Chiral synthesis via organoboranes. 45. Asymmetric hydroboration of 1-cyclopentenol derivatives using diisopinocampheylborane. Synthesis of optically active cyclopentane-1,2-diol derivatives of high optical purity ☆

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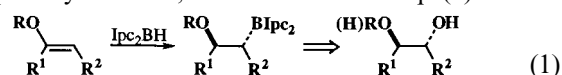
Abstract

The asymmetric hydroboration of 1-cyclopentenol derivatives, such as ethers, acetate, silyl ether and borinate, was investigated using diisopinocampheylborane, ^{d}Ipc$_2$BH. The product trialkylboranes were treated with excess of acetaldehyde to give the corresponding diethyl boronate esters. These boronate esters on oxidation using alkaline hydrogen peroxide gave optically active *trans*-cyclopentane-1,2-diol derivatives in 50–85% enantiomeric excess and up to 95% overall yield. Some of the optically active *trans*-2-alkoxycyclopentanols were converted by ether cleavage to optically active *trans*-(1R,2R)-cyclopentane-1,2-diol. The asymmetric hydroboration-oxidation of 3-methoxy-2,5-dihydrofuran gave *trans*-(3R,4R)-4-methoxytetrahydrofuran-3-ol of 75% ee in 70% overall yield. © 1999 Elsevier Science S.A. All rights reserved.

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1. Introduction

Optically active 1,2-diols are valuable chiral synthons and are employed as chiral auxiliaries and as chiral ligands in a wide range of asymmetric catalysts [1]. However, it appears that the asymmetric hydroxylation of alkenes using osmium reagents [2a] and the enzymatic hydrolysis [2b] of racemic 1,2-diacetates are the only general methods available for the preparation of optically active 1,2-diols. Achiral hydroboration of oxy-substituted alkenes, such as enol ethers [3], enol acetates [3,4], enol silyl ethers [5], and enolates [5e] has already been reported in the literature to give the corresponding 1,2-diol derivatives. In our continuing study on asym-

metric hydroborations, we were interested in the asymmetric hydroboration of oxy-substituted alkenes using diisopinocampheylborane (^{d}Ipc$_2$BH) of > 99% ee. The hydroboration products upon oxidation would then give optically active 1,2-diol derivatives Eq. (1).

$$RO\text{—}\diagdown_{R^1}^{R^2} \xrightarrow{Ipc_2BH} RO\diagdown_{R^1}^{BIpc_2}{}_{R^2} \Longrightarrow (H)RO\diagdown_{R^1}^{OH}{}_{R^2} \qquad (1)$$

For the present study, we chose 1-cyclopentenol derivatives **1**–**7** as substrates for asymmetric hydroboration using ^{d}Ipc$_2$BH (Scheme 1). The five-membered ring compounds were chosen mainly because of their ease of preparation. Additionally, five-membered cycloalkenes are more reactive [6,7] compared to their six-membered counterparts towards hydroboration with ^{d}Ipc$_2$BH and other bulky hydroborating reagents.

2. Results and discussions

The enol derivatives **1**–**7** were treated with crystalline, enantiomerically pure ^{d}Ipc$_2$BH [8], obtained

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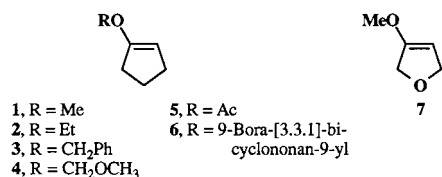
Scheme 1. 1-Cyclopentenol derivatives used for the asymmetric hydroboration.

from (+)-α-pinene, in THF solvent. (+)-α-Pinene (15% excess) was added prior to the addition of the cyclopentenol derivatives to suppress the dissociation of $^dIpc_2BH$ to monoisopinocampheylborane ($^dIpcBH_2$) and α-pinene. The reactions were carried out at low temperatures and were monitored by ^{11}B-NMR spectroscopy. Since $^dIpc_2BH$ is only sparingly soluble in THF, dissolution of the solid $^dIpc_2BH$ usually indicates completion of the reaction. The trialkylborane products were treated with excess of acetaldehyde to eliminate selectively the isopinocampheyl group as α-pinene providing the corresponding diethyl boronate esters. These boronate esters were then oxidized using alkaline 30% hydrogen peroxide to the corresponding alcohols Eq. (2).

