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Enantioselective catalysis Part 124. Enantioselective Michael reaction catalyzed by optically active transition metal complexes [1]

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Abstract

The Michael reaction of acrolein **2** with ethyl 2-oxocyclohexanecarboxylate **1** can be catalyzed enantioselectively with a number of optically active transition metal complexes or in situ combinations of transition metal compounds and optically active ligands. The best results up to 47% ee could be obtained with $Co(acac)_2$ and 1,2-diphenylethylenediamine.

Keywords: Michael reaction; Enantioselective catalysis; Transition metal complexes

1. Introduction

In 1984, the first application of optically active transition metal catalysts in Michael reactions was reported [2]. The in situ combination of bis(2,4-pentanedionato)cobalt(II) and (+)- or (−)-1,2-diphenylethylenediamine was found by Brunner and Hammer to be an efficient catalyst in the reaction of methyl 1-oxo-2-indanecarboxylate with methyl vinyl ketone which gave optical inductions up to 66% ee [2]. The same catalyst was used in different systems of unsymmetrical 1,3-dicarbonyl Michael donors and α,β-unsaturated Michael acceptors by Brunner and Kraus in 1989 [3]. The best result was achieved in the addition of acrolein to ethyl 2-oxocyclohexanecarboxylate with optical yields of 39% ee [3]. In 1990, Botteghi et al. obtained 6% ee in the reaction of methyl vinyl ketone with ethyl 2-methylacetoacetate promoted by chiral bis-bidentate nickel(II) Schiff base complexes derived from 2-hydroxy-1-naphthaldehyde [4]. One year later 38% ee were attained in the addition of methyl vinyl ketone to methyl 1-oxo-2-indanecarboxylate and 59% ee in the reaction of nitromethane with chalcone using proline-derived ligands in combination with nickel(II) [5]. With similar ligands in ruthenium(III) complexes Yamaguchi et al. obtained up to 77% ee in the addition of malonate anions to prochiral α,β-unsaturated aldehydes and ketones [6]. In the Michael reaction of methyl vinyl ketone with methyl 1-oxo-2-indanecarboxylate Desimoni et al. reported optical yields

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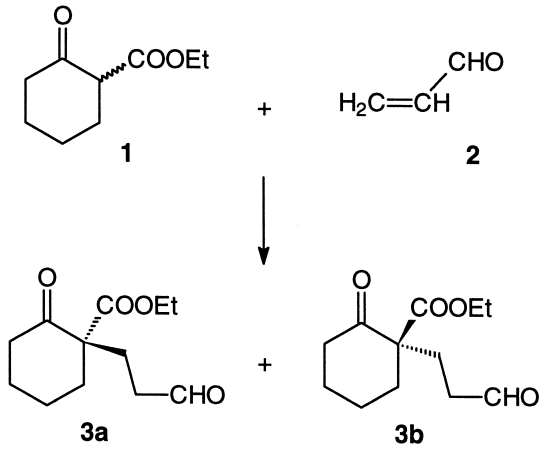
up to 70% ee with copper(II) complexes of tetradentate Schiff base ligands derived from salicylaldehyde [7]. They were improved to 75% ee in 1995 [8]. With rhodium(I) complexes of an optically active ferrocenyl–phosphane ligand Ito et al. achieved optical inductions up to 89% ee in the addition of 2-cyanopropionates to α,β-unsaturated ketones [9]. A recent paper of Nozaki et al. reported optical yields up to 73% ee in a similar Michael system with an optically active rhodium(I) catalyst containing binaphthyl–bisphosphane ligands [10]. In 1996, binaphthyl ligands were used by Jørgenson and Falborg in the titanium(IV)-catalyzed reaction of alkenoyl-1,3-oxazolidine-2-ones with *O*-benzyl-hydroxylamine (42% ee) [11], and by Shibasaki et al. in the addition of methyl vinyl ketone to methyl 1-oxo-2-indanecarboxylate (93% ee) catalyzed by lanthanoid(III) complexes [12]. As reported by Scettri et al. in 1993, $Eu(tfc)_3$ is able to catalyze the reaction of methyl vinyl ketone and ethyl 2-ethylacetoacetate with an enantioselectivity of 36% ee [13]. Bernardi et al. obtained optical inductions up to 63% ee using chiral bis(oxazoline) copper(II) complexes in the Mukaiyama Michael addition of propionate silyl ketene acetal to 2-(carbomethoxy)cyclopentenone [14]. In this paper we describe our results with respect to the Michael reaction of acrolein with ethyl 2-oxocyclohexanecarboxylate [15].

