Dynamic Kinetic Transformation of Sulfinyl Chlorides: Synthesis of Enantiomerically Pure C_2-Symmetric Bis-Sulfoxides

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Two modular and highly convergent approaches for the synthesis of both isomers of a large number of optically pure C_2-symmetric bis-sulfoxides have been developed, and their scope and limitations have been assessed. The first one uses as intermediate diastereomerically pure C_2-symmetric bis-sulfinate esters **6(*S*$_S$,*S*$_S$)** and **6(*R*$_S$,*R*$_S$)**, obtained by dynamic kinetic resolution of ethane-1,2-bis-sulfinyl chloride **5**. A single inducer of chirality, the glucose-derived DAG (diacetone-D-glucose) **1** is used for the enantioselective synthesis of both diastereomerically pure C_2-symmetric bis-sulfinate esters, thanks to the opposite stereodirecting effect of pyridine and ^{i}Pr$_2$NEt used to catalyze the reaction. The second approach is based on the copper-catalyzed oxidative coupling of optically pure lithiomethyl sulfoxides. Both isomers of a large number of methyl sulfoxides can be obtained in a convergent manner using (R_S)- and (S_S)-DAG methanesulfinate esters **8*R*$_S$** and **8*S*$_S$**. Methanesulfinates **8*R*$_S$** and **8*S*$_S$** are also obtained in an enantioselective way by a dynamic kinetic resolution of methane sulfinyl chloride **24**. The final bis-sulfoxides are obtained with enhanced enantioselectivities compared to the corresponding monomers, as a result of the Horeau effect which is operating in both approaches. A model based on the formation of pentacoordinated sulfur intermediate is proposed. This model can explain the dynamic kinetic resolution observed via Berry pseudorotations, without the commonly accepted in situ racemization of the starting material. The usefulness of the approaches is demonstrated by the preparation of complexes of Pd(II) and Ru(II) bearing bidentated chiral sulfoxides as ligands.

Introduction.

The search for new and efficient methods for the synthesis of optically pure compounds has been an active area of research in organic synthesis.[1] While tremendous advances have been made in asymmetric synthesis, either substrate driven or catalytically induced, resolution of racemates is still the most important industrial approach to the synthesis of enantiomerically pure compounds.[2] A kinetic resolution is defined as a process where the two enantiomers of a racemate are transformed to products at different rates.[3] Thus, in an efficient kinetic resolution, one of the enantiomers of the racemic mixture is transformed to the desired product while the other is recovered intact (Figure 1A). Although efficient in terms of producing highly enantiomerically pure compounds, it has the limitation of having a maximum theoretical yield of 50%. Many efforts have been devoted to overcome this limitation and to afford compounds with high enantiomeric purity, but with improved yields.[4] Among the various solutions developed to date, dynamic kinetic resolution (DKR) strategies have enjoyed increasing attention in the past few years (Figure 1B).[5]

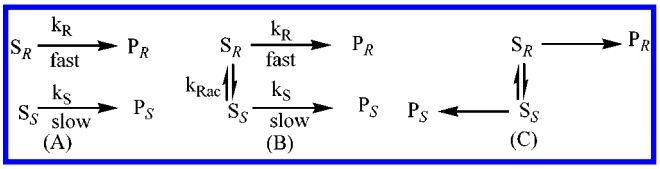

Figure 1. Kinetic (A), dynamic kinetic (B), and enantiodivergent dynamic kinetic (C) resolution of racemates.

DKR combines the resolution step of kinetic resolution with an in situ equilibration or racemization of the chirally labile substrate, which leads to an efficient use of the starting material. In such a process, one can in principle obtain a quantitative yield of one of the enan-

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tiomers. Additionally, provided that the rate of equilibration of the substrate enantiomers is about the same or higher than that of the removal of one enantiomer from the system, DKR will lead to a higher enantiomeric ratio of the product. Racemization of the substrate can occur either chemically, enzymatically, or spontaneously; conditions must be chosen to avoid the racemization of product. Several examples of efficient dynamic kinetic resolution of enantiomers and diastereoisomers have recently been reported.[6] Nevertheless, a drawback for a DKR, especially for enzymatic DKR, is that only one of the two enantiomers is accessible. In the case of chemical DKR, a change to the enantiomer (generally the nonnatural one) of the chiral inducer is needed. Thus, an ideal asymmetric synthesis involving a dynamic kinetic resolution would be one able to furnish both enantiomers with high ee, in two pathways equivalent in energy, that is in an enantiodivergent manner[7] (Figure 1C). We have recently been involved in the synthesis of chiral sulfoxides,[8] and in the present work we report a detailed study of two complementary routes for the synthesis of both enantiomers of C_2-symmetric sulfoxides.[9] The two methods rely on a dynamic kinetic resolution of either mono- or bis-sulfinyl chlorides. Additionally, as a simple change of the tertiary amine used to catalyze the reaction induces a complete change in the stereocourse of the reaction pathway, the methods presented here allow the synthesis of both isomers in an enantioselective manner. As nucleophilic substitution on sulfur atom can take place via an addition−elimination pathway with a sulfurane intermediate, this method may be one of the rare examples of a DKR that does not rely on the general accepted rule of an in situ racemization of one of the enantiomers. A plausible model for dynamic kinetic resolution occurring via a Berry pseudorotation is proposed. The product bis-sulfoxides are used for the synthesis of complexes of transition metals, including palladium and ruthenium, of synthetic and pharmacological interest.

Results and Discussion

Advances in metal-catalyzed enantioselective reactions have accelerated research on the synthesis of chiral ligands.[10] In this regard, the use of C_2 symmetry as a chiral ligand design element is a well-recognized strategy for restricting the number of diastereomeric transition states in metal-catalyzed enantioselective processes.[11]

Figure 2. Structural similarities of ethane-bridged C_2-symmetric bis-sulfoxides and P-chiral diphosphines.

While there are a variety of P/P[12] and N/N[13] ligands, the use of S/S[14] ligands is scarce.[15] Enantiopure sulfoxides, especially C_2-symmetric bis-sulfoxides, offer unique features as transition-metal ligands; the inherent chirality of the coordinating sulfinyl sulfur atom is able to transfer efficiently the chiral information to the coordination sphere of the transition metal. The bidentate complex of ruthenium(II) of various racemic ethane- and propane-bridged bis-sulfoxides have been shown recently to accumulate inside the cell and to interact with DNA, suggesting their potential use as anticancer agents.[16] The main limitation for these applications is the absence of a general method able to form compounds with two stereogenic sulfur atoms in enantiopure form. Inspired by good results obtained in metal catalyzed asymmetric reactions by P-chiral ligands, such as the DIPAMP and analogues,[17] we started a program for the synthesis of ethane-bridged C_2-symmetric bis-sulfoxides (Figure 2).

For the general synthesis of ethane-bridged C_2-symmetric bis-sulfoxides, three approaches are considered: enantioselective oxidation of bis-sulfides[18](Scheme 1A), nucleophilic substitution of chiral bis-sulfinate esters[19,20]

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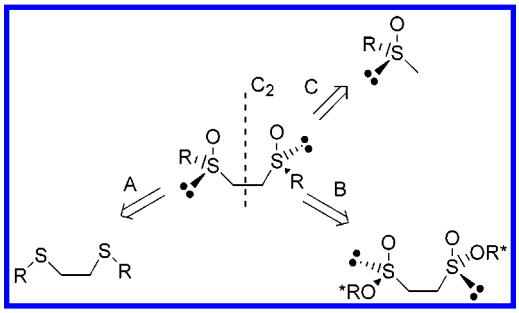
Scheme 1. Different Routes to Optically Pure C_2-Symmetric Bis-sulfoxides



(Scheme 1B), and copper-catalyzed dimerization of lithiomethyl sulfoxides[21,22] (Scheme 1C).

The enantioselective oxidation of both sulfur atoms in bis-sulfides (Scheme 1A) is the most direct approach to C_2-symmetric bis-sulfoxides. However, this approach, which has been used to oxidize aryl sulfides, gives the desired sulfoxides with moderate diastereoselectivity, together with a mixture of monosulfoxides as well as sulfoxide sulfone.[23]

Dynamic Kinetic Resolution of Ethane 1,2-Bis-sulfinyl Chlorides: Enantiodivergent Synthesis of Bis-sulfinate Esters and Bis-sulfoxides. The most convergent and general method for the synthesis of enantiopure C_2-symmetric bis-sulfoxides is the nucleophilic addition of an organometallic reagent to a compound having two electrophilic sulfurs with established chirality and the subsequent displacement of the bis-sulfoxide (Scheme 1B). Either kinetic resolution of ethane-1,2-bis-sulfinyl chloride or a high separation factor of the intermediate diastereomers that are formed permits the bis-sulfinylating agent to be obtained in high de. An Andersen-type method should be a good adaptation of this strategy.[24] The first step is the synthesis of bis-sulfinate esters, by condensation of ethane-1,2-bis-sulfinyl chloride and a secondary chiral alcohol. As both chiral sulfur atoms are simultaneously formed, the diastereomeric ratio of the C_2-symmetric isomers should be much higher than the diastereomeric ratio of mono-sulfinate substrate, as a consequence of the Horeau effect.[25a,b] This effect, which has been used to describe the stereochemical outcome in the dimerization of a scalemic compound (vide infra), applies to the simultaneous diastereoselective bis-functionalization of a substrate.[25c] In theory, if a reaction gives x:1 diastereomeric ratio in the mono-diastereoselective process, such as the formation of monosulfinate ester, for instance, assuming that there is no double stereodifferentiation in the formation of bis-sulfinate esters (the formation of the second sulfinate is not influenced by the formation of the first one), the diastereomeric ratio of C_2-symmetric bis-sulfinate should be x^2:1. The bisfunctionalization process thus gives rise to C_2-symmetric bis-sulfinate esters in higher diastereomeric ratio than the formation of monosulfinate, and also generates a non-C_2-symmetric diastereoisomer in a $2x$ amount.[26] The determination of the S_S/R_S ratio in the methanesulfinates may help in the design of the best approach for the synthesis of bis-sulfinate esters, and so also for bis-sulfoxides. Recently, we have reported a study of the stereochemical outcome of the reaction of various secondary carbinols with methanesulfinyl chloride.[27] The commercially available diacetone-D-glucose **1** and dicyclohexylidene-D-glucose **2** were shown to be the best inducers of chirality and thus were used in the present study.

The starting bis-sulfinyl chloride **5** was obtained in two steps from 1,2-ethanedithiol **3.** Condensation of chlorine and **3** leads to the formation of the corresponding polymer **4**, and further treatment with chlorine in acetic acid afforded the desired 1,2-bis-sulfinyl chloride **5** in good yield (Scheme 2). The bis-sulfinates were obtained by condensation of ethane-1,2-bis-sulfinyl chloride[28] and a chiral alcohol in the presence of pyridine (Scheme 3), and the results are presented in Table 1.