$$(2)$$
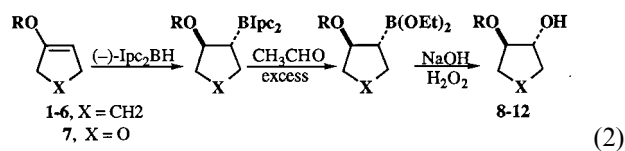
The enantiomeric purities of the product alcohols were determined by capillary GC analyses of the corresponding esters of (R)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) [10]. In the present study, the enantiomeric excess (ee) of the product alcohols were not optimized and the reaction temperatures were chosen such that the reaction proceeded at a reasonable rate. In the cases of 1-methoxy- and 1-ethoxycyclopentenes (**1** and **2**), the solid $^dIpc_2BH$ disappeared completely and the ^{11}B-NMR of the reaction mixture showed the presence of only the trialkylboranes, indicating complete hydroboration in these cases. Oxidation of the corresponding alkylboronates *trans*-2-methoxy- and *trans*-2-ethoxycyclopentanols in 85 and 75% ee, respectively. The hydroboration of **3** was not complete, as indicated by the residual solid $^dIpc_2BH$. Upon oxidation, the product 2-benzyloxycyclopentanol was obtained in 77% ee. Similarly, methoxymethyl-1-cyclopentenyl ether (**4**), after the hydroboration-oxidation reaction, gave the corresponding mono methoxymethyl ether of *trans*-cyclopentane-1,2-diol in 50% ee. In the case of 1-acetoxycyclopentene, the hydroboration was very slow. Even after 7 days at −10°C most of the $^dIpc_2BH$ remained unreacted. Consequently, we did not process this reaction further. We then extended this asymmetric hydroboration reaction to the dihydrofuran derivative (**7**). This enol ether behaved very similar to the other cyclopentenyl ethers. Thus, hydroboration–oxidation of the methyl enol ether **7** gave the methoxy alcohol **12** of 75% ee in 77% overall yield. The results are summarized in Table 1.

The enol derivatives are related structurally to trialkylsubstituted olefins, where the oxy group is replaced by an alkyl group. It has been previously reported in the literature that $^dIpc_2BH$ reacts sluggishly with trisubstituted alkenes and the products are obtained in low optical purity [7]. The reaction of trisubstituted alkenes with $^dIpc_2BH$ proceed with the displacement of one mole of α-pinene per mole of alkene reacted. It has been shown previously in our laboratories that $^dIpc_2BH$ exists as the dimer, *sym*-tetraisopinocampheyldiborane $(^dIpc_2BH)_2$, in THF or diglyme solution and that there was a small measurable dissociation of the reagent into triisopinocampheyldiborane $(Ipc_3B_2H_3)$ and α-pinene

Table 1
Hydroboration of enol derivatives **1-7**, with $^dIpc_2BH$.

Subtrate	Hydroboration		Oxidation product	% ee[a]	% Yield
	Temp	Time			
1[b]	−25°	76 h	(1R,2R)-(−)-2-methoxy-cyclopentanol, **8**	85	93
2[c]	−25°	80 h	(1R,2R)-(−)-2-ethoxy-cyclopentanol, **9**	76	95
3[d]	−15°	5 d	(1R,2R)-(−)-2-benzyloxy-cyclopentanol, **10**	77	75 (95)[e]
4[f]	−15°	5 d	(1R,2R)-(−)-2-(methoxy–methoxy)cyclopentanol, **11**	50	77
6	−10°	3 d	(1R,2R)-(−)-cyclopentane-1,2-diol	86	40
7[g]	−25°	30 h	(3R,4R)-(+)-4-methoxy-tetrahydrofuran-3-ol, **12**	75	70

[a] The ee values were determined by capillary GC analysis of the corresponding MTPA esters.
[b] R. Wohl, Synthesis (1974) 38.
[c] I. Ryu, T. Aya, S. Otani, S. Murai, N. Senoda, J. Organomet. Chem. 321 (1987) 279.
[d] Ref. [10].
[e] Yield given in parentheses was based on alkene reacted.
[f] Ref. [18].
[g] S. Hoff, L. Brandsma, J.F. Arens, Recl. Trav. Chim. Pays-Bas 88 (1969) 609.