2. The Michael system ethyl 2-oxocyclohexanecarboxylate / acrolein

The addition of acrolein **2** to ethyl 2-oxocyclohexanecarboxylate **1** gives the configurationally stable adduct ethyl 1-(2′-formylethyl)-2-oxocyclohexanecarboxylate **3** (Scheme 1).

The reactions were performed with an 1.1-fold excess of acrolein in toluene solution in the presence of 1–3 mol% of the catalyst. For work-up the mixture was acidified with 2% HCl to remove the catalyst and the ligands. The solvent was evaporated and the chemical yield



Scheme 1.

was determined by ^1H NMR spectroscopy of the crude product, using the decrease of the enol proton of the donor **1** and the increase of the aldehyde proton of the adduct **3**. The ratio of enol-**1** to keto-**1** in $CHCl_3$ solution was determined to be 0.67 by ^1H NMR integration. The product was purified by distillation. As the rotatory power of the enantiomerically pure adduct **3** was unknown, the optical induction had to be determined by comparison of the optical rotation after oxidation of the aldehyde to the corresponding carboxylic acid with the rotation of the pure acid. The rotatory power of the pure (+)-acid was found to be $+94.6 \pm 0.6°$ after resolution with brucine via five-fold recrystallization in acetone solution, being slightly more precise than previously reported [3]. As the optically active ligands used in the catalyst are removed by the acid treatment and the distillation, enantiomer analysis by measuring the optical rotation is considered to be reliable.

3. Catalytically active metal acetylacetonates

As a first survey some metal acetylacetonates were tested for their catalytic activity in the Michael reaction of Scheme 1 (Table 1).

The acetylacetonato complexes of the 3d-elements cobalt(II), copper(II), nickel(II) and zinc(II) were found to be catalysts for the Michael

Table 1
Metal acetylacetonates as catalysts in the Michael reaction **1 + 2 → 3a/3b** (room temperature, 50 ml of toluene)

Entry	Catalyst	Molar ratio cat./**1**	Reaction time [h]	Chemical yield [%]	No. runs
1	$Cr(acac)_3$	1:35	283	0	3
2	$Co(acac)_2$	1:35	283	91–97	8
3	$Ni(acac)_2$	1:35	286	72–77	5
4	$Cu(acac)_2$	1:35	286	78–81	4
5	$Zn(acac)_2$	1:35	388	72–80	8
6	$Pd(acac)_2$	1:105	484	3–5	3
7	$La(acac)_3$	1:35	450	79–85	3
8	$Eu(acac)_3$	1:35	450	50–52	2
9	$Yb(acac)_3$	1:35	472	74–78	3

system **1/2** (entries 2–5). Their activity decreases in the given order. In this series, $Co(acac)_2$ was the most efficient catalyst with chemical yields up to 97% in reaction times of 288 h. Tris(acetylacetonato)chromium(III) did not promote the reaction at all (entry 1). Only small yields of product could be obtained with the palladium(II) compound (entry 6). The complexes of the rare earth metals lanthanum(III), europium(III) and ytterbium(III) did show some activity, but the reaction times had to be almost twice as long as with the 3d-elements to get similar yields of the adduct **3** (entries 7–9).

4. Optically active ethylenediamines as ligands

(*R*,*R*)-(−)-1,2-Diphenylethylenediamine [16] **L1** was used as a ligand in the Co-catalyzed Michael reaction **1 + 2 → 3a/3b** [15]. The results are listed in Table 2.

