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Stereoselective Formation of a Chiral Ether by Intramolecular O–H Insertion Reaction of a Metal Carbenoid Generated from Diazoacetoacetate

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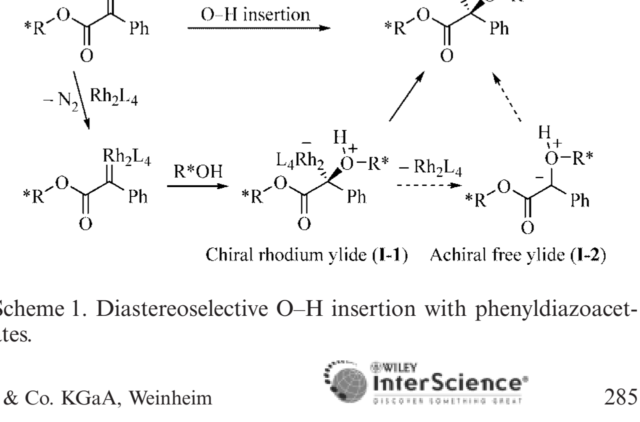
Intermolecular O–H insertion reactions of rhodium carbenoids generated from chiral diazoacetoacetates are less efficient and less stereoselective than the reactions of those generated from the corresponding phenyldiazoacetates. Nevertheless, when the diazoacetoacetate is connected to a phenolic moiety through a 2,4-pentanediol tether, the carbenoid generated shows a high potential in both efficiency and stereoselectivity during the intramolecular O–H insertion reaction to give a cyclic ether in up to 88 % diastereomeric excess (*de*) in quantitative yield. The *de* value depends on the structure of the tether, but is independent of the catalyst employed. The isomerization of the cyclic ether has been studied under the conditions of equilibrium and kinetic protonation of the corresponding enolate. The similarity between the *de* values obtained by insertion and those obtained under equilibrium suggests that the rhodium catalyst is eliminated during the early stages of the O–H insertion reaction and that proton transfer, which determines the stereoselectivity, occurs after the elimination of the rhodium metal, independent of the stereochemistry of the initial addition.

Introduction

Carbenoid addition to a hydroxy group by O–H insertion is a synthetically useful method for the formation of an ethereal bond under mild reaction conditions. In the presence of an appropriate catalyst, a diazo compound can be a good precursor of such a carbenoid, and its reaction with an alcohol or a phenol gives an ethereal product.[1] Since the diazo carbon atom is achiral and the ethereal α-carbon atom of the product can be chiral, stereocontrol of the O–H insertion reaction leads to a useful asymmetric synthesis. Enantioselective O–H insertion reactions using chiral catalysts have not been successful, and only a very recent report has disclosed such a reaction in which a chiral copper catalyst and methyl triethylsilyldiazoacetates were employed.[2] Diastereoselective reactions using achiral rhodium catalysts have been reported to give poor to moderate selectivities except for one case which gave a very high selectivity.[3] In the presence of an alcohol, the chiral phenylmenthyl and pantolactone esters of phenyldiazoacetate produced 53[4] and 70% *de*,[5] respectively. Similarly, a chiral phenyldiazoacetamide gave 90% *de* with a copper catalyst.[6] The reaction of a trifluoromethyldiazo ester in the presence of $Rh_2(OAc)_4$ with chiral alcohols also showed stereoselectivity, 60% *de* with menthol[7] and 98% *de* with fencol.[3] The intramolecular reaction of ethyl 2-diazo-4-(1-hydroxycyclohexyl)-4-methoxy-3-oxobutanoate is reported to result in 22% *de* by catalysis with $Rh_2(OAc)_4$.[8]

The rhodium-catalyzed O–H insertion reaction starts with the addition of a rhodium(II) catalyst to a diazo compound to generate the rhodium carbenoid by denitrogenation in the presence of an alcohol (or water). Stereoselective addition to the coexisting alcohol produces an optically active rhodium-associated ylide (**I-1**), the stereochemical purity of which will be carried over to the final product by substitution of the rhodium atom by a proton (Scheme 1). However, if the rhodium catalyst is eliminated prior to the proton transfer, the generated metal-free ylide (**I-2**) loses its chirality at the reaction site. Proton transfer by deprotonation/protonation in **I-2** regenerates the chirality, of which strict stereocontrol must be difficult unless the chiral auxiliary participates at the reaction center, the carbanion or proton in **I-2**.[5]



Scheme 1. Diastereoselective O–H insertion with phenyldiazoacetates.

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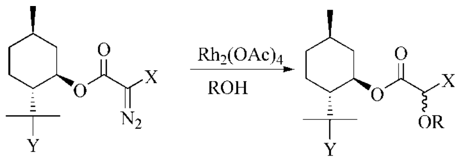
Among the many reaction designs intending to achieve efficient stereocontrol, intramolecular reactions using 2,4-pentanediol (PD) as a chiral tether to connect a reactant with a reagent are distinctive in their strict stereocontrol and wide applicability.[9] In addition, the chiral tether also has the potential to control an intermolecular reaction of a cyclic intermediate generated by the intramolecular addition.[10] Hence, a PD tether connecting a diazo ester to an alcoholic function is expected to control the stereochemistry of the O–H insertion even if the chirality is established either during or after the initial addition.[11,12] As a matter of fact, the stereoselectivity observed with a diazoacetoacetate ester was high giving an 88% diastereomeric excess (*de*) even though the product chirality seems to have been established in the metal-free ylide during the proton-transfer step independent of the stereochemistry of the initial metal ylide formation.[13]

Results and Discussion

Intermolecular Reaction with Diazoacetoacetates

As a preliminary investigation, the effect of the structure of the diazo moiety on the reaction efficiency and selectivity was examined by performing intermolecular O–H insertion reactions in accord with the reaction procedure reported previously.[4] Moody et al. reported that the selectivity of the reaction of a phenyldiazoacetate (Scheme 2; X = Ph) in the presence of an alcohol (2 mol of methanol or *tert*-butyl alcohol) catalyzed by $Rh_2(OAc)_4$ at room temperature is low with menthol ester **1** (Y = H), but is high with phenylmenthyl ester **2** (Y = Ph) with a *de* of up to 53% (40% yield). The relationship between the structure and the *de* clearly indicates that the chiral moiety works as a steric fence against the external alcohol during the insertion reaction. With the same substrate design, the catalysis of the diazoacetoacetate analogues (X = Ac; **3** and **4**) was also studied. The reactivity of the generated carbenoid towards the alcohols was lower than those obtained with **1** and **2**, and only a small amount (<10% yield) of the product was obtained by using a combination of **3** and methanol (0% *de*). The yield was improved to 75% when the reaction was carried out in methanol, but again no stereoselectivity was observed (0% *de*). Under the same conditions, **4** produced a product in poor yield (<10%) and in 26% *de*. The reaction with *tert*-butyl alcohol was also sluggish, and no O–H insertion was observed under any conditions (<3% yield). The reaction with phenol also did not give the O–H insertion product. The use of $Rh_2(OCOC_3F_7)_4$ instead of $Rh_2(OAc)_4$ led to a slight increase in the yield but only of a few percent. The results indicate that the carbenoids generated from the diazoacetoacetates are less reactive towards O–H insertion than those generated from the phenyldiazoacetates. Since the stabilization effect of the carbanion in the metal-free intermediate is greater in the acetoacetate than in the phenylacetate, the lower selectivity can reasonably be explained by the elimination of the rhodium catalyst prior to proton transfer, and the stereoselectivity of the transfer is poor in the metal-free intermediate.

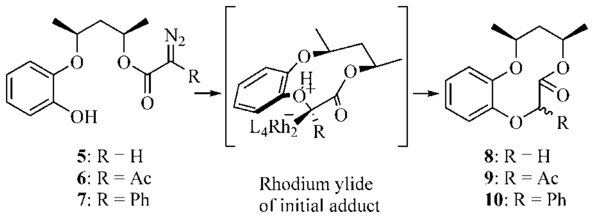


	MeOH (% yield)		*t*BuOH (% yield)	
	2 equiv.	as solvent	2 equiv.	as solvent
1: X = Ph, Y = H	10% *de* (83)	—	14% *de* (43)	—
2: X = Ph, Y = Ph	44% *de* (63)	—	53% *de* (40)	—
3: X = Ac, Y = H	0% *de* (<10)	0% *de* (75)	—	— (<3)
4: X = Ac, Y = Ph	26% *de* (<3)	26% *de* (<10)	—	— (<3)

Scheme 2. Intermolecular O–H insertion with 2 mol-equiv. of alcohol or in alcohol as solvent.

