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Enantioselective Formal Synthesis of (−)-Podophyllotoxin from (2*S*,3*R*)-3-Arylaziridine-2-carboxylate

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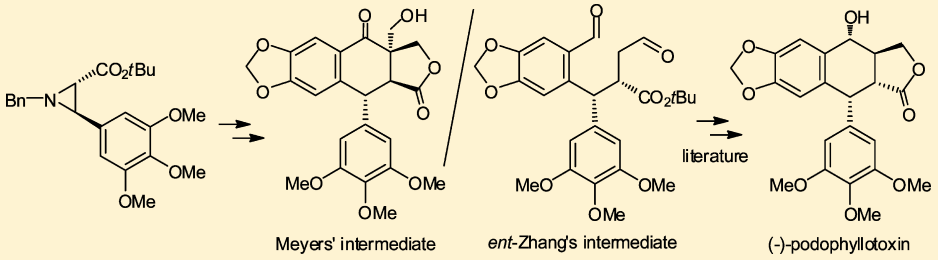
Supporting Information



ABSTRACT: Meyers' 4-aryl-1-tetralone-lactone and *ent*-Zhang's 2-diarylmethyl-4-oxobutanoate were synthesized in the formal synthesis of (−)-podophyllotoxin from (2*S*,3*R*)-3-arylaziridine-2-carboxylate, via 3,3-diarylpropanoate as a common intermediate, in an overall 42% yield through 10 steps and 31% yield through 6 steps, respectively. The key steps in the synthesis were regio- and diastereoselective ring opening with an aromatic nucleophile, samarium iodide promoted reductive C−N bond cleavage, and Stille coupling for introducing the vinyl functionality. The starting aziridine was enantioselectively prepared from 3,4,5-trimethoxybenzaldehyde by guanidinium ylide mediated asymmetric aziridination. All nitrogen components used in the reaction sequence are reusable as the starting guanidinium source.

INTRODUCTION

Lignans are a family of compounds consisting of dimerized C6−C3 phenylpropanoids, which are biosynthetically derived from shikimic acid via an aromatic α-amino acid such as phenylalanine or tyrosine. Among lignans, the aryltetralin-lactone (−)-podophyllotoxin (**1**) is an important natural product because of its potent antitumor activity; in fact, sugar-modified analogues, such as etoposide and etopophos, are clinically used as anticancer drugs.[1] In the stereoselective synthesis of **1** and its analogues, the challenges are the four contiguous stereocenters and the presence of a base-sensitive *trans*-lactone moiety. Although many approaches[2] to the racemic synthesis of podophyllotoxin can be found in the literature, to the best of our knowledge, only eight groups[3] have reported its enantioselective total synthesis. Meyers and co-workers[3g] used conjugate addition of 3,4,5-trimethoxyphenyl anion to a chiral 2-naphthalenyloxazoline to construct an aryltetralin skeleton in the asymmetric induction step and succeeded in the first total synthesis of natural (−)-podophyllotoxin (**1**) through an aryltetralone-lactone, (−)-3-(hydroxymethyl)-picropodophyllone (**2**). Recently, Zhang and co-workers[3a] completed a concise total synthesis of *ent*-(+)-podophyllotoxin (*ent*-**1**) by applying a tandem Michael addition−allylation of a chirally masked 2-piperonyl anion to cinnamate and allyl bromide as an asymmetric induction step, in which they used 2-diarylmethyl-4-oxobutanoate **3** as a key precursor for constructing the aryltetralin skeleton.

We[4] have previously developed an atom-economical method, applicable to asymmetric synthesis, for preparing aziridine-2-carboxylates by reaction of a guanidinium salt with an aromatic (or unsaturated) aldehyde: a *trans*-aziridine is formed as the major product when an electron-rich aldehyde is used as the electrophile, and the coformed urea can be reused to prepare the starting guanidinium salt. We[4c,e,5] also examined the ring opening of the generated 3-aryl (or unsaturated) aziridine-2-carboxylates by various nucleophiles, which provided the nucleophile-inserted 2-amino-3-aryl (or unsaturated) propanoates. The 2-amino-3,3-diarylpropanoate derivative formed by the reaction with an aromatic (*Ar*) nucleophile is a suitable synthetic precursor for 4-aryltetralin-type lignans.

In this paper we disclose new enantioselective syntheses of Meyers' 4-aryl-1-tetralone-lactone (**2**) and *ent*-Zhang's 2-diarylmethyl-4-oxobutanoate (**3**), which are useful synthetic intermediates for (−)-podophyllotoxin (**1**), from *trans*-(2*S*,3*R*)-3-arylaziridine-2-carboxylate through the ring-opened 2-amino-3-arylpropanoate. The key steps in the synthesis are guanidinium ylide mediated asymmetric aziridination of 3,4,5-trimethoxybenzaldehyde, regio- and diastereoselective ring opening of the generated *trans*-(2*S*,3*R*)-3-(3,4,5-trimethoxyphenyl)aziridine-2-carboxylate with sesamol (3,4-methylenedioxyphenol) as an *Ar* nucleophile, samarium iodide (SmI_2) promoted reductive C−N bond cleavage of the ring-opened 2-amino-3,3-diarylpropanoate derivative, and Stille coupling for introducing a vinyl functionality to the 2-hydroxy-4,5-(methylenedioxy)phenyl substituent. In addition, each nitrogen component generated in the aziridination and in the C−N bond cleavage reaction could be recovered and recycled to prepare the guanidinium starting source.

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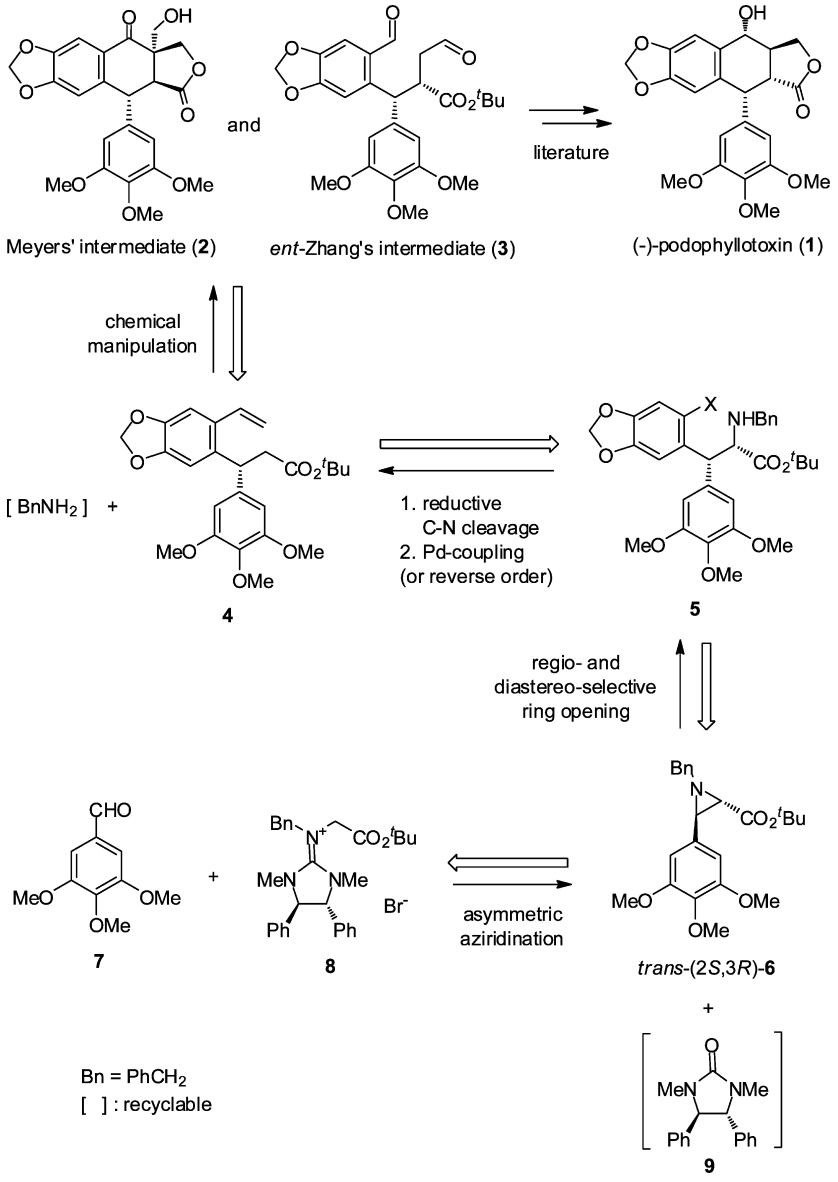
Scheme 1. Retrosynthetic Analysis



RESULTS AND DISCUSSION

We observed that nonactivated *N*-benzyl-3-arylaziridine-2-carboxylates were attacked exclusively at the C3 benzylic position by electron-rich *Ar* nucleophiles in the presence of indium chloride ($InCl_3$) as a Lewis acid (LA) catalyst to give 2-benzylamino-3,3-diarylpropanoates with high diastereoselectivity.[5b] X-ray crystallographic analysis of a ring-opened product established that the stereochemistry of an *Ar*-inserted C3 stereogenic center was controlled by an *anti*-mode nucleophilic opening process (inversion). Against this background, our retrosynthetic analysis of Meyers' 4-aryl-1-tetralone-lactone (**2**) and *ent*-Zhang's 2-diarylmethyl-4-oxobutanoate (**3**) is shown in Scheme 1. *trans*-(2*S*,3*R*)-*N*-Benzyl-3-(3,4,5-trimethoxyphenyl)-aziridine-2-carboxylate *trans*-(2*S*,3*R*)-**6**, prepared by an asymmetric aziridination reaction[4,5] of 3,4,5-trimethoxybenzaldehyde (**7**) using the (*R*,*R*)-guanidinium salt **8**, is converted to (2*S*,3*R*)-2-benzylamino-3,3-diarylpropanoate **5** by regio- and diastereoselective ring opening with a 4-substituted methylenedioxybenzene. Reductive cleavage of the C−N bond in the aminopropanoate **5** provides the propanoate **4** and benzylamine, either before or after vinylation through a palladium (Pd)-catalyzed coupling reaction. The benzylamine obtained could be reused as the external nitrogen source in the preparation of a starting guanidinium salt **8** by reaction with urea **9**, coproduced in the aziridination reaction, after chlorination. The propanoate **4** could then be converted to the targeted **2** and **3** by suitable chemical manipulations.

In our synthetic scheme, the key step is the stereoselective construction of the C3 stereogenic center in 2-amino-3,3-diarylpropanoates **5** by ring opening of *trans*-(2*S*,3*R*)-3-(3,4,5-trimethoxyphenyl)aziridine-2-carboxylate *trans*-(2*S*,3*R*)-**6**. The starting *trans*-(2*S*,3*R*)-**6** was prepared in 84% yield and with 82% enantiomeric excess (ee) by asymmetric aziridination using the (*R*,*R*)-guanidinium salt **8** under one of our standard conditions using tetramethylguanidine (TMG) as base,[4,5] in which the diastereoisomeric *cis*-(2*S*,3*S*)-**6** and urea **9** were coproduced in 4% (84% ee) and 83% yields, respectively. In addition, the corresponding racemic aziridines (±)-*trans*- and (±)-*cis*-**6** were also prepared by using guanidinium salt **10**, which lacks phenyl pendants, under an alternative standard condition (NaH in DMF)[4,5] as a model source for ring-opening experiments (Scheme 2).