The previously reported chemical and optical yields (75% and 39% ee, respectively) obtained with the combination $Co(acac)_2$/**L1** [3] could be confirmed (entry 1). It could be shown that extending the reaction time to 250 h improved the chemical yield to almost quantitative (entry 2). In these experiments, surprisingly, the enantiomeric excess of the product increased from 36–38 to 43–47% ee. Thus, the optical induction in the Michael reaction **1 + 2 → 3a/3b**, catalyzed by $Co(acac)_2$/**L1**, is not constant but rises in the course of the reaction. It must be assumed that the accumulating product interacts with the catalyst enhancing the stereoselectivity of the reaction. This assumption could be corroborated by recording the chemical yields and the enantiomeric excess obtained in a time period of 0–250 h in intervals of about 25 h (Fig. 1). The diagram clearly shows an almost linear increase of the enantiomeric excess from 27% ee (22% chemical yield after 25 h) to 47% ee (100% chemical yield after 250 h).

On changing the molar ratio of the catalyst $Co(acac)_2$/**L1** to the substrate **1** from 1:35 to 1:105 the reaction time had to be increased to get reasonable chemical yields. However, the stereoselectivity did not change significantly (entry 3). The use of the isolated complex $Co(acac)_2$(**L1**), prepared by refluxing stoichiometric amounts of $Co(acac)_2$ and **L1** in toluene [1,2], as the catalyst did not show any differences to the in situ combination $Co(acac)_2$/**L1**

Table 2
L1 as a ligand in the Michael reaction **1 + 2 → 3a/3b**, catalyzed by metal acetylacetonates (room temperature, 50 ml of toluene)

Entry	Catalyst	Molar ratio cat./**1**	Reaction time [h]	Chemical yield [%]	Enantioselectivity [% ee]	No. runs
1	$Co(acac)_2$/**L1**	1:35	163	72–76	36–38 (−)	5
2	$Co(acac)_2$/**L1**	1:35	250	97–100	43–47 (−)	15
3	$Co(acac)_2$/**L1**	1:105	310	86–88	40–42 (−)	3
4	$Co(acac)_2$(**L1**)[a]	1:35	250	94–97	40–46 (−)	3
5	$Ni(acac)_2$/**L1**	1:35	186	92–96	6–7 (−)	3
6	$Cu(acac)_2$/**L1**	1:35	234	89–93	21–23 (+)	4

[a] The complex $Co(acac)_2$(**L1**) [1,2] was isolated and used as the catalyst instead of the in situ combination $Co(acac)_2$/**L1**.

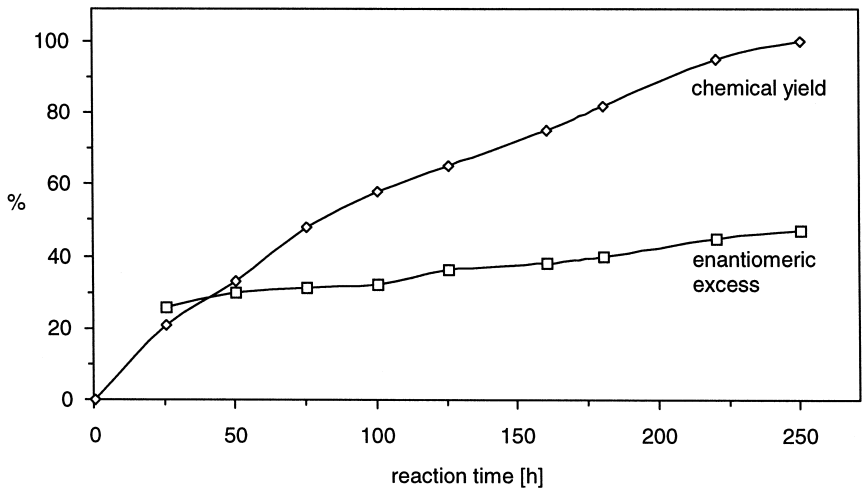


Fig. 1. Dependence of the enantiomeric excess from the chemical yield in the Michael reaction **1 + 2 → 3a / 3b**, catalyzed by $Co(acac)_2$/**L1**.