Intramolecular Reaction with a (2*R*,4*S*)-PD Tether

Substrates **5**–**7** carrying different diazo groups with a (2*R*,4*S*)-PD tether were prepared from stereochemically pure (2*R*,4*R*)-2,4-pentanediol by Mitsunobu reaction with a monoprotected catechol followed by the introduction of the diazo ester and deprotection. Upon addition of $Rh_2(OCOCF_3)_4$ (5 mol-%) in dichloromethane, diazoacetate **5** was quantitatively converted into cyclic ether **8** by intramolecular O–H insertion (Scheme 3). In the presence of the same catalyst, diazoacetoacetate **6** was converted into cyclic ether **9** only upon heating, but the conversion occurred readily at room temperature when $Rh_2(OCOC_3F_7)_4$ was employed as the catalyst (5 mol-%). However, the reaction of phenyldiazoacetate **7** did not afford any of the expected product **10** (<2%) but resulted only in intermolecular addition reactions with contaminants to give α-hydroxy and α-keto analogues.[14] These results contrast those obtained in the preliminary experiments of the intermolecular O–H insertion reactions of phenyldiazoacetates **1** and **2**, which are more reactive and gave better yields than diazoacetoacetates **3** and **4**. It is assumed that use of the PD tether causes the acetoacetate carbenoid and hydroxy groups to adopt an arrangement with an appropriate relative geometry for reaction, but causes a fatal strain during the reaction of the phenylacetate carbenoid, presumably due to steric repulsion between the two aromatic groups. The stereochemical purity of **9**, as obtained by the insertion reaction, was 86% *de* as determined by ^1H NMR analysis. The observed stereoselectivity is high for an O–H insertion reaction but low for



5: R = H
6: R = Ac
7: R = Ph

8: R = H
9: R = Ac
10: R = Ph

Scheme 3. Intramolecular O–H insertion with various diazo esters.

a PD-tethered intramolecular reaction. To understand the factors affecting the stereocontrol of the reaction of diazoacetoacetate **6**, related diazoacetoacetate substrates **11**–**13** (Figure 1) were next studied.

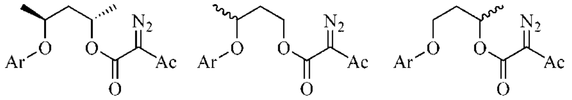
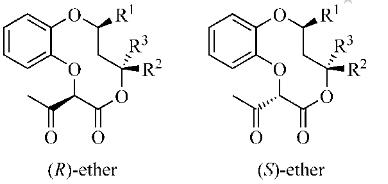


Figure 1. Substrates **11**–**13** carrying different tethers.



9: $R^1 = R^2 = Me, R^3 = H$
14: $R^1 = R^3 = Me, R^2 = H$
15: $R^1 = Me, R^2 = R^3 = H$
16: $R^2 = Me, R^1 = R^3 = H$

Figure 2. Diastereomers of intramolecular insertion products **9** and **14**–**16**.

Diazoacetoacetate Esters with Different Tethers

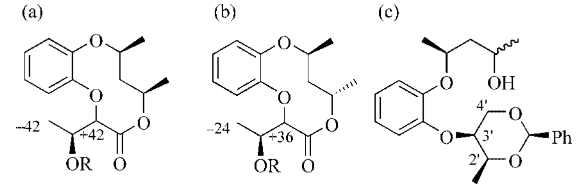
Substrate **11** carrying a (2*S*,4*S*)-PD tether (Figure 1) was prepared similarly to **6**, except for the use of an additional Mitsunobu inversion prior to the introduction of the diazo group. Substrates **12** and **13** were prepared from 1,3-butanediol derivatives as racemic compounds. Compared with the reaction of **6** to give **9**, which proceeds in a quantitative yield, the reactions of the substrates **11**–**13** with $Rh_2(OCOC_3F_7)_4$ were not very efficient which resulted in lower isolated yields (see Table 1) of the cyclic ethers **14**–**16** (Figure 2). The side-products were intermolecular adducts formed with contaminated water and dimers formed at the diazo carbon atom. The reactions with $Rh_2(OCOCF_3)_4$ and $Rh_2(OAc)_4$ were less efficient than those with $Rh_2(OCOC_3F_7)_4$.

The cyclic ethers **9** and **14**–**16** consisted of pairs of diastereomers, but the enolic isomers were not detected (<1%) by ^1H NMR in $CDCl_3$. The stereochemistry of the O–H insertion was studied for the reaction of **6** and **11** using PD tethers by determining the major isomers of **9** and **14**. Treatment of **9** and **14** with a limited amount of $LiAlH_4$ at –78 °C resulted in regioselective reduction to give **17a** and **18a**. The isomeric ratios determined by ^1H NMR were 73:27 and 67:31, respectively. The major stereoisomers were transformed into α-methoxy-α-(trifluoromethyl)phenylacetate (MTPA) esters **17b** and **18b** with both of the enantiomeric reagents. The differential chemical shifts ($\Delta\delta = \delta_{(S)} - \delta_{(R)}$) between the (*S*)-MTPA and (*R*)-MTPA esters shown in Figure 3 indicate that the stereochemistry of the hydroxy carbon atom generated by the reduction was (*S*) for both **17** and **18**.[15] The relative stereochemistries of **17** and **18** at the α and β positions of the esters were determined as follows. Reduction of **9** and **14** with excess $LiAlH_4$ resulted in diols, the major isomers of which were converted into the acetals of benzaldehyde, **19** and **20**. The ^1H NMR spectra of the acetal ring region of **19** and **20** are very similar to each other. The coupling constants of the acetal protons are $J_{3'-4'}$ = 1.4 and 1.4 Hz and $J_{3'-2'}$ = 1.4 Hz, indicating that the conformation of 3′-H is equatorial. Since the acid-catalyzed formation of the acetal must give thermodynamically stable compounds under the present benzene/reflux conditions, the 2′-Me and 6′-Ph groups must be in equatorial positions. Thus, the 3′-substituents in the axial positions are *cis* to 2′-Me, and **9** and **14** have been assigned as (*R*)-ethers.

The selectivities of the reactions of **6** and **11**–**13** to give diastereomers of **9** and **14**–**16** under different conditions are summarized in Table 1. The reaction time required was much shorter with $Rh_2(OCOC_3F_7)_4$, but also largely depended on the substrate/catalyst ratio. The stereoselectivity among the substrates is **6** > **11** and **12** > **13**; thus, the two methyl groups of the PD tether have a matching stereodirection in (2*R*,4*S*)-**6**, but compete in (2*S*,4*S*)-**11**. The notable

Table 1. Stereoselectivity of the O–H insertion reaction with **6** and **11**–**13**.

Substrate	Catalyst	Solvent	Temp. [°C] (time)	*de* [%] (isolated yield [%])
6	$Rh_2(OAc)_4$	$CDCl_3$	50 (1 d)	88
	$Rh_2(OCOCF_3)_4$	$CDCl_3$	40 (1 d)	86
		C_6H_6	50 (1 d)	86 (76)
		C_6D_6	r.t. (5 d)	84
	$Rh_2(OCOC_3F_7)_4$	$CDCl_3$	r.t. (5 min)	86
		CH_2Cl_2	r.t. (4 h)	86 (48)
11	$Rh_2(OAc)_4$	$CDCl_3$	60 (1 d)	66
	$Rh_2(OCOCF_3)_4$	$CDCl_3$	60 (1 d)	68
	$Rh_2(OCOC_3F_7)_4$	$CDCl_3$	r.t. (5 min)	68
		CH_2Cl_2	r.t. (4 h)	68 (46)
12	$Rh_2(OCOCF_3)_4$	$CDCl_3$	r.t. (5 h)	80
	$Rh_2(OCOC_3F_7)_4$	$CDCl_3$	r.t. (2 d)	80 (54)
		CH_2Cl_2	r.t. (4 h)	80 (54)
13	$Rh_2(OCOC_3F_7)_4$	$CDCl_3$	r.t. (2 d)	20
		CH_2Cl_2	r.t. (3 h)	20



17a: R = H
17b: R = MTPA
18a: R = H
18b: R = MTPA
19 and **20**

Figure 3. (a) and (b) Modified Mosher's method for determining the absolute configuration of **9** and **14**. The values shown in the structures of **17** and **18** are the differential chemical shifts of the MTPA esters (**17b** and **18b**) ($\Delta\delta = \delta_{(S)} - \delta_{(R)}$). (c) Stereochemistry of acetals **19** and **20**.

feature of this reaction is that the *de* values are almost independent of the catalyst. So far the (2*R*,4*S*)-PD tether of **6** was found to be the best with an 88% *de*.

Structural Analysis of (*R*)-9 and (*R*)-14

A single crystallization of the diastereomeric mixture of **9** from an ether solution gave crystals with not only a high stereochemical purity (>99% *de*), but also of sufficient quality for X-ray analysis (33% yield). By the same procedure, pure crystals of **14** were obtained (24% yield). Their crystallographic data are given in Table 2, and the ORTEP drawings are shown in Figures 4 and 5. As seen in Figure 4, the crystal of (*R*)-**9** contains two different conformers, but they are almost identical. The five carbon atoms of the tether align in an antiperiplanar conformation, and the acetate group sticks out to avoid any steric hindrance. The structure of (*R*)-**14** shown in Figure 5 has one of the methyl groups of the tether in a pseudoaxial position. Interestingly, R^1 in **14** (Figure 2), having the same stereochemistry as that of **9**, is axial and R^3, having the opposite stereochemistry, is pseudoequatorial. Therefore, the tether, including the R^3 group, adopts an antiperiplanar conformation. Accordingly, the conformation of the ester carbonyl group is different in **9** and **14**, s-*cis* to the acetate group in **14**, whereas an s-*trans* conformation is seen in **9**. In both **9** and **14**, the acidic proton at the position α to the carbonyl group is inside the molecule near the aromatic ring. Overall, the structures of the major isomers seem to have stable conformations.