[9]. Triisopinocampheyldiborane can be considered as a 1:1 mixture of ^{d}Ipc$_2$BH and ^{d}IpcBH$_2$. When the substrate is hindered sufficiently to retard the direct reaction of ^{d}Ipc$_2$BH, the reaction proceeds partially through an alternate pathway—reaction with ^{d}IpcBH$_2$, the less bulky dissociation product. It is known that ^{d}Ipc$_2$BH and ^{d}IpcBH$_2$ exhibit opposite enantiofacial selectivity in the hydroboration [7,9]. Consequently, low enantioselectivities are realized in the asymmetric hydroboration of hindered alkenes as a result of the competitive dissociation of ^{d}Ipc$_2$BH. In the present study, α-pinene (15% excess) was added prior to the addition of the cyclopentenol derivatives to retard such dissociation of ^{d}Ipc$_2$BH.

Peterson and Stepanian [11] reported that the hydroboration-oxidation of 1-methoxy- and 1-benzyloxy-cyclopentenes using ^{l}Ipc$_2$BH at 25 °C produced *trans*-2-methoxy- and 2-benzyloxycyclopentanols in 29 and 23% ee, respectively. Neither absolute configuration, nor the optical rotation of these products, were reported. Since these authors carried out the reaction at a considerably higher temperature (25°C), compared to the reaction temperature reported in the present study (− 25 and − 15°C), and have not added additional α-pinene to suppress the dissociation of ^{d}Ipc$_2$BH, it is most likely that the low asymmetric induction was due to the participation of mixed hydroborating agents arising from the dissociation of ^{d}Ipc$_2$BH.

2.1. Determination of absolute configuration of the product alcohols

The absolute configuration of optically active *trans*-cyclopentane-1,2-diol has been reported in the literature [12]. Hence, the absolute configuration of the hydroboration–oxidation products, the optically active *trans*-2-alkoxycyclopentanols, were determined by converting them to *trans*-cyclopentane-1,2-diol. The methoxy alcohol **8** (85% ee) was silylated using trimethylsilyl chloride-triethylamine. This silyl ether **13** was converted to (1R,2R)-*trans*-(+)-cyclopentane-1,2-diol **15** by reaction with in situ generated trimethylsilyl iodide followed by hydrolysis of the intermediate bis-silyl ether **14** with methanol. Thus the absolute configuration of the methoxy alcohol **8**, obtained by the hydroboration–oxidation of **1** using ^{d}Ipc$_2$BH could be determined as 1R,2R (Eq. (3)).

(3)
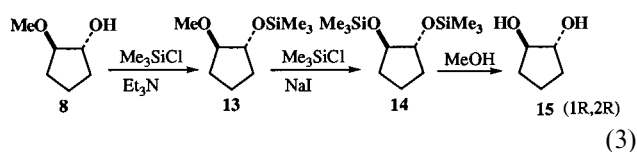
The absolute configuration of the benzyloxy alcohol **10** was established to be 1R,2R by hydrogenating [13] it over 10% Pd–C to give (1R,2R)-*trans*-(+)-cyclopen-

tane-1,2-diol in 90% yield. The monomethoxymethyl ether of *trans*-cyclopentane-1,2-diol **11** was converted to (1R,2R)-*trans*-(+)-cyclopentane-1,2-diol in 92% yield by treatment with HCl in THF, establishing that absolute configuration of **11** as 1R,2R.

The absolute configuration of the tetrahydrofurane-diol **16** is available in the literature [14]. Unfortunately, reaction of the methoxy alcohol **12** with NaI/Me$_3$SiCl in acetonitrile gave a complex reaction mixture from which the required diol **16** could not be isolated. Consequently, we converted alcohol **12** to 3-methoxytetrahydrofuran **17**, easily prepared from the commercially available 3-hydroxytetrahydrofuran of known absolute configuration. Thus, the methoxy alcohol **12** was converted to the corresponding tosylate and reduced using lithium triethylborohydride [15] to afford (S)-(+)-3-methoxytetrahydrofuran in 50% yield (Eq. (4)).

(4)
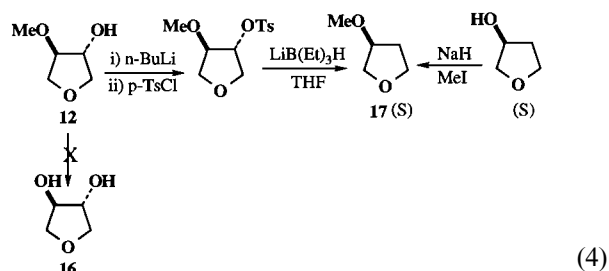
An authentic sample of (S)-(+)-3-methoxytetrahydrofuran was obtained by methylation of commercially available (S)-(+)-3-hydroxytetrahydrofuran. Chiroptical comparison of these two samples of (S)-(+)-3-methoxytetrahydrofuran confirmed an absolute configuration of 3R,4R for **12**.