The bis-sulfinate esters are formed in good chemical yield and variable diastereoselectivity depending on the chiral auxiliary used. Both secondary carbinols **1** and **2** gave the C_2-symmetric diastereisomer (R_S,R_S) as the major isomer in more than 98% diastereomeric excess with regard to the other C_2-symmetric bis-sulfinate (Table 1, entries 1 and 3).

The ^{1}H NMR spectrum of the crude mixture in $CDCl_3$ did not permit the determination of the diastereomeric ratio. Variation of solvent revealed that deuterated benzene was best for the determination of the stereochemical outcome of the reaction, with clean separation of all the anomeric protons for the species present in the mixture.

By successive addition of the secondary carbinol and the minor diastereoisomer **6(S_S,S_S)** (vide infra) to the crude mixture of bis-sulfinate esters obtained with pyridine as the base, the doublet at 5.76 ppm was assigned to the anomeric protons of **6(S_S,S_S)**; the doublet at 5.83 ppm corresponds to the anomeric protons of **6(R_S,R_S),** while the non-C_2-symmetric **6(R_S,S_S)** has two different anomeric protons that appear as two doublets at 5.79 and 5.85 ppm (Figure 3). The same assignment protocol was

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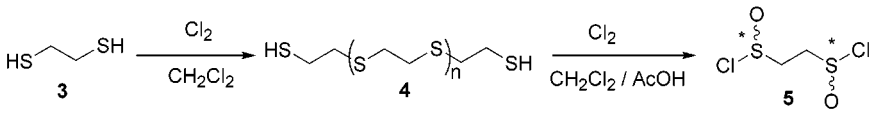
Scheme 2. Synthesis of Ethane 1,2-Bis-sulfinyl Chloride



Scheme 3. Enantioselective Dynamic Kinetic Resolution of Ethane-1,2-Bis-sulfinyl Chloride 5

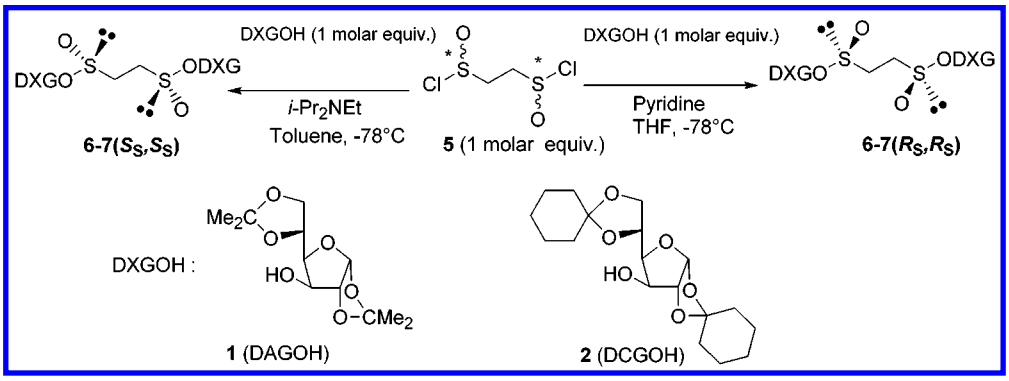
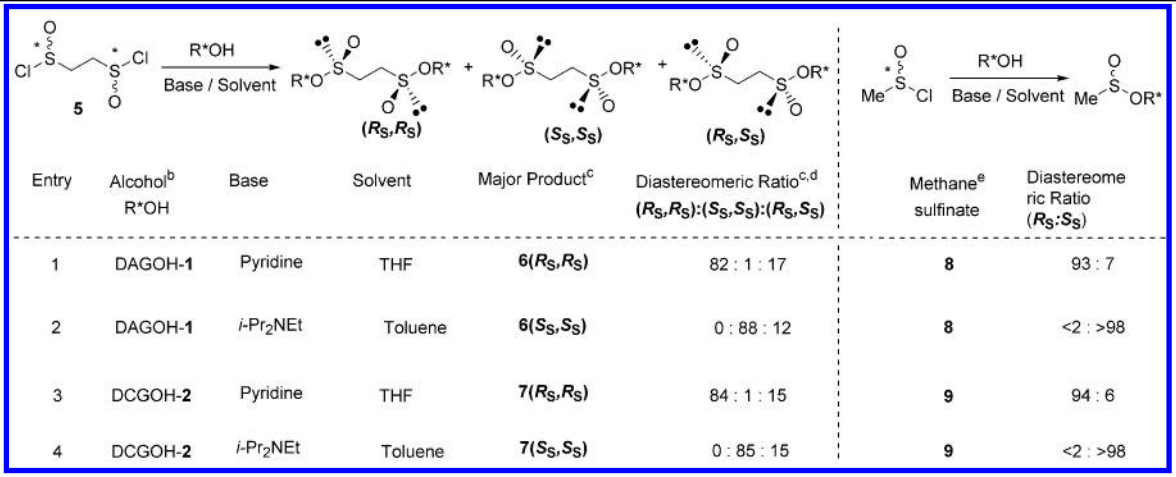


Table 1. Reaction of Ethane-1,2-bis-sulfinyl Chloride with Glucose-Derived Carbinols[a]



Entry	Alcohol[b] R*OH	Base	Solvent	Major Product[c]	Diastereomeric Ratio[c,d] (R_S,R_S):(S_S,S_S):(R_S,S_S)	Methane sulfinate[e]	Diastereomeric Ratio (R_S:S_S)
1	DAGOH-**1**	Pyridine	THF	**6**(R_S,R_S)	82 : 1 : 17	**8**	93 : 7
2	DAGOH-**1**	*i*-Pr_2NEt	Toluene	**6**(S_S,S_S)	0 : 88 : 12	**8**	<2 : >98
3	DCGOH-**2**	Pyridine	THF	**7**(R_S,R_S)	84 : 1 : 15	**9**	94 : 6
4	DCGOH-**2**	*i*-Pr_2NEt	Toluene	**7**(S_S,S_S)	0 : 85 : 15	**9**	<2 : >98

used in the case of DCG bis-sulfinate esters **7(S_S,S_S)**, **7-(R_S,R_S)**, and **7(R_S,S_S)** (Figure 4).

A simple change in the amine used to catalyze the reaction from the aromatic pyridine to the aliphatic and hindered diisopropylethylamine (DIPEA) completely changed the diastereoselectivity of the reaction (Table 1, entries 2 and 4). Only the C_2-symmetric bis-sulfinate ester **6(S_S,S_S)**, together with the non-C_2-symmetric bis-sulfinate ester **6(R_S,S_S)**, are obtained in an 88:12 ratio (Table 1, entry 2). Likewise, no trace of the other C_2-symmetric bis-sulfinate **7(R_S,R_S)** was detected when the DCGOH was used as chiral auxiliary in the presence of Hünig's base (Table 1, entry 4). A single recrystallization from diethyl ether−hexanes mixture allowed the isolation of diastereomerically pure C_2-symmetric bis-sulfinate ester **6(S_S,S_S)** in 65% yield, and the bis-sulfinate ester **7(S_S,S_S)** in 60%. It is worth noting that the major isomer obtained has the absolute configuration at the sulfinyl sulfurs opposite to that formed with pyridine as base. Accordingly, the opposite stereochemical course observed by the simple change of the (achiral) amine used to catalyze the reaction is formally equivalent to the change of the inducer of chirality from the cheap and commercially available diacetone-D-glucose to the unnatural diacetone-L-glucose.

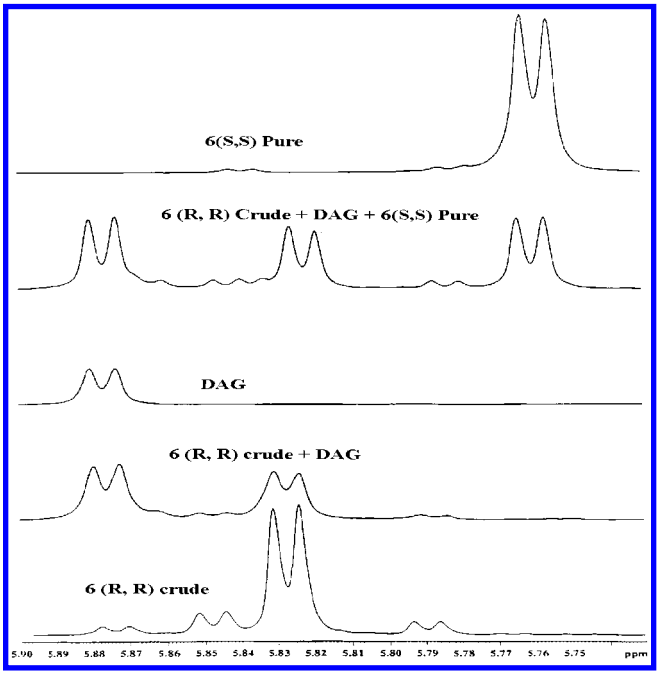


Figure 3. ^1H NMR analysis of the anomeric signals of DAG bis-sulfinate esters **6**.

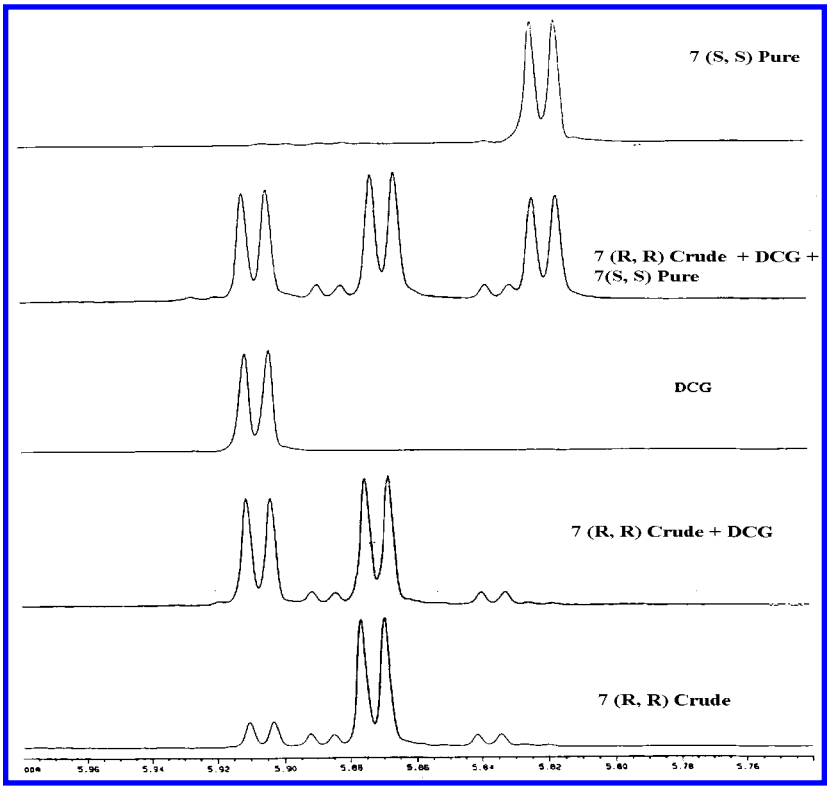


Figure 4. ^{1}H NMR analysis of the anomeric signals of DCG bis-sulfinate esters **7**.