Table 2. Crystallographic data for compounds (*R*)-**9** and (*R*)-**14**.

	(*R*)-**9**	(*R*)-**14**
Empirical formula	$C_{30}H_{36}O_{10}$	$C_{15}H_{18}O_5$
Formula mass	278.30	278.30
Crystal system	orthorhombic	orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
a [Å]	8.9016(7)	9.581(4)
b [Å]	11.8711(10)	9.5266(9)
c [Å]	27.806(2)	16.2213(17)
V [Å^3]	2938.3(4)	1480.6(7)
Z	8	4
$D_{\text{calcd.}}$ [g cm^{-3}]	1.26	1.25
Independent reflections	3612	2004
R (R_w)	0.062 (0.054)	0.070 (0.066)

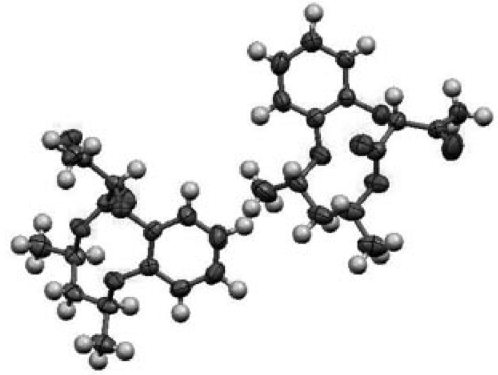


Figure 4. ORTEP drawing of the molecular structures of (*R*)-**9**.

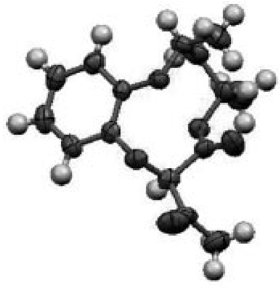


Figure 5. ORTEP drawing of the molecular structure of (*R*)-**14**.

Isomerization between the Diastereomers of the Cyclic Ethers 9 and 14–16

The β-keto ester moiety of **9** and **14**–**16** allows isomerization between the diastereomers at the α position under basic conditions. The isomerization was observed by ^{1}H NMR spectroscopy in a $CDCl_3$ solution containing DABCO (3% w/v) at –60 to 60 °C. Even at –60 °C, the isomerization was quick enough to attain equilibrium within 20 min, and the change in the isomeric ratio with temperature was fully reversible. As shown in Table 3, higher *de* values were observed at lower temperatures for all the ethers and the *de* of **9** reached 96%, although it decreased to 86% on warming to room temperature. Based on this experiment, the *de* values obtained by the O–H insertion reactions (Table 1) were found to be similar to those obtained under thermodynamic equilibrium at room temperature.

The irreversible protonation of the enolates was also studied. Such a kinetic protonation was attempted by the treatment of **9** or **14**–**16** with *t*BuOK in *t*BuOH at 30 °C followed by quick neutralization with a saturated aqueous NH_4Cl solution. The *de* values decreased with **14** and **15** and increased with **16** by 8–10%. A significant change was observed with (*R*)-**9** of 86% *de*; stereoinversion occurred with the formation of (*S*)-**9** in up to 40% *de*. The stereoin-

Table 3. Variation of the diastereomeric excesses of **9** and **14**–**16** with temperature.

Ether[a]	*de* [%]				
	–60 °C	–30 °C	0 °C	23 °C	60 °C
9	96	90	88	86	78
14	82	78	76	68	54
15	92	88	82	80	70
16	30	26	22	20	14

[a] The initial *de* values were >99% for **9** and **14** and the same as those at 23 °C for **15** and **16**.

version is attributable to conformational regulation by the tether, that is, the tether in the stable antiperiplanar structure maintains the conformations with the same inside and outside faces at the keto ester part throughout the deprotonation/protonation process.

The stereochemical transformability of **9** and **14**–**16** suggests that the diastereomeric ratios obtained by the O–H insertion reaction may not indicate the stereoselectivity of the reaction, but be a result of the isomerization. Here, evidence that the isomerization did not occur during the insertion reaction is indispensable for discussing the stereoselectivity of the insertion reaction. In $CDCl_3$, the stereochemistries proved to be stable at room temperature for several days. Addition of a rhodium catalyst to the solution also did not lead to any change. For example, the diastereomeric mixture of **9** of 0% *de* was still 0% *de* in the presence of $Rh_2(OCOC_3F_7)_4$ after 24 h. However, addition of acetic acid (3% v/v) caused a change in the isomeric ratio. The approximate half-life periods of the isomerization at room temperature were 12 h for **9**, **14**, and **16**, and 4 h for **15**. Acid contamination may occur during the insertion reaction, but the acid-catalyzed isomerizations are too slow to affect the product ratios during the O–H insertion reactions. Isomerization during the O–H insertion reaction was finally excluded by the following experiments. The O–H insertion reaction with **11** was carried out in the presence of stereochemically pure **9** (>99% *de*). The product **14** had the same 68% *de* as that obtained in the absence of **9**, and the recovered **9** had an unchanged stereochemical purity of >99%. Thus, the *de* values obtained by the O–H insertion reactions are not affected by the isomerization.

Stereocontrol Mechanism of the O–H Insertion

The stereoselectivities of the O–H insertion reactions were insensitive to the ligands of the employed rhodium catalysts. This must be a characteristic property of the carbenoids generated from diazoacetoacetate esters, because other asymmetric O–H insertions with phenyl- or styryldiazoacetate depend on the employed catalyst for their stereoselectivities.[4,5,16] Since the acetoacetate structure stabilizes the negative charge at the central carbon atom, the rhodium atom and its ligands tend to easily dissociate from the rhodium ylide. As a result, proton transfer to generate chirality in the product occurs in the metal-free ylide. In such a reaction, the chirality generated by carbenoid addition to the O–H function disappears, and then the proton transfer in the resulting metal-free ylide needs extra stereocontrol to stereoselectively furnish the product. The stereocontrol of the reaction involving a medium-sized ring is usually poor, but inclusion of a PD tether can be different, as deduced by the fact that strict stereocontrol is observed in hydrogen abstraction in a 10-membered-ring radical intermediate.[10] The similarity between the *de* values of the insertion products and the same compounds obtained under thermodynamic stationary states supports this mechanism, because the stereodeterminng step of the proton transfer is close to the end of the reaction coordinate for the metal-free ylide mechanism. The initial intermediate of the metal ylide is chiral and forms under a certain amount of stereocontrol exerted by the chiral PD tether, but that stereoselectivity should not be carried over to the product. The product *de* of 86% is high for an O–H insertion reaction, but it is not achieved by the strict stereocontrol exerted by the PD tether in the intramolecular reaction, but by the stereocontrol of the PD that operates in the intermolecular reaction of the cyclic intermediate.

Conclusion

In the present report it has been shown that the PD-tethered reaction is effective for the stereocontrol of the O–H insertion reaction with diazoacetoacetate esters. The mode of stereocontrol is apparently different to that occurring in inter- and intramolecular asymmetric O–H insertion reactions with other diazo esters, and the stereoselectivity seems to be governed by proton transfer in the metal-free ylide. The chiral catechol ethers obtained are structures found in natural lignans as well as in some medicines,[17] and thus the present PD-tethered O–H insertion reaction can be used as an alternative method for their asymmetric synthesis.

