

Enantioselective Oxidation of Secondary Alcohols Catalyzed by Soluble Chiral Polymeric [*N,N*-Bis(salicylidene)ethane-1,2-diaminato(2–)]manganese(III) ([Mn^{III}(salen)]) Type Complexes in a Biphasic System

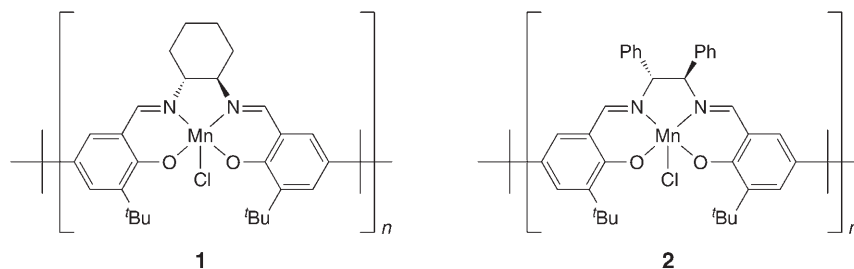
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The polymeric [*N,N*-bis(salicylidene)ethane-1,2-diaminato(2–)]manganese(III) ([Mn^{III}(salen)]) type complexes **1** and **2** were successfully applied to the oxidative kinetic resolution of secondary alcohols. The reaction proceeded readily at room temperature with excellent enantioselectivities of up to 99.9% ee. A variety of substrates, including aromatic and aliphatic alcohols, could be tolerated. The polymeric catalysts could easily be recovered and recycled.

Introduction. – The covalent attachment of homogeneous catalysts to insoluble polymer supports or inorganic supports has been studied widely as an attractive strategy for extending the practical advantages of heterogeneous catalysis to homogeneous system [1]. The potential benefits of heterogenization include facilitation of catalyst separation from reaction products and simplification of catalyst recycling. However, immobilization often results in catalysts with lower enantioselectivities or efficiencies than the solution-phase counterparts. Chiral catalysts can also be bound to a soluble support; in this case, the catalytic process can be performed under homogeneous conditions and lead to activities similar to those of their monomeric analogues. Dendrimers and poly(ethylene glycol) as soluble support have gained significant attention [2]. *Zheng* and co-workers [3] disclosed a new approach to soluble linear polymeric salen-type ligands with main-chain chirality; the corresponding chiral polymeric (salen)metal complexes were employed in the enantioselective epoxidation of olefins and the hydrolytic kinetic resolution of terminal epoxides with excellent enantioselectivity. In addition, the catalyst can be easily recovered and reused several times without loss of enantioselectivity [3].

Recently, we have discovered a successful method for oxidative kinetic resolution of alcohols [4][5] with chiral [Mn(salen)]-type complexes as catalyst in the presence of the phase-transfer catalyst (PTC) tetraethylammonium bromide or of an inorganic salt containing the bromide anion [6]. In continuation of our work, we now report the application of polymeric salenmanganese(III)-type complexes **1** and **2** to the oxidative kinetic resolution of secondary alcohols. These systems allow a simplified catalyst separation from the product mixtures, and the recovered catalysts are demonstrated to retain their full activity and enantioselectivity.



Results and Discussion. – In our previous work, water has proved to be the solvent of choice in the kinetic resolution of alcohols catalyzed by chiral [Mn^{III}(salen)]-type complexes [6]. However, for the polymeric chiral salenmanganese(III) catalytic system **1**, a moderate enantioselectivity was observed in the kinetic resolution of α -methylbenzyl alcohol in H₂O (Table 1, Entries 1 and 2). When mixtures of H₂O and CH₂Cl₂ were used as reaction media with the polymeric salenmanganese(III) complex **1** as catalyst, up to 95.2% ee was observed, with high k_{rel}^1 values, up to 24.5 (Entries 3 and 4). The use of polymeric salenmanganese(III) complex **2** resulted in slightly decreased enantioselectivities (Entries 5 and 6).

Table 1. The Influence of the Solvent on the Oxidative Kinetic Resolution of α -Methylbenzyl Alcohol^{a)}

Entry	Catalyst	Additive	Solvent	Conversion [%] ^{b)}	ee [%] ^{b)}	k_{rel}
1	1	Et ₄ NBr	H ₂ O	60.0	61.0	4.2
2	1	KBr	H ₂ O	60.5	82.3	8.1
3	1	Et ₄ NBr	H ₂ O/CH ₂ Cl ₂ 2:1	55.6	94.1	24.5
4	1	KBr	H ₂ O/CH ₂ Cl ₂ 2:1	58.8	95.2	18.0
5	2	Et ₄ NBr	H ₂ O/CH ₂ Cl ₂ 2:1	56.9	81.4	10.3
6	2	KBr	H ₂ O/CH ₂ Cl ₂ 2:1	54.6	77.8	10.7

^{a)} The reaction was carried out at room temperature (20°) for 1 h, with catalyst (2 mol-%, based on the monomer of the chiral salenmanganese(III) complex), Et₄NBr or KBr (8 mol-%), α -methylbenzyl alcohol (0.25 mmol), PhI(OAc)₂ (0.175 mmol), and H₂O (1 ml) or H₂O /CH₂Cl₂ 2:1 (1.5 ml). ^{b)} Determined by GC (HP 6890GC) with a CP-Chirasil-Dex-CB capillary column.

