding the crude aldehyde (3.01 g, 13.0 mmol, 95%) as a red oil, which was used immediately in the next step without further purification. To a solution of the crude aldehyde (2.76 g, 11.9 mmol) in dry $CHCl_3$ (60 mL) was added freshly prepared Wittig reagent **3** (8.93 g, 17.85 mmol) in dry $CHCl_3$ (60 mL) at 5 °C. The reaction mixture was stirred at 5 °C for 30 min (longer times were used on larger scales, monitored by TLC), and $CHCl_3$ was then removed under reduced pressure. The residue was purified by chromatography on silica gel (petroleum ether/EtOAc 6:1, R_f = 0.3) to yield **4** (5.80 g, 12.7 mmol, 93%) as a colorless oil. $[\alpha]_D^{20}$ = 1.30 (*c* 1.54, $CHCl_3$). IR (KBr): 3374, 2923, 2854, 1747, 1648 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.59 (d, *J* = 9.40 Hz, 1H), 5.23 (s, 1H), 4.81 (s, 1H), 4.19 (q, *J* = 7.08 Hz, 2H), 3.70 (s, 3H), 2.66 (dd, *J* = 16.01, 4.32 Hz, 1H), 2.59 (dd, *J* = 16.21, 5.63 Hz, 1H), 2.48−2.27 (m, 2H), 1.43 (s, 9H), 1.35−1.23 (m, 21H), 0.88 (t, *J* = 7.12 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 167.6, 154.7,

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138.3, 135.0, 79.7, 60.7, 51.8, 45.2, 39.5, 31.9, 29.6, 29.6, 29.4, 29.3, 28.3, 14.2, 14.1. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{25}H_{45}NO_6Na$ 478.3145, found 478.3146. The ee value of 98% was determined using a Chiralpak IC (250 mm × 4.6 mm, 5 μm) at an oven temperature of 25 °C, a flow rate of 0.8 mL/min, a mobile phase of *n*-hexane/isopropanol (70:30), and a maximum absorption wavelength of 212 nm. The retention times for the *R* and *S* isomers were 48.888 and 39.414 min, respectively.

(*R*,*E*)-Dimethyl 4-(Dibenzylamino)-2-undecylhex-2-enedioate (5). The experimental procedure was identical to the procedure for the analogous compound in ref 4. Compound **5** was obtained as a colorless oil (486 mg, 91% based on 1 mmol of substrate). Petroleum ether/EtOAc 20:1, R_f = 0.3. $[\alpha]_D^{20}$ = −4.11 (*c* 0.764, $CHCl_3$). IR (KBr): 3062, 3027, 2925, 1743, 1713 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.30 (m, 8H), 7.29−7.23 (m, 2H), 6.79 (d, *J* = 10.31 Hz, 1H), 4.27 (q, *J* = 7.12 Hz, 2H), 4.06 (td, *J* = 9.82, 6.32 Hz, 1H), 3.89 (d, *J* = 13.79 Hz, 2H), 3.45 (d, *J* = 13.79 Hz, 2H), 3.68 (s, 3H), 2.86 (dd, *J* = 14.10, 9.03 Hz, 1H), 2.42 (dd, *J* = 14.12, 9.02 Hz, 1H), 1.37 (t, *J* = 7.21 Hz, 3H), 1.34−1.15 (m, 18H), 0.93 (t, *J* = 6.42 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 167.6, 139.4, 136.8, 136.8, 128.7, 128.2, 127.0, 60.7, 53.8, 53.6, 51.6, 38.0, 32.0, 29.7, 29.6, 29.6, 29.4, 29.4, 29.2, 22.7, 14.3, 14.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{34}H_{49}NO_4Na$ 558.3559, found 558.3560.

(2*E*,4*E*)-Dimethyl 2-Undecylhexa-2,4-dienedioate (6). To a solution of compound **5** (535 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) was added 80% content *m*-CPBA (225 mg, 1.05 mmol) at 5 °C. The reaction mixture was stirred at this temperature for 10 min. The CH_2Cl_2 was removed under reduced pressure, and the residue was purified by chromatography on silica gel (petroleum ether/ether 20:1, R_f = 0.3) to yield **6** (0.334 g, 1.0 mmol, 99%) as a colorless oil. IR (KBr): 3025, 1712 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (dd, *J* = 15.20, 11.92 Hz, 1H), 7.19 (d, *J* = 11.96 Hz, 1H), 6.17 (d, *J* = 15.24 Hz, 1H), 4.25 (q, *J* = 7.12 Hz, 2H), 3.79 (s, 3H), 2.51 (t, *J* = 7.40 Hz, 2H), 1.48−1.39 (m, 2H), 1.36−1.21 (m, 19H), 0.88 (t, *J* = 7.08 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 166.8, 140.5, 138.6, 134.2, 126.5, 61.0, 51.8, 31.9, 29.9, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 27.5, 22.7, 14.2, 14.1. HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{20}H_{35}O_4$ 339.2535, found 339.2538.

(*R*,*E*)-4-(Dibenzylamino)-2-undecylhex-2-ene-1,6-diol (7). To a suspended solution of lithium aluminum hydride (0.52 g, 13.24 mmol) in dry ether (25 mL) was added a solution of **5** (1.435 g, 2.68 mmol) in dry ether dropwise at 5 °C under N_2. The reaction mixture was stirred at this temperature for 10 min. Water (0.502 mL), aqueous sodium hydroxide (15% w/v; 0.502 mL), and then more water (1.506 mL) were added cautiously with vigorous stirring, causing the gray suspension to turn white. Ethyl acetate (50 mL) was added, and the mixture was stirred for 30 min before being filtered through Celite, dried (magnesium sulfate), filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc 2:1) to give **7** as a clear colorless oil (1.185 g, 95%). $[\alpha]_D^{20}$ = −25.82 (*c* 0.30, $CHCl_3$). IR (KBr): 3420, 3028 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.30 (m, 8H), 7.29−7.23 (m, 2H), 5.63 (d, *J* = 10.20 Hz, 1H), 4.19 (d, *J* = 13.68 Hz, 1H), 4.15 (d, *J* = 13.68 Hz, 1H), 3.99 (d, *J* = 13.52 Hz, 2H), 3.86−3.78 (m, 1H), 3.74−3.66 (td, *J* = 10.68, 3.56 Hz, 2H), 3.36 (d, *J* = 13.52 Hz, 2H), 2.21−2.12 (m, 1H), 2.07−1.98 (m, 1H), 1.95−1.88 (m, 2H), 1.42−1.14 (m, 20H), 0.92 (t, *J* = 6.52 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.4, 139.3, 128.8, 128.5, 127.2, 121.3, 66.3, 62.4, 55.7, 53.9, 34.5, 31.9, 29.8, 29.6, 29.6, 29.4, 29.3, 28.7, 28.6, 22.7, 14.1. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{47}NO_2Na$ 488.3504, found 488.3505.

