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Use of Aziridines for the Stereocontrolled Synthesis of (−)-LL-C10037α, (+)-MT35214, and (+)-4-epi-MT35214

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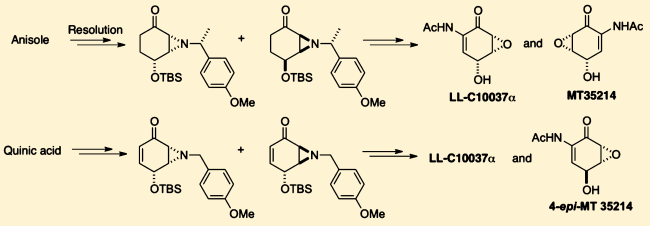
Supporting Information

ABSTRACT: Strategies for the synthesis of the title compounds have been developed using a diastereoselective aziridination reaction of 4-O-substituted cyclohexenones. Aziridination using a chiral amine permitted resolution of a 4-hydroxycyclohexane derivative, and this resulted in the synthesis of both enantiomers of the title compound. Alternatively, the chiral 4-hydroxycyclohexenone starting material was derived from quinic acid. In both cases stereoselective epoxidation and opening of the aziridine ring with hydrazoic acid afforded the 2-azidocyclohexenone, which was transformed to the 2-acetamido group present in the natural product.



INTRODUCTION

Antibiotics LL-C10037α (**1**) and MM 14201 (**2**) (Figure 1) are representative examples of small metabolites with structural similarities to the mC_7N unit of the manumycin group of compounds.[1] LL-C10037α (**1**) is an antitumor antibiotic isolated from the fermentation filtrate of *Streptomyces* LL-C10037 by Lee and co-workers,[2] for which the correct structural assignment[3] and absolute stereochemistry[4] were established by Gould and collaborators. MM 14201 (**2**) is an antibiotic with a broad antibacterial spectrum produced by *Streptomyces* sp. NCIB 11813, which due to its unstable nature was isolated as the acetamide MT 35214 (**3**).[5] The manumycins show a variety of biological activities, including antibiotic, cytotoxic, and insecticidal properties, as well as a number of enzyme inhibition activities, the most important of which is the inhibition of the Ras farnesyltransferase, an enzyme linked to many human cancers.[4] Ansamycin antibiotics, such as Rifamycin B, Mitomycin C, and Ansamitocin, also present a mC_7N unit[5] even though it is not in the form of an amido epoxycyclohexenone core, indicating that both classes of compounds are derived from the shikimate pathway.[5−7]

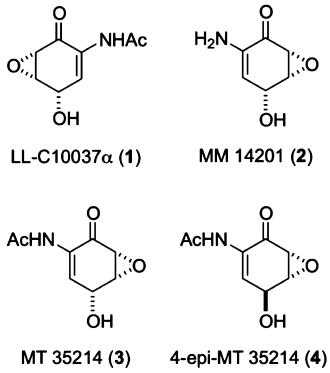


Figure 1. Antibiotics LL-C10037α and MM14201 and their stereoisomers.

Due to these important biological activities and the scarcity of the natural compounds in nature, several syntheses have been developed. The syntheses in the racemic form of enantiomers **1** and **3** as well as its 4-epimer **4** have been reported by Wipf's[6,7] and Taylor's[8] groups. By a similar procedure using a chiral acetal protecting group, Wipf et al.[7] synthesized the optically active LL-C10037α (**1**), whereas Johnson[9] and Altenbach[10] reported the enantioselective synthesis of **1** from benzoquinone by enzymatic resolution of a racemic intermediate. An asymmetric synthesis of MT 35214 (**3**) from 2,5-dimethoxyaniline was achieved by Taylor and co-workers[11] employing a chiral phase-transfer catalyst to effect an enantioselective epoxidation. All published stereoselective syntheses started from the achiral compounds 2,5-dimethoxyaniline (Wipf[7] and Taylor[11]) and benzoquinone (Johnson[9] and Altenbach[10]); thus, a resolution step was necessary during these syntheses.

As part of our studies on 4-hydroxy-α-halocycloenones, we report herein our approach to the synthesis of (−)-LL-C10037α (**1**) and (+)-MT 35214 (**3**) in optically active form starting from racemic 4-TBSO-2-iodocyclohexenone, via resolution by an aziridination protocol. We also report the asymmetric synthesis of the (+)-4-epimer MT 35214 (**4**) from (−)-quinic acid.

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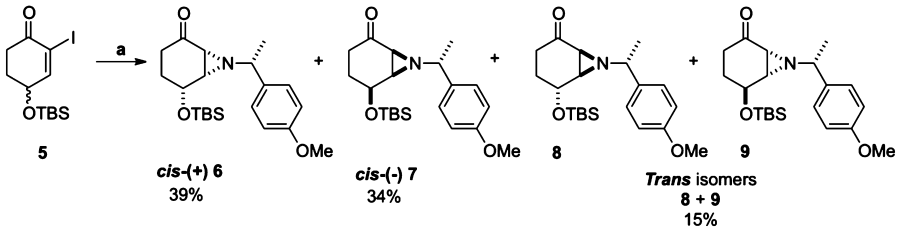
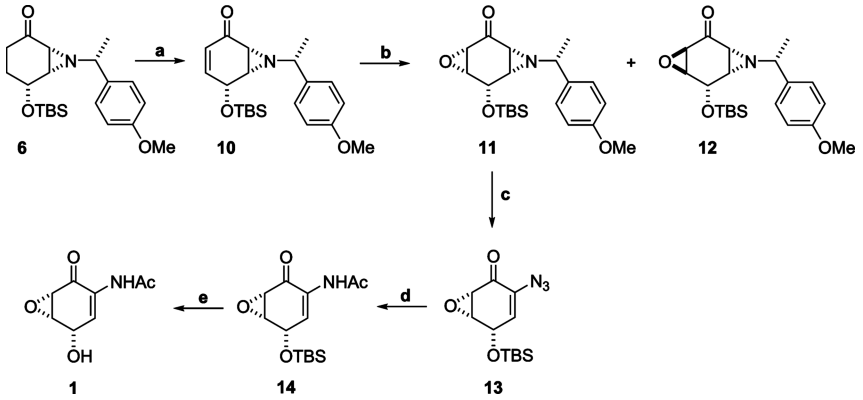
Scheme 1. [a]



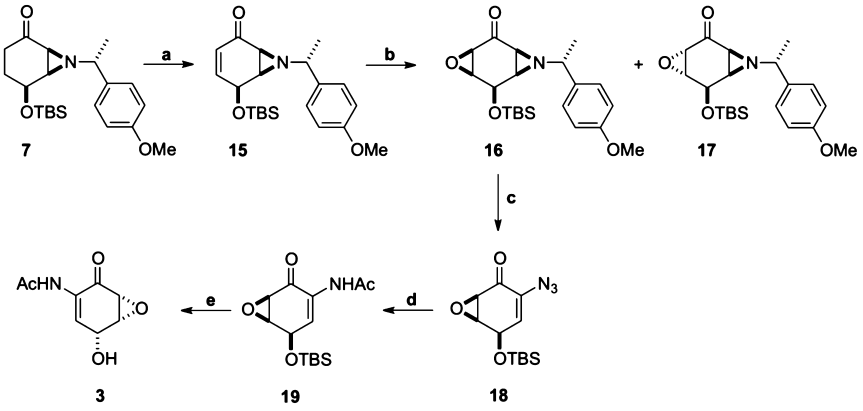
[a]Legend: (a) toluene, 1,10-phenanthroline, Cs_2CO_3, (*R*)-(+)-4-OMe-α-MeBnNH$_2$, room temperature, 88%, *cis*:*trans* 5:1.

Scheme 2. [a]



[a]Legend: (a) THF, LDA, PhSCl*N*t*Bu*, −78 °C, 73%; (b) THF, H_2O_2, Triton B, 0 °C, 87%, *syn*:*anti* 4:1; (c) toluene, HN_3, room temperature, 89%; (d) THF, Ph_3P, H_2O, Ac_2O, room temperature, 89%; (e) THF, H_2O, TBAF, room temperature, 93%.

Scheme 3. [a]



[a]Legend: (a) THF, LDA, PhSCl*N*t*Bu*, −78 °C, 76%; (b) THF, H_2O_2, Triton B, 0 °C, 84%, *syn*:*anti* 5:1; (c) toluene, HN_3, room temperature, 74%; (d) THF, Ph_3P, H_2O, Ac_2O, room temperature, 73%; (e) THF, H_2O, TBAF, room temperature, 84%.

RESULTS AND DISCUSSION

Synthesis of (−)-LL-C10037α and (+)-MT 35214 from Racemic 4-TBSO-2-iodocyclohexenone. Starting from *rac*-4-TBSO-2-iodocyclohexenone[12] ((±)-**5**), the strategy used comprised the following steps: (i) resolution via an aziridination reaction with a chiral amine,[13] (ii) formation of a new α,β-unsaturated system, (iii) incorporation of the epoxide ring, (iv) formation of an α-azidoenone, (v) formation of the enamide, and (vi) deprotection.