On the basis of these results, we are schematically representing the lowest energy transition state structure proposed [16] for the hydroboration of the 1-cyclopentenol derivatives with ^{d}Ipc$_2$BH in Fig. 1.

In this model, the Ipc groups attached to the carbon bearing the boron atom are shown using the symbols S (small) for the hydrogen, M (medium) for the methylene and L (large) for the methylene attached to the methyl group. With trisubstituted olefins, the steric interaction between the inside L group and the alkyl group is large enough to slow down the reaction con-
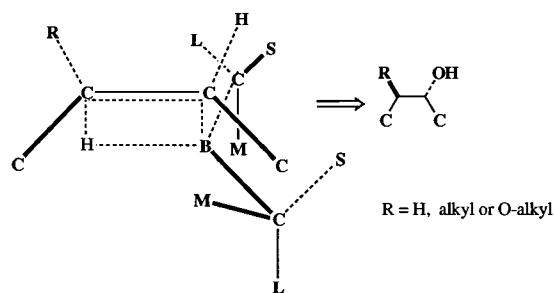
Fig. 1. Preferred transition state structure for hydroboration of olefins with ^{d}Ipc$_2$BH.

siderably. In the case of simple enol ethers **1**–**3** and **7**, the increased electron density at the β-carbon, due to the + R effect, increases the coordination between the β-carbon and the boron atom. This energetically favorable coordination of the β-carbon of the double bond to the boron atom apparently overcomes the steric repulsion between the L-group and the alkoxy group.

3. Conclusions

Of the several cyclopentyl enol derivatives used in the present study of asymmetric hydroboration using ^{d}Ipc$_2$BH, the simple derivatives, such as methyl, ethyl and benzyl enol ethers, appear to be the more favorable substrates. In these cases, the hydroboration–oxidation products were obtained in high optical purity (75–85% ee) and good overall yield (70–95%), under unoptimized reaction conditions. Optically active 2-methoxy- and 2-benzyloxycyclopentanols were converted to optically active *trans*-(1*R*,2*R*)-cyclopentane-1,2-diol in high enantiomeric purity, thus constituting a formal synthesis of the latter.

4. Experimental

All b.p.s are uncorrected. All operations involving organoboranes were carried out under an inert atmosphere. Detailed procedures for handling air-sensitive compounds have been reported elsewhere [17]. The ^{11}B-NMR spectra were obtained at 25.5 MHz on a Varian FT-80A instrument. The ^{11}B chemical shifts are given in δ units relative to BF$_3$:OEt$_2$. The ^{1}H-NMR spectra were recorded at 200 MHz (Gemini-200). The ^{13}C-NMR measurements were made at 50.3 MHz (Gemini-200). The ^{1}H- and ^{13}C-NMR chemical shifts are reported in δ units relative to TMS standard. Optical rotations were measured on a Rudolph polarimeter Autopol III, at 25°C. The enantiomeric excesses of the product alcohols were determined by capillary GC analysis of the corresponding esters of (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid [10] (MTPA), on a 50 ft methylsilicone or SPB-5 column using Hewlett–Packard 5890A chromatograph. For all the optically active alcohols reported in this paper, the corresponding racemic alcohols were prepared by known procedures and their MTPA esters showed 50–50 baseline separation on capillary GC analysis. THF was distilled over sodium and benzo-phenone ketyl. Anhydrous ether obtained from Mallinckrodt, was used with out further purification. Dimethyl sulfoxide (DMSO) was dried by distilling over CaH.

