DOI: 10.1021/ic100229e

Inorganic Chemistry
Article

Chiral Salicyloxazolines as Auxiliaries for the Asymmetric Synthesis of Ruthenium Polypyridyl Complexes

Lei Gong, Seann P. Mulcahy, Deepa Devarajan, Klaus Harms, Gernot Frenking, and Eric Meggers*

Fachbereich Chemie, Philipps-Universität Marburg, Hans-Meerwein-Strasse, 35032 Marburg, Germany

Received February 4, 2010

Chiral auxiliaries are promising emerging tools for the asymmetric synthesis of octahedral metal complexes. We recently introduced chiral salicyloxazolines as coordinating bidentate chiral ligands which provide excellent control over the metal-centered configuration in the course of ligand substitution reactions and can be removed afterward in an acid-induced fashion under complete retention of configuration (*J. Am. Chem. Soc.* **2009**, *131*, 9602−9603). Here reported is our detailed investigation of this sequence of reactions, affording virtually enantiopure ruthenium polypyridyl complexes. The control of the metal-centered chirality by the coordinated chiral salicyloxazolinate ligand was evaluated as a function of reaction conditions, the employed bidentate 2,2′-bipyridine and 1,10-phenanthroline ligands, and the substituent at the asymmetric 5-position of the oxazoline heterocycle. Most striking was the strong influence of the reaction solvent, with aprotic solvents of lower polarity providing the most favorable diastereoselectivities. Through a combination of computational and experimental results, it was revealed that the observed stereoselectivities are under thermodynamic control. The removal of the chiral salicyloxazoline auxiliary under retention of the configuration requires acidic conditions and a coordinating solvent such as MeCN or THF in order to prevent partial racemization. This method represents the first general strategy for the asymmetric synthesis of enantiopure heteroleptic ruthenium polypyridyl complexes.

Introduction

Optically pure octahedral metal complexes play an increasingly important role in the life sciences as structural scaffolds for the selective molecular recognition of biological macromolecules such as nucleic acids and proteins.[1,2] Unfortunately, in contrast to the availability of highly sophisticated methods for the asymmetric synthesis of organic compounds, general methods for the asymmetric synthesis of optically pure, configurationally stable octahedral metal complexes are scarce, and if single enantiomers are desired, racemic mixtures are typically resolved by chiral separation techniques.[3]

In the most straightforward approach of controlling metal-centered chirality, chiral coordinating ligands have been employed for diastereoselective coordination chemistry.[3] For example, in 1920, Smirnoff reported the first diastereoselective synthesis of chiral octahedral platinum(IV) complexes by using nonracemic 1,2-diaminopropane.[4] von Zelewsky et al. later investigated intensively the control of metal-centered chirality in octahedral ruthenium complexes by using enantiopure chiral tetradentate bis-2,2′-bipyridines, so-called CHIRAGENs (from CHIRAlity GENerator), to control the chirality at the metal center, and they were the first to report the diastereoselective synthesis of an optically pure octahedral ruthenium polypyridyl complex without the need for the separation of stereoisomers.[5] Scott and co-workers recently reported the highly diastereoselective synthesis of optically pure single isomers of *fac*-tris(diimine) complexes of iron(II) from chiral 2-iminopyridines.[6] However, these and related approaches are not quite general because they are limited to the synthesis of optically pure octahedral complexes which contain carefully designed chiral ligands in their coordination sphere.

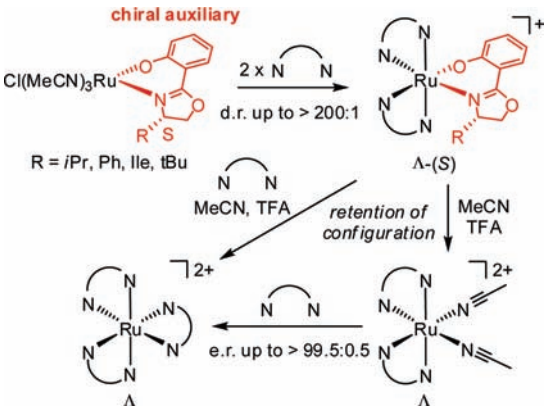
An attractive, more broadly applicable strategy for asymmetric coordination chemistry is to employ chiral coordinating ligands as chiral auxiliaries. Such auxiliaries have the task of controlling the implementation of the absolute configuration at the metal center during ligand exchange reactions, followed by a traceless removal of the chiral ligand afterward.[7] In pioneering work, Bailar et al. reported in 1948 the first asymmetric synthesis of (+)-$[Co(en)]^{3+}$, (+)-$[Co(en)_2Cl_2]^{+}$,

*Email: meggers@chemie.uni-marburg.de.

(1) Zeglis, B. M.; Pierre, V. C.; Barton, J. K. *Chem. Commun.* **2007**, 4565–4579.
(2) Meggers, E. *Chem. Commun.* **2009**, 1001–1010.
(3) Reviews on stereoselective synthesis in coordination chemistry: (a) Knof, U.; von Zelewsky, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 302–322. (b) Knight, P. D.; Scott, P. *Coord. Chem. Rev.* **2003**, *242*, 125–143. (c) Lacour, J.; Hebbe-Viton, V. *Chem. Soc. Rev.* **2003**, *32*, 373–382.
(4) Smirnoff, A. P. *Helv. Chim. Acta* **1920**, *3*, 177–195.
(5) Hayoz, P.; von Zelewsky, A.; Stoeckli-Evans, H. *J. Am. Chem. Soc.* **1993**, *115*, 5111–5114.
(6) Howson, S. E.; Allan, L. E. N.; Chmel, N. P.; Clarkson, G. J.; van Gorkum, R.; Scott, P. *Chem. Commun.* **2009**, 1727–1729.
(7) For a recent review on chiral auxiliaries in asymmetric coordination chemistry, see: Meggers, E. *Chem.—Eur. J.* **2010**, *16*, 752–758.

Published on Web 07/28/2010

Scheme 1. Chiral Salicyloxazolines as Auxiliaries for the Asymmetric Synthesis of Octahedral Ruthenium Polypyridyl Complexes

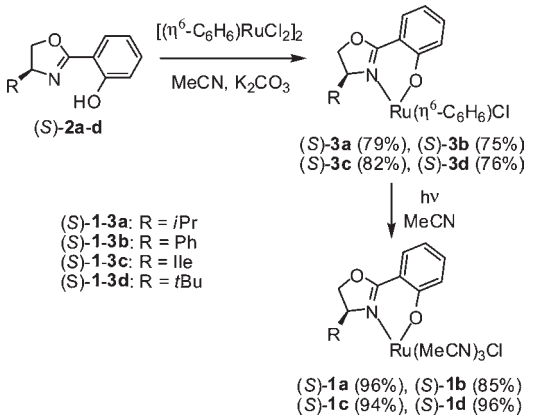


and (+)-$[Co(en)_2(NO_2)_2]^+$, en = 1,2-ethylenediamine (the Λ-enantiomers), by using (*R*,*R*)-(+)-tartrate as the coordinating chiral auxiliary.[8] In 1964, Bailar et al. also demonstrated the first asymmetric synthesis of enantiomerically enriched $[Ru(bpy)_3]^{2+}$, bpy = 2,2′-bipyridine, by reacting first K_2RuCl_6 with (*R*,*R*)-(+)-tartrate, affording an undefined "tartratoruthenium complex", followed by the reaction with an excess of 2,2′-bipyridine to yield the ruthenium complex $[Ru(bpy)_3]^{2+}$ with a Λ/Δ ratio of 63:37.[9,10] In a similar fashion, $[Ru(phen)_3]^{2+}$ (phen = 1,10-phenanthroline) and $[Os(bpy)_3]^{2+}$ were synthesized in an enantiomerically enriched form.[9]

