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Tetrahedron: *Asymmetry* 19 (2008) 543–548

Tetrahedron: *Asymmetry*

# Synthesis and optical activity analysis of chiral titanium(IV) *sec*-butoxide and its group IV analogues

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Received 4 September 2007; accepted 4 February 2008

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**Abstract**—The complete series of chiral group IV *sec*-butoxides has been obtained by the treatment of $M(NMe_2)_4$ ($M = Ti, Zr, Hf$) with resolved (*R*)-(−)- or (*S*)-(+)-2-butanol. These complexes were analyzed by polarimetry, revealing a decreasing trend in molar rotation down the group, from titanium to hafnium. Catalysis screenings showed that the resolved titanium *sec*-butoxides, in conjunction with the resolved BINOL (BINOL = 1,1′-bi-2-naphthol) of the opposite configuration designation, catalyzed the addition of dimethyl zinc to benzaldehyde with higher enanteoselectivity than that observed for resolved BINOL with titanium(IV) isopropoxide or with the titanium(IV) *sec*-butoxide of the same configuration designation.

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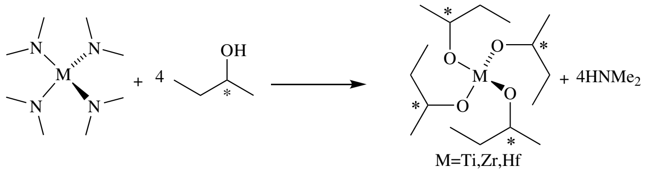
## 1. Introduction

Group IV alkoxides are a topic of continued interest with respect to their structure and varied chemistry.[1–5] These compounds act as important precursors in metal oxide materials; high dielectric constant hafnium materials will soon be used in sub-100 nm computer chip technology.[5] Group IV alkoxides, most notably $Ti(O^iPr)_4$, also serve as catalysts in numerous organic transformations. As growth in the pharmaceutical and chemical industries has increased the demand for the production of enantiomerically pure products, strategies employing chiral intermediates have been developed to carry out enantioselective syntheses with high stereoselectivity.[6–9] Increased enantiomeric excess has been observed when bulky or coordinating groups are added to chiral ligand frameworks, necessitating multi-step organic ligand synthesis prior to metal coordination and catalyst screening. In the stereoselective addition of alkyl groups to aromatic aldehydes, strategies include the use of chelating chiral auxiliary ligands, such as amino alcohols,[10,11] BINOL,[12–14] TADDOL,[15,16] Salan,[17] N-sulfonylated amino alcohols,[18,19] and bis(sulfonamide)[20,21] to afford high enantiomeric excess. Employing simple *terminal* chiral alkoxides is an alternative approach.[12,21–24] Herein, we report the synthesis and characterization of the previously unreported complete series of chiral group IV *sec*-butoxides, $M(O^2Bu)_4$ ($M = Ti, Zr, Hf$), and the results of the stereoselective addition of dimethyl zinc to benzaldehyde, mediated by the resolved $Ti(O^2Bu)_4$ species.

## 2. Results and discussion

### 2.1. Synthesis

Alcoholysis of tetrakis(dimethylamido)titanium with an excess (6 equiv) of (*R*)-(−)- or (*S*)-(+)-2-butanol in benzene, followed by vacuum distillation, provided the chiral titanium(IV) alkoxides, $Ti(O^{R\text{-}2}Bu)_4$ and $Ti(O^{S\text{-}2}Bu)_4$, as colorless liquids in high yield (Scheme 1). The procedure for the synthesis of the zirconium and hafnium complexes was similar; the treatment of tetrakis(dimethylamido)zirconium and hafnium with a stoichiometric amount of (*R*)-(−)- or (*S*)-(+)-2-butanol in benzene, followed by a high temperature vacuum distillation, gave the corresponding chiral



**Scheme 1.** Synthesis of resolved group IV *sec*-butoxides ($M = Ti, Zr, Hf$).

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doi:10.1016/j.tetasy.2008.02.008

zirconium(IV) and hafnium(IV) alkoxides as colorless, viscous oils.

## 2.2. Optical activity analysis

Optical activity analyses were performed for each of the alkoxides synthesized. Both the specific rotation (α) and molar rotation (*Φ*) were determined (Table 1), and were found to decrease down the group, from titanium to hafnium. Although not a complete series, a similar trend was found for the group 10 complexes [(1*R*,1′*R*)-2,6-bis-[1-(diphenylphosphino)ethyl]phenyl]chloro-platinum and -palladium, with specific rotations of −297.8 and −323.6, respectively.[25] To date, no other complete series of homologues of a transition metal group with chiral ligands, homoleptic or heteroleptic, characterized by optical activity has been reported.

When comparing the specific rotation of homologues, this decreasing trend is not unexpected; if two substances have unequal molecular weights, but similar rotatory strength, or power to rotate polarized light, the substance with the smaller molecular weight will have a larger rotation simply because there are more molecules per unit weight.[26] For the group IV *sec*-butoxides, the decreasing trend in molar rotation may be due to differences in both rotatory strength and molecular size. The $Zr(O^2Bu)_4$ and $Hf(O^2Bu)_4$ alkoxides have similar molar rotations and may reflect that these complexes are similar in size due to the metals having essentially equivalent covalent radii. In order to evaluate the concentration dependence of the optical activity, polarimetry analyses were carried out for the (*R*)-isomers of the group IV *sec*-butoxides at concentrations of 1, 5, and 10 (Fig. 1). The slope of each line of best fit is equal to the specific rotation of the corresponding complex. Over the range of concentrations studied, the rotation for each compound decreases linearly with sample concentration, indicating that solution structure does not affect the magnitude of rotation.