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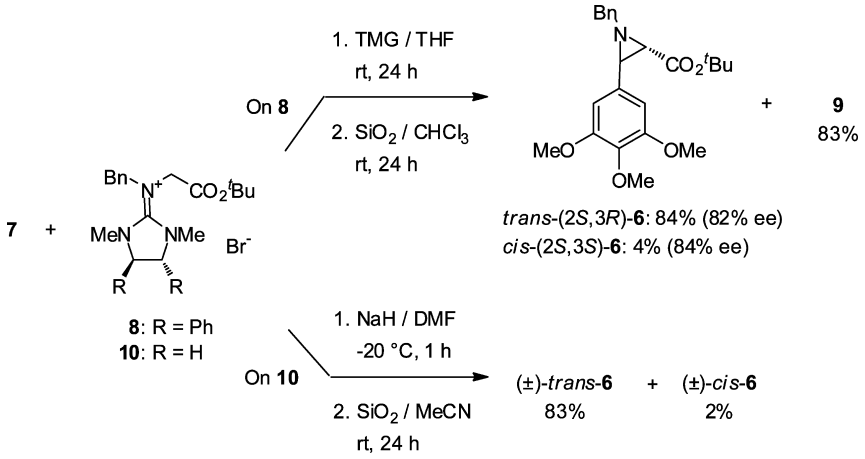
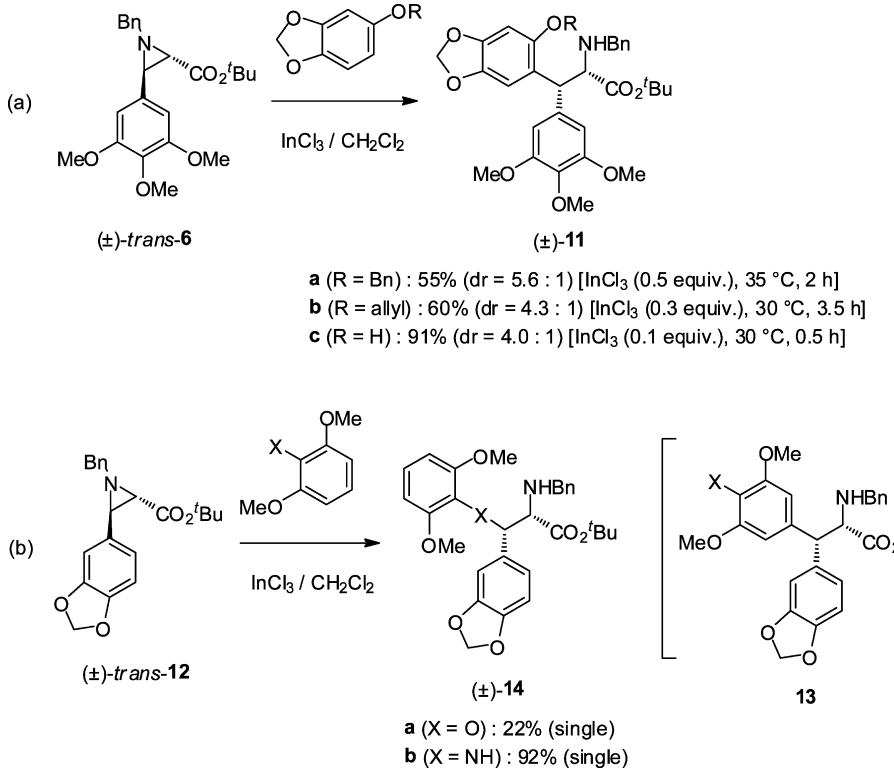
Scheme 2. Aziridination



Scheme 3. Preliminary Examination of $InCl_3$-Catalyzed Ring-Opening Reactions



At first, we preliminarily examined the ring-opening reaction using the racemic *trans*-aziridine (±)-*trans*-**6** with sesamol derivatives (Scheme 3a). Treatment with sesamol benzyl ether in the presence of a 0.5 mol amount of $InCl_3$ afforded the desired carbon-inserted ring-opened product (±)-**11a** (R = Bn) in 55% yield with a moderate diastereomeric ratio (dr = 5.6:1). Similar results were obtained with an allyl ether, even when the amount of $InCl_3$ was reduced (0.5 equiv → 0.3 equiv) ((±)-**11b**: 60% yield, dr = 4.3:1). Gratifyingly, the use of sesamol led to satisfactory conversion, even with the lower amount (0.1 equiv) of $InCl_3$, in which the ring-opened 2-amino-3,3-diarylpropanoate (±)-**11c** (R = H) was provided in 91% yield, but the diastereoselectivity was slightly lowered (dr = 4.0:1).

An alternative approach involving interchange of the aziridine unit from the trimethoxyphenyl- (±)-*trans*-**6** with the methylenedioxyphenylaziridine (±)-*trans*-**12**[4e,f,5] and the *Ar* nucleophile unit from sesamol with the trimethoxybenzene derivative, respectively, may also be possible, despite the undesired formation of the diastereomeric ring-opened product **13** (X = OMe) with an opposite stereochemistry at the C3 stereogenic center. It had been reported that the 2,3,4-trimethoxyphenyl-inserted product, not the corresponding 3,4,5-trimethoxyphenyl derivative, was provided in the ring opening of an activated *N*-tosylaziridine derivative with 1,2,3-trimethoxybenzene.[6] Furthermore, we experienced unsuccessful ring opening when anisole was used as an *Ar* nucleophile.[5b] Thus, more electron-rich 2,6-dimethoxyphenol and 2,6-dimethoxyaniline were selected as potential 3,4,5-trimethoxyphenyl-type nucleophiles and we comparably attempted the $InCl_3$-catalyzed ring opening of the methylenedioxyphenylaziridine (±)-*trans*-**12** (Scheme 3b). However, different from the sesamol-type nucleophiles, they functioned as heteroatom nucleophiles, not as *Ar* nucleophiles, to give the

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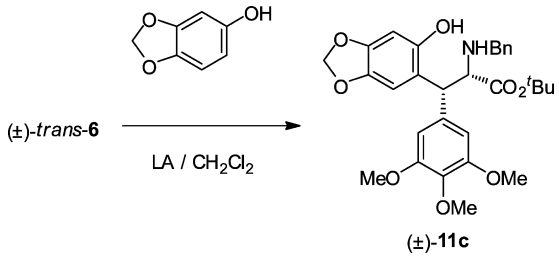
heteroatom-inserted 2-aminopropanoate (±)-**14** as a single diastereoisomer, in place of carbon-inserted 2-amino-3,3-diarylpropanoates **13**. In particular, the product (±)-**14b** (X = NH) was provided in high yield (92%) when 2,6-dimethoxyaniline was used as a nucleophile. These facts may suggest that a softer C6 atom of sesamol, doubly activated by two electron-donating groups at 1,3-positions, in comparison to the phenolic oxygen atom serves as the nucleophilic center in the ring-opening reaction of an aziridine substrate through C−C bond formation.[7]

The result regarding ring opening of trimethoxyphenylaziridine (±)-*trans*-**6** with sesamol prompted us to optimize an LA catalyst (Table 1). Although conversion was slightly increased by the replacement of $InCl_3$ with indium triflate ($In(OTf)_3$) or scandium triflate ($Sc(OTf)_3$), no improvement in dr was observed (Table 1, entries 1−3). High dr (10:1) was attained

Table 1. Screening of LAs for the Ring Opening of the Trimethoxyphenylaziridine (±)-*trans*-6 with Sesamol



(±)-**11c**

			(±)-11c	
entry	LA (amt, equiv)	conditions	yield, %	dr
1	$InCl_3$ (0.1)	30 °C, 4 h	91	4:1
2	$In(OTf)_3$ (0.3)	30 °C, 4 h	93	4:1
3	$Sc(OTf)_3$ (0.1)	30 °C, 4 h	94	4:1
4	$Zn(OTf)_2$ (0.1)	30 °C, 9 h	89	10:1
5	$Cu(OTf)_2$ (0.1)	30 °C, 9 h	61	10:1
6	$BF_3{\cdot}Et_2O$ (1.0)	0 °C, 1 h	85	4.3:1
7	ZnI_2 (0.1)	30 °C, 24 h	79	3:1

with zinc triflate [$Zn(OTf)_2$] or copper triflate [$Cu(OTf)_2$], and in the former case, the high conversion (89%) was maintained (Table 1, entries 4 and 5). On the other hand, boron trifluoride etherate ($BF_3{\cdot}Et_2O$) or zinc iodide (ZnI_2) led to unsatisfactory results (Table 1, entries 6 and 7). Thus, we selected $Zn(OTf)_2$ as the most suitable LA catalyst for the sesamol-participated ring opening and obtained the same results when the enantio-rich aziridine *trans*-(2*S*,3*R*)-**6** was applied to the ring-opening reaction.

Next, we attempted to introduce a vinyl unit into the sesamol-inserted 2-amino-3-arylpropanoate **11c**, derived from *trans*-(2*S*,3*R*)-**6**, by Pd-catalyzed coupling before reductive C−N cleavage (Scheme 4). After the phenolic function in **11c** was activated by making trifluoromethanesulfonate, the *N*-benzyl (*N*-Bn) derivative **15** was subjected to a Stille-type reaction.[8] Coupling product **16** was afforded in moderate yield; however, subsequent reductive C−N cleavage of **16** under the optimized conditions discussed later was unsatisfactory (**4**: 30%, see Scheme 5).

Independent trials for introduction of a C3 unit under Heck[9] or Sonogashira[10] reaction conditions as alternative approaches to the Meyers intermediate (**2**) were attempted. However, starting materials were mainly recovered in both coupling reactions using either the *N*-Bn (**15**) or *N*-(*tert*-butoxycarbonyl) (*N*-Boc) derivative (**17**), which was derived from **15** by catalytic hydrogenation in the presence of di-*tert*-butyl dicarbonate ($(Boc)_2O$). Therefore, 2-aminopropanoate **11c** was subjected to a reductive C−N bond cleavage reaction before introduction of the C unit.

Honda and Ishikawa[11] reported the SmI_2-promoted C−N bond cleavage of α-amino carbonyl compounds containing amino esters. In this reaction, a combination of tetrahydrofuran (THF), hexamethylphosphoric triamide (HMPA), and methanol (MeOH), serving as a solvent, additive, and proton source, respectively, played an important role in reaction completion. However, we observed no reaction when 2-aminopropanoate **11c** was subjected to Honda and Ishikawa's condition using MeOH as a proton source. Successful C−N bond cleavage was accomplished by replacing MeOH with water, which provided propanoate **18** and benzylamine in the same 93% yield (Scheme 5). The vinyl-inserted product **4** was smoothly provided by a Pd-coupling reaction of **18** under Stille-type conditions,[8] after conversion to trifluoromethanesulfonate **19**, in better yield (90% at 50 °C for 7 h), in comparison with the case of 2-aminopropanoate **15** (64% at 90 °C for 8 h; Scheme 4). The ee of **4** was estimated as 81%, without the loss of enantiopurity through reactions, and the ee could be increased to 99% after recrystallization from hexane/MeOH (10/1). This fact is relevant to our synthetic strategy, because vinyl product **4** was the common key precursor for Meyer's (**2**) and *ent*-Zhang's intermediates (**3**). In trials for introduction of a C3 unit into the deaminated product **19** under Heck reaction conditions,[9] different from the case of 2-aminopropanoates **15** and **17** (Scheme 4), the coupling product **20** was obtained, even in moderate yield. However, reduction of the acrylate in **20** to the allyl alcohol failed under the conditions examined.

On the basis of these experimental facts, chemical manipulation of **4** toward the Meyers intermediate (**2**) was examined. Straightforward preparation of tetralinol (**23**) and/or tetralone systems (**26**) were initially attempted (Scheme 6). Direct epoxidation of **4** under conventional conditions failed, but the intended epoxide **21** was afforded in good yield by a stepwise approach (93% in two steps) through iodohydrin **22**, which was provided in 95% yield by treatment of **4** with *N*-iodosuccinimide (NIS) in aqueous THF. Although the diastereoselectivity in the products was low (dr = 2:1), the newly created benzylic stereogenic center will be destroyed in a later conversion to a ketone. Unfortunately, cyclization of epoxide **21** or iodohydrin **22** to tetralinol **23** was unsuccessful. Instead, indane derivative **24** displaced at the benzylic position was obtained in approximately 30% yield. Trial reactions for constructing the tetralone system **26** from iodo ketone **25**, which was available as an unstable product from iodohydrin **22** by Dess−Martin periodinane (DMP) oxidation, also failed.

