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Synthesis and X-ray structures of (biphenoxide)Ti species: four and five coordinate complexes that crystallize as mixtures of diastereomers

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This paper is dedicated to Professor Pascual Royo on the occasion of his 65th birthday

Abstract

A set of novel Ti(IV) crystal structures are described, where two diastereomers prefer to crystallize together in a 1:1 ratio in the unit cell. The achiral ligand 4,4′,6,6′-tetra-*tert*-butyl-2,2′-biphenol (**1**) reacted with chiral Ti(IV) complexes of the type Ti(O*i*-Pr)$_2$(OR*)$_2$ to give (biphenoxide)Ti(OR*)$_2$ [OR* = mentholate (**4a**) or borneolate (**4b**)] as a mixture of diastereomers (**4a** and **4a**′, **4b** and **4b**′), in which the bis(phenoxide) ligand has the *R* and *S* configuration. An attempt to separate diastereomers **4a** and **4a**′ by crystallization resulted in a 1:1 mixture of these compounds in the unit cell. Diastereomers of **4a** and **4b** crystallized in the presence of CH_3CN to give five coordinate trigonal bipyramidal complexes (biphenoxide)Ti(OR*)$_2$(NCCH$_3$) (**5a**, **5a**′, **5b**, **5b**′). Compounds **5a** and **5a**′, and **5b** and **5b**′ again crystallized as a 1:1 mixture of diastereomers.

Keywords: Menthol; Borneol; Biphenol; Axial chirality; Diastereomeric structures

1. Introduction

The traditional approach to asymmetric catalysis involves the synthesis of enantiopure ligands that are then attached to metals and screened in reactions to test their enantioselectivities and activities [1–3]. A severe impediment to this technique is that it often requires the synthesis of many enantiopure ligands before an acceptable catalyst can be found. The synthesis of such ligands is usually labor intensive and the limiting step in optimization of asymmetric processes [4]. Another approach to asymmetric catalysis that holds great promise is the optimization of chiral catalysts with a single chiral ligand (L*) and a series of achiral ligands (L_1–L_x) [5–9]. Thus, one can synthesize many chiral catalysts from a single chiral ligand [M(L*)L_1–M(L*)L_x] and expedite the optimization of asymmetric processes. Our interest has been in using achiral and *meso*-ligands that have low energy chiral conformations. The idea is that these achiral and *meso*-ligands bind to a metal bearing a chiral ligand and preferentially adopt a chiral conformation. If they behave in this manner, the achiral ligand in the chiral conformation will form an integral part of the chiral environment of the catalyst.

In our initial investigations [8,9], we chose to use achiral and *meso*-ligands that were expected to have a low barrier to interconversion of the enantiomeric conformations when bound to a metal center. This choice was made to avoid the generation of diastereomeric catalysts that do not interconvert readily under the reaction conditions and would promote the reaction with different enantioselectivities and activities [10].

It has also been demonstrated by Gagné and coworkers [11] that reaction of a chiral metal complex with an achiral ligand that binds in chiral conformations can proceed with high diastereoselectivity. In their case, the barrier to interconversion of the resulting diastereomers was high. After the diastereomers were separated, the chiral ligand was displaced from the metal leaving the metal center with an achiral ligand locked in a chiral conformation (with excellent enantiomeric excess). This

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complex was then used as a catalyst in an asymmetric reaction and was found to be highly enantioselective.

We were interested in a similar approach employing biphenol ligands and chiral titanium alkoxides to generate (biphenoxide)Ti(OR*)$_2$ complexes. We imagined that the stereochemistry of the biphenoxide ligand would be set on its reaction with the chiral alkoxide complex. Similar strategies have been successfully employed by others using BINOL as the chiral ligand, however, [12] the structure of these catalysts are unknown. Our idea was to start from chiral titanium alkoxide complexes, Ti(OR*)$_2$(O*i*-Pr)$_2$, derived from inexpensive, readily available resolved alcohols. These would be treated with achiral biphenols in a reaction that we hoped would be diastereoselective. Separation of the diastereomers by crystallization was envisaged to provide a (biphenoxide)Ti species that would behave like a (BINOLate)Ti derivative and could be used in asymmetric catalysis [13]. However, this idea was thwarted by a rare and interesting property of the (biphenoxide)Ti-moiety. The compounds of the type (biphenoxide)Ti(OR*)$_2$ and (biphenoxide)Ti(OR*)$_2$(NCCH$_3$) that we examined crystallize as a 1:1 mixture of two diastereomers. We report here the synthesis and structures of these unusual compounds, all of which contain two diastereomers in the unit cell.

2. Results and discussion

The achiral biphenol ligand that we employed in this study is 4,4′,6,6′-tetra-*tert*-butyl-2,2′-biphenol (**1**, Fig. 1). Reaction of this achiral biphenol with titanium tetraisopropoxide will give a racemic mixture of the enantiomeric biphenoxide complexes (Fig. 2). We envisioned that the barrier to racemization of the titanium biphenoxide complexes would be high, because racemization would likely involve either a strained transition state or cleavage of one of the strong Ti–O bonds of the biphenoxide ligand. Reaction of **1** with a chiral titanium alkoxide complex, Ti(OR*)$_2$(O*i*-Pr)$_2$, could give two diastereomers.