The resolution of (±)-**5** was achieved via a Gabriel−Cromwell aziridination reaction[14] with optically pure (*R*)-(+)-4-methoxy-α-methylbenzylamine. Carrying out the reaction at room temperature for 17 h afforded a 5:1 mixture of *cis* and *trans* isomers in 88% yield. Chromatographic separation afforded *cis*-aziridine ***cis*-(+)-6** ($[\alpha]_D^{20}$ = +107.3 (*c* 2.44, CH_2Cl_2)), *cis*-aziridine ***cis*-(−)-7** ($[\alpha]_D^{20}$ = −64.1 (*c* 3.05, CH_2Cl_2)), and an inseparable mixture of *trans*-aziridines **8** and **9** (Scheme 1). We believe that the *cis* stereoselectivity of this reaction is due to hydrogen bonding between the amine proton and the adjacent ether or hydroxyl group during the Michael addition. This is the first reaction to occur and determines the relative stereochemistry of the aziridine formed. Under these conditions the amine is not deprotonated. However, tosylamide under these conditions adds to form the *trans*-aziridine, and here we assume the formation of an anion that does not hydrogen bond to the adjacent ether or alcohol and hence the sterically controlled product is formed. A study of this reaction

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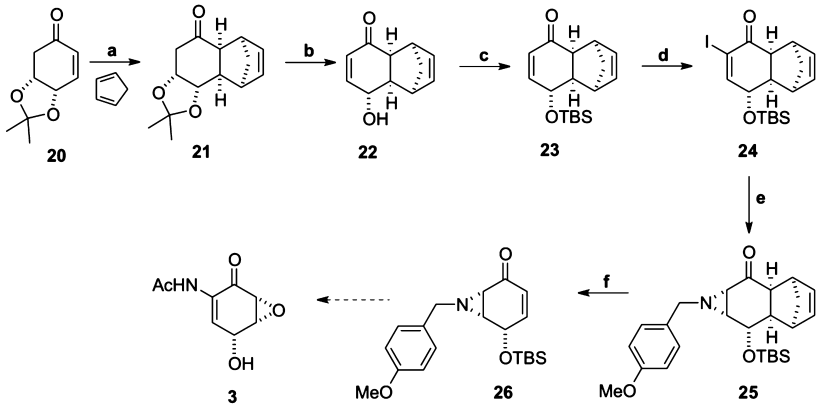
Scheme 4. [a]



[a]Legend: (a) $AlCl_3$, toluene, −78 °C, 88%; (b) THF, NaOH 0.5 M, 0 °C, 75%; (c) CH_2Cl_2, DIPEA, TBSCl, DMAP, room temperature, 98%; (d) Py:CCl_4 1:1, I_2, DMAP, room temperature, 94%; (e) toluene, 1,10-phen, Cs_2CO_3, 4-OMeBnNH$_2$, room temperature, 92%; (f) Ph_2O, reflux, 91%.

under different conditions has been carried out and will be published separately.

With the optically pure *cis* diastereomers separated, the subsequent steps of our strategy were carried out using *cis*-aziridine ***cis*-(+)-6** (Scheme 2) and *cis*-aziridine ***cis*-(−)-7** (Scheme 3).

A key step in the strategy was the formation of the enone ***cis*-(+)-10** (Scheme 2). Although several oxidative elimination protocols were attempted, most were unsuccessful and a little-used method discovered by Mukaiyama et al.[15] gave excellent results. Thus reaction of the enolate of ketone ***cis*-(+)-6** with *N*-*tert*-butyl phenylsulfinimidoyl chloride followed by a basic workup[15] afforded directly the enone ***cis*-(+)-10** ($[\alpha]_D^{20}$ = +103.8 (*c* 1.05, CH_2Cl_2)), in 73% yield.

Epoxidation of the *cis*-aziridine ***cis*-(+)-10** with hydrogen peroxide, in the presence of Triton B, afforded *syn*-epoxy-*cis*-aziridine **11** ($[\alpha]_D^{20}$ = +47.9 (*c* 1.49, CH_2Cl_2)) and *anti*-epoxy-*cis*-aziridine **12** ($[\alpha]_D^{20}$ = +109.7 (*c* 2.38, CH_2Cl_2)) in 87% total yield and in a 4:1 ratio. Under the same conditions but in the absence of the aziridine ring, the peroxide approached the enone from the face opposite to the OTBS group, affording exclusively the *trans* diastereomer.[16] Therefore, formation of the *syn*-epoxy-*cis*-aziridine **11** in a 4:1 ratio provided good evidence for the stereodirecting effect of the aziridine ring on the diastereofacial selectivity of the epoxidation. The directing ability of an aziridine group during the epoxidation of adjacent double bonds has been demonstrated previously in the synthesis of (+)-Bromoxone.[17] In this work it was shown that the stereodirecting effect of the aziridine ring was much stronger than the effect of a free hydroxyl group for the stereochemical outcome of the epoxidation reaction and that the influence of the bulky silyl group was steric.

For the formation of the α-azidoenone, an acid-catalyzed aziridine ring cleavage−elimination reaction was used.[17] Treatment of *syn*-epoxy-*cis*-aziridine **11** with HN_3 at room temperature for 20 min gave *syn*-epoxy-azide **13** ($[\alpha]_D^{20}$ = −107.9 (*c* 0.82, CH_2Cl_2)) in 89% yield.

The conversion of *syn*-epoxy-azide **13** into *syn*-epoxy-acetamide **14** ($[\alpha]_D^{20}$ = −110.5 (*c* 1.69, CH_2Cl_2)) was achieved by *N*-acetylation, with acetic anhydride, during the Staudinger reduction of the azido group, with triphenylphosphine in the presence of water,[18] at room temperature in 89% yield.

Finally, a controlled cleavage of the TBS group of *syn*-epoxy-acetamide **14** by the addition of a small amount of water[19] before the addition of the TBAF solution afforded (−)-LL-C10037α (**1**), in 93% yield, after 15 min at room temperature.

The specific rotations obtained for (−)-LL-C10037α (**1**), $[\alpha]_D^{20}$ = −199.1 (*c* 0.11, CH_2Cl_2) and $[\alpha]_D^{20}$ = −238.8 (*c* 0.08, MeOH), were in accord with those reported, $[\alpha]_D^{20}$ = −202 (*c* 0.334, MeOH),[4] $[\alpha]_D^{20}$ = −201 (*c* 0.34, MeOH),[9] and $[\alpha]_D^{20}$ = −194 (*c* 1.1, MeOH),[10] and the spectroscopic data were identical with those previously described.[5]

The synthesis of MT 35214 (**3**), the enantiomer of LL-C10037α (**1**), was accomplished from the *cis*-aziridine ***cis*-(−)-7** (Scheme 3). The same strategy described in Scheme 2 was followed, but in this case the aziridine ring of ***cis*-(−)-7**, being on the opposite plane of the molecule in comparison to ***cis*-(+)-6**, directed the epoxide formation to afford the correct configuration present in the final product **3**.

Dehydrogenation (LDA, PhSClN*t*Bu, −78 °C, 76%) of *cis*-aziridine ***cis*-(−)-7** afforded the α,β-enone ***cis*-(−)-15** ($[\alpha]_D^{20}$ = −49.1 (*c* 0.66, CH_2Cl_2)) in 76% yield. Epoxidation (H_2O_2, Triton B, 84%) afforeded *syn*-epoxy-*cis*-aziridine **16** ($[\alpha]_D^{20}$ = +13.4 (*c* 1.51, CH_2Cl_2)) and *anti*-epoxy-*cis*-aziridine **17** ($[\alpha]_D^{20}$ = −62.6 (*c* 1.0, CH_2Cl_2)) in a 5:1 ratio.

Aziridine ring cleavage of *syn*-epoxy-*cis*-aziridine **16**, with HN_3 at room temperature for 20 min, gave *syn*-epoxy-azide **18** ($[\alpha]_D^{20}$ = +111.2 (*c* 1.03, CH_2Cl_2)) in 74% yield, that after Staudinger reduction and *in situ* *N*-acetylation (Ph_3P, H_2O, Ac_2O) afforded *syn*-epoxy-acetamide **19** ($[\alpha]_D^{20}$ = +119.6 (*c* 1.21, CH_2Cl_2)) in 74% yield.

The spectroscopic data for compounds **18** ($[\alpha]_D^{20}$ = +111.2 (*c* 1.03, CH_2Cl_2)) and **19** ($[\alpha]_D^{20}$ = +119.6 (*c* 1.21, CH_2Cl_2)) were identical with those for *syn*-epoxy-azide **13** ($[\alpha]_D^{20}$ = −107.9 (*c* 0.82, CH_2Cl_2)) and *syn*-epoxy-acetamide **14** ($[\alpha]_D^{20}$ = −110.5 (*c* 1.69, CH_2Cl_2)), and their specific rotations confirmed the enantiomeric relationship.

Desilylation (H_2O, TBAF) of *syn*-epoxy-acetamide **19** afforded (+)-MT 35214 (**3**) in 83% yield, which had spectroscopic data identical with those published.[5] The obtained specific rotation, $[\alpha]_D^{20}$ = +225.0 (*c* 0.02, MeOH), indicated that it forms an enantiomeric pair with (−)-LL-C10037α (**1**) and was comparable with the reported value, $[\alpha]_D^{20}$ = +186.7 (*c* 0.35, MeOH).[11]

Synthesis of (+)-MT 35214 Precursor and 4-epi-MT 35214 from (−)-Quinic Acid Derivatives. *(+)-MT 35214 Precursor.* Starting from the (−)-quinic acid derived 4,5-isopropylidene-cyclohexenone[19,20] **20**, we were able to obtain

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the (+)-MT 35214 precursor ***cis*-(−)-26** by a different approach (Scheme 4). Quinic acid is a chiral, abundant, and relatively inexpensive starting material, isolated from the plant species *Cinchona*. It has the advantage of being readily available and suitably functionalized for conversion to a wide range of interesting structures, particularly polysubsituted cyclohexanes. To protect the double bond of enone **20**, a Diels−Alder reaction with cyclopentadiene was used. The stereochemistry of the cycloadduct obtained was expected to influence the stereochemical outcome of the aziridination. A retro-Diels−Alder reaction would re-form the double bond.

The Diels−Alder reaction of enone **20** with cyclopentadiene, in the presence of $AlCl_3$ in toluene at −78 °C, proceeded smoothly and cleanly in a completely diastereofacial and *endo*-selective manner to provide the correspondent cycloadduct **21** ($[\alpha]_D^{20}$ = +36.9 (*c* 3.24, CH_2Cl_2)) in 88% yield. In accordance with the results reported by Danishefsky and co-workers,[21] cycloadduct **21** corresponds to the product resulting from addition to the less hindered face of the bicyclic system **20**.

Treatment of *trans,endo*-norbornene-acetonide **21** with a catalytic amount of aqueous NaOH solution in THF[19] afforded *trans,endo*-norbornene-hydroxy enone **22** as a white solid ($[\alpha]_D^{20}$ = +36.5 (*c* 2.31, CH_2Cl_2)) in 75% yield. The measured physical properties of *trans,endo*-**22** were different from those reported for the *cis,endo* isomer,[22,23] providing further evidence for the proposed stereochemistry.