Wild and co-workers recently reported the asymmetric synthesis of iron(II) complexes by using a tartratic-acid-based chiral linker between two tridentate ligands, which led to the formation of only one diastereomer.[11] Saponification of the linker resulted in removal of the chiral auxiliary under slight racemization with an observed enantiomeric ratio of the final iron complex of 85:15. Inoue and co-workers described the use of monodentate chiral sulfoxides as chiral auxiliaries.[12] Accordingly, racemic *cis*- or *trans*-$[Ru(pp)_2Cl_2]$ (pp = 2,2′-bipyridine or 4,4′-dimethyl-2,2′-bipyridine) were reacted with a chiral sulfoxide, affording with modest diastereoselectivities (d.e. ≤ 60%) the compounds *cis*-$[Ru(pp)_2(sulfoxide)Cl]Cl$, which themselves can subsequently serve as precursors for the conversion to enantiomerically enriched tris(2,2′-bipyridine) complexes. In a related study, Aït-Haddou et al. achieved higher asymmetric inductions of up to 76% d.e. by performing the reactions under microwave irradiation, and diastereomeric ratios could be further improved by making use of the different solubilities of the two formed diastereomers.[13]

Our group recently introduced salicyloxazolines as chiral auxiliaries for asymmetric coordination chemistry and applied the strategy to the asymmetric synthesis of enantiopure tris-heteroleptic ruthenium polypyridyl complexes $[Ru(pp)(pp')(pp'')]^{2+}$, with pp, pp′, and pp″ = achiral 2,2′-bipyridines (Scheme 1).[14] Herein, we report our detailed investigation of this reaction sequence, reveal the scope of this method, and provide a guide to optimal standard reaction conditions.

Scheme 2. Synthesis of Salicyloxazolinate Precursor Complexes (*S*)-**1a**−**d**



Results and Discussion

Salicyloxazolinate Precursor Complexes. The salicyloxazolinate complexes **1a**−**d** (Scheme 2), containing a deprotonated chiral (*S*)-5-alkyl- or (*S*)-5-aryl-2-(2′-hydroxyphenyl)oxazoline ligand in addition to four exchangable, labile ligands (three MeCN ligands and one chloride), serve as our canonical starting complexes for diastereoselective coordination chemistry. In these complexes, the substituents at the asymmetric 5- position of the oxazoline moiety have the function of controlling the metal-centered chirality in the course of the replacement of the four labile monodentate against two bidentate ligands. Chiral salicyloxazoline ligands are readily accessible from chiral α-amino acids in just two steps[15] and converted to the ruthenium precursor complexes by the reaction with first $[(\eta^6\text{-}C_6H_6)RuCl_2]_2$ in the presence of K_2CO_3, affording (*S*)-**3a**−**d** in yields of 75−82%, followed by a subsequent photolysis with a medium pressure mercury lamp in acetonitrile providing the precursor complexes (*S*)-**1a**−**d** in yields of 85−96% as mixtures of isomers (Scheme 2).[16] It is noteworthy that these precursor complexes have a limited stability and are preferably prepared freshly before use and should be stored dry at −20 °C for not longer than approximately 2 weeks. Complex (*S*)-**1d** with R = *tert*-butyl is particularly unstable and cannot be obtained in a completely pure fashion. This is most likely due to a strong steric interference between the bulky *tert*-butyl group and the neighboring acetonitrile and chloride ligands, leading to a destabilizing of the entire coordination sphere.

Diastereoselective Coordination Chemistry. The reactions of the precursors (*S*)-**1a**−**d** with 2.2 equivalents of plain or derivatized 2,2-bipyridine or 1,10-phenanthroline ligands afford in a diastereoselective fashion the Λ-(*S*) complexes as the main products (Scheme 3). Diastereomeric ratios between Λ-(*S*) and Δ-(*S*) complexes depend on the reaction conditions, the nature of the bidentate ligands, and the substituent at the 5- position of the oxazoline moiety. These data will be presented and discussed in the following.

(8) Jonassen, H. B.; Bailar, J. C.; Huffman, E. H. *J. Am. Chem. Soc.* **1948**, *70*, 756–758.
(9) Liu, C. F.; Liu, N. C.; Bailar, J. C. *Inorg. Chem.* **1964**, *3*, 1085–1087.
(10) Gillard, R. D.; Hill, R. E. E.; Maskill, R. *J. Chem. Soc. A* **1970**, 707–710.
(11) Warr, R. J.; Willis, A. C.; Wild, S. B. *Inorg. Chem.* **2006**, *45*, 8618–8627.
(12) Hesek, D.; Inoue, Y.; Everitt, S. R. L.; Ishida, H.; Kunieda, M.; Drew, M. G. B. *Inorg. Chem.* **2000**, *39*, 317–324.
(13) Pezet, F.; Daran, J.-C.; Sasaki, I.; Aït-Haddou, H.; Balavoine, G. G. A. *Organometallics* **2000**, *19*, 4008–4015.
(14) Gong, L.; Mulcahy, S. P.; Harms, K.; Meggers, E. *J. Am. Chem. Soc.* **2009**, *131*, 9602–9603.
(15) Bolm, C.; Weickhardt, K.; Zehnder, M.; Ranff, T. *Chem. Ber.* **1991**, *124*, 1173–1180.
(16) For a related synthetic strategy, see: Freedman, D. A.; Evju, J. K.; Pomije, M. K.; Mann, K. R. *Inorg. Chem.* **2001**, *40*, 5711–5715.

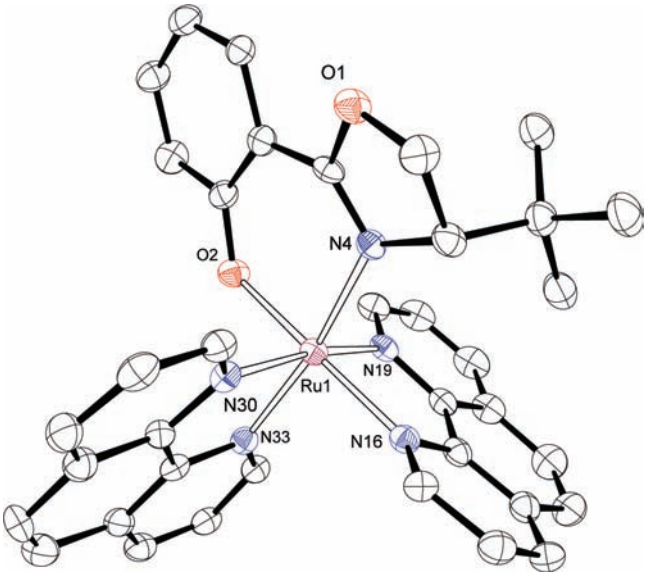
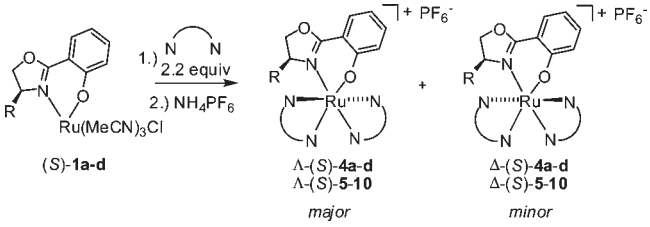


Figure 1. Crystal structure of Λ-(*S*)-**4d** in which the absolute stereochemistry was determined. The PF_6^- counterion and a CH_2Cl_2 solvent molecule are omitted for clarity. ORTEP drawing with 50% probability thermal elipsoids. Selected bond distances (Å) and angles (deg): Ru1−N4 = 2.135(3), Ru1−N16 = 2.038(2), Ru1−N19 = 2.041(3), Ru1−N30 = 2.063(3), Ru1−N33 = 2.056(3), Ru1−O2 = 2.063(2), N16−Ru1−N4 = 94.55(11), N19−Ru1−N4 = 98.01(9), N30−Ru1−N4 = 90.70(11), N33−Ru1−N4 = 169.41(12), O2−Ru1−N4 = 90.00(10), N16−Ru1−N19 = 80.25(11), N16−Ru1−N30 = 96.37(12), N19−Ru1−N30 = 170.86(11), N33−Ru1−N30 = 80.12(9).