Therefore, we applied a stepwise approach to the tetralin systems (Scheme 7). After protection of the alcohol group of **22** with a *tert*-butyldimethylsilyl (TBS) group, treatment of the silyl ether **27** with lithium hexamethyldisilazide (LHMDS) in the presence of HMPA afforded the desired cyclized tetralin **28** in 90% yield as expected. The ^1H NMR spectrum showed that the 2:1 dr of starting material **22** was preserved in product **28**, indicating that highly stereocontrolled ring closure occurred; however, the relative stereochemistry between C3 and C4 configurations (numbering based on tetralin-1-ol) could not be assigned because of complex signal patterns in the ^1H NMR spectrum. After deprotection, oxidation of tetralinol **23** with DMP provided the corresponding ketone **26** as a single isomer in 92% yield. The desired cyclization from protected iodohydrin **27** to tetralinol system **28** with a *trans*-(3*R*,4*R*) configuration was deduced by comparison with the coupling constant between C3−H and C4−H (J = 8.0 Hz) in tetralone system **26**.[12] Aldol

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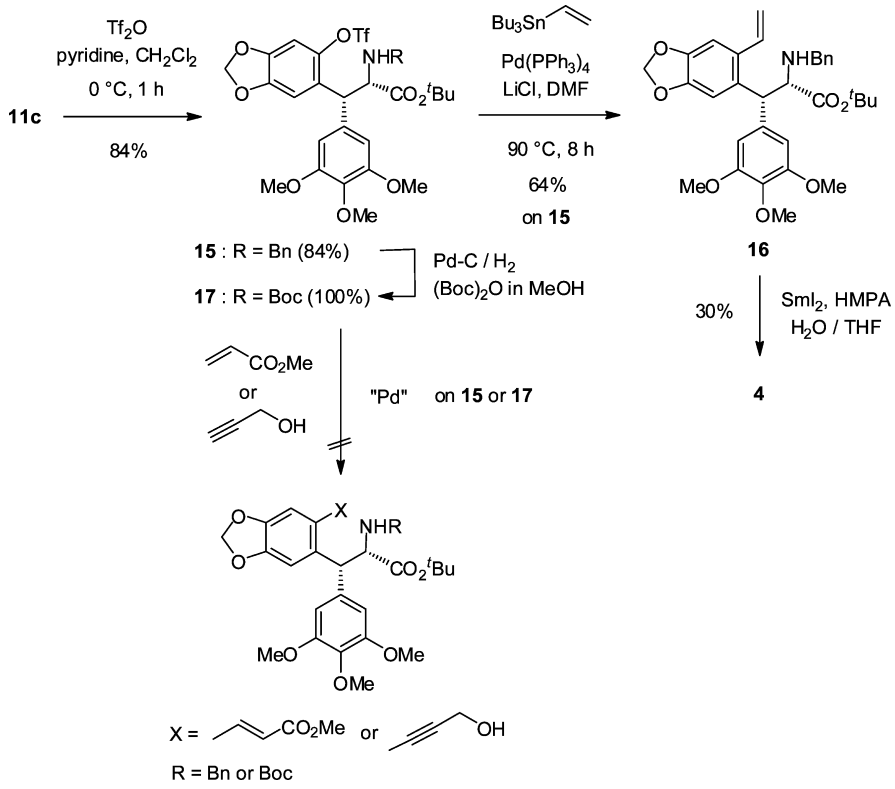
Scheme 4. Trials for Introducing a C Unit into 2-Amino-3,3-diarylpropanoates



condensation of **26** with excess formalin solution smoothly provided (−)-3-(hydroxymethyl)picropodophyllone (**2**), Meyers' intermediate, in 95% yield. Product data were identical with reported data,[3g] and the overall yield was 35% from a commercially available 3,4,5-trimethoxybenzaldehyde (**7**) through 11 steps with an average 91% yield. On the other hand, Meyers and co-workers synthesized the intermediate **2** in overall 10% yield from piperonal through 19 steps with an average yield of 89%.

Finally, synthesis of *ent*-Zhang's intermediate (**3**) from a common precursor (vinyl-inserted product **4**) was attempted (Scheme 8). Alkylation with allyl bromide provided 2-diarylmethyl-4-pentenoate **29** in 92% yield with a 3:1 dr. Oxidative cleavage of two vinyl functions with an osmium tetraoxide (OsO_4) and sodium periodate ($NaIO_4$) system proceeded smoothly to give the desired 2-diarylmethyl-4-oxobutanoate (**3**), *ent*-Zhang's intermediate, in 49% isolated yield after purification of the diastereoisomeric dicarbonyl compounds obtained. These findings indicate that the major diastereoisomer of the pentenoate **29** was the 2*S* derivative. The data on the product **3** were identical with the reported data, except for a specific rotation,[3a] and the overall yield was 26% from 3,4,5-trimethoxybenzaldehyde (**7**) through seven steps with an average yield of 84%. The synthetic efficiency was almost comparable to that of Zhang's route (overall 34% yield from bromopiperonal through four steps with an average yield of 78%).

CONCLUSION

We effectively achieved the enantioselective syntheses of Meyers' 4-aryl-1-tetralone-lactone and *ent*-Zhang's 2-diarylmethyl-4-oxobutanoate as useful synthetic intermediates for (−)-podophyllotoxin from *trans*-(2*S*,3*R*)-3-(3,4,5-trimethoxyphenyl)aziridine-2-carboxylate, which was derived from 3,4,5-trimethoxybenzaldehyde by guanidinium ylide mediated asymmetric aziridination. This strategy may appear to have low atom economy because nitrogen atoms are not incorporated into the products, but the nitrogen components (urea and benzylamine) released during the reaction sequence can be recovered and reused to prepare the guanidinium starting material. In addition, not only is the aziridine system likely analogous to an aromatic α-amino acid derivative—a biosynthetic precursor of phenylpropanoid as a monomeric lignan component—but it might also contribute greatly to controlling the new stereogenic center of the diaryl-substituted carbon in the ring-opened product. Thus, this approach provides a new strategy for the synthesis of biologically important 4-aryltetralin lignans.

EXPERIMENTAL SECTION

Melting points were determined with a melting point hot-stage instrument and are uncorrected. ^1H and ^{13}C NMR spectra were recorded with 400 and 600 MHz spectrometers in $CDCl_3$. FAB and ESI mass spectra were obtained using a double-focusing magnetic sector mass spectrometer and time-of-flight mass spectrometer, respectively. For column and flash chromatography silica gel 60 (63-210 μm) and NH-coated silica gel (100−200 mesh) and silica gel 60 (40−100 μm), respectively, were used. All reactions were carried out using dry solvents under an argon atmosphere, and organic extracts were evaporated under reduced pressure after drying over $MgSO_4$, unless otherwise noted.

Asymmetric Aziridination of 3,4,5-Trimethoxybenzaldehyde (7) and (*R*,*R*)-Guanidinium Bromide (8). A freshly distilled TMG (0.4 mL, 3.20 mmol) was added dropwise to a stirred solution of **7** (0.589 g, 3.00 mmol) and **8** (1.732 g, 3.146 mmol) in THF (3.0 mL) at 0 °C. The mixture was stirred at room temperature for 1 day, and then SiO_2 (30 g) was added after dilution with $CHCl_3$ (30 mL). The resulting slurry was stirred at room temperature for 1 day. The SiO_2 was filtered through Celite and washed with AcOEt. After evaporation of the filtrate, column chromatography of the residue (SiO_2, AcOEt/hexane 1/6) gave *trans*-(2*S*,3*R*)-**6** (1.01 g, 84%, 82% ee), *cis*-(2*S*,3*S*)-**6** (43 mg, 4%, 84% ee), and urea **9** (colorless prisms (692 mg, 83%), mp 149−151 °C).

*trans-(2S,3R)-tert-Butyl 3-(3,4,5-trimethoxyphenyl)aziridine-2-carboxylate (trans-(2S,3R)-**6**):* colorless needles, mp 130−133 °C;

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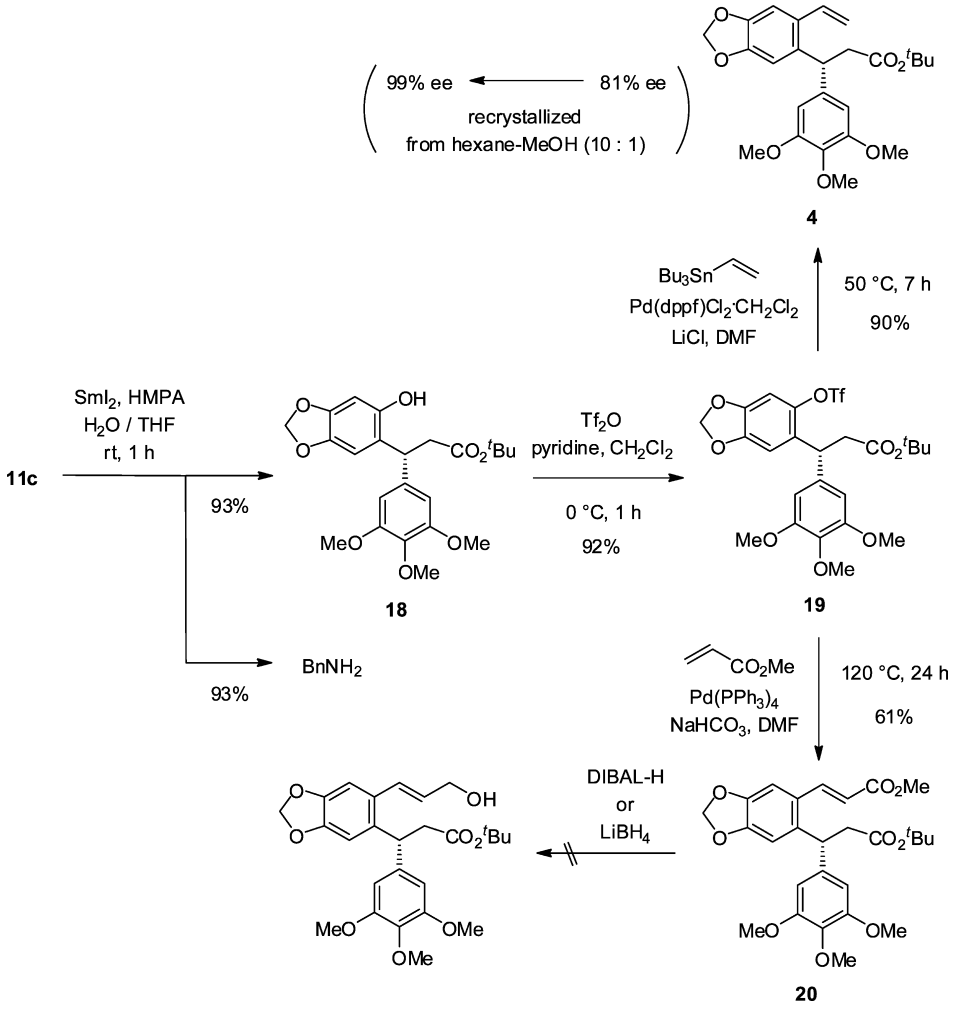
Scheme 5. Introduction of a C Unit after Reductive C−N Bond Cleavage



$[\alpha]^{27}_{D}$ = +1.3° (*c* 1.00, $CHCl_3$); IR (ATR) 1719 cm^{-1}; ^1H NMR (400 MHz) δ 1.40 (s, 9H), 2.69 (d, *J* = 2.2 Hz, 1H), 3.21 (d, *J* = 2.2 Hz, 1H), 3.82 (s, 3H), 3.84 (s, 6H), 4.08 (d, *J* = 14.0 Hz, 1H), 4.23 (d, *J* = 14.0 Hz, 1H), 6.53 (s, 2H), 7.24 (t, *J* = 6.0 Hz, 1H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.40 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz) δ 28.0, 45.7, 48.1, 54.6, 56.1, 60.8, 81.8, 103.0, 126.9, 128.1, 128.2, 134.1, 137.3, 139.2, 153.3, 167.6; HPLC (CHIRALCEL OD-H, λ 254 nm, hexane/^{i}PrOH 100/1, flow rate 1.0 mL/min) t_R for a major isomer 12.1 min, t_R for a minor isomer 17.9 min. Anal. Calcd for $C_{23}H_{29}NO_5$: C, 69.15; H, 7.32; N, 3.51. Found: C, 69.37; H, 7.38; N, 3.51.

cis-(2S,3S)-tert-Butyl 3-(3,4,5-trimethoxyphenyl)aziridine-2-carboxylate (cis-(2S,3S)-6): colorless oil; $[\alpha]^{27}_{D}$ = +3.3° (*c* 1.09, $CHCl_3$); IR (ATR) 1731 cm^{-1}; ^1H NMR (400 MHz) δ 1.21 (s, 9H), 2.53 (d, *J* = 7.0 Hz, 1H), 2.93 (d, *J* = 7.0 Hz, 1H), 3.52 (d, *J* = 13.8 Hz, 1H), 3.80 (s, 3H), 3.83 (s, 6H), 4.03 (d, *J* = 13.8 Hz, 1H), 6.63 (s, 2H), 7.26−7.46 (m, 5H); ^{13}C NMR (100 MHz) δ 27.8, 46.8, 47.1, 56.0, 60.7, 63.1, 81.0, 104.6, 127.1, 127.9, 128.3, 131.1, 137.0, 137.9, 152.7, 167.0; HRMS (FAB) calcd for $C_{23}H_{30}NO_5$ 400.2124, found 400.2123; HPLC (CHIRALCEL OD-H, λ 254 nm, hexane/^{i}PrOH 50/1, flow rate 1.0 mL/min) t_R for a major isomer 15.6 min, t_R for a minor isomer 13.5 min.

