Chapter 5

Studies on the Synthesis of 2-Amino-2-(chroman-2-yl)ethanols via a Late-Stage Dienone-Phenol Rearrangement of Spirocyclohexadienone Scaffolds

Work of this Chapter has resulted in the following publication:

Devi, R. and Das, S. K. Combining spiro-fused cyclohexadienone – tetrahydrofuran ring system with glycine: Asymmetric synthesis of a new class of α-amino acid derivatives. *Tetrahedron Letters*, 59(23):2281-2283, 2018.

5.1. Introduction

β-Amino alcohol, also known as vicinal amino alcohol or 1,2-amino alcohol, is a privileged motif that serve as an indispensable structural unit in a very large number of bioactive compounds, clinical drugs, agrochemicals, and natural products [1-8]. Representative examples of this class of compounds are presented in Figure 5.1. It is important to mention that the biological activities of β-amino alcohols are often dependent on their absolute and relative stereochemistry. Apart from their proven pharmacological effects for a wide variety of human diseases and disorders, they are also interesting from a synthetic viewpoint. For examples, they can be readily converted into other useful building blocks, such as aziridines, 1,2-diamines, and α-amino acids and their derivatives.

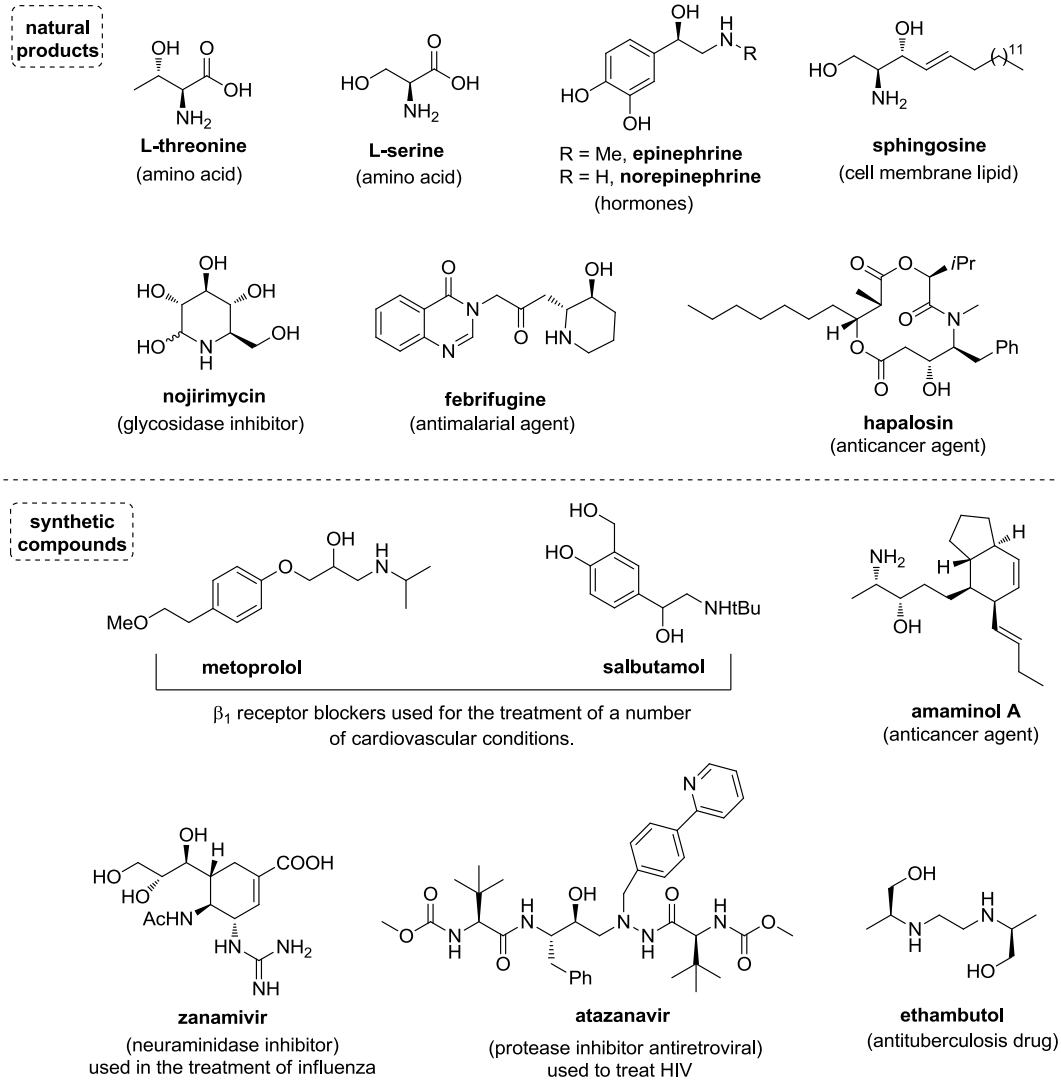


Figure 5.1. Representative examples of biologically important β-amino alcohols

They can also serve as excellent starting materials for the synthesis of diverse N- and N,O-heterocycles. Thus, β-amino alcohols have been extensively used as chiral synthons in the synthesis of biologically important natural products and synthetic compounds [9-11]. During the past few decades, enantiomerically pure β-amino alcohols ─ most commonly derived from natural sources ─ have also been used as chiral ligands and chiral auxiliaries in asymmetric catalysis [12-15]. These β-amino alcohols are generally derivatized to improve their chelating ability or to increase their steric directing effect.

Considerable research efforts have resulted in significant number of synthetic methods for β-amino alcohols [1,16,17]. Some common methods of synthesizing chiral β-amino alcohols are:

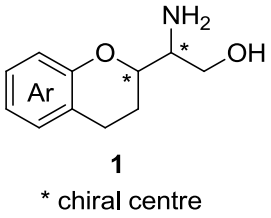
- reduction of β-amino acids (or their derivatives) and α-amino carbonyl compound,
- stereo-, regio-, and enantioselective ring opening of epoxides by N-nucleophiles,
- amino hydroxylation of olefins, and
- asymmetric hydroboration of enamines.

β-Amino alcohols can also be obtained in enantiomerically enriched/pure form via resolution of the corresponding racemic mixtures that are easily prepared through a variety of procedures.

5.2. Background and Objectives

Over the past few decades, tremendous advances have been made in the stereoselective synthesis of racemic and enantiomerically enriched/pure β-amino alcohols. To broaden the diversity, however, it is still highly desirable to synthesize new varieties of substituted β-amino alcohols, particularly those linked to another privileged structural unit via either the α or β carbon atom. As already mentioned in the **Chapter 1** of this thesis, incorporation of a privileged structure like the chroman scaffold has significant impact on chemical and biological properties of molecules. On the other hand, combination of two or more privileged structures has become a productive drug-design strategy as marrying two or more different privileged structures, which might have different mechanisms of action and targets, has often resulted into a hybrid compound with enhanced efficacy and the ability to overcome resistance to the parent drug [18,19]. In this context, synthesis of 2-amino-2-(chroman-2-yl)ethanols (Figure 5.2)

should be very attractive. Although diverse β-amino alcohols have been synthesized over past several decades, to the best of our knowledge, 2-amino-2-(chroman-2-yl)ethanols have never been reported in the literature. Thus, the aim of the research work described in this chapter was to access 2-amino-2-(chroman-2-yl)ethanols through the development of an efficient stereocontrolled synthetic route.



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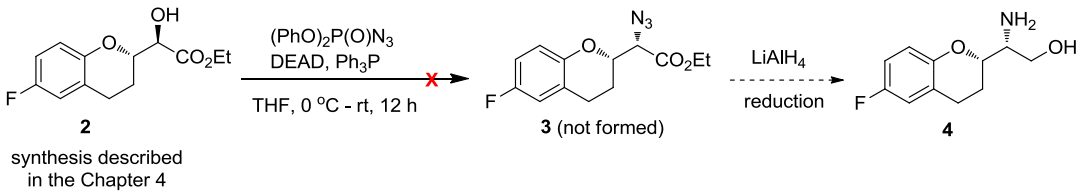
* chiral centre

Figure 5.2. Representative examples of biologically important β-amino alcohols

5.3. Results and Discussion

5.3.1. Attempted Synthesis of 2-Amino-2-(chroman-2-yl)ethanols from a Chroman-Bearing α-Hydroxy Ester

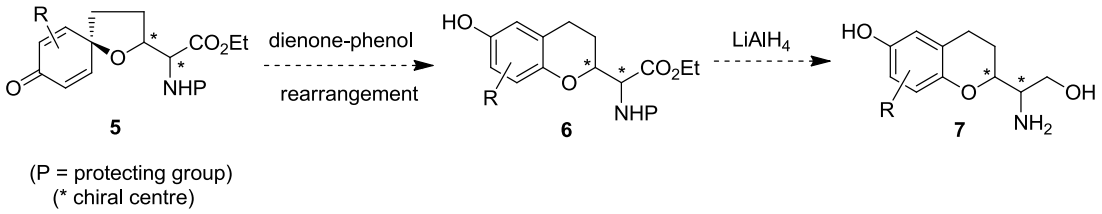
Since α-hydroxy esters are established starting materials for the synthesis of β-amino alcohols, our initial aim was to start with chroman-based α-hydroxy esters to synthesize 2-amino-2-(chroman-2-yl)ethanols. In the **Chapter 4** of this thesis, in the context of synthesizing nebivolol intermediates, we have demonstrated the synthesis of chroman-based α-hydroxy ester **2** in enantio- and diastereomerically pure form (Scheme 5.1). This helped us to quickly investigate the conversion of **2** into the corresponding chroman-based β-amino alcohol **4**. Unfortunately, attempt to synthesize **3** by azidation of **2** under Mitsunobu conditions ($(PhO)_2P(O)N_3$, DEAD, Ph_3P) failed (Scheme 5.1). S_N2 reactions of tosylate and triflate derivatives of **2** with NaN_3 in DMF were also disappointing (not shown here), resulting in either recovery or decomposition of the starting material. Therefore, we could not materialize the planned synthesis of **4** by $LiAlH_4$ reduction of **3**.