The method summarized in Scheme 3 furnishes both C_2-symmetric bis-sulfinate esters epimers at the sulfinyl sulfur with high de in two very similar pathways. Moreover, the ratio of C_2-symmetric bis-sulfinate esters **6** and **7** corresponds closely to the square of the ratio of methanesulfinate diastereoisomers **8** and **9**, respectively (Table 1), demonstrating the operation of Horeau effect. The crude reaction mixture can lead to C_2-symmetric bis-sulfoxides in high ee and may be used directly in the next step without further purification.

The sulfur atom in the sulfinyl chloride is tetrahedral and can thus exist in two enantiomeric forms. Hence, the symmetric ethane-1,2-bis-sulfinyl chloride **5**[29] is a mixture of *meso* (*R*,*S*) and *dl* pair [(*R*,*R*), (*S*,*S*)] in a 1:1 ratio. In the hypothetic case of a reaction of a chiral substrate (Aux*) with ethane 1,2-bis-sulfinyl chloride mixture, a good kinetic resolution will lead to up to 50% yield of the diastereoisomers Aux*(R_S,S_S), to 25% of the diastereisomer Aux*(R_S,R_S) and finally to up to 25% of the diastereisomer Aux*(S_S,S_S).[30] Condensation of 2 molar equiv of glucose-derived secondary carbinols, diacetone-D-glucose (DAGOH) **1** or dicyclohexylidene-D-glucose (DCGOH) **2**, and 1 molar equiv of ethane-1,2-bis-sulfinyl chloride[6] **5** in the presence of pyridine or Hunig's base gave 1,2-bis-sulfinate esters **6** and **7,** respectively, in high yield and high diastereoselectivity (Table 1). Taking into account that (i) stoechiometric quantities of reagents has been used in all runs, (ii) the conversion is occurring with nearly quantitative yield, and (iii) the diastereomeric ratio of the major diastereoisomer is always higher than 50%, it is clear that the reaction is occurring via a DKR process,[6] rather than a simple kinetic resolution of the starting bis-sulfinyl chloride **5**. As far as we know, this represents a unique example of a process leading to the simultaneous creation of two chiral centers with an enantiodivergent dynamic kinetic resolution.

Determination of the Absolute Configuration of the Bis-sulfinate Esters. To determine the ability of the bis-sulfinate esters **6** and **7** to transfer two stereogenic sulfur atoms, as well as to determine the absolute configuration at the sulfinyl sulfur, their reactions with organometallic reagents were assessed. Condensation of the Grignard reagents on the crude sulfinate esters mixture led to the corresponding C_2-symmetric bis-sulfoxide together with the meso compound, easily separable by column chromatography (Scheme 4).

As can be seen in Table 2, a large number of bis-alkyl (Table 2, entries 1−5), bis-aryl (Table 2, entries 6 and 7), as well as functionalized bis-sulfoxides (Table 2, entries 8−11) have been obtained in modest to good yields. The specific rotations of the known sulfoxides (**10**, **14**, and **15**) are higher than those previously described,[18c,19,21a] indicating the high optical purities of the bis-sulfoxides obtained by this method. Among the bis-sulfoxides prepared, the synthesis of both isomers of bis-(methylsulfinyl)ethane **10(*R*,*R*)** and **10(*S*,*S*)** (Table 2, entries 1 and 2), is worth of comment as they cannot be easily prepared by other methods (Scheme 1).

Since the absolute configuration of various bis-sulfoxides is known, we were able to assign the absolute configuration of the bis-sulfinates, assuming that the displacement step occurs with complete inversion of configuration at sulfur, as it is proposed and proved for many Andersen type reactions.[24,31] The absolute config-

(29) Douglass, I. B.; Farah, B. S.; Thomas, E. J. *J. Org. Chem*. **1961**, *26*, 1996.

(30) For a mathematical treatment of the kinetics in DKR, see: (a) Kitamura, M.; Tokunaga, M.; Noyori, R. *J. Am. Chem. Soc.* **1993**, *115*, 144. (b) Kitamura, M.; Tokunaga, M.; Noyori, R. *Tetrahedron* **1993**, *49*, 1853.

(31) (a) Jacobus, J.; Mislow, K. *J. Am. Chem. Soc.* **1967**, *89*, 5228. (b) *The Chemistry of Sulfinic acids, esters and their derivatives*; Patai, S., Ed.; Wiley & Sons: New York, 1990.

Scheme 4. Enantioselective Dynamic Kinetic Resolution Route to Optically Pure C_2-Symmetric Bis-sulfoxides

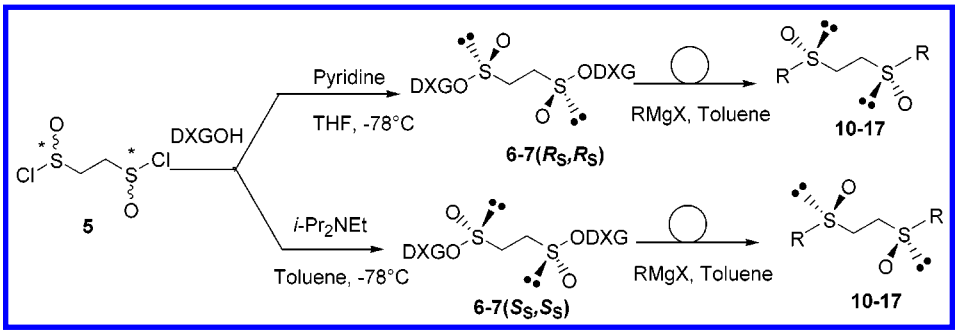
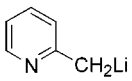
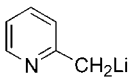


Table 2. Synthesis of Optically Active C_2-Symmetric 1,2-Bis-sulfinylethane RS(O)CH$_2$CH$_2$S(O)R from Chiral Ethane-1,2-bis-sulfinate Esters and RM[a]

	Bis-Sulfinate			Bis-Sulfoxide			
Entry	Comp.	Conf. at S[b]	RM	Comp.	Yield (%)[c]	Config.	$[\alpha]_D$ (*c*, Solvent)[d]
1	**6**	(*R*, *R*)[b]	MeMgI	**10**	40	(*S*, *S*)	+ 281 (*c* 0.5, EtOH)
2	**6**	(*S*, *S*)	MeMgI	**10**	50	(*R*, *R*)	-153 (*c* 0.5, $CHCl_3$)
3	**6**	(*S*, *S*)	EtMgI	**11**	45	(*R*, *R*)	-142 (*c* 0.6, $CHCl_3$)
4	**6**	(*S*, *S*)	^{i}PrMgI	**12**	30	(*S*, *S*)	-145 (*c* 0.6, $CHCl_3$)
5	**6**	(*R*, *R*)[b]	^{t}BuMgCl	**13**	46	(*R*, *R*)	+ 245 (*c* 0.5, EtOH)
6	**6**	(*R*, *R*)[b]	*o*-AnMgI	**14**	52	(*R*, *R*)	+650 (*c* 0.5, $CHCl_3$)
7	**6**	(*S*, *S*)	*p*-TolMgBr	**15**	54	(*S*, *S*)	-272 (*c* 0.5 MeOH)[e]
8	**6**	(*R*, *R*)[b]		**16**	60	(*S*, *S*)	+105 (*c* 1.0, $CHCl_3$)
9	**7**	(*S*, *S*)		**16**	50	(*R*, *R*)	-110 (*c* 0.8, $CHCl_3$)
10	**6**	(*R*, *R*)[b]	^{t}BuO$_2$CCH$_2$Li	**17**	60	(*S*, *S*)	+137 (*c* 1.0, $CHCl_3$)
11	**7**	(*S*, *S*)	^{t}BuO$_2$CCH$_2$Li	**17**	70	(*R*, *R*)	-138 (*c* 1.0, $CHCl_3$)

[a] All reactions were carried out by adding 2 molar equiv of the organometallic reagent to a 0.05 M solution of 1,2-bis-sulfinate ester in toluene. [b] Configuration of the major isomer. [c] Isolated yield after flash chromatography. [d] Optical rotations are among the highest ones reported in the literature (see text). [e] Contain 7% of *meso*-**15(*R*,*S*)**.

uration at the sulfinyl sulfur in the major 1,2-bis-sulfinate ester obtained using pyridine as base should be (R_S,R_S), while the major isomer obtained with Hünig's base should be (S_S,S_S).

The modest yield obtained in the case of simple dialkyl and diaryl sulfoxides (Table 2, entries 1−7) can be rationalized by a competing elimination reaction occurring after the first displacement step, as a consequence of the basicity of the protons α to the sulfoxide group.[32] Supporting this assumption, the ^{1}H NMR spectra of the crude mixture shows absorption at 5.8−6.7 ppm, corresponding to vinyl sulfoxides. The better yields observed in the case of functionalized bis-sulfoxides (Table 2, entries 10 and 11), where the carbanion α to the sulfoxide and the ester group is stabilized and inhibits elimination, supports this interpretation.

Dynamic Kinetic Resolution of Methanesulfinyl Chloride. Enantioselective Synthesis of 1,2-Bis-sulfoxides by Copper-Catalyzed Dimerization of Lithiomethylsulfoxides. The moderate yields in the formation of some of the C_2-symmetric bis-sulfoxides from the bis-sulfinate route prompted us to search for an alternative method of synthesis. Among the possible approaches (vide supra), the copper-catalyzed dimerization of enantiopure lithiomethylsulfoxides (Scheme 1C) presented the following advantages: (i) both isomers of a large number of methylsulfoxides are accessible, and (ii) it should lead to the final bis-sulfoxides with high enantiomeric excesses as a consequence of the Horeau effect. An Andersen-type approach using a diastereomerically pure methyl sulfinylating agent constitutes a general and convergent route to optically pure methyl

(32) The sulfinyl group enhance the kinetic and the thermodynamic acidity of the protons in the α-position. For instance, the pk_a of DMSO (35) is between that of *N*,*N*-diethyl acetamide (34.5) and that of 1,2-dithiane (39): Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

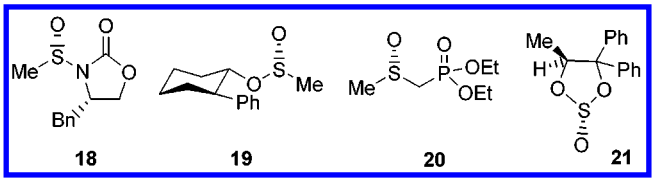
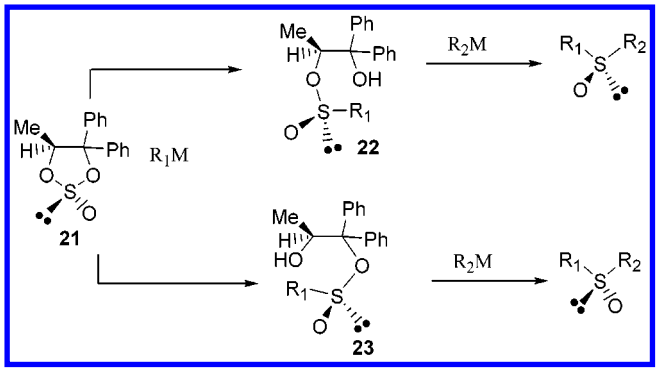


Figure 5. Different methanesulfinylating agents.