The chiral alkoxide ligands chosen for this study were [(1*S*)-*endo*]-(−)-borneol **2a** and (1*R*,2*S*,5*R*)-(−)-menthol **2b** (Fig. 1). Borneol and menthol can be bought in bulk for ca. \$0.25 g^{-1}. The chiral titanium alkoxide precursors were prepared by reaction of titanium tetraisopropoxide with two equivalents of R*OH with the hopes of generating Ti(OR*)$_2$(O*i*-Pr)$_2$. Borneol or menthol (two equivalents) was combined with titanium tetraisopropoxide and stirred under vacuum to remove the liberated isopropanol and provide **3a** and **3b**, respectively (Scheme 1). The 500 MHz ^{1}H-NMR spectra of **3a** and **3b** show a 1:1 ratio of isopropoxy ligands to chiral alkoxide ligands, but the ^{13}C{^{1}H}-NMR spectra reveal that these compounds exist as mixtures of titanium complexes Ti(O*i*-Pr)$_n$(OR*)$_{4-n}$. Rather than attempting to purify these mixtures, they were generated and used without isolation. Addition of biphenol **1** to the mixture containing **3a** or **3b** and removal of the isopropanol under reduced pressure resulted in the formation of the borneolate derivative **4a** and the mentholate adduct **4b** (Scheme 1).

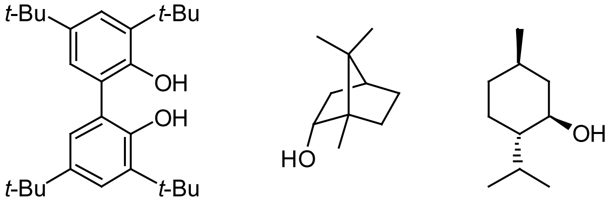


Fig. 1. Structures of ligands **1**, **2a**, and **2b**.

Analysis of the crude 500 MHz ^{1}H-NMR spectrum of **4a** indicated it was a 1:1 mixture of diastereomers, in which the bis(phenoxide) ligand has the *R* and *S* configuration. The ^{1}H-NMR spectrum of these diastereomers, **4a** and **4a′**, are identical except for one set of non-overlapping methyl resonances. The diastereomeric ratio was determined by integration of these methyl resonances (0.66 ppm for one diastereomer and 0.87 ppm for the other). The 125 MHz ^{13}C{^{1}H}-NMR spectrum also indicated that diastereomers **4a** and **4a′** have very similar spectra. Only a single set of six aromatic carbon peaks of the 1:1 mixture of diastereomers was observed in the ^{13}C{^{1}H}-NMR spectrum. Four of the aliphatic carbon resonances of the alkoxides appeared as separate peaks for the two diastereomers **4a** and **4a′** with the maximum difference in chemical shifts being 0.2 ppm. One of these resonances belongs to the alkoxide carbon of the borneolate ligand.

The ^{1}H- and ^{13}C{^{1}H}-NMR spectra of **4b** are analogous to that of **4a**. Like **4a** and **4a′**, **4b** were also formed as a mixture of diastereomers (**4b** and **4b′**). Determination of the ratio of diastereomers **4b** and **4b′** was more difficult, however, because all the resonances of the diastereomers are overlapping in the 500 MHz ^{1}H-NMR spectrum. In the ^{13}C{^{1}H}-NMR spectrum of **4b** and **4b′**, three of the aliphatic peaks from the mentholate ligands have slightly different chemical shifts. These peaks have equal intensity and indicate a ca. 1:1 ratio of diastereomers.

Despite the low diastereoselectivities in the syntheses in Scheme 1, we hoped to separate the diastereomers by crystallization. Thus, a saturated solution of **4a** in dichloromethane was cooled to −35 °C and orange X-ray quality crystals formed and were isolated by filtration in 71% yield. The structure was somewhat of a surprise, however, instead of isolating one of the two diastereomers by crystallization, the crystal that formed contained a 1:1 mixture of diastereomers **4a** and **4a′**