Scheme 5.1. Failed synthetic approach for chroman-linked α-amino alcohol

5.3.2. Attempted Synthesis of 2-Amino-2-(chroman-2-yl)ethanols via a Late-Stage Dienone-Phenol Rearrangement

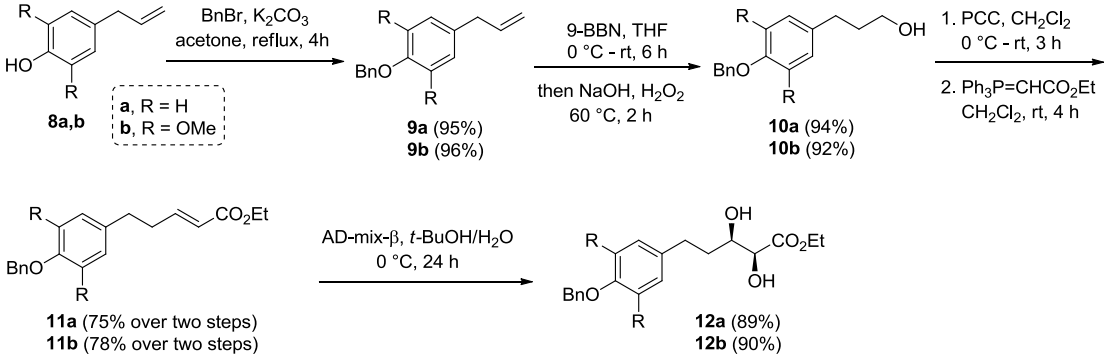
With the disappointing observations in the attempted conversion of **2** to **3**, we turned our attention for an alternative strategy. Acid-catalyzed/mediated dienone-phenol rearrangement of appropriate spirocyclic cyclohexadienone systems (1-oxaspiro[4.5]deca-6,9-dien-8-ones) is a powerful tool for the synthesis of chroman derivatives with free phenolic-OH group on the benzene ring [20-24]. Employing dienone-phenol rearrangement as a key step, the synthesis of 2-unsubstitued chromans is well established [25-28]. However, there exist only limited reports on the synthesis of 2-functionalized ones using this strategy [29,30], although synthesis of these later compounds would greatly increase the structural diversity of chroman derivatives. Along this direction, we sought to develop an alternative method for the synthesis of 2-(chroman-2-yl)glycine esters **6** via acid-catalyzed/mediated dienone-phenol rearrangement of spirocyclohexadienone-embedded glycine esters **5** (Scheme 5.2). The major advantage of this new proposed route would be the incorporation of an amine group prior to a late-stage construction of the chroman ring, thus ducking the difficulty we faced while attempting to synthesize **4** (Scheme 5.1). However, in order to accomplish this goal it was necessary to overcome a key obstacle. Treatment of **5** with catalytic/stoichiometric amount of a Brønsted/Lewis acid must either induce simultaneous removal of the amino protecting group and the dienone-phenol rearrangement reaction, or bring up only the rearrangement reaction without affecting the protecting group. Compound **6**, if successfully synthesized, was expected to provide chroman-linked β-(*N*-protected)amino alcohols **7** by its $LiAlH_4$ reduction.



Scheme 5.2. Revised synthetic approach for chroman-linked α-amino alcohol

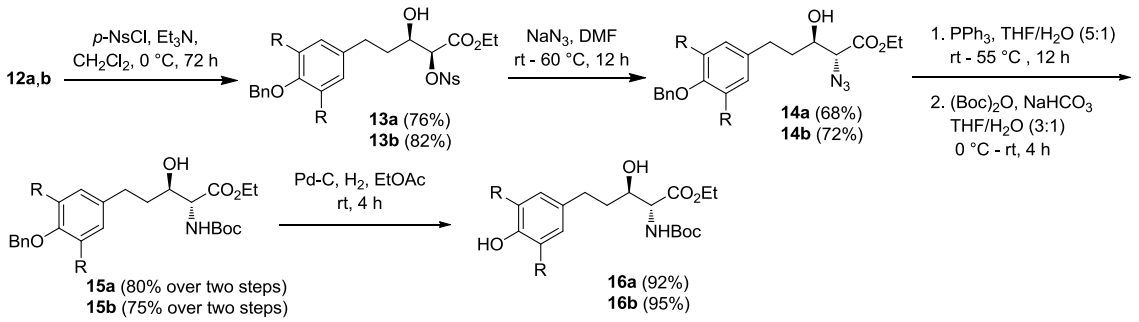
The rather unpredictable nature of this revised designed strategy toward **7** dictated a number of model studies prior to its finalization. As shown in Scheme 5.3, we first set out to synthesize enantiomerically pure α,β-dihydroxy esters **12a** and **12b** that would be

used as starting materials for the synthesis of spirocyclohexadienone-embedded glycine esters. Compounds **12a** and **12b** were conveniently prepared in from commercially available 4-allylphenols **8a** and **8b**, respectively. Thus, benzylation of **8a** and **8b** with BnBr in the presence of K_2CO_3 followed by hydroboration (9-BBN)─oxidation (H_2O_2, NaOH) of the resulting compounds **9a**,**b** gave primary alcohols **10a** and **10b**, respectively. PCC oxidation of **10a**,**b** followed by Wittig olefination of the resulting crude aldehydes with $Ph_3P{=}CHCO_2Et$ furnished **11a** and **11b**, respectively. Dihydroxylation of **11a**,**b** under the Sharpless asymmetric dihydroxylation conditions (AD mix β) provided α,β-dihydroxy esters **12a** (*ee*: 96.2%) and **12b** (*ee*: 95.1%), respectively.



Scheme 5.3. Synthesis of precursor diols

Next, regioselective mononosylation of **12a**,**b** followed by azidation of the resulting β-hydroxy-α-nosyloxy esters **13a**,**b** with NaN_3 afforded β-hydroxy-α-azido esters **14a** and **14b**, respectively (Scheme 5.4). Subsequent attempted one-pot debenzylation ─ azide reduction ─ *N*-Boc protection of **14a** and **14b** to provide **15a**,**b** under standard debenzylation conditions (Pd-C, H_2) and in the presence of $(Boc)_2O$ was unsuccessful (not shown here). Consequently, a stepwise protocol was followed.

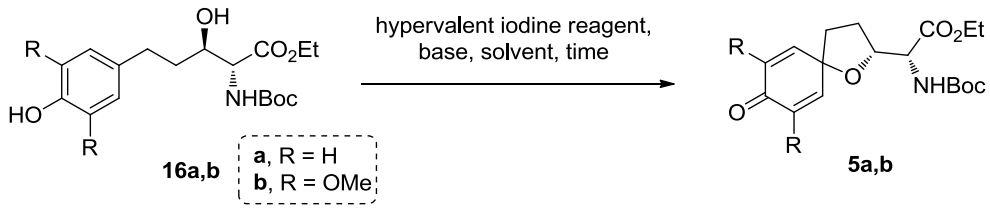


Scheme 5.4. Synthesis of Synthesis of *N*-Boc-protected α-hydroxy-β-amino esters

Thus, Staudinger reduction (PPh_3, THF, H_2O) of **14a**,**b** followed by *N*-Boc protection of the resulting crude amines yielded **15a** and **15b**, respectively. Finally, compounds **15a,b** were subjected to debenzylation with Pd-C and H_2 to afford phenols **16a** and **16b**, respectively.

With the key compounds **16a,b** in hand, our attention was turned for their conversion to spiro-fused cyclohexadienone ─ tetrahydrofuran (SFCT) system-embedded glycine esters **5a,b**. Toward that objective, we decided to employ hypervalent iodine(III)-based reagents to effect the oxidative dearomatization [31-35] of **16a,b** under six different reaction conditions (Table 5.1). Treatment of compounds **16a,b** with phenyliodine(III) diacetate (PIDA) in MeCN led to complete consumption of starting materials within 15 min and formation of desired products **5a,b**, albeit in very low yields (Table 5.1, entry 1). The other well-known hypervalent iodine(III) reagent, i.e., phenyliodine(III) bis(trifluoroacetate) (PIFA) in MeCN also furnished similar yields (entry 2). With PIDA and PIFA as the oxidizing agents, the screening showed that the reaction gave better yields in trifluoroethanol (TFE) and hexafluoroisopropanol (HFIP) (entries 3-6).

Table 5.1. Screening of reaction conditions on the oxidative dearomatization ─ regioselective spirocyclization of 16a,b



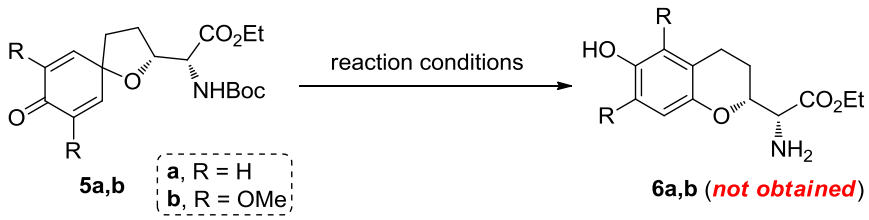
entry	conditions[a]	yield[b]
1	PIDA, K_2CO_3, MeCN	27% (**5a**); 36% (**5b**)
2	PIFA, pyridine, MeCN	29% (**5a**); 35% (**5b**)
3	PIDA, K_2CO_3, TFE	52% (**5a**); 55% (**5b**)
4	PIFA, pyridine, TFE	55% (**5a**); 59% (**5b**)
5	PIDA, K_2CO_3, HFIP	65% (**5a**); 62% (**5b**)
6	PIFA, K_2CO_3, HFIP	57% (**5a**); 58% (**5b**)

[a]Reaction conditions: **6a** or **6b** (0.1 mmol), K_2CO_3 (0.12 mmol) or pyridine (0.2 mL), solvent (2 mL) at 0 °C – rt for 15 min (for entries 1 and 2) or 10 min (for entries 3-6); [b]Isolated yields after column chromatography

Compared to their non-fluorinated alcohol analogues, TFE and HFIP have low pKa, low nucleophilicity, and very high ionizing power [36]. These are major stabilizing factors for the intermediate phenoxenium cation formed during an oxidative dearomatization process mediated by hypervalent iodine(III) ragents [31-35]. Thus, the higher yields in TFE and HFIP compared to that in acetonitrile were not surprising. Nevertheless, this transformation was best carried out using PIDA as an oxidizing agent and K_2CO_3 as a base in HFIP (entry 5). It is important to mention that Boc group was not affected by HFIP which has been reported to cause Boc deprotection, albeit under much harsher reaction conditions (compared to the conditions described in Table 5.1) [37].

With the establishment of successful spirocyclization reaction conditions, the stage was set for the much anticipated simultaneous *N*-Boc deprotection and dienone-phenol rearrangement of **5a** and **5b**, leading to the formation of the corresponding 2-(chroman-2-yl)glycine esters **6a**,**b**. We evaluated a variety of literature known conditions to effect this transformation; however, the desired products **6a**,**b** were never formed ─ in each trial starting material was either decomposed or a complex product mixture was generated (Table 5.2).