Scheme 3. Diastereoselective Coordination Chemistry of Precursor Complexes (*S*)-**1a**−**d** with 2.2 Equivalents of Bidentate Ligands[a]



[a] R = *i*Pr (**4a**, **5**−**10**), Ph (**4b**), Ile (**4c**), and *t*Bu (**4d**). Bidentate ligands: Phen (**4a**−**d**), bpy (**5**), 4,4′-Me_2bpy (**6**), 5,5′-Me_2bpy (**7**), 4,4′-$(MeO)_2$bpy (**8**), 4,7-Ph_2phen (**9**), and 3,4,7,8-Me_4phen (**10**).

a. Determination of the Metal-Centered Configuration. The absolute metal-centered configuration was assigned by X-ray crystallography for two complexes, one recently published example[14] in addition to the complex Λ-(*S*)-**4d** shown in Figure 1. Complex Λ-(*S*)-**4d** was obtained from the highly diastereoselective reaction of (*S*)-**1d** with 2.2 equivalents of 1,10-phenanthroline (phen) in chlorobenzene (see below). The structure verifies a Λ configuration at the ruthenium center and a strong steric interference between the *tert*-butyl group and one of the phen ligands. Apparently, the steric strain results in a slightly distorted octahedral coordination sphere and a twisted salicyloxazoline ligand. This twist was not observed in a related structure bearing an isopropyl group at the oxazoline moiety.[14] Metal-centered configurations of all other here presented complexes were assigned relative to these two crystal structures by means of CD spectroscopy. Figure 2 depicts the CD spectra of the two diastereomers Λ-(*S*)-**4a** and Δ-(*S*)-**4a**.

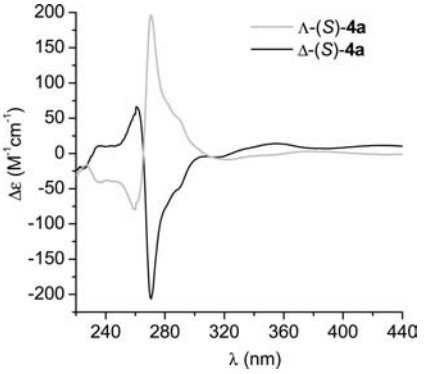


Figure 2. CD spectra of the purified diastereomeric products Λ-(*S*)-**4a** and Δ-(*S*)-**4a**. The spectra were measured in MeCN at concentrations of 0.2 mM.

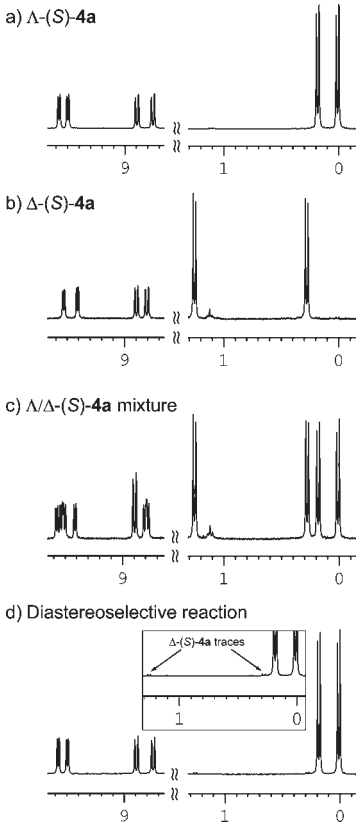


Figure 3. ^{1}H NMR spectra excerpts of the diastereomeric products (a) Λ-(*S*)-**4a** and (b) Δ-(*S*)-**4a**, (c) a 1:1 Λ/Δ-mixture, and (d) a reaction that yielded Λ-(*S*)-**4a** with a high diastereoselectivity (e.r. = 82:1). Shown are the signals of the phenanthroline protons in the α position relative to the coordinating nitrogens and the isopropyl CH_3 groups. Diastereomeric ratios were determined by an integration of the isopropyl signals (see inset in d).

b. Determination of Diastereomeric Ratios by ^{1}H NMR. Figure 3 displays excerpts of the ^{1}H NMR spectra of the purified diastereomers Λ-(*S*)-**4a** (Figure 3a), Δ-(*S*)-**4a** (Figure 3b), and their 1:1 Λ/Δ mixture (Figure 3c). The ^{1}H NMR spectra of the two diastereomers differ strongly in the chemical shifts of their protons in the ortho position to the pyridine N atoms of the phen ligands in addition to the isopropyl CH_3 groups, allowing for a determination of diastereomeric ratios conveniently by peak integration. Figure 3d displays an example of a reaction, (*S*)-**1a** → Λ-(*S*)-**4a**, affording a high Λ/Δ ratio, which was determined as 82:1 from

Table 1. Solvent Dependence of the Diastereoselective Formation of Λ-(*S*)-**4a** from (*S*)-**1a**[a]

entry	solvent	*T*/°C	*t*/h	yield/%	d.r.[b]
1	EtOH/H_2O 9:1	reflux	3	80	2:1
2	EtOH	reflux	4	70	3:1
3	CH_3CN	100 (sealed vial)	20	59	6:1
4	$ClCH_2CH_2Cl$	70	1	57	18:1
5	DMF	70	1	77	23:1
6	CH_2Cl_2	70 (sealed vial)	1	58	26:1
7	acetone	70 (sealed vial)	1	71	47:1
8	THF	70 (sealed vial)	1	67	60:1
9	C_6H_5Cl	70	1	79	82:1

[a] Reaction conditions: Reaction of 2.5 mM (*S*)-**1a** with 2.2 equiv of phen at the indicated time and temperature. [b] Diastereomeric ratios determined by ^{1}H NMR.

Table 2. Concentration Dependence of the Diastereoselective Formation of Λ-**4a** from (*S*)-**1a**[a]

entry	*c*/mM[b]	*t*/h	Yield/%	d.r.[c]
1	50	1.0	74	17:1
2	25	1.0	71	28:1
3	10	1.0	80	40:1
4	2.5	1.0	79	82:1
5	1.0	1.5	84	65:1

[a] Reaction with 2.2 equiv of phen in C_6H_5Cl at 70 °C for 1 h. [b] Concentration of (*S*)-**1a**. [c] Diastereomeric ratios determined by ^{1}H NMR.

the ratio of the integrals of the isopropyl CH_3 groups of the two diastereomers.

c. Solvent Dependence of the Diastereoselectivities. The influence of the solvent on the diastereoselectivity of the asymmetric ligand substitution chemistry was investigated by reacting (*S*)-**1a** in different solvents with 2.2 equivalents of phen. Table 1 reveals that the solvent has a dramatic influence on the distereoselective formation of Λ-(*S*)-**4a** over Δ-(*S*)-**4a**. Whereas wet EtOH (10% H_2O) under reflux yielded a very low 2:1 d.r., the reaction in C_6H_5Cl afforded Λ-(*S*)-**4a** with an excellent 82:1 d.r. and with a good yield of 79%. As a trend, high diastereoselectivities were observed in noncoordinating aprotic solvents, whereas EtOH/H_2O (2:1 d.r.), EtOH (3:1 d.r.), and MeCN (6:1 d.r.) gave poor results. It can be speculated that coordinating solvents are disadvantageous because of the need for higher reaction temperatures or reaction times, whereas protic solvents might form hydrogen bonds to the phenolate oxygen of the salox ligand, thus potentially reducing the binding strength and facilitating isomerization.

d. Concentration Dependence. We also noticed an influence of the concentration of precursor complex (*S*)-**1a** on the observed diastereoselectivities. Table 2 lists the results obtained from the reaction of (*S*)-**1a** at different concentrations with 2.2 equiv of phen in C_6H_5Cl at 70 °C for 1 h. Diastereomeric ratios Λ/Δ-(*S*)-**4a** range from 17:1 (50 mM (*S*)-**1a**) to 82:1 (2.5 mM (*S*)-**1a**) and demonstrate that lower concentrations afford better diastereoselectivities with an optimal concentration at around 2.5 mM. The large decrease in diastereoselectivity observed at higher concentrations is unexpected and might at least in part be explained by a chiral recognition process between the involved chiral complexes.[17] Another possible explanation takes into account the inverse effect of the substrate concentrations on the lifetime of the reaction intermediate (single phen ligand coordinated to the ruthenium), with a shorter lifetime being in principle desirable for a reaction under kinetic control and a longer lifetime for a reaction under thermodynamic control, thus being consistent with the below suggested mechanism.