**Table 1.** Specific and molar rotation values for $M(O^2Bu)_4$ (*c* 1, $C_6H_6$)

| $M(O^2Bu)_4$ | α (deg.) | $[\alpha]_D$ ($10^{-1}$ deg cm$^2$ g$^{-1}$) | [*Φ*] (10 deg cm$^2$ mol$^{-1}$) |
|---|---|---|---|
| $Ti(O^{R\text{-}2}Bu)_4$ | −0.906 | −83.1 | −282.9 |
| $Ti(O^{S\text{-}2}Bu)_4$ | +0.881 | +83.1 | +282.85 |
| $Zr(O^{R\text{-}2}Bu)_4$ | −0.230 | −20.9 | −80.2 |
| $Zr(O^{S\text{-}2}Bu)_4$ | +0.222 | +22.65 | +86.9 |
| $Hf(O^{R\text{-}2}Bu)_4$ | −0.121 | −11.75 | −55.3 |
| $Hf(O^{S\text{-}2}Bu)_4$ | +0.120 | +12.4 | +58.3 |

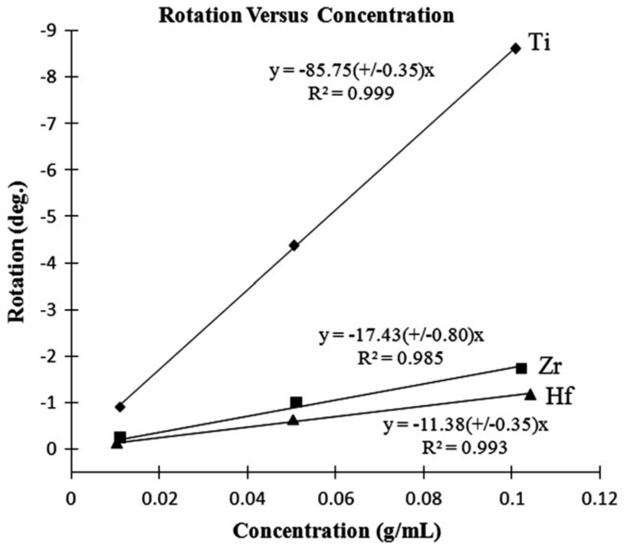
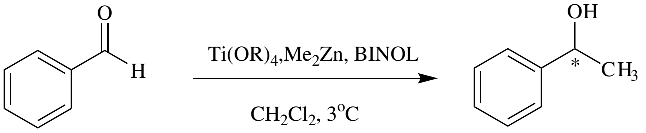


**Figure 1.** Concentration dependence of observed rotations for $M(O^{R\text{-}2}Bu)_4$ (M = Ti, Zr, Hf).

## 2.3. Asymmetric methylation of benzaldehyde

To assess the potential of chiral group IV *sec*-butoxides as asymmetric catalysts, the methylation of benzaldehyde to give 1-phenylethanol in the presence of dimethyl zinc and $Ti(OR)_4$ (R = $^i$Pr, $^{R\text{-}2}$Bu, or $^{S\text{-}2}$Bu) was studied, employing a procedure similar to that previously developed for diethyl zinc (Scheme 2).[27] Analogous studies employing diethyl zinc and achrial $Ti(O^iPr)_4$ have already been reported.[14,27] The alkylation of aldehydes with dimethyl zinc gives much lower enantiomeric excesses than diethyl zinc,[13,16,19,28] although it is known that for both the cases, the dialkyl zinc reagent does not directly alkylate the aldehyde substrate.[13]

In the presence of $Ti(O^{R\text{-}2}Bu)_4$ and $Ti(O^{S\text{-}2}Bu)_4$, a 17% excess of *R*- and 12% excess of *S*-1-phenylethanol were observed, respectively (Table 2).[29]



**Scheme 2.** Dimethyl zinc addition to benzaldehyde.

**Table 2.** Data for the addition of dimethyl zinc to benzaldehyde[a]

| Entry | $Ti(OR)_4$ | BINOL | % Conv[b] | % ee[c] | Config.[d] |
|---|---|---|---|---|---|
| 1 | $O^iPr$ | None | 81 | — | — |
| 2 | $O^{R\text{-}2}Bu$ | None | 54 | 17 | (*R*) |
| 3 | $O^{S\text{-}2}Bu$ | None | 33 | 12 | (*S*) |
| 4 | $O^iPr$ | Racemic | 98 | — | — |
| 5 | $O^{R\text{-}2}Bu$ | Racemic | 99 | 8 | (*S*) |
| 6 | $O^{S\text{-}2}Bu$ | Racemic | 99 | 11 | (*R*) |
| 7 | $O^iPr$ | (*R*) | 99 | 46 | (*R*) |
| 8 | $O^iPr$ | (*S*) | 99 | 40 | (*S*) |
| 9 | $O^{R\text{-}2}Bu$ | (*R*) | 99 | 37 | (*R*) |
| 10 | $O^{S\text{-}2}Bu$ | (*S*) | 99 | 40 | (*S*) |
| 11 | $O^{R\text{-}2}Bu$ | (*S*) | 99 | 58 | (*S*) |
| 12 | $O^{S\text{-}2}Bu$ | (*R*) | 99 | 56 | (*R*) |

[a] $Ti(OR)_4$ (1.4 mmol in 5 mL $CH_2Cl_2$), 0.21 mmol BINOL, 6.0 mmol $Me_2Zn$/toluene, 1.0 mmol benzaldehyde.

[b] After 24 h, as determined by $^1H$ NMR.

[c] Determined by chiral GC, Alltech Chiraldex B-DM.

[d] As determined by the analysis of an authentic sample of (*R*)-(+)-1-phenylethanol.