Table 5.2. Attempted one-pot dienone-phenol rearrangement and Boc-deprotection of 5a,b



5a,b

a, R = H
b, R = OMe

6a,b (***not obtained***)

entry	conditions[a]	result
1	$BF_3{\cdot}OEt_2$, 0 °C – rt,	decomposition
2	TsOH, CH_2Cl_2, rt, 1 h	complex product mixture
3	TsOH, MeCN, 80 °C, 1 h	complex product mixture
4	TsOH, EtOH, 80 °C, 1 h	decomposition
5	TsOH, 1:1 H_2O/MeOH, 60 °C, 1 h	decomposition
6	TFA, CH_2Cl_2, rt, 2 h	complex product mixture
6	HCl, $CHCl_3$, 60 °C, 1 h	complex product mixture

[a]Reaction conditions: **5a** or **5b** (0.1 mmol), 0.1 M substrate concentration and Brønsted/Lewis acid (0.4 mmol)

The failure to materialize this transformation could not be explained. At this point in the project, we were forced to confess that the crucial dienone-phenol rearrangement of these substrates might never be realized, at least by our hands. Therefore, we abandoned this approach for the synthesis of the desired 2-amino-2-(chroman-2-yl)ethanols. The synthesis of 2-amino-2-(chroman-2-yl)ethanols was subsequently successful following an entirely different approach which will be discussed separately in the next chapter (**Chapter 6**) of this thesis.

5.4. Conclusion

In summary, we have described our efforts toward the synthesis of 2-amino-2-(chroman-2-yl)ethanols for which we chose a particularly attractive but challenging synthetic route involving an one-pot dienone-phenol rearrangement and Boc-deprotection as key step. Unfortunately, in the end, the synthesis was embittered as we were unable to effect this crucial rearrangement reaction. While disappointed with failure of the planned synthesis of 2-amino-2-(chroman-2-yl)ethanols, we were delighted to find that the study provided synthetic access to spirocyclohexadienone containing glycine esters through an intramolecular oxidative dearomatization reaction. On the other hand, spirocyclohexadienones are present as substructures in many bioactive natural products, pharmaceuticals, and compounds for diverse other applications. The spiro-fused cyclohexadienone ─ tetrahydrofuran (SFCT) system is small subset of spirocyclohexadienones. During the past decades, diverse SFCT systems have been reported ─ but those bearing an α-amino acid derivative moiety like **5** have never been synthesized. Such hybrid compounds bearing three different well-known structural units (cyclohexadienone ─ tetrahydrofuran ─ α-amino ester) might be useful in the drug discovery process.

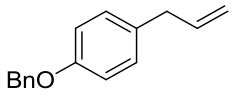
5.5. Experimental Section

5.5.1. General Remarks

Same as described in the **Chapter 2**, **Section 2.6.1** of this thesis.

5.5.2. Preparation of Compounds

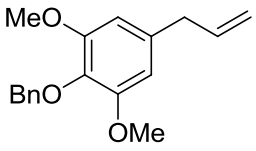
1-Allyl-4-(benzyloxy)benzene (9a):



9a

A mixture of 4-allylphenol **8a** (3.0 g, 22.35 mmol, 1.50 equiv), K_2CO_3 (4.63 g, 33.52 mmol) and benzyl bromide (2.90 mL, 24.52 mmol, 1.10 equiv) in acetone (80 mL) was stirred under reflux for 4 h. The mixture was filtered to remove the solid and the filtrate was concentrated to dryness under reduced pressure. The resulting residue was dissolved in EtOAc (50 mL), and washed with water (50 mL) and brine (50 mL). The separated organic layer was dried over anh. Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (0-5% EtOAc in hexanes) to obtain the title compound **9a** as a colorless oil**.** Yield: (4.76 g, 95%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46-7.40 (m, 2H), 7.40-7.35 (m, 2H), 7.34-7.28 (m, 1H), 7.10 (d, 2H, *J* = 8.6 Hz), 6.91 (d, 2H, *J* = 8.6 Hz), 6.01-5.89 (m, 1H), 5.10-5.01 (m, 2H), 5.04 (s, 2H), 3.33 (d, 2H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.2, 137.8, 137.2, 132.4, 129.5, 128.5, 127.9, 127.4, 115.4, 114.8, 70.1, 39.3. The spectral data exactly matched with the literature data [38].

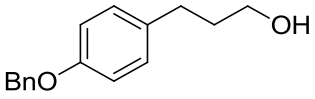
5-Allyl-2-(benzyloxy)-1,3-dimethoxybenzene (9b):



9b

Following the above-described procedure, compound **8b** (3.0 g, 15.44 mmol) was subjected to the benzylation reaction. The resulting crude product was purified by silica gel column chromatography (0-10% EtOAc in hexanes) to obtain the title compound **9b** as a colorless semi-solid**.** Yield: (4.21 g, 96%); R_f: 0.42 (silica gel, 40% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.3 Hz, 2H), 7.35-7.25 (m, 3H), 6.40 (s, 2H), 5.99-5.82 (m, 1H), 5.09-4.99 (m, 2H), 5.02 (s, 2H), 3.31 (d, *J* = 7.0 Hz, 2H); This is a known molecule [39].

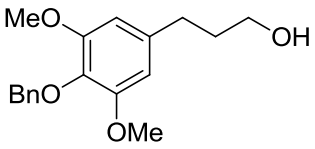
3-(4-(Benzyloxy)phenyl)propan-1-ol (10a).



10a

To stirred solution of **9a** (4.0 g, 17.83 mmol, 1.00 equiv) in anh. THF (80 mL) was added 9-BBN (0.5 M solution in THF, 70.0 mL, 35.0 mmol, 1.96 equiv) dropwise under a nitrogen atmosphere at 0 °C. The mixture was then stirred at rt for 6 h. The reaction was carefully terminated by the addition of H_2O (5 mL) at 0 °C. Next, 3 N NaOH solution (50 mL) and 30% H_2O_2 (40 mL) were added to it sequentially. The reaction mixture was then stirred for an additional 2 h at 60 °C. After cooling to rt, the reaction mixture was then partitioned between brine (80 mL) and EtOAc (80 mL). The layers were separated and the aqueous phase was extracted with EtOAc (50 mL). The combined organic extracts were washed with brine (100 mL), dried over anh. Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (5-20% EtOAc in hexanes) to obtain the title compound **10a** as a white solid**.** Yield: (4.06 g, 94%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* =7.0 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.35-7.32 (m, 1H), 7.13 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 5.06 (s, 2H), 3.68 (t, *J* = 6.3 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.90-1.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 137.1, 134.1, 129.3, 128.5, 127.9, 127.4, 114.7, 70.0, 62.2, 34.4, 31.1. The spectral data matched with the literature data [40].

3-(4-(Benzyloxy)-3,5-dimethoxyphenyl)propan-1-ol (10b):

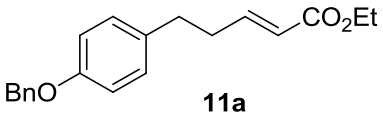


10b

Following the above-described procedure, compound **9b** (4.0 g, 14.06 mmol) was subjected to the hydroboration-oxidation reaction. The resulting crude product was purified by silica gel column chromatography (5-25% EtOAc in hexanes) to obtain the title compound **10b** as a colorless semi-solid**.** Yield: (3.91 g, 92%); R_f: 0.42 (silica gel, 40% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* =7.3 Hz, 2H), 7.35-7.25 (m, 3H), 6.40 (s, 2H), 4.97 (s, 2H), 3.79 (s, 6H), 3.62 (t, *J* = 5.9 Hz, 2H), 2.62 (t, *J* = 7.3 Hz, 2H), 1.89-1.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.1, 137.7, 134.7,

128.2, 127.9, 127.5, 105.1, 74.8, 61.7, 55.8, 34.0, 32.3; Anal. Calcd. for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33, found: C, 71.37; H, 7.28.

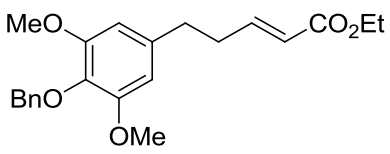
(*E*)-Ethyl 5-(4-(benzyloxy)phenyl)pent-2-enoate (11a):



11a

To a stirred solution of compound **10a** (3.5 g, 14.44 mmol, 1.00 equiv) in anh. CH_2Cl_2 (60 mL) was added PCC (4.67 g, 21.66 mmol, 1.50 equiv) under an atmosphere of nitrogen at 0 °C. The reaction mixture was stirred vigorously for 3 h at rt. The solvent was evaporated under reduced pressure and the residue was suspended in anh. Et_2O (50 mL) and stirred vigorously for 5 min. The resulting mixture was filtered through a small pad of silica gel. The filtrate was concentrated to dryness under reduced pressure. The resulting residual oil (crude aldehyde) was dissolved in CH_2Cl_2 (30 mL) and (carbethoxymethylene)triphenylphosphorane (5.67 g, 16.25 mmol) was added. The reaction mixture was stirred for 4 h at rt. Solvent was removed under reduced pressure and the resulting residue was purified by silica gel column chromatography (0-5% EtOAc in hexanes) to obtain the title compound **11a** as a colorless oil**.** Yield: (3.36 g, 75%); R_f: 0.46 (silica gel, 20% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45-7.31 (m, 5H), 7.10 (d, *J* = 8.7 Hz, 2H), 7.00 (dt, *J* = 15.6, 6.9 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 2H), 5.84 (dt, *J* = 15.6, 1.4 Hz, 1H), 5.05 (s, 2H), 4.19 (q, *J* = 7.0, 2H), 2.73 (t, *J* = 8.0, 2H), 2.53-2.47 (m, 2H), 1.29 (t, *J* = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 157.2, 148.1, 137.1, 133.2, 129.3, 128.6, 127.9, 127.5, 121.8, 114.9, 70.0, 60.2, 34.1, 33.5, 14.3; Anal. Calcd. for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14, found: C, 77.46; H, 7.18.

(*E*)-Ethyl 5-(4-(benzyloxy)-3,5-dimethoxyphenyl)pent-2-enoate (11b):

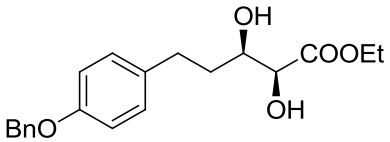


11b

Following the above-described procedure, compound **10b** (3.5 g, 11.57 mmol) was subjected to the PCC oxidation ─ Wittig olefination reaction sequence. The resulting crude product was purified by silica gel column chromatography (0-15% EtOAc in

hexanes) to obtain the title compound **11b** as a colorless oil**.** Yield: (3.34 g, 78%); R_f: 0.42 (silica gel, 25% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* =7.3 Hz, 2H), 7.35-7.25 (m, 3H), 6.99 (dt, *J* = 16.0, 6.9 Hz, 1H), 6.37 (s, 2H), 5.84 (dt, *J* = 15.6, 1.4 Hz, 1H), 4.97 (s, 2H), 4.18 (q, *J* = 7.0, 2H), 3.79 (s, 6H), 2.70 (t, *J* = 8.0, 2H), 2.53-2.47 (m, 2H), 1.27 (t, *J* = 7.0, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 153.3, 147.8, 137.8, 136.5, 135.2, 128.3, 128.0, 127.6, 121.8, 115.3, 74.9, 60.1, 56.0, 34.7, 33.8, 14.2; Anal. Calcd. for $C_{22}H_{26}O_5$: C, 71.33; H, 7.07, found: C, 71.45; H, 7.14.