Experimental Section

General: Melting points were determined with a Yanaco melting point apparatus. All the substrates and products were characterized by NMR spectroscopy with a JEOL ECA-600 spectrometer at 600 MHz for the ^1H spectra and 150 MHz for the ^{13}C spectra, and by IR with a JASCO FT/IR-410 spectrometer. High-resolution mass spectra were obtained with a JEOL JMS-T100LC spectrometer using electron spray ionization (ESI). Optical rotations were measured with a Perkin-Elmer-243B polarimeter. All dry solvents were purified by distillation from appropriate drying agents. All reactions were carried out under dry nitrogen. The X-ray diffraction data were recorded with a Rigaku AFC-7R diffractometer using a Quantum CCD area detector at room temperature. CCDC-281652 and -281653 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Preparation of 3 and 4: Diketene (1.3 mol) was slowly added to a solution of (–)-menthol (5 g) and Et_3N (0.3 mol) in CH_2Cl_2 (100 mL) at room temperature. After stirring for 3 h, the mixture was treated with water and extracted with CH_2Cl_2. Drying with $MgSO_4$, concentration, and column chromatography on silica gel (elution with 20% ethyl acetate in hexane) afforded a quantitative yield of menthyl acetoacetate. $[\alpha]_{\mathrm{D}}^{20}$ = –64.43 (*c* = 0.70, CH_2Cl_2). IR (NaCl, neat): $\tilde{\nu}$ = 2956, 1716, 1646, 1455, 1242, 1149, 984, 845 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 4.70 (td, *J* = 11.0, 4.1 Hz, 1 H), 3.40 (d, *J* = 2.7 Hz, 2 H), 2.23 (s, 3 H), 2.01–1.97 (m, 1 H), 1.84 (m, 1 H), 1.65 (dt, *J* = 10.3, 2.7 Hz, 2 H), 1.46 (m, 1 H), 1.34 (tt, *J* = 11.7, 3.4 Hz, 1 H), 1.05–0.93 (m, 2 H), 0.87 (d, *J* = 7.6 Hz, 3 H), 0.85 (d, *J* = 6.9 Hz, 3 H), 0.83 (m, 1 H), 0.73 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 200.57, 166.68, 75.47, 50.51, 46.85, 40.66, 34.12, 31.36, 29.99, 26.11, 23.28, 21.92, 20.68, 16.11 ppm. HRMS (ESI): calcd. for $C_{14}H_{24}NaO_3$ [M + Na]$^+$ 263.1623; found 263.1613. According to the same procedure, except for the use of (–)-8-phenylmenthol (150 mg) in CH_2Cl_2 (10 mL), the ester was obtained in a quantitative yield after a silica gel column chromatography (elution with 10% ethyl acetate in hexane). $[\alpha]_{\mathrm{D}}^{20}$ = +13.96 (*c* = 0.48, CH_2Cl_2). IR (NaCl, neat): $\tilde{\nu}$ = 2955, 1714, 1644, 1496, 1242, 1031, 982, 848, 767, 701 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 7.26 (m, 4 H), 7.12 (tt, *J* = 8.2, 4.1 Hz, 1 H), 4.81 (td, *J* = 11.0, 4.1 Hz, 1 H), 2.74 (d, *J* = 15.8 Hz, 1 H), 2.62 (d, *J* = 15.8 Hz, 1 H), 2.08 (s, 3 H), 2.03 (td, *J* = 12.4, 3.4 Hz, 1 H), 1.89 (m, 1 H), 1.79 (dd, *J* = 13.7, 3.4 Hz, 1 H), 1.66 (dt, *J* = 12.4, 2.7 Hz, 1 H), 1.44 (m, 1 H), 1.28 (s, 3 H), 1.12 (td, *J* = 13.7, 2.7 Hz, 1 H), 1.18 (s, 3 H), 0.97–0.84 (m, 2 H), 0.86 (d, *J* = 7.6 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 200.77, 166.42, 151.80, 127.90, 125.35, 125.01, 75.06, 50.14, 49.76, 41.37, 39.46, 34.46, 31.24, 30.03, 29.09, 26.28, 23.40, 21.71 ppm. HRMS (ESI): calcd. for $C_{20}H_{28}NaO_3$ [M + Na]$^+$ 339.1936; found 339.1942. Et_3N (1.3 mol) was added slowly to a solution of menthyl acetoacetate (5 g) and 4-acetamidobenzenesulfonyl azide (1.2 mol) in CH_3CN (100 mL) at room temperature. After 5 h, the mixture was treated with water, extracted with diethyl ether, and washed with water and then brine. Drying with $MgSO_4$, concentration, and column chromatography on silica gel (elution with 20% ethyl acetate in hexane) afforded **3** (78% yield) as a yellow oil. $[\alpha]_{\mathrm{D}}^{20}$ = –80.8 (*c* = 0.53, CH_2Cl_2). IR (NaCl, neat): $\tilde{\nu}$ = 2957, 2139, 1713, 1309, 1165, 1068, 954, 743, 637 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 4.76 (td, *J* = 11.0, 4.8 Hz, 1 H), 2.40 (s, 3 H), 2.00 (d, *J* = 11.7 Hz, 1 H), 1.79 (m, 1 H), 1.64 (d, *J* = 11.7 Hz, 2 H), 1.45 (m, 1 H), 1.36 (tt, *J* = 11.7, 2.7 Hz, 1 H), 1.06–0.95 (m, 2 H), 0.86 (d, *J* = 6.2 Hz, 3 H), 0.84 (d, *J* = 6.9 Hz, 3 H), 0.81 (m, 1 H), 0.73 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 190.05, 160.89, 75.65, 46.98, 41.07, 34.01, 31.04, 28.09, 26.49, 23.55, 21.81, 20.54, 16.43 ppm. HRMS (ESI): calcd. for $C_{14}H_{22}N_2NaO_3$ [M + Na]$^+$ 289.1528; found 289.1544. According to the same procedure, except for the use of phenylmenthyl acetoacetate (200 mg) in CH_3CN (10 mL), reaction for 12 h gave **4** as a yellow oil in 98% yield. $[\alpha]_{\mathrm{D}}^{20}$ = –106.2 (*c* = 0.52, CH_2Cl_2). IR (NaCl, neat): $\tilde{\nu}$ = 2958, 2142, 1712, 1311, 1158, 1066, 965, 763, 701, 637 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 7.23–7.19 (m, 4 H), 7.12 (t, *J* = 6.9 Hz, 1 H), 4.99 (td, *J* = 11.0, 4.8 Hz, 1 H), 2.32 (s, 3 H), 2.06 (td, *J* = 13.7, 3.4 Hz, 1 H), 1.90 (dd, *J* = 13.7, 3.4 Hz, 1 H), 1.82 (d, *J* = 12.4 Hz, 1 H), 1.70 (dt, *J* = 13.7, 2.7 Hz, 1 H), 1.47 (m, 1 H), 1.31 (s, 3 H), 1.19 (m, 1 H), 1.19 (s, 3 H), 1.03–0.90 (m, 2 H), 0.88 (d, *J* = 6.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 190.07, 160.37, 151.54, 127.91, 125.33, 125.14, 74.80, 50.75, 42.12, 39.37, 34.40, 31.41, 29.76, 28.02, 26.37, 22.61, 21.73 ppm. HRMS (ESI): calcd. for $C_{20}H_{26}N_2NaO_3$ [M + Na]$^+$ 365.1841; found 365.1811.

Rhodium-Catalyzed Reaction of 3 with Alcohols: $Rh_2(OAc)_4$ (ca. 2 mg) was added to a solution of **3** (50 mg) in methanol (2 mL) at room temperature. After stirring at room temperature for 18 h, the solution was concentrated under vacuum. The residue was purified by silica gel chromatography (elution with 10% ethyl acetate in hexane) to give the insertion product as a mixture of diastereomers in a 1:1 ratio in 75% yield. IR (NaCl, neat): $\tilde{\nu}$ = 2956, 1739, 1456, 1202, 952, 912 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 4.84 (m, 1 H), 4.23 (s, 0.5 H), 4.21 (s, 0.5 H), 3.45 (s, 1.5 H), 3.44 (s, 1.5 H), 2.23 (d, *J* = 4.1 Hz, 3 H), 2.03–1.77 (m, 3 H), 1.71–1.64 (m, 2 H), 1.56–1.39 (m, 2 H), 1.12–0.96 (m, 2 H), 0.88 (d, *J* = 6.9 Hz, 3 H), 0.87 (d, *J* = 6.9 Hz, 3 H), 0.74 (d, *J* = 6.9 Hz, 1.5 H), 0.71 (d, *J* = 6.9 Hz, 1.5 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 201.95, 201.72, 166.59, 166.51, 87.40, 87.26, 76.47, 76.22, 58.44, 58.31, 47.00, 46.75, 40.64, 40.44, 34.19, 34.09, 31.42, 31.40, 26.32, 26.22, 25.97, 25.91, 23.36, 23.05, 21.98, 21.91, 20.72, 20.64, 16.16, 15.78 ppm. HRMS (ESI): calcd. for $C_{15}H_{26}NaO_4$ [M + Na]$^+$ 293.1729; found 293.1776.

Preparation of 6: (2*R*,4*S*)-2-Acetylacetoxy-4-(2-hydroxyphenoxy)pentane was prepared according to a reported method.[18] Et_3N (1.75 mL, 1.5 mol) was added slowly to a solution of this compound (2.32 g) and 4-acetamidobenzenesulfonyl azide (2.26 g, 1.1 mol) in CH_3CN (60 mL) at room temperature. After 15 h, the mixture was treated with water, extracted with diethyl ether, and washed with water and brine. Drying with $MgSO_4$, concentration, and column chromatography on silica gel (elution with 20% ethyl acetate in hexane) afforded **6** as a colorless solid (2.21 g, 87% yield). M.p. 99.6–99.7 °C. $[\alpha]_{\mathrm{D}}^{20}$ = –39.61 (*c* = 0.87, CH_2Cl_2). IR (NaCl, neat): $\tilde{\nu}$ = 3365, 2979, 2149, 1714, 1641, 1609, 1500, 1457, 1374, 1316, 1264, 1157, 1109, 1070, 968, 924, 742 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 6.90 (dd, *J* = 7.6, 1.4 Hz, 1 H), 6.83 (td, *J* = 7.6, 2.1 Hz, 1 H), 6.81–6.77 (m, 2 H), 5.93 (s, OH), 5.26 (td, *J* = 12.4, 6.2 Hz, 1 H), 4.48 (td, *J* = 12.4, 6.2 Hz, 1 H), 2.38 (s, 3 H), 2.20 (td, *J* = 14.4, 7.6 Hz, 1 H), 1.80 (td, *J* = 14.4, 5.5 Hz, 1 H), 1.34 (d, *J* = 6.2 Hz, 3 H), 1.32 (d, *J* = 6.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 190.02, 161.03, 146.61, 144.25, 121.80, 119.97, 115.06, 113.02, 72.32, 69.84, 42.87, 28.12, 20.43, 20.17 ppm. HRMS (ESI): calcd. for $C_{15}H_{18}N_2NaO_5$ [M + Na]$^+$ 329.1113; found 329.1124.