4.1. Preparation of methoxymethyl-1-cyclopentenyl ether **4**

The literature [18] procedure for the *O*-alkylation of ketone enolates was modified as follows. To LDA (prepared from diisopropylamine (2.02 g, 20 mmol) and 2M *n*-BuLi in hexane (10 ml, 20 mmol) at 0°C in THF), at − 78°C cyclopentanone (1.68 g, 20 mmol) was added dropwise with stirring. After an hour at − 78°C the mixture was warmed to 25°C. THF was evaporated under reduced pressure, DMSO (250 ml) was added to the residue, followed by dropwise addition of methoxymethyl chloride (1.77 g, 22 mmol). The mixture was stirred for 5 min. Pentane (3 × 75 ml) was then added to the mixture with stirring and the pentane layer was removed using a double-ended needle. The pentane solution was distilled under reduced pressure to give pure **4** (b.p. 50–52°C, 14 Torr): yield 1.0 g (40%); ^{1}H-NMR (CDCl$_3$) δ 1.8–2.0 (m, 2 H, CH$_2$CH$_2$CH$_2$), 2.3–2.4 (m, 4 H, CH$_2$CH$_2$CH$_2$), 3.4 (s, 3 H, OCH$_3$), 4.7 (m, 1 H, CH), 4.9 (s, 2 H, OCH$_2$). ^{13}C-NMR (CDCl$_3$) δ 21.0 (C-4), 29.3 (C-3), 31.8 (C-5), 56.5 (OCH$_3$), 95.2 (OCH$_2$), 97.4 (C-2), 157.4 (C-1).

4.2. General procedure for hydroboration of enol derivatives **1**–**7**

The following procedure for the preparation of (1*R*,2*R*)-(-)-*trans*-2-methoxycyclopentanol is representative. A slurry of enantiomerically pure ^{d}Ipc$_2$BH [8] (5.72 g, 20 mmol) and α-pinene (3 mmol) in THF (10 ml) was cooled to − 25°C and 1-methoxycyclopentene (1.96 g, 20 mmol) was added with stirring. The reaction mixture was stirred for 76 h at − 25°C when all the ^{d}Ipc$_2$BH completely dissolved. The complete formation of the intermediate trialkylborane was confirmed by ^{11}B-NMR spectrum of an aliquot (δ + 82, s). Acetaldehyde (4.67 ml, 80 mmol) was added to the reaction mixture at 0°C, and stirred at 25°C for 24 h. Most of the unreacted acetaldehyde was removed under reduced pressure and aqueous NaOH (3 M, 5 ml)was added to the reaction mixture followed careful addition of 30% aq. H$_2$O$_2$ (5 ml). The reaction mixture was stirred at 25°C for 6 h. After saturating the aqueous layer of the reaction mixture with K$_2$CO$_3$ (5 g), the product was extracted with ether (3 × 20 ml). The combined organic layers were dried over anhydrous MgSO$_4$. The solvent was evaporated (25°C, 12 Torr), and residue was purified by distillation: 2.2g (93%); b.p. 146–148°C (745 Torr) (lit. [19] b.p. 81–83°C/10 Torr). The product, *trans*-2-methoxycyclopentanol, was further purified by preparative GC: $[\alpha]_D$ − 17.1° (c, 3.4, EtOH), 85% ee (by capillary GC analysis of MTPA); ^{1}H-NMR (CCl$_4$) δ 1.3–2.2 (m, 6 H, CH$_2$CH$_2$CH$_2$), 3.2 (s, 1 H, OH), 3.3

(s, 3 H, OCH₃), 3.4–3.7 (m, 1 H, CH), 3.9–4.2 (m, 1 H, CH). ¹³C-NMR (CDCl₃) δ 20.8 (C-4), 29.1 (C-3), 32.4 (C-5), 56.9 (OCH₃), 76.7 (C-1), 88.7 (C-2). Anal. Calc. for C₆H₁₂O₂: C, 62.04; H, 10.41. Found: C, 61.87; H, 10.78.

4.3. (1R,2R)-(−)-2-Ethoxycyclopentanol, 9

B.p. 160°C/745 mm (lit. [20] b.p. 182°C/760 Torr). [α]$_D$ − 19.6° (c, 4.8, EtOH), 76% ee (by capillary GC analysis of MTPA ester); ¹H-NMR (CCl₄) δ 1.2 (t, $J = 7$ Hz, 3 H, CH₃), 1.3–2.3 (m, 6 H, CH₂CH₂CH₂), 2.8 (bs, 1 H, OH), 3.5 (q, $J = 7$ Hz, 2 H, CH₂CH₃), 3.5–3.8 (m, 1 H, CH), 3.9–4.3 (m, 1 H, CH). ¹³C-NMR (CDCl₃) δ 15.6 (CH₃), 20.8 (C-4), 29.7 (C-3), 32.3 (C-5), 64.7 (OCH₂), 77.0 (C-1), 87.0 (C-2). Anal. Calc. for C₇H₁₄O₂: C, 64.58; H, 10.84. Found: C, 64.83; H, 11.12.