(2*S*,3*R*)-Ethyl 5-(4-(benzyloxy)phenyl)-2,3-dihydroxypentanoate (12a):

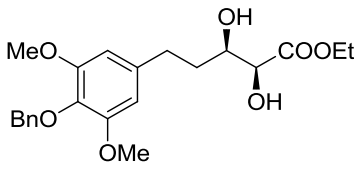


12a

To a stirred solution of *tert*-butyl alcohol (25 mL) and water (30 mL) were added AD-mix-β (7.04 g, 1.4 g/mmol of **11a**) and methanesulfonamide (0.62 g, 6.44 mmol, 1.28 equiv) at rt. The mixture was vigorously stirred at rt until both phases were clear and then cooled to 0 °C. A solution of compound **11a** (1.56 g, 5.02 mmol, 1.00 equiv) in *tert*-butyl alcohol (5 mL) was added at 0 °C. The reaction mixture was stirred at the same temperature for 24 h. The reaction was quenched at 0 °C by the addition of sodium bisulfite (5 g), warmed to rt, and further stirred for 1 h. The reaction mixture was then extracted with EtOAc (3×100 mL). The combined organic layers were washed with aqueous 2 N KOH solution (50 mL), water (50 mL), and brine (50 mL), dried over anh. Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (15-40% EtOAc in hexanes) to obtain the title compound **12a** as a colorless gum (1.54 g, 89%); R_f: 0.32 (silica gel, 50% EtOAc in hexanes); *ee* = 96.2% (HPLC column: ChiralPac-1A; temp: 25 °C; mobile phase: hexane/2-propanol (75/25 v/v); flow rate: 0.8 mL/min; wavelength: 220 nm; major enantiomer: t_R = 11.48 min, minor enantiomer: t_R = 13.83 min); $[\alpha]^D_{25}$ = +11.43 (*c* = 1.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45-7.31 (m, 5H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.92 (d, *J* = 8.7 Hz, 2H), 5.05 (s, 2H), 4.33-4.25 (m, 2H), 4.10-4.09 (m, 1H), 3.92-3.91 (m, 1H), 3.09 (br s, 1H), 2.82-2.63 (m, 2H), 2.02-1.87 (m, 3H), 1.32 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 157.1, 137.1, 133.8, 129.3, 128.5, 127.9,

127.4, 114.8, 73.1, 71.8, 70.0, 62.2, 35.6, 31.0, 14.1; Anal. Calcd. for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02, found: C, 69.83; H, 7.04.

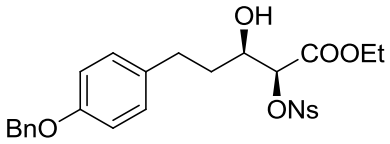
(2*S*,3*R*)-Ethyl 5-(4-(benzyloxy)-3,5-dimethoxyphenyl)-2,3-dihydroxypentanoate (12b):



12b

Following the above-described procedure, compound **11b** (1.5 g, 4.05 mmol) was subjected to the dihydroxylation reaction. The resulting crude product was purified by silica gel column chromatography (15-50% EtOAc in hexanes) to obtain the title compound **12b** as a white solid (1.47 g, 90%); R_f: 0.38 (silica gel, 60% EtOAc in hexanes); *ee* = 95.1% (HPLC column: ChiralPac-1A; temp: 25 °C; mobile phase: hexane/2-propanol (75/25 v/v); flow rate: 0.8 mL/min; wavelength: 220 nm; major enantiomer: t_R = 15.11 min, minor enantiomer: t_R = 18.48 min); $[\alpha]^D_{25}$ = +9.67 (*c* = 1.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 6.9 Hz, 2H), 7.34-7.24 (m, 3H), 6.40 (s, 2H), 4.95 (s, 2H), 4.25 (q, *J* = 6.9 Hz, 2H), 4.09 (d, *J* = 2.3 Hz, 1H), 3.93-3.89 (m, 1H), 3.78 (s, 6H), 3.33 (br s, 1H), 2.79-2.59 (m, 2H), 2.37 (br s, 1H), 1.95-1.87 (m, 2H), 1.28 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 173.4, 153.5, 137.8, 137.4, 135.0, 128.4, 128.0, 127.7, 105.3, 75.0, 73.1, 71.8, 62.1, 56.0, 35.4, 32.3, 14.1; Anal. Calcd. for $C_{22}H_{28}O_7$: C, 65.33; H, 6.98, found: C, 65.19; H, 6.92.

(2*S*,3*R*)-Ethyl 5-(4-(benzyloxy)phenyl)-3-hydroxy-2-(((4-nitrophenyl)sulfonyl)oxy) pentanoate (13a):

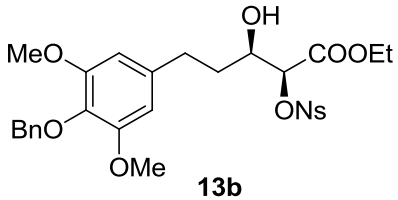


13a

To a stirred solution of **12a** (1.0 g , 2.70 mmol, 1.00 equiv) in anh. CH_2Cl_2 (20 mL) were added triethylamine (0.61 mL, 4.35 mmol, 1.60 equiv) and 4-nitrobenzenesulfonyl chloride (688 mg, 3.10 mmol, 1.15 equiv) at 0 °C. The resulting reaction mixture was stirred for 72 h at 0 °C. The reaction was quenched by the addition of 1N HCl (15 mL),

and then diluted with CH_2Cl_2 (20 mL). The phases were separated, the organic layer was washed with saturated aqueous $NaHCO_3$ (15 mL), brine (15 mL), dried over anh. Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (10-25% EtOAc in hexanes) to obtain the title compound **13a** as a light yellow gum**.** Yield: (1.09 g, 76%); R_f: 0.37 (silica gel, 40% EtOAc in hexanes); $[\alpha]^D_{25}$ = -28.59 (*c* = 2.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (d, *J* = 8.70 Hz, 2H), 8.15 (d, *J* = 8.70 Hz, 2H), 7.46-7.33 (m, 5H), 7.08 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.70 Hz, 2H), 5.05 (s, 2H), 5.00 (d, *J* = 3.2 Hz, 1H), 4.20-4.12 (m, 2H), 4.10-4.06 (m, 1H), 2.79-2.60 (m, 2H), 1.92-1.76 (m, 3H), 1.20 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 157.2, 150.8, 141.8, 137.0, 129.5, 129.3, 128.5, 127.9, 127.4, 124.2, 114.9, 70.7, 70.0, 62.4, 34.8, 30.9, 30.5, 13.9; Anal. Calcd. for $C_{26}H_{27}NO_9S$: C, 58.97; H, 5.14; N, 2.64, found: C, 58.84; H, 5.18; N, 2.56.

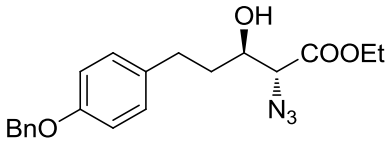
(2*S*,3*R*)-Ethyl 5-(4-(benzyloxy)-3,5-dimethoxyphenyl)-3-hydroxy-2-(((4-nitrophenyl)sulfonyl)oxy)pentanoate (13b):



13b

Following the above-described procedure, diol **12b** (1.0 g, 2.47 mmol) was subjected to the regioselective nosylation reaction. Purification of the crude product by silica gel column chromatography (15-30% EtOAc in hexanes) furnished the title compound **13b** as a light yellow semi-solid**.** Yield: (1.19 g, 82%); R_f: 0.28 (silica gel, 40% EtOAc in hexanes). $[\alpha]^D_{25}$ = -19.18 (*c* = 1.92, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.70 Hz, 2H), 8.17 (d, *J* = 8.70 Hz, 2H), 7.50 (d, *J* = 7.3 Hz, 2H), 7.37-7.30 (m, 3H), 6.42 (s, 2H), 5.04 (d, *J* = 3.2 Hz, 1H), 4.99 (s, 2H), 4.19-4.02 (m, 3H), 3.82 (s, 6H), 2.81-2.64 (m, 2H), 2.03 (d, *J* = 8.7 Hz, 1H), 1.98-1.87 (m, 2H), 1.21 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 153.6, 150.9, 141.8, 137.9, 136.4, 135.5, 128.4, 128.1, 127.7, 124.2, 105.5, 80.8, 75.0, 70.8, 62.4, 56.1, 34.8, 31.9, 14.0. Anal. Calcd. for $C_{22}H_{27}N_3O_6$: C, 57.04; H, 5.30, found: C, 57.21; H, 5.37.

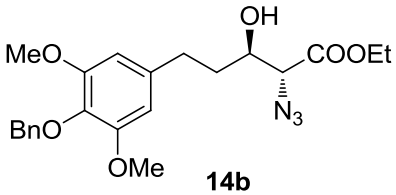
(2*R*,3*R*)-Ethyl 2-azido-5-(4-(benzyloxy)phenyl)-3-hydroxypentanoate (14a):



14a

To a solution of compound **13a** (900 mg, 1.70 mmol, 1.00 equiv) in anh. DMF (10 mL) was added NaN_3 (551 mg, 8.5 mmol, 5.00 equiv) under an atmosphere of N_2. The reaction mixture was heated to 50 °C and stirred for 12 h. After cooling to rt, the reaction mixture was diluted with Et_2O (20 mL) and water (20 mL), and the phases were separated. The aqueous phase was extracted with Et_2O (20 mL), and the combined organic extracts were washed with brine (20 mL), dried over anh. Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (5-15% EtOAc in hexanes) to obtain the title compound **14a** as a gummy yellow liquid**.** Yield: (427 mg, 68%); R_f: 0.46 (silica gel, 30% EtOAc in hexanes). $[\alpha]^D_{25}$ = +4.83 (*c* = 1.42, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45-7.31 (m, 5H), 7.12 (d, *J* = 8.2 Hz, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 5.05 (s, 2H), 4.28 (q, *J* = 7.3 Hz, 2H), 3.96-3.91 (m, 2H), 2.85-2.78 (m, 1H), 2.69-2.62 (m, 1H), 2.46 (br s, 1H), 1.87-1.81 (m, 2H), 1.31 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 157.2, 137.1, 133.5, 129.3, 128.5, 127.9, 127.4, 114.9, 71.0, 70.0, 66.2, 62.1, 34.7, 30.6, 14.1. Anal. Calcd. for $C_{20}H_{23}N_3O_4$: C, 65.03; H, 6.28; N, 11.37, found: C, 65.21; H, 6.16; N, 11.23.