(±)-*tert*-Butyl 2-Benzylamino-3-(2-benzyloxy-4,5-methylenedioxyphenyl)-3-(3,4,5-trimethoxyphenyl)propanoate ((±)-11a). A solution of (±)-*trans*-**6** (104 mg, 0.259 mmol), $InCl_3$ (27 mg, 0.122 mmol), and sesamol benzyl ether (68 mg, 0.297 mmol) in CH_2Cl_2 (1.2 mL) was stirred at 35 °C for 2 h, quenched by addition of saturated $NaHCO_3$ solution (2 mL), and extracted with AcOEt (10 mL × 3). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 4/1) gave (±)-**11a** (89 mg, 55%, dr 5.6/1), which was recrystallized from hexane/Et_2O (1/1) to give a single isomer (60 mg, 37%) as colorless prisms, mp 125−126 °C: IR (ATR) 3676, 1721 cm^{-1}; ^1H NMR (400 MHz) δ 1.18 (s, 9H), 3.61 (d, *J* = 13.4 Hz, 1H), 3.63 (s, 6H) 3.75 (s, 3H), 3.77 (d, *J* = 10.5 Hz, 1H), 3.85 (d, *J* = 13.4 Hz, 1H), 4.48 (d, *J* = 10.5 Hz, 1H), 4.85 (d, *J* = 11.5 Hz, 1H), 4.94 (d, *J* = 11.5 Hz, 1H), 5.89 (d, *J* = 1.5 Hz, 1H), 5.94 (d, *J* = 1.5 Hz, 1H), 6.38 (s, 2H), 6.54 (s, 1H), 6.73 (s, 1H), 7.23−7.33 (m, 10H); ^{13}C NMR (100 MHz) δ 27.7, 47.6, 51.9, 55.8, 60.7, 64.1, 71.1, 80.8, 96.0, 101.0, 106.1, 107.6, 122.4, 127.0, 127.4, 127.8, 128.2, 128.4, 128.5, 136.4, 136.8, 137.0, 139.6, 141.3, 146.3, 151.4, 152.6, 173.8; HRMS (FAB) calcd for $C_{37}H_{42}NO_8$ 628.2911, found 628.2889. Anal. Calcd for $C_{37}H_{42}NO_8$: C, 70.79; H, 6.58; N, 2.23. Found: C, 70.67; H, 6.60; N, 2.26.

(±)-*tert*-Butyl 2-Benzylamino-3-(2-allyloxy-4,5-methylenedioxyphenyl)-3-(3,4,5-trimethoxyphenyl)propanoate ((±)-11b). A solution of (±)-*trans*-**6** (101 mg, 0.252 mmol), $InCl_3$ (18 mg, 0.08 mmol), and sesamol allyl ether (195 mg, 1.10 mmol) in CH_2Cl_2 (1.0 mL) was stirred at 30 °C for 3.5 h, quenched by addition of saturated $NaHCO_3$ solution (2 mL), and extracted with AcOEt (15 mL × 3). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 4/1) gave (±)-**11b** (87 mg, 60%, dr 4.3/1), which was recrystallized from hexane/Et_2O (1/1) to give a single isomer (46 mg, 32%) as colorless prisms, mp 113−114 °C: IR (ATR) 3676, 1721 cm^{-1}; ^1H NMR (400 MHz) δ 1.20 (s, 9H), 3.61 (d, *J* = 13.4 Hz, 1H), 3.75−3.81 (m, 10H), 3.84 (d, *J* = 13.4 Hz, 1H), 4.32−4.46 (m, 2H), 4.52 (d, *J* = 10.6 Hz, 1H), 5.19−5.40 (m, 2H), 5.88 (d, *J* = 1.5 Hz, 1H), 5.92 (d, *J* = 1.5 Hz, 1H), 5.92−6.03 (m, 1H), 6.47 (s, 1H), 6.49 (s, 2H), 6.71 (s, 1H), 7.16−7.33 (m, 5H); ^{13}C NMR (100 MHz,) δ 27.8, 51.9, 56.1, 60.7, 64.4, 65.8, 70.1, 80.9, 96.2, 101.5, 106.2, 107.7, 117.2, 122.7, 127.0, 128.2,

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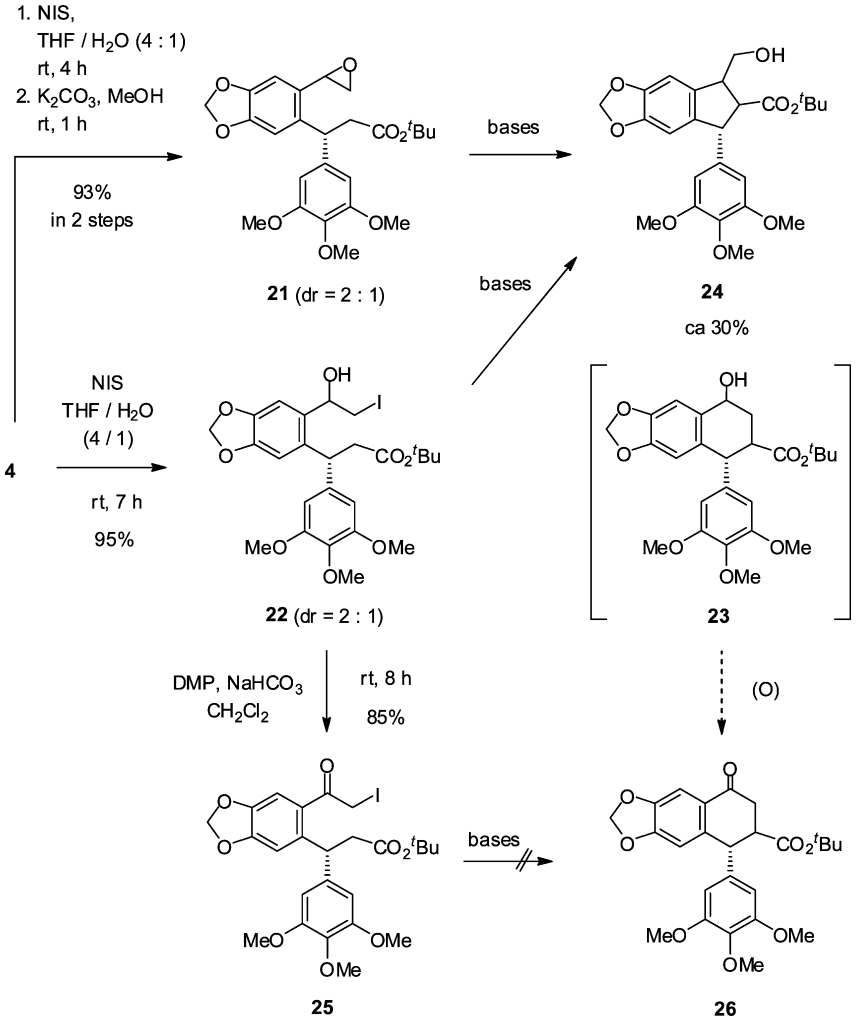
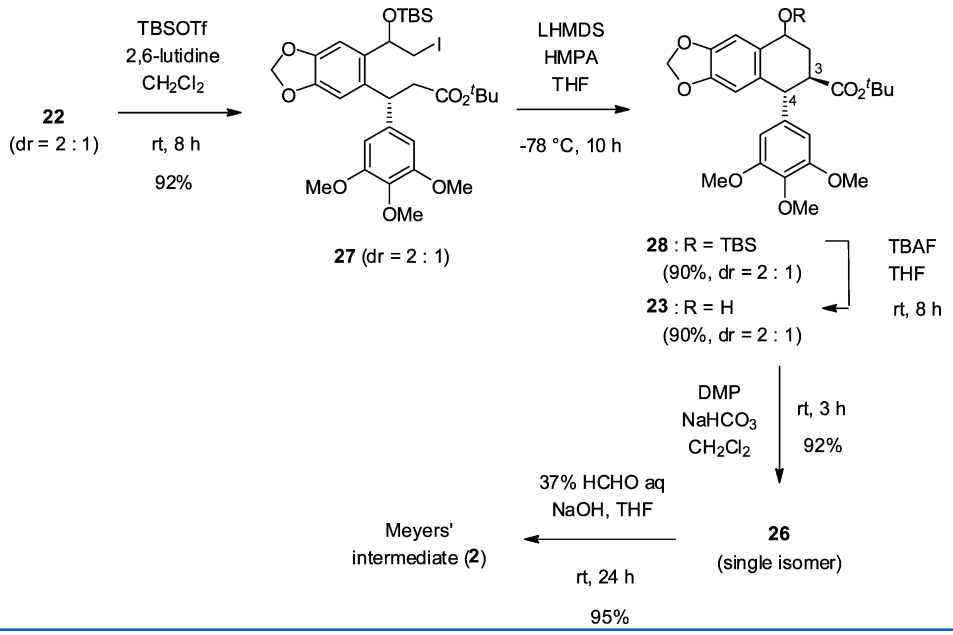
Scheme 6. Chemical Manipulation Trials for Preparation of 4-Aryltetralin Systems



Scheme 7. Preparation of Meyers' Intermediate 2



128.4, 133.5, 136.7, 139.8, 141.3, 146.4, 146.4, 151.4, 152.7, 173.9. Anal. Calcd for $C_{33}H_{39}NO_8$: C, 68.61; H, 6.80; N, 2.42. Found: C, 68.56; H, 6.80; N, 2.29.

(2*S*,3*R*)-*tert*-Butyl 2-Benzylamino-3-(2-hydroxy-4,5-methylenedioxyphenyl)-3-(3,4,5-trimethoxyphenyl)propanoate (11c). A solution of *trans*-(2*S*,3*R*)-**6** (50 mg, 0.125 mmol), $Zn(OTf)_2$ (4 mg,

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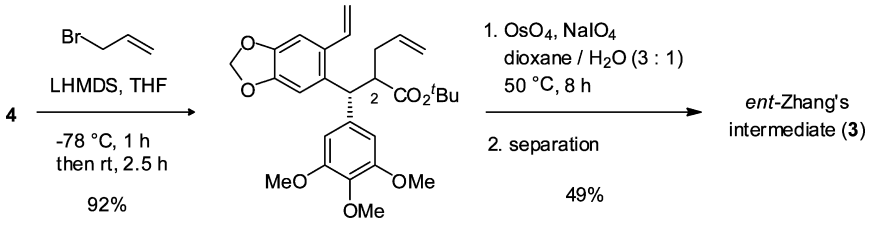
Scheme 8. Preparation of *ent*-Zhang's Intermediate 3



0.011 mmol), and sesamol (21 mg, 0.153 mmol) in CH_2Cl_2 (1.2 mL) was stirred at 30 °C for 9 h, quenched by addition of saturated $NaHCO_3$ solution (2 mL), and extracted with AcOEt (15 mL × 3). The combined organic solutions were washed with H_2O (5 mL × 2) and brine (5 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 6/1) gave **11c** (60 mg, 89%, dr 10/1) as colorless prisms, mp 145−147 °C, which were twice washed with hexane/Et_2O (1/1): $[\alpha]^{27}_D$ = +17.1° (*c* 1.09, $CHCl_3$); IR (ATR) 3278, 1722 cm^{-1}; ^1H NMR (400 MHz) δ 1.29 (s, 9H,), 3.48 (d, *J* = 13.4 Hz, 1H), 3.54 (d, *J* = 13.4 Hz, 1H), 3.80 (s, 6H), 3.82 (s, 3H), 3.84 (d, *J* = 5.6 Hz, 1H), 4.41 (d, *J* = 5.6 Hz, 1H), 5.85 (s, 2H), 6.42 (s, 1H), 6.52 (s, 1H), 6.56 (s, 2H), 7.09 (d, *J* = 6.8 Hz, 2H), 7.25−7.55 (m, 3H); ^{13}C NMR (100 MHz) δ 27.7, 52.2, 54.4, 56.0, 60.9, 64.8, 82.6, 100.3, 100.9, 105.5, 111.2, 115.7, 127.7, 128.1, 128.7, 134.8, 136.8, 137.4, 140.2, 147.8, 152.4, 153.3, 170.1; HRMS (FAB) calcd for $C_{30}H_{36}NO_8$ 538.2441, found 538.2427.