Preparation of 7: (2*S*,4*R*)-4-Hydroxy-2-(2-hydroxyphenoxy)pentane was prepared according to a reported method.[18] Et_3N (0.33 mL, 1.5 mol) was added slowly to a solution of this compound (300 mg) and 2-oxophenylacetyl chloride tosylhydrazone[19] (527 mg, 1 mol) in CH_3CN (5 mL) at room temperature. After stirring for 26 h, the mixture was treated with water, extracted with diethyl ether, and washed with water and then brine. Drying with $MgSO_4$, concentration, and column chromatography on silica gel (elution with 30% ethyl acetate in hexane) afforded **7** (120.4 mg, 22% yield) as a yellow oil; a substantial amount of reactant (140.7 mg, 45%) was recovered. $[\alpha]_{\mathrm{D}}^{20}$ = –44.00 (*c* = 0.60, CH_2Cl_2). IR (NaCl, neat): $\tilde{\nu}$ = 3446, 3055, 2978, 2089, 1704, 1699, 1695, 1683, 1674, 1496, 1456, 1362, 1011, 956, 816, 755, 691, 667 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 7.45 (d, *J* = 8.2 Hz, 2 H), 7.37 (t, *J* = 7.6 Hz, 2 H), 7.17 (t, *J* = 7.6 Hz, 1 H), 6.92 (d, *J* = 7.6 Hz, 1 H), 6.89–6.77 (m, 3 H), 5.95 (s, 1 H, OH), 5.29 (m, 1 H), 4.50 (m, 1 H), 2.25 (td, *J* = 14.4, 6.9 Hz, 1 H), 1.80 (dt, *J* = 14.4, 5.5 Hz, 1 H), 1.37 (d, *J* = 6.2 Hz, 3 H), 1.35 (d, *J* = 6.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 164.85, 146.70, 144.44, 128.93, 125.91, 125.84, 125.36, 124.10, 124.00, 121.71, 119.99, 115.01, 113.07, 72.31, 69.11, 51.95, 42.90, 20.67, 20.18 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}N_2NaO_4$ [M + Na]$^+$ 363.1321; found 363.1320.

Preparation of 11: (2*S*,4*S*)-2-Acetylacetoxy-4-(2-hydroxyphenoxy)pentane was prepared by the two Mitsunobu reactions and esterification according to a reported method.[18] Et_3N (0.6 mL, 1.4 mol) was added slowly to a solution of this compound (852.4 mg) and 4-acetamidobenzenesulfonyl azide (888 mg, 1.2 mol) in CH_3CN

(40 mL) at room temperature. After 2 h, the mixture was treated with water, extracted with diethyl ether, and washed with water and then brine. Drying with $MgSO_4$, concentration, and column chromatography on silica gel (elution with 30% ethyl acetate in hexane) afforded **11** as a colorless oil (815.4 mg, 89% yield). $[\alpha]_D^{20}$ = +99.75 (c = 0.79, CH_2Cl_2). IR (NaCl, neat): $\tilde{\nu}$ = 3446, 2979, 2143, 1717, 1699, 1695, 1652, 1635, 1505, 1456, 1362, 965, 816, 742 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 6.91 (dd, J = 7.6, 1.4 Hz, 1 H), 6.85 (td, J = 7.6, 2.1 Hz, 1 H), 6.81–6.77 (m, 2 H), 5.67 (s, 1 H, OH), 5.33 (td, J = 12.4, 6.2 Hz, 1 H), 4.47 (td, J = 12.4, 6.2 Hz, 1 H), 2.40 (s, 3 H), 1.99 (t, J = 6.2 Hz, 2 H), 1.35 (d, J = 6.2 Hz, 3 H), 1.31 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 190.08, 160.92, 146.91, 144.28, 122.19, 120.11, 115.18, 113.99, 72.16, 69.33, 43.00, 28.18, 20.94, 20.16, 15.23 ppm. HRMS (ESI): calcd. for $C_{15}H_{18}N_2NaO_5$ $[M + Na]^+$ 329.1113; found 329.1117.

Preparation of Substrates 12: A THF (120 mL) solution of diisopropyl azodicarboxylate (6.0 mL, 1.3 mol) was added dropwise to a solution of O-TBS-catechol (5.17 g), 3-hydroxybutyl benzoate (6.43 g, 1.4 mol), and triphenylphosphane (7.24 g, 1.2 mol) in THF (80 mL). After stirring at room temperature for 90 h, the mixture was concentrated and then purified by column chromatography on silica gel (elution with 10% ethyl acetate in hexane) to give the catechol ether (6.55 g, 71% yield). IR (NaCl, neat): $\tilde{\nu}$ = 2929, 2858, 1722, 1592, 1505, 1451, 1390, 1362, 1271, 1176, 1112, 1070, 1027, 933, 839, 748, 711 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 8.01 (dd, J = 7.6, 1.4 Hz, 2 H), 7.54 (tt, J = 7.6, 1.4 Hz, 1 H), 7.42 (t, J = 7.6 Hz, 2 H), 6.89–6.77 (m, 4 H), 4.57 (td, J = 12.4, 6.2 Hz, 1 H), 4.50 (dt, J = 11.0, 6.2 Hz, 1 H), 4.45 (dt, J = 11.0, 6.2 Hz, 1 H), 2.22 (m, 1 H), 2.05 (m, 1 H), 1.35 (d, J = 6.2 Hz, 3 H), 0.99 (s, 9 H), 0.15 (d, J = 2.1 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 166.50, 149.07, 146.17, 132.90, 129.57, 128.36, 121.67, 121.38, 121.24, 115.64, 71.56, 61.83, 35.71, 25.96, 19.97, –4.40, –4.44 ppm. HRMS (ESI): calcd. for $C_{23}H_{32}NaO_4Si$ $[M + Na]^+$ 423.1968; found 423.1927. $LiAlH_4$ (680 mg, 1.1 mol) was added to a solution of this compound (6.40 g) in diethyl ether (200 mL) at 0 °C. After stirring at 0 °C for 3 h, the mixture was treated with a 1 M NaOH aqueous solution (80 mL), extracted with diethyl ether, and washed with 1 M NaOH and then water. Drying with Na_2SO_4, concentration, and column chromatography on silica gel (elution with 20% ethyl acetate in hexane) gave 2.35 g of a colorless oil (49.5% yield). IR (NaCl, neat): $\tilde{\nu}$ = 3349, 2930, 1591, 1505, 1456, 1265, 1113, 1044, 929, 838, 746, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 6.89–6.78 (m, 4 H), 4.57 (tdt, J = 12.4, 6.2, 1.4 Hz, 1 H), 3.84 (m, 1 H), 3.77 (m, 1 H), 1.98 (m, 1 H), 1.88 (m, 1 H), 1.31 (d, J = 6.2 Hz, 3 H), 0.98 (s, 9 H), 0.17 (s, 3 H), 0.15 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 148.90, 145.96, 121.68, 121.16, 115.28, 73.68, 60.42, 39.03, 19.84, –4.31, –4.43 ppm. HRMS (ESI): calcd. for $C_{16}H_{28}NaO_3Si$ $[M + Na]^+$ 319.1705; found 319.1691. Diketene (0.62 mL, 1.6 mol) was added slowly to a solution of this compound (1.5 g) and Et_3N (0.25 mL, 0.4 mol) in CH_2Cl_2 (50 mL) at room temperature. After stirring for 26 h, the mixture was treated with water, extracted with CH_2Cl_2, and washed with water. Drying with Na_2SO_4, concentration, and column chromatography on silica gel (elution with 20% ethyl acetate in hexane) afforded 1.22 g of the acetoacetate ester as a colorless oil (62.9%). IR (NaCl, neat): $\tilde{\nu}$ = 2930, 1750, 1717, 1700, 1652, 1591, 1505, 1456, 1362, 1265, 1044, 910, 839, 748 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 6.89–6.78 (m, 4 H), 4.46 (td, J = 12.4, 6.2 Hz, 1 H), 4.33–4.25 (m, 2 H), 3.42 (s, 2 H), 2.22 (s, 3 H), 2.08 (m, 1 H), 1.94 (m, 1 H), 1.29 (d, J = 6.2 Hz, 3 H), 0.98 (s, 9 H), 0.14 (d, J = 3.4 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 200.37, 167.00, 148.99, 146.07, 121.69, 121.39, 121.24, 115.53, 71.24, 62.25, 50.04, 35.49, 30.09, 25.73, 19.83, –4.42, –4.48 ppm. HRMS (ESI): calcd. for $C_{20}H_{32}NaO_5Si$ $[M + Na]^+$ 403.1917; found 403.1960. Tetrabutylammonium fluoride (1.6 g, 2.1 mol) was added to a solution of the above product (1.15 g) in THF (50 mL) at room temperature. After stirring for 3 h, the mixture was treated with water, extracted with diethyl ether, and washed with water and brine. Drying with Na_2SO_4, concentration, and column chromatography on silica gel (elution with 20% ethyl acetate in hexane) gave 722 mg of the desilylated compound as a yellow oil (90.4%). IR (NaCl, neat): $\tilde{\nu}$ = 3446, 2977, 1750, 1717, 1700, 1695, 1652, 1635, 1594, 1505, 1456, 1419, 748 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 6.91 (dd, J = 7.6, 1.4 Hz, 1 H), 6.85 (tt, J = 8.9, 1.4 Hz, 2 H), 6.80 (td, J = 8.9, 1.4 Hz, 1 H), 5.71 (s, 1 H, OH), 4.53 (tdt, J = 12.4, 6.2, 1.4 Hz, 1 H), 4.35–4.27 (m, 2 H), 3.45 (s, 2 H), 2.23 (s, 3 H), 2.08 (m, 1 H), 2.01 (m, 1 H), 1.33 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 200.33, 166.91, 146.78, 144.43, 121.99, 120.12, 114.96, 113.85, 72.54, 61.95, 49.96, 35.46, 30.18, 19.96 ppm. HRMS (ESI): calcd. for $C_{14}H_{18}NaO_5$ $[M + Na]^+$ 289.1052; found 289.1080. Et_3N (0.42 mL, 1.2 mol) was slowly added to a solution of this compound (661.2 mg) and 4-acetamidobenzenesulfonyl azide (753 mg, 1.2 mol) in CH_3CN (30 mL) at room temperature. After 12 h, the mixture was treated with water, extracted with diethyl ether, and washed with water and brine. Drying with Na_2SO_4, concentration, and column chromatography on silica gel (elution with 30% ethyl acetate in hexane) afforded 635 mg of **12** as a yellow oil (87% yield). IR (NaCl, neat): $\tilde{\nu}$ = 3439, 2977, 2143, 1715, 1656, 1595, 1499, 1467, 1365, 1321, 1262, 1156, 1109, 1075, 966, 743 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 6.92 (dd, J = 7.6, 1.4 Hz, 1 H), 6.86 (m, 1 H), 6.83–6.79 (m, 2 H), 5.64 (s, 1 H, OH), 4.52 (tdt, J = 12.4, 6.2, 1.4 Hz, 1 H), 4.44 (dt, J = 11.7, 6.2 Hz, 1 H), 4.38 (dtd, J = 11.7, 6.2, 1.4 Hz, 1 H), 2.43 (s, 3 H), 2.14 (m, 1 H), 2.06 (m, 1 H), 1.35 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 189.86, 161.28, 146.73, 144.29, 122.09, 120.12, 115.11, 113.59, 76.16, 72.36, 61.88, 35.65, 28.13, 20.02 ppm. HRMS (ESI): calcd. for $C_{14}H_{16}N_2NaO_5$ $[M + Na]^+$ 315.0957; found 315.0909.