(2*R*,3*R*)-Ethyl 2-azido -5-(4-(benzyloxy)-3,5-dimethoxyphenyl)-3-hydroxypentanoate (14b):

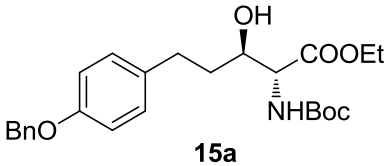


14b

Compound **13b** (1.0 g, 1.70 mmol, 1.00 equiv) was reacted with NaN_3 (551 mg, 8.5 mmol, 5.00 equiv) in DMF (10 mL) following the above described procedure. Purification of the crude product by silica gel column chromatography (5-25% EtOAc in hexanes) furnished the title compound **14b** as a light yellow semi-solid**.** Yield: (526 mg, 72%); R_f: 0.35 (silica gel, 35% EtOAc in hexanes). $[\alpha]^D_{25}$ = +6.72 (*c* = 1.75, $CHCl_3$); ^{1}H

NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 6.9 Hz, 2H), 7.37-7.29 (m, 3H), 6.41 (s, 2H), 4.97 (s, 2H), 4.29 (q, *J* = 7.3 Hz, 2H), 3.99-3.90 (m, 2H), 3.81 (s, 6H), 2.85-2.60 (m, 2H), 2.52 (br s, 1H), 1.97-1.79 (m, 2H), 1.32 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 153.4, 137.9, 137.1, 135.2, 128.4, 128.1, 127.7, 105.4, 75.0, 71.0, 70.0, 66.1, 62.2, 56.1, 34.6, 32.0, 14.1. Anal. Calcd. for $C_{22}H_{27}N_3O_6$: C, 61.53; H, 6.34; N, 9.78, found: C, 61.66; H, 6.41; N, 9.63.

(2*R*,3*R*)-Ethyl 5-(4-(benzyloxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)-3-hydroxy pentanoate (15a):

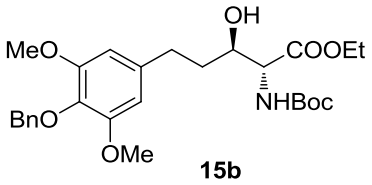


15a

To a solution of compound **14a** (400 mg, 1.08 mmol, 1.00 equiv) in THF/H_2O (5:1, 6 mL) was added PPh_3 (368 mg, 1.40 mmol, 1.30 equiv), and the resulting mixture was stirred at 55 °C overnight. The reaction mixture was concentrated under reduced pressure and the resulting residue was dissolved in diethyl ether (15 mL) and HCl (0.1 N, 10 mL). The mixture was stirred vigorously for 10 min and the two phases were then separated. The aqueous layer was collected and neutralized with 10% aqueous Na_2CO_3 solution. The mixture was extracted with EtOAc (15 mL). The organic layer was dried over anh. Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude amine was treated with $NaHCO_3$ (168 mg, 2.0 mmol) and $(Boc)_2O$ (0.23 mL, 1.0 mmol in THF/H_2O (3:1, 4 mL) at 0˚ C. The reaction mixture was stirred for 4 h at rt. The reaction mixture was diluted with EtOAc (10 mL) and water (10 mL), and the phases were separated. The aqueous phase was extracted with EtOAc (10 mL), and the combined organic extracts were washed with brine (10 mL), dried over anh. Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (5-10% EtOAc in hexanes) to obtain the title compound **15a** as a colorless semi-solid**.** Yield: (384 mg, 80%); R_f: 0.52 (silica gel, 25% EtOAc in hexanes); $[\alpha]^{D}_{25}$ = -12.35 (*c* = 1.08, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45-7.31 (m, 5H), 7.11 (d, *J* = 8.2 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.49 (d, *J* = 5.5 Hz, 1H), 5.05 (s, 2H), 4.40 (br s, 1H), 4.23-4.17 (m, 2H), 3.92 (br s, 1H), 3.08 (br s, 1H), 2.84-2.61 (m, 2H), 1.84-1.79 (m, 2H), 1.46 (s, 9H), 1.25 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 170.5, 157.1, 156.1, 137.2, 133.8, 129.3, 128.5, 127.8, 127.4, 114.8, 80.4, 72.3, 70.0, 61.7, 58.5, 35.0, 30.9, 28.2, 14.1. Anal. Calcd. for $C_{25}H_{33}NO_6$: C, 67.70; H, 7.50; N, 3.16, found: C, 67.79; H, 7.55; N, 3.12.

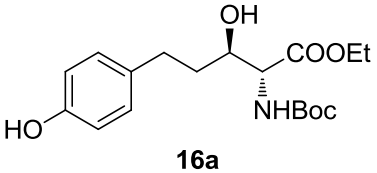
(2*R*,3*R*)-Ethyl 5-(4-(benzyloxy)-3,5-dimethoxyphenyl)-2-((*tert*-butoxycarbonyl) amino)-3-hydroxypentanoate (15b):



15b

Following the above described procedures, compound **14b** (500 mg, 1.16 mmol, 1.00 equiv) was first reduced with PPh_3 (397 mg, 1.51 mmol, 1.30 equiv) in THF/H_2O (5:1, 6 mL) and then the resulting crude amine was treated with $NaHCO_3$ (252 mg, 3.0 mmol) and $(Boc)_2O$ (0.27 mL, 1.2 mmol in THF/H_2O (3:1, 4 mL). Purification of the crude product by silica gel column chromatography (5-25% EtOAc in hexanes) furnished the title compound **15b** as a colorless semi-solid**.** Yield: (578 mg, 75%); R_f: 0.45 (silica gel, 25% EtOAc in hexanes). $[\alpha]^D_{25}$ = -9.11 (*c* = 0.75, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.3 Hz, 2H), 7.35-7.26 (m, 3H), 6.4 (s, 2H), 5.52 (d, *J* = 6.9 Hz, 1H), 4.96 (s, 2H), 4.41-4.34 (m, 1H), 4.24-4.16 (m, 2H), 3.92 (br s, 1H), 3.80 (s, 6H), 3.24 (br s, 1H), 2.83-2.58 (m, 2H), 1.92-1.74 (m, 2H), 1.45 (s, 9H), 1.26 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 156.1, 153.3, 137.8, 137.4, 135.0, 128.4, 128.0, 127.7, 105.3, 80.4, 75.0, 72.3, 61.6, 58.4, 56.0, 34.8, 32.3, 28.2, 14.1. Anal. Calcd. for $C_{27}H_{37}NO_8$: C, 64.40; H, 7.41; N, 2.78, found: C, 64.58; H, 7.48; N, 2.82.

(2*R*,3*R*)-Ethyl 2-((*tert*-butoxycarbonyl)amino)-3-hydroxy-5-(4-hydroxyphenyl)pentanoate (16a):

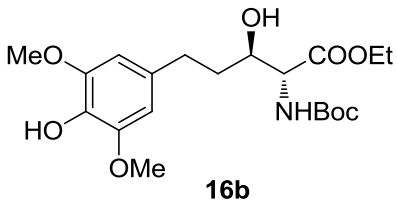


16a

To a stirred solution of **15a** (350 mg, 0.789 mmol, 1.00 equiv) in EtOAc (5 mL) was added 10% Pd-C (45 mg). The reaction mixture was purged with hydrogen gas five times and the resulting suspension was stirred under pressure of a hydrogen balloon at rt for 4 h. The catalyst was removed by filtration through a pad of Celite®. The Celite® pad was

washed with EtOAc (10 mL) and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (30% EtOAc/hexanes) to afford 1**6a** as a white solid compound. Yield: (256 mg, 92%); R_f: 0.48 (silica gel, 50% EtOAc in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* = 8.2 Hz, 2H), 6.74 (d, *J* = 8.2 Hz, 2H), 6.59 (br s, 1H), 5.59 (d, *J* = 3.7 Hz, 1H), 4.39-4.38 (m, 1H), 4.23-4.10 (m, 2H), 3.93-3.91 (m, 1H), 3.41 (br s, 1H), 2.78-2.55 (m, 2H), 1.82-1.69 (m, 2H), 1.44 (s, 9H), 1.22 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 156.3, 154.2, 132.9, 129.4, 115.3, 80.7, 72.3, 61.8, 58.5, 35.0, 30.9, 28.2, 14.0. Anal. Calcd. for $C_{18}H_{27}NO_6$: C, 61.17; H, 7.70; N, 3.96, found: C, 61.06; H, 7.78; N, 3.90.

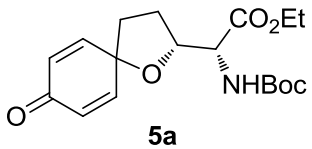
(2*R*,3*R*)-Ethyl 2-((*tert*-butoxycarbonyl)amino)-3-hydroxy-5-(4-hydroxy-3,5-dimethoxyphenyl) pentanoate (16b):



16b

Compound **15b** (500 mg, 0.993 mmol) was debenzylated by Pd-C/H_2 conditions following the above described procedure. The product 1**6b** was obtained (white solid, 390 mg, 95%) in sufficiently pure form after the debenzylation, and immediately used for the next step without further purification.

(*R*)-Ethyl 2-((*tert*-butoxycarbonyl)amino)-2-((*R*)-8-oxo-1-oxaspiro[4.5]deca-6,9-dien-2-yl)acetate (5a).

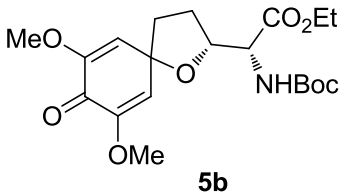


5a

To a mixture of **16a** (34 mg, 0.1 mmol, 1.00 equiv) and K_2CO_3 (27 mg, 0.2 mmol, 2.00 equiv) in HFIP (2 mL) at 0 °C was added $PhI(OAc)_2$ (37 mg, 0.12 mmol, 1.20 equiv). After 10 min, the reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with EtOAc (25 mL × 2). The combined organic extracts were washed with brine ((10 mL), dried over anh. Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by

silica gel column chromatography (20-30% EtOAc/hexanes) to afford **5a** as a colorless liquid. Yield: (23 mg, 65%); R_f: 0.52 (silica gel, 40% EtOAc in hexanes); $[\alpha]^{D}_{25}$ = +17.04 (*c* = 0.45, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.77 (dd, *J* = 10.1, 3.2 Hz, 1H), 6.71 (dd, *J* = 9.6, 2.3 Hz, 1H), 6.09 (dd, *J* =10.1, 1.4 Hz, 2H), 5.35 (s br, 1H), 4.46-4.41 (m, 2H), 4.22 (q, *J* = 7.3 Hz, 2H), 2.26-2.18 (m, 2H), 2.12-2.00 (m, 2H), 1.42 (s, 9H), 1.28 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.3, 170.0, 155.2, 148.8, 127.5, 127.2, 81.7, 80.2, 78.4, 61.6, 56.5, 36.2, 28.4, 28.2, 14.1; Anal. Calcd. for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99, found: C, 61.67; H, 7.12; N, 4.07.