With the optimal conditions in hand, we explored the generality of the oxidative kinetic resolution of secondary alcohols in the presence of polymeric chiral salenmanganese(III) complexes as catalyst (Table 2). The behavior of secondary aromatic alcohols was first investigated. A variety of aromatic alcohols bearing various *para*-substituents underwent the kinetic reaction with high enantioselectivities in the presence of catalyst **1**. The reaction of the *ortho*-substituted aromatic alcohols proceeded with low enantioselectivities (Entry 4). The polymeric catalyst was also applicable to secondary aliphatic alcohols, resulting in excellent enantioselectivities (99.9% ee, Entry 12).

¹⁾ $k_{rel} = \ln[(1 - C)(1 - ee)] / \ln[(1 - C)(1 + ee)]$ where C is the conversion and ee is the enantiomeric excess. For an excellent discussion of kinetic resolution, see [7].

Table 2. *Asymmetric Kinetic Resolution of Secondary Alcohols Catalyzed by Polymeric Chiral Salen-manganese(III)-Type Complexes^a*

Entry	Substrate		Catalyst	Conversion [%] ^b	ee [%] ^b	<i>k</i> _{rel}
	R ¹	R ²				
1	4-Me-C ₆ H ₄	Me	1	59.0	90.1	12.9
2	4-F-C ₆ H ₄	Me	1	60.3	98.1	20.3
3	4-Cl-C ₆ H ₄	Me	1	58.0	96.8	22.6
4	2-Cl-C ₆ H ₄	Me	1	6.6	0	–
5	4-Br-C ₆ H ₄	Me	1	59.0	94.2	16.4
6	4-F ₃ C-C ₆ H ₄	Me	1	58.7	90.4	13.1
7	naphthalen-2-yl	Me	1	55.8	90.3	18.2
8	PhCH ₂	Me	1	56.3	96.4	27.2
9	4-Me-C ₆ H ₄	Et	1	52.4	7.6	1.2
10	4-Me-C ₆ H ₄	Et	2	50.3	31.4	2.5
11	1,2,3,4-tetrahydronaphthalen-1-ol (R ¹ –CHOH–R ²)		1	56.9	77.1	8.6
12	^t Bu	Me	1	56.5	99.9	55.4
13	Pr	Me	1	51	86	28.9
14 ^c)	Ph	Me	1	57.7	94.5	19.3
15 ^d)	Ph	Me	1	59.8	92.4	13.6

^a) The reaction was carried out at room temperature (20°) for 1 h, catalyst (2 mol-%, based on the monomer of the catalysts), KBr (8 mol-%), substrate (0.25 mmol), PhI(OAc)₂ (0.175 mmol), mixtures of H₂O/CH₂Cl₂ 2 : 1 (1.5 ml). ^b) Determined by GC (HP 6890GC) with a *CP-Chirasil-Dex-CB* capillary column. ^c) Second run (recycling), Et₄NBr as additive. ^d) Fourth run (recycling), Et₄NBr as additive.

The recycling of polymeric complex **1** was examined in the case of the enantioselective oxidation of α -methylbenzyl alcohol with the PTC Et₄NBr system. After the kinetic reaction, the polymeric catalyst was precipitated by adding hexane to the reaction mixture. The recovered catalyst was then subjected to further catalytic reactions with only a slight loss of enantioselectivity (*Table 1, Entry 3* (first run, 94.1% ee); *Table 2, Entries 14 and 15* (fourth run, 92.4% ee)).

In summary, we have established the first kinetic resolution of secondary alcohols in a biphasic system catalyzed by polymeric salenmanganese(III)-type complexes. The reaction proceeded readily at room temperature with excellent enantioselectivities of up to 99.9% ee. The polymeric system demonstrated broad tolerance of substrates, including secondary aromatic alcohols and secondary aliphatic alcohols. The polymeric catalysts could easily be recovered and recycled several times without loss of the high enantioselectivities.

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Experimental Part

General. All the secondary alcohols are commercially available and used without further purification. GC Analysis: *HP-6890* gas chromatograph, *CP-Chirasil-Dex-CB* column.

Chloro[2,2'-(cyclohexane-1,2-diyl)bis[(nitrilo-κN)methylidyne]]bis[phenolato-κO](2-)}manganese Homopolymer (1) and Chloro[2,2'-(1,2-diphenylethane-1,2-diyl)bis[(nitrilo-κN)methylidyne]]bis[phenolato-κO](2-)}manganese Homopolymer (2). Complexes 1 and 2 were synthesized by modification of the procedure reported in [3].

Kinetic Resolution of Secondary Alcohols: General Procedure 1. A mixture of the secondary alcohol (0.25 mmol), catalyst 1 (0.005 mmol, based on the catalyst monomer), KBr (0.02 mmol), and H₂O/CH₂Cl₂ 2:1 (1.5 ml) in a 5-ml tube was stirred for a few minutes at r.t. The co-oxidant PhI(OAc)₂ (0.175 mmol) was then added, and the mixture was stirred for a further hour. The products were extracted with Et₂O and the conversion and ee values were determined by GC analysis.

Recycling of the Polymeric Salenmanganese(III) Complex in the Kinetic Resolution Reaction: General Procedure 2. As described in the *General Procedure 1*, with *α*-methylbenzyl alcohol (0.25 mmol), catalyst 1 (0.005 mmol), Et₄NBr (0.02 mmol), H₂O/CH₂Cl₂ 2:1 (1.5 ml), and PhI(OAc)₂ (0.175 mmol). When the reaction was complete, hexane was added to the stirred mixture, and the hexane was decanted. The catalyst was recovered by filtration and dried before the next use.

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