(*R*,*E*)-2-((Dibenzylamino)oxy)-2-undecylhex-3-ene-1,6-diol (13), (2*R*,3*S*,4*R*)-*N*,*N*-Dibenzyl-3-hydroxy-2-(hydroxymethyl)-2-undecyltetrahydro-2*H*-pyran-4-amine Oxide (20), and (2*R*,3*R*)-*N*,*N*-Dibenzyl-2-((*S*)-1,2-dihydroxytridecan-2-yl)tetrahydrofuran-3-amine Oxide (21). To a solution of **7** (1.725 g, 3.70 mmol) in dry CH_2Cl_2 (15 mL) was added *m*-CPBA (0.836 g, 80%, 3.89 mmol) at room temperature, and the mixture was kept at reflux for 2 h (or kept stirring at room temperature for 24 h). The reaction mixture was diluted with CH_2Cl_2 (100 mL), washed successively with 10% NaOH (2 × 10 mL) and saturated brine (2 × 10 mL), dried (magnesium sulfate), filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc 1:2) to give pure **13** as a clear colorless oil (0.355 g, 20%) and **20** and **21** (0.736 g, 40%) as an inseparable mixture. After recrystallization from acetone, pure **20** was obtained as a white jelly (0.132 g, 7%). Compound **13**: $[\alpha]_D^{20}$ = −12.01 (*c* 1.16, $CHCl_3$). IR (KBr): 3421, 3029 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.29 (m, 10H), 5.72 (dt, *J* = 16.04, 6.84 Hz, 1H), 5.46 (d, *J* = 16.08 Hz, 1H), 4.11 (d, *J* = 12.56 Hz, 1H), 4.01−3.75 (m, 4H), 3.64 (t, *J* = 6.42 Hz, 2H), 3.43 (d, *J* = 12.04 Hz, 1H), 3.31 (d, *J* = 12.04 Hz, 1H), 2.71 (brs, 1H), 2.30 (q, *J* = 6.48 Hz, 2H), 1.61−1.43 (m, 2H), 1.37−1.16 (m, 18H), 0.92 (t, *J* = 6.52 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 133.8, 130.0, 128.4, 128.2, 127.8, 83.5, 66.9, 63.3, 62.8, 61.8, 36.4, 35.3, 32.0, 30.2, 29.7, 29.7, 29.6, 29.4, 23.7, 22.7, 14.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{47}NO_3Na$ 504.3454, found 504.3455. Compound **20**: Mp 115.1−116.3 °C (petroleum ether/CH_2Cl_2). IR (KBr): 3400, 3029 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72−7.65 (m, 2H), 7.62 (d, *J* = 6.72 Hz, 2H), 7.48−7.43 (m, 3H), 7.43−7.35 (m, 3H), 4.76 (d, *J* = 11.83 Hz, 1H), 4.43 (d, *J* = 10.52 Hz, 1H), 4.35 (d, *J* = 11.90 Hz, 1H), 4.15 (d, *J* = 12.82 Hz, 1H), 3.99 (d, *J* = 12.82 Hz, 1H), 3.76 (dd, *J* = 11.91, 3.62 Hz, 1H), 3.66 (d, *J* = 11.12 Hz, 1H), 3.57 (d, *J* = 11.12 Hz, 1H), 3.55−3.45 (m, 1H), 3.34 (t, *J* = 11.02 Hz, 1H), 2.75 (s, 1H), 2.05 (d, *J* = 10.03 Hz, 1H), 1.95 (qd, *J* = 12.02, 4.91 Hz, 1H), 1.63 (m, 1H), 1.26 (m, 20H), 0.91 (t, *J* = 6.83 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.2, 131.8, 129.8, 129.6, 129.5, 129.4, 128.5, 128.4, 79.1, 72.2, 67.9, 67.7, 66.5, 66.2, 59.3, 31.9, 30.1, 29.7, 29.6, 29.6, 29.5, 29.4, 28.4, 24.5, 22.7, 21.5, 14.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{47}NO_4Na$ 520.3403, found 520.3405.

(*R*,*E*)-4-(Dibenzylamino)-2-undecylhex-2-ene-1,6-diyl Diacetate (10). To a solution of **7** (1.406 g, 3.02 mmol) in dry CH_2Cl_2 (25 mL) were added dry Et_3N (1.691 mL, 12.08 mmol), acetic anhydride (0.66 mL, 6.80 mmol), and DMAP (0.050 g, 0.41 mmol) at room temperature. The reaction mixture was stirred at room temperature for 30 min and then diluted with CH_2Cl_2 (100 mL). The diluted solution was washed successively with 0.1 N HCl (2 × 10 mL), saturated $NaHCO_3$ (2 × 10 mL), and saturated brine (2 × 10 mL) and then dried over magnesium sulfate, after which the filtered organics were concentrated in vacuo. The resultant residue was purified by column chromatography on silica gel (petroleum ether/EtOAc 13:1), affording pure **10** as a clear colorless oil (1.658 g, 100%). $[\alpha]_D^{20}$ = −8.73 (*c* 1.24, $CHCl_3$). IR (KBr): 3027, 2925, 2853, 1741 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−7.29 (m, 8H), 7.26−7.21 (m, 2H), 5.56 (d, *J* = 10.12 Hz, 1H), 4.59 (d, *J* = 12.76 Hz, 1H), 4.58 (d, *J* = 12.76 Hz, 1H), 4.36−4.27 (m, 1H), 4.11−4.04 (m, 1H), 3.84 (d, *J* = 13.84 Hz, 2H), 3.62−3.55 (m, 1H), 3.39 (d, *J* = 13.84 Hz, 2H), 2.15 (s, 3H), 2.12−2.06 (m, 1H), 1.99−1.91 (m, 1H), 1.89 (s, 3H), 1.87−1.81 (m, 1H), 1.72−1.61 (m, 1H), 1.39−1.09 (m, 18H), 0.93 (t, *J* = 6.52 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 170.8, 140.1, 139.0, 128.6, 128.2, 126.9, 126.1, 67.9, 61.9, 53.8, 51.7, 31.9, 29.9, 29.7, 29.4, 29.3, 28.7, 28.5, 22.7, 21.1, 20.8, 14.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{35}H_{51}NO_4Na$ 572.3216, found 572.3217.

(*R*,*E*)-2-((Dibenzylamino)oxy)-2-undecylhex-3-ene-1,6-diyl Diacetate (12). To a solution of **10** (1.533 g, 2.79 mmol) in dry CH_2Cl_2 (15 mL) was added *m*-CPBA (0.595 g, 80%, 2.93 mmol) at room temperature, and then the mixture was kept stirring at 35 °C for 3 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL), washed successively with 10% NaOH (2 × 10 mL) and saturated brine (2 × 10 mL), dried (magnesium sulfate), filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc 13:1) to give pure **12** as a colorless oil (1.308 g, 83%). $[\alpha]_D^{20}$ = −6.64 (*c* 0.46, $CHCl_3$). IR (KBr): 3030, 1742 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.26 (m, 10H), 5.55 (dt, *J* = 16.24, 6.76 Hz, 1H), 5.35 (d, *J* = 16.28 Hz, 1H), 4.23 (d, *J* = 11.68 Hz, 1H), 4.19 (d, *J* = 11.68 Hz, 1H), 4.07 (t, *J* = 6.64 Hz, 2H), 3.90−3.80 (m, 5H), 2.90 (q, *J* = 6.56 Hz, 2H), 2.06 (s, 3H), 2.01 (s, 3H), 1.60−1.45 (m, 2H), 1.35−1.15 (m, 18H), 0.92 (t, *J* = 6.53 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 170.9, 137.6, 133.7, 129.9, 129.5, 128.3, 128.2, 127.3, 126.6, 81.7, 65.1, 64.1, 63.6, 61.9, 32.3, 31.9, 30.1, 29.7, 29.7, 29.6, 29.5, 29.4, 23.5, 22.7, 21.0, 20.9, 14.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{35}H_{51}NO_5Na$ 588.3665, found 588.3669.