(entry 4). **L1** in combination with nickel(II) and copper(II) acetylacetonate gave good chemical yields but lower enantioselectivities than with cobalt(II) acetylacetonate (entries 5, 6). The product obtained in the catalyses of **L1** with the acetylacetonates of zinc(II), lanthanum(III) and ytterbium(III) was racemic throughout [15]. The results of the three- and four-fold *N*-methylated derivatives of **L1** as well as (+)-*N*,*N*′-dimethyl-*N*, *N*′-di[(*S*)-1-phenylethyl]ethylenediamine and (+)-*N*,*N*′-dimethyl-*N*,*N*′-di[(*S*)-1-cyclohexylethyl]ethylenediamine in combination with $Co(acac)_2$ showed a distinct decrease of both chemical and optical yields in comparison to the non-methylated ligand **L1** [15].

5. Cinchona alkaloids as catalysts

The successful use of cinchona alkaloids as chiral catalysts for the Michael reaction is well documented. [2] In our study the catalysis of the reaction **1 + 2 → 3a / 3b** by cinchona alkaloids with and without additional $Zn(acac)_2$ revealed some unexpected trends (Table 3). The free bases cinchonidine and quinine were found to be good catalysts with enantiomeric excesses up to 72 and 56% ee, respectively (entries 1, 3). Surprisingly, if used with additional $Zn(acac)_2$ as a metal component, the optical induction dropped appreciably to 25% ee for cinchonidine and 36% ee for quinine (entries 2, 4).

On the other hand, the addition of $Zn(acac)_2$ to the alkaloids cinchonine and quinidine gave a distinct increase of the enantiomeric excess in the product obtained. For cinchonine, it rose from 35% ee without to 48% ee with additional $Zn(acac)_2$ (entries 5, 6), and quinidine as a base catalyst alone gave 31% ee, but 42% ee in combination with $Zn(acac)_2$ (entries 7, 8). Similar results were obtained with $Co(acac)_2$ as metal component [15].

6. Salicylaldimines and their nitro and dinitro derivatives

The salicylaldimines **L2** [18], **L5**, **L8** [7] as well as their mononitro derivatives **L3** [19], **L6** [20], **L9** and their dinitro derivatives **L4**, **L7**, **L10** (Scheme 2) were tested as ligands for $Zn(acac)_2$ in the Michael reaction **1 + 2 → 3a / 3b**. The results are listed in Table 4.

[2] For a review, see Ref. [17]

Table 3
Cinchona alkaloids with and without $Zn(acac)_2$ as catalysts in the Michael reaction **1 + 2 → 3a / 3b** (room temperature, 50 ml of toluene)

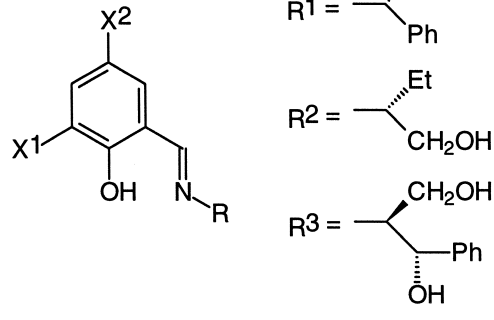
Entry	Catalyst	Molar ratio cat./**1**	Reaction time [h]	Chemical yield [%]	Enantioselectivity [% ee]	No. runs
1	cinchonidine	1:35	497	82–88	67–72 (+)	5
2	$Zn(acac)_2$/cinchonidine	1:35	497	93–97	22–25 (+)	3
3	quinine	1:35	474	80–84	52–56 (+)	5
4	$Zn(acac)_2$/quinine	1:35	474	90–95	32–36 (+)	3
5	cinchonine	1:35	497	76–81	33–35 (−)	4
6	$Zn(acac)_2$/cinchonine	1:35	497	86–92	45–48 (−)	4
7	quinidine	1:35	474	65–72	25–31 (−)	4
8	$Zn(acac)_2$/quinidine	1:35	474	69–73	39–42 (−)	4

Table 4
Nitro-substituted salicylaldimines as ligands for $Zn(acac)_2$ in the Michael reaction **1 + 2 → 3a / 3b** (room temperature, 50 ml of toluene)