The following reactions were straightforward. Protection of the free hydroxyl group of enone **22** with TBSCl, in the presence of DIPEA and catalytic DMAP in CH_2Cl_2, gave silyloxy **23** ($[\alpha]_D^{20}$ = −49.5 (*c* 2.13, CH_2Cl_2)) in 98% yield. Treatment with iodine, in a 1:1 mixture of pyridine and CCl_4,[17] afforded α-iodoenone **24** ($[\alpha]_D^{20}$ = −79.2 (*c* 3.04, CH_2Cl_2)) in 94% yield. Aziridination of α-iodoenone **24** in toluene with 4-methoxybenzylamine, in the presence of 1,10-phenanthroline and Cs_2CO_3 at room temperature, occurred at the convex face to provide only *cis*-aziridine ***cis*-(−)-25** ($[\alpha]_D^{20}$ = −62.3 (*c* 0.87, CH_2Cl_2)) in 92% yield.

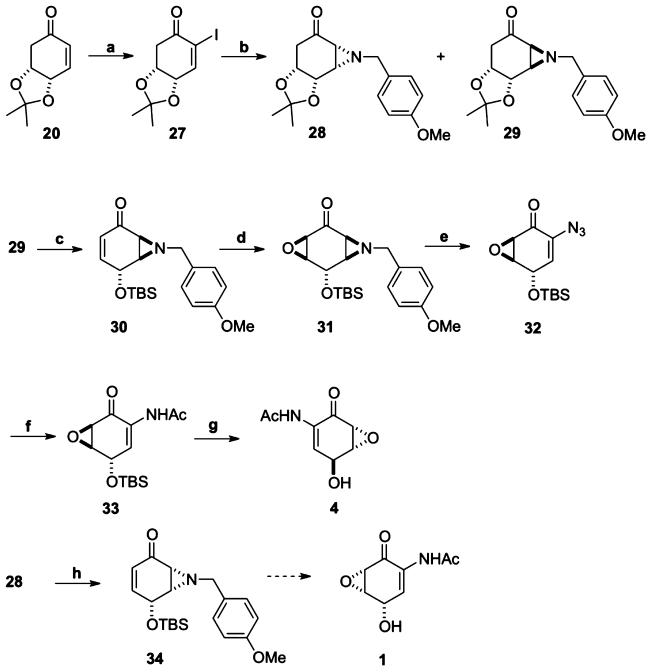
The retro-Diels−Alder reaction of *cis*-aziridine-*trans*-norbornene **25** proceeded effectively, by thermolysis in diphenyl ether under reflux, to afford *cis*-aziridine-enone ***cis*-(−)-26** ($[\alpha]_D^{20}$ = −139.2 (*c* 0.97, CH_2Cl_2)) in 91% yield, demonstrating the stability of the aziridine ring under these conditions. Following the same synthetic strategy described in Scheme 3 from aziridine ***cis*-(-) 15**, (+)-MT 35214 (**3**) should be obtained.

(−)-LL-C10037α Precursor and (+)-4-epi-MT 35214. Derivatisation of 4,5-isopropylidene-cyclohexenone **20** also enabled us to obtain the (−)-LL-C10037α precursor ***cis*-(+) 34** and (+)-4-epi-MT 35214 (**4**) (Scheme 5).

The first part of the synthesis (steps a−d) followed previous work by our group, in which the major diastereomer **29** (**28**:**29** = 1:4) led to *anti*-epoxy-*trans*-aziridine **31**, an intermediate in the stereoselective synthesis of natural product (+)-bromoxone.[17]

The acid-catalyzed regioselective aziridine ring cleavage of **31**, with a 2 M HN_3 solution for 12 h at 60 °C, afforded α-azidoenone **32** ($[\alpha]_D^{20}$ = +171.5 (*c* 0.2, CH_2Cl_2)) in 78% yield. N-acetylation during the Staudinger azide reduction (THF, Ph_3P, DMAP, Ac_2O, room temperature) of α-azidoenone **32** gave α-enamide **33** in 82% yield. Desilylation (CH_3CN, HF, room temperature) afforded *trans*-epoxy alcohol **4** ($[\alpha]_D^{20}$ = +72 (*c* 0.05; MeOH)) in 80% yield. The spectroscopic data of **4** were in accord with those reported[6] for racemic 4-epi-MT 35214.

Scheme 5. [a]



[a]Legend: (a) Et_2O:Py (1:1), I_2, DMAP, room temperature, 85%; (b) toluene, 1,10-phenanthroline, Cs_2CO_3, 4-MeOBnNH$_2$, 95 °C, 84%, *cis*:*trans* 1:4; (c) (i) THF, NaOH 0.5 M, 0 °C, (ii) CH_2Cl_2, DIPEA, TBSCl, DMAP, room temperature, 80%; (d) THF, H_2O_2, Triton B, 0 °C, 90%; (e) HN_3, benzene, 60 °C, 78%; (f) THF, PPh_3, Ac_2O, DMAP, room temperature, 82%; (g) CH_3CN, HF, room temperature, 80%; (h) (i) THF, NaOH 0.5 M, 0 °C, (ii) CH_2Cl_2, DIPEA, TBSCl, DMAP, room temperature, 69%.

Treatment of the minor diastereomer *cis*-aziridine **28**[17] in THF with aqueous NaOH, followed by protection of the allylic alcohol in CH_2Cl_2 with TBSCl, in the presence of DIPEA and DMAP, afforded *cis*-aziridine-enone ***cis*-(+)-34** ($[\alpha]_D^{20}$ = +149.2 (*c* 0.63; CH_2Cl_2)) in 69% yield. NMR data and specific rotation of ***cis*-(+)-34** showed that it forms an enantiomeric pair with *cis*-aziridine-enone ***cis*-(−)-26** and therefore should provide (−)-LL-C10037α.

CONCLUSION

A stereoselective synthesis of the enantiopure target compounds (−)-LL-C10037α (**1**) and (+)-MT 35214 (**3**) from (±)-4-TBSO-2-iodocyclohexenone ((±)-**5**) has been achieved, as have the syntheses of (+)-4-epi-MT 35214 (**4**) from (−)-quinic acid derivatives.

Separation of (±)-**5** via the aziridination protocol allowed us to obtain both enantiomers (−)-LL-C10037α (**1**) and (+)-MT 35214 (**3**) along with all intermediates in optically pure form. The presence of the aziridine nitrogen atom was also shown to be important in the sequence of reactions, due to its stereodirecting effect on the epoxidation reaction. It allowed the formation of an α-azidoenone via acid-catalyzed regioselective ring cleavage followed by spontaneous elimination of the amine moiety.

The (+)-MT 35214 precursor **26** was obtained from the quinic acid derivative **20** by combining a stereoselective Diels−Alder/aziridination/retro-Diels−Alder sequence. Applying our strategy to the major diastereomer of the aziridination of the quinic acid derivative **27** afforded (+)-4-epi-MT 35214 (**4**),

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whereas the minor diastereomer led to the (−)-LL-C10037α precursor **34**.

EXPERIMENTAL SECTION

General Considerations. When required, solvents and reagents were purified or dried according to standard procedures[24] prior to use. All commercial reagents were purchased from Sigma-Aldrich. Reactions requiring anhydrous conditions were performed under an argon atmosphere. After workup the organic layers were dried over anhydrous $MgSO_4$. Purification was performed on silica gel 60 for flash chromatography (230−400 mesh) or on silica gel 60 GF_{254} for preparative TLC. NMR chemical shifts are reported in ppm downfield from TMS or using the residual solvent peak as reference. Peak assignments were based on COSY and HMQC experiments. The NMR spectra were measured on a Bruker Avance II+ 400 MHz instrument, specific rotations were obtained with a Perkin-Elmer 241 automatic polarimeter, infrared spectra were recorded using a Mattson Research Series FTIR, and melting points were determined on a Buchi B-540 apparatus.

Abbreviations: 1,10-phen, 1,10-phenanthroline; Cs_2CO_3, cesium carbonate; (*R*)-(+)-4-OMe-α-MeBnNH$_2$, (*R*)-(+)-4-methoxy-α-methylbenzylamine; THF, tetrahydrofuran; LDA, lithium diisopropylamide; PhSClN*t*Bu, *N*-*tert*-butyl phenylsulfinimidoyl chloride; H_2O_2, hydrogen peroxide; Triton B, benzyltrimethylammonium hydroxide; HN_3, hydrazoic acid; Ph_3P, triphenylphosphine; Ac_2O, acetic anhydride; TBAF, tetrabutylammonium fluoride; $AlCl_3$, aluminum chloride; NaOH, sodium hydroxide; CH_2Cl_2, dichloromethane; DIPEA, diisopropylethylamine; TBDMSCl, *tert*-butyldimethylsilyl chloride; DMAP, 4-(dimethylamino)pyridine; Py, pyridine; CCl_4, carbon tetrachloride; I_2, iodine; Ph_2O, diphenyl ether; Et_2O, diethyl ether; CH_3CN, acetonitrile; HF, hydrofluoric acid.

(1*R*,5*R*,6*S*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(1*R*)-1-(4-methoxyphenyl)ethyl]-7-azabicyclo[4.1.0]heptan-2-one (6), (1*S*,5*S*,6*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(1*R*)-1-(4-Methoxyphenyl)ethyl]-7-azabicyclo[4.1.0]heptan-2-one (7), (1*S*,5*R*,6*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(1*R*)-1-(4-methoxyphenyl)ethyl]-7-azabicyclo[4.1.0]heptan-2-one (8), and (1*R*,5*S*,6*S*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(1*R*)-1-(4-methoxyphenyl)ethyl]-7-azabicyclo[4.1.0]heptan-2-one (9). *At 96 °C.* To a solution of *rac*-4-TBSO-2-iodocyclohexenone[12] ((±)-**5**; 0.123 g, 0.35 mmol) in toluene (1 mL) were added 1,10-phenanthroline (0.063 g, 0.35 mmol), Cs_2CO_3 (0.126 g, 0.39 mmol), and (*R*)-(+)-4-methoxy-α-methylbenzylamine (0.078 mL, 0.53 mmol). The reaction mixture was stirred for 1 h at 96 °C and after rapid cooling was quenched with water and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated. The residue was purified by preparative TLC (hexane/EtOAc 9/1), affording, in ascending order of polarity, an inseparable mixture of *trans*-aziridines **8** and **9** as a colorless oil (0.051 g, 39%), *cis*-aziridine **6** as a colorless oil (0.030 g, 23%), and *cis*-aziridine **7** as a colorless oil (0.026 g, 20%).