(*R*,*E*)-2-((Dibenzylamino)oxy)-2-undecylhex-3-ene-1,6-diol (13). To a solution of **12** (1.109 g, 1.962 mmol) in THF (25 mL) was

added a solution of KOH (0.220 g, 3.92 mmol) in MeOH (2 mL) at room temperature. The reaction mixture was stirred at room temperature for 30 min, and then 1 N HCl (10 mL) was added. After 10 min, the THF was removed under reduced pressure. The reaction mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were washed with brine (2 × 10 mL), dried (magnesium sulfate), filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/acetone 5:l) to give pure **13** as a colorless oil (0.897 g, 95%). The NMR data were completely identical to the data reported above. The ee value of 98% was determined using a Chiralpak IC (250 mm × 4.6 mm, 5 μm) at an oven column temperature of 25 °C, a flow rate of 0.8 mL/min, a mobile phase of *n*-hexane/isopropanol 70:30, and a maximum absorption wavelength of 205 nm. The retention times for the *R* and *S* isomers were 10.467 and 11.772 min, respectively.

(*R*)-2-Undecylhexane-1,2,6-triol (14). The experimental procedure was identical to the procedure used for the analogous compound in ref 4. Compound **14** was obtained as a white solid (267 mg, 93% based on 1 mmol of substrate **13**). Mp 60.1−61.3 °C (EtOAc). $[\alpha]_D^{20}$ = 1.72 (*c* 1.06, $CHCl_3$). IR (KBr): 3420 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.64 (t, *J* = 5.88 Hz, 2H), 3.62−3.47 (brs, 3H), 3.44 (t, *J* = 12.16 Hz, 2H), 1.60−1.53 (m, 2H), 1.50−1.35 (m, 6H), 1.33−1.22 (m, 18H), 0.89 (t, *J* = 6.52 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 75.0, 67.8, 61.9, 35.9, 34.9, 32.7, 31.9, 30.4, 29.7, 29.7, 29.4, 23.5, 22.7, 19.5, 14.1. HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{36}NO_3Na$ 311.2562, found 311.2564.

(*R*)-4-(2,2-Dimethyl-4-undecyl-1,3-dioxolan-4-yl)butan-1-ol (15). To a solution of **14** (0.342 mg, 1.19 mmol) in acetone (4 mL) were added 2,2-dimethoxypropane (0.39 mL, 3.18 mmol) and $TsOH·H_2O$ (15 mg, 0.08 mmol) at room temperature. After the mixture was stirred for 30 min, the acetone was removed under reduced pressure. To the residue was added saturated $NaHCO_3$ (20 mL), and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic phases were washed with brine (2 × 10 mL), dried (magnesium sulfate), filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/acetone 5:1) to give pure **15** as a colorless oil (0.390 g, 100%). $[\alpha]_D^{20}$ = 2.42 (*c* 0.31, $CHCl_3$). IR (KBr): 3434 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.75 (s, 2H), 3.65 (t, *J* = 5.88 Hz, 2H), 1.77−1.67 (brs, 1H), 1.67−1.42 (m, 7H), 1.42−1.35 (m, 7H), 1.35−1.20 (m, 18H), 0.89 (t, *J* = 6.52 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.8, 83.6, 72.8, 62.6, 37.4, 37.0, 33.1, 31.9, 30.2, 29.6, 29.6, 29.6, 29.3, 27.2, 27.1, 24.2, 22.7, 20.4, 14.1. HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{40}NO_3Na$ 351.2875, found 351.2876.

(*R*)-6-(Hydroxymethyl)-6-undecyltetrahydro-2*H*-pyran-2-one [(+)-Tanikolide (1)]. A 0.67 M buffer solution was prepared by adding NaH_2PO_4 (2.091g) and Na_2HPO_4 (4.799 g) to H_2O (40 mL).[37] To a solution of **15** (0.22g, 0.7 mmol) in acetonitrile (3.6 mL) were added the buffer solution (0.67M, 2.72 mL) and TEMPO (33 mg, 0.21 mmol) at 35 °C. Over 2 h, a solution of NaClO (1.11 mL of 10% NaClO dissolved in 1.69 mL of H_2O) and a solution of $NaClO_2$ (1.59 g of $NaClO_2$ dissolved in 0.7 mL of H_2O) were added dropwise from separate syringes at 35 °C with stirring. (*Caution:* Do not mix sodium hypochlorite solution and $NaClO_2$ before adding them to the reaction mixture!). After the dropwise additions were complete, conc. HCl (2 mL) was added dropwise to the reaction mixture at 5 °C over 30 min. The reaction system was extracted with EtOAc (3 × 30 mL), and the combined organic phases were dried (magnesium sulfate), filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc 8:1) to give pure (+)-tanikolide (**1**) as a colorless oil (0.177 g, 89%). $[\alpha]_D^{20}$ = 2.77 (*c* 1.32, $CHCl_3$) {lit.[1] $[\alpha]_D^{20}$ = +2.3 (*c* = 0.65, CH_3Cl)}. IR (KBr): 3434, 1728 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): 3.66 (d, *J* = 11.90 Hz, 1H), 3.55 (d, *J* = 11.90 Hz, 1H), 2.65 (brs, 1H), 2.48 (t, *J* = 6.23 Hz, 2H), 1.97−1.80 (m, 3H), 1.77−1.66 (m, 3H), 1.65−1.56 (m, 1H), 1.33−1.24 (m, 18H), 0.88 (t, *J* = 6.32 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 86.6, 67.4, 36.7, 31.9, 30.0, 29.8, 29.6, 29.6, 29.5, 29.5, 29.3, 26.6, 23.4, 22.7, 16.1, 14.1. HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{32}NO_3Na$ 307.2249, found 307.2250.

(*R*)-*N*,*N*-Dibenzyl-3-hydroxy-1-((2*S*,3*S*)-3-(hydroxymethyl)-3-undecyloxiran-2-yl)propan-1-amine Oxide (8). *Our Method.* To a solution of **7** (0.200 g, 0.43 mmol) in dry CH_2Cl_2 (6 mL) was added *m*-CPBA (0.205 g, 80%, 0.95 mmol) at 5 °C. The reaction mixture was stirred for 5 min. CH_2Cl_2 was removed under reduced pressure at 35 °C water bath temperature. The residue was purified by column chromatography on basic alumina (gradient elution, EtOAc at first, then acetone) to give pure **8** as a white powder (0.209 g, 98%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 6.60 Hz, 4H), 7.42−7.36 (m, 3H), 7.34−7.22 (m, 3H), 4.64−4.45 (m, 3H), 4.32 (d, *J* = 12.52 Hz, 1H), 3.70 (t, *J* = 12.60 Hz, 2H), 3.62−3.58 (m, 2H), 3.55−3.44 (m, 1H), 3.36 (t, *J* = 9.80 Hz, 1H), 2.49−2.36 (m, 1H), 1.79 (d, *J* = 15.41 Hz, 1H), 1.57−1.39 (m, 2H), 1.39−1.10 (m, 20H), 0.90 (t, *J* = 6.72 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.2, 132.8, 130.7, 130.3, 129.2, 129.1, 128.3, 127.9, 73.4, 68.8, 67.1, 64.9, 62.3, 59.5, 58.4, 31.9, 31.2, 30.0, 29.6, 29.6, 29.5, 29.4, 28.7, 25.0, 22.7, 14.2. HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{31}H_{47}NaNO_4$ 520.3403, found 520.3404.