Ring Opening of the Methylenedioxyphenylaziridine (±)-*trans*-12 with 2,6-Dimethoxyphenol. A mixture of (±)-*trans*-**12** (102 mg, 0.290 mmol), $InCl_3$ (6 mg, 0.029 mmol), and 2,6-dimethoxyphenol (67 mg, 0.433 mmol) in CH_2Cl_2 (3 mL) was stirred at 40 °C for 14 h, quenched by addition of saturated $NaHCO_3$ solution (1 mL), and extracted with AcOEt (15 mL × 3). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 8/1) gave 2-aminopropanoate (±)-**14a** (32 mg, 22%) and the isomerized *cis*-aziridine (±)-*cis*-**12** (32 mg, 31%).

*(±)-tert-Butyl 2-benzylamino-3-[(2,6-dimethoxyphenyl)oxy]-3-(3,4-methylenedioxyphenyl)propanoate ((±)-**14a**):* colorless oil; IR (ATR) 1729 cm^{-1}; ^1H NMR (400 MHz) δ 1.20 (s, 9H), 3.658 (s, 6H), 3.660 (d, *J* = 6.7 Hz, 1H), 3.78 (d, *J* = 13.0 Hz, 1H), 3.94 (d, *J* = 13.0 Hz, 1H), 5.30 (d, *J* = 6.7 Hz, 1H), 5.90 (s, 2H), 6.44 (d, *J* = 8.4 Hz, 2H), 6.66 (d, *J* = 8.1 Hz, 1H), 6.83 (dd, *J* = 8.1, 1.6 Hz, 1H), 6.88 (t, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 1.6 Hz, 1H), 7.18−7.36 (m, 5H); ^{13}C NMR (100 MHz) δ 27.7, 52.4, 55.7, 67.9, 80.8, 84.5, 100.7, 105.2, 107.1, 109.1, 122.0, 123.5, 126.7, 128.2, 128.3, 132.9, 135.8, 140.3, 146.8, 147.1, 153.2, 171.2; HRMS (ESI) calcd for $C_{29}H_{34}NO_7$ 508.2335, found 508.2318.

*(±)-cis-tert-Butyl 3-(3,4-methylenedioxyphenyl)aziridine-2-carboxylate ((±)-cis-**12**):* mp 176−178 °C; IR (ATR) 1731 cm^{-1}; ^1H NMR (400 MHz) δ 1.24 (s, 9H), 2.48 (d, *J* = 7.0 Hz, 1H), 2.93 (d, *J* = 6.8 Hz, 1H), 3.53 (d, *J* = 14.0 Hz, 1H), 3.96 (d, *J* = 14.0 Hz, 1H), 5.90 (s, 2H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 7.22−7.44 (m, 5H); ^{13}C NMR (100 MHz) δ 27.8, 46.8, 47.1, 63.3, 81.1, 100.8, 107.7, 108.6, 121.2, 127.1, 127.8, 128.3, 129.3, 138.0, 146.7, 147.0, 167.2; HRMS (ESI) calcd for $C_{21}H_{23}NaNO_4$ 376.1525, found 376.1522.

(±)-*tert*-Butyl 2-Benzylamino-3-[(2,6-dimethoxyphenyl)-amino]-3-(3,4-methylenedioxyphenyl)propanoate ((±)-14b). A mixture of (±)-*trans*-**12** (64 mg, 0.181 mmol), $InCl_3$ (2 mg, 0.01 mmol), and 2,6-dimethoxyaniline (27 mg, 0.178 mmol) in CH_2Cl_2 (1.0 mL) was stirred at room temperature for 1.5 h, quenched by addition of saturated $NaHCO_3$ solution (3 mL), and extracted with AcOEt (5 mL × 3). The combined organic solutions were washed with H_2O (2 mL × 2) and brine (2 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 4/1) gave (±)-**14b** (83 mg, 92%) as colorless prisms, mp 97−99 °C: IR (ATR) 3334, 1711 cm^{-1}; ^1H NMR (400 MHz) δ 1.41 (s, 9H), 3.63 (d, *J* = 4.0 Hz, 1H), 3.66 (d, *J* = 13.1 Hz, 1H), 3.82 (s, 6H), 3.91 (d, *J* = 13.1 Hz, 1H), 5.25 (br s, 1H), 5.71 (br, 1H, exchangeable), 5.82 (s, 2H), 6.45 (d, *J* = 8.2 Hz, 2H), 6.58 (d, *J* = 8.1 Hz, 1H), 6.63 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.69 (t, *J* = 8.2 Hz, 1H), 6.73 (d, *J* = 1.5 Hz, 1H), 7.24−7.27 (m, 1H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.44 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (100 MHz) δ 28.1, 53.1, 55.8, 60.0, 66.1, 81.4, 100.6, 104.7, 107.5, 107.9, 119.3, 121.0, 125.8, 127.0, 128.27, 128.29, 133.8, 140.4, 146.4, 147.1, 150.6, 171.9; HRMS (ESI) calcd for $C_{29}H_{34}N_2NaO_6$ 529.2315, found 529.2334.

***tert*-Butyl 2-Benzylamino-3-[4,5-methylenedioxy-2-(trifluoromethanesulfonyloxy)phenyl]-3-(3,4,5-trimethoxyphenyl)-propanoate (15).** Tf_2O (0.2 mL, 1.17 mmol) was added dropwise to a stirred solution of **11c** (416 mg, 0.773 mmol) and pyridine (0.1 mL, 1.24 mmol) in CH_2Cl_2 (4.0 mL) at 0 °C, and the mixture was stirred at 0 °C for 5 h. After addition of saturated $NaHCO_3$ solution (10 mL), the mixture was extracted with AcOEt (30 mL × 3). The combined organic solutions were washed with H_2O (5 mL × 2) and brine (5 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 8/1) gave **15** (436 mg, 84%) as colorless prisms, mp 133−134 °C: IR (ATR) 1726 cm^{-1}; ^1H NMR (400 MHz) δ 1.26 (s, 9H), 3.62 (d, *J* = 13.5 Hz, 1H), 3.64 (d, *J* = 9.9 Hz, 1H), 3.78 (s, 3H), 3.80 (s, 6H), 3.85 (d, *J* = 13.5 Hz,1H), 4.39 (d, *J* = 9.9 Hz, 1H), 6.00 (d, *J* = 1.3 Hz, 1H), 6.05 (d, *J* = 1.3 Hz, 1H), 6.52 (s, 2H), 6.73 (s, 1H), 6.78 (s, 1H), 7.16−7.32 (m, 5H); ^{13}C NMR (100 MHz) δ 27.7, 47.1, 51.6, 56.1, 60.7, 64.5), 81.5, 102.4, 102.6, 105.9, 108.0, 116.9, 120.0, 127.1, 128.2, 135.0, 137.1, 139.3, 141.3, 146.8, 147.3, 153.0, 172.7; HRMS (ESI) calcd for $C_{31}H_{34}F_3NNaO_{10}S$ 692.1753, found 692.1733.

***tert*-Butyl 2-Benzylamino-3-(4,5-methylenedioxy-2-vinylphenyl)-3-(3,4,5-trimethoxyphenyl)propanoate (16).** Tributylvinyltin (0.1 mL, 0.342 mmol) was added dropwise to a stirred mixture of **15** (200 mg, 0.299 mmol), $Pd(PPh_3)_4$ (35 mg, 0.030 mmol), and LiCl (25 mg, 0.599 mmol) in DMF (3.0 mL) at room temperature, and the mixture was stirred at 90 °C for 8 h. After addition of 10% KF solution (2 mL), the mixture was stirred for 30 min and filtered through Celite, which was washed with AcOEt (10 mL). After separation of the organic solution the aqueous solution was extracted with AcOEt (20 mL × 2). The combined organic solutions were washed with H_2O (2 mL × 2) and brine (2 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 6/1) gave **16** (105 mg, 64%) as colorless prisms, mp 145−147 °C: IR (ATR) 3671, 1716 cm^{-1}; ^1H NMR (400 MHz) δ 1.22 (s, 9H), 3.58 (d, *J* = 13.0 Hz, 1H), 3.73 (d, *J* = 9.9 Hz, 1H), 3.77 (s, 3H), 3.78 (s, 6H), 3.81 (d, *J* = 13.0 Hz, 1H), 4.39 (d, *J* = 9.9 Hz, 1H), 5.22 (dd, *J* = 10.8, 1.3 Hz, 1H), 5.45 (dd, *J* = 17.2, 1.3 Hz, 1H), 5.92 (d, *J* = 1.5 Hz, 1H), 5.97 (d, *J* = 1.5 Hz, 1H), 6.43 (s, 2H), 6.80 (s, 1H), 6.92 (s, 1H), 7.05 (dd, *J* = 17.2, 10.8 Hz, 1H), 7.18−7.33 (m, 5H); ^{13}C NMR (100 MHz) δ 27.8, 49.3, 52.0, 56.1, 60.8, 65.1, 81.2, 101.0, 106.0, 106.5, 107.2, 115.4, 127.0, 128.2, 128.4, 131.6, 132.3, 134.6, 136.5, 139.5, 146.4, 147.4, 152.9, 173.5; HRMS (ESI) calcd for $C_{32}H_{38}NO_7$ 548.2648, found 548.2666.

***tert*-Butyl 2-(*tert*-Butoxycarbonylamino)-3-[4,5-methylenedioxy-2-(trifluoromethanesulfonyloxy)phenyl]-3-(3,4,5-trimethoxyphenyl)propanoate (17).** A mixture of **15** (202 mg, 0.301 mmol), Pd/C (21 mg), and Boc_2O (0.15 mL, 0.653 mmol) in AcOEt (2.0 mL) was vigorously stirred at room temperature for 6 h under a hydrogen atmosphere. The mixture was filtered through Celite, which was washed with AcOEt. After evaporation of the filtrate, column chromatography of the residue (SiO_2, hexane/AcOEt 4/1) gave **17** (204 mg, 100%) as colorless prisms, mp 65−67 °C: IR (ATR) 3649, 1734, 1716 cm^{-1}; ^1H NMR (400 MHz) δ 1.22 (s, 9H), 1.35 (s, 9H), 3.80 (s,

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3H), 3.83 (s, 6H), 4.44 (d, J = 9.9 Hz, 1H), 4.90 (t, J = 9.9 Hz, 1H), 4.97 (d, J = 9.5 Hz, 1H), 6.01 (s, 2H), 6.56 (s, 2H), 6.72 (s, 1H), 7.03 (s, 1H); ^{13}C NMR (100 MHz) δ 27.5, 28.1, 47.6, 56.0, 56.8, 60.8, 80.1, 82.1, 102.5, 102.8, 105.6, 108.1, 115.3, 117.4, 119.5, 121.6, 127.0, 133.8, 137.3, 140.9, 147.3, 147.6, 153.1, 155.1, 170.3; HRMS (FAB) calcd for $C_{29}H_{36}F_3NNaO_{12}S$ 702.1808, found 702.1779.