At Room Temperature. To a solution of *rac*-4-TBSO-2-iodocyclohexenone[12] ((±)-**5**; 1.320 g, 3.75 mmol) in toluene (10 mL) were added 1,10-phenanthroline (0.676 g, 3.75 mmol), Cs_2CO_3 (1.344 g, 4.13 mmol), and (*R*)-(+)-4-methoxy-α-methylbenzylamine (0.831 mL, 5.63 mmol). After it was stirred for 17 h at room temperature, the reaction mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 9/1), a mixture of *trans*-aziridines **8** and **9** eluting first as a colorless oil (0.215 g, 15%), followed by *cis*-aziridine **6** as a colorless oil (0.554 g, 39%), and finally *cis*-aziridine **7** as a colorless oil (0.482 g, 34%).

cis-Aziridine ***6***. R_f = 0.61 (hexane:EtOAc 8:2). $[\alpha]_D^{20}$ = +107.3 (*c* 2.44, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (2H, d, *J* = 8.4 Hz, Ar-H), 6.83 (2H, d, *J* = 8.4 Hz, Ar-H), 4.00 (1H, ddd, *J* = 10.8 Hz, *J* = 4.8 Hz, *J* = 1.6 Hz, H-5), 3.78 (3H, s, OMe), 2.67 (1H, q, *J* = 6.4 Hz, H-8), 2.45 (1H, ddd, *J* = 18.4 Hz, *J* = 5.4 Hz, *J* = 1.8 Hz, H-3), 2.28−2.19 (1H, m, H-4), 2.17 (1H, br d, *J* = 6.0 Hz, H-6), 2.13 (1H, d, *J* = 6.4 Hz, H-1), 2.07 (1H, ddd, *J* = 18.6 Hz, *J* = 12.6 Hz, *J* = 6.4 Hz, H-3), 1.61−1.55 (1H, m, H-4), 1.40 (3H, d, *J* = 6.4 Hz, CH_3), 0.71 [9H, s, $(CH_3)_3$C-Si], −0.03 (3H, s, CH_3-Si), −0.15 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.0 (C═O), 158.6 (Ar-C), 135.9 (Ar-C), 127.8 (Ar-C), 113.6 (Ar-C), 68.0 (C-8), 67.6 (C-5), 55.2 (OMe), 47.2 (C-1), 46.8 (C-6), 35.6 (C-3), 25.8 (C-4), 25.6 [$(CH_3)_3$C-Si], 23.7 (CH_3), 17.8 [$(CH_3)_3$-C-Si], −4.8 (CH_3-Si), −5.0 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1711 (C═O) cm^{-1}. Anal. Calcd for $C_{21}H_{33}NO_3Si$: C, 67.16; H, 8.86; N, 3.73. Found: C, 67.35; H, 8.72; N, 3.71.

cis-Aziridine ***7***. R_f = 0.55 (hexane:EtOAc 8:2). $[\alpha]_D^{20}$ = −64.1 (*c* 3.05, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (2H, d, *J* = 8.8 Hz, Ar-H), 6.83 (2H, d, *J* = 8.4 Hz, Ar-H), 4.12 (1H, ddd, *J* = 10.6 Hz, *J* = 5.2 Hz, *J* = 1.8 Hz, H-5), 3.78 (3H, s, OMe), 2.67 (1H, q, *J* = 6.4 Hz, H-8), 2.40 (1H, ddd, *J* = 18.4 Hz, *J* = 5.6 Hz, *J* = 2.0 Hz, H-3), 2.31−2.20 (2H, m, H-4, H-6), 2.07−1.98 (2H, m, H-1, H-3), 1.65−1.59 (1H, m, H-4), 1.42 (3H, d, *J* = 6.4 Hz, CH_3), 0.95 [9H, s, $(CH_3)_3$C-Si], 0.15 (3H, s, CH_3-Si), 0.18 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.5 (C═O), 158.6 (Ar-C), 135.8 (Ar-C-1), 127.5 (Ar-C), 113.7 (Ar-C), 67.7 (C-8), 67.6 (C-5), 55.2 (OMe), 47.8 (C-6), 46.7 (C-1), 35.4 (C-3), 25.9 (C-5), 25.8 [$(CH_3)_3$C-Si], 23.8 (CH_3), 18.1 [$(CH_3)_3$C-Si], −4.6 (CH_3-Si), −4.7 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1711 (C═O) cm^{-1}. HRMS (ESI-FIA-TOF): *m*/*z* calcd for $C_{21}H_{34}NO_3Si$, 376.2308; found, 376.2287 (M + H).

Inseparable Mixture of trans-Aziridines ***8*** *and* ***9***. R_f = 0.67 (hexane:EtOAc 8:2). FTIR (neat): ν_{max} 1709 (C═O) cm^{-1}. Anal. Calcd for $C_{21}H_{33}NO_3Si$: C, 67.16; H, 8.86; N, 3.73. Found: C, 67.24; H, 8.86; N, 3.71.

trans-Aziridine ***8***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (2H, d, *J* = 8.8 Hz, Ar-H), 6.82 (2H, d, *J* = 8.8 Hz, Ar-H), 4.41−4.39 (1H, m, H-5), 3.76 (3H, s, OMe), 2.69 (1H, q, *J* = 6.6 Hz, H-8), 2.31−2.25 (6H, m, 2xH-3, H-4, H-6 of **8**, and 2xH-3 of **9**), 2.05 (1H, d, *J* = 6.0 Hz, H-1), 1.65−1.56 (2H, m, H-4′ of **8**, and H-4′ of **9**), 1.38 (3H, d, *J* = 6.8 Hz, CH_3), 0.90 [9H, s, $(CH_3)_3$C-Si], 0.13 (3H, s, CH_3-Si), 0.10 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.6 (C═O), 158.7 (Ar-C), 136.6 (Ar-C-1), 127.4 (Ar-C), 113.80 (Ar-C), 67.7 (C-8), 66.1 (C-5), 55.19 (OMe), 48.7 (C-6), 45.9 (C-1), 32.2 (C-3 of **8**, and C-3 of **9**), 27.4 (C-4), 25.8 [$(CH_3)_3$C-Si], 23.8 (CH_3), 18.1 [$(CH_3)_3$C-Si], −4.6 (CH_3-Si), −4.7 (CH_3-Si) ppm.

trans-Aziridine ***9***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (2H, d, *J* = 8.8 Hz, Ar-H), 6.87 (2H, d, *J* = 8.8 Hz, Ar-H), 4.10 (1H, dt, *J* = 4.0 Hz, *J* = *J* = 2.8 Hz, H-5), 3.80 (3H, s, OMe), 2.64 (1H, q, *J* = 6.6 Hz, H-8), 2.31−2.25 (6H, m, 2 × H-3 of **9**, and 2 × H-3, H-4, H-6 of **8**), 2.18−2.13 (3H, m, H-1, H-4, H-6), 1.65−1.56 (2H, m, H-4′ of **9**, and H-4′ of **8**), 1.35 (3H, d, *J* = 6.4 Hz, CH_3), 0.82 [9H, s, $(CH_3)_3$C-Si], −0.03 (3H, s, CH_3-Si), −0.04 (3H, s, CH_3−Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.9 (C═O), 158.8 (Ar-C), 136.3 (Ar-C-1), 127.5 (Ar-C), 113.84 (Ar-C), 68.1 (C-8), 65.5 (C-5), 55.24 (OMe), 48.0 (C-6), 46.5 (C-1), 32.2 (C-3 of **9**, and C-3 of **8**), 27.1 (C-4), 25.7 [$(CH_3)_3$C-Si], 23.4 (CH_3), 18.0 [$(CH_3)_3$C-Si], −4.8 (CH_3-Si), −4.9 (CH_3-Si) ppm.

(1*R*,5*R*,6*S*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(1*R*)-1-(4-methoxyphenyl)ethyl]-7-azabicyclo[4.1.0]hept-3-en-2-one (10). To a solution of LDA (prepared at 0 °C from *n*-BuLi (0.806 mL, 1.6 M in hexane, 1.29 mmol) and DIPA (0.217 mL, 1.55 mmol) in THF (2 mL)) cooled to −78 °C was added a solution of ketone **6** (0.385 g, 1.03 mmol) in THF (3 mL). After 10 min, a solution of PhSClN*t*Bu[25] (0.334 g, 1.55 mmol) in THF (3 mL) was added and stirring continued for 3 h at this temperature. The reaction mixture was quenched with $NaHCO_3$ saturated solution and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated. Purification by flash chromatography (hexane:EtOAc 9:1) yielded enone **10** as a viscous oil (0.280 g, 73%). $[\alpha]_D^{20}$ = +103.8 (*c* 1.05, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (2H, d, *J* = 8.4 Hz, Ar-H), 6.83 (2H, d, *J* = 8.8 Hz, Ar-H), 6.33 (1H, dt, *J* = 10.4 Hz, *J* = 2.4 Hz, H-4), 5.81 (1H, dt, *J* = 10.8 Hz, *J* = 2.0 Hz, H-3), 4.59 (1H, dt, *J* = 4.4 Hz, *J* = 2.0 Hz, H-5), 3.77 (3H, s, OMe), 2.70 (1H, q, *J* = 6.4 Hz, H-8), 2.37 (1H, ddd, *J* = 6.4 Hz, *J* = 4.2 Hz, *J* = 2.2 Hz, H-6), 2.24 (1H, dd, *J* = 6.2 Hz, *J* = 1.8 Hz, H-1), 1.43 (3H, d, *J* = 6.4 Hz, CH_3), 0.74 [9H, s, $(CH_3)_3$C-Si], −0.01 (3H, s, CH_3-Si), −0.18 (3H, s,

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CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.1 (C═O), 158.8 (Ar-C), 148.3 (C-4), 135.3 (Ar-C-1), 128.2 (Ar-C), 125.5 (C-3), 113.8 (Ar-C), 68.6 (C-8), 65.7 (C-5), 55.2 (OMe), 44.3 (C-1), 42.5 (C-6), 25.7 [$(CH_3)_3$C-Si], 23.5 (CH_3), 18.1 [$(CH_3)_3$C-Si], −5.0 (CH_3-Si), −5.1 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1685 (C═O) cm^{-1}. HRMS (ESI-FIA-TOF): m/z calcd for $C_{21}H_{31}NO_3SiNa$, 396.1971; found, 396.1960 (M + Na).