Davies' Method. The experimental procedure for **7** → **7a** → **7b** strictly conformed to that reported by Davies.[8] When **7b** (1 mmol) was formed in CH_2Cl_2 solution, the solution was diluted with CH_2Cl_2 (50 mL) and washed with saturated Na_2CO_3 (4 × 7 mL) and brine (2 × 7 mL). The CH_2Cl_2 was concentrated to 10 mL under reduced pressure. To the concentrated solution was added *m*-CPBA (1 mmol) at room temperature. The reaction mixture was stirred for 10 min at this temperature. CH_2Cl_2 was removed under reduced pressure at 35 °C water bath temperature. The residue was purified by column chromatography on basic alumina (gradient elution, EtOAc at first, then acetone) to give pure **8** as a white powder (0.209 g, 98%). The NMR data for **8** obtained by this method were completely identical to those for **8** obtained using our method.

(*R*,*E*)-4-(Dibenzylamino)-2-methylpent-2-en-1-ol (16a). Compound **16a** was prepared according to the experimental procedure used for compound **7**. Compound **16a** was obtained as a colorless liquid (277 mg, 94% based on 1 mmol of substrate). R_f = 0.3 (petroleum ether/EtOAc 5:1). IR (KBr): 3386, 3061 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.47−7.45 (m, 4H), 7.39−7.34 (m, 4H), 7.31−7.25 (m, 2H), 5.57 (d, *J* = 9.36 Hz, 1H), 4.09 (s, 2H), 3.81 (d, *J* = 13.92 Hz, 2H), 3.68−3.60 (m, 1H), 3.55 (d, *J* = 13.96 Hz, 2H), 1.77 (brs, 1H), 1.57 (s, 3H), 1.26 (d, *J* = 6.76 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 137.0, 128.6, 128.2, 126.7, 125.9, 68.6, 54.0, 51.1, 18.2, 14.1. HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{26}NO$ 296.2014, found 296.2014.

(*R*,*E*)-4-(Dibenzylamino)-2-propylhex-2-ene-1,6-diol (16b). Compound **16b** was prepared according to the experimental procedure used for compound **7**. Compound **16b** was obtained as a colorless liquid (335 mg, 95% based on 1 mmol of substrate). R_f = 0.3 (petroleum ether/EtOAc 1.5:1). IR (KBr): 3419, 3027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40−7.32 (m, 8H), 7.29−7.24 (m, 2H), 5.65 (d, *J* = 10.20 Hz, 1H), 4.19 (d, *J* = 13.60 Hz, 1H), 4.15 (d, *J* = 13.52 Hz, 1H), 3.99 (d, *J* = 13.52 Hz, 2H), 3.86−3.78 (m, 1H), 3.74−3.66 (td, *J* = 9.56, 3.92 Hz, 2H), 3.36 (d, *J* = 13.48 Hz, 2H), 2.22−2.11 (m, 1H), 2.06−1.88 (m, 2H), 1.48−1.27 (m, 3H), 0.82 (t, *J* = 7.32 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.4, 139.3, 128.8, 128.5, 127.2, 121.6, 66.3, 62.4, 55.6, 53.9, 34.5, 30.7, 21.8, 14.2. HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{31}NO_2Na$ 376.2252, found 376.2252.

(*R*,*E*)-*N*,*N*-Dibenzyl-4-methylhex-3-en-2-amine (16c). To a solution of **16a** (285 mg, 0.965 mmol) in dry CH_2Cl_2 (7 mL) were added MsCl (235.9 mg, 1.931 mmol), Et_3N (195.4 mg, 1.931 mmol), and DMAP (23.6 mg, 0.193 mmol) at 5 °C. After the reactin mixture was stirred at 5 °C for 1 h, MsCl (235.9 mg, 1.931 mmol) and Et_3N (195.4 mg, 1.931 mmol) were further added to the reaction mixture, which was stirred for an additional 1 h. Next, the reaction temperature was elevated to room temperature, and the reaction was further continued for 2 h. The reaction mixture was poured into ice−water (30 mL) and extracted with EtOAc (3 × 60 mL), which was washed successively with 5% aq. HCl (30 mL), saturated aq. $NaHCO_3$ (30 mL) and brine (50 mL), after which the organic layer was dried over Na_2SO_4. This mesylate was employed without further purification for the next reaction. To a solution of the crude mesylate in dry THF (10 mL) was added $LiAlH_4$ (128.23 mg, 3.38 mmol) in a small portion over 30 min. After the reaction mixture was stirred at room temperature for 1 h, the reaction

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was quenched by the addition of H_2O (0.128 mL), 15% NaOH (0.128 mL), and H_2O (0.384 mL) subsequently. The white solids were filtered. The filtrate was concentrated, and the residue was purified by chromatography on silica gel (petroleum ether/EtOAc 20:1, R_f = 0.3) to yield **16c** (218 mg, 81%) as a colorless oil. IR (KBr): 3084, 3061, 3026, 1602 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.50−7.45 (m, 4H), 7.39−7.35 (m, 4H), 7.35−7.26 (m, 2H), 5.31 (d, J = 9.24 Hz, 1H), 3.81 (d, J = 13.92 Hz, 2H), 3.59−3.50 (m, 1H), 3.52 (d, J = 14.08 Hz, 2H), 1.84 (s, 3H), 1.55 (s, 3H), 1.24 (d, J = 6.60 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.1, 134.1, 128.6, 128.1, 126.6, 125.3, 53.9, 51.3, 26.0, 18.6, 18.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{21}H_{27}NNa$ 316.2041, found 316.2041.

((2*S*,3*S*)-3-((*R*)-1-(Dibenzylamino)ethyl)-2-methyloxiran-2-yl)methanol (19a). Colorless oil (318 mg, 96%). R_f = 0.3 (petroleum ether/EtOAc 5:1). IR (KBr): 3445, 3084, 3061, 3027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 7.92 Hz, 4H), 7.37−7.33 (m, 4H), 7.28−7.24 (m, 2H), 3.86 (s, 4H), 3.73 (d, J = 12.2 Hz, 1H), 3.63−3.60 (m, 1H), 3.27 (d, J = 9.12 Hz, 1H), 2.86−2.80 (m, 1H), 2.23 (brs, 1H), 1.18 (s, 3H), 1.15 (d, J = 6.92 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0, 129.4, 128.5, 127.3, 63.2, 61.6, 61.0, 59.7, 54.8, 54.4, 30.8, 30.6, 18.3, 14.5. HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{20}H_{25}NO_2Na$ 334.1783, found 334.1782. The NMR data obtained by our method were completely identical to those obtained by Davies' method.