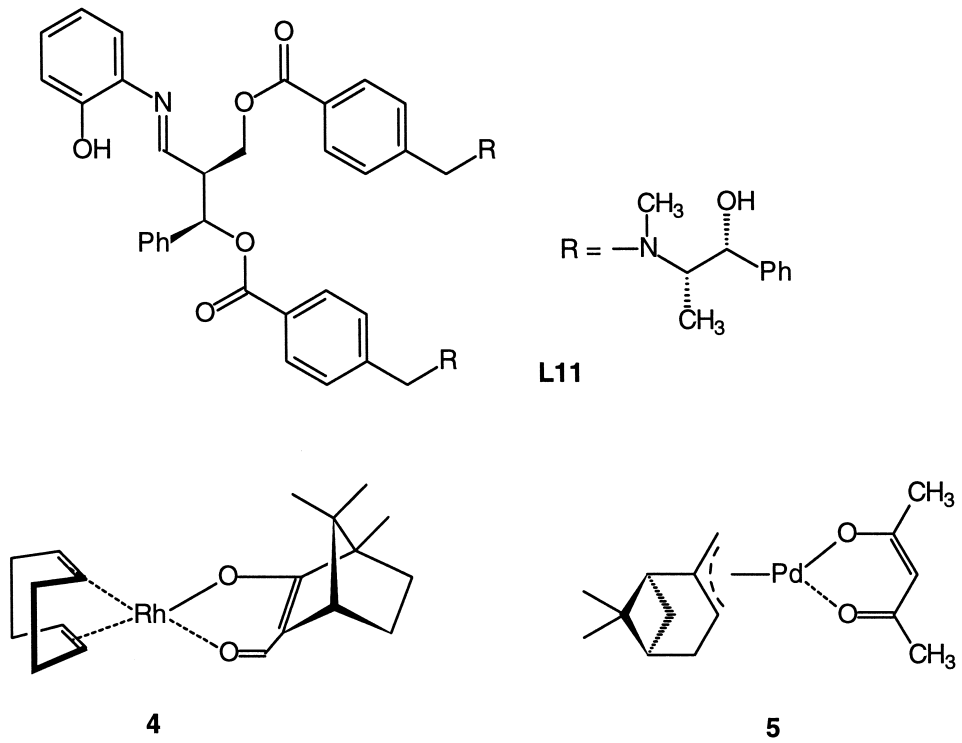
Entry	Catalyst	Molar ratio cat./**1**	Reaction time [h]	Chemical yield [%]	Enantioselectivity [% ee]	No. runs
1	$Zn(acac)_2$/**L2**	1:105	386	56–58	0	4
2	$Zn(acac)_2$/**L3**	1:105	386	61–65	7–9 (−)	4
3	$Zn(acac)_2$/**L4**	1:105	386	54–57	11–13 (−)	4
4	$Zn(acac)_2$/**L5**	1:105	386	46–49	8–11 (−)	4
5	$Zn(acac)_2$/**L6**	1:105	386	60–65	10–13 (−)	4
6	$Zn(acac)_2$/**L7**	1:105	386	55–59	17–21 (−)	4
7	$Zn(acac)_2$/**L8**	1:105	386	41–44	15–17 (+)	4
8	$Zn(acac)_2$/**L9**	1:105	386	61–65	19–22 (+)	4
9	$Zn(acac)_2$/**L10**	1:105	386	58–64	21–24 (+)	4
10	$Co(acac)_2$/**L6**	1:105	214	42–46	29–32 (−)	3

The positive effect of the nitro substitution is remarkable. For **L2–L4** the enantioselectivity rose from 0 to 13% ee (entries 1–3), the only difference in these ligands being additional nitro groups. The same effect can be seen in the other ligand families **L5–L7** (entries 4–6) and **L8–L10** (entries 7–9). Surprisingly, (*R*)-(+)-*N*-(1-hydroxybut-2-yl)-2-hydroxy-5-nitrobenzaldimine **L6** in combination with $Co(acac)_2$ gave higher optical inductions up to 32% ee with chemical yields of 46% (entry 10) than with $Zn(acac)_2$ (entry 5). However, both the non-nitrated ligand **L5** and the 3,5-dinitro derivative **L7** of the same ligand system did not promote

	X^1	X^2	R
L2	H	H	R^1
L3	NO_2	H	R^1
L4	NO_2	NO_2	R^1
L5	H	H	R^2
L6	NO_2	H	R^2
L7	NO_2	NO_2	R^2
L8	H	H	R^3
L9	NO_2	H	R^3
L10	NO_2	NO_2	R^3



Scheme 2.