(1*R*,3*S*,5*R*,6*S*,7*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-8-[(1*R*)-1-(4-methoxyphenyl)ethyl]-4-oxa-8-azatricyclo[5.1.0.0^{3,5}]octan-2-one (11) and (1*R*,3*R*,5*S*,6*S*,7*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-8-[(1*R*)-1-(4-methoxyphenyl)ethyl]-4-oxa-8-azatricyclo-[5.1.0.0^{3,5}]octan-2-one (12). To a an ice-cooled solution of enone **10** (0.230 g, 0.62 mmol) in THF (2 mL) were added H_2O_2 (0.6 mL, 30 wt.% in water, 5.88 mmol) and Triton B (1 mL, 40 wt.% in methanol, 2.2 mmol). After it was stirred for 30 min at this temperature, the reaction mixture was quenched with NH_4Cl saturated solution and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated. The residue was purified by preparative TLC (hexane:EtOAc 9:1) to yield the less polar *anti*-epoxide **12** as a colorless oil (0.042 g, 17%) and the more polar *syn*-epoxide **11** as a colorless oil (0.170 g, 70%).

*syn-epoxide **11***. R_f = 0.20 (hexane:EtOAc 9:1). $[\alpha]_D^{20}$ = +47.9 (*c* 1.49, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.35 (2H, d, *J* = 8.8 Hz, Ar-H), 6.85 (2H, d, *J* = 8.4 Hz, Ar-H), 4.33 (1H, dd, *J* = 4.2 Hz, *J* = 2.2 Hz, H-6), 3.79 (3H, s, OMe), 3.43 (1H, dt, *J* = 4.0 Hz, *J* = 2.4 Hz, H-5), 3.31 (1H, dd, *J* = 4.0 Hz, *J* = 2.0 Hz, H-3), 2.37 (1H, q, *J* = 6.6 Hz, H-9), 2.26−2.20 (2H, m, H-1, H-7), 1.39 (3H, d, *J* = 6.4 Hz, CH_3), 0.77 [9H, s, $(CH_3)_3$C-Si], 0.02 (3H, s, CH_3-Si), −0.16 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.9 (C═O), 158.7 (Ar-C), 135.3 (Ar-C-1), 128.2 (Ar-C), 113.7 (Ar-C), 70.1 (C-9), 65.6 (C-6), 61.1 (C-5), 55.5 (C-3), 55.2 (OMe), 49.3 (C-7), 46.3 (C-1), 25.7 [$(CH_3)_3$C-Si], 23.6 (CH_3), 18.1 [$(CH_3)_3$C-Si], −4.91 (CH_3-Si), −4.95 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1699 (C═O) cm^{-1}. HRMS (ESI-FIA-TOF): m/z calcd for $C_{21}H_{31}NO_4SiNa$, 412.1920; found, 412.1917 (M + Na).

*anti-Epoxide **12***. R_f = 0.34 (hexane:EtOAc 9:1). $[\alpha]_D^{20}$ = +109.7 (*c* 2.38, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.26 (2H, d, *J* = 8.4 Hz, Ar-H), 6.84 (2H, d, *J* = 8.4 Hz, Ar-H), 4.25 (1H, d, *J* = 4.0 Hz, H-6), 3.79 (3H, s, OMe), 3.20 (1H, d, *J* = 3.2 Hz, H-3), 3.17 (1H, dd, *J* = 3.2 Hz, *J* = 1.2 Hz, H-5), 2.76 (1H, q, *J* = 6.6 Hz, H-9), 2.19 (1H, ddd, *J* = 5.4 Hz, *J* = 4.4 Hz, *J* = 1.0 Hz, H-7), 2.11 (1H, dd, *J* = 5.6 Hz, *J* = 0.8 Hz, H-1), 1.42 (3H, d, *J* = 6.4 Hz, CH_3), 0.75 [9H, s, $(CH_3)_3$C-Si], 0.00 (3H, s, CH_3-Si), −0.17 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2 (C═O), 159.0 (Ar-C), 134.9 (Ar-C-1), 128.3 (Ar-C), 113.9 (Ar-C), 68.9 (C-9), 64.5 (C-6), 56.5 (C-5), 55.3 (OMe), 51.2 (C-3), 43.0 (C-7), 42.3 (C-1), 25.8 [$(CH_3)_3$C-Si], 23.2 (CH_3), 18.2 [$(CH_3)_3$C-Si], −5.0 (CH_3-Si), −5.1 (CH_3-Si) ppm.

(1*S*,5*S*,6*R*)-3-Azido-5-[(*tert*-butyldimethylsilyl)oxy]-7-oxabicyclo[4.1.0]hept-3-en-2-one (13). A solution of aziridine **11** (0.059 g, 0.152 mmol) in HN_3 (1 mL, 2 M in toluene; HN_3 is volatile and highly toxic) was stirred at room temperature for 20 min. The reaction mixture was cooled to 0 °C, quenched with $NaHCO_3$ saturated solution, and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated. Purification by preparative TLC (hexane:EtOAc 9:1) afforded vinyl azide **13** as a colorless oil (0.038 g, 89%). $[\alpha]_D^{20}$ = −107.9 (*c* 0.82, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 5.85 (1H, t, *J* = 2.6 Hz, H-4), 4.88 (1H, t, *J* = 2.8 Hz, H-5), 3.69 (1H, dt, *J* = 3.6 Hz, *J* = 2.8 Hz, H-6), 3.52 (1H, d, *J* = 4.0 Hz, H-1), 0.95 [9H, s, $(CH_3)_3$C-Si], 0.19 (3H, s, CH_3-Si), 0.18 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.5 (C═O), 131.3 (C-3), 128.1 (C-4), 65.8 (C-5), 54.1 (C-6), 52.8 (C-1), 25.7 [$(CH_3)_3$C-Si], 18.2 [$(CH_3)_3$C-Si], −4.6 (CH_3-Si), −4.7 (CH_3-Si) ppm. FTIR (neat): ν_{max} 2114 (N_3), 1697 (C═O) cm^{-1}. HRMS (ESI-FIA-TOF): m/z calcd for $C_{12}H_{19}N_3O_3SiNa$, 304.1093; found, 304.1078 (M + Na).

***N*-[(1*S*,5*S*,6*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-2-oxo-7-oxabicyclo[4.1.0]hept-3-en-3-yl]acetamide (14).** Ph_3P (0.0307 g, 0.117 mmol) was added to a solution of azide **13** (0.0328 g, 0.117 mmol) in THF (1 mL) at 0 °C. After the mixture was stirred for 2 h at room temperature, H_2O (10 drops, ca. 0.120 mL, 6.7 mmol) was added and stirring continued for 3 h more. Ac_2O (0.0557 mL, 0.585 mmol) was added at 0 °C, and the mixture was again warmed to room temperature. After 5 h, the reaction mixture was neutralized with $NaHCO_3$ saturated solution and extracted with EtOAc. The combined organic layers were dried, filtered, and concentrated. Purification by preparative TLC (hexane:EtOAc 8:2) yielded acetamide **14** as a viscous oil (0.031 mg, 89%). $[\alpha]_D^{20}$ = −110.5 (*c* 1.69, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 (1H, br s, NH), 7.38 (1H, t, *J* = 2.8 Hz, H-4), 4.97 (1H, t, *J* = 3.0 Hz, H-5), 3.72 (1H, dt, *J* = 4.0 Hz, *J* = 2.8 Hz, H-6), 3.52 (1H, d, *J* = 4.0 Hz, H-1), 2.11 (3H, s, CH_3C═O), 0.96 [9H, s, $(CH_3)_3$C-Si], 0.202 (3H, s, CH_3-Si), 0.198 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.8 (C═O enone), 169.1 (C═O acetamide), 127.9 (C-3), 126.2 (C-4), 65.6 (C-5), 53.7 (C-6), 52.0 (C-1), 25.7 [$(CH_3)_3$C-Si], 24.5 (CH_3−C═O), 18.2 [$(CH_3)_3$C-Si], −4.52 (CH_3-Si), −4.54 (CH_3-Si) ppm. FTIR (neat): ν_{max} 3280 (NH), 1674 (C═O) cm^{-1}. HRMS (ESI-FIA-TOF): m/z calcd for $C_{14}H_{23}NO_4SiNa$, 320.1294; found, 320.1277 (M + Na).