Table 3. Influence of the Oxazoline Substituent in (*S*)-**1a**−**d** on the Diastereoselective Formation of Λ-(*S*)-**4a**−**d**[a]

entry	precursor	yield/%	d.r.[b]
1	**1a** (R = *i*Pr)	79	82:1
2	**1b** (R = Ph)	72	87:1
3	**1c** (R = Ile)	84	91:1
4	**1d** (R = *t*Bu)	70	95:1

[a] Conditions: Reaction with 2.2 equiv of phen in C_6H_5Cl at 70 °C for 1 h. [b] Diastereomeric ratios determined by ^{1}H NMR.

Table 4. Diastereoselectivity of the Formation of Λ-(*S*)-**4a**−**10** from (*S*)-**1a**[a]

entry	ligand[b]	main product	*t*/h	yield/%	d.r.[c]
1	bpy	Λ-(*S*)-**5**	2.5	66	120:1
2	4,4′-Me_2bpy	Λ-(*S*)-**6**	2.5	73	200:1
3	5,5′-Me_2bpy	Λ-(*S*)-**7**	2.5	63	>200:1
4	4,4′-$(MeO)_2$bpy	Λ-(*S*)-**8**	2.5	63	46:1
5	phen	Λ-(*S*)-**4a**	1.0	79	82:1
6	4,7-Ph_2phen	Λ-(*S*)-**9**	1.0	85	51:1
7	3,4,7,8-Me_4phen	Λ-(*S*)-**10**	1.0	74	45:1

[a] Conditions: 2.5 mM (*S*)-**1a** in C_6H_5Cl at 70 °C with 2.2 equiv of phen ligands or 4.0 equiv of bpy ligands. [b] bpy = 2,2′-bipyridine, phen = 1,10-phenanthroline. [c] Diastereoselectivities determined by ^{1}H NMR.

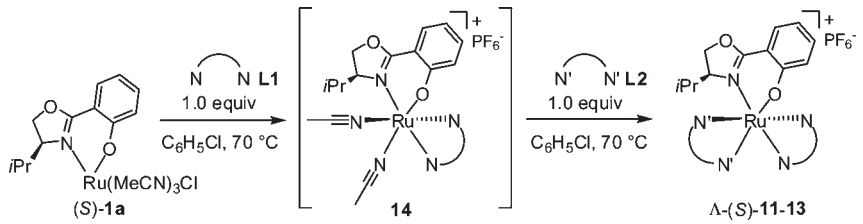
e. Influence of the Oxazoline Substituent. We investigated the influence of the substituent at the 5- position of the oxazoline moiety on the asymmetric induction step by using the reaction of precursor complexes (*S*)-**1a**−**d** with 2.2 equivalents of phen in chlorobenzene at 70 °C as the test system. In all four cases, the products Λ-(*S*)-**4a**−**d** were formed with high diastereoselectivities.[18] As shown in Table 3, replacing the isopropyl group in (*S*)-**1a** (82:1 d.r.) against phenyl ((*S*)-**1b**, 87:1 d.r.), isobutyl ((*S*)-**1c**, 91:1 d.r.), or *tert*-butyl ((*S*)-**1d**, 95:1 d.r.) resulted in the expected trend for the diastereomeric ratios Λ/Δ observed for **4a**−**d**, with the sterically most demanding *tert*-butyl group producing the highest asymmetric induction. However, the differences between the individual substituents are surprisingly subtle. This might be related to the high steric crowding of the chiral oxazoline within the octahedral coordination sphere, providing an already almost optimal asymmetric induction with the isopropyl substituent.

f. Ligand Dependence. In order to evaluate the effect of the nature of the bidentate ligand on the diastereoselectivity, we reacted (*S*)-**1a** in C_6H_5Cl at 70 °C with different bpy and phen ligands. Table 4 reveals that the d.r. values of the products Λ-(*S*)-**4a**−**10** range from 45:1 for 3,4,7,8-tetramethyl-1,10-phenanthroline (Λ-(*S*)-**10**) to higher than 200:1 for substituted bpy ligands such as 5,5′-dimethyl-2,2′-bipyridine (Λ-(*S*)-**7**). As a trend, bpy ligands provide a higher

(17) For an example, see: Gut, D.; Rudi, A.; Kopilov, J.; Goldberg, I.; Kol, M. *J. Am. Chem. Soc.* **2002**, *124*, 5449–5456.

(18) For the stereoselective coordination of chiral salicyloxazolines in half-sandwich complexes, see: (a) Brunner, H.; Nuber, B.; Prommesberger, M. *Tetrahedron: Asymmetry* **1998**, *9*, 3223–3229. (b) Davenport, A. J.; Davies, D. L.; Fawcett, J.; Russell, D. R. *Dalton Trans.* **2004**, 1481–1492. (c) Gott, A. L.; Clarke, A. J.; Clarkson, G. J.; Munslow, I. J.; Wade, A. R.; Scott, P. *Organometallics* **2008**, *27*, 2706–2714.

Scheme 4. Synthesis of the Mixed Polypyridine Ruthenium Salicylate Complexes Λ-(*S*)-**11-13** Starting from (*S*)-**1a** in a Two-Step Reaction Sequence with Complex **14** as the Identified Intermediate (Verified for **L1** = 4,4′-*t*Bu$_2$bpy)[a]



[a] See Table 5 for the identities of **L1** and **L2**.

Table 5. Diastereoselectivity of the Formation of the Mixed Ligand Complexes Λ-(*S*)-**11**−**13** from (*S*)-**1a**[a]

entry	L1	L2	main product	yield	d.r.[b]
1	bpy	5,5′-Me$_2$bpy	Λ-(*S*)-**11**	61%	62:1
2	5,5′-Me$_2$bpy	bpy	Λ-(*S*)-**12**	59%	142:1
3	4,4′-*t*Bu$_2$bpy	5,5′-Me$_2$bpy	Λ-(*S*)-**13**	64%	250:1

[a] Conditions: 2.5 mM (*S*)-**1a** in C_6H_5Cl at 70 °C first with 1 equiv of **L1** (1.0 h) and then with 2 equiv of **L2** (2.5 h). [b] Diastereoselectivities determined by ^{1}H NMR; d.r. = ratio between the main and the sum of the remaining diastereomers.

diastereoselectivity than the more rigid phen ligands, and additional substituents at the bpy ligands have beneficial effects, whereas this trend is just the opposite for phen ligands. The reasons for these trends are unclear; however, we can conclude that the observed diastereoselectivities range from satisfactory to excellent for every investigated bpy and phen ligand.

g. Synthesis of Mixed Ligand Complexes. The reactions of (*S*)-**1a** with consecutively two different 2,2′-bipyridine ligands afford mixed ligand ruthenium polypyridyl salicyloxazolinate complexes with high diastereoselectivities.[14] For example, the heating of (*S*)-**1a** with 1 equiv of bpy in chlorobenzene at 70 °C for 1 h and subsequently with 5,5′-Me$_2$bpy again in chlorobenzene at 70 °C for 2.5 h afforded Λ-(*S*)-**11** (61% yield) as the main diastereomer with a diastereomeric ratio of the main and the sum of the remaining isomers of d.r. = 62:1 (Scheme 4, Table 5, entry 1). Changing the order of ligands by first adding the larger 5,5′-Me$_2$bpy ligand followed by bpy afforded complex Λ-(*S*)-**12** with a further improved d.r. value of 142:1 (Table 5, entry 2). Finally, the reaction of (*S*)-**1a** with first 4,4′-*t*Bu$_2$bpy and then 5,5′-Me$_2$bpy afforded Λ-(*S*)-**13** with virtually complete diastereoselectivity out of four possible diastereomers (250:1 d.r.; Table 5, entry 3). Small amounts of side products which contain two of the same bidentate ligands were removed by silica gel flash chromatography.