Reductive C−N Bond Cleavage of Aminopropanoate 11c. A 0.1 M solution of SmI_2 in THF (125 mL, 12.3 mmol) was prepared with CH_2I_2 (1.0 mL, 12.3 mmol), Sm (2.132 g, 14.2 mmol), and THF (125 mL) at room temperature. To the solution were successively added HMPA (2.2 mL, 12.4 mmol), H_2O (0.3 mL, 16.7 mmol), and a solution of **11c** (1.36 g, 2.52 mmol) in THF (7 mL), and the mixture was stirred at room temperature for 1 h and then for 10 min in air after addition of H_2O (20 mL). The precipitates were removed by filtration through Celite and repeatedly washed with AcOEt. After evaporation of the combined filtrates, the residue was diluted with AcOEt (200 mL). The organic solution was washed with 10% HCl solution (20 mL × 3), H_2O (10 mL × 2), and brine (10 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 3/1) gave **18** (1.01 g, 93%). The aqueous layer was made alkaline (pH >12) by addition of 10% NaOH solution and extracted with AcOEt (50 mL × 2). The combined organic solutions were washed with H_2O (10 mL × 2) and brine (10 mL × 2), dried (K_2CO_3), and evaporated. Column chromatography of the residue (NH-SiO_2, hexane/$CHCl_3$ 1/1) gave $BnNH_2$ (250 mg, 93%) as a colorless oil.

*(R)-tert-Butyl 3-(2-hydroxy-4,5-methylenedioxyphenyl)-3-(3,4,5-trimethoxyphenyl)propanoate (**18**):* colorless needles, mp 175−177 °C; $[\alpha]^{27}_D$ = −22.2° (*c* 1.01, $CHCl_3$); IR (ATR) 3422, 1716 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.39 (s, 9H), 2.92 (dd, J = 16.4, 10.4 Hz, 1H), 3.02 (dd, J = 16.4, 4.8 Hz, 1H), 3.82 (s, 3H), 3.83 (s, 6H), 4.66 (dd, J = 10.4, 4.8 Hz, 1H), 5.85 (d, J = 1.4 Hz, 1H), 5.86 (d, J = 1.4 Hz, 1H), 6.43 (s, 2H), 6.45 (s, 1H), 6.48 (s, 1H), 6.70 (s, 1H); ^{13}C NMR (100 MHz) δ 27.9, 39.1, 41.4, 56.1, 60.8, 82.0, 100.0, 101.0, 104.8, 107.2, 123.2, 136.6, 139.0, 141.8, 146.4, 148.0, 153.2, 173.4. Anal. Calcd for $C_{23}H_{28}O_8$: C, 63.88; H, 6.53. Found: C, 63.50; H, 6.56.

(*R*)-*tert*-Butyl 3-[4,5-Methylenedioxy-2-(trifluoromethanesulfonyloxy)phenyl]-3-(3,4,5-trimethoxyphenyl)propanoate (19). Tf_2O (0.03 mL, 0.175 mmol) was added dropwise to a stirred solution of **18** (50 mg, 0.116 mmol) and pyridine (0.03 mL, 0.372 mmol) in CH_2Cl_2 (1.2 mL) at −40 °C, and the mixture was stirred at 0 °C for 1 h. After addition of saturated $NaHCO_3$ solution (1 mL), the mixture was extracted with AcOEt (15 mL × 2). The combined organic solutions were washed with H_2O (1 mL) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 6/1) gave **19** (60 mg, 92%) as a colorless oil: $[\alpha]^{25}_D$ = −10.4° (*c* 1.02, $CHCl_3$); IR (ATR) 1718 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.32 (s, 9H), 2.81 (dd, J = 15.2, 7.8 Hz, 1H), 2.89 (dd, J = 15.2, 8.8 Hz, 1H), 3.81 (s, 3H), 3.83 (s, 6H), 4.72 (t, J = 8.2 Hz, 1H), 6.01 (d, J = 1.2 Hz, 1H), 6.02 (d, J = 1.2 Hz, 1H), 6.48 (s, 2H), 6.74 (s, 1H), 6.75 (s, 1H); ^{13}C NMR (100 MHz) δ 27.6, 40.4, 41.4, 56.0, 60.7, 80.8, 102.4, 102.8, 104.7, 107.5, 116.8, 120.0, 129.9, 136.8, 136.9, 140.1, 146.8, 147.5, 153.1, 169.8; HRMS (ESI) calcd for $C_{24}H_{27}F_3NaO_{10}S$ 587.1175, found 587.1151.

(*R*)-*tert*-Butyl 3-(4,5-Methylenedioxy-2-vinylphenyl)-3-(3,4,5-trimethoxyphenyl)propanoate (4). Tributylvinyltin (0.5 mL, 1.71 mmol) was added dropwise to a stirred solution of **19** (769 mg, 1.36 mmol), Pd(dppf)Cl_2·CH_2Cl_2 (110 mg, 0.135 mmol), and LiCl (118 mg, 2.79 mmol) in DMF (7.7 mL) at room temperature, and the mixture was stirred at 50 °C for 7 h. After addition of 10% KF solution (5 mL), the mixture was stirred at room temperature for 30 min and filtered through Celite, which was washed with AcOEt. After separation of the organic solution the aqueous solution was extracted with AcOEt (50 mL × 2). The combined organic solutions were washed with H_2O (5 mL × 2) and brine (5 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 6/1) gave **4** (541 mg, 90%, 81% ee) as colorless needles, mp 115−116 °C, which were twice recrystallized from hexane/MeOH (10/1) to give optically pure **4** (338 mg, 56%, 99% ee) as colorless needles, mp 115−116 °C: $[\alpha]^{25}_D$ = −20.2° (*c* 1.02, $CHCl_3$); IR (ATR) 1717 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.31 (s, 9H), 2.81 (dd, J = 15.3, 7.7 Hz, 1H), 2.88 (dd, J = 15.3, 8.4 Hz, 1H), 3.80 (s, 9H), 4.72 (t, J = 8.0 Hz, 1H), 5.26 (dd, J = 11.2, 1.3 Hz, 1H), 5.51 (dd, J = 17.2, 1.3 Hz, 1H), 5.92 (d, J = 1.5 Hz, 1H), 5.93 (d, J = 1.5 Hz, 1H), 6.41 (s, 2H), 6.66 (s, 1H), 6.96 (s, 1H), 7.09 (dd, J = 17.2, 11.2 Hz, 1H); ^{13}C NMR (100 MHz) δ 27.9, 42.1, 42.5, 56.1, 60.8, 80.7, 101.0, 104.8, 106.3, 107.2, 115.2, 130.4, 134.3, 134.7, 136.5, 138.8, 146.3, 147.5, 153.1, 170.9; HRMS (ESI) calcd for $C_{25}H_{30}NaO_7$ 465.1889, found 465.1878; HPLC (CHIRALCEL OD-H, λ 254 nm, hexane/^{i}PrOH 9/1, flow rate 1.0 mL/min) t_R for the major isomer 9.3 min, t_R for the minor isomer 10.9 min.

***trans*-Methyl 2-[2-(*tert*-Butoxycarbonyl)-1-(3,4,5-trimethoxyphenyl)ethyl]-4,5-methylenedioxyphenylpropenoate (20).** Methyl acrylate (0.05 mL, 0.555 mmol) was added dropwise to a stirred mixture of **19** (50 mg, 0.0893 mmol), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol), and $NaHCO_3$ (39 mg, 0.458 mmol) in DMF (1.0 mL) at room temperature, and the mixture was stirred at 120 °C for 24 h. After addition of H_2O (2 mL), the mixture was extracted with AcOEt (15 mL × 3). The combined organic solutions were washed with H_2O (2 mL × 3) and brine (2 mL × 3), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 3/1) gave **20** (27 mg, 61%) as colorless prisms, mp 168−170 °C: IR (ATR) 1717 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.31 (s, 9H), 2.85 (dd, J = 15.2, 8.1 Hz, 1H), 2.92 (dd, J = 15.2, 8.1 Hz, 1H), 3.78 (s, 3H), 3.80 (s, 3H), 3.81 (s, 6H), 4.79 (t, J = 8.1 Hz, 1H), 5.98 (d, J = 1.3 Hz, 1H), 5.99 (d, J = 1.3 Hz, 1H), 6.18 (d, J = 15.7 Hz, 1H), 6.41 (s, 1H), 6.79 (s, 1H), 7.01 (s, 1H), 8.17 (d, J = 15.7 Hz, 1H); ^{13}C NMR (100 MHz) δ 27.9, 42.2, 42.8, 51.6, 56.1, 60.8, 80.9, 101.5, 104.7, 106.4, 107.2, 118.0, 126.8, 136.5, 137.8, 138.4, 141.8, 146.6, 149.6, 153.2, 167.3, 170.4; HRMS (FAB) calcd for $C_{27}H_{32}O_9$ 500.2046, found 500.2043.

***tert*-Butyl 3-[4,5-Methylenedioxy-2-(oxacyclopropyl)-phenyl]-3-(3,4,5-trimethoxyphenyl)propanoate (21).** A solution of **4** (100 mg, 0.226 mmol) and NIS (61 mg, 0.270 mmol) in THF/H_2O (4/1, 1.0 mL) was stirred at room temperature for 4 h. After addition of K_2CO_3 (81 mg, 0.589 mmol) and MeOH (1.0 mL), the mixture was stirred at room temperature for 1 h, quenched by addition of saturated $Na_2S_2O_3$ solution (1 mL), and extracted with AcOEt (20 mL × 2). The combined organic solutions were washed with H_2O (1 mL × 2), dried, and evaporated to give **21** (97 mg, 93%, dr 2/1) as pale yellow needles, mp 78−82 °C, which were used in the next reaction without further purification: IR (ATR) 1717 cm^{-1}; ^{1}H NMR (400 MHz) for the major isomer δ 1.33 (s, 9H), 2.39 (dd, J = 5.7, 2.7 Hz, 1H), 2.92 (d, J = 8.1 Hz, 2H), 2.95 (dd, J = 5.7, 4.1 Hz, 1H), 3.79 (s, 6H), 3.803 (s, 3H), 4.12 (dd, J = 4.1, 2.7 Hz, 1H), 4.74 (t, J = 8.1 Hz, 1H), 5.92−5.95 (m, 2H), 6.38 (s, 2H), 6.758 (s, 1H), 6.79 (s, 1H); ^{1}H NMR (400 MHz) for the minor isomer δ 1.31 (s, 9H), 2.70 (dd, J = 5.8, 2.7 Hz, 1H), 2.88 (dd, J = 8.0, 7.0 Hz, 2H), 3.17 (dd, J = 5.8, 4.2 Hz, 1H), 3.801 (s, 6H), 3.81 (s, 3H), 4.01 (dd, J = 4.2, 2.7 Hz, 1H), 4.75 (t, J = 8.0 Hz,1H), 5.92−5.95 (m, 2H), 6.46 (s, 2H), 6.75 (s, 1H), 6.762 (s, 1H); ^{13}C NMR (100 MHz) for the major isomer δ 27.9, 42.2, 42.6, 50.3, 50.4, 56.1, 60.8, 80.8, 101.1, 104.8, 105.4, 106.9, 129.34, 135.1, 136.6, 138.9, 146.4, 147.25, 153.1, 170.78; ^{13}C NMR (100 MHz) for the minor isomer δ 27.9, 42.3, 42.5, 50.3, 50.4, 56.1, 60.7, 80.7, 101.1, 104.9, 105.4, 107.0, 129.28, 135.2, 136.7, 138.5, 146.3, 147.27, 153.2, 170.81; HRMS (ESI) calcd for $C_{25}H_{30}NaO_8$ 481.1838, found 481.1840.