(*R*)-3-(Dibenzylamino)-3-((2*S*,3*S*)-3-(hydroxymethyl)-3-propyloxiran-2-yl)propan-1-ol (19b). Colorless oil (354 mg, 96%). R_f = 0.3 (petroleum ether/EtOAc 1.5:1). IR (KBr): 3435, 3040 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.41−7.25 (m, 10H), 4.06 (d, J = 12.76 Hz, 2H), 3.79−3.70 (m, 5H), 3.55−3.45 (m, 1H), 3.32 (d, J = 9.72 Hz, 1H), 2.92−2.87 (m, 1H), 2.06−1.94 (m, 1H), 1.50−1.25 (m, 5H), 0.90 (t, J = 6.84 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0, 129.4, 128.5, 127.3, 63.2, 61.6, 61.0, 59.7, 54.8, 54.4, 30.8, 30.6, 18.3, 14.5. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{20}H_{25}NO_2Na$ 392.2202, found 392.2202.

(*R*)-*N*,*N*-Dibenzyl-1-((*S*)-3,3-dimethyloxiran-2-yl)ethanamine (19c). Colorless oil (280 mg, 95%). R_f = 0.3 (petroleum ether/EtOAc 18:1). IR (KBr): 3061, 3028, 1602 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.47−7.45 (m, 4H), 7.35−7.30 (m, 4H), 7.26−7.22 (m, 2H), 3.85 (s, 4H), 2.93 (d, J = 9.04 Hz, 1H), 2.77−2.60 (m, 1H), 1.36 (s, 3H), 1.15 (s, 3H), 1.14 (d, J = 7.16 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 128.8, 128.1, 126.7, 64.9, 56.0, 54.1, 52.4, 25.0, 18.9, 15.0. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{20}H_{25}NNaO$ 318.1834, found 318.1838.

(*R*)-3-(Dibenzylamino)-3-((2*S*,3*S*)-3-(hydroxymethyl)-3-undecyloxiran-2-yl)propan-1-ol (19d). Colorless oil (461 mg, 96%). R_f = 0.3 (petroleum ether/EtOAc 2:1). IR (KBr): 3420, 3062, 3068 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.41−7.25 (m, 10H), 4.06 (d, J = 12.76 Hz, 2H), 3.70−3.60 (m, 5H), 3.55−3.45 (m, 1H), 3.32 (d, J = 9.68 Hz, 1H), 2.93−2.87 (m, 1H), 1.90−2.10 (m, 1H), 1.75 (brs, 1H), 1.45−1.43 (m, 3H), 1.43−1.25 (m, 19H), 0.92 (t, J = 6.64 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0, 129.4, 128.5, 127.3, 63.3, 61.7, 61.1, 59.8, 54.9, 54.4, 29.6, 29.6, 29.4, 29.3, 28.5, 24.9, 22.7, 14.1. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{20}H_{25}NO_2Na$ 504.3454, found 504.3454.

(2*R*,3*S*,4*R*)-*N*,*N*-Dibenzyl-3-hydroxy-2-(hydroxymethyl)-2-undecyltetrahydro-2*H*-pyran-4-amine Oxide (20) and (2*R*,3*R*)-*N*,*N*-Dibenzyl-2-((*S*)-1,2-dihydroxytridecan-2-yl)tetrahydrofuran-3-amine Oxide (21). To a solution of **7** (2.00 g, 4.3 mmol) in dry CH_2Cl_2 (60 mL) was added *m*-CPBA (2.04 g, 80%, 9.5 mmol) at 5 °C. Compound **8** was immediately produced. The reaction mixture was stirred for 12 h. CH_2Cl_2 was removed under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc 2:1) to give **20** and **21** as an inseparable mixture (1.95 g, 3.9 mmol, 91%). Recrystallization of the mixture from acetone afforded pure **20** as a white solid (0.53 g, 1.06 mmol). Mp 115.1−116.3 °C (petroleum ether/CH_2Cl_2). IR (KBr): 3400, 3029 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.72−7.65 (m, 2H), 7.62 (d, J = 6.72 Hz, 2H), 7.48−7.43 (m, 3H), 7.43−7.35 (m, 3H), 4.76 (d, J = 11.83 Hz, 1H), 4.43 (d, J = 10.52 Hz, 1H), 4.35 (d, J = 11.90 Hz, 1H), 4.15 (d, J = 12.82 Hz, 1H), 3.99 (d, J = 12.82 Hz, 1H), 3.76 (dd, J = 11.91, 3.62 Hz, 1H), 3.66 (d, J = 11.12 Hz, 1H), 3.57 (d, J = 11.12 Hz, 1H), 3.55−3.45 (m, 1H), 3.34 (t, J = 11.02 Hz, 1H), 2.75 (s, 1H), 2.05 (d, J = 10.03 Hz, 1H), 1.95 (qd, J = 12.02, 4.91 Hz, 1H), 1.63 (m, 1H), 1.26 (m, 20H), 0.91 (t, J = 6.83 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.2, 131.8, 129.8, 129.6, 129.5, 129.4, 128.5, 128.4, 79.1, 72.2, 67.9, 67.7, 66.5, 66.2, 59.3, 31.9, 30.1, 29.7, 29.6, 29.6, 29.5, 29.4, 28.4, 24.5, 22.7, 21.5, 14.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{47}NO_4Na$ 520.3403, found 520.3405.

(2*R*,3*S*,4*R*)-4-(Dibenzylamino)-2-(hydroxymethyl)-2-undecyltetrahydro-2*H*-pyran-3-ol (22). Colorless crystals (466 mg, 97%), mp 61.5−63.1 °C. IR (KBr): 3462, 3062, 3027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39−7.33 (m, 4H), 7.32−7.26 (m, 6H), 3.94 (d, J = 13.30 Hz, 2H), 3.87 (d, J = 10.52 Hz, 1H), 3.81 (dd, J = 11.82, 4.11 Hz, 1H), 3.61 (d, J = 3.19 Hz, 2H), 3.49 (td, J = 12.10, 2.10 Hz, 1H), 3.42 (s, 2H), 3.39 (s, 1H), 2.95 (td, J = 11.89, 3.78 Hz, 1H), 2.32 (s, 1H), 1.83 (d, J = 12.48 Hz, 1H), 1.69 (qd, J = 12.42, 5.02 Hz, 1H), 1.40−1.10 (m, 20H), 0.92 (t, J = 6.80 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.0, 128.9, 128.6, 127.3, 78.4, 68.9, 66.2, 60.8, 56.3, 53.6, 31.9, 30.3, 29.7, 29.7, 29.6, 29.4, 25.1, 23.5, 22.8, 21.8, 14.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{47}NO_3Na$ 504.3454, found 504.3454.