(−)-LL-C10037α^2 (1). To a solution of silyl ether **14** (0.0186 g, 0.0625 mmol) in THF (1 mL) at room temperature was added H_2O (2 drops, ca. 0.024 mL, 1.33 mmol) followed by TBAF (0.0625 mL, 1 M in THF, 0.0625 mmol). After 15 min, the reaction mixture was diluted with water (1 mL) and extracted with EtOAc. The combined organic layers were dried, filtered, and concentrated. Purification by preparative TLC (hexane:EtOAc 2:8) yielded the title compound (0.0107 g, 93%), which had spectroscopic data identical with those published.[5] $[\alpha]_D^{20}$ = −199.1 (*c* 0.11, CH_2Cl_2) and $[\alpha]_D^{20}$ = −238.8 (*c* 0.08, MeOH). Lit.: $[\alpha]_D^{20}$ = −202 (*c* 0.334, MeOH),[4] $[\alpha]_D^{20}$ = −201 (*c* 0.34, MeOH),[9] $[\alpha]_D^{20}$ = −194 (*c* 1.1, MeOH).[10] ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (1H, br s, NH), 7.44 (1H, t, *J* = 2.8 Hz, H-4), 4.85 (1H, dt, *J* = 10.0 Hz, *J* = 3.0 Hz, H-5), 3.88 (1H, dd, *J* = 3.4 Hz, *J* = 2.8 Hz, H-6), 3.60 (1H, d, *J* = 4.0 Hz, H-1), 2.40 (1H, d, *J* = 10.4 Hz, OH), 2.13 (3H, s, CH_3−C═O) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.5 (C═O enone), 169.2 (C═O acetamide), 128.4 (C-3), 124.7 (C-4), 64.5 (C-5), 54.1 (C-6), 52.6 (C-1), 24.6 (CH_3−C═O) ppm. FTIR (neat): ν_{max} 3345 (NH and OH), 1655 (C═O) cm^{-1}. MS (calcd for $C_8H_9NO_4$ 183.1): m/z 184.0 (M + 1, 100%).

(1*S*,5*S*,6*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(1*R*)-1-(4-methoxyphenyl)ethyl]-7-azabicyclo[4.1.0]hept-3-en-2-one (15). To a solution of LDA (prepared at 0 °C from *n*-BuLi (0.508 mL, 1.6 M in hexane, 0.81 mmol) and DIPA (0.137 mL, 0.98 mmol) in THF (2 mL)) cooled to −78 °C was added a solution of ketone **7** (0.244 g, 0.66 mmol) in THF (2 mL). After 10 min, a solution of PhSClN*t*Bu[24] (0.210 g, 0.98 mmol) in THF (2 mL) was added and stirring continued for 3 h at this temperature. The reaction mixture was quenched with $NaHCO_3$ saturated solution and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated. Purification by flash chromatography (hexane:EtOAc 9:1) yielded enone **15** as a viscous oil (0.185 g, 76%). $[\alpha]_D^{20}$ = −49.1 (*c* 0.66, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.20 (2H, d, *J* = 8.8 Hz, Ar-H), 6.81 (2H, d, *J* = 8.8 Hz, Ar-H), 6.37 (1H, dt, *J* = 10.4 Hz, *J* = 2.2 Hz, H-4), 5.77 (1H, dt, *J* = 10.8 Hz, *J* = 1.8 Hz, H-3), 4.73 (1H, dt, *J* = 4.4 Hz, *J* = 2.0 Hz, H-5), 3.76 (3H, s, OMe), 2.75 (1H, q, *J* = 6.6 Hz, H-8), 2.45 (1H, ddd, *J* = 6.4 Hz, *J* = 4.6 Hz, *J* = 2.4 Hz, H-6), 2.17 (1H, dd, *J* = 6.0 Hz, *J* = 1.6 Hz, H-1), 1.47 (3H, d, *J* = 6.4 Hz, CH_3), 0.98 [9H, s, $(CH_3)_3$C-Si], 0.21 (3H, s, CH_3-Si), 0.20 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.5 (C═O), 158.6 (Ar-C), 147.3 (C-4), 135.2 (Ar-C-1), 127.6 (Ar-C), 125.7 (C-3), 113.7 (Ar-C), 68.1 (C-8), 65.6 (C-5), 55.1 (OMe), 44.1 (C-6), 43.3 (C-1), 25.8 [$(CH_3)_3$C-Si], 23.7 (CH_3), 18.2 [$(CH_3)_3$C-Si], −4.6 (CH_3-Si), −4.9 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1687 (C═O) cm^{-1}. Anal. Calcd for $C_{21}H_{31}NO_3Si$: C, 67.52; H, 8.36; N, 3.75. Found: C, 67.53; H, 8.44; N, 3.70.

(1*S*,3*R*,5*S*,6*R*,7*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-8-[(1*R*)-1-(4-methoxyphenyl)ethyl]-4-oxa-8-azatricyclo[5.1.0.0^{3,5}]octan-2-one (16) and (1*S*,3*S*,5*R*,6*R*,7*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-8-[(1*R*)-1-(4-methoxyphenyl)ethyl]-4-oxa-8-azatricyclo-[5.1.0.0^{3,5}]octan-2-one (17). To a 0 °C cooled solution of enone **15** (0.112 g, 0.30 mmol) in THF (2 mL) were added H_2O_2 (0.3 mL, 30 wt % in water, 2.94 mmol) and Triton B (0.5 mL, 40 wt % in methanol, 0.22 mmol). After it was stirred for 1 h at this temperature,

the reaction mixture was quenched with NH_4Cl saturated solution and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated. The residue was purified by preparative TLC (hexane:EtOAc 9:1) to yield the less polar *anti*-epoxide **17** as a colorless oil (0.016 g, 14%) and the more polar *syn*-epoxide **16** as a colorless oil (0.086 g, 74%).

syn-Epoxide ***16.*** R_f = 0.26 (hexane:EtOAc 9:1, twice). $[\alpha]_D^{20}$ = +13.4 (*c* 1.51, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (2H, d, *J* = 8.8 Hz, Ar-H), 6.83 (2H, d, *J* = 8.8 Hz, Ar-H), 4.47 (1H, dd, *J* = 4.0 Hz, *J* = 2.4 Hz, H-6), 3.78 (3H, s, OMe), 3.48 (1H, dt, *J* = 4.0 Hz, *J* = 2.4 Hz, H-5), 3.28 (1H, dd, *J* = 4.0 Hz, *J* = 2.4 Hz, H-3), 2.39−2.35 (2H, m, H-7, H-9), 2.10 (1H, dd, *J* = 6.4 Hz, *J* = 2.4 Hz, H-1), 1.45 (3H, d, *J* = 6.4 Hz, CH_3), 1.00 [9H, s, $(CH_3)_3$C-Si], 0.23 (3H, s, CH_3-Si), 0.22 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.4 (C═O), 158.7 (Ar-C), 135.2 (Ar-C-1), 127.7 (Ar-C), 113.8 (Ar-C), 70.0 (C-9), 65.6 (C-6), 60.8 (C-5), 55.6 (C-3), 55.2 (OMe), 50.5 (C-7), 46.1 (C-1), 25.9 [$(CH_3)_3$C-Si], 23.7 (CH_3), 18.3 [$(CH_3)_3$C-Si], −4.5 (CH_3-Si), −4.6 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1705 (C═O) cm^{-1}. HRMS (ESI-FIA-TOF): *m*/*z* calcd for $C_{21}H_{31}NO_4SiNa$, 412.1920; found, 412.1924 (M + Na).

anti-Epoxide ***17.*** R_f = 0.44 (hexane:EtOAc 9:1, twice). $[\alpha]_D^{20}$ = −62.6 (*c* 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (2H, d, *J* = 8.8 Hz, Ar-H), 6.84 (2H, d, *J* = 8.8 Hz, Ar-H), 4.38 (1H, d, *J* = 4.0 Hz, H-6), 3.79 (3H, s, OMe), 3.24 (1H, dd, *J* = 3.2 Hz, *J* = 1.6 Hz, H-5), 3.16 (1H, d, *J* = 3.2 Hz, H-3), 2.81 (1H, q, *J* = 6.6 Hz, H-9), 2.23 (1H, ddd, *J* = 5.6 Hz, *J* = 4.2 Hz, *J* = 1.4 Hz, H-7), 2.06 (1H, dd, *J* = 5.6 Hz, *J* = 1.2 Hz, H-1), 1.47 (3H, d, *J* = 6.4 Hz, CH_3), 1.00 [9H, s, $(CH_3)_3$C-Si], 0.24 (3H, s, CH_3-Si), 0.23 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6 (C═O), 158.9 (Ar-C), 134.7 (Ar-C-1), 127.7 (Ar-C), 113.8 (Ar-C), 68.3 (C-9), 64.6 (C-6), 56.3 (C-5), 55.2 (OMe), 51.0 (C-3), 44.4 (C-7), 41.7 (C-1), 25.9 [$(CH_3)_3$-C-Si], 23.6 (CH_3), 18.4 [$(CH_3)_3$C-Si], −4.5 (CH_3-Si), −4.8 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1720 (C═O) cm^{-1}. Anal. Calcd for $C_{21}H_{31}NO_4Si$: C, 64.75; H, 8.02; N, 3.60. Found: C, 64.54; H, 7.92; N, 3.60.

(1*R*,5*R*,6*S*)-3-Azido-5-[(*tert*-butyldimethylsilyl)oxy]-7-oxabicyclo[4.1.0]hept-3-en-2-one (18). Following the procedure for **13**, aziridine **16** (0.067 g, 0.17 mmol) and HN_3 (1 mL, 1.5 M in toluene, HN_3 is volatile and highly toxic) afforded vinyl azide **18** as a colorless oil (0.036 g, 74%), which had spectroscopic data identical with those of vinyl azide **13**. $[\alpha]_D^{20}$ = +111.2 (*c* 1.03, CH_2Cl_2).

***N*-[(1*R*,5*R*,6*S*)-5-[(*tert*-butyldimethylsilyl)oxy]-2-oxo-7-oxabicyclo[4.1.0]hept-3-en-3-yl]acetamide (19).** Following the procedure for **14**, azide **18** (0.0207 g, 0.074 mmol), Ph_3P (0.0193 mg, 0.074 mmol), H_2O (6 drops, ca. 0.072 mL, 4 mmol), and Ac_2O (0.035 mL, 0.367 mmol) in THF (1 mL) yielded acetamide **19** as a viscous oil (0.016 mg, 73%), which had spectroscopic data identical with those of acetamide **14**. $[\alpha]_D^{20}$ = +119.6 (*c* 1.21, CH_2Cl_2).