Scheme 3. Some other examples of ligands/catalysts.

the reaction as well (12% and 9% chemical yield, respectively) [15].

7. Other ligands and systems

Apart from ethylenediamines, cinchona alkaloids and salicylaldimines other ligand types were tested in the Michael reaction **1 + 2 → 3a / 3b** [15,21]. Some examples are given in Scheme 3 and Table 5.

The ligand (+)-*N*-salicylidene-2-amino-1-phenyl-1, 3-propanediylbis[(1*S*,2 *R*)-*N*-(2-hydroxy-1-methyl-2-phenylethyl) -*N*-methyl-4-aminomethylbenzoate] **L11** [22] gave a maximum chemical yield of 10% in a reaction time of 449 h if used with $Co(acac)_2$ at a molar ratio of 1:1 [21]. On addition of a stoichiometric amount of $Cu(acac)_2$ to $Co(acac)_2$/**L11** the chemical yield increased to 55–57% and the stereoselectivity obtained was up to 35% ee (entry 1).

Catalysis of the Michael reaction **1 + 2** with (+)-η^4-1,5-cyclooctadiene[3-(hydroxymethyl-

Table 5
Other systems used as catalysts for the Michael reaction **1 + 2 → 3a / 3b** (room temperature, 50 ml of toluene)

Entry	Catalyst	Molar ratio cat./**1**	Reaction time [h]	Chemical yield [%]	Enantioselectivity [% ee]	No. runs
1	$Co(acac)_2$/$Cu(acac)_2$/**L11**[a]	1:52	475	55–57	31–35 (+)	2
2	**4**	1:105	478	65–71	0	3
3	**5**	1:105	484[b]	27–36	6–9 (+)	2

[a] Molar ratio Co/Cu/**L11** 1:1:1.
[b] At 40°C.

ene)-(1*R*)-camphorato]rhodium(I) **4** [23] gave good chemical yields, but racemic product **3** (entry 2). This is not surprising, as the chiral information of the catalyst is lost due to ligand–ligand exchange of the optical active *O,O*-ligand with the substrate **1** during catalysis. However, (−)-acetylacetonato(η^3-6,6-dimethyl-2-methylenebicyclo[3.1.1]hept-3-yl)palladium **5** [24] gave a small enrichment of (+)-product (entry 3), because its optically active ligand remains in the catalyst during the reaction.

Other ligands such as aminoalcohols, salicyloxazolines and macrocycles containing three and four nitrogen atoms were tested in the reaction **1 + 2 → 3a / 3b**, but the chemical yields and/or the stereoselectivities were low [15].

8. Variation of solvent and temperature

The system $Co(acac)_2$/**L1** was used to examine the effects of different solvents and temperatures on chemical and optical yields (Table 6). The stereoselectivity of the Michael reaction **1 + 2 → 3a / 3b** decreased significantly if carried out in methylene chloride or acetonitrile (entries 1, 2). If mixtures of toluene and petroleum ether 40/60 were used as solvents, the reaction time had to be increased to get reasonable chemical yields. The enantioselectivity did not change much for 3:1 and 2:1 mixtures (entries 4, 5), but declined from 47% ee to 38% ee for a 1:1 mixture of toluene/PE (entry 6).

The reaction proceeded much faster when raising the temperature from room temperature to 110°C, but both the chemical yield and the stereoselectivity decreased (entries 7–9). Cooling below room temperature did not lead to higher optical inductions but to impracticable reaction times (entries 10, 11).

9. Experimental

The substrates ethyl 2-oxocyclohexanecarboxylate **1** and acrolein **2** were commercially available and purified by distillation under nitrogen. ^{1}H NMR spectra: Bruker WM 250 (250 MHz). Optical rotation: Perkin–Elmer polarimeter 241. All reactions were carried out under nitrogen.