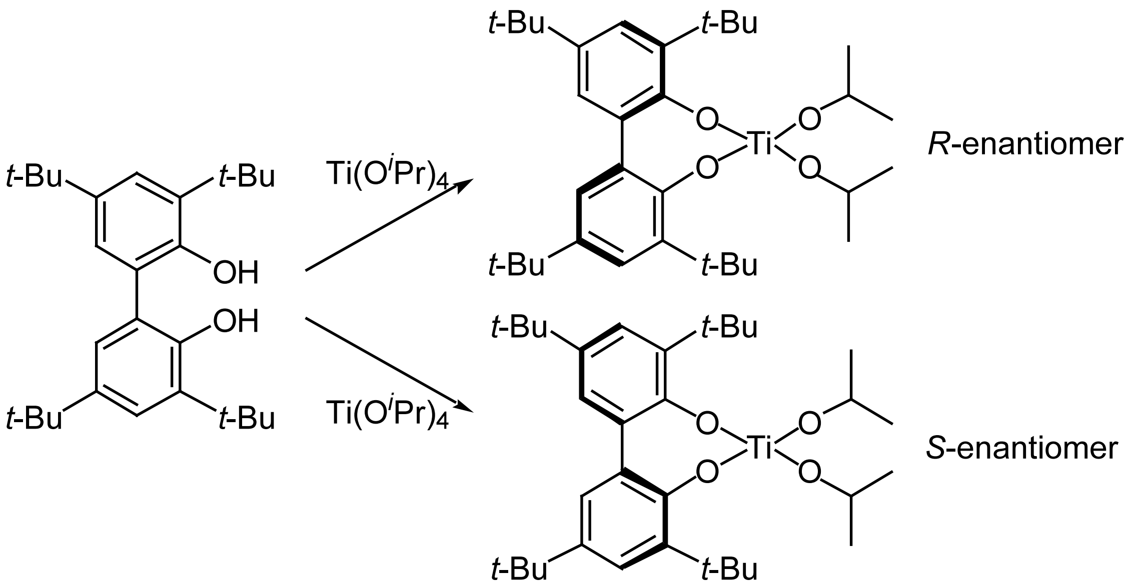
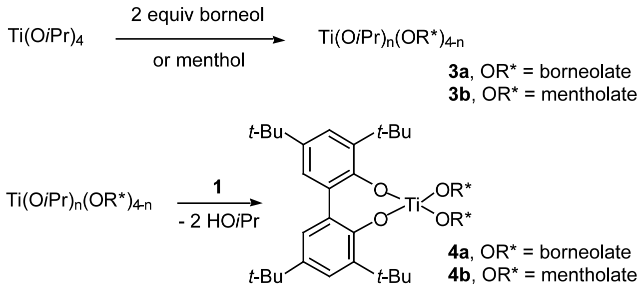


Fig. 2. Reaction of **1** with titanium tetraisopropoxide.



Scheme 1.

(Fig. 3) with three molecules of dichloromethane per titanium complex. This mixture was recrystallized under different conditions (CH_2Cl_2:hexanes, 1:1, −35 °C), and the unit cell of the crystal was identical indicating that the crystal contained both diastereomers. As seen in Fig. 3, the diastereomers **4a** and **4a**′ differ in the configuration of the bis(phenoxide) group. The bond distances and bond angles are listed in Table 1, and the data collection parameters are listed in Table 3. The unit cell contained three molecules of CH_2Cl_2. Both diastereomers are monomeric and ca. C_2-symmetric, with titanium in a distorted tetrahedral environment. The dihedral angle between the two biphenol rings is 53.0° in the (*R*)-diastereomer, and 52.0° in the (*S*)-diastereomer. The titanium phenoxide Ti–O distances in **4a** and **4a**′ range from 1.823 to 1.841 Å, and are longer than the alkoxide Ti–O distances, which are between 1.746 and 1.760 Å. These bond distances fall within the expected range for titanium alkoxides and phenoxides, [14] and are similar to those found for $[(BINOLate)Ti(O\textit{i}\text{-}Pr)_2]_3$ [9].

In an attempt to separate the diastereomers **4a** and **4a**′, we performed the recrystallization in the presence of CH_3CN. We envisioned that crystallization using CH_3CN might produce five coordinate titanium complexes with bound CH_3CN ligands. These five coordinate diastereomers might have different solubility properties and therefore, be separable by crystallization. Recrystallization of the 1:1 ratio of diastereomers **4a** and **4a**′ was performed by dissolving the diastereomers in a mixture of CH_2Cl_2 and CH_3CN and cooling to −35 °C. X-ray quality crystals of the CH_3CN adduct, **5a**, grew under these conditions. The structure determination was performed at low temperature. However, this structure also contained a 1:1 mixture of diastereomers (Fig. 4).

We then proceeded to recrystallize the menthol derived **4b** and **4b**′ from a mixture of CH_2Cl_2 and CH_3CN. This yielded crystals of the expected CH_3CN adduct, but yet again the structure consisted of a 1:1 mixture of diastereomers with one molecule of dichloromethane per titanium complex (**5b** and **5b**′, Fig. 5).

Both sets of diastereomers, **5a**, **5a**′, **5b** and **5b**′, are monomeric in the solid state, and the central titanium is in a distorted trigonal bipyramidal environment. Selected bond distances and bond angles are given in Table 2, and are very similar for the four complexes. In each case, the apical positions are occupied by the CH_3CN ligand and one oxygen of the biphenol. The dihedral angle between the biphenol rings of **5a** and **5a**′ are 55.3° in the (*R*)-diastereomer and 56.2° in the (*S*)-diastereomer, and for **5b** and **5b**′ the (*R*)-diastereomer and the (*S*)-diastereomers have dihedral angles of 59.1 and 60.4°. The titanium phenoxide Ti–O distances range from 1.837 to 1.888 Å, and are longer than the alkoxide Ti–O distances, which range from 1.759 to 1.788 Å. The Ti–N bond distances range from 2.342 to 2.387 Å, with Ti–N–C bond angles from 167.2 to 175.8°.