Preparation of Substrates 13: A THF (30 mL) solution of diisopropyl azodicarboxylate (1.25 mL, 1.4 mol) was added dropwise to a solution of O-TBS-catechol (1.04 g), 1,3-butanediol (580 mg, 1.4 mol), and triphenylphosphane (1.49 g, 1.2 mol) in THF (20 mL) at room temperature. After stirring for 19 h, the solution was concentrated and then purified by column chromatography on silica gel (elution with 10% ethyl acetate in hexane) to give 985.6 mg of the primary ether (72% yield). IR (NaCl, neat): $\tilde{\nu}$ = 3365, 3063, 2930, 1593, 1505, 1471, 1390, 1266, 1114, 1044, 1006, 923, 781, 745, 705, 662 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 6.89–6.79 (m, 4 H), 4.15 (dt, J = 8.9, 6.2 Hz, 1 H), 4.11–4.04 (m, 2 H), 1.92 (t, J = 6.2 Hz, 2 H), 1.24 (d, J = 8.9 Hz, 3 H), 0.98 (s, 9 H), 0.16 (d, J = 4.1 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 150.26, 145.15, 121.71, 121.14, 120.86, 113.50, 66.73, 66.44, 38.22, 25.77, 23.65, –4.42, –4.47 ppm. HRMS (ESI): calcd. for $C_{16}H_{28}NaO_3Si$ $[M + Na]^+$ 319.1705; found 319.1743. The following procedure is almost the same as that described for **12**. Diketene addition to the above ether (934.6 mg) gave 1.07 g of the acetoacetate (88%). IR (NaCl, neat): $\tilde{\nu}$ = 2931, 1717, 1652, 1591, 1506, 1473, 1362, 1269, 1045, 923, 839, 748, 705, 662 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 6.89–6.78 (m, 4 H), 5.19 (m, 1 H), 3.98 (t, J = 6.9 Hz, 2 H), 3.41 (s, 2 H), 2.22 (s, 3 H), 2.12–2.00 (m, 2 H), 1.32 (d, J = 6.2 Hz, 3 H), 0.98 (s, 9 H), 0.14 (d, J = 2.7 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 223.94, 166.57, 150.29, 145.17, 121.77, 121.16, 121.12, 113.59, 69.77, 64.85, 50.39, 35.64, 30.05, 25.72, 20.13, –4.57 ppm. HRMS (ESI): calcd. for $C_{20}H_{32}NaO_5Si$ $[M + Na]^+$ 403.1917; found 403.1960. Deprotection of the TBS group starting with 1.01 g of the substrate gave 626.9 mg of the deprotected product (88.9%). IR (NaCl, neat): ṽ = 3446, 2979, 1717, 1699, 1695, 1683, 1674, 1652, 1635, 1616, 1575, 1557, 1505, 1456, 1419, 746 cm^{-1}. ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 6.91 (dd, J = 8.2, 2.1 Hz, 1 H), 6.87–6.79 (m, 3 H), 5.83 (br. s, 1 H, OH), 5.25 (td, J = 12.4, 6.2 Hz, 1 H), 4.12–4.05 (m, 2 H), 3.44 (s, 2 H), 2.22 (s, 3 H), 2.08–2.04 (m, 2 H), 1.32 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 150 MHz): δ = 223.84, 166.75, 145.59, 121.89, 120.09, 114.96, 112.28, 69.20, 65.19, 50.32, 35.48, 30.13, 20.36, 20.19, 19.96 ppm. HRMS (ESI): calcd. for $C_{14}H_{18}NaO_5$ [M + Na]$^+$ 289.1052; found 289.1072. Formation of the diazo group with 557 mg of this substrate gave 595.3 mg of **13** (92.6%). IR (NaCl, neat): ṽ = 3446, 2979, 2146, 1739, 1716, 1700, 1695, 1683, 1675, 1652, 1616, 1575, 1505, 1456, 1419, 744 cm^{-1}. ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 6.92 (dd, J = 7.6, 1.4 Hz, 1 H), 6.88–6.79 (m, 3 H), 5.80 (d, J = 2.1 Hz, 1 H, OH), 5.37 (td, J = 12.4, 6.2 Hz, 1 H), 4.11 (td, J = 9.6, 6.2 Hz, 1 H), 4.05 (dt, J = 9.6, 6.2 Hz, 1 H), 2.44 (s, 3 H), 2.11 (q, J = 6.2 Hz, 2 H), 1.38 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 150 MHz): δ = 189.95, 161.16, 146.11, 145.47, 122.07, 120.09, 115.12, 112.30, 76.37, 69.45, 65.14, 35.70, 28.23, 20.49 ppm. HRMS (ESI): calcd. for $C_{14}H_{16}N_2NaO_5$ [M + Na]$^+$ 315.0957; found 315.0909.