Theoretically, in the course of the reaction of (*S*)-**1a** with **L1** and subsequently **L2**, overall, four diastereomers can be formed if **L1** ≠ **L2**: two with a Λ and two with a Δ configuration at the ruthenium center. However, in all three investigated examples, virtually no Δ diastereomers could be detected. The predominant minor diastereomer in the formation of Λ-(*S*)-**11** (Table 5, entry 1) is Λ-(*S*)-**12** (Table 5, entry 2) and vice versa. Thus, the coordinated salicyloxazoline in precursor complex (*S*)-**1a** provides an excellent control over the absolute metal-centered configuration.

Mechanistic Investigations. The crystal structure of the recently reported monocation of Λ-(*S*)-**11** (Figure 4)[14] provides valuable insight into the mechanism of the

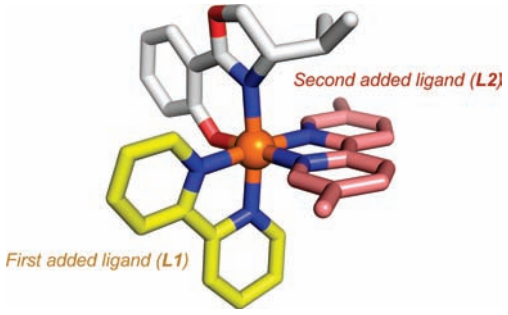


Figure 4. Structure of the tris-heteroleptic complex cation of Λ-(*S*)-**11**. This reveals the order in which the coordination sites at the ruthenium center are getting occupied in the course of the reaction of (*S*)-**1a** with first **L1** and subsequently **L2**. For crystallographic data, see ref 14.

consecutive incorporation of two different bpy ligands into the coordination sphere of (*S*)-**1a**. The observed relative and absolute stereochemistry of Λ-(*S*)-**11** is consistent with the intuitive assumption that the stereoselective incorporation of the first added bidentate ligand (**L1**) should occur at the two coordination sites at the farthest distance from the bulky *i*Pr group, whereas the second ligand **L2** would then replace the remaining two leaving groups, which are in direct proximity to the *i*Pr group.

In order to gain further insight into the reaction mechanism, we isolated and purified the unstable intermediate formed from the reaction of (*S*)-**1a** with one equivalent of 4,4′-*t*Bu$_2$bpy (**L1**) in C_6H_5Cl at 70 °C for 2.5 h. Analytical data and ^{1}H−^{1}H ROESY correlation measurements (see Supporting Information) reveal the formation of the single diastereomeric complex **14** (**L1** = 4,4′-*t*Bu$_2$bpy), in which one chloride and MeCN ligand of (*S*)-**1a** are replaced by 4,4′-*t*Bu$_2$bpy (Scheme 4). This stereochemistry thus confirms the incorporation of the first bidentate ligand at the coordination sites farthest away from the bulky *i*Pr group. To gain a better understanding of the reasons for the highly diastereoselective reaction (*S*)-**1a** → Λ-(*S*)-**13** (Table 5, entry 3), we calculated the relative energies of all four possible monocationic diastereomeric intermediates: the observed complex **14** plus the theoretically possible diastereomers **15**−**17** (Figure 5). For this, the geometries were optimized at RBP86/SVP and the relative energies calculated at RBP86/TZVPP//RBP86/SVP (Figure 5). Interestingly, relative to the experimentally observed complex **14**, the other diastereomers **15**−**17** are destabilized by 0.5−1.2 kcal/mol. This energy difference increases further to 0.8−1.7 kcal/mol in the presence of acetonitrile as the solvent (COSMO calculated energies), revealing that intermediate **14** is indeed thermodynamically favored over the three other possible diastereomeric intermediates.

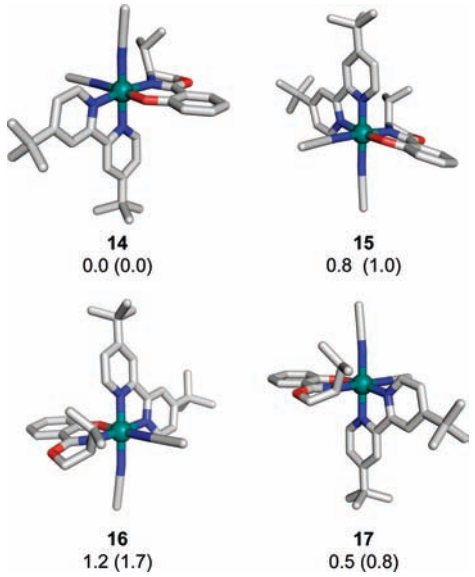


Figure 5. The reaction of (*S*)-**1a** with one equivalent of 4,4′-*t*Bu$_2$bpy under replacement of one MeCN and one chloride ligand. This can lead to the four diastereomers **14**−**17**. Shown are optimized geometries of the intermediates **14**−**17** at RBP86/SVP. Relative energies (kcal/mol) were calculated at RBP86/TZVPP//RBP86/SVP, and the COSMO calculated energies in acetonitrile are given in parentheses. All complexes are monocationic.

If the diastereoselective formation of the intermediate **14** is under thermodynamic control as suggested by the relative stabilities of the individual intermediates **14**−**17**, the individual diastereomers should be in equilibrium. To test this hypothesis, we varied the solvent for the conversion (*S*)-**1a** → Λ-(*S*)-**13**, exploiting the strong solvent effects. Accordingly, the reaction of (*S*)-**1a** with first 4,4′-*t*Bu$_2$bpy in EtOH at reflux for 2.5 h, followed by 5,5′-Me$_2$bpy also in EtOH for another 2.5 h at reflux, afforded all four possible diastereomers, with a low diastereomeric ratio of only 1.4:1 between Λ-(*S*)-**13** and the sum of the remaining isomers. Thus, whereas the reaction in the aprotic solvent C_6H_5Cl provided complete diastereoselectivity, this is not the case in EtOH. However, when we reacted (*S*)-**1a** first with 4,4′-*t*Bu$_2$bpy in EtOH at reflux for 2.5 h, followed by changing the solvent and heating for another 2.5 h but now in C_6H_5Cl at 80 °C, followed by the addition of 5,5′-Me$_2$bpy and heating again in C_6H_5Cl at 80 °C for another 1.5 h, Λ-(*S*)-**13** was formed with a significantly improved d.r. = 24:1. These experiments in different solvents lead to the following conclusions: First, whereas in C_6H_5Cl only the intermediate **14** is formed, in EtOH all four diastereomeric complexes **15**−**17** must be generated as intermediates, which has as a consequence an overall low diastereoselectivity for the formation of Λ-(*S*)-**13**. Second, the high diastereoselectivity obtained by reacting (*S*)-**1a** with the first bidentate ligand in EtOH and later with the second one in C_6H_5Cl strongly suggests that the four diastereomers **14**−**17**, all of which were initially formed in EtOH, subsequently convert to **14** upon changing the solvent to C_6H_5Cl, thus resulting in an overall high diastereomeric ratio of Λ-(*S*)-**13**. Consequently, the diastereomers **14**−**17** must be in equilibrium with each other, and this equilibrium is strongly influenced by the nature of the solvent. The conversion of individual diastereomers into each other is most likely induced by a MeCN ligand dissociation, leading to configurationally labile pentacoordinated intermediates. Since the calculated energy differences between the intermediates **14**−**17** cannot fully account for the experimentally observed high diastereoselectivities, it is more likely that the energy differences between the related diastereomeric pentacoordinated intermediates actually determine the overall diastereoselectivity of the reaction sequence. Additional kinetic effects may also play a role.