*9.1. Ethyl 1-(2′-formylethyl)-2-oxocyclohexanecarboxylate (**3**)*

A total of 0.180 mmol of the metal acetylacetonate and 0.181 mmol of the ligand were dis-

Table 6
Variation of solvent and temperature in the Michael reaction **1 + 2 → 3a / 3b** with $Co(acac)_2$/**L1** used as catalyst

Entry	Solvent[a]	Temp. [°C]	Reaction time [h]	Chemical yield [%]	Enantioselectivity [% ee]
1	CH_3CN	RT	474	34	12 (−)
2	CH_2Cl_2	RT	473	85	17 (−)
3	toluene	RT	250	100	47 (−)
4	toluene/PE 3:1	RT	474	93	45 (−)
5	toluene/PE 2:1	RT	521	83	49 (−)
6	toluene/PE 1:1	RT	541	44	38 (−)
7	toluene	110	24	37	21 (−)
8	toluene	60	100	78	31 (−)
9	toluene	30	188	85	35 (−)
10	toluene	0	474	46	32 (−)
11	toluene	−20	907	12	n.d.[b]

[a] PE = petroleum ether 40/60.
[b] n.d. = could not be determined.
RT = room temperature.

solved in 50 ml of toluene. After 10–15 min, ethyl 2-oxocyclohexanecarboxylate **1** (1.00 ml, 6.29 mmol) and acrolein (0.45 ml, 6.74 mmol) were added. After the specified reaction time the excess of acrolein was removed in vacuo. To remove the catalyst, the mixture was washed 3 times with 10 ml of 2% HCl and once with 10 ml of H_2O and dried over Na_2SO_4. After filtration and evaporation of the solvent, the chemical yield was determined by ^1H NMR integration prior to purification by Kugelrohr distillation at 78°C/0.01 Torr (lit. 140–143°C/1.5 Torr [25]) to give a colorless oil. The enantiomeric excess was measured by polarimetry after oxidation of the purified aldehyde **3** to its corresponding carboxylic acid [3]. ^1H NMR (250 MHz, $CDCl_3$, *i*-TMS): δ 1.28 (t, $J = 7.1$ Hz, 3H, CH_3), 1.41–2.67 (m, 12H, CH_2), 4.21/4.22 (dq, $J = 10.7$ Hz, $J = 7.1$ Hz, 2H, OCH_2), 9.74 (t, $J = 1.2$ Hz, 1H, CHO).

9.2. The new salicylaldimines

Method A: 10.0 mmol of salicylaldehyde and 10.0 mmol of the optically active amine were dissolved in 25 ml of MeOH. After addition of 2 g $MgSO_4$ the mixture was stirred for 20 h at room temperature. Filtration and evaporation of the solvent gave the crude product, which was purified by recrystallization from MeOH or CH_2Cl_2.

Method B: Same reaction mixture as above without $MgSO_4$. After a few minutes the product precipitated. It was filtered off, washed with few ml of MeOH and dried.

9.2.1. (R)-(−)-N-(1-Phenylethyl)-2-hydroxy-3,5-dinitrobenzaldimine ***L4***

Preparation according to method B with 2.12 g (10.0 mmol) of 2-hydroxy-3,5-dinitrobenzaldehyde [26] and 1.27 ml (10.0 mmol) of (*R*)-(+)-1-phenylethylamine. Yield: 2.27 g (72%), yellow–orange precipitate, m.p. 152–153°C, $[\alpha]_D^{20} = -177.3°$ (*c* 0.30, acetone). ^1H NMR (250 MHz, $CDCl_3$, *i*-TMS): δ 1.86 (d, $J = 6.9$ Hz, 3H, CH_3), 5.01 (q, $J = 6.9$ Hz, 1H, CH), 7.34–7.51 (m, 5H, PhH), 8.22 (s, 1H, =CH), 8.38 (d, $J = 3.0$ Hz, 1H, PhH), 8.96 (d, $J = 3.0$ Hz, 1H, PhH), 15.34 (br s, 1H, OH). $C_{15}H_{13}N_3O_5$ (315.3): calc.: C 57.14, H 4.16, N 13.33; found: C 57.44, H 4.21, N 13.26.