(*R*)-Ethyl 2-((*tert*-butoxycarbonyl)amino)-2-((*R*)-7,9-dimethoxy-8-oxo-1-oxaspiro[4.5]deca-6,9-dien-2-yl)acetate (5b):



5b

Following the above described procedure, compound **16b** (41 mg, 0.1 mmol) was subjected to the oxidative dearomatization reaction. Purification of the crude product by silica gel column chromatography (30-40% EtOAc/hexanes) afforded **5b** as a light yellow gum. Yield: (25 mg, 62%); R_f: 0.51 (silica gel, 50% EtOAc in hexanes);); $[\alpha]^{D}_{25}$ = +9.63 (*c* = 0.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.71 (d, *J* = 2.7 Hz, 1H), 5.67 (d, *J* = 2.3 Hz, 1H), 5.35 (d, *J* = 7.3 Hz, 1H), 4.47-4.40 (m, 2H), 4.24 (q, *J* = 6.9 Hz, 2H), 3.66 (s, 3H), 3.67 (s, 3H), 2.36-2.21 (m, 2H), 2.15-2.07 (m, 2H), 1.44 (s, 9H), 1.30 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.4, 170.2, 155.3, 149.14, 149.12, 117.2, 116.1, 80.9, 80.3, 80.0, 61.6, 56.7, 55.2, 38.0, 28.6, 28.2, 14.2; Anal. Calcd. for $C_{20}H_{29}NO_8$: C, 58.38; H, 7.10; N, 3.40, found: C, 58.25; H, 7.16; N, 3.34.

5.6. References

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5.7. NMR Spectra of Selected Compounds