Scheme 5. Synthesis of Chiral Sulfoxides by the Sulfite Approach



sulfoxides.[33] However, while there are various methods[34] for the synthesis of diastereomerically pure aryl sulfinylating agents,[35] the synthesis of enantiopure alkyl sulfinylating agents is more challenging. Several recent contributions toward resolving this problem from the groups of Kagan,[36] Evans,[37] Whitessell,[38] Naso,[39] and ours[8a] allow the synthesis of diastereomerically pure methyl sulfinating agents **18**−**21** (Figure 5).

Among these approaches, Kagan's sulfite **21**[36] and our DAG method[8a] are the only ones that can give both enantiomers on desire of a given sulfoxide. In Kagan's approach, this result is generally achieved by permutation of the organometallics R_1 leading to hydroxysulfinates **22** and **23** and R_2 leading to the sulfoxides (Scheme 5) as long as both R_1 and R_2 are either small or bulky (when one of the groups is small and the other bulky, this approach leads to the same sulfoxide).

In the DAG method, both sulfoxides are accessible from diastereomerically pure sulfinate esters, epimeric at the sulfinyl sulfur, obtained using the same inducer of chirality and changing only the tertiary amine used to catalyze the reaction (Scheme 6). Additionaly, the formation of methanesulfinate esters takes place with *dynamic kinetic resolution* of the starting methanesulfinyl chloride, enhancing the scope of the reported DAG methodology. Accordingly, condensation of only 1.2 molar equiv of the racemic methanesulfinyl chloride (**24**) with 1 molar equiv of DAG **1** using either pyridine or DIPEA as base induces the stereoselective formation of the $\mathbf{8}\boldsymbol{R}_\mathbf{S}$ or $\mathbf{8}\boldsymbol{S}_\mathbf{S}$ methanesulfinates in 86 and 98% diastereomeric excess, respectively. A flash column chromatography or a recrystallization from hexanes yields diastereomerically pure (R_S)-DAG methanesulfinate $\mathbf{8}\boldsymbol{R}_\mathbf{S}$ and (S_S)-DAG methanesulfinate $\mathbf{8}\boldsymbol{S}_\mathbf{S}$ in 86% and 90% isolated yields, respectively.

The high isolated yields of both isomers using only 1.2 molar equiv of the racemic MeSOCl (**24**) unambiguously demonstrate that the DAG methodology occurs with dynamic kinetic resolution of the starting methanesulfinyl chloride. These results are general to all sulfinyl chlorides and may indeed be occurring in other asymmetric approaches to compounds with a chiral tetrahedral sulfur atom. Methanesulfinates, $\mathbf{8}\boldsymbol{R}_\mathbf{S}$ and $\mathbf{8}\boldsymbol{S}_\mathbf{S}$ were used as key intermediates (Table 3) for the synthesis of optically pure *tert*-butyl methyl sulfoxide **25**, as well as various aryl methyl sulfoxides **26**−**28**, by condensation with Grignards reagents.

The obtained methyl sulfoxides were used for the synthesis of C_2-symmetric bis-sulfoxides by copper-catalyzed oxidative coupling of the corresponding α anions (Scheme 7). The results are collected in Table 3. Various 1,2-bis-aryl as well as 1,2-bis-*tert*-butylsulfoxides have been obtained by the reported dimerization method in high yields and high optical purities.

The diastereoselectivity of the dimerization process is worthy of comment; another consequence of the Horeau effect, it reflects the enantiomeric excess of the starting methyl sulfoxide. We have already shown that the enantiomeric excesses of the final sulfoxides reproduce exactly the diastereomeric excesses of the intermediate DAG-sulfinate esters. Thus, an *x*:1 diastereomeric mixture of DAG-sulfinate esters will generate an *x*:1 mixture of scalemic methyl sulfoxides. The dimerization process (which does not alter the configuration at sulfur) will give a mixture of optically pure bis-sulfoxides in a x^2:1 ratio along with 2*x* of the *meso*-bis-sulfoxide, as easily determined by ^{1}H NMR analysis of the crude product. Taking into account that the $\mathbf{8}\boldsymbol{R}_\mathbf{S}$ and $\mathbf{8}\boldsymbol{S}_\mathbf{S}$ methanesulfinates are obtained in 86 and 98% diastereomeric excess respectively, both isomers of the final bis-sulfoxides will be obtained in greater than 98% ee, allowing the crude reaction mixture of DAG methanesulfinate to be used without purification. The high chemical yields of the final sulfoxides make the dimerization process, coupled with the DAG method, a powerful tool for the synthesis of enantiopure bis-sulfoxides.

Mechanism of the Enantioselective Dynamic Kinetic Transformation of Ethane-1,2-bis-sulfinyl Chloride. Most dynamic kinetic resolutions reported to date are based on an in situ equilibration or racemization of the chirally labile substrate, associated with a classical kinetic resolution.[5] However, when the chiral atom belongs to groups IV−VI, both enantiomers can be of equal reactivity and lead to the same diastereoisomer, as a consequence of the intermediacy of hypervalent compounds that can undergo pseudorotation.[40] The mechanism of the synthesis of sulfinate esters described in this work should explain not only the dynamic kinetic

(33) For reviews on the synthesis and utilization in C−C bond formation of chiral sulfoxides, see: (a) Solladié, G. *Synthesis* **1981**, 185. (b) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717. (c) Khiar, N.; Fernández, I.; Alcudia, A.; Alcudia, F. *Adv. Sulf. Chem.*, *2*; Rayner, C. M., Ed.; JAI Press, Inc.: Stamford, 2000; Chapter 3.

(34) Solladié, G.; Hutt, J.; Girardin, A. *Synthesis* **1987**, 173.

(35) Payne, S. G.; Hajipour, A. R.; Prabakaran, K. *Tetrahedron Lett.* **1994**, *35*, 645.

(36) (a) Rebiere, F.; Kagan, H. B. *Tetrahedron Lett.* **1989**, *30*, 3659. (b) Rebiere, F.; Samuel, O.; Ricard, L.; Kagan, H. B. *J. Org. Chem.* **1991**, *56*, 6, 5991.

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(38) Whitesell, J. K.; Wong, M.-S. *J. Org. Chem.* **1994**, *59*, 597.

(39) Cappozzi, M. A. M. Cardellicchio, C.; Fracchiolla, G.; Naso, F.; Tortorella, P. *J. Am. Chem. Soc.* **1999**, *121*, 4708.

(40) (a) For a good discussion on the stereochemical outcome of nucleophilic substitution on tricoordinated sulfur atom, see: Okuyama, T. In *The Chemistry of Sulphinic Acids, Esters and Their derivatives*; Patai, S., Ed.; John Wiley & Sons: Chichester, England, 1990; Chapter 21. (b) For an excellent account on the stereochemical outcome on the nucleophilic substitution on tricoordinated phosphorus atom, see: Mislow, K. *Acc. Chem. Res.* **1970**, *3*, 321.

Scheme 6. Enantioselective Synthesis of DAG-Methanesulfinates $8R_S$ and $8S_S$

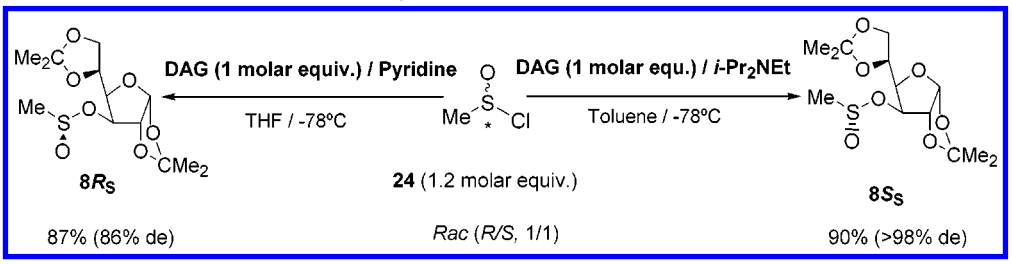
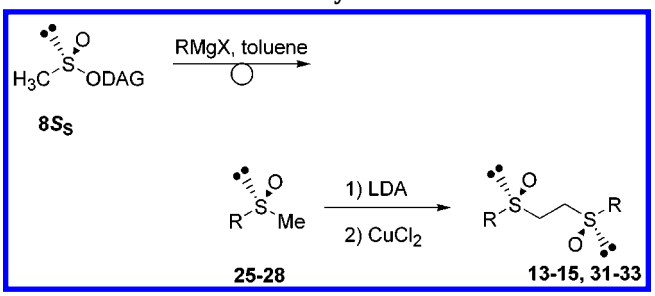


Table 3. Synthesis of C_2-Symmetric 1,2-Bis-sulfinylethanes $RS(O)CH_2CH_2S(O)R$ by Cu(II) Oxidative Coupling of the Corresponding Methyl Sulfoxides, RS(O)Me

	RS(O)Me					bis-sulfoxide			
entry	compd	config	R	yield[a] (%)	$[\alpha]_D$ (*c*, solvent)	compd	yield[a] (%)	config	$[\alpha]_D$ (*c*, solvent)[d]
1	**25**	*S*	^{t}Bu	80	+19 (*c* 1.0, MeOH)	13	75	(*S*,*S*)	−245 (*c* 0.5, EtOH)
2	**26**[b]	*S*	*o*-Tol	82	−222 (*c* 0.9, $CHCl_3$)	31	66	(*S*,*S*)	−529 (*c* 0.8, $CHCl_3$
3	**27**[b]	*S*	*o*-An	77	−271 (*c* 0.7, $CHCl_3$	14	80	(*S*,*S*)	−622 (*c* 0.4, $CHCl_3$
4	**28**[b]	*S*	mesityl	82	−390 (*c* 1.0, $CHCl_3$	32	90	(*S*,*S*)	−369 (*c* 0.8, $CHCl_3$
5	**29**[c]	*R*	*p*-Tol	75	+145 (*c* 1.5, $CHCl_3$	15	70	(*R*,*R*)	+275 (*c* 0.5, $CHCl_3$
6	**30**[c]	*R*	Napht	73	+107 (*c* 0.1, $CHCl_3$	33	78	(*R*,*R*)	+169 (*c* 0.9, $CHCl_3$

[a] Isolated yield after flash chromatography. [b] Obtained from (*S*)-DAG methanesulfinate. [c] Obtained from the corresponding (*S*)-menthyl arenesulfinate. [d] Optical rotations are among the highest ones reported in the literature (see text).