(+)-MT 35214[5] (3). Following the procedure for **1**, silyl ether **19** (0.0123 g, 0.0414 mmol), THF (1 mL), H_2O (1 drop, ca. 0.012 mL, 0.67 mmol), and TBAF (0.0414 mL, 1 M in THF, 0.0414 mmol) yielded the title compound (0.0064 g, 84%), which had spectroscopic data identical with those for **1** and with those published.[5] $[\alpha]_D^{20}$ = +225.0 (*c* 0.02, MeOH); lit. $[\alpha]_D^{20}$ = +186.7 (*c* 0.35, MeOH).[11]

(1*S*,2*R*,3*S*,7*R*,10*S*,11*R*)-5,5-Dimethyl-4,6-dioxatetracyclo-[9.2.1.0.^{2,10}0^{3,7}]tetradec-12-en-9-one (21). A solution of cyclohexenone[19,20] **20** (0.900 g, 5.35 mmol) in toluene (14 mL) was added dropwise to a solution of $AlCl_3$ (0.656 g, 4.92 mmol) in toluene (20 mL) at −78 °C. After 10 min, a solution of cyclopentadiene (2.2 mL, 27.29 mmol) in toluene (7 mL) was added dropwise. The resulting mixture was stirred for 15 min and then poured onto an ice-$NaHCO_3$ saturated solution and extracted with Et_2O. The combined organic layers were dried, filtered, and concentrated. Purification by flash chromatography (hexane:EtOAc 8:2) yielded adduct **21** as a colorless viscous oil (1.107 g, 88%). $[\alpha]_D^{20}$ = +36.9 (*c* 3.24, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.22 (1H, dd, J_1 = 5.6 Hz, *J* = 2.8 Hz, H-12), 6.16 (1H, dd, *J* = 5.6 Hz, *J* = 2.8 Hz, H-13), 4.10−4.03 (2H, m, H-3 and H-7), 3.26 (1H, br s, H-11), 3.16 (1H, br s, H-1), 3.04−2.97 (2H, m, H-2 and H-10), 2.50−2.40 (2H, m, 2xH-8), 1.48−1.47 (4H, m, H-14a and CH_3a), 1.37 (1H, d, *J* = 8.4 Hz, H-14b), 1.34 (3H, s, CH_3b) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.1 (C═O), 138.4 (C-12), 134.6 (C-13), 108.0 (C-5), 75.9 (C-3), 75.1 (C-7), 52.4 (C-10), 49.0 (C-14), 47.2 (C-1), 46.4 (C-11), 44.6 (C-2), 44.4 (C-8), 28.2 (CH_3a), 25.9 (CH_3b) ppm. FTIR (neat): ν_{max} 1709 (C═O) cm^{-1}. HRMS (ESI-FIA-TOF): *m*/*z* calcd for $C_{14}H_{18}O_3Na$, 257.1154; found, 257.1149 (M + Na).

(1*R*,2*S*,6*S*,7*R*,8*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-4-iodotricyclo[6.2.1.0^{2,7}]undeca-4,9-dien-3-one (24). To a solution of acetonide **21** (0.200 g, 0.854 mmol) in THF (2 mL) at 0 °C was added dropwise a 0.5 M NaOH solution, until no starting material was detected by TLC. The reaction mixture was quenched with NH_4Cl saturated solution and extracted with EtOAc. The combined organic layers were dried, filtered, and concentrated. Allyl alcohol **22** was obtained as a white solid (0.113 g, 75%). Mp: 167.4−168.6 °C. $[\alpha]_D^{20}$ = +36.5 (*c* 2.31, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.68 (1H, dd, *J* = 10.4 Hz, *J* = 3.2 Hz, H-5), 6.16 (1H, dd, *J* = 5.6 Hz, *J* = 2.8 Hz, H-10), 6.09 (1H, dd, *J* = 5.6 Hz, *J* = 2.8 Hz, H-9), 5.87 (1H, dd, *J* = 10.0 Hz, *J* = 2.0 Hz, H-4), 4.06−4.03 (1H, m, H-6), 3.36 (1H, br s, H-1), 3.27 (1H, br s, H-8), 2.99 (1H, dd, *J* = 10.2 Hz, *J* = 3.8 Hz, H-2), 2.79 (1H, dt, *J* = 10.0 Hz, *J* = 4.2 Hz, H-7), 2.52 (1H, br s, OH), 1.52 (1H, dt, J_1 = 8.4 Hz, *J* = 1.6 Hz, H-11a), 1.40 (1H, d, *J* = 8.4 Hz, H-11b) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.2 (C═O), 150.4 (C-5), 137.9 (C-10), 135.3 (C-9), 129.4 (C-4), 67.3 (C-6), 49.3 (C-2), 48.2 (C-11), 46.47 (C-7), 46.44 (C-1), 46.40 (C-8) ppm. FTIR (neat): ν_{max} 3407 (OH), 1661 (C═O) cm^{-1}.

To a 0 °C cooled solution of alcohol **22** (0.081 g, 0.46 mmol) in CH_2Cl_2 (2 mL) were added DIPEA (0.200 mL, 1.15 mmol), TBSCl (0.139 g, 0.92 mmol), and a catalytic amount of DMAP. The solution was stirred for 12 h at room temperature and then diluted with EtOAc and washed with water. The organic layer was dried, filtered, and concentrated. Silyloxy **23** was obtained as a colorless viscous oil (0.131 g, 98%). $[\alpha]_D^{20}$ = −49.5 (*c* 2.13, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.52 (1H, dd, *J* = 10.0 Hz, *J* = 2.8 Hz, H-5), 6.20 (1H, dd, *J* = 5.6 Hz, *J* = 2.8 Hz, H-10), 6.08 (1H, dd, *J* = 5.6 Hz, *J* = 2.8 Hz, H-9), 5.81 (1H, dd, *J* = 10.2 Hz, *J* = 2.2 Hz, H-4), 3.99 (1H, dt, *J* = 4.8 Hz, *J* = 2.4 Hz, H-6), 3.34 (1H, br s, H-1), 3.18 (1H, br s, H-8), 2.98 (1H, dd, *J* = 10.6 Hz, *J* = 3.8 Hz, H-2), 2.80−2.74 (1H, dt, *J* = 10.8 Hz, *J* = 4.4 Hz, H-7), 1.50 (1H, dt, *J* = 8.4 Hz, *J* = 1.6 Hz, H-11a), 1.39 (1H, d, *J* = 8.8 Hz, H-11b), 0.93 [9H, s, $(CH_3)_3$C-Si], 0.15 (3H, s, CH_3-Si), 0.11 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.0 (C═O), 151.6 (C-5), 138.3 (C-10), 135.3 (C-9), 128.6 (C-4), 68.3 (C-6), 49.6 (C-2), 48.2 (C-11), 46.9 (C-7), 46.0 (C-8), 45.9 (C-1), 25.7 [$(CH_3)_3$C-Si], 18.0 [$(CH_3)_3$C-Si], −4.5 (CH_3-Si), −4.6 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1679 (C═O) cm^{-1}.

To a 0 °C cooled solution of enone **23** (0.104 g, 0.36 mmol) in Py:CCl_4 1:1 (2 mL) were added a solution of I_2 (0.183 g, 0.72 mmol) in Py:CCl_4 1:1 (2 mL) and a catalytic amount of DMAP. After it was stirred for 25 min at room temperature, the reaction mixture was diluted with EtOAc and washed with 20% $Na_2S_2O_3$ solution and water. The organic layer was dried, filtered, and concentrated. Purification by flash chromatography (hexane:EtOAc 9:1) yielded *α*-iodoenone **24** as a yellow viscous oil (0.140 g, 94%). $[\alpha]_D^{20}$ = −79.2 (*c* 3.04, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (1H, d, *J* = 3.2 Hz, H-5), 6.21 (1H, dd, *J* = 5.8 Hz, *J* = 3.0 Hz, H-10), 6.09 (1H, dd, *J* = 5.6 Hz, *J* = 2.8 Hz, H-9), 3.98 (1H, dd, *J* = 5.2 Hz, *J* = 3.2 Hz, H-6), 3.37 (1H, br s, H-1), 3.16 (1H, br s, H-8), 3.11 (1H, dd, *J* = 10.4 Hz, *J* = 4.0 Hz, H-2), 2.84 (1H, ddd, *J* = 10.4 Hz, *J* = 5.2 Hz, *J* = 4.0 Hz, H-7), 1.50 (1H, dt, *J* = 8.8 Hz, *J* = 1.8 Hz, H-11a), 1.41 (1H, d, *J* = 8.8 Hz, H-11b), 0.93 [9H, s, $(CH_3)_3$C-Si], 0.14 (3H, s, CH_3-Si), 0.12 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3 (C═O), 160.0 (C-5), 138.5 (C-10), 135.5 (C-9), 102.2 (C-4), 70.9 (C-6), 49.4 (C-2), 48.3 (C-11), 47.3 (C-7), 46.7 (C-1), 45.9 (C-8), 25.7 [$(CH_3)_3$C-Si], 17.9 [$(CH_3)_3$C-Si], −4.5 (CH_3-Si), −4.6 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1687 (C═O) cm^{-1}. HRMS (ESI-FIA-TOF): *m*/*z* calcd for $C_{17}H_{25}IO_2SiNa$, 439.0566; found, 439.0553 (M + Na).