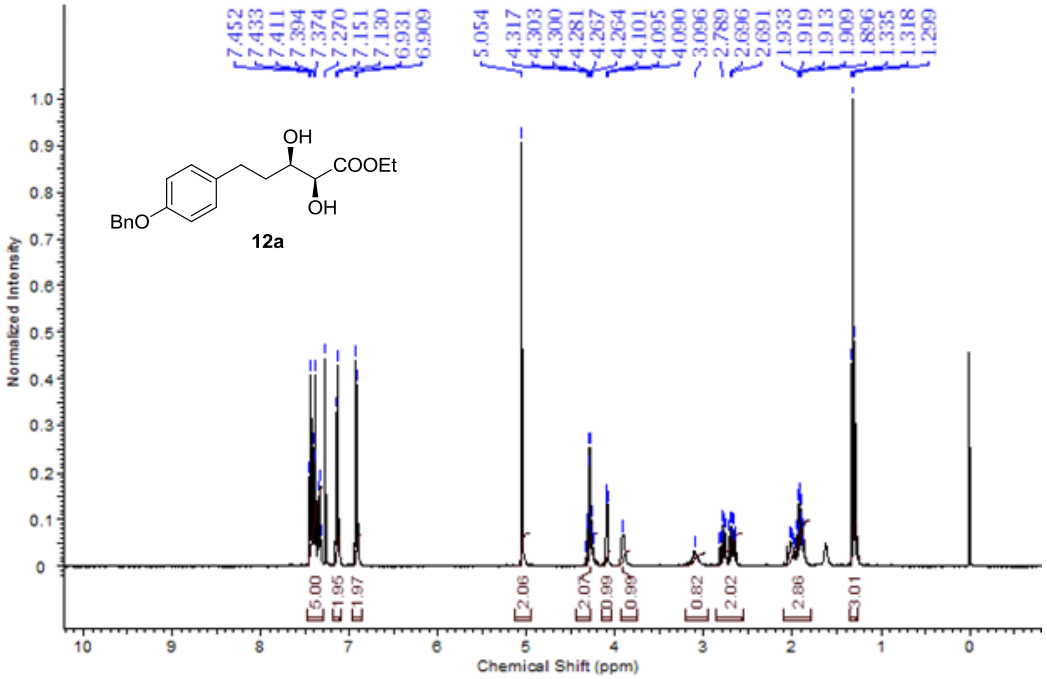


Figure 5.3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 12a

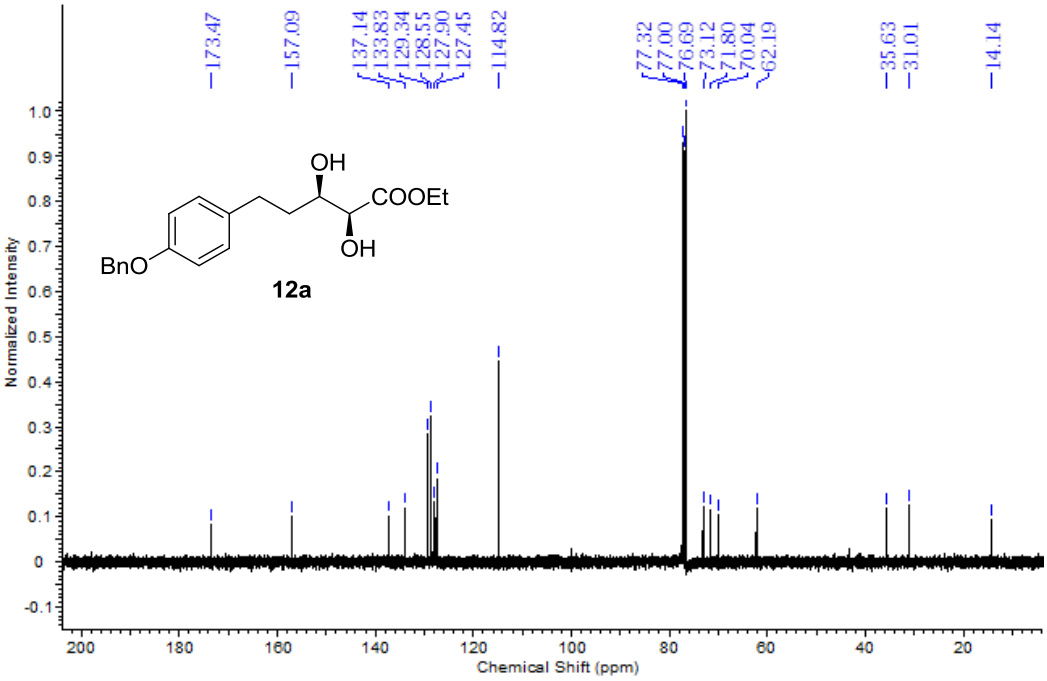


Figure 5.4. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 12a

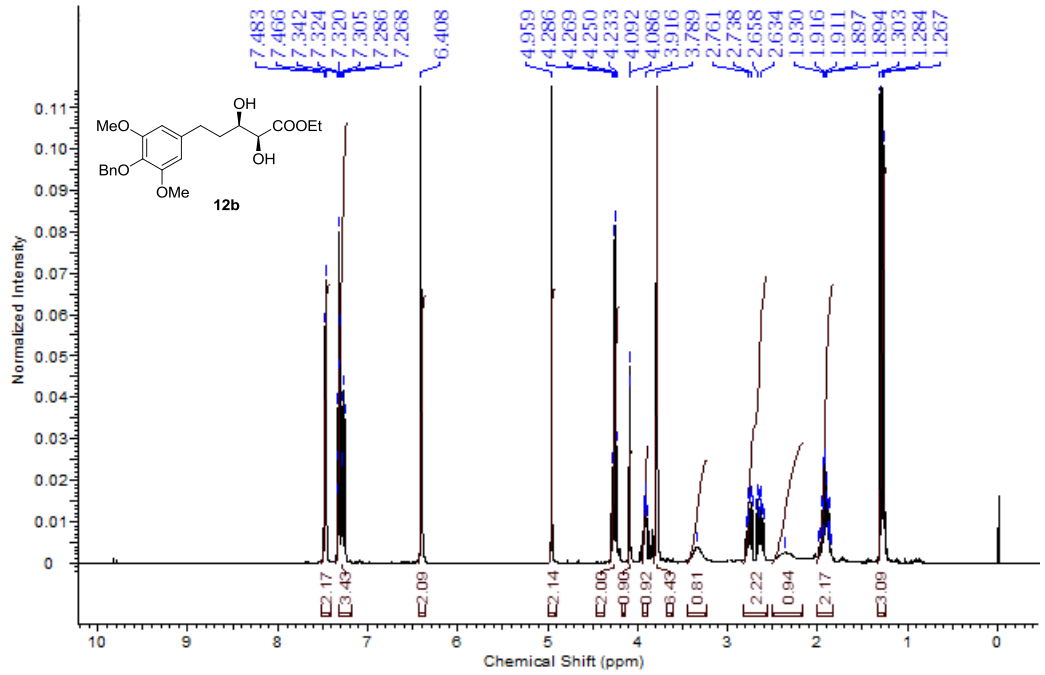


Figure 5.5. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 12b

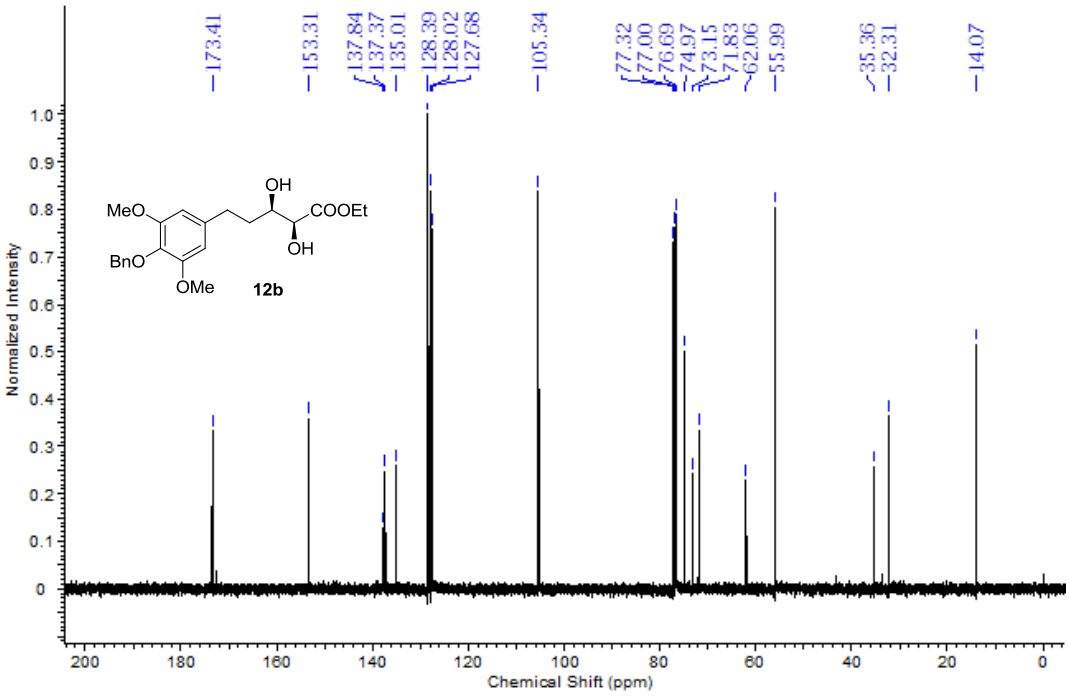


Figure 5.6. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 12b

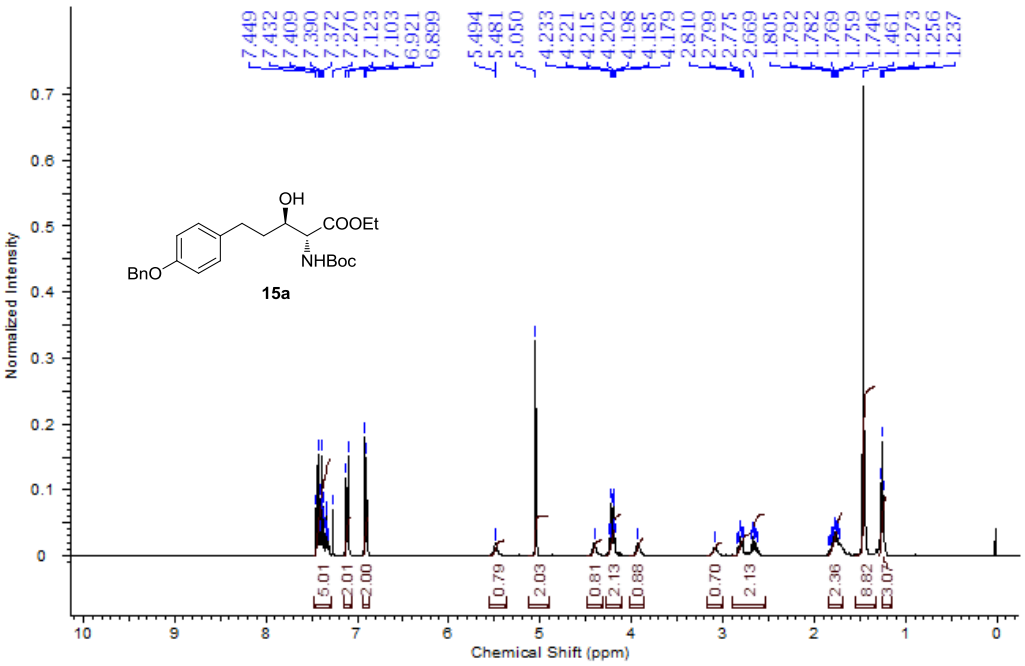


Figure 5.7. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 15a

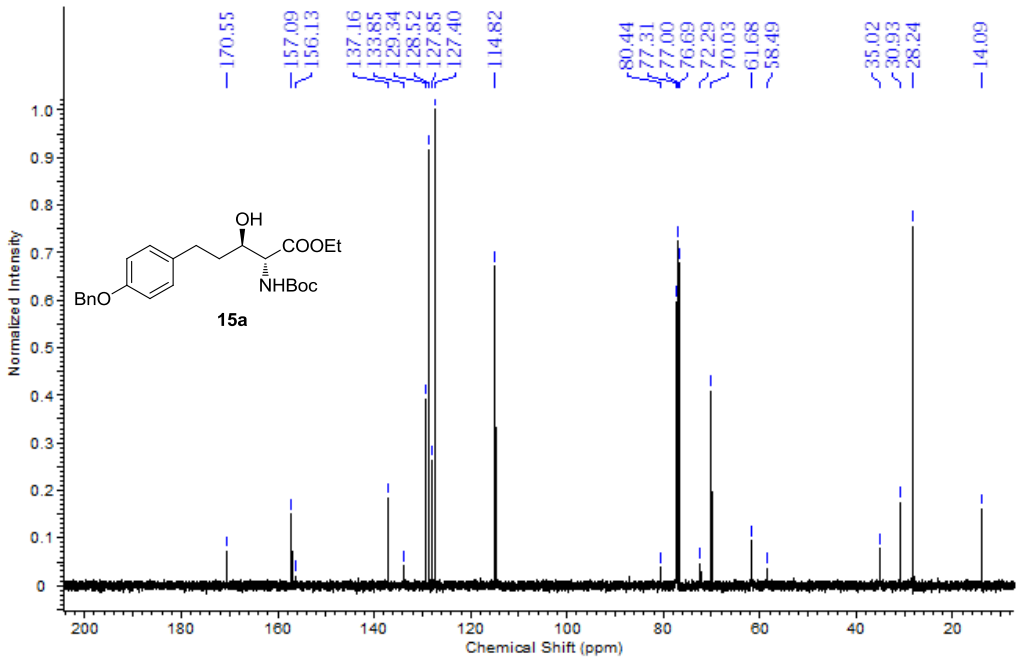


Figure 5.8. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 15a

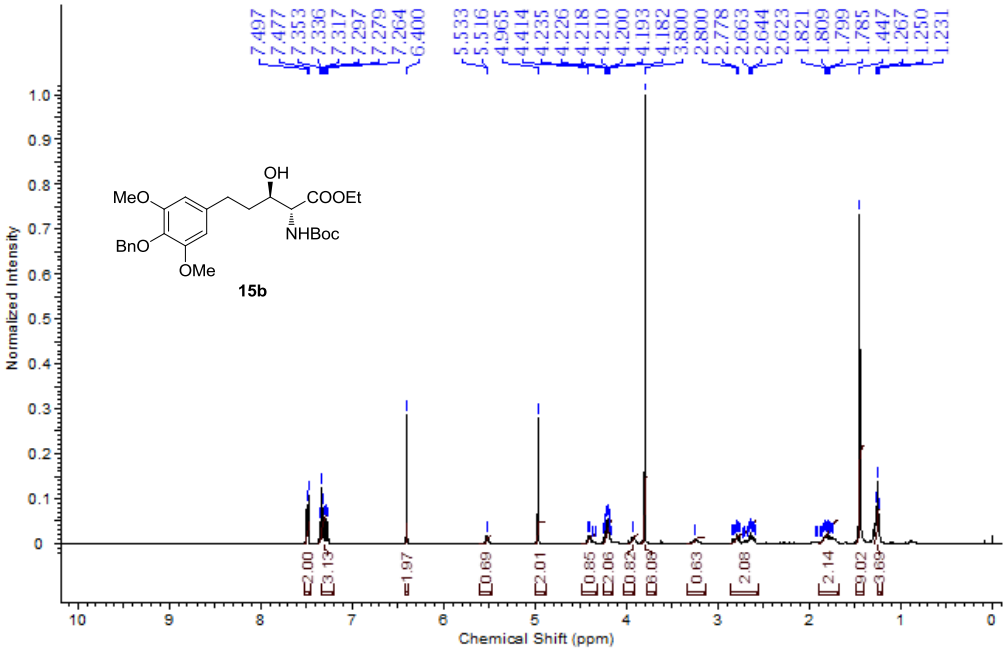


Figure 5.9. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 15b

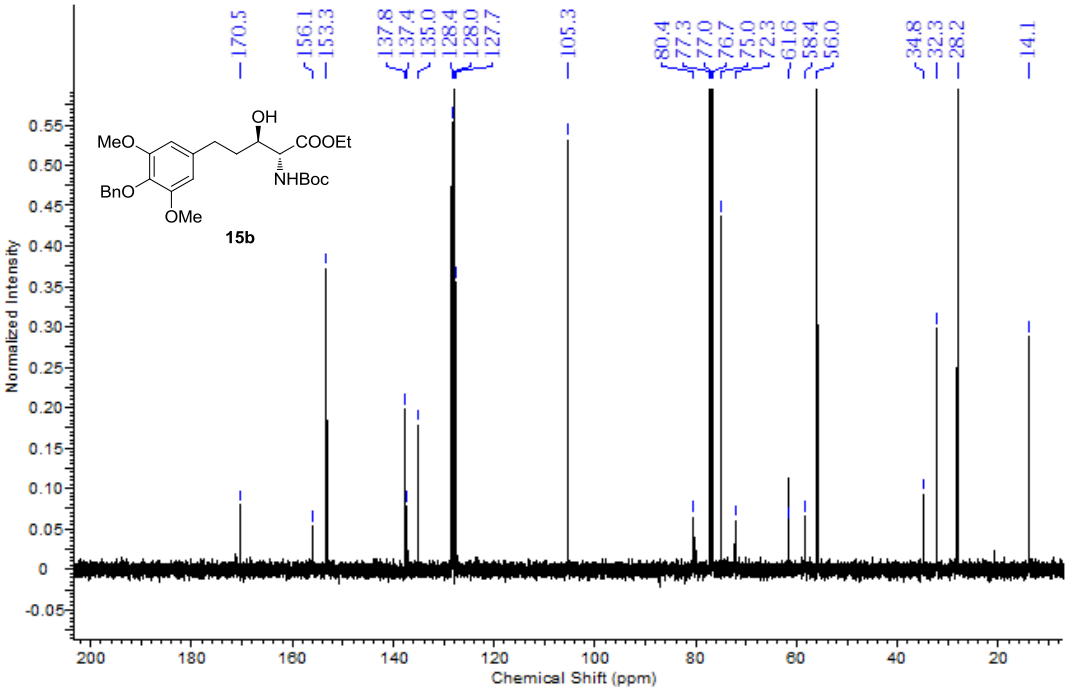


Figure 5.10. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 15b

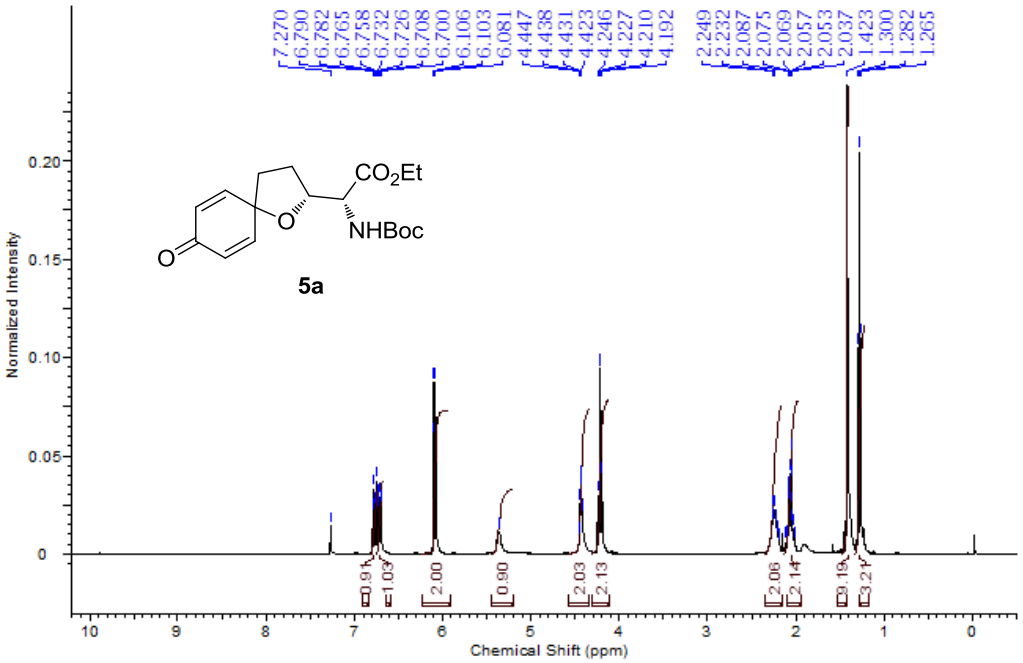