(*S*)-2-((2*R*,3*R*)-3-(Dibenzylamino)tetrahydrofuran-2-yl)-tridecane-1,2-diol (23). Colorless oil (466 mg, 97%). IR (KBr): 3446, 3062, 3027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40−7.34 (m, 4H), 7.34−7.28 (m, 6H), 4.07 (s, 1H), 4.01−3.88 (m, 5H), 3.69 (q, J = 8.30 Hz, 1H), 3.44 (d, J = 11.79 Hz, 1H), 3.38 (d, J = 13.02 Hz, 2H), 3.20 (d, J = 11.82 Hz, 1H), 3.12 (s, 1H), 2.16 (dq, J = 14.80, 7.51 Hz, 1H), 2.03−1.91 (m, 1H), 1.55−1.45 (m, 1H), 1.36−1.12 (m, 20H), 0.91 (t, J = 6.82 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.6, 129.5, 128.7, 127.7, 80.9, 74.8, 67.7, 65.8, 59.2, 55.2, 35.0, 32.0, 30.3, 29.7, 29.7, 29.7, 29.4, 23.1, 22.8, 22.7, 14.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{47}NO_3Na$ 504.3454, found 504.3454.

(4a*R*,8*R*,8a*R*)-*N*-Benzyl-*N*-chloro-2-phenyl-4a-undecylhexahydropyrano[3,2-*d*][1,3]dioxin-8-amine (24). Colorless oil (436 mg, 85%). IR (KBr): 3500, 3032 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 6.60 Hz, 2H), 7.49−7.30 (m, 8H), 5.75 (s, 1H), 4.42 (s, 2H), 4.19 (dd, J = 17.02, 10.29 Hz, 2H), 3.81 (dd, J = 11.90, 5.92 Hz, 1H), 3.71 (td, J = 12.38, 2.51 Hz, 1H), 3.60 (d, J = 10.53 Hz, 1H), 3.53 (td, J = 10.68, 4.37 Hz, 1H), 2.23−2.08 (m, 2H), 1.94 (d, J = 13.32 Hz, 1H), 1.81−1.68 (m, 1H), 1.48−1.20 (m, 19H), 0.92 (t, J = 6.72 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9, 137.7, 129.2, 129.0, 128.3, 127.7, 126.2, 102.5, 83.7, 72.6, 71.2, 66.4, 60.2, 60.0, 31.9, 30.1, 29.7, 29.7, 29.6, 29.5, 29.3, 25.0, 22.7, 21.3, 14.1. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{44}ClNO_3Na$ 536.2907, found 536.2907.

(*S*)-2-((2*R*,3*R*)-3-(Benzylchloroamino)tetrahydrofuran-2-yl)-2-hydroxytridecyl Benzoate (25). Colorless oil (449 mg, 85%). IR (KBr): 3446, 1723 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 7.20 Hz, 2H), 7.58 (t, J = 7.38 Hz, 1H), 7.46 (t, J = 7.67 Hz, 2H), 7.35−7.30 (m, 5H), 4.34 (dd, J = 27.78, 11.46 Hz, 2H), 4.18 (d, J = 6.12 Hz, 1H), 4.13 (d, J = 2.21 Hz, 2H), 4.10−4.00 (m, 2H), 4.00−3.92 (m, 1H), 2.48−2.38 (m, 1H), 2.30 (s, 1H), 2.10−1.98 (m, 1H), 1.83−1.72 (m, 2H), 1.54−1.37 (m, 2H), 1.39−1.19 (m, 18H), 0.90 (t, J = 6.99 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 136.5, 133.0, 130.1, 129.7, 129.0, 128.5, 128.4, 128.1, 82.8, 74.4, 68.5, 68.0, 66.6, 65.9, 35.4, 31.9, 30.2, 29.6, 29.63, 29.6, 29.5, 29.3, 26.9, 23.2, 22.7, 14.1. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{44}ClNNaO_4$ 552.2857, found 552.2861.

(*S*)-2-(Dibenzylamino)butane-1,4-diyl Diacetate (26). The preparation of compound **26** was analogous to that used for compound **10**. Compound **26** was obtained as a colorless oil (361 mg, 98% based on 1 mmol of substrate). R_f = 0.3 (petroleum ether/EtOAc 30:1). IR (KBr): 1738, 1645 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.20 (m, 10H), 4.38−4.33 (m, 1H), 4.25−4.19 (m, 2H), 3.82 (d, J = 13.52 Hz, 2H), 3.59 (d, J = 13.56 Hz, 2H), 3.09−3.06 (m, 1H), 2.14 (s, 3H), 1.98−1.90 (m, 1H), 1.88(s, 3H), 1.75−1.66 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 170.9, 139.6, 128.8, 128.3, 127.1, 63.7, 61.8, 53.9, 52.5, 27.9, 21.1, 20.9. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{22}H_{27}NNaO_4$ 392.1838, found 392.1840.

(*S*)-2-(Benzylchloroamino)butane-1,4-diyl Diacetate (27). Colorless oil (297 mg, 95%). R_f = 0.3 (petroleum ether/EtOAc 30:1). IR (KBr): 3445, 1741 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.50−7.30 (m, 5H), 4.56−4.50 (m, 1H), 4.30−4.10 (m, 5H), 3.36−3.30 (m, 1H), 2.12 (s, 3H), 2.10−2.00 (m, 1H), 1.99 (s, 3H), 1.89−1.79 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 170.7, 137.1, 128.9, 128.4, 128.0,

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64.9, 63.7, 61.5, 61.2, 28.7, 21.0, 20.9. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{20}ClNNaO_4$ 336.0979, found 336.0979.

(*S*,*E*)-3-(2-(Dibenzylamino)-4-methylpentylidene)dihydrofuran-2(3*H*)-one (28). Compound **28** was prepared according to the procedure developed in ref 4.[38] Compound **28** was obtained as white needlelike crystals (308 mg, 85% based on 1 mmol of substrate). R_f = 0.3 (petroleum ether/EtOAc 8:1). Mp 103.2−103.6 °C (petroleum ether). $[\alpha]_D^{20}$ = 6.30 (c 1.04, $CHCl_3$). IR (KBr): 2954, 1759, 1639 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42−7.26 (m, 10H), 6.92 (dt, J = 10.0, 2.76 Hz, 1H,), 4.40−4.29 (td, J = 7.64, 3.88 Hz, 1H), 3.92 (d, J = 13.78 Hz, 2H), 3.45 (d, J = 13.81 Hz, 2H), 3.42−3.37 (m, 1H), 2.60−2.53 (td, J = 7.96, 2.68 Hz, 2H), 1.82−1.71 (m, 2H), 1.37−1.25 (m, 1H), 0.87 (d, J = 6.18 Hz, 3H), 0.80 (d, J = 6.16 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 139.7, 139.6, 128.6, 128.3, 127.5, 127.1, 65.5, 55.5, 54.1, 40.8, 25.0, 24.6, 22.8, 22.5. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{24}H_{29}NNaO_2$ 386.2096, found 386.2095.