Replacement of the Salicyloxazolinate Ligand under Retention of Configuration. A chiral auxiliary for the asymmetric synthesis of metal complexes must not only control the metal-centered chirality in the course of ligand exchange reactions but also needs to be removable without affecting the metal-centered configuration. Salicyloxazolinate ligands fulfill both requirements since binding strength of the salicyloxazolinate ligand can be decreased in the presence of acid, presumably through protonation of the phenolate oxygen. Accordingly, by the treatment of Λ-(*S*)-**13** with 5 equiv of TFA at 50 °C in freshly distilled dry acetonitrile for 3.5 h in the dark, the salicyloxazoline ligand was smoothly replaced by two acetonitriles to afford intermediate **18**, followed by subsequent reaction with bpy to afford Λ-**19** with virtually complete retention of the configuration as determined by chiral HPLC analysis (e.r. = 166:1, Table 6, Entry 1, Scheme 5).[19] More conveniently, complex Λ-(*S*)-**13** can be converted into enantiopure Λ-**19** in a one-pot procedure by the reaction in dry MeCN with 15 equiv of bpy in the presence of 5 equiv of TFA at 110 °C in a sealed vial for just 2 h (e.r. = 250:1, Table 6, Entry 2). The absolute stereochemistry of Λ-**19** was verified by X-ray crystallography and CD analysis.[14]

Other bidentate ligands such as 4,4′-(MeO)$_2$bpy and phen, affording the virtually enantiopure complexes Λ-**20** and Λ-**21**, respectively (Table 6, Entries 3 and 4), demonstrate the generality of this one step auxiliary replacement under retention of the configuration. Interestingly, Table 6 also reveals the importance of the solvent (Table 6, entries 5−7). DMF and C_6H_5Cl lead to significant racemization, whereas in THF the enantiopurity comes close to MeCN. Apparently, a coordinating solvent is advantageous for suppressing racemization, which is consistent with the assumption that racemization is promoted by coordinatively unsaturated pentacoordinated intermediates, which become suppressed in coordinating solvents. Furthermore, it is noteworthy that other acids, such as HCl, lead to significant racemization, presumably through the interference of the counterion as a coordinating ligand (Table 6, entries 8 and 9).

Conclusions

We here demonstrated that chiral salicyloxazolines, conveniently accessible from chiral amino acids in just two steps, are highly valuable auxiliaries for the asymmetric synthesis of ruthenium polypyridyl complexes. We investigated the influence of coordinated chiral salicyloxazolinate ligands on the diastereoselective formation of octahedral polypyridine

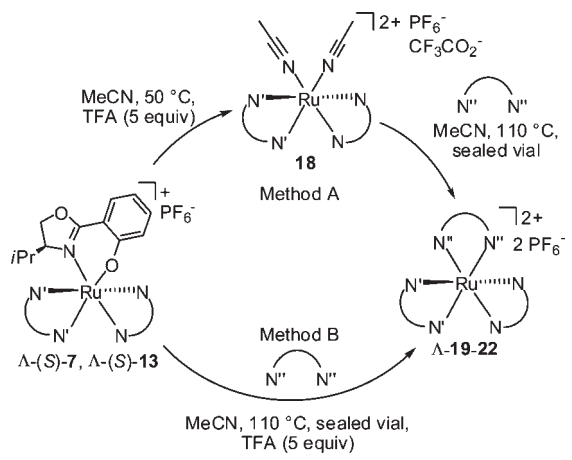
(19) For the substitution of two pyridines or two CO ligands under retention of configuration, see: (a) Rutherford, T. J.; Quagliotto, M. G.; Keene, F. R. *Inorg. Chem.* **1995**, *34*, 3857–3858. (b) Hua, X.; von Zelewsky, A. *Inorg. Chem.* **1995**, *34*, 5791–5797.

Table 6. Acid-Induced Substitution of the Chiral Salicyloxazoline under Retention of Configuration

entry	substrate	ligand **L3**	conditions	product	yield	e.r.[a]
1	Λ-(*S*)-**13**	bpy	TFA in MeCN, method A[b,c]	Λ-**19**	88%	166:1
2	Λ-(*S*)-**13**	bpy	TFA in MeCN, method B[b,d]	Λ-**19**	91%	250:1
3	Λ-(*S*)-**13**	4,4′-$(MeO)_2$bpy	TFA in MeCN, method B[b,d]	Λ-**20**	85%	200:1
4	Λ-(*S*)-**13**	phen	TFA in MeCN, method B[b,d]	Λ-**21**	85%	330:1
5	Λ-(*S*)-**7**	5,5′-Me_2bpy	TFA in C_6H_5Cl[e]	Λ-**22**	77%	25:1
6	Λ-(*S*)-**7**	5,5′-Me_2bpy	TFA in DMF[f]	Λ-**22**	48%	42:1
7	Λ-(*S*)-**7**	5,5′-Me_2bpy	TFA in THF[g]	Λ-**22**	75%	178:1
8	Λ-(*S*)-**7**	5,5′-Me_2bpy	HCl in C_6H_5Cl[h]	Λ-**22**	64%	4.4:1
9	Λ-(*S*)-**7**	5,5′-Me_2bpy	HCl in MeCN[i]	Λ-**22**	60%	2.6:1

[a] Enantiomeric ratios determined by chiral HPLC analysis. [b] Best results were obtained with freshly distilled MeCN over CaH_2. [c] Method A: (i) MeCN, 50 mM Λ-(*S*)-**13**, 5 equiv TFA, 50 °C, 3.5 h. (ii) 10 mM **18**, 15 equiv **L3**, 110 °C in sealed vial, 2 h. [d] Method B: One step substitution, MeCN, 50 mM Λ-(*S*)-**13**, 5 equiv TFA, 15 equiv **L3**, 110 °C in sealed vial, 2 h. [e] C_6H_5Cl, 25 mM Λ-(*S*)-**7**, 95 °C, 8 equiv of **L3**, 5 equiv TFA, 2 h. [f] DMF, 25 mM Λ-(*S*)-**7**, 95 °C, 8 equiv of **L3**, 5 equiv TFA, 5 h. [g] THF, 25 mM Λ-(*S*)-**7**, 95 °C, 8 equiv of **L3**, 5 equiv TFA, 3 h, sealed vial. [h] Saturated solution of HCl(g) in C_6H_5Cl, 25 mM Λ-(*S*)-**7**, 8 equiv **L3**, 95 °C in sealed vial, 24 h. [i] Saturated solution of HCl(g) in MeCN, 25 mM Λ-(*S*)-**7**, 8 equiv **L3**, 95 °C in sealed vial, 24 h.

Scheme 5. Acid-Promoted Replacement of the Salicyloxazoline Chiral Auxiliary under Retention of Configuration[a]



[a] Intermediate **18** was synthesized from Λ-(*S*)-**13**. See Table 6 for more details.

salicyloxazolinate ruthenium complexes and determined the most favorable reaction conditions. Most striking is the strong influence of the solvent on the observed diastereoselectivity with aprotic less polar solvents giving the best results. Computational and experimental results imply that the diastereoselectivity is under thermodynamic control. The following acid-promoted replacement of the salicyloxazoline occurs under retention of configuration and without any racemization if a coordinating solvent such as MeCN is used. The application of this and related chiral auxiliaries for the asymmetric synthesis of biologically active ruthenium complexes is underway in our laboratory.