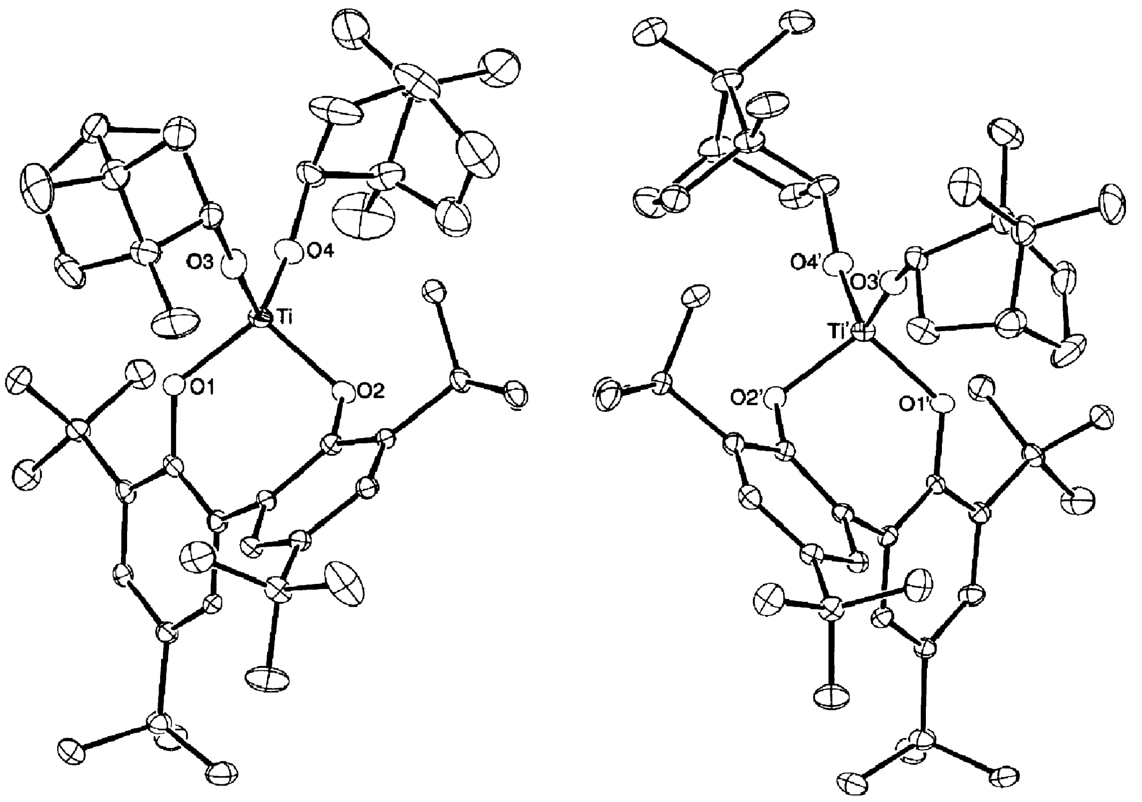


Fig. 3. ORTEP drawing of **4a** and **4a′**. Ellipsoids are at the 20% probability level. Selected bond distances and bond angles are listed in Table 1.

Table 1
Selected bond lengths (Å) and bond angles (°) for **4a** and **4a′**

	4a	**4a′**
Bond lengths		
Ti–O1	1.823(3)	1.833(3)
Ti–O2	1.833(3)	1.841(3)
Ti–O3	1.746(2)	1.747(3)
Ti–O4	1.757(2)	1.760(3)
Bond angles		
O1–Ti–O2	100.97(11)	100.43(11)
O1–Ti–O3	108.51(12)	108.32(13)
O1–Ti–O4	112.94(13)	113.08(13)
O2–Ti–O3	112.73(13)	114.67(13)
O2–Ti–O4	107.09(13)	107.91(12)
O3–Ti–O4	113.93(12)	111.98(14)
Ti–O1–C	130.1(2)	130.5(2)
Ti–O2–C	112.9(2)	113.5(2)
Ti–O3–C	168.5(2)	175.3(3)
Ti–O4–C	156.4(2)	153.4(3)

Table 2
Selected bond lengths (Å) and bond angles (°) for **5a**, **5a′**, **5b** and **5b′**

	5a	**5a′**	**5b**	**5b′**
Bond lengths				
Ti–O1	1.839(3)	1.848(3)	1.849(4)	1.837(4)
Ti–O2	1.888(3)	1.871(3)	1.877(3)	1.882(3)
Ti–O3	1.781(3)	1.779(3)	1.759(4)	1.780(4)
Ti–O4	1.773(3)	1.784(3)	1.771(3)	1.788(3)
Ti–N1	2.387(4)	2.372(4)	2.342(5)	2.348(5)
Bond angles				
O1–Ti–O2	91.74(11)	93.18(11)	93.6(2)	94.65(14)
O1–Ti–O3	116.17(14)	115.44(13)	113.9(2)	113.6(2)
O1–Ti–O4	123.04(14)	121.98(14)	122.3(2)	121.8(2)
O2–Ti–O3	102.17(12)	103.49(13)	101.3(2)	102.6(2)
O2–Ti–O4	95.89(13)	95.83(13)	94.7(2)	97.3(2)
O3–Ti–O4	116.99(14)	117.65(14)	120.0(2)	118.7(2)
N1–Ti–O1	81.76(12)	82.08(12)	80.9(2)	81.1(2)
N1–Ti–O2	172.07(11)	173.58(12)	173.8(2)	174.7(2)
N1–Ti–O3	84.85(13)	82.52(13)	83.8(2)	82.0(2)
N1–Ti–O4	83.99(14)	83.14(14)	85.8(2)	82.5(2)
Ti–O1–C	133.7(2)	132.2(2)	134.0(3)	132.1(3)
Ti–O2–C	117.0(2)	119.9(2)	113.9(3)	115.2(3)
Ti–O3–C	146.2(3)	141.3(3)	156.4(3)	144.2(3)
Ti–O4–C	174.0(3)	139.9(3)	156.2(4)	148.6(3)
Ti–N1–C	167.2(3)	172.6(3)	175.8(5)	171.5(5)