(*S*,*E*)-3-(2-(Benzylchloroamino)-4-methylpentylidene)-dihydrofuran-2(3*H*)-one (29). White solid (298 mg, 97%). R_f = 0.3 (petroleum ether/EtOAc 9:1). Mp 89.2−90.6 °C (EtOAc). IR (KBr): 3431, 1743 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.32 (m, 5H), 7.03 (dt, J = 10.0, 2.76 Hz, 1H,), 4.40 (t, J = 7.36 Hz, 1H), 4.22 (d, J = 13.2 Hz, 1H), 3.97 (d, J = 13.2 Hz, 1H), 3.69−3.62 (m, 1H), 2.77−2.74 (m, 2H), 1.87−1.73 (m, 2H), 1.37−1.30 (m, 1H), 0.93 (d, J = 6.56 Hz, 3H), 0.89 (d, J = 6.52 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 137.7, 136.9, 128.8, 128.6, 128.5, 128.1, 65.4, 64.5, 64.4, 41.3, 25.5, 24.4, 22.9, 22.3. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{17}H_{22}ClNNaO_2$ 330.1237, found 330.1238.

(*R*,*E*)-2-(Dibenzylamino)-5-methoxy-4-methyl-5-oxopent-3-en-1-yl Benzoate (30). Compound **30** was prepared according to the procedure developed in ref 4. Compound **30** was obtained as a white solid (410 mg, 97% based on 1 mmol of substrate). Mp 73.7−74.5 °C. R_f = 0.3 (petroleum ether/EtOAc 6:1). IR (KBr): 3062, 3028, 1715 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08−8.06 (m, 2H), 7.64−7.62 (m, 1H), 7.53−7.50 (m, 2H), 7.53−7.50 (m, 2H), 7.50−7.48 (m, 4H), 7.39−7.27 (m, 6H), 6.94 (d, J = 1.44 Hz, 1H), 4.65−4.59 (m, 1H), 4.40−4.35 (m, 1H), 4.07−4.02 (m, 1H), 3.98 (d, J = 13.8 Hz, 2H), 3.83 (s, 3H), 3.57 (d, J = 13.8 Hz, 1H), 1.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0, 166.3, 139.4, 135.9, 133.1, 132.8, 130.1, 129.7, 128.6, 128.5, 128.3, 127.1, 64.2, 55.3, 54.5, 52.1, 13.3. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{28}H_{29}NNaO_4$ 446.1994, found 446.1996.

(*R*,*E*)-2-(Benzylchloroamino)-5-methoxy-4-methyl-5-oxopent-3-en-1-yl Benzoate (31). Colorless oil (360 mg, 93%). R_f = 0.3 (petroleum ether/EtOAc 8:1). IR (KBr): 1722, 1600 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 7.08 Hz, 2H), 7.62−7.58 (m, 1H), 7.50−7.46 (m, 2H), 7.33 (s, 5H), 7.05 (d, J = 9.12 Hz, 1H), 4.69−4.64 (m, 1H), 4.50−4.45 (m, 1H), 4.29−4.23 (m, 2H), 4.09 (d, J = 13.2 Hz, 1H), 3.83 (s, 3H), 1.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 166.3, 136.5, 133.7, 133.2, 129.7, 128.9, 128.5, 128.5, 128.1, 65.2, 64.5, 63.3, 52.2, 13.7. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{21}H_{22}ClNNaO_4$ 410.1135, found 410.1132.

(*S*)-*N*,*N*-Dibenzyl-1,4-bis(benzyloxy)butan-2-amine (32). The preparation of compound **32** was analogous to that used for the preparation of compound **27**. Compound **30** was obtained as a colorless oil (339 mg, 73% based on 1 mmol of substrate). R_f = 0.3 (petroleum ether/EtOAc 40:1). IR (KBr): 3085, 3062, 3028 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42−7.26 (m, 20H), 4.61−4.40 (m, 4H), 3.86 (d, J = 13.7 Hz, 2H), 3.75−3.50 (m, 6H), 3.17−3.11 (m, 1H), 2.04−1.95 (m, 1H), 1.88−1.71 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 138.7, 128.9, 128.4, 128.3, 128.2, 127.8, 127.5, 126.8, 73.2, 72.9, 71.0, 68.4, 54.4, 54.2, 29.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{32}H_{35}NNaO_2$ 488.2565, found 488.2565.

(*S*)-*N*-Benzyl-1,4-bis(benzyloxy)-*N*-chlorobutan-2-amine (33). Colorless oil (389 mg, 95%). R_f = 0.3 (petroleum ether/EtOAc 40:1). IR (KBr): 3061, 3029, 1720, 1641 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.25 (m, 15H), 4.60 (s, 2H), 4.56 (s, 2H), 4.33 (q, J = 13.8 Hz, 2H), 4.02−3.97 (m, 1H), 3.70−3.67 (m, 1H), 3.67−3.60 (m, 2H), 3.60−3.50 (m, 1H), 2.06−1.99 (m, 1H), 1.90−1.83 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.5, 138.3, 138.0, 128.9, 128.4, 128.4, 128.3, 127.7, 127.6, 127.6, 73.3, 73.0, 70.8, 67.2, 65.2, 64.2, 30.1. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{25}H_{28}ClNNaO_2$ 432.1706, found 432.1707.

(*S*)-*N*,*N*-Dibenzyl-2,2,3,3,10,10,11,11-octamethyl-4,9-dioxa-3,10-disiladodecan-6-amine (34). The preparation of compound **34** was analogous to that used for the preparation of compound **27**. Compound **34** was obtained as a colorless oil (456 mg, 89%). R_f = 0.3 (petroleum ether). IR (KBr): 3085, 3063, 3027 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42−7.34 (m, 4H), 7.33−7.31 (m, 4H), 7.29−7.22 (m, 2H), 3.85−7.73 (m, 7H), 3.66−3.60 (m, 1H), 2.91−2.85 (m, 1H), 1.91−1.85 (m, 1H), 1.73−1.66 (m, 1H), 0.98 (s, 9H), 0.91 (s, 9H), 0.11 (s, 6H), 0.06 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 128.7, 128.1, 126.6, 63.5, 61.7, 55.7, 54.5, 31.9, 26.0, 18.4, 18.2, −5.2, −5.2, −5.4, −5.5. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{30}H_{51}NNaO_2Si_2$ 536.3356, found 536.3356.

(*S*)-*N*-Benzyl-*N*-chloro-2,2,3,3,10,10,11,11-octamethyl-4,9-dioxa-3,10-disiladodecan-6-amine (35). Colorless oil (434 mg, 95%). R_f = 0.3 (petroleum ether). IR (KBr): 3031 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.31 (m, 5H), 4.41 (d, J = 14.28 Hz, 1H), 4.30 (d, J = 14.28 Hz, 1H), 4.14−4.09 (m, 1H), 3.86−3.76 (m, 3H), 3.69−3.33 (m, 1H), 1.98−1.85 (m, 1H), 1.85−1.75 (m, 1H), 0.99 (s, 9H), 0.96 (s, 9H), 0.17 (s, 6H), 0.12 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 128.7, 128.3, 127.5, 66.4, 65.1, 63.7, 60.3, 32.5, 26.0, 26.0, 18.3, 18.3, −5.2, −5.3, −5.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{23}H_{44}NNaO_2Si_2$ 480.2497, found 480.2498.