Scheme 7. Synthesis of C_2-Symmetric Bis-sulfoxides by Dimerization



resolution but also the change in the enantioselectivity introduced by the nature of the tertiary amine. We have previously demonstrated that the reaction of sulfinyl chlorides with chiral secondary alcohols occurs under kinetic control, and that the base effect observed is related with the steric rather than on the electronic structure of the tertiary amine. A plausible explanation is the formation of a pentavalent sulfurane[41] intermediate able to undergo pseudorotation during the reaction.[42] A number of achiral[43] as well as chiral sulfuranes[44] have been prepared and their chemical and structural properties determined. Interestingly, Koizumi's group has recently reported a complete opposite stereochemical outcome in the acidic or basic hydrolysis of an optically pure spiro-λ^4-sulfurane.[45] To explain the enantioselectivity observed, we propose that the first step of the process is the formation of racemic sulfinamides,[46] as the *reactive species*, which interact with the chiral alcohol (Scheme 8). As it has been proposed for most dynamic kinetic resolution processes,[5] the enantioselective dynamic kinetic resolution of bis-sulfinyl chlorides can be rationalized by a continuous racemization process of two bis-sulfinamide intermediates along with the formation of a major bis-sulfinate ester from the third bis-sulfinamide, induced by the chiral secondary alcohol. Nevertheless, as the sulfur atom can undergo Berry pseudorotation[47] during the reaction, the DKR reported here can be also explained by the formation of bis-sulfurane[48] intermediates with two pentavalent sulfur atoms. Depending on whether the base used is pyridine or *i*-Pr_2NEt, all the bis-sulfurane intermediates evolve by a Berry pseudorotation process to bis-sulfurane type **A** or bis-sulfurane type **B** (Scheme 8), which yield (*R*,*R*)- or (*S*,*S*)-bis-sulfinate esters, respectively, by extrusion of the amine.[49]

The model presented in Scheme 8 may not be limited to sulfinate esters, but should be general to compounds with a chiral atom of the group IV−VI, such as the phosphinate esters for instance.[50]

(41) (a) Sulfurane as intermediate: Martin, J. C.; Paul, I. C. *Science* **1976**, *191*, 154. For reviews, see: (b) Hayes, R. A.; Martin, J. C. In *Organic Sulfur Chemistry, Theoretical and Experimental Advances*; Bernardi, I. G., Csimadia, I. G., Mangini, A., Eds.; Elsevier: Amesterdam, 1985; Chapter 8. (c) Oae, S. In *Reviews on Heteroatom Chemistry*; MYO, Tokyo, 1988; Vol. 1, p 304. (d) Furokawa, N. *Heteroatom Chemistry*; Block, Ed.; VCH: New York, 1990; p 165.

(42) (a) Jacobus, J.; Mislow, K. *J. Am. Chem. Soc.* **1967**, *89*, 5228. (b) Lockard, J. P.; Schroeck, C. W.; Johnson, C. R. *Synthesis* **1973**, 485. (c) Oae, S.; Kawai, T.; Furukawa, N.; Iwasaki, F. *J. Chem. Soc., Perkin Trans.* **1987**, *2*, 405.

(43) For achiral sulfuranes, see: (a) Hornbuckle, S. F.; Livant, P.; Webb, T. R. *J. Org. Chem.* **1995**, *60*, 4153. (b) Rabai, J.; Kapovits, I.; Argay, G.; Koritsanszky, T.; Kalaman, A. *J. Chem. Soc., Chem. Commun.* **1995**, 1069. (c) Szabó, D.; Kapovitz, I.; Argay, G.; Czugler, M.; Kálmán, A.; Koritsánsky, T. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1045.

(44) For chiral sulfuranes: (a) Drabowicz, J.; Martin, J. C. *Pure Appl. Chem.* **1996**, *68*, 951. (b) Szabó, D.; Szendeffy, S.; Kapovitz, I.; Kucsman, A.; Czugler, M.; Kálmán, A.; Nagy, P. *Tetrahedron*: *Asymmetry* **1997**, *8*, 2411, and references therein.

(45) Zhang, J.; Sito, S.; Koizumi, T. *J. Am. Chem. Soc.* **1998**, *120*, 1631.

(46) Synthesis of sulfinamide, see: (a) Mikolajczyk, M.; Drabowicz, J.; Bujnicki, B. *J. Chem. Soc., Chem. Commun.* **1976**, 568. (b) Alonso, R.; Garcia-Ruano, J. L.; Noheda, P.; Zarzuelo, M. M. *Tetrahedron*: *Asymmetry* **1995**, *6*, 1133.

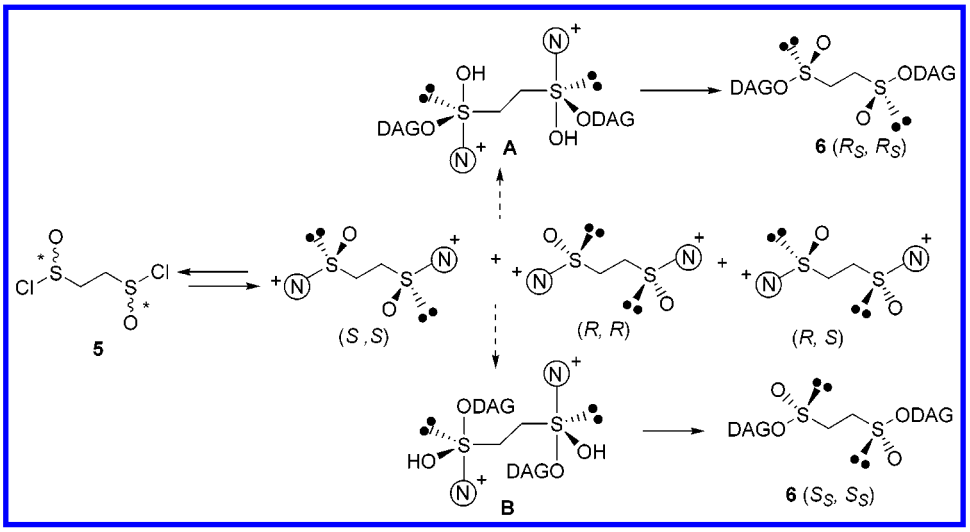
(47) Berry, R. S. *J. Chem. Phys.* **1960**, *32*, 933.

(48) The analysis of pseudorotational interconversions described in detail for phosphoranes can be applied to potential interconversions of the hypothetical pentacoordinated hypervalent sulfuranes. See: (a) DeBruin, K. E.; Naumann, K.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7031. (b) Muetterties, E. L. *J. Am. Chem. Soc.* **1969**, *91*, 1636.

(49) A plausible explanation of the dramatic change in the stereochemical outcome of the reaction induced by the achiral tertiary amine could be that in the case of the bulky and electronegative Hunig's base there is a formation of three bis-sulfurane intermediates where the chiral alcohol and the tertiary amine are the apical positions, whereas, in the case of reaction promoted by pyridine, there is formation of three bis-sulfurane, where the incoming alcohol is in apical position and the less bulky aromatic base is in equatorial position.

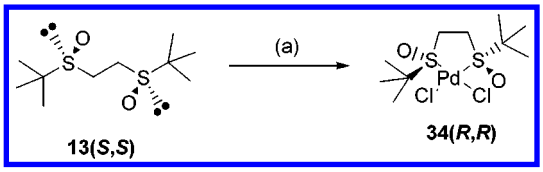
(50) Benabra, A.; Alcudia, A.; Khiar, N.; Fernández, I.; Alcudia, F. *Tetrahedron*: *Asymmetry* **1996**, *7*, 3353.

Scheme 8. Possible Pathways for the Enantioselective Dynamic Kinetic Resolution of Ethane-1,2-bis-sulfinyl Chloride 5



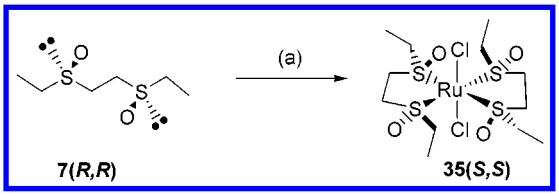
Synthesis of Palladium(II) and Ruthenium(II) Chiral Complexes Containing C_2-Symmetric Bis-sulfoxides. Very few examples of transition-metal complexes with chiral sulfoxides as ligands are described in the literature.[51] Interestingly, the sulfoxide group can behave as a bidentate ligand, able to coordinate a metal either through the oxygen or through the sulfur atom.[52] This feature has been analyzed from the perspective of a valence bond model and HSAB theory taking into account steric effects.[53] As a rule, in accordance with the relative hardness of oxygen and sulfur, hard metals give O-coordinated complexes, while soft metals give S-coordinated complexes.[54] It should be noted that we[14a] and others[14b,c] have recently reported promising results for the use of bis-sulfoxides in metal-catalyzed enantiomeric reactions. Fe(III) complexes having (*S*,*S*)-bis(*p*-tolylsulfinyl)methane and (*S*,*S*)-2,2-bis(*p*-tolylsulfinyl)-propane[14a] have been used in metal-catalyzed enantioselective Diels−Alder reaction, while Pd(0) complexes with (*S*,*S*)-1,2-bis(*p*-tolylsulfinyl)benzene[14c] as ligands were used in Pd-catalyzed allylic substitution,[55] with moderate enantioselectivity in both cases. Additionally, a family of *cis*- and *trans*-Ru(II) complexes with the general formula $RuCl_2$(*meso* or *rac*-bis-sulfoxide)$_2$ have recently been synthesized, characterized, and studied for their antitumor activity. Preliminary in vitro experiments with Chinese hamster ovary cells indicate that the trans complexes accumulate in the cells and bind to DNA to a greater degree than the cis complexes. The modular design of our ligands, together with the possibility of easy access to both enantiomers, prompted us to investigate the synthesis of their metal complexes. This work is preliminary to catalytic asymmetric synthesis[56] and the study of the effect of the chirality of the sulfinyl sulfur in Ru(II) complexes on the molecular recognition with DNA and thus on their anticancer activity. To investigate how our ligands coordinate to transition metals, we prepared Pd and Ru complexes of bis-sulfoxides **13(*S*,*S*)** and **11(*R*,*R*)** with different structures.

Scheme 9[a]



[a] Key: $PdCl_2(MeCN)_2$, EtOH, rt.

Scheme 10[a]



[a] Key: $RuCl_2(3H_2O)$, MeOH, reflux.

cis-Dichloro[(*R*,*R*)-bis-*tert*-butylsulfinyl)ethane]palladium(II) **34(*R*,*R*)** (Scheme 9) was readily prepared by treating **13(*S*,*S*)** with $PdCl_2(CH_3CN)_2$, in ethanol.

trans-Dichloro[(*S*,*S*)-1,2-bis(ethylsulfinyl)ethane]ruthenium(II) **35(*S*,*S*)** was obtained in 70% yield by refluxing **11(*R*,*R*)** with 1 molar equiv of $RuCl_2 \cdot 3H_2O$ in methanol, during 3 h (Scheme 10). The complex is air stable enough for its purification by silica gel column chromatography.