It is interesting to note that the titanium centers in the sets of diastereomers **5a** and **5a′**, as well as **5b** and **5b′**, are stereogenic centers as a result of the trigonal bipyramidal geometry of the titanium center. The configuration at the titanium center can be scrambled by pseudo rotation, dissociation of acetonitrile to give one of the diastereomers **4a** and **4a′** or **4b** and **4b′**, or association of an acetonitrile to give an octahedral intermediate that can then loose the original acetonitrile.

We have demonstrated that this family of biphenoxide compounds preferentially crystallizes as a mixture of diastereomers. This behavior appears to be indepen-

Table 3
Crystallographic data and collection parameters

	4a and **4a**′	**5a** and **5a**′	**5b** and **5b**′
Empirical formula	$TiC_{51}H_{80}O_4Cl_6$	$TiC_{50}H_{77}NO_4$	$TiC_{51}H_{83}NO_4Cl_2$
Formula weight	1017.75	804.03	892.98
Crystal class	Monoclinic	Monoclinic	Triclinic
Space group	$P2_1$ (#4)	$P2_1$ (#4)	$P\bar{1}$ (#1)
Temperature (K)	120	180	200
Z	4	4	2
a (Å)	19.8926(1)	13.3080(2)	12.3385(3)
b (Å)	13.1375(1)	23.0791(6)	20.0888(7)
c (Å)	20.2330(1)	15.9441(3)	11.1495(3)
α (°)	90	90	90.932(2)
β (°)	107.960(1)	106.486(1)	105.473(2)
γ (°)	90	90	80.841(2)
V (Å^3)	5030.01(5)	4695.7(2)	2628.46(13)
μ (cm^{-1})	5.32	2.24	3.05
D_{calc} (g cm^{-1})	1.344	1.137	1.128
λ (Å)	0.71069	0.71069	0.71069
R_1 [a] (%)	5.73	5.87	6.01
wR_2 [b] (%)	13.98	15.12	15.10

[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$.

[b] $wR_2 = [\Sigma\ w(F_o^2 - F_c^2)^2/\Sigma\ w(F_o^2)^2]^{1/2}$.

dent of metal center geometry, as crystals containing a mixture of diastereomers were formed for both four and five coordinate titanium centers. The origin of this rare behavior, however, is not clear. It appears that the biphenoxide ligand controls the crystallization process and that the chiral alkoxide ligands have little impact on crystal formation. We believe that co-crystallization of diastereomers is rare [15,16], however, there is no simple method for searching the literature or crystallographic data bases for such occurrences. Certainly, fractional crystallization is a common method of separating mixtures of compounds and is expected to be more likely than co-crystallization.

In summary, a study initially designed to investigate the use of chiral biphenol ligands in asymmetric catalysis has led to a set of novel Ti(IV) crystal structures, where two diastereomers prefer to crystallize together in a 1:1 ratio in the unit cell. We remain optimistic that the axially chiral conformations of achiral biphenol ligands can be of use in asymmetric catalysis, and continue to investigate their properties.

3. Experimental

3.1. General

All manipulations involving titanium alkoxides were carried out under an inert atmosphere in a Vacuum Atmospheres drybox with attached MO-40 Dritrain, or by using standard Schlenk or vacuum line techniques. ^{1}H-NMR spectra were obtained on a Bruker 500 MHz Fourier transform NMR spectrometer at the University of Pennsylvania NMR facility. Chemical shifts are reported in units of parts per million downfield from tetramethylsilane and all coupling constants are reported in Hz. ^{13}C{^{1}H}-NMR spectra were obtained at 125 MHz on the 500 MHz instrument, and chemical shifts were recorded relative to the solvent resonance. Unless otherwise specified, all reagents were purchased from Aldrich Chemical Co. and used without further purification. Titanium tetraisopropoxide was distilled under vacuum and stored in a glass vessel sealed with Teflon stopper. Hexanes (UV grade, alkene free), dichloromethane, and CH_3CN were dried using alumina