4.4. (1R,2R)-(−)-2-Benzyloxycyclopentanol, 10 [21]

B.p. 110°C/1 mm; [α]$_D$ − 23.3° (c, 2.7, EtOH), 77% ee (by capillary GC analysis of MTPA ester); ¹H-NMR (CCl₄) δ 1.3–2.2 (m, 6 H, CH₂CH₂CH₂), 2.0 (bs, 1 H, OH), 3.6–3.9 (m, 1 H, CH), 4.0–4.3 (m, 1 H, CH), 4.6 (s, 2 H, OCH₂), 7.3 (s, 5 H, C₆H₅). ¹³C-NMR (CDCl₃) δ 20.6 (C-4), 29.4 (C-3), 32.2 (C-5), 71.3 (OCH₂), 77.1 (C-1), 86.6 (C-2), 127.6 (C-3′, C-4′ and C-5′), 128.3 (C-2′ and C-6′), 138.6 (C-1′). Anal. Calc. for C₁₂H₁₆O₂: C, 74.97; H, 8.39. Found: C, 75.14; H, 8.72.

4.5. (1R,2R)-(−)- Mono methoxymethyl ether of trans-cyclopentane-1,2-diol, 11

Purified by prep GC 10% SE-30 at 150°C; [α]$_D$ − 11.6° (c, 2.2, MeOH), 50% ee (by capillary GC analysis of the corresponding cyclopentane-1,2-diol on SPB-5 column); ¹H-NMR (CDCl₃) δ 1.4–1.7 (m, 4 H, CH₂CH₂CH₂), 1.8–2.2 (m, 2 H, CH₂CH₂CH₂), 3.3 (s, 1 H, OH), 3.4 (s, 3 H, OCH₃), 3.7 (dd, $J = 5.7$ and 12.9 Hz, 1 H, CH), 4.0 (dd, $J = 5.7$ and 12.9 Hz, 1 H, CH), 4.64, 4.68 (ABq, 2 H, $J = 7$ Hz). ¹³C-NMR (CDCl₃) δ 19.5 (C-4), 29.6 (C-3), 31.0 (C-5), 55.8 (OCH₃), 77.7 (C-1), 88.0 (C-2), 97.2 (OCH₂).

4.6. (3R,4R)-(+)-4-Methoxytetrahydrofuran-3-ol, 12

Purified by prep GC (10% carbowax column at 150°C; [α]$_D$ + 14.0° (c, 3.2, EtOH), 75% ee (by capillary GC analysis of MTPA ester on SPB-5, 165°C). ¹H-NMR (CCl₄) δ 3.4 (s, 3 H, OCH₃), 3.5–4.2 (m, 6 H, CH₂CHCHCH₂), 4.3 (bs, 1 H, OH). ¹³C-NMR

(CDCl₃) δ 57.1 (OCH₃), 71.2 (C-3), 73.8 (C-5), 74.7 (C-1), 86.9 (C-2).

4.7. Conversion of methoxy alcohol 8 to (1R,2R)-(−)-cyclopentane-1,2-diol, 15

A mixture of methoxy alcohol 8 (1.74 g, 15 mmol), triethylamine (8.37 ml, 60 mmol), trimethylsilyl chloride (3.57 g, 33 mmol) and ether (150 ml) was stirred at 25°C for 24 h. The precipitated amine hydrochloride was filtered off and the filtrate was distilled. The residue after removing volatiles was found to be pure 13, which was used as such for the next step: yield 2.7 g (95%); ¹H-NMR (CCl₄) δ 0.08 (s, 9 H, Si(CH₃)₃), 1.2–2.1 (s, 3 H, OCH₃), 3.3–3.6 (m, 1 H, CH), 3.8–4.3 (m, 1 H, CH).

To a mixture of 13 (1.9 g, 10 mmol), NaI (1.5 g, 10 mmol), and acetonitrile (15 ml) was added trimethylsilyl chloride (1.08 g, 10 mmol), and stirred at 25°C. The reaction was monitored by GC and after 6 h most of the starting materials disappeared. Methanol (5 ml) was added to the reaction mixture and stirred at 25°C for 6 h. The solids were filtered off and the filtrate evaporated under reduced pressure (12 Torr). The residue was purified by prep GC (10% SE-30 at 140°C), to give pure (1R,2R)-cyclopentane-1,2-diol [12]: [α]$_D$ − 20.0° (EtOH); yield 0.3 g (40%); ¹H-NMR (CDCl₃) δ 1.2-2.2 (m, 6 H, CH₂CH₂CH₂), 3.91 (m, 2 H, CHCH), 4.2 (bs, 2 H, 2 OH).