Figure 5.11. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 5a

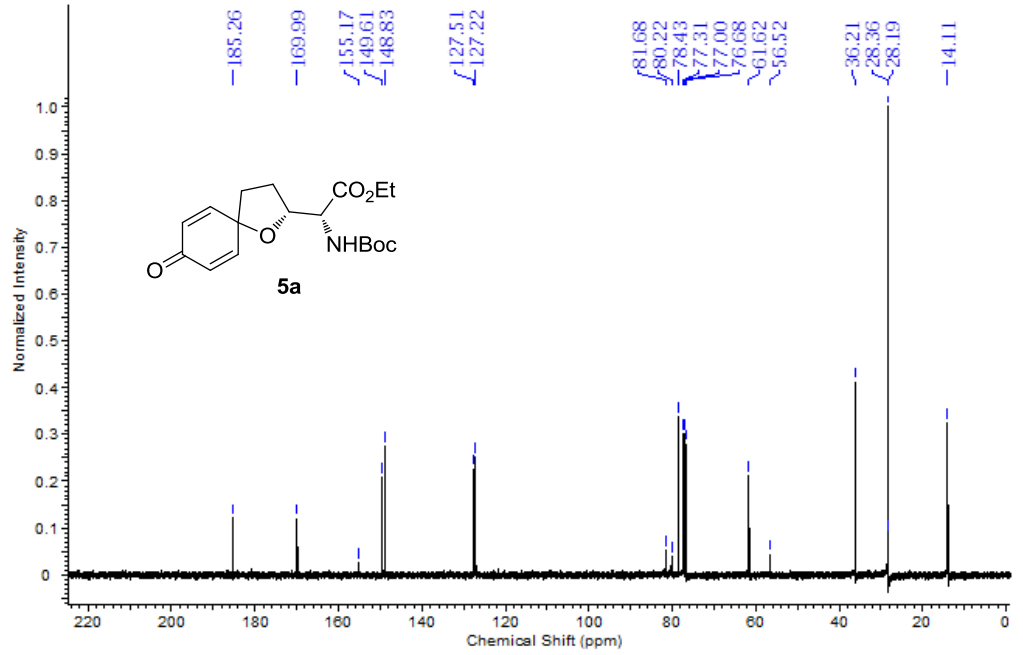


Figure 5.12. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 5a

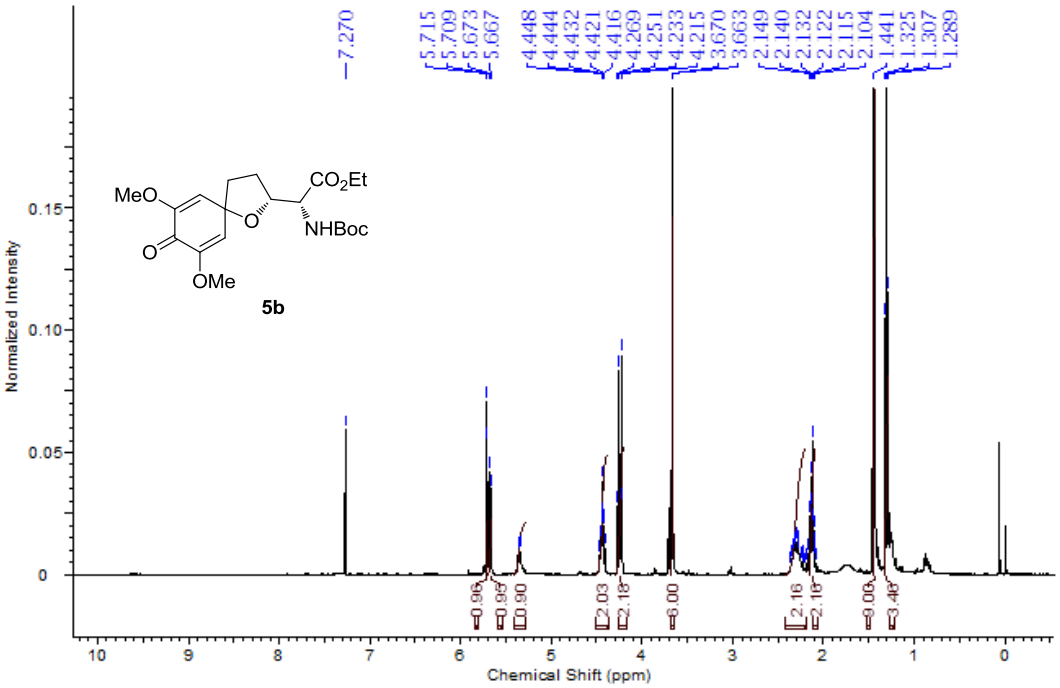


Figure 5.13. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 5b

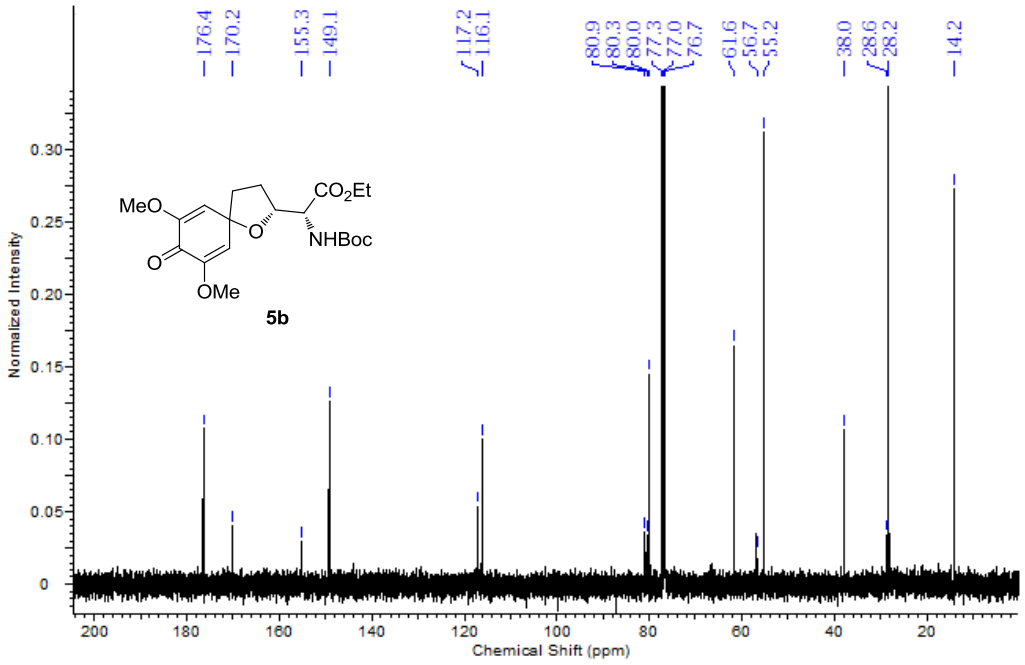
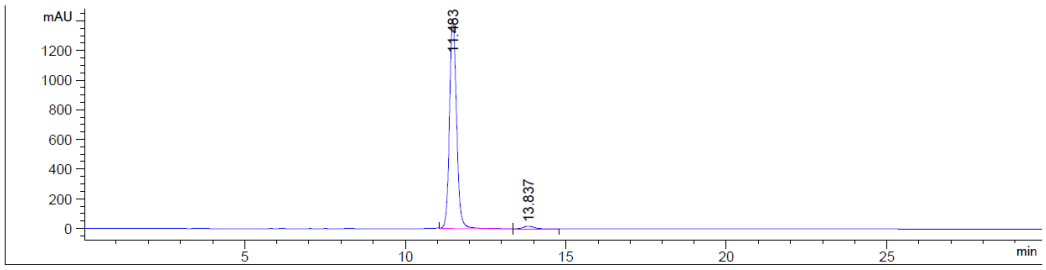


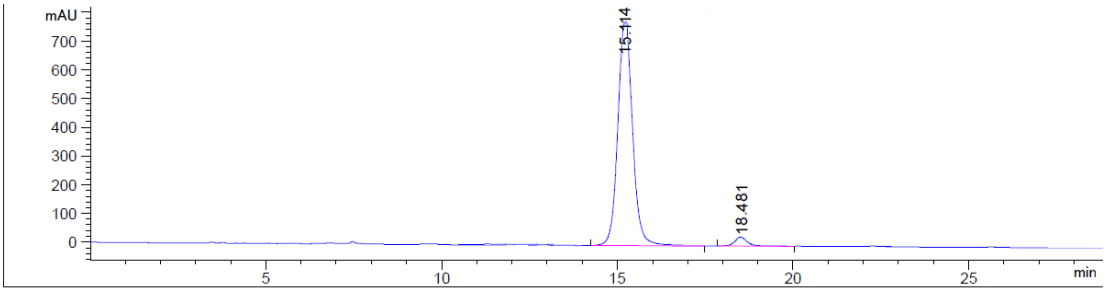
Figure 5.14. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 5b

5.8. HPLC Traces of Diols 12a,b



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.483	VB	0.2364	2.15447e4	1408.62646	98.1644
2	13.837	BB	0.3468	402.87610	18.16271	1.8356
Totals :				2.19475e4	1426.78917	

Figure 5.15. HPLC chromatogram of 12a



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.114	BB	0.4419	2.28230e4	792.73810	96.8774
2	18.481	BB	0.3678	735.65332	30.23878	3.1226
Totals :				2.35586e4	822.97688	

Figure 5.16. HPLC chromatogram of 12b