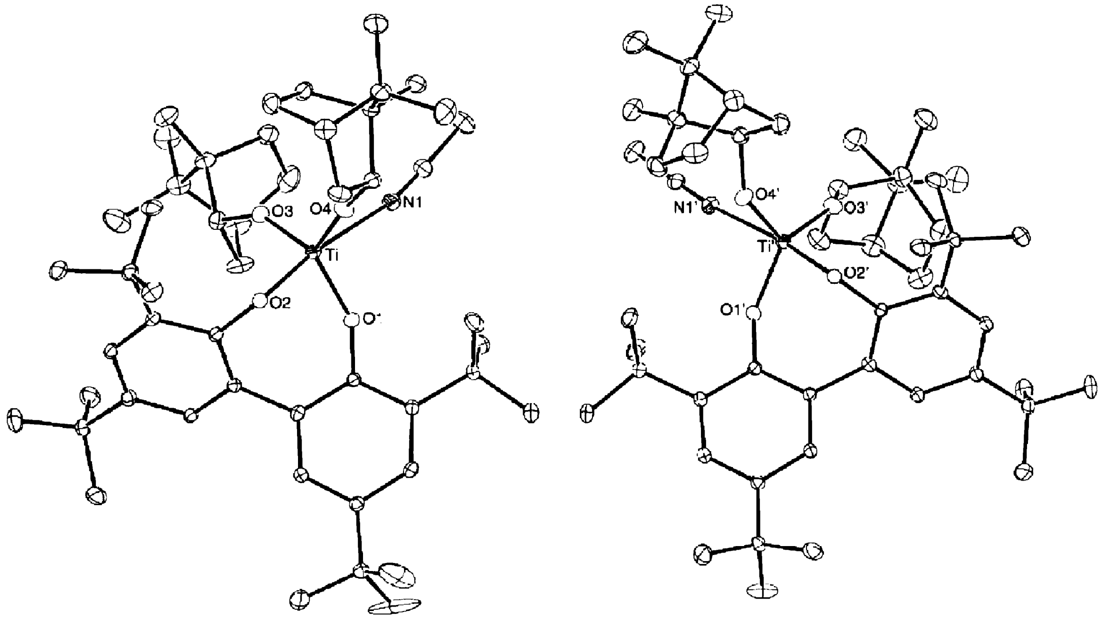


Fig. 4. ORTEP drawing of **5a** and **5a**′. Ellipsoids are at the 20% probability level. Selected bond distances and bond angles are listed in Table 2.

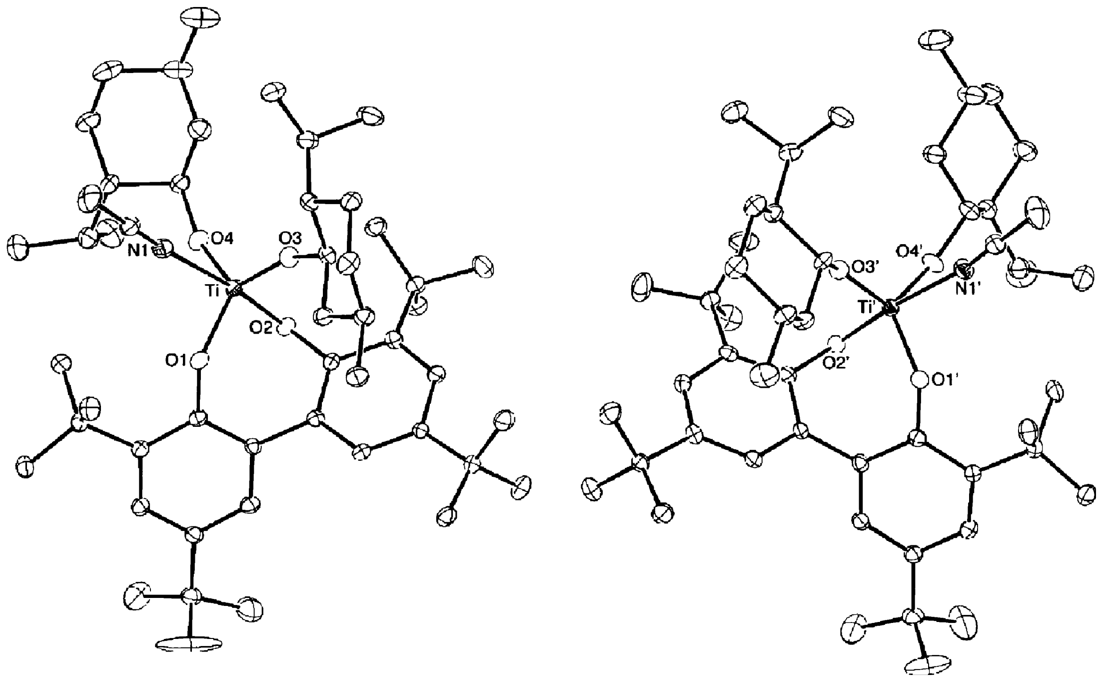


Fig. 5. ORTEP drawing of **5b** and **5b**′. Ellipsoids are at the 20% probability level. Selected bond distances and bond angles are listed in Table 2.

columns under nitrogen. $CDCl_3$ was dried over calcium hydride and vacuum transferred.

3.2. Preparation of *3a*

(1*S*)-*endo*-Borneol (309 mg, 2.00 mmol) was dissolved in 5 ml of dichloromethane, and titanium isopropoxide (284 mg, 1.00 mmol) was added. The reaction was allowed to stir for 15 min at room temperature (r.t.), and then was subjected to high vacuum for 4 h to remove two equivalents of isopropanol and give **3a** in 100% yield. The ^{1}H-NMR shows a 1:1 ratio of isopropoxy ligands to borneolate ligands, but the $^{13}C\{^1H\}$-NMR reveals that **3a** exists as a mixture of compounds $Ti(O\textit{i}\text{-}Pr)_n(OR^*)_{4-n}$. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 0.84 (s, 6H), 0.85 (s, 6H), 0.90 (s, 6H), 1.1–1.3 (m, 6H), 1.26 (d, $J = 6.1$ Hz, 12H), 1.61 (m, 2H), 1.70 (m, 2H), 2.10 (m, 2H), 2.29 (m, 2H), 4.52 (septet, $J = 6.1$ Hz, 2H), 4.6–4.7 (m, 2H) ppm.