Simple ^{1}H NMR analysis of the crude mixtures shows the C_2-symmetric structure of all the complexes formed, including the octahedral ruthenium complex for which cis complexes lacking C_2-symmetry have been described,

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(52) Baldenius, K. U.; Kagan, H. B. *Tetrahedron*: *Asymmetry* **1990**, *1*, 597.

(53) (a) Quirós Méndez, N.; Arif, A. M.; Gladysz, J. A. *Organometallics* **1991**, *10*, 2199. (b) Davies, J. A. *Adv. Inorg.Chem. Radiochem.* **1981**, *24*, 115.

(54) Pettinari, C.; Pellei, M.; Cavicchio, G:, Crucianelli, M.; Panzeri, W.; Colapietro, M.; Casseta, A. *Organometallics* **1999**, *18*, 555.

(55) Hiroi, K.; Suzuki, Y.; Abe, I.; Kawagishi, R. *Tetrahedron* **2000**, *56*, 4710 and references therein.

(56) For the recent utilization of chiral sulfoxides as chiral auxiliaries in metal-catalyzed asymmetric reactions, see: (a) Montenegro, E.; Moyano, A.; Pericàs, M. A.; Riera, A.; Alvarez,-Larena, A.; Piniella, J.-F. *Tetrahedron*: *Asymmetry* **1999**, *10*, 457. (b) Carretero, J. C.; Adrio, J. *J. Am. Chem. Soc.* **1999**, *121*, 7411 and references therein.

from *meso*-**11(*R*,*S*)** as ligand. The IR spectra of the palladium and ruthenium complexes show a ν(S−O) band at higher frequencies than in the free ligands. According to a simple diagnostic method for the determination of the coordination of sulfoxides and according to HSAB theory, we suggest S-complexation in both palladium and ruthenium derivatives. The methylene protons α to the sulfinyl group exhibited quite different ^{1}H NMR signal pattern and chemical shifts, allowing their utilization as chemical probes for the coordination mode.

S-Bonding deshields α protons by 0.6 ppm in the palladium complex **34(*R*,*R*)** and by 0.58 ppm in the ruthenium complex **35(*S*,*S*).** The larger nonequivalence in the metal complexes versus free ligands of the α methylene protons can be accounted for by a fixed conformation while the magnitude of this parameter in the different complexes reflects the strength of the metal sulfur bond.

Conclusions

Two complementary procedures for the synthesis of enantiopure C_2-symmetric bis-sulfoxides were developed. Both procedures take place with enantiodivergent dynamic kinetic resolution of either a mono- or a bis-sulfinyl chloride leading to diastereomerically pure sulfinate esters. As a consequence of the Horeau effect, the bis-sulfinate esters and the bis-sulfoxides are obtained with enhanced diastereo and enantioselectivity. The work reported may represent an example of DKR that does not rely necessarily on the epimerization of the starting substrate, as a consequence of the hypervalent intermediates able to undergo pseudorotations. A large number of bis-sulfoxides were produced, and some of them were used for the synthesis of new transition metal complexes. We are confident that these results will accelerate the utilization of the useful chiral bis-sulfoxides as chiral ligands in metal catalyzed enantioselective reactions. These aspects are actively being pursued in our group.

Experimental Section

General Methods. All reactions were run under an atmosphere of dry argon using oven-dried glassware and freshly distilled and dried solvents. THF and diethyl ether were distilled from sodium benzophenone ketyl. Dichloromethane was distilled from calcium hydride. TLC was performed on silica gel GF_{254} (Merck) with detection by charring with phosphomolybdic acid/EtOH. For flash chromatography, silica gel (Merck 230−400 mesh) was used. Columns were eluted with positive air pressure. Chromatographic eluents are given as volume-to-volume ratios (v/v). NMR spectra were recorded with a Bruker AMX_{500} (^{1}H, 500 MHz) and Bruker Avance DRX_{500} (^{1}H, 500 MHz) spectrometers. Chemical shifts are reported in ppm, and coupling constants are reported in Hz. Routine spectra were referenced to the residual proton or carbon signals of the solvent. High-resolution mass spectra were recorded on a Kratos MS-80RFA 241-MC apparatus. Optical rotations were determined with a Perkin-Elmer 341 polarimeter. Elemental analyses were recorded on a Leco CHNS-932 apparatus. The organic extracts were dried over anhydrous sodium sulfate and concentrated in vacuo.

Ethane-1,2-bis-sulfinyl Chloride (5). Compound **5** was prepared according to the procedure reported by Douglas et al.,[29] with slight modifications. Chlorine (11.4 g) [generated in situ by treating potassium permanganate (10.15 g) with an excess of concentrated HCl] was added to a solution of 1,2-ethanedithiol **3** (15.2 g, 0.16 mol) in methylene chloride (20 mL) to yield 13.1 g of the corresponding polymer **4**. A suspension of this polymer (6.86 g) in methylene chloride (30 mL) and glacial acetic acid (8.5 mL) was treated again with chlorine (15.8 g) to give a yellow solution. After removal of the solvent under vacuum, ethane-1,2-bis-sulfinyl chloride **5** was obtained as a white solid pure enough to be used in the next reaction without further purification. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 3.88−4.07 (m, 4H).

General Procedure for Preparation of Chiral Ethane-1,2-bis-sulfinates. Method A. A solution of ethane-1,2-bis-sulfinyl chloride **5** (1.1 mmol, 1.1 equiv) in THF (5 mL) was added dropwise over a mixture of the chiral alcohol (2 mmol) and pyridine (2.2 mmol, 1.1 equiv) in THF (5 mL) at −78 °C. After being stirred for 1 h at −78 °C under argon atmosphere, the reaction mixture was quenched with water and diluted with CH_2Cl_2. The organic layer was washed with 5% HCl aqueous solution, 2% $NaHCO_3$ aqueous solution, and saturated NaCl aqueous solution and dried over Na_2SO_4. After the solvent was removed under vacuum, the bis-sulfinate esters obtained (in almost quantitative yield) were usually used in the next reaction without further purifications.

Method B. Method B is similar to method A; the only changes are that *i*-Pr_2NEt is used instead of pyridine as base and that toluene is used instead of THF as solvent.

Di(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl) (*R*,*R*)-Ethane-1,2-bis-sulfinate [6(R_S,R_S)]. The reaction of diacetone-D-glucose (**1**) and ethane-1,2-bis-sulfinyl chloride (**5**) using method A afforded 1,2-bis-sulfinate ester **6(R_S,R_S)** as the major product, together with **6(S_S,S_S)** and **6(R_S,S_S)** diastereoisomers in a 82:1:17 ratio, as determined by ^{1}H NMR spectra of the crude. ^{1}H NMR (C_6D_6, 500 MHz) δ: 0.97, 1.28, 1.30 and 1.31 (4s, 24H), 2.95−3.10 (m, 4H), 3.90−4.00 (m, 4H), 4.18−4.24 (m, 2H), 4.31−4.34 (m, 2H), 4.79−4.81 (m, 4H), 5.83 (d, 2H, J = 3.6 Hz). ^{13}C NMR (C_6D_6, 125 MHz) δ: 25.3, 26.1, 26.8, 26.9, 48.7, 68.0, 72.7, 81.4, 83.8, 84.3, 105.8, 109.7 and 112.4. HRMS: calcd for $C_{26}H_{43}O_{14}S_2$ $(M + 1)^+$ 643.2094, found 643.2089 (0.7 ppm).

Di(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl) (*S*,*S*)-Ethane-1,2-bis-sulfinate [6(S_S,S_S)]. The reaction of diacetone-D-glucose (**1**) and ethane-1,2-bis-sulfinyl chloride (**5**) according to method B afforded 1,2-bis-sulfinate ester **6(S_S,S_S)** as the major product, together with the **6(R_S,S_S)** diastereoisomer in 88:12 ratio, as determined by ^{1}H NMR spectra of the crude. Recrystallization from ether−hexane afforded the optically pure **6(S_S,S_S)** bis-sulfinate in 62% yield as a white solid. Mp: 113−114 °C. $[\alpha]^{25}_D$ = +85 (*c* 1.0, $CHCl_3$). ^{1}H NMR (C_6D_6, 500 MHz) δ: 1.04, 1.31 and 1.39 (3s, 24H), 2.78−2.98 (m, 4H), 4.04 (m, 4H), 4.31−4.40 (m, 4H), 4.45 (d, 2H, J = 3.6 Hz), 4.80 (d, 2H, J = 2.8 Hz), 5.76 (d, 2H, J = 3.6 Hz). ^{13}C NMR (C_6D_6, 50 MHz) δ: 25.3, 26.2, 26.8, 27.0, 47.6, 67.4, 72.6, 79.1, 80.8, 84.0, 105.5, 109.7 and 112.3. HRMS: calcd for $C_{26}H_{43}O_{14}S_2$ $(M + 1)^+$ 643.2094, found 643.2033 (9.4 ppm).

Di(1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranosyl) (*R*,*R*)-Ethane-1,2-bis-sulfinate [7(R_S,R_S)]. The reaction of di-*O*-cyclohexylidene-D-glucose (**2**) and ethane-1,2-bis-sulfinyl chloride (**5**) according to method A afforded bis-sulfinate ester **7(R_S,R_S)** as the major product, together with the **7(S_S,S_S)** and **7(R_S,S_S)** diastereoisomers in a 84:1:15 ratio, as determined by ^{1}H NMR spectra of the crude. ^{1}H NMR (C_6D_6, 500 MHz) δ: 1.18−1.83 (m, 40H), 3.10−3.26 (m, 4H), 4.02−4.12 (m, 4H), 4.30−4.34 (m, 2H), 4.46 (dd, 2H, J = 8.8 and 2.9 Hz), 4.91 (d, 2H, J = 3.5 Hz), 4.95 (d, 2H, J = 2.9 Hz), 5.95 (d, 2H, J = 3.5 Hz). ^{13}C NMR (C_6D_6, 125 MHz) δ: 23.6, 23.9, 24.0, 24.2, 24.8, 25.2, 34.9, 35.8, 36.6, 36.8, 48.2, 72.3, 81.2, 83.7, 83.8, 105.3, 110.09, 112.9. HRMS: calcd for $C_{38}H_{58}O_{14}NaS_2$ $(M + Na)^+$ 825.3165, found 825.3179 (−1.7 ppm).