(*R*)-*tert*-Butyl 3-{2-[(1-Hydroxy-2-iodo)ethyl]-4,5-methylenedioxyphenyl}-3-(3,4,5-trimethoxyphenyl)propanoate (22). A solution of **4** (200 mg, 0.452 mmol) and NIS (121 mg, 0.537 mmol) in THF/H_2O (4/1, 2.0 mL) was stirred at room temperature for 7 h in air, quenched by addition of saturated $Na_2S_2O_3$ solution (1 mL), and extracted with AcOEt (20 mL × 2). The combined organic solutions were washed with saturated $Na_2S_2O_3$ solution (1 mL), H_2O (1 mL × 2), and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 3/1) gave **22** (253 mg, 95%, dr 2/1) as colorless prisms, mp 182−184 °C: $[\alpha]^{25.5}_D$ = +22.1° (*c* 1.08, $CHCl_3$); IR (ATR) 3508, 1723 cm^{-1}; ^{1}H NMR (400 MHz) for the major isomer δ 1.32 (s, 9H), 2.71 (dd, J = 10.3, 3.2 Hz, 1H), 2.90 (d, J = 8.0 Hz, 2H), 3.00 (d, J = 2.4 Hz, 1H, exchangeable), 3.13 (t, J = 9.8 Hz, 1H), 3.796 (s, 3H), 3.83 (s, 6H), 4.61 (t, J = 8.0 Hz, 1H), 5.30 (dt, J = 9.3, 3.2 Hz, 1H), 5.96 (s, 2H), 6.40 (s, 2H), 6.81 (s, 1H), 7.00 (s, 1H); ^{1}H NMR (400 MHz) for the minor isomer δ 1.34 (s, 9H), 2.57 (d, J = 3.1 Hz, 1H, exchangeable), 2.89 (d, J = 8.0 Hz, 2H), 3.30 (t, J = 10.0 Hz, 1H), 3.55 (dd, J = 10.3, 3.0 Hz, 1H), 3.803 (s, 3H), 3.81 (s, 6H), 4.54 (t, J = 8.0 Hz, 1H), 5.11 (dt, J = 9.6,

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2.8 Hz, 1H), 5.96 (s, 2H), 6.37 (s, 2H), 6.83 (s, 1H), 7.03 (s, 1H); ^{13}C NMR (100 MHz) for the major isomer δ 13.1, 27.9, 42.2, 42.8, 56.2, 60.8, 70.1, 81.1, 101.2, 104.6, 106.0, 106.6, 133.0, 133.5, 136.7, 139.0, 146.5, 147.5, 153.3, 171.1; ^{13}C NMR (100 MHz) for the minor isomer δ 13.9, 27.9, 42.4, 42.5, 56.1, 60.7, 70.9, 81.0, 101.2, 104.8, 106.4, 107.2, 133.0, 133.2, 136.7, 138.6, 146.5, 147.4, 153.2, 170.8; HRMS (ESI) calcd for $C_{25}H_{31}IKO_8$ 625.0701, found 625.0709.

2-(*tert*-Butoxycarbonyl)-3-hydroxymethyl-5,6-methylenedioxy-1-(3,4,5-trimethoxyphenyl)indane (24). The reaction flask was dried by heat gun under reduced pressure for 1 h. A 1.6 M solution of LiHMDS in THF (0.16 mL, 0.256 mmol) was added dropwise to a stirred solution of epoxide **21** (50 mg, 0.109 mmol) in THF (2.2 mL) at −78 °C, and the mixture was stirred at −78 °C for 18 h. After addition of saturated NH_4Cl solution (1 mL) at 0 °C, the mixture was extracted with AcOEt (20 mL × 2). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 3/1) gave **24** (15 mg, 30%) as a colorless needles, mp 66−68 °C: IR (ATR) 3504, 1723 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.45 (s, 9H), 3.10 (t, J = 9.2 Hz, 1H), 3.47−3.54 (m,1H), 3.81 (s, 6H), 3.85 (s, 3H), 3.96 (dd, J = 11.2, 6.2 Hz, 1H), 4.06 (dd, J = 11.2, 4.2 Hz, 1H), 4.48 (d, J = 9.2 Hz, 1H), 5.92 (d, J = 1.3 Hz, 1H), 5.95 (d, J = 1.3 Hz, 1H), 6.40 (s, 1H), 6.43 (s, 2H), 6.74 (s, 1H); ^{13}C NMR (100 MHz) δ 28.1, 49.9, 53.6, 56.1, 59.2, 60.8, 65.3, 81.4, 101.2, 103.6, 105.3, 105.6, 133.9, 136.9, 138.2, 139.4, 147.5, 147.7, 153.2, 173.6; HRMS (ESI) calcd for $C_{25}H_{30}NaO_8$ 481.1838, found 481.1827.

***tert*-Butyl 3-(2-Iodoacetyl-4,5-methylenedioxyphenyl)-3-(3,4,5-trimethoxyphenyl)propanoate (25).** A mixture of **22** (50 mg, 0.085 mmol), DMP (54 mg, 0.128 mmol), and $NaHCO_3$ (22 mg, 0.256 mmol) in CH_2Cl_2 (0.9 mL) was stirred at room temperature for 4 h. After addition of saturated $NaHCO_3$ solution (1 mL) with ice cooling, the mixture was extracted with AcOEt (20 mL × 2). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 4/1) gave **25** (43 mg, 85%) as labile colorless prisms, mp 116−118 °C: ^{1}H NMR^{13} (400 MHz) δ 1.31 (s, 9H), 2.85 (dd, J = 15.6, 8.8 Hz, 1H), 2.93 (dd, J = 15.6, 7.3 Hz, 1H), 3.80 (s, 3H), 3.83 (s, 6H), 4.23 (d, J = 10.8 Hz, 1H), 4.30 (d, J = 10.8 Hz, 1H), 5.05 (t, J = 8.1 Hz, 1H), 5.99 (d, J = 1.3 Hz, 1H), 6.01 (d, J = 1.3 Hz, 1H), 6.53 (s, 2H), 6.78 (s, 1H), 7.04 (s, 1H).

(*R*)-*tert*-Butyl 3-{2-[1-(*tert*-Butyldimethylsilyloxy)-2-iodoethyl]-4,5-methylenedioxyphenyl}-3-(3,4,5-trimethoxyphenyl)-propanoate (27). TBSOTf (0.03 mL, 0.128 mmol) was added to a stirred solution of **22** (50 mg, 0.086 mmol, dr 2/1) and 2,6-lutidine (0.03 mL, 0.259 mmol) in CH_2Cl_2 (0.9 mL) at 0 °C, and the mixture was stirred at room temperature for 8 h. After addition of saturated $NaHCO_3$ solution (1 mL) at 0 °C, the mixture was extracted with AcOEt (20 mL × 2). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 6/1) gave **27** (55 mg, 92%, dr 2/1) as a colorless oil: $[\alpha]^{26}_D$ = +104.1° (c 0.954, $CHCl_3$); IR (ATR) 1731 cm^{-1}; ^{1}H NMR (400 MHz) for the major isomer δ −0.08 (s, 3H), 0.21 (s, 3H), 0.91 (s, 9H), 1.35 (s, 9H), 2.77−2.93 (m, 4H), 3.783 (s, 3H), 3.83 (s, 6H), 4.52 (t, J = 7.8 Hz, 1H), 5.15 (dd, J = 9.6, 1.7 Hz, 1H), 5.96 (d, J = 1.5 Hz, 1H), 5.99 (d, J = 1.5 Hz, 1H), 6.35 (s, 2H), 6.87 (s, 1H), 7.00 (s, 1H); ^{1}H NMR (400 MHz) for the minor isomer δ −0.24 (s, 3H), 0.10 (s, 3H), 0.79 (s, 9H), 1.35 (s, 9H), 2.34 (dd, J = 10.2, 1.9 Hz, 2H), 3.15 (dd, J = 10.4, 9.6 Hz, 1H), 3.57 (dd, J = 10.4, 2.0 Hz, 1H), 3.78 (s, 3H), 3.81 (s, 6H), 4.36 (dd, J = 9.4, 6.5 Hz, 1H), 4.96 (dd, J = 9.6, 2.0 Hz, 1H), 5.96 (d, J = 1.5 Hz, 1H), 6.01 (d, J = 1.5 Hz, 1H), 6.37 (s, 2H), 6.88 (s, 1H), 7.06 (s, 1H); ^{13}C NMR (100 MHz) for the major isomer δ −4.77, −4.63, 14.3, 18.2, 25.8, 28.0, 43.1, 43.4, 56.2, 60.9, 71.0, 80.8, 101.1, 104.6, 106.3, 107.0, 132.0, 135.4, 136.7, 139.3, 146.4, 147.1, 153.4, 170.6; ^{13}C NMR (100 MHz) for the minor isomer δ −5.43, −3.61, 14.1, 18.1, 25.7, 28.0, 43.0, 43.3, 56.1, 60.7, 67.9, 80.9, 101.1, 105.3, 106.2, 106.7, 131.4, 135.8, 136.8, 138.6, 146.3, 147.0, 153.4, 170.5; HRMS (ESI) calcd for $C_{31}H_{45}INaO_8Si$ 723.1826, found 723.1849.

(1*R*,2*R*)-2-(*tert*-Butoxylcarbonyl)-4-(*tert*-butyldimethylsilyloxy)-6,7-methylenedioxy-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydronaphthalene (28). The reaction flask was dried by heat gun under reduced pressure for 1 h. A 1.6 M solution of LHMDS in THF (0.1 mL, 0.16 mmol) was added dropwise to a stirred solution of **27** (65 mg, 0.092 mmol, dr 2/1) and HMPA (0.05 mL, 0.282 mmol) in THF (1.0 mL) at −78 °C, and the mixture was stirred at −78 °C for 10 h. After addition of saturated NH_4Cl solution (1 mL) at −78 °C, the mixture was extracted with AcOEt (20 mL × 2). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 6/1) gave **28** (47 mg, 90%, dr 2/1) as colorless needles, mp 69−74 °C: $[\alpha]^{26.5}_D$ = +34.0° (c 1.04, $CHCl_3$); IR (ATR) 1727 cm^{-1}; ^{1}H NMR (400 MHz) for the major isomer δ 0.18 (s, 3H), 0.24 (s, 3H), 0.98 (s, 9H), 1.27 (s, 9H), 1.96−2.11 (m, 2H), 2.82 (ddd, J = 13.2, 11.2, 2.0 Hz, 1H), 3.78 (s, 3H), 3.795 (s, 6H), 4.09−4.15 (m, 1H), 4.94 (dd, J = 11.2, 4.8 Hz, 1H), 5.86−5.90 (m, 2H), 6.22 (s, 1H), 6.33 (s, 2H), 6.95 (s, 1H); ^{1}H NMR (400 MHz) for the minor isomer δ 0.15 (s, 3H), 0.18 (s, 3H), 0.92 (s, 9H), 1.32 (s, 9H), 2.25 (dd, J = 5.3, 2.6 Hz, 1H), 2.28 (dd, J = 5.5, 2.4 Hz, 1H), 3.18 (dt, J = 10.7, 3.4 Hz, 1H), 3.799 (s, 3H), 3.83 (s, 6H), 4.09−4.15 (m, 1H), 4.75 (t, J = 3.7 Hz, 1H), 5.86−5.90 (m, 2H), 6.32 (s, 1H), 6.37 (s, 2H), 6.67 (s, 1H); ^{13}C NMR (100 MHz) for the major isomer δ −4.68, −3.92, 18.1, 25.9, 27.8, 36.7, 49.2, 49.5, 56.1, 60.9, 69.6, 80.5, 100.8, 106.0, 106.3, 108.8, 131.8, 133.6, 136.8, 139.5, 146.3, 146.6, 153.1, 173.1; ^{13}C NMR (100 MHz) for the minor isomer δ −4.45, −4.26, 18.0, 25.8, 27.9, 35.1, 45.0, 47.9, 56.0, 60.8, 67.7, 80.2, 101.0, 106.2, 108.1, 109.3, 131.7, 132.0, 136.9, 139.5, 145.9, 147.2, 153.0, 174.5; HRMS (ESI) calcd for $C_{31}H_{44}NaO_8Si$ 595.2703, found: 595.2707.