3.3. Preparation of *3b*

Compound **3b** was prepared using (1*R*,2*S*,5*R*)-(−)-menthol in the same procedure as **3a**. The ^{1}H-NMR shows a 1:1 ratio of isopropoxy ligands to mentholate ligands, but the $^{13}C\{^1H\}$-NMR reveals that **3b** exists as a mixture of compounds $Ti(O\textit{i}\text{-}Pr)_n(OR^*)_{4-n}$. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 0.8–1.0 (m, 8H), 0.92 (d, $J = 6.5$ Hz, 12H), 1.0–1.2 (m, 6H), 1.25 (d, $J = 6.0$ Hz, 12H), 1.40 (m, 2H), 1.56 (m, 2H), 1.62 (m, 2H), 2.12 (m, 2H), 2.38 (m, 2H), 3.90 (m, 2H), 4.50 (septet, $J = 6.0$ Hz, 12H) ppm.

3.4. Preparation of diastereomers *4a* and *4a*′

(1*S*)-*endo*-Borneol (309 mg, 2.00 mmol) was dissolved in 5 ml of dichloromethane and titanium isopropoxide (284 mg, 1.00 mmol) was added. The reaction was allowed to stir for 15 min, and then was subjected to high vacuum for 4 h to remove two equivalents of isopropanol. 3,3′,5,5′-*t*-butyl-2,2′-biphenol (411 mg, 1.00 mmol) was then added, and the resulting mixture was stirred at r.t. for 30 min. The volatile materials were removed under reduced pressure. The remaining solid was redissolved in 5 ml of dichloromethane, and the volatile materials were again removed under reduced pressure. This process of redissolving the reaction mixture and then removal of volatile materials was repeated three more times, after which the product was left under vacuum for 2 h. Recrystallization of the resulting solid by dissolving it in a minimal amount of dichloromethane and cooling to −35 °C yielded X-ray quality orange crystals of diastereomers **4a** and **4a**′. The yield was 71% (542 mg, 0.71 mmol). ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 0.66 (b, 3H), 0.76 (s, 6H), 0.79 (s, 6H), 0.87 (b, 3H), 1.1–1.2 (m, 4H), 1.32 (s, 18H), 1.46 (s, 18H), 1.5–1.7 (m, 4H), 1.9–2.1 (m, 4H), 2.2–2.3 (m, 2H), 4.56 (m, 2H), 7.12 (d, $J = 2.5$ Hz, 2H), 7.39 (d, $J = 2.5$ Hz, 2H) ppm; $^{13}C\{^1H\}$-NMR ($CDCl_3$, 125 MHz) δ 13.3, 13.6, 18.7, 20.2, 26.5, 28.0, 28.2, 30.5, 31.7, 34.5, 35.5, 39.4, 40.5, 45.1, 45.2, 47.6, 51.4, 93.8, 94.0, 123.8, 127.9, 129.1, 136.3, 143.7, 154.7 ppm; IR (CH_2Cl_2) 3943, 3054, 2957, 2872, 2305, 1422, 1390, 1264, 1112, 1069, 895, 854, 738 cm^{-1}.

3.5. Preparation of diastereomers **4b** and **4b′**

Diastereomers **4b** and **4b′** were prepared using menthol in the same procedure as **4a**. The solid was dissolved in a minimal amount of CH_2Cl_2 and recrystallized by cooling to −35 °C to give orange crystals of **4b** and **4b′** in 66% yield. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 0.6–1.1 (m, 26H), 1.33 (s, 18H), 1.46 (s, 18H), 1.5–1.6 (m, 6H), 1.8–2.1 (m, 2H), 2.24 (b, 2H), 3.98 (m, 2H), 7.10 (d, $J = 2.5$ Hz, 2H), 7.37 (d, $J = 2.5$ Hz, 2H) ppm; $^{13}C\{^1H\}$-NMR ($CDCl_3$, 125 MHz) δ 15.7, 21.2, 22.2, 22.6, 25.8, 30.6, 31.6, 31.7, 34.4, 34.5, 35.5, 45.5, 45.9, 50.8, 51.2, 87.8 (b), 123.6, 128.1, 128.8, 135.8, 143.3, 155.0 ppm; IR (CH_2Cl_2) 4194, 3942, 3528, 3052, 2957, 2684, 2305, 1780, 1592, 1550, 1458, 1423, 1401, 1362, 1265, 1096, 997, 927, 895, 855, 796, 740, 677, 584 cm^{-1}.