4.8. Conversion of benzyloxy alcohol 10 to (1R,2R)-(−)-cyclopentane-1,2-diol

The benzyloxy alcohol 10 (1.0 g, of 65% ee) was hydrogenated over 10% Pd–C (0.2 g) in ethanol (20 ml) using a Brown hydrogenator [13]. Hydrogen was generated by adding aq. NaBH₄ to glacial acetic acid. When the uptake of hydrogen stopped, the mixture was filtered, solvent removed to give pure (1R,2R)-cyclopentane-1,2-diol [12]: yield 0.43 g (90%). The diol was further purified by prep GC (10% SE-30, 140°C): [α]$_D$ − 15.7° (c, 5.3, EtOH).

4.9. Conversion of alcohol 11 to (1R,2R)-(−)-cyclopentane-1,2-diol

To a mixture of 11 (1 g), THF (5 ml) and water (1 ml) was added conc. HCl (12 M, 0.1 ml), and the mixture was stirred at 25°C for 12 h. Solid K₂CO₃ (1g) was added carefully. The supernatant solution was decanted and the solvent was evaporated to give (1R,2R)-cyclopentane-1,2-diol [11]: yield 0.6 g (92%). The product was further purified by preparative GC. Capillary GC analysis of its MTPA ester (SPB-5, 240°) showed a 50% ee for the diol.

4.10. Conversion of methoxy alcohol 12 to (S)-(+)-3-methoxytetrahydrofuran 17

To a solution of **12** (0.6 g, 5.0 mmol) in ether (15 ml), *n*-BuLi in hexane (2.0 ml, 5.0 mmol) was added dropwise. To this mixture *p*-toluenesulfonyl chloride (0.97 g, 5.1 mmol) was added and the mixture stirred at 25°C for 12 h. The precipitated LiCl was filtered off and the solvent was evaporated from the filtrate. ^{1}H-NMR of the residue showed it to be pure tosylate, which was used as such for the next step: ^{1}H-NMR (CDCl$_3$) δ 2.5 (s, 3 H, ArCH$_3$), 3.3 (s, 3 H, OCH$_3$), 3.5–4.2 (m, 5 H,CH$_2$OCH$_2$CHOCH$_3$), 4.9 (m, 1 H, CHOTs), 7.4 (d, $J = 8$ Hz, 2 H, ArH$_3$ and H$_5$), 7.8 (d, $J = 8$ Hz, 2 H, ArH$_4$ and H$_6$).

To a solution of crude tosylate in THF (10 ml) was added a 1.0 M solution of lithium triethylborohydride in THF (5 ml). The mixture was stirred at 25°C for 12 h. The precipitated solids were filtered off and the filtrate was fractionated at atmospheric pressure. The fraction distilling at 98°C was found to be pure (S)-3-methoxytetrahydrofuran **17**: yield 0.25 g (50%). $[\alpha]_D$ + 15.4° (c, 6.0, THF), ^{1}H-NMR (CCl$_4$) δ 1.7–2.3 (m, 2 H,OCH$_2$CH$_2$), 3.3 (s, 3 H, OCH$_3$), 3.7–4.2 (m, 5 H,OCHCH$_2$OCH$_2$).

4.11. Methylation of commercial (S)-(+)-3-hydroxytetrahydrofuran

To a slurry of NaH (from 0.45 g, 10 mmol of 60% NaH emulsion) in ether (15 ml), (S)-(+)-3-hydroxy-tetrahydrofuran of 95% optical purity (1 g, 11.4 mmol) in ether (5 ml) was added at such a rate that the ether was refluxing gently. The mixture was stirred at 25°C for 1 h. Methyl iodide (1.7 g, 12 mmol) added to the mixture and stirred at 25°C for 24 h. The ether solution was filtered and the filtrate was distilled. The fraction distilling between 100–105° was found to be pure (S)-(+)-3-hydroxytetrahydrofuran **17**: Yield 1.0 g (90%); $[\alpha]_D$ + 25.9° (c, 4.5, THF).

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