(1*R*,2*R*)-2-(*tert*-Butoxylcarbonyl)-4-hydroxy-6,7-methylenedioxy-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydronaphthalene (23). A 1.0 M solution of TBAF in THF (0.67 mL, 0.67 mmol) was added to a solution of **28** (192 mg, 0.335 mmol, dr 2/1) in THF (3 mL) at room temperature, and the mixture was stirred at the same temperature for 8 h in air. After addition of H_2O (3 mL), the mixture was extracted with AcOEt (30 mL × 2). The combined organic solutions were washed with H_2O (2 mL × 2) and brine (2 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 3/1) gave **23** (139 mg, 90%, dr 2/1) as colorless needles, mp 65−67 °C: $[\alpha]^{25}_D$ = +24.6° (c 0.97, $CHCl_3$); IR (ATR) 3733, 1717 cm^{-1}; ^{1}H NMR (400 MHz) for the major isomer δ 1.31 (s, 9H), 2.01 (ddd, J = 13.2, 10.0, 8.0 Hz, 1H), 2.35 (ddd, J = 13.2, 6.0, 3.2 Hz, 1H), 2.45 (d, J = 8.8 Hz, 1H), 2.85 (ddd, J = 10.0, 8.4, 3.2 Hz, 1H), 3.78 (s, 6H), 3.83 (s, 3H), 4.22 (d, J = 8.0 Hz, 1H), 4.80−4.86 (m, 1H), 5.90 (d, J = 1.2 Hz, 1H), 5.91 (d, J = 1.2 Hz, 1H), 6.26 (s, 2H), 6.39 (s, 1H), 7.08 (s, 1H); ^{1}H NMR (400 MHz) for the minor isomer δ 1.25 (s, 9H), 1.89 (d, J = 4.0 Hz, 1H), 2.13 (ddd, J = 13.6, 12.3, 3.2 Hz, 1H), 2.24 (dt, J = 13.6, 3.2 Hz, 1H), 3.13 (ddd, J = 12.3, 11.0, 2.8 Hz, 1H), 3.80 (s, 6H), 3.84 (s, 3H), 4.01 (d, J = 10.4 Hz, 1H), 4.80−4.86 (m, 1H), 5.90 (s,2H), 6.30 (s, 2H), 6.31 (s, 1H), 6.81 (s, 1H); ^{13}C NMR (150 MHz) for the major isomer δ 27.9, 34.48, 48.0, 48.7, 56.15, 60.87, 67.8, 81.0, 101.0, 106.1, 106.9, 108.9, 130.9, 132.8, 136.80, 139.5, 146.7, 147.1, 153.1, 173.9; ^{13}C NMR (150 MHz) for the minor isomer δ 27.8, 34.52, 44.6, 49.3, 56.17, 60.89, 67.1, 80.4, 101.1, 106.5, 108.5, 109.2, 130.4, 132.6, 136.85, 139.1, 146.4, 147.7, 153.1, 174.2; HRMS (ESI) calcd for $C_{25}H_{30}NaO_8$ 481.1838, found 481.1824.

(1*R*,2*R*)-2-(*tert*-Butoxylcarbonyl)-6,7-methylenedioxy-1-(3,4,5-trimethoxyphenyl)-2,3-dihydro-4(1*H*)-naphthalenone (26). A mixture of **23** (52 mg, 0.114 mmol, dr 2/1), DMP (66 mg, 0.155 mmol), and $NaHCO_3$ (25 mg, 0.299 mmol) in CH_2Cl_2 (1.1 mL) was stirred at room temperature for 3 h. After addition of saturated $NaHCO_3$ solution (1 mL) with ice cooling, the mixture was extracted with AcOEt (20 mL × 2). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 4/1) gave **26** (48 mg, 92%) as colorless prisms, mp 116−118 °C: $[\alpha]^{23}_D$ = +41.7° (c 1.01, $CHCl_3$); IR (ATR) 1721, 1666 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.24 (s, 9H), 2.78 (dd, J = 17.0, 4.6 Hz, 1H), 2.87 (dd, J = 17.0, 9.0 Hz, 1H), 3.22 (ddd, J = 9.0, 8.0, 4.6 Hz, 1H), 3.79 (s, 6H), 3.84 (s, 3H), 4.40 (d, J = 8.0 Hz, 1H), 6.00 (br s, 1H), 6.01 (br s, 1H), 6.34 (s, 2H), 6.41 (s, 1H), 7.52 (s, 1H); ^{13}C NMR (100 MHz) δ 27.7, 38.7, 48.6, 49.3, 56.2, 60.9, 81.4, 101.8, 105.8, 106.1, 108.8, 127.2, 136.9, 137.2, 140.8, 147.4, 152.5, 153.3, 171.8, 193.9; HRMS (ESI) calcd for $C_{25}H_{28}NaO_8$ 479.1682, found 479.1664.

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Preparation of Meyers' Intermediate 2. A mixture of **26** (30 mg, 0.066 mmol), 37% HCHO solution (1.0 mL), and 1 N NaOH solution (0.14 mL, 0.14 mmol) in THF (1.0 mL) was stirred at room temperature for 1 day in air. After addition of saturated NH_4Cl solution (1 mL), the mixture was extracted with AcOEt (20 mL × 2). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 3/1) gave **2** (28 mg, 95%) as colorless prisms, mp 106−108 °C (lit.[3g] mp 105−108 °C): $[\alpha]^{25}_D$ = −23.9° (*c* 0.98, $CHCl_3$) (lit.[3g] $[\alpha]^{23}_D$ = −23.7° (*c* 0.38, $CHCl_3$)); IR (ATR) 3505, 2921, 1770, 1659, 1593, 1474 cm^{-1}; ^1H NMR (400 MHz) δ 3.26 (br d, *J* = 11.4 Hz, 1H), 3.36 (d, *J* = 2.2 Hz, 1H), 3.64 (d, *J* = 11.4 Hz, 1H), 3.74 (s, 6H), 3.81 (s, 3H), 4.35 (d, *J* = 9.4 Hz, 1H), 4.59 (d, *J* = 9.4 Hz, 1H), 4.78 (d, *J* = 2.2 Hz, 1H), 6.07 (s, 1H), 6.10 (s, 1H), 6.15 (s, 2H), 6.70 (s, 1H), 7.47 (s, 1H); ^{13}C NMR (100 MHz) δ 42.8, 48.0, 54.0, 56.3, 60.9, 64.2, 72.7, 102.3, 105.1, 106.3, 109.7, 127.2, 137.3, 137.9, 138.8, 148.6, 153.6, 154.0, 176.0, 196.8; HRMS (ESI) calcd for $C_{23}H_{22}NaO_9$ 465.1162, found 465.1157.

***tert*-Butyl 2-Allyl-3-(4,5-methylenedioxy-2-vinylphenyl)-3-(3,4,5-trimethoxyphenyl)propanoate (29).** The reaction flask was dried by heat gun under reduced pressure for 1 h. A 1.6 M solution of LHMDS in THF (0.15 mL, 0.24 mmol) was added dropwise to a stirred solution of **4** (50 mg, 0.113 mmol) in THF (2.2 mL) at −78 °C, and the mixture was stirred at −78 °C for 30 min. After addition of allyl bromide (0.03 mL, 0.344 mmol) at −78 °C, the mixture was stirred at −78 °C for 1 h and then at room temperature for 2.5 h. After addition of saturated NH_4Cl solution (2 mL) with ice cooling, the mixture was extracted with AcOEt (15 mL × 3). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 6/1) gave **29** (50 mg, 92%, dr 3/1) as a colorless oil: IR (ATR) 1724 cm^{-1}; ^1H NMR (400 MHz) for the major isomer δ 1.19 (s, 9H), 2.24 (t, *J* = 7.0 Hz, 1H), 3.05−3.15 (m, 1H), 3.79 (s, 3H), 3.83 (s, 6H), 4.27 (d, *J* = 11.6 Hz, 1H), 4.96−5.05 (m, 2H), 5.27 (dd, *J* = 10.9, 1.2 Hz, 1H), 5.44 (dd, *J* = 17.1, 1.2 Hz, 1H), 5.67−5.81 (m, 1H), 5.88 (d, *J* = 1.3 Hz, 1H), 5.92 (d, *J* = 1.3 Hz, 1H), 6.47 (s, 2H), 6.87 (s, 1H), 6.97 (s, 1H), 7.19 (dd, *J* = 17.1, 10.9 Hz, 1H); ^1H NMR (400 MHz) for the minor isomer δ 1.21 (s, 9H), 2.24 (t, *J* = 7.0 Hz, 1H), 3.05−3.15 (m, 1H), 3.76 (s, 3H), 3.83 (s, 6H), 4.39 (d, *J* = 11.7 Hz, 1H), 4.96−5.05 (m, 2H), 5.30 (dd, *J* = 10.7, 1.2 Hz, 1H), 5.44 (dd, *J* = 16.8, 1.2 Hz, 1H), 5.67−5.81 (m, 1H), 5.90 (d, *J* = 1.2 Hz, 1H), 5.95 (d, *J* = 1.2 Hz, 1H), 6.51 (s, 2H), 6.80 (s, 1H), 6.92 (s, 1H), 7.18−7.22 (m, 1H); ^{13}C NMR (100 MHz) for the major isomer δ 27.7, 36.0, 48.5, 51.5, 56.1, 60.7, 80.5, 100.9, 105.0, 106.6, 106.9, 115.4, 116.8, 130.8, 134.1, 135.04, 135.1, 136.60, 137.4, 146.2, 147.3, 153.2, 172.7; ^{13}C NMR (100 MHz) for the minor isomer δ 27.8, 35.6, 48.0, 51.4, 56.0, 60.7, 80.6, 101.1, 105.2, 106.2, 106.5, 115.6, 116.8, 131.3, 133.5, 134.8, 134.96, 136.56, 138.2, 146.3, 147.8, 152.9, 173.5; HRMS (ESI) calcd for $C_{28}H_{34}NaO_7$ 505.2202, found 505.2188.

Preparation of *ent*-Zhang's Intermediate 3. A solution of **29** (31 mg, 0.064 mmol, dr 3/1), $NaIO_4$ (82 mg, 0.384 mmol), and 0.1 M OsO_4 solution (0.06 mL, 0.006 mmol) in 1,4-dioxane/H_2O (4/1, 2.0 mL) was stirred at 50 °C for 8 h in air, quenched by addition of saturated $Na_2S_2O_3$ solution (2 mL) with ice cooling, and extracted with AcOEt (15 mL × 3). The combined organic solutions were washed with H_2O (1 mL × 2) and brine (1 mL × 2), dried, and evaporated. Column chromatography of the residue (SiO_2, hexane/AcOEt 6/1) gave **3** (15 mg, 49%) as a colorless oil: $[\alpha]_D^{27}$ +94.74° (*c* 1.03, $CHCl_3$) (lit.[3a] $[\alpha]_D^{27}$ = −95.38° (*c* 1.66, $CHCl_3$)); IR (ATR) 1724, 1676 cm^{-1}; ^1H NMR (400 MHz) δ 1.19 (s, 9H), 2.60 (dd, *J* = 18.3, 3.7 Hz, 1H), 2.88 (ddd, *J* = 18.3, 10.0, 1.3 Hz, 1H), 3.56−3.64 (m, 1H), 3.79 (s, 3H), 3.84 (s, 6H), 5.23 (d, *J* = 11.7 Hz, 1H), 6.02 (d, *J* = 1.6 Hz, 1H), 6.06 (d, *J* = 1.6 Hz, 1H), 6.52 (s, 2H), 7.14 (s, 1H), 7.24 (s, 1H), 9.67 (s, 1H), 10.3 (s, 1H); ^{13}C NMR (100 MHz) δ 27.5, 44.9, 45.5, 45.6, 56.2, 60.7, 81.3, 102.1, 105.1, 108.3, 110.2, 128.2, 136.1, 137.2, 141.2, 146.9, 152.2, 153.5, 172.2, 189.6, 199.4; HRMS (ESI) calcd for $C_{26}H_{30}NaO_9$ 509.1788, found 509.1773.

■ ASSOCIATED CONTENT

Supporting Information

Figures giving NMR spectra for compounds **2**−**4**, *trans*-(2*S*,3*R*)- and *cis*-(2*S*,3*S*)-**6**, (±)-**11a,b**, **11c**, (±)-*cis*-**12**, (±)-**14a,b**, and **15**−**29** (only ^1H NMR spectrum for **25**) and HPLC traces for (±)-*trans*- and *trans*-(2*S*,3*R*)-**6**, (±)-*cis*- and *cis*-(2*S*,3*S*)-**6**, and (±)- and (*R*)-**4**. 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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