9.2.2. (R)-(+)-N-(1-Hydroxybut-2-yl)-2-hydroxy-3,5-dinitrobenzaldimine ***L7***

Preparation according to method B with 2.12 g (10.0 mmol) of 2-hydroxy-3,5-dinitrobenzaldehyde and 0.96 ml (10.0 mmol) of (*R*)-(−)-2-amino-1-butanol. Yield: 2.53 g (89%), yellow precipitate, m.p. 220°C (dec.), $[\alpha]_D^{20} = +44.0°$ (*c* 0.30, acetone). ^1H NMR (250 MHz, $CDCl_3$, *i*-TMS): 0.98 (t, $J = 7.5$ Hz, 3H, CH_3), 1.70–1.93 (m, 2H, CH_2), 3.49–3.75 (m, 2H, CH_2OH), 5.38–5.50 (m, 1H, CH), 8.50 (d, $J = 3.0$ Hz, 1H, PhH), 8.61 (s, 1H, =CH), 8.75 (d, $J = 3.0$ Hz, 1H, PhH), 14.86 (br s, 1H, OH). $C_{11}H_{13}N_3O_6$ (283.2): calc.: C 46.65, H 4.63, N 14.84; found: C 46.55, H 4.70, N 14.68.

9.2.3. (1S,2S)-(+)-N-(1,3-Dihydroxy-1-phenylprop-2-yl)-2-hydroxy-5-nitrobenzaldimine ***L9***

Preparation according to method A with 1.67 g (10.0 mmol) of 2-hydroxy-5-nitrobenzaldehyde [27] and 1.67 g (10.0 mmol) of (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol and recrystallization from MeOH. Yield: 1.34 g (42%), yellow crystals, m.p. 201–202°C, $[\alpha]_D^{20} = +289.3$ (*c* 0.30, acetone). ^1H NMR (250 MHz, DMSO-d_6, *i*-TMS): δ 3.52–3.76 (m, 3H, CH_2, CH), 4.91 (t, $J = 4.1$ Hz, 1H, OH), 5.21 (m, 1H, CH), 6.03 (d, $J = 4.4$ Hz, 1H, OH), 6.60 (d, $J = 9.7$ Hz, 1H, PhH), 7.22–7.41 (m, 5H, PhH), 8.03 (dd, $J = 9.7$ Hz, $J = 3.0$ Hz, 1H, PhH), 8.40 (d, $J = 3.0$ Hz, 1H, PhH), 8.59 (s, 1H, =CH), 14.48 (br s, 1H, OH). $C_{16}H_{16}N_2O_5$ (316.3): calc.: C 60.75, H 5.10, N 8.86; found: C 60.87, H 5.12, N 8.74.

9.2.4. (1S,2S)-(+)-N-(1,3-Dihydroxy-1-phenylprop-2-yl)-2-hydroxy-3,5-dinitrobenzaldimine ***L10***

A total of 2.12 g (10.0 mmol) of 2-hydroxy-3,5-dinitrobenzaldehyde and 1.67 g (10.0 mmol)

of (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol were dissolved in 50 ml of toluene. The solution was refluxed using a water extractor for 20 h. The product precipitated as a dark yellow solid, which was filtered off, washed with PE and dried. Recrystallization from acetone/PE gave the pure product as yellow crystals. Yield: 2.43 g (67%), m.p. 222–223°C (dec.), $[\alpha]_D^{20} = +479.0°$ (*c* 0.30, acetone). ^{1}H NMR (250 MHz, DMSO-d_6, *i*-TMS): δ 3.57–3.88 (m, 3H, CH_2, CH), 4.95 (br s, 1H, OH), 5.37 (br s, 1H, OH), 6.24 (d, $J = 3.4$ Hz, 1H, CH), 7.25–7.43 (m, 5H, PhH), 8.70 (d, $J = 3.1$ Hz, 1H, PhH), 8.75 (d, $J = 3.1$ Hz, 1H, PhH), 8.84 (s, 1H, =CH), 13.76 (br s, 1H, OH). $C_{16}H_{15}N_3O_7$ (361.3): calc.: C 53.19, H 4.18, N 11.63; found: C 53.02, H 4.23, N 11.59.

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