Synthesis of New Chiral Cyclopentadienes Suited for Chelation

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A new family chiral cyclopentadienes suitable for chelation are obtained by the functionalization of sodium cyclopentadienide with chiral tosylates.

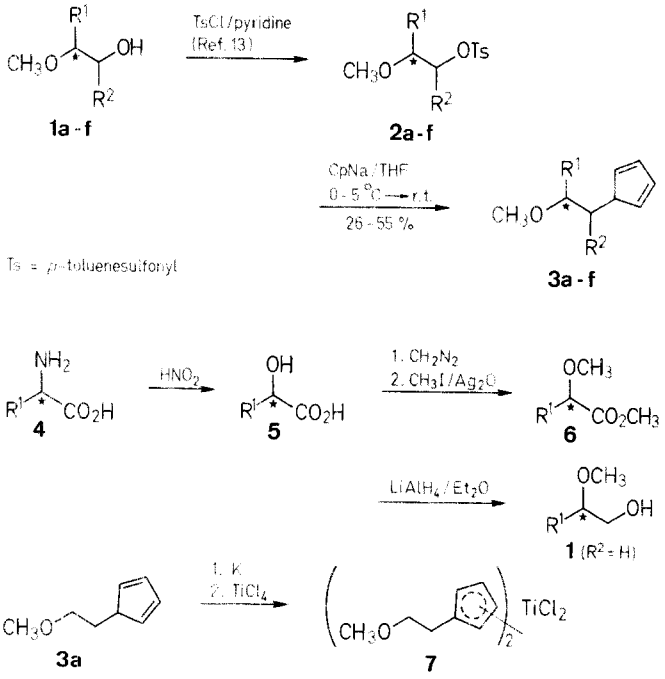
Asymmetric synthesis benefits greatly from the preparation of new chiral reagents or new chiral catalysts. Cyclopentadienyl (Cp) is a very common ligand in organometallic chemistry. It appears in many catalyst precursors such as Cp_2TiCl_2, Cp_2V and Cp_2Ni. The Cp ligand is also frequently encountered in complexes undergoing stoichiometric reaction, such as Cp_2ZrClH or Cp_2MoH_2. It is therefore of interst to synthesize chiral cyclopentadienes. However, the syntheses of chiral cyclopentadienes is still limited to a few examples, such as $CpCH(CH_3)Ph$ (17.3% optical purity),[1] menthylcyclopentadienyl (MCp), neomenthylcyclopentadienyl (NMCp)[2] and other two allylic cyclopentadienes.[3] Of these only MCp and NMCp have been used to prepare complexes such as $(MCp)_2TiCl_2$, $(NMCp)_2TiCl_2$, $(MCp)CpTiCl_2$, $(MCp)(MeCp)TiCl_2$ and $(NMCp)CpTiCl_2$. Their application to the asymmetric catalytic hydrogenation of 2-phenyl-1-butene at room temperature under 1 atmosphere of hydrogen gave 2-phenylbutane with 28% ee.[4]

Table. Chiral Cyclopentadiene Derivatives **3a–f** Prepared.

Product	R^1	R^2	Yield (%)	b.p. (°C/Torr)	Molecular Formula[a]	$[\alpha]_D$ (c; t; solvent)	^{1}H-NMR (TMS, $CDCl_3$) δ	MS (M^+) m/z
3a	H	H	44	40/4	$C_8H_{12}O$ (124.2)		1.6–2.3 (m); 2.8–3.0 (m); 2.7 (s); 5.4–6.6 (m)	124
(*R*)-**3b**	C_6H_5	H	26	83–5/0.5	$C_{14}H_{16}O$ (200.3)	−37.3° (1.47; 14°C; C_6H_6)	2.6 (m); 3.1 (s); 4.2 (m); 5.9–6.3 (m); 7.3 (s)	200
(*S*)-**3b**						+37.8° (1.50; 14°C; C_6H_6)		
(*R*)-**3c**	CH_3	H	28	38–42/2	$C_9H_{14}O$ (138.2)	+4.62° (2.50; 23°C; THF)[b]	0.7 (d); 1.8 (m); 2.1 (s); 2.45 (m); 2.8 (s); 5.6–6.6 (m)	138
(*S*)-**3c**						−46.7° (2.50; 20°C; THF)		
(*S*)-**3d**	*i*-C_3H_7	H	40	28/0.1	$C_{11}H_{18}O$ (166.25)	−9.05° (2.10; 21.5°C; THF)	0.45 (d); 1.2 (m); 1.8 (m); 2.1 (m); 2.4 (m); 2.8 (s); 5.6–6.5 (m)	166
(*R*)-**3e**	H	CH_3	55	34–7/1.5	$C_9H_{14}O$ (138.2)	−5.0° (2.10; 17°C; THF)[c]	1.0 (t); 2.05 (m); 2.75 (d); 3.6 (t); 3.05 (s); 5.7–6.8 (m)	138
(*S*)-**3e**						+9.95° (2.04; 16.5°C; THF)		
(*R*)-**3f**			37	48–50/0.4	$C_{10}H_{14}O$ (150.2)	+7.60° (2.18; 24°C; THF)	1.1–2.1 (m); 2.4 (d); 2.7 (s); 3.3–3.9 (m); 5.8–6.4 (m)	150
(*S*)-**3f**						−6.75° (2.00; 26°C; THF)		