3.6. Preparation of diastereomers **5a** and **5a′**

Diastereomers **5a** and **5a′** were prepared using the same procedure as **4a**. Diastereomers **5a** and **5a′** were crystallized by dissolving the solid in a minimal amount of CH_2Cl_2 followed by addition of 1 ml of CH_3CN. Cooling to −35 °C gave X-ray quality orange crystals of **5a** and **5a′** in 63% yield. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 0.65 (b, 3H), 0.76 (s, 6H), 0.79 (s, 6H), 0.87 (b, 3H), 1.0–1.2 (m, 4H), 1.32 (s, 18H), 1.45 (s, 18H), 1.5–1.7 (m, 4H), 1.9–2.1 (m, 4H), 1.99 (s, 3H), 2.2–2.3 (m, 2H), 4.55 (m, 2H), 7.11 (d, $J = 2.5$ Hz, 2H), 7.38 (d, $J = 2.5$ Hz, 2H) ppm; $^{13}C\{^1H\}$-NMR ($CDCl_3$, 125 MHz) δ 1.8, 13.3, 13.5, 18.7, 20.2, 26.5, 28.0, 28.2, 30.5, 30.7, 31.6, 34.5, 35.5, 39.4, 40.4, 45.1, 45.2, 47.6, 51.3, 93.8, 94.0, 123.8, 127.9, 129.0, 136.3, 143.6, 154.7 ppm; IR (CH_2Cl_2) 3054, 2960, 2958, 2305, 1422, 1265, 1113, 1091, 1069, 1036, 896, 750, 740 cm^{-1}.

3.7. Preparation of diastereomers **5b** and **5b′**

Diastereomers **5b** and **5b′** were prepared using the same procedure as **4b**. Diastereomers **5b** and **5b′** were crystallized by dissolving the solid in a minimal amount of CH_2Cl_2 followed by addition of 1 ml of CH_3CN. Cooling to −35 °C gave X-ray quality orange crystals of **5b** and **5b′** in 54% yield. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 0.6–1.0 (m, 26H), 1.32 (s, 18H), 1.45 (s, 18H), 1.5–1.6 (m, 6H), 1.9–2.1 (m, 2H), 1.99 (s, 3H), 2.24 (b, 2H), 3.97 (m, 2H), 7.09 (d, $J = 2.5$ Hz, 2H), 7.36 (d, $J = 2.5$ Hz, 2H) ppm; $^{13}C\{^1H\}$-NMR ($CDCl_3$, 125 MHz) δ 1.8, 15.7, 21.2, 22.2, 22.6, 25.8, 29.7, 30.6, 31.6, 31.7, 34.4, 34.5, 35.5, 45.9 (b), 50.8 (b), 87.8 (b), 123.5, 128.1, 128.7, 135.8, 143.3, 155.0 ppm; IR (CH_2Cl_2) 2870, 2305, 1422, 1402, 1389, 1362, 1260, 1157, 1108, 1098, 1067, 1046, 997, 927, 855, 705 cm^{-1}.

3.8. X-ray crystallographic procedures

A representative procedure for the structure determinations is provided. Air-sensitive crystals of **5a** were grown as described above. Crystals were isolated from the mother liquor and immediately immersed in paratone under a nitrogen atmosphere in a drybox. A crystal was selected for the X-ray diffraction study and mounted in paratone on a quartz fiber and rapidly placed in a nitrogen gas cold stream of the cryostat system at 180 K. Compound **5a** crystallizes in the Monoclinic space group $P2_1$ (systematic absences $0k0$: $k = \text{odd}$) with $a = 13.3080(2)$ Å, $b = 23.0791(6)$ Å, $c = 15.9441(3)$ Å, $\beta = 106.486(1)°$, $V = 4695.7(2)$ Å^3, $Z = 4$ and $D_{calc} = 1.137$ g cm^{-3}. X-ray intensity data were collected on an Rigaku R-AXIS IIc area detector employing graphite-monochromated Mo–K$_\alpha$ radiation ($\lambda = 0.71069$ Å). Indexing was performed from a series of 1° oscillation images with exposures of 50 s per frame. A hemisphere of data was collected using 5° oscillation angles with exposures of 300 s per frame and a crystal-to-detector distance of 82 mm. Oscillation images were processed using bioteX producing a listing of unaveraged F^2 and $\sigma(F^2)$ values which were then passed to the TEXSAN program package for further processing and structure solution on a Silicon Graphics Indigo R4000 computer. A total of 31956 reflections were measured over the ranges $5.02 \le 2\theta \le 50.7°$, $-16 \le h \le 15$, $-27 \le k \le 26$, $-18 \le l \le 18$ yielding 15 015 unique reflections ($R_{int} = 0.0634$). The intensity data were corrected for Lorentz and polarization effects but not for absorption.

The structure was solved by direct methods (SIR-92). Refinement was by full-matrix least-squares based on F^2 using SHELXL-93. All reflections were used during refinement (F^2's that were experimentally negative were replaced by $F^2 = 0$). The weighting scheme used was $w = 1/[\sigma^2(F_o^2) + 0.0808P^2 + 3.7084P]$ where $P = (F_o^2 + 2F_c^2)/3$. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using a 'riding' model. Refinement converged to $R_1 = 0.0587$ and $wR_2 = 0.1512$ for 14 043 reflections for which $F > 4\sigma(F)$ and $R_1 = 0.0634$, $wR_2 = 0.1567$ and GOF = 1.058 for all 15 015 unique, non-zero reflections and 1047 variables, The maximum Δ/σ in the final cycle of least-squares was −0.012 and the two most prominent peaks in the final difference Fourier were +0.409 and −0.343 e Å^{-3}.

4. Supplementary Material

Crystallographic data for the structural analysis has been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 184157, 184158, and 184159 for compounds **4a** and **4a′**, **5b** and **5b′**, and **5a** and **5a′**, respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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