(*S*)-1,4-Bis(allyloxy)-*N*,*N*-dibenzylbutan-2-amine (36). The preparation of compound **36** was analogous to that used for the preparation of compound **27**. Compound **36** was obtained as a colorless oil (290 mg, 85%). R_f = 0.3 (petroleum ether/EtOAc 35:1). IR (KBr): 3083, 3062, 3027, 1646 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.29 (m, 10H), 6.04−5.91 (m, 2H), 5.43−5.23 (m, 4H), 4.07 (d, J = 5.12 Hz, 2H), 3.97 (d, J = 5.56 Hz, 2H), 3.90 (d, J = 13.72 Hz, 2H), 3.77 (d, J = 12.96 Hz, 2H), 3.79−3.74 (m, 1H), 3.74−3.50 (m, 3H), 3.15−3.08 (m, 1H), 2.03−1.94 (m, 1H), 1.86−1.77 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 135.2, 129.0, 128.2, 126.8, 116.6, 116.5, 72.1, 71.8, 71.1, 68.4, 54.4, 54.1, 29.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{24}H_{21}NNaO_2$ 365.2355, found 365.2357.

(*S*)-1,4-Bis(allyloxy)-*N*-benzyl-*N*-chlorobutan-2-amine (37). Colorless oil (287 mg, 93%). R_f = 0.3 (petroleum ether/EtOAc 35:1). IR (KBr): 2953, 2924, 2853, 1646 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.29 (m, 5H), 5.99−5.88 (m, 2H), 5.36−5.21 (m, 4H), 4.35−4.25 (m, 2H), 4.10−3.92 (m, 5H), 3.92−3.53 (m, 4H), 2.02−1.94 (m, 1H), 1.84−1.76 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 135.0, 134.8, 128.9, 128.3, 127.6, 116.9, 72.1, 71.9, 70.7, 67.2, 65.2, 64.1, 30.0. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{17}H_{24}ClNNaO_2$ 332.1393, found 332.1395.

(*S*,*E*)-3-(2-(Benzylchloroamino)propylidene)dihydrofuran-2(3*H*)-one (39). The known compound **38**[4,39] was transformed into **39** according to the general procedure above. Compound **39** was obtained as a colorless oil (241 mg, 91%). R_f = 0.3 (petroleum ether/EtOAc 4:1). IR (KBr): 3030, 1754, 1680 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.30 (m, 5H), 6.96 (dt, J = 8.52, 2.84 Hz, 1H), 4.42−4.38 (m, 2H), 4.16 (d, J = 13.36 Hz, 1H), 4.05 (d, J = 13.36 Hz, 1H), 3.84−3.76 (m, 1H), 2,87−2.82 (m, 1H), 1.43 (d, J = 6.52 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 138.6, 136.8, 128.9, 128.5, 128.0, 127.8, 65.5, 64.5, 62.7, 25.4, 17.6. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{14}H_{16}ClNNaO_2$ 288.0767, found 288.0768.

(*R*,*E*)-3-(2-(Dibenzylamino)-3-hydroxypropylidene)dihydrofuran-2(3*H*)-one (40). Compound **40** was prepared according to the procedure developed in ref 4. Compound **40** was obtained as a white solid (300 mg, 89% based on 1 mmol of substrate). Mp 139.7−140.5 °C (EtOAc). R_f = 0.3 (petroleum ether/EtOAc 5:1). IR (KBr): 3445, 3025, 1748, 1678 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.28 (m, 10H), 6.91 (d, J = 9.88 Hz, 1H), 4.50−4.30 (m, 2H), 4.02 (d, J = 13.52 Hz, 2H), 3.80−3.75 (m, 1H), 3.75−3.55 (m, 1H), 3.48 (d, J = 13.52 Hz, 2H), 3.50−3.40 (m, 1H), 3.00−2.80 (brs, 1H), 2.80−2,65 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 138.6, 134.1, 130.7, 128.7, 128.7, 127.5, 65.5, 60.3, 59.9, 54.1, 25.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{21}H_{23}NNaO_3$ 360.1576, found 360.1578.

(*2S*,*3S*,*4S*)-1-Benzyl-4-chloro-2-(chloromethyl)-4-(2-hydroxyethyl)-5-oxopyrrolidin-3-yl Benzoate (41). Crystalline solid (316

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mg, 75%), mp 65.5−66.4 °C (EtOAc). R_f = 0.3 (petroleum ether/EtOAc 4:1). IR (KBr): 3445, 3064, 3031, 1715 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 2.96 Hz, 2H), 7.75−7.65 (m, 1H), 7.65−7.49 (m, 2H), 7.49−7.25 (m, 5H), 5.79 (d, J = 7.16 Hz, 1H), 5.13 (d, J = 14.88 Hz, 1H), 4.42 (d, J = 14.92 Hz, 1H), 4.20−4.10 (m, 1H), 4.10−4.00 (m, 1H), 4.00−3.90 (m, 1H), 3.90−3.80 (m, 2H), 3.16 (brs, 1H), 2.34−2.30 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 165.3, 134.9, 134.1, 130.0, 129.2, 128.8, 128.4, 128.4, 128.2, 71.2, 68.9, 59.1, 58.3, 46.1, 41.0, 39.9. HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{21}H_{21}Cl_2NNaO_4$ 444.0745, found 444.0749.

***N*-Butyl-*N*-chlorobutan-1-amine (43) and *N*-Benzylbutan-1-amine (44).** The known compound **42**[40] was transformed into compounds **43** and **44**. The NMR, IR, and HRMS data of **43** and **44** were identical to those reported in the literature.[41,42] Compound **43** (102 mg, 65%): Colorless oil, R_f = 0.7 (petroleum ether). IR (KBr): 2958, 2872, 1466, 1379, 1070 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.93 (t, J = 7.16 Hz, 4H), 1.70−1.60 (m, 4H), 1.45−1.30 (m, 4H), 0.95 (t, J = 7.36 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 64.1, 30.0, 20.0, 13.9. HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_8H_{18}ClNNa$ 186.1025, found 186.1026. Compound **44** (57 mg, 35%): Colorless oil, R_f = 0.3 (petroleum ether/EtOAc 1:1). IR (KBr): 3419, 3074 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40−7.25 (m, 5H), 3.83 (s, 2H), 3.48 (brs, 1H), 2.66 (t, J = 6.84 Hz, 2H), 1.60−1.40 (m, 2H), 1.40−1.25 (m, 2H), 0.93 (t, J = 7.12 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1, 128.5, 127.2, 53.6, 48.7, 31.6, 20.4, 14.0. HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{11}H_{17}NNa$ 186.1259, found 186.1261.

Methyl 2-Oxo-2-phenylacetate (51). The known compound **50**[43] was transformed into the known compound **51**[44] according to the general procedure above. Compound **51** (139 mg, 85%): Yellow oil, R_f = 0.3 (petroleum ether/EtOAc 30:1). IR (KBr): 1741, 1692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 8.48 Hz, 2H), 7.71−7.67 (m, 1H), 7.56−7.52 (m, 2H), 4.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.1, 164.1, 135.0, 132.4, 130.1, 128.9, 52.8. HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_9H_8NaO_3$ 187.0371, found 187.0373.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H NMR and ^{13}C NMR spectra for compounds **4**−**19** and **26**−**51** and copies of 1D and 2D NMR spectra for compounds **20**, **22**−**25**, and **41**. 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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