Experimental Section

Materials and General Methods. All reactions were carried out under a nitrogen atmosphere. The reactions involving the formation of chiral ruthenium complexes were carried out in the dark as a precaution against light-induced decomposition and isomerization. Solvents were distilled under nitrogen from calcium hydride (CH_3CN, CH_2Cl_2, DMF, $ClCH_2CH_2Cl$) or sodium/benzophenone (Et_2O, THF). Chlorobenzene, acetone, and ethanol were HPLC grade without further drying. Reagents were purchased from Acros, Aldrich, or Alfa and used without further purification. Column chromatography was performed with silica gel (230−400 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance (300 MHz), a Bruker DRX (400 MHz), or a Bruker AM (500 MHz) spectrometer at ambient temperature. NMR standards used are as follows: (^{1}H NMR) CD_3CN = 1.94 ppm, $CDCl_3$ = 7.26 ppm. (^{13}C NMR) CD_3CN = 1.32 ppm, $CDCl_3$ = 77.16 ppm. ^{13}C NMR chemical shifts are reported in parts per million downfield from tetramethylsilane. IR spectra were obtained on a Bruker Alpha-P series FT-IR spectrometer. CD spectra were recorded on a JASCO J-810 CD spectropolarimeter. Chiral HPLC chromatograms were obtained with an Agilent 1200 Series HPLC System. High-resolution mass spectra were recorded on a Micromass AutoSpec instrument using ESI techniques. Elemental analysis data were obtained on an Elemental Analysensystem GmbH Vario EL III instrument and Heraeus CHN-Rapid-Analyzer. Diastereomeric ratios were determined by ^{1}H NMR. Enantiomeric ratios were determined with a Daicel Chiralcel OD-R (250 × 4 mm) HPLC column on an Agilent 1200 Series HPLC System. The flow rate was 0.5 mL/min, the column temperature was 40 °C, and UV-absorption was measured at 254 nm. Solvent A = 0.087% H_3PO_4, solvent B = MeCN, with a typical linear gradient of 30% to 60% B in 20 min. $[(\eta^6\text{-}C_6H_6)RuCl_2]_2$ and salicyloxazolines (*S*)-**2a**−**d** were prepared according to published procedures.[14,15] The complexes Λ-(*S*)-**11**−**13** and Λ-**19**−**21** have been reported previously.[14] See the Supporting Information for the synthesis and analytical data of the complexes (*S*)-**3b**−**d**, (*S*)-**1b**−**d**, Λ-(*S*)-**4b**−**d**, Λ-(*S*)-**5**−**10**, and the intermediates **14** and **18**.

Benzene Half-Sandwich Complex (*S*)-3a. A solution of $[(\eta^6\text{-}C_6H_6)_2RuCl_2]_2$ (200 mg, 0.40 mmol), (*S*)-5-isopropyl-2-(2′-hydroxyphenyl)oxazoline [(*S*)-**2a**] (174 mg, 084 mmol), and K_2CO_3 (122 mg, 0.88 mmol) in CH_3CN (32 mL) was purged with N_2 for 20 min and then stirred at 70 °C (oil bath temperature) for 3 h. The reaction mixture was cooled to room temperature and separated from unsoluble salts by filtration. The addition of ether (10 mL) into the concentrated filtrate (5 mL) gave a brown-orange precipitate, which was centrifuged, washed twice with ether, and dried under a high vacuum to yield (*S*)-**3a** as a single diastereomer (265 mg, 79%).

^{1}H NMR (300.1 MHz, $CDCl_3$): δ (ppm) 7.35 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.12 (td, *J* = 7.8, 1.8 Hz, 1H), 6.68 (d, *J* = 8.1 Hz, 1H), 6.36 (t, *J* = 7.8 Hz, 1H), 5.60 (s, 6H), 4.77 (dt, *J* = 9.3, 3.0 Hz, 1H), 4.58 (dd, *J* = 9.0, 3.6 Hz, 1H), 4.46 (t, *J* = 9.3 Hz, 1H), 2.66 (m, 1H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ (ppm) 168.5, 162.9, 134.2, 129.2, 122.6, 114.1, 109.0, 83.8, 75.9, 67.2, 30.2, 19.9, 14.9.

IR (neat): ν (cm^{-1}) 3065, 2954, 2916, 2868, 1622, 1542, 1488, 1470, 1445, 1430, 1388, 1349, 1239, 1141, 1118, 1068, 992, 979, 934, 925, 894, 853, 825, 761, 684, 663, 612, 576, 542, 506, 441, 435, 405.

HRMS calcd for $RuO_2NC_{18}H_{20}$: $(M - Cl)^+$ 384.0532. Found: 384.0536.

Elem anal. calcd for $RuClO_2NC_{18}H_{20}$: N, 3.34; C, 51.61; H, 4.81. Found: N, 3.32; C, 52.00; H, 4.65.

Precursor Complex (*S*)-1a. A solution of (*S*)-**3a** (200 mg, 0.48 mmol) in dry CH_3CN (210 mL) was purged with N_2 for 20 min and then irradiated with a mercury medium pressure lamp (Heraeus UV Reactor System, Heraeus Noblelight power source, UV immersion

lamp TQ 150, 150 W, quartz cooling jacket) in combination with a uranium filter for 2 h while nitrogen was bubbled through the solution. The resulting solution was dried in vacuo at room temperature to afford the yellow precursor complex (*S*)-**1a** as a mixture of two diastereomers (6:1; 221 mg, 96%). Compound (*S*)-**1a** is quite unstable and should be used freshly or stored under nitrogen at −20 °C for not more than two weeks.

^{1}H NMR (300.1 MHz, CD_3CN) for the major diastereomer: δ (ppm) 7.43 (dd, J = 8.1, 1.8 Hz, 1H), 6.88 (td, J = 7.8, 1.8 Hz, 1H), 6.46 (d, J = 8.1 Hz, 1H), 6.17 (td, J = 7.8, 1.2 Hz, 1H), 4.58 (dt, J = 9.3, 3.0 Hz, 1H), 4.42 (dd, J = 8.7, 3.3 Hz, 1H), 4.25 (t, J = 9.0 Hz, 1H), 2.52 (s, 3H), 2.34 (s, 3H), 2.26 (s, 3H), 0.89 (m, 1H), 0.79 (d, J = 7.2 Hz, 3H), 0.66 (d, J = 7.2 Hz, 3H).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ (ppm) 170.8, 161.8, 159.9, 130.9, 129.2, 122.7, 111.0, 70.8, 66.2, 28.3, 17.8, 12.9, 3.2, 2.94, 2.88.

IR (thin film): ν (cm^{-1}) 3459, 2962, 2919, 2871, 2267, 1618, 1539, 1471, 1445, 1382, 1350, 1232, 1156, 1066, 854, 755.

HRMS calcd for $RuClO_2N_4C_{18}H_{23}$: $(M)^+$ 464.0548. Found: 464.0550.

Diastereoselective Coordination Chemistry: Synthesis of Λ-(*S*)-4a. A solution of fresh precursor (*S*)-**1a** (23.2 mg, 0.050 mmol) and 1,10-phenanthroline (19.6 mg, 0.11 mmol) in chlorobenzene (20 mL) was purged with N_2 for 15 min and then heated at 70 °C for 1 h. The resulting brown solution was cooled to room temperature, dried in vacuo, and the crude material subjected to silica gel chromatography with acetonitrile and later acetonitrile/water/saturated aqueous KNO_3 (200:3:1) as the eluent. The product eluents were concentrated to dryness, and the resulting material was dissolved in minimal amounts of ethanol/water. The product was precipitated by the addition of excess solid NH_4PF_6. The purple precipitate was centrifuged, washed twice with water, and dried under a high vacuum to afford Λ-(*S*)-**4a** as a PF_6 salt in 79% (32.1 mg) with 82:1 d.r.