Di(1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranosyl) (*R*,*R*)-Ethane-1,2-bis-sulfinate [7(S_S,S_S)]. The reaction of di-*O*-cyclohexylidene-D-glucose (**2**) and ethane-1,2-bis-sulfinyl chloride (**5**) according to method B afforded the bis-sulfinate ester **7(S_S,S_S)** as the major product, together with the **7(R_S,S_S)** diastereoisomer in a 85:15 diastereomeric ratio, as determined by ^{1}H NMR spectra of the crude mixture. Crystallization from ether−hexane afforded the optically pure bis-sulfinate **7(*S*,*S*)** as a white solid in 60% yield. Mp: 96−98 °C. $[\alpha]^{25}_D$ = +69 (*c* 1.0, $CHCl_3$). ^{1}H NMR (C_6D_6, 500 MHz) δ: 1.10−1.70 (m, 40H), 2.82−3.00 (m, 4H), 4.08 (m, 4H), 4.35−4.45 (m, 4H), 4.48 (d,

2H, J = 3.6 Hz), 4.84 (d, 2H, J = 2.9 Hz), 5.82 (d, 2H, J = 3.6 Hz). ^{13}C NMR (C_6D_6, 125 MHz) δ: 23.8, 24.1, 24.2, 24.4, 25.1, 25.5, 35.1, 36.1, 36.8, 37.0, 47.8, 67.2, 72.4, 79.5, 81.1, 83.6, 105.2, 110.3, 113.1. HRMS: calcd for $C_{38}H_{58}O_{14}NaS_2$ $(M + Na)^+$ 825.3165, found 825.3164 (0.2 ppm).

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl Methanesulfinate (8). Diasteoreomerically pure methanesulfinate **8*R*$_S$** and **8*S*$_S$** were prepared by condensation of 1 equiv of DAG **1** and 1.2 equiv of methanesulfinyl chloride **24** at −78 °C using pyridine in THF or DIPEA in toluene according to the published method.[8a] Methanesulfinyl chloride **24** was obtained using Hermann methodology, by treating dimethyl disulfide with sulfuryl chloride in acetic acid.[57]

General Procedure for Preparation of Chiral Bissulfoxides by Nucleophilic Substitution on Chiral Bisulfinates. Bis-sulfoxides **10**−**17** were obtained by addition of 2 equiv of RM (R = alkyl or aryl, M = MgBr or Li) to a solution of 1,2-bis-sulfinate esters **6** or **7** in toluene, at 0 °C. The mixture was stirred for 1 h, quenched with saturated aqueous NH_4Cl solution, extracted with ethyl acetate and Cl_2CH_2, and purified by flash chromatography.

In the case of 1,2-bis-(alkylsulfinyl)ethanes **10**−**12**, the workup was different: After the reaction mixture was stirred for 1 h, 1 equiv of TFA was added and the solvent removed under vacuo. The residue was extracted with ether in order to remove the DAGOH, and after treatment with Mixed bed resin (Sigma TMD-8; 1:1 mixture of strong cation and anion-exchange resin) to remove the remaining salts, it was purified by column chromatography on silica gel. The starting bis-sulfinate ester, yields, specific rotations, and absolute configurations are collected in Table 2.

(*S*,*S*)-Bis(methylsulfinyl)ethane [10(*S*,*S*)]. White solid. Crystallized from ethanol−ethyl acetate. Mp: 130−132 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.66 (s, 6H), 2.97−3.06 (m, 2H), 3.21−3.29 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 38.8, 46.2. IR (cm^{-1}, ν_{SO}) 1026. $[\alpha]^{25}_D$ = +281 (*c* 0.5, ethanol). Anal. Calcd for $C_4H_{10}O_2S_2$: C, 31.15; H, 6.53. Found: C, 31.49; H, 6.50.

(*R*,*R*)-Bis(methylsulfinyl)ethane [10(*R*,*R*)]. This compound shows the same spectroscopic data as the **10(*S*,*S*)** enantiomer. $[\alpha]^{25}_D$ = −153 (*c* 0.5, $CHCl_3$). HRMS: calcd for $C_4H_{11}O_2S_2$ $(M + 1)^+$ 155.0200, found 155.0199 (1.1 ppm).

(*R*,*S*)-Bis(methylsulfinyl)ethane [10(*R*,*S*)]. The spectroscopic data of *meso*-**10** are taken from a mixture of bis-sulfoxides **10**, enriched in the **(*R*,*S*)** diastereoisomer. ^{1}H NMR ($CDCl_3$ 500 MHz) δ: 2.65 (s, 6H), 2.99−3.03 (m, 2H), 3.20−3.24 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 39.2, 46.5.

(*R*,*R*)-Bis(ethylsulfinyl)ethane [11(*R*,*R*)]. White solid. Crystallized from ethanol−ethyl acetate. Mp: 98−100 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.33 (t, 6H, J = 7.5 Hz), 2.72−2.82 (AB fragment of an ABX_3 system, 4H), 2.94−3.01 (m, 2H), 3.13−3.20 (m, 2H). ^{13} C NMR ($CDCl_3$) δ: 6.9, 43.6, 46.2. IR (cm^{-1}, ν_{SO}): 1015. $[\alpha]^{25}_D$ = −142 (*c* 0.9, EtOH). HRMS: calcd for $C_6H_{15}O_2S_2$ $(M + 1)^+$ 183.0513, found 183.0516 (−1.3 ppm).

(*S*,*S*)-Bis(isopropylsulfinyl)ethane [12(*S*,*S*)]. White solid. Crystallized from ethanol−ethyl acetate. Mp: 65−70 °C. ^{1}H NMR ($CDCl_3$) δ: 1.25 (d, 6H, J = 6.9 Hz), 1.32 (d, 6H, J = 6.9 Hz), 2.85 (hept, 2H, J = 6.9 Hz), 2.90−2.99 (m, 2H), 3.06−3.15 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 15.1, 15.8, 41.3, 51.2. IR (cm^{-1}, ν_{SO}): 1030. $[\alpha]^{25}_D$ = −149 (*c* 0.8, EtOH). HRMS: calcd for $C_8H_{19}O_2S_2$ $(M + 1)^+$ 211.0826, found 211.0828 (−0.9 ppm).

(*R*,*R*)-Bis(*tert*-butylsulfinyl)ethane [13(*R*,*R*)]. White solid. Crystallized from ethyl acetate−hexane. Mp: 154−156 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.23 (s, 18H), 2.84−3.00 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 22.8, 39.3, 53.8. IR (cm^{-1}, ν_{SO}): 1033. $[\alpha]^{25}_D$ = +245 (*c* 0.5, ethanol). HRMS: calcd for $C_{10}H_{23}O_2S_2$ $(M + 1)^+$ 239.1139, found 239.1137 (0.8 ppm).

(*R*,*S*)-Bis(*tert*-butylsulfinyl)ethane [13(*R*,*S*)]. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.27 (s, 18H), 2.75−2.79 (m, 2H), 2.95−2.99 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 22.8, 40.4, 54.1.

(*R*,*R*)-Bis(*o*-anisylsulfinyl)ethane [14(*R*,*R*)]. Purified by flash column chomatography (CH_2Cl_2/acetone/hexane, 3:2:6). White solid. Mp: 148−150 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.66−2.79 (m, 2H), 3.47−3.55 (m, 2H), 3.67(s, 6H), 6.75(d, 2H, J = 8.2 Hz), 7.07(t, 2H, J = 7.5 Hz), 7.36(ddd, 2H, J = 1.7, 7.5, 8.2 Hz), 7.58 (dd, 2H, J = 1.7, 7.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 43.6, 55.5, 110.6, 121.3, 125.8, 129.5, 132.2, 154.8. IR (cm^{-1}, ν_{SO}): 1036. $[\alpha]^{25}_D$ = +446 (*c* 0.5, ethanol). $[\alpha]_D$ = +650 (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{16}H_{18}O_4S_2$: C, 56.78; H, 5.36. Found: C, 56.75; H, 5.25.

(*R*,*S*)-Bis(*o*-anisylsulfinyl)ethane [14(*R*,*S*)]. Purified by flash column chomatography (CH_2Cl_2/acetone/hexane, 3:2:6). White solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 3.03−3.07 (m, 2H), 3.23−3.27 (m, 2H), 3.83(s, 6H), 6.89(d, 2H, J = 8.2 Hz), 7.14 (t, 2H, J = 7.7 Hz), 7.44 (ddd, 2H, J = 1.6, 7.7, 8.2 Hz), 7.67 (dd, 2H, J = 1.6, 7.7 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 43.1, 55.8, 110.9, 121.4, 125.8, 129.3, 132.4, 155.1.

(*S*,*S*)-Bis(*p*-tolylsulfinyl)ethane [15(*S*,*S*)]. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.38 (s, 6H), 2.68−2.75 (m, 2H), 3.27−3.34 (m, 2H), 7.37 and 7.26 (AA'BB' system, 8H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 21.3, 47.7, 123.8, 130.0, 139.0, 141.7. $[\alpha]^{25}_D$ = −272 (*c* 0.5, methanol). HRMS: calcd for $C_{16}H_{18}O_2S_2$ 306.0748, found 306.0754 (2.2 ppm).

(*R*,*S*)-Bis(*p*-tolylsulfinyl)ethane [15(*R*,*S*)]. The spectroscopical data of the *meso*-**11(*R*,*S*)** are taken from a mixture of bis-sulfoxides **11**, enriched in the **(*R*,*S*)** diastereoisomer. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.39 (s, 6H), 2.98 (s, 4H), 7.30 and 7.40 (AA′BB′ system, 8H).

(*S*,*S*)-Bis(2-pyridylmethanesulfinyl)ethane [16(*S*,*S*)]. Purified by column chromatography (ethyl acetate/methanol 10:1). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 3.00−3.29 (m, 4H), 4.18-(AB system, 4H, J = 12.9 Hz, $\Delta\nu$ = 31.4 Hz), 7.18 (ddd, 2H, J = 1.1, 4.9, 7.7 Hz), 7.30 (dt, 2H, J = 1.1, 7.7 Hz), 7.66 (td, 2H, J = 1.8, 7.7 Hz), 8.55 (ddd, 2H, J = 1.1, 1.8, 74.9 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 42.8, 59.2, 123.0, 125.1, 136.7, 149.8. $[\alpha]^{25}_D$ = +105 (*c* 1.0, $CHCl_3$). HRMS: calcd for $C_{14}H_{17}N_2O_2S_2$ $(M + 1)^+$ 309.0731, found 309.0726 (1.8 ppm).

(*R*,*R*)-Bis(2-pyridylmethanesulfinyl)ethane [16(*R*,*R*)]. Purified by column chomatography (ethyl acetate/methanol, 10:1). Spectroscopical data identical to those of 12(*S*,*S*). $[\alpha]^{25}_D$ = −110 (*c* 0.8, $CHCl_3$).

(*S*,*S*)-Bis(*tert*-butoxycarbonylmethanesulfinyl)ethane [17(*S*,*S*)]. Purified by crystallization from ethanol/hexane and ethyl acetate/hexane. White solid. Mp: 110−111 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.49 (s, 9H), 3.22−3.29 (m, 2H), 3.37−3.44 (m, 2H), 3.70 (s, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 27.9, 44.2, 57.0, 84.0, 163.6. $[\alpha]^{25}_D$ = +137 (*c* 1.05, $CHCl_3$). Anal. Calcd for $C_{14}H_{26}O_6S_2$: C, 47.44; H, 7.39. Found: C, 47.35; H, 7.21.