(1*R*,2*S*,4*S*,6*R*,7*S*,8*R*,9*S*)-7-[(*tert*-Butyldimethylsilyl)oxy]-5-[(4-methoxyphenyl)methyl]-5-azatetracyclo[7.2.1.0.^{2,8}0^{4,6}]dodec-10-en-3-one (25). To a solution of *α*-iodoenone **24** (0.089 g, 0.21 mmol) in toluene (1 mL) were added 1,10-phenanthroline (0.038 g, 0.21 mmol), Cs_2CO_3 (0.075 g, 0.23 mmol), and 4-methoxybenzylamine (0.042 mL, 0.32 mmol). After it was stirred for 4 h at room

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temperature, the reaction mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated. Purification by flash chromatography (hexane:EtOAc 9:1) afforded aziridine **25** (0.082 g, 92%). $[\alpha]_D^{20}$ = −62.3 (*c* 0.87, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (2H, d, *J* = 8.4 Hz, Ar-H), 6.85 (2H, d, *J* = 8.8 Hz, Ar-H), 6.25 (1H, dd, *J* = 5.6 Hz, *J* = 2.4 Hz, H-11), 5.96 (1H, dd, *J* = 5.8 Hz, *J* = 3.0 Hz, H-10), 3.79 (3H, s, OMe), 3.73 (1H, d, *J* = 13.6 Hz, H-13a), 3.49 (1H, dd, *J* = 8.8 Hz, *J* = 0.8 Hz, H-7), 3.31 (1H, d, *J* = 13.6 Hz, H-13b), 3.09−3.06 (2H, m, H-2 and H-1), 2.94 (1H, br s, H-9), 2.77 (1H, ddd, *J* = 11.0 Hz, *J* = 8.6 Hz, *J* = 2.8 Hz, H-8), 2.17 (1H, dd, *J* = 6.6 Hz, *J* = 1.0 Hz, H-6), 2.12 (1H, d, *J* = 6.8 Hz, H-4), 1.45 (1H, d, *J* = 8.4 Hz, H-12a), 1.26 (1H, d, *J* = 8.4 Hz, H-12b), 0.89 [9H, s, $(CH_3)_3$C-Si], 0.09 (3H, s, CH_3-Si), 0.02 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.2 (C=O), 158.8 (Ar-C), 138.7 (C-11), 134.5 (C-10), 130.3 (Ar-C-1), 128.7 (Ar-C), 113.8 (Ar-C), 72.1 (C-7), 61.4 (C-13), 55.3 (OMe), 52.6 (C-6), 50.8 (C-2), 47.8 (C-12), 47.0 (C-4), 46.7 (C-8), 44.2 (C-9), 43.1 (C-1), 25.7 [$(CH_3)_3$C-Si], 17.9 [$(CH_3)_3$C-Si], −4.1 (CH_3-Si), −4.7 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1705 (C=O) cm^{-1}. Anal. Calcd for $C_{25}H_{35}NO_3Si$: C, 70.55; H, 8.29; N, 3.29. Found: C, 70.40; H, 8.45; N, 3.24.

(1*S*,5*S*,6*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(4-methoxyphenyl)methyl]-7-azabicyclo[4.1.0]hept-3-en-2-one (26). To diphenyl ether (1.5 mL) under reflux was added a solution of adduct **25** (0.013 g, 0.03 mmol) in diphenyl ether (0.5 mL). After 45 min, the mixture was cooled and loaded onto a pad of silica gel (hexane:EtOAc 9:1), affording enone **26** as a viscous oil (0.010 g, 91%). $[\alpha]_D^{20}$ = −139.2 (*c* 0.97, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (2H, d, *J* = 8.4 Hz, Ar-H), 6.84 (2H, d, *J* = 8.4 Hz, Ar-H), 6.36 (1H, dt, *J* = 10.4 Hz, *J* = 2.4 Hz, H-4), 5.80 (1H, dt, *J* = 10.8 Hz, *J* = 2.0 Hz, H-3), 4.70 (1H, dt, *J* = 4.4 Hz, *J* = 2.0 Hz, H-5), 3.78 (3H, s, OMe), 3.75 (1H, d, *J* = 13.6 Hz, H-8), 3.51 (1H, d, *J* = 13.6 Hz, H-8′), 2.46 (1H, ddd, *J* = 6.4 Hz, *J* = 4.4 Hz, *J* = 2.4 Hz, H-6), 2.29 (1H, dd, *J* = 6.0 Hz, *J* = 1.6 Hz, H-1), 0.90 [9H, s, $(CH_3)_3$C-Si], 0.13 (3H, s, CH_3-Si), 0.08 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.8 (C=O), 158.9 (Ar-C), 147.8 (C-4), 129.5 (Ar-C-1), 129.3 (Ar-C), 125.5 (C-3), 113.8 (Ar-C), 65.9 (C-5), 62.5 (C-8), 55.2 (OMe), 43.6 (C-1), 43.2 (C-6), 25.7 [$(CH_3)_3$C-Si], 18.2 [$(CH_3)_3$C-Si], −4.7 (CH_3-Si), −4.9 (CH_3-Si) ppm. FTIR (neat): ν_{max} 1687 (C=O) cm^{-1}. HRMS (ESI-FIA-TOF): *m*/*z* calcd for $C_{20}H_{30}NO_3Si$, 360.1995; found, 360.1989 (M + H).

(1*R*,5*S*,6*S*)-3-Azido-5-[(*tert*-butyldimethylsilyl)oxy]-7-oxabicyclo[4.1.0]hept-3-en-2-one (32). In a screw-capped vial, a solution of aziridine[17] **31** (0.019 g, 0.051 mmol) in HN_3 (2 mL, 1.3 M in benzene; HN_3 is volatile and highly toxic) was stirred at 60 °C for 12 h. After rapid cooling, the reaction mixture was loaded onto a preparative TLC (hexane:EtOAc 8:2), affording vinyl azide **32** as a colorless oil (0.011 g, 78%). $[\alpha]_D^{20}$ = +171.5 (*c* 0.2, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.96 (1H, dd, *J* = 5.2 Hz, *J* = 2.4 Hz, H-4), 4.79 (1H, dt, *J* = 5.2 Hz, *J* = 1.2 Hz, H-5), 3.66 (1H, ddd, *J* = 3.6 Hz, *J* = 2.4 Hz, *J* = 1.2 Hz, H-6), 3.59 (1H, dd, *J* = 3.6 Hz, *J* = 1.2 Hz, H-1), 0.92 [9H, s, $(CH_3)_3$C-Si], 0.18 (3H, s, CH_3-Si), 0.15 (3H, s, CH_3-Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.6 (C=O), 133.5 (C-3), 126.0 (C-4), 64.0 (C-5), 58.2 (C-6), 53.6 (C-1), 25.6 [$(CH_3)_3$C-Si], 18.1 [$(CH_3)_3$C-Si], −4.4 (CH_3-Si), −4.7 (CH_3-Si) ppm. FTIR (neat): ν_{max} 2107 (N_3), 1694 (C=O) cm^{-1}.

***N*-[(1*R*,5*S*,6*S*)-5-[(*tert*-butyldimethylsilyl)oxy]-2-oxo-7-oxabicyclo[4.1.0]hept-3-en-3-yl]acetamide (33).** Ph_3P (0.0068 g, 0.026 mmol) was added to a solution of azide **32** (0.0089 g, 0.032 mmol) in THF (1 mL) at 0 °C. After the mixture was stirred for 20 min, Ac_2O (0.007 mL, 0.074 mmol) and DMAP (0.0039 g, 0.032 mmol) were added and the mixture was warmed to room temperature. After 5 h, the mixture was concentrated and loaded onto a preparative TLC (hexane:EtOAc 8:2), affording acetamide **33** as a colorless oil (0.0077 g, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (1H, br s, NH), 7.50 (1H, dd, *J* = 5.2 Hz, *J* = 2.4 Hz, H-4), 4.87 (1H, dt, *J* = 5.2 Hz, *J* = 1.2 Hz, H-5), 3.70 (1H, ddd, *J* = 3.6 Hz, *J* = 2.4 Hz, *J* = 1.2 Hz, H-6), 3.59 (1H, dd, *J* = 3.6 Hz, *J* = 1.2 Hz, H-1), 2.13 (3H, s, CH_3−C=O), 0.92 [9H, s, $(CH_3)_3$C-Si], 0.19 (3H, s, CH_3-Si), 0.17 (3H, s, CH_3-Si) ppm. HRMS (ESI-FIA-TOF): *m*/*z* calcd for $C_{14}H_{23}NNaO_4Si$, 320.12940; found, 320.12921 (M + Na).

***N*-[(1*R*,5*S*,6*R*)-5-Hydroxy-2-oxo-7-oxabicyclo[4.1.0]hept-3-en-3-yl]acetamide (4).** To a solution of silyl ether **33** (0.0040 g, 0.0135 mmol) in CH_3CN (0.6 mL) was added HF (0.0845 mL, 0.4% in water, 0.0169 mmol), and the mixture was stirred at room temperature for 2 h. The reaction was quenched with $NaHCO_3$ saturated solution and extracted with EtOAc. The combined organic layers were dried, filtered, and concentrated. The residue was purified by preparative TLC (hexane:EtOAc 3:7) to yield epoxy alcohol **4** as a colorless oil (0.002 g, 80%), which had spectroscopic data consistent with those reported for *rac*-4-*epi*-MT35214.[6] $[\alpha]_D^{20}$ = +72 (*c* 0.05, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69 (1H, br s, NH), 7.61 (1H, dd, *J* = 5.3 Hz, *J* = 2.3 Hz, H-4), 4.92−4.88 (1H, m, H-5), 3.86−3.83 (1H, m, H-6), 3.62 (1H, d, *J* = 3.4 Hz, H-1), 2.14 (3H, s, CH_3C=O) ppm.

(1*R*,5*R*,6*S*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(4-methoxyphenyl)methyl]-7-azabicyclo[4.1.0]hept-3-en-2-one (34). To a solution of acetonide[17] **28** (0.061 g, 0.20 mmol) in THF (1 mL) at 0 °C was added dropwise a 0.5 M NaOH solution, until no starting material was detected by TLC. The reaction mixture was quenched with NH_4Cl saturated solution and extracted with CH_2Cl_2. The combined organic layers were dried, filtered, and evaporated. The crude residue was dissolved in CH_2Cl_2 (2 mL), and at 0 °C were added DIPEA (0.087 mL, 0.50 mmol), TBSCl (0.060 g, 0.40 mmol), and a catalytic amount of DMAP. The mixture was stirred overnight at room temperature and then diluted with EtOAc and washed with water. The organic layer was dried, filtered, and concentrated. Purification by preparative TLC (hexane:EtOAc 8:2) afforded enone **34** as a viscous oil (0.050 g, 69%), which had spectroscopic data identical with those of **26**. $[\alpha]_D^{20}$ = +149.2 (*c* 0.63, CH_2Cl_2).

■ ASSOCIATED CONTENT

Supporting Information

Figures giving ^{1}H and ^{13}C NMR spectra of new compounds. 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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