^{1}H NMR (300.1 MHz, CD_3CN): δ (ppm) 9.57 (dd, J = 5.4, 1.2 Hz, 1H), 9.49 (dd, J = 5.3, 1.1 Hz, 1H), 8.89 (dd, J = 8.2, 1.1 Hz, 1H), 8.75 (dd, J = 8.2, 1.1 Hz, 1H), 8.46−8.50 (m, 3H), 8.23−8.38 (m, 5H), 8.18 (dd, J = 8.2, 5.3 Hz, 1H), 7.84 (dd, J = 8.5, 2.6 Hz, 1H), 7.65 (dd, J = 5.3, 1.2 Hz, 1H), 7.51−7.59 (m, 2H), 7.21 (m, 1H), 6.55 (m, 2H), 4.78 (t, J = 9.3 Hz, 1H), 4.61 (dd, J = 9.4, 3.5 Hz, 1H), 4.17 (dt, J = 9.2, 3.1 Hz, 1H), 0.18 (d, J = 7.0 Hz, 3H), 0.01 (d, J = 7.0 Hz, 3H), −0.42 (m, 1H).

^{13}C NMR (125.8 MHz, CD_3CN): δ (ppm) 171.5, 164.0, 155.3, 153.0, 152.8, 152.7, 151.7, 150.1, 150.0, 135.92, 135.85, 135.6, 134.4, 133.7, 131.6, 131.3, 131.1, 130.7, 128.69, 128,68, 128.61, 128.47, 126.4, 126.1, 125.9, 125.4, 124.3, 113.9, 110.7, 73.3, 68.1, 30.9, 18.4, 13.1.

IR (neat): ν (cm^{-1}) 3057, 2961, 1606, 1537, 1469, 1442, 1424, 1408, 1287, 1262, 1199, 1156, 1066, 964, 829, 754, 731, 555.

HRMS calcd for $RuO_2N_5C_{36}H_{30}$ $(M - PF_6)^+$: 666.1438. Found: 666.1425.

Elem anal. calcd for $RuPF_6O_2N_5C_{36}H_{30}$: N, 8.64; C, 53.34; H, 3.73. Found: N, 8.44; C, 53.78; H, 3.39.

CD (MeCN): λ, nm ($\Delta\varepsilon$, M^{-1} cm^{-1}) 260 (−79), 270 (+197).

Replacement of the Chiral Auxiliary: Synthesis of Complex Λ-22. In a closed brown glass vial, a solution of Λ-(*S*)-**7** (4.1 mg, 0.0050 mmol), trifluoroacetic acid (1.9 μL, 0.025 mmol), and 5,5′-dimethyl-2,2′-bipyridine (7.4 mg, 0.040 mmol) in freshly distilled dry THF (0.2 mL) was heated at 95 °C for 3 h under a nitrogen atmosphere. The reaction mixture was cooled to room temperature and dried in vacuo. The crude material was subjected to silica gel chromatography with acetonitrile and later acetonitrile/water/saturated aqueous KNO_3 (80:3:1). The product eluents were concentrated to dryness, and the resulting material was dissolved in minimal amounts of ethanol/water. The product was precipitated by the addition of excess solid NH_4PF_6. The orange precipitate was centrifuged, washed twice with water, and dried under a vacuum to yield Λ-**22** as the hexafluorphosphate salt (3.5 mg, 75%). The enantiopurity (178:1) was determined by chiral HPLC analysis.

^{1}H NMR (300.1 MHz, CD_3CN): δ (ppm) 8.32 (d, J = 8.4 Hz, 6H), 7.85 (d, J = 8.1 Hz, 6H), 7.45 (s, 6H), 2.21 (s, 18H).

^{13}C NMR (125.8 MHz, CD_3CN): δ (ppm) 154.3, 151.01, 137.74, 137.68, 122.9, 17.28.

IR (neat): ν (cm^{-1}) 2926, 1606, 1579, 1476, 1388, 1312, 1275, 1243, 1146, 1043, 833, 818, 739, 555, 521, 432.

HRMS calcd for $RuN_6C_{36}H_{36}PF_6$: $(M - PF_6)^+$ 799.1681. Found: 799.1684.

CD (MeCN): λ, nm ($\Delta\varepsilon$, $M^{-1}cm^{-1}$): 284 (−50), 299 (+111).

Elem anal. calcd for $RuP_2F_{12}N_6C_{36}H_{36}$: N, 8.90; C, 45.82; H, 3.85. Found: N, 8.60; C, 45.47; H, 3.47.

General Method for the Replacement of the Chiral Auxiliary. In a sealed brown glass vial, a solution of a salicyloxazolinate ruthenium complex (0.010 mmol), trifluoroacetic acid (3.8 μL, 0.050 mmol), and a 2,2′-bipyridine or 1,10-phenanthroline ligand (0.15 mmol) in CH_3CN (0.2 mL) was heated at 110 °C (oil bath temperature) for 2 h under a nitrogen atmosphere. The reaction mixture was cooled to room temperature and dried in vacuo. The crude material was subjected to silica gel chromatography with acetonitrile and later acetonitrile/water/saturated aqueous KNO_3 (50:3:1). The product eluents were concentrated to dryness, and the resulting material was dissolved in minimal ethanol/water. The product was precipitated by the addition of excess solid NH_4PF_6. The orange precipitate was centrifuged, washed twice with water, and dried under a high vacuum to yield the ruthenium polypyridyl complex with high enantiopurity as the Λ enantiomer.

Crystal Structure Determination of Λ-(*S*)-4d. Crystals of Λ-(*S*)-**4d** were obtained by slow diffusion of a solution of Λ-(*S*)-**4d** in CH_2Cl_2 layered with Et_2O. The data were collected on an STOE IPDS2 diffractometer using Mo Kα radiation at 100 K. The structure was solved using direct methods (SIR-92[20]) and refined on F2 using the full matrix least-squares procedure in SHELXL-97,[21] all nonhydrogen atoms anisotropically and H atoms "riding" on calculated positions. The absolute structure could be determined ("Flack parameter" −0.02(2)). See the Supporting Information for crystallographic data.

Computational Details. The geometries of the intermediates **14**−**17** were optimized at the RBP86/SVP[22,23] level of theory using the RI (Resolution of Identity)[24] approximation in the TURBOMOLE[25] program package. The optimized structures have been verified as energy minima by calculating the vibrational frequencies. Single point energy calculations were done with larger basis set[22] using RBP86/SVP optimized structures. This level of theory is denoted as RBP86/TZVPP//RBP86/SVP. The effect of a solvent was estimated with the continuum solvation model COSMO.[26] The COSMO calculations were carried out with a dielectricity constant ε = 36.64 for the solvent acetonitrile.

Acknowledgment. This work was supported by the German Research Foundation (DFG). We thank Prof. Haiping Xia (Xiamen University, Xiamen, P. R. China) for the measurement of several elemental analyses.

Supporting Information Available: X-ray crystallographic data for complex Λ-(*S*)-**4d**, synthesis procedures, analytical data, and CD spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

(20) Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A. *J. Appl. Crystallogr.* **1993**, *26*, 343–350.
(21) Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *A64*, 112–122.
(22) (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098–3100. (b) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822–8824.
(23) Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305.
(24) Eichkorn, K.; Treutler, O.; Öhm, H.; Häser, M.; Ahlrichs, R. *Chem. Phys. Lett.* **1995**, *242*, 652–660.
(25) Ahlrichs, R.; Bär, M.; Häser, M.; Horn, H.; Kölmel, C. *Chem. Phys. Lett.* **1989**, *162*, 165–169.
(26) Schäfer, A.; Klamt, A.; Sattel, D.; Lohrenz, J. C. W.; Eckert, F. *Phys. Chem. Chem. Phys.* **2000**, *2*, 2187–2193.