[a] Satisfactory microanalyses obtained: C ± 0.5, H ± 0.3.
[b] Optical purity is about 9.7%.
[c] Optical purity is about 50%.

We describe here the synthesis of a new family of chiral cyclopentadienes suitable for chelation.



The starting chiral materials are: (*R*)- and (*S*)-mandelic acid,[7] (*R*)- and (*S*)-tetrahydrofur-2-ylmethanol,[8] optical active 1-methyl-2-methoxyethanol[9] [absolute configuration determined by X-ray analysis, optical purity is 100% for (*S*)-, but 50% for (*R*)-], (*R*)-2-methoxypropanoic acid,[10] L-lactic acid[11] and L-Valine.[12] In the case of the α-amino carboxylic acids and the α-hydroxy carboxylic acids, the corresponding substituted β-methoxyethanols were prepared according to the scheme. The results are shown in the following Table. All products gave satisfactory elemental analyses, ^{1}H-NMR and mass spectra.

These chiral ligands have been used to prepare titanium and zirconium complexes.[5] In the former case, the results of X-ray analysis show that the ether oxygen atom in the chiral side chain of the cyclopentadienyl group can coordinate to the titanium atom to form a chelating ring in the catalytic active intermediate [Cp_2^*TiH][5] (Cp^* = substituted cyclopentadienyl), thus bringing the chiral atom nearby the reaction center of the catalyst molecule. Therefore, these catalysts are expected to give better results than unchelated chiral cyclopentadienyl, derivatives such as MCp or NMCp, in some asymmetric catalytic reactions. Complex **7** was used as catalyst to isomerize 1,5-hexadiene into methylenecyclopentane with a yield of 90%.[5] Asymmetric catalysis studies using our chiral ligands are in progress.

Oxidation of L-Valine to (*S*)-2-Hydroxy-3-methylbutanoic Acid:
The oxidation is carried out according to Ref. 12.

Methyl α-Methoxy Esters 6:
Methyl α-methoxy esters **6** are prepared as described in Ref. 11.

β-Methoxyethanol Derivatives 1:
β-Methoxyethanol derivatives **1** are prepared as described in Ref. 10.

Substituted 2-Methoxyethyl *p*-Toluenesulfonates 2:
Tosylates of chiral alcohols **1** are prepared as described in Ref. 13 and in the references cited therein.

(Substituted 2-alkoxyalkyl)cyclopentadienes 3; Typical Procedure:
Under argon, a solution of sodium cyclopentadienide (prepared according to Ref. 14; 0.275 mol) in THF (200 mL) is added slowly to a solution

of (*S*)-1-methyl-2-methoxyethyl *p*-toluenesulfonate (0.217 mol) in THF (100 mL), with stirring, and at a temperature between 0 and 5 °C. The reaction mixture is stirred for a further 4 h at room temperature and treated with H_2O (50 mL). The aqueous phase is extracted with ether (5 × 50 mL) and the combined organic phase is dried (Na_2SO_4), concentrated and distilled *in vacuo* to give *1-methyl-2-methoxyethylcyclopentadiene* **3e** as a colorless oil; yield: 18.9 g (55%); b.p. 32–35 °C/1 Torr.

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