General Procedure for Decomposition of the Diazo Compounds: Analytical runs: $Rh_2(L)_4$ (5 mol-%) was added to a solution of a diazo substrate in CDCl$_3$ (0.7 mL) at room temperature. After stirring at room temperature for 2 h, the crude mixture was analyzed by ^{1}H NMR spectroscopy. Synthetic runs: A CH_2Cl_2 (10–30 mL) solution of the substrate was added dropwise to a solution of $Rh_2(OCOC_3F_7)_4$ (5 mol-%) in CH_2Cl_2 (10–20 mL) at room temperature. After stirring at room temperature for 2 h, the solution was concentrated under vacuum. The residue was purified by silica gel chromatography (elution with 30% ethyl acetate in hexane). **Ether 9:** Yield: 76%. M.p. 108–110 °C. $[\alpha]_D^{20}$ = +201.75 (c = 0.63, CH_2Cl_2). IR (NaCl, neat): ṽ = 2978, 2934, 1739, 1596, 1496, 1452, 1417, 1380, 1357, 1258, 1193, 1109, 1084, 994, 945, 912, 818, 754 cm^{-1}. ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 7.10–7.07 (m, 2 H), 6.97 (dd, J = 8.2, 1.4 Hz, 1 H), 6.93 (td, J = 7.6, 1.4 Hz, 1 H), 5.17 (m, 1 H), 4.58 (s, 1 H), 4.24 (m, 1 H), 2.47 (s, 3 H), 2.23 (dt, J = 15.1, 11.0 Hz, 1 H), 1.61 (dt, J = 15.1, 1.4 Hz, 1 H), 1.51 (d, J = 6.2 Hz, 3 H), 1.30 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 150 MHz): δ = 201.84, 166.14, 153.02, 146.78, 126.59, 123.01, 122.38, 116.24, 90.23, 79.33, 72.57, 42.97, 26.65, 23.23, 20.83 ppm. HRMS (ESI): calcd. for $C_{15}H_{18}NaO_5$ [M + Na]$^+$ 301.1052; found 301.1055. **Ether 14:** Yield: 63% yield. M.p. 120–122 °C. $[\alpha]_D^{20}$ = +2.2 (c = 0.50, CH_2Cl_2). IR (NaCl, neat): ṽ = 2981, 2934, 1734, 1652, 1596, 1498, 1456, 1419, 1360, 1260, 1081, 941, 912, 826, 806, 752, 667 cm^{-1}. ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 7.13 (td, J = 8.2, 1.4 Hz, 1 H), 7.07 (dd, J = 7.9, 1.4 Hz, 1 H), 6.99 (dd, J = 8.2, 1.4 Hz, 1 H), 6.91 (td, J = 7.9, 1.4 Hz, 1 H), 5.40 (ddd, J = 12.4, 6.5, 3.4 Hz, 1 H), 4.72 (ddd, J = 12.4, 6.5, 2.7 Hz, 1 H), 4.21 (s, 1 H), 2.50 (s, 3 H), 1.98 (ddd, J = 15.4, 6.5, 3.4 Hz, 1 H), 1.86 (ddd, J = 15.4, 6.5, 2.7 Hz, 1 H), 1.52 (d, J = 6.5 Hz, 3 H), 1.20 (d, J = 6.5 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 150 MHz): δ = 203.87, 166.34, 151.93, 148.39, 126.29, 123.14, 121.83, 115.15, 87.44, 72.71, 68.27, 36.75, 26.98, 20.72, 20.02 ppm. HRMS (ESI): calcd. for $C_{15}H_{18}NaO_5$ [M + Na]$^+$ 301.1052; found 301.1046. **Ether 15:** Yield: 54%. Colorless oil. IR (NaCl, neat): ṽ = 2925, 1744, 1596, 1496, 1453, 1259, 928, 758 cm^{-1}. ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 7.12 (td, J = 8.2, 1.4 Hz, 1 H), 7.08 (dd, J = 7.9, 1.7 Hz, 1 H), 6.99 (dd, J = 8.2, 1.4 Hz, 1 H), 6.92 (td, J = 7.9, 1.4 Hz, 1 H), 4.76 (dtd, J = 11.3, 4.8, 1.4 Hz, 1 H), 4.54 (m, 1 H), 4.40 (s, 1 H), 4.09 (tt, J = 11.3, 1.4 Hz, 1 H), 2.50 (s, 3 H), 2.15 (m, 1 H), 1.85 (m, 1 H), 1.53 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 150 MHz): δ = 216.40, 166.53, 152.28, 126.44, 123.04, 122.12, 115.90, 88.17, 62.96, 32.07, 30.90, 29.69, 26.90, 21.39 ppm. HRMS (ESI): calcd. for $C_{14}H_{16}NaO_5$ [M + Na]$^+$ 287.0895; found 287.0937. **Ether 16:** Yield: 38%. Colorless oil. IR (NaCl, neat): ṽ = 2979, 1747, 1597, 1496, 1260, 756 cm^{-1}. ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 7.14–7.07 (m, 4 H), 6.96 (m, 1 H), 5.40–5.35 (m, 2 H), 4.69 (s, 1 H, assigned to S), 4.48 (s, 1 H, R), 4.44 (ddd, J = 10.0, 5.5, 2.4 Hz, 1 H, S), 4.39 (ddd, J = 11.0, 5.5, 2.7 Hz, 1 H, R), 4.29 (td, J = 11.0, 2.1 Hz, 1 H, R), 3.99 (td, J = 10.0, 1.4 Hz, 1 H, S), 2.48 (s, 3 H, R), 2.46 (s, 3 H, S), 2.07–1.98 (m, 2 H), 1.95–1.89 (m, 2 H), 1.32 (d, J = 6.2 Hz, 3 H, S), 1.26 (d, J = 6.2 Hz, 3 H, R) ppm. ^{13}C NMR (CDCl$_3$, 150 MHz): δ = 203.30, 201.24, 166.85, 166.68, 150.57, 148.00, 125.90, 125.54, 123.33, 122.72, 122.59, 122.33, 118, 40, 115.70, 89.06, 87.02, 71.90, 71.32, 70.27, 67.28, 34.37, 31.98, 30.89, 26.82, 26.69, 20.19 ppm. HRMS (ESI): calcd. for $C_{14}H_{16}NaO_5$ [M + Na]$^+$ 287.0895; found 287.0908.

Preparation of 17a and 17b: $LiAlH_4$ (2.2 mg, 1.5 mol) was added to a stirred solution of **9** (10 mg) in diethyl ether (3 mL) at –78 °C. After stirring for 2 h, the mixture was treated with water at –78 °C. This mixture was warmed to room temperature, extracted with diethyl ether, and washed with water and then brine. Drying with Na_2SO_4, concentration, and column chromatography on silica gel (elution with 40% ethyl acetate in hexane) afforded **17a** (77% yield as a diastereomeric ratio (73:27). IR of the isomeric mixture: IR (NaCl, neat): ṽ = 3497, 2976, 2932, 1734, 1595, 1496, 1451, 1378, 1257, 1197, 1175, 1109, 1084, 1039, 956, 758 cm^{-1}. Major isomer: ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 7.02 (dt, J = 16.5, 7.6 Hz, 2 H), 6.97 (dd, J = 7.6, 1.4 Hz, 1 H), 6.93 (td, J = 7.6, 1.4 Hz, 1 H), 5.16 (m, 1 H), 4.32 (m, 1 H), 4.24 (m, 1 H), 3.90 (d, J = 8.9 Hz, 1 H), 2.91 (br. s, 1 H), 2.28 (dt, J = 15.1, 11.0 Hz, 1 H), 1.62 (d, J = 15.1 Hz, 1 H), 1.52 (d, J = 6.2 Hz, 3 H), 1.32 (d, J = 6.2 Hz, 3 H), 1.21 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 150 MHz): δ = 168.84, 153.13, 147.49, 126.29, 123.42, 122.51, 116.46, 91.68, 79.74, 72.08, 66.71, 42.97, 23.34, 21.01, 17.18 ppm. HRMS (ESI): calcd. for $C_{15}H_{20}NaO_5$ [M + Na]$^+$ 303.1208; found 303.1149. Minor isomer: ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 7.02 (dt, J = 16.5, 7.6 Hz, 2 H), 6.95–6.89 (m, 2 H), 5.09 (m, 1 H), 4.32 (m, 1 H), 4.24 (m, 1 H), 3.89 (d, J = 7.6 Hz, 1 H), 2.35 (dt, J = 15.1, 11.0 Hz, 1 H), 1.60 (d, J = 15.1 Hz, 1 H), 1.51 (d, J = 6.2 Hz, 3 H), 1.45 (d, J = 6.2 Hz, 3 H), 1.37 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 150 MHz): δ = 169.41, 153.13, 147.85, 126.08, 123.35, 122.35, 116.40, 90.00, 79.74, 72.63, 67.12, 42.63, 23.30, 21.10, 19.71 ppm. (S)- or (R)-MTPACl (10 µL) and DMAP (ca. 10 mg) were added to a solution of **17a** (5 mg) in CH_3CN (2 mL) at room temperature. After stirring for 1 h, the mixture was quenched with a 2 M HCl aqueous solution. This mixture was extracted with diethyl ether and washed with the HCl solution, water, and then brine. Drying with Na_2SO_4 and concentration afforded (R)-**17b** when the (S) reagent was employed and (S)-**17b** when the (R) reagent was employed. **(*R*)-17b:** ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 7.57 (dt, J = 25.4, 4.8 Hz, 2 H), 7.42 (dd, J = 5.8, 2.1 Hz, 2 H), 7.34 (d, J = 2.1 Hz, 1 H), 7.01 (dd, J = 7.6, 1.0 Hz, 1 H), 6.92 (dd, J = 8.2, 1.4 Hz, 1 H), 6.79 (td, J = 7.6, 1.0 Hz, 1 H), 6.56 (dd, J = 8.2, 1.4 Hz, 1 H), 5.73 (m, 1 H), 5.19 (m, 1 H), 4.22 (m, 1 H), 4.11 (d, J = 9.3 Hz, 1 H), 3.59 (s, 3 H), 2.38–2.27 (m, 1 H), 1.61 (dt, J = 15.8, 1.4 Hz, 1 H), 1.51 (d, J = 6.5 Hz, 3 H), 1.36 (d, J = 6.9 Hz, 3 H), 1.34 (d, J = 6.5 Hz, 3 H) ppm. HRMS (ESI): calcd. for $C_{25}H_{27}F_3NaO_7$ [M + Na]$^+$ 519.1607; found 519.1660. **(*S*)-17b:** ^{1}H NMR (CDCl$_3$, 600 MHz): δ = 7.64 (d, J = 7.6 Hz, 2 H), 7.48 (d, J = 6.9 Hz, 1 H), 7.35–7.32 (m, 2 H), 7.08–7.08 (m, 2 H), 6.98–6.93 (m, 2 H), 5.71 (m, 1 H), 5.24 (m, 1 H), 4.25 (m, 1 H), 4.18 (d, J = 7.6 Hz, 1 H), 3.60 (s, 3 H), 2.31 (m, 1 H), 1.63 (dt, J = 15.1, 1.4 Hz, 1 H), 1.53 (d, J = 6.2 Hz, 3 H), 1.34 (d, J = 6.2 Hz, 3 H), 1.29 (d, J = 6.9 Hz, 3 H) ppm. HRMS (ESI): calcd. for $C_{25}H_{27}NaO_7$ [M + Na]$^+$ F_3 519.1607; found 519.1659.