(*R*,*S*)-Bis(*tert*-butoxycarbonylmethanesulfinyl)ethane [17(*R*,*S*)]. The spectroscopical data of the *meso*-**17(*R*,*S*)** are taken from a mixture of bis-sulfoxides **17**, enriched in the **(*R*,*S*)** diastereoisomer. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.47 (s, 18H), 3.20−3.24 (m, 2H), 3.68 (AB system, 4H, J = 14 Hz, $\Delta\nu$ = 16.3 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 29.9, 44.3, 55.3, 84.0, 163.6.

(*R*,*R*)-Bis(*tert*-butoxycarbonylmethanesulfinyl)ethane [17(*R*,*R*)]. Purified by crystallization from ethanol/hexane and ethyl acetate/hexane. Specrospcopical data are identical to those of the **17(*S*,*S*)** enantiomer. $[\alpha]^{25}_D$ = −138 (*c* 1.0, $CHCl_3$).

Preparation of Enantiopure Aryl (or Alkyl) Methyl Sulfoxides. General Procedure. Methyl sulfoxides **25**−**28** were obtained in high yields by the addition of 1.2 equiv of ArMgX (or RMgX) to a solution of diaceton-D-glucose (*S*)-methanesulfinate **8*S*$_S$** in toluene at 0 °C. The mixture was then stirred for 1h, quenched with saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2, and purified by flash chromatography. Yields, specific rotations, and absolute configurations are collected in Table 2.

(*S*)-*tert*-Butyl Methyl Sulfoxide (25). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.25 (s, 9H), 2.35 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 22.5, 31.5, 52.6. $[\alpha]^{25}_D$ = +7.8 (c. 7, $CHCl_3$). HRMS: calcd for $C_5H_{12}OS$ $(M + 1)^+$ 120.0608, found 120.0609 (−0.5 ppm).

(*S*)-*o*-Tolyl Methyl Sulfoxide (26). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.33 (s, 3H), 2.64 (s, 3H), 7.13−7.18 (m, 1H), 7.34−7.41 (m, 2H), 7.88−7.93 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz)

(57) Youn, J. H.; Hermann, R. *Tetrahedron Lett.* **1986**, *27*, 1493.

δ: 17.9, 41.9, 122.8, 127.3, 130.5, 130.6, 133.8, 143.8. IR (cm^{-1}, ν_{SO}): 1033. $[\alpha]^{25}_D = -222$ (c. 0.9, $CHCl_3$). HRMS: calcd for $C_8H_{11}OS$ $(M + 1)^+$ 155.0531, found 155.0527 (2.1 ppm).

(*S*)-*o*-Anisyl Methyl Sulfoxide (27). White solid. Mp: 75−79 °C. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.55 (s, 3H), 3.66 (s, 3H), 6.72 (dd, 1H, $J = 8.1$, 0.6 Hz), 6.95 (td, 1H, $J = 7.6$, 0.6 Hz), 7.24 (ddd, 1H, $J = 8.1$, 7.6, 1.7 Hz), 7.59 (dd, 1H, $J = 7.6$, 1.7 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 41.1, 55.6, 110.5, 121.6, 124.5, 131.8, 132.9, 154.7. IR (cm^{-1}, ν_{SO}): 1032. $[\alpha]^{25}_D = -271$ (*c* 0.7, $CHCl_3$). HRMS: calcd for $C_8H_{11}O_2S$ $(M + 1)^+$ 171.0479, found 171.0474 (3.3 ppm).

(*S*)-Mesityl Methyl Sulfoxide (28). ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.22 (s, 3H), 2.49 (s, 6H), 2.78 (s, 3H), 6.80 (s, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 18.7, 20.8, 38.2, 130.7, 137.6, 140.8. IR (cm^{-1}, ν_{SO}): 1069. $[\alpha]^{25}_D = -390$ (*c* 1.0, $CHCl_3$). HRMS: calcd for $C_{10}H_{15}OS$ $(M + 1)^+$ 183.0843, found 183.0838 (3.3 ppm).

General Procedure for Preparation of Chiral Bissulfoxides by Oxidative Cu(II) Dimerization of Enantiopure Methylsulfinyl Anion. Bissulfoxides **13**−**15** and **31**−**33** were prepared by addition of 1.6 equiv of $CuCl_2$ to a solution of the corresponding alkyl or aryl methylsulfinyl carbanion in THF at −78 °C. After being stirred for 15 min at −78 °C, the reaction mixture was stirred at room temperature for 1 h, quenched with 10% aqueous H_2SO_4 solution, extracted with chloroform, and washed with aqueous NH_3 solution and brine. The product was purified by flash chromatography.

(*S,S*)-Bis(*tert*-butylsulfinyl)ethane [13(*S,S*)]. Spectroscopic data identical to those of the **13(*R,R*)** enantiomer. $[\alpha]^{25}_D = -272$ (*c* 0.5, methanol). HRMS: calcd for $C_{16}H_{18}O_2S_2$ 306.0748, found 306.0754 (2.2 ppm).

(*S,S*)-Bis(*o*-anisylsulfinyl)ethane [14(*S,S*)]. Spectroscopil data identical to those of the enantiomer **14(*R,R*).** $[\alpha]^{25}_D = -622$ (*c* 0.4, $CHCl_3$). HRMS: calcd for $C_{16}H_{19}O_4S_2$ $(M + 1)^+$ 339.0725, found 339.0720 (1.4 ppm).

(*R,R*)-Bis(*p*-tolylsulfinyl)ethane [15(*R,R*)]. Spectroscopical data identical to those of the **15(*S,S*)** enantiomer. $[\alpha]^{25}_D = +275$ (*c* 0.5, methanol). HRMS: calcd for $C_{16}H_{18}O_2S_2$ 306.0748, found 306.0754 (2.2 ppm).

(*S,S*)-Bis(*o*-tolylsulfinyl)ethane [31(*S,S*)]. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.21 (s, 6H), 2.58−2.74 (m, 2H), 3.29−3.45 (m, 2H), 7.09−7.15 (m, 2H), 7.24−7.36(m, 4H), 7.63−7.70 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 17.9, 44.9, 123.7, 126.9, 130.9, 134.2, 140.1. IR (cm^{-1}, ν_{SO}): 1031. $[\alpha]^{25}_D = -529$ (*c* 0.8, $CHCl_3$). HRMS calcd for $C_{16}H_{19}O_2S_2$ $(M + 1)^+$ 307.0826, found 307.0821-(1.9 ppm).

(*S,S*)-Bis(mesitylsulfinyl)ethane [32(*S,S*)]. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.24 (s, 6H), 3.10−3.25 (m, 2H), 3.45−3.60 (m, 2H), 6.81 (s, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ:18.9, 20.9, 45.5, 131.0, 133.7, 138.2, 141.5. IR (cm^{-1}, ν_{SO}): 1022, 1065. $[\alpha]^{25}_D = -369$ (*c* 0.8, $CHCl_3$). HRMS: calcd for $C_{20}H_{27}O_2S_2$ $(M + 1)^+$ 363.1452, found 363.1446 (1.7 ppm). Anal. Calcd for $C_{20}H_{26}O_2S_2$: C, 66.26; H, 7.32. Found: C, 65.81; H, 7.68.

(*R,R*)-Bis-(2-Methoxy-1-naphthylsulfinyl)ethane [33-(*R,R*)]. White solid. Mp: 180−181 °C. ^1H NMR ($CDCl_3$, 500 MHz) δ: 3.50−3.80 (m, 4H), 3.79 (s, 6H), 7.09 (d, 2H, $J = 9$ Hz), 7.30−7.45 (m, 4H), 7.72−7.77 (m, 2H), 7.87 (d, 2H, $J = 9$ Hz), 8.76−8.80 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 45.6, 56.5, 112.5, 119.5, 122.3, 124.5, 128.0, 128.7, 129.0, 132.5, 134.5, 156.4. IR (cm^{-1}, ν_{SO}): 1047. $[\alpha]^{25}_D = +169$ (*c* 0.9, $CHCl_3$). HRMS: calcd for $C_{24}H_{23}O_4S_2$ $(M + 1)^+$ 439.1023, found 439.1037 (3.3 ppm). Anal. Calcd for $C_{24}H_{22}O_4S_2$: C, 65.73; H, 5.06. Found: C, 65.56; H, 5.49.

***cis*-Dichloro[(*R,R*)-bis-*tert*-butylsulfinyl)ethane]palladium(II) [34(*R,R*)].** To a stirred ethanol suspension (3 mL) of bis(acetonitrile)dichloropalladium(II) (54.3 mg, 0.209 mmol), at room temperature and under argon, was added dropwise an ethanol solution (3 mL) of **13(*S,S*)** (50 mg, 0.209 mmol). After the mixture was stirred 45 min, the precipitate was filtered off and washed with diethyl ether to give **34(*R,R*)** (40 mg, 46%) as a yellow solid. ^1H NMR ($CDCl_3$, 500 MHz) δ: 1.80 (s, 18H), 3.38−3.50 (m, 2H), 3.68−3.80 (m, 2H). ^1H NMR (CD_3OD, 200 MHz) δ: 1.80 (s, 18H), 3.61−4.04 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 24.4, 48.5, 86.6. ^{13}C NMR (CD_3OD, 50 MHz) δ: 24.3, 49.7, 70.4. IR (cm^{-1}, υ_{S-O}): 1047. $[\alpha]_D = +272$ (*c* 0.1, $CHCl_3$). Anal. Calcd for $C_{16}H_{18}O_2S_2PdCl_2$: C, 28.89; H, 5.33. Found: C, 29.32; H, 5.38.

***trans*-Dichloro[bis-(*S,S*)-1,2-bis(ethylsulfinyl)ethane]-ruthenium(II) [35(*S,S*)]**. To a solution of $RuCl_3 \cdot 3H_2O$ (40 mg, 0.15 mmol) in methanol (8 mL), previously refluxed under argon until orange color (3−4 h), was added a solution of bissulfoxide **11(*R,R*)** (60 mg, 0.31 mmol) in methanol (4 mL). After being refluxed for another 3 h, the hot solution was filtered to remove the small amount of the Ru metal formed during the reaction. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography under argon (Cl_2CH_2/MeOH, 17:1), to give **35(*S,S*)** (70%) as a yellow solid. ^1H NMR (D_2O, 500 MHz) δ: 1.43 (t, 6H, $J = 7.3$ Hz), 3.60−3.90 (m, 8H). ^{13}C NMR (D_2O, 125 MHz) δ: 4.6, 46.8, 49.9. IR (cm^{-1}, υ_{SO}): 1079. $[\alpha]^{25}_D = -67$ (*c* 0.7, MeOH). HRMS: calcd for $C_{12}H_{28}O_4NaS_4Cl_2Ru$ $(M + Na)^+$ 558.9188, found 558.9184 (0.8 ppm).

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