Preparation of 18a and 18b: According to the same procedure as used for **17a** and **17b**, **18a** and **18b** were prepared from **14**. Ester **18a**: Yield: 30%; diastereomeric ratio: 69:31. Major isomer: ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.12–7.06 (m, 2 H), 6.97 (d, J = 7.6 Hz, 1 H), 6.91 (td, J = 7.6, 1.4 Hz, 1 H), 5.43 (m, 1 H), 4.72 (m, 1 H), 4.33 (m, 1 H), 3.58 (d, J = 8.2 Hz, 1 H), 3.04 (br. s, 1 H, OH), 1.96–1.85 (m, 2 H), 1.52 (d, J = 6.9 Hz, 3 H), 1.25 (d, J = 6.2 Hz, 3 H), 1.19 (d, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 168.47, 152.04, 125.91, 123.33, 121.80, 115.06, 87.05, 72.58, 67.42, 66.50, 36.79, 30.89, 20.72, 20.18, 17.46 ppm. HRMS (ESI): calcd. for $C_{15}H_{20}NaO_5$ [M + Na]$^+$ 303.1208; found 303.1217. Minor isomer: ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.07 (m, 1 H), 7.03 (dd, J = 7.6, 1.4 Hz, 1 H), 6.97 (d, J = 7.6 Hz, 1 H), 6.91 (td, J = 7.6, 1.4 Hz, 1 H), 5.43 (m, 1 H), 4.72 (m, 1 H), 4.37 (m, 1 H), 3.61 (d, J = 8.2 Hz, 1 H), 2.47 (br. s, 1 H, OH), 1.96–1.85 (m, 2 H), 1.51 (d, J = 6.9 Hz, 3 H), 1.49 (d, J = 6.2 Hz, 3 H), 1.18 (d, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 168.45, 153.13, 125.68, 123.06, 121.84, 115.35, 87.85, 72.74, 67.57, 66.23, 36.90, 30.89, 20.80, 20.11, 17.46 ppm. **(*R*)-18b:** ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.57 (dt, J = 8.2, 1.4 Hz, 2 H), 7.32–7.30 (m, 3 H), 7.00 (td, J = 8.2, 1.4 Hz, 1 H), 6.89 (dd, J = 8.2, 1.0 Hz, 1 H), 6.66 (td, J = 8.2, 1.4 Hz, 1 H), 6.26 (dd, J = 8.2, 1.4 Hz, 1 H), 5.74 (m, 1 H), 5.41 (m, 1 H), 4.67 (m, 1 H), 3.83 (d, J = 9.6 Hz, 1 H), 3.61 (s, 3 H), 1.96–1.82 (m, 2 H), 1.50 (d, J = 6.2 Hz, 3 H), 1.37 (d, J = 6.5 Hz, 3 H), 1.17 (d, J = 6.2 Hz, 3 H) ppm. **(*S*)-18b:** ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.63 (d, J = 7.6 Hz, 2 H), 7.34–7.30 (m, 3 H), 7.06 (td, J = 7.9, 2.1 Hz, 1 H), 6.95 (t, J = 8.2 Hz, 1 H), 6.82–6.77 (m, 2 H), 5.70 (m, 1 H), 5.45 (m, 1 H), 4.73 (m, 1 H), 3.89 (d, J = 9.6 Hz, 1 H), 3.56 (s, 3 H), 2.00–1.85 (m, 2 H), 1.53 (d, J = 6.9 Hz, 3 H), 1.33 (d, J = 6.2 Hz, 3 H), 1.19 (d, J = 6.9 Hz, 3 H) ppm.

Preparation of 19: $LiAlH_4$ (2.3 mg, 2.1 mol) was added to a stirred solution of **7** (8.1 mg) in diethyl ether (3 mL) cooled to –78 °C, and then this solution was warmed to room temperature. After stirring for 2 h, the mixture was treated with water. The mixture was then extracted with diethyl ether and washed with water and brine. Drying with Na_2SO_4, concentration, and column chromatography on silica gel (elution with 75% ethyl acetate in hexane) afforded 2.4 mg of diol (29% yield). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.00–6.90 (m, 4 H), 4.45 (m, 1 H), 4.17–4.12 (m, 2 H), 4.05 (m, 1 H), 3.91 (dd, J = 12.4, 3.1 Hz, 1 H), 3.81 (dd, J = 12.4, 3.4 Hz, 1 H), 3.74 (br. s, 1 H, OH), 3.44 (br. s, 1 H, OH), 1.93 (dt, J = 14.4, 10.0 Hz, 1 H), 1.71 (dt, J = 14.4, 2.1 Hz, 1 H), 1.37 (d, J = 6.2 Hz, 3 H), 1.26 (d, J = 6.5 Hz, 3 H), 1.19 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 149.01, 147.67, 122.88, 121.92, 118.25, 115.64, 83.86, 78.19, 68.15, 67.72, 62.06, 45.39, 23.51, 20.77, 19.18 ppm. HRMS (ESI): calcd. for $C_{15}H_{24}NaO_5$ [M + Na]$^+$ 307.1521; found 307.1551. Benzaldehyde (ca. 5 mg) and TsOH·Py (trace) were added to a stirred solution of the diol (1.9 mg) in benzene (2 mL), and then this solution was refluxed for 4 h. After the mixture had cooled to room temperature, it was treated with water. This mixture was then extracted with diethyl ether and washed with water and brine. Drying with Na_2SO_4, concentration, and column chromatography on silica gel (elution with 35% ethyl acetate in hexane) afforded 3.4 mg of **19** (>95% yield). IR (NaCl, neat): $\tilde{\nu}$ = 3534, 2928, 1717, 1594, 1496, 1454, 1378, 1257, 1206, 1150, 1094, 992, 749, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.53 (dd, J = 7.6, 1.4 Hz, 2 H), 7.36–7.32 (m, 3 H), 6.98–6.90 (m, 4 H), 5.62 (s, 1 H), 4.73 (m, 1 H), 4.43 (dd, J = 12.4, 1.4 Hz, 1 H), 4.25 (qd, J = 6.9, 1.4 Hz, 1 H), 4.19 (m, 1 H), 4.10 (d, J = 1.4 Hz, 1 H), 3.98 (dd, J = 12.4, 1.4 Hz, 1 H), 1.84 (dt, J = 14.4, 8.9 Hz, 1 H), 1.55 (m, 1 H), 1.50 (d, J = 6.9 Hz, 3 H), 1.18 (d, J = 6.2 Hz, 3 H), 1.08 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 149.39, 148.48, 138.31, 128.86, 128.12, 126.29, 122.75, 122.17, 120.38, 117.09, 101.42, 75.08, 71.73, 67.76, 66.76, 46.04, 23.52, 20.27, 17.33 ppm. HRMS (ESI): calcd. for $C_{22}H_{28}NaO_5$ [M + Na]$^+$ 395.1834; found 395.1845.

Preparation of 20: According to the same procedure employed for the synthesis of **19**, **20** was obtained in 52% yield in the two steps. **Diol:** ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.03–6.91 (m, 4 H), 4.70 (m, 1 H), 4.27 (m, 1 H), 4.15 (m, 1 H), 4.04 (m, 1 H), 3.91 (dd, J = 13.4, 2.7 Hz, 1 H), 3.77 (dd, J = 13.4, 4.1 Hz, 1 H), 1.86–1.76 (m, 2 H), 1.37 (d, J = 6.2 Hz, 3 H), 1.27 (d, J = 6.5 Hz, 3 H), 1.20 (d, J = 6.2 Hz, 3 H) ppm. **Acetal 20:** ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.55 (dd, J = 6.9, 1.4 Hz, 2 H), 7.36–7.32 (m, 3 H), 6.98 (m, 1 H), 6.93–6.91 (m, 3 H), 5.62 (s, 1 H), 4.73 (m, 1 H), 4.45 (dd, J = 13.1, 1.4 Hz, 1 H), 4.27–4.21 (m, 2 H), 4.08 (d, J = 1.4 Hz, 1 H), 3.98 (dd, J = 13.1, 1.4 Hz, 1 H), 1.75–1.65 (m, 2 H), 1.47 (d, J = 6.2 Hz, 3 H), 1.23 (d, J = 6.2 Hz, 3 H), 1.11 (d, J = 6.2 Hz, 3 H) ppm.

Isomerization of the Cyclic Ethers: The isomeric ratios of the cyclic ethers **9** and **14**–**16** were determined by ^{1}H NMR spectroscopy. DABCO (3% wt/v), as catalyst, was added to a solution of **9** or **14**–**16** (5 mg) in $CDCl_3$ (0.5 mL) in an NMR tube at room temperature. The isomeric ratios were determined by ^{1}H NMR spectroscopy at –60, –30, 0, 23, and 60 °C. The kinetic protonation was carried out as follows. *t*BuOK (ca. 3 mg) was added to a solution of **9** or **14**–**16** (8 mg) in *t*BuOH (3 mL) at 30 °C. After stirring at 30 °C for 2 h, the mixture was quenched with a saturated solution of aqueous NH_4Cl. This mixture was then extracted with diethyl ether and washed with water and brine. After drying with $MgSO_4$ and concentration, the crude mixture was analyzed by ^{1}H NMR spectroscopy.

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