Preparation of 2 and 9. Gaseous formaldehyde, prepared from paraformaldehyde (0.571 g, 19 mmol) by heating a flask containing the solid with a flame, was bubbled into a solution of hydroxylamine **8** (0.295 g, 1.9 mmol) in 50 mL of toluene containing 18 g of anhydrous sodium sulfate under nitrogen.[5a] The mixture was stirred for 15 min at 0 °C and then heated at reflux for 24 h. The mixture was cooled, filtered through Celite, and evaporated to give 0.327 g of an orange oil. Chromatography on silica gel (ether) gave 0.234 g (74%, 70% based on **7**) of a 2.5:1 mixture of **2** and **9** as determined by GC analysis. Pure samples of **2** and **9** were isolated by preparative GC on a 10 ft × $^1/_4$ in. 4% KOH, 15% Carbowax 20 M on 60/80 Chromosorb W column at 200 °C at a flow rate of 50 mL/min.

The data for **2** follow: NMR ($CDCl_3$) δ 3.93 (dd, 1, J = 6, 9 Hz), 3.38 (d, 1, J = 11 Hz), 3.27 (dd, 1, J = 12.5, 4.5 Hz), 2.63 (ddd, 1, J = 12.5, 12, 5 Hz), 2.57 (d, 1, J = 11 Hz), 1.17–2.17 (m, 12); IR (neat) 2940, 2865, 1460, 980, 920, 905, 900, 875, 765 cm^{-1}; MS, m/e (relative intensity) 167 (M^+, 39) 150 (70), 96 (28), 93 (36), 81 (40), 79 (53), 67 (33), 60 (31), 55 (31), 43 (30), 42 (28), 41 (35), 40 (100); GC (200 °C) t_R 13.8 min. Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.28, H, 10.18; N, 8.21.

The data for **9** follow: NMR ($CDCl_3$, 500 MHz) δ 3.29 (ddd, 1, J = 5, 8, 13.5 Hz), 3.27 (d, 1, J = 11.5 Hz), 2.94 (dd, 1, J = 11.5, 4 Hz), 2.75 (dd, 1, J = 13.5, 5.5 Hz), 2.39–2.25 (m, 1), 1.77–1.00 (m, 12); IR (neat) 2940, 2870, 1455, 1020, 955, 870, 830, 780, 620 cm^{-1}; MS, m/e (relative intensity) 167 (M^+, 43), 150 (100), 93 (41), 91 (42), 81 (47), 79 (58), 67 (38), 55 (62), 43 (42), 42 (58), 41 (95), 39 (48); GC (200 °C) t_R 11.1 min. Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.65; H, 10.15; N, 8.17.

(±)-Nitramine (1a). 10% Pd on carbon (0.017 g) was added to a solution of **2** (0.042 g, 0.25 mmol) in 6 mL of ethanol. The resulting mixture was stirred under 1 atm of hydrogen for 2 h, filtered through Celite, and evaporated to give 0.041 g (96%) of (±)-nitramine (**1a**): NMR ($CDCl_3$) δ 5.33 (br s, 2), 3.53 (dd, 1, J = 9, 4 Hz), 3.37 (d, 1, J = 12 Hz), 3.17–2.83 (m, 1), 2.65 (ddd, 1, J = 11.5, 11.5, 3 Hz), 2.43 (d, 1, J = 12 Hz), 2.2–0.8 (m, 12); ^{13}C NMR (C_6D_6) δ 78.5 (C-7), 52.7 (C-1), 47.3 (C-3), 39.0, 37.5, 36.3, 33.2, 24.7, 24.2, 21.5; IR (CCl_4) 3300, 2940, 2870, 2820, 1455, 1440, 1125, 1080, 1050 cm^{-1}. The ^1H and ^{13}C NMR data correspond closely to those reported for the natural product.[2a]

An acetone solution of nitramine was mixed with an ethanolic solution of hydrogen chloride. The solvent was evaporated to give a yellowish solid, mp 180–185 °C, which was recrystallized twice from acetone to give pure (±)-nitramine hydrochloride, mp 225–228 °C.

(±)-*N*-Methylnitramine (1b). A solution of **1a** (40 mg, 0.28 mmol) in 0.5 mL of EtOH and 0.5 mL of methyl iodide was heated for 2 h at 90 °C in a sealed tube. The solvent and excess methyl iodide were evaporated. The residue was treated with ice water, and the solution was made alkaline with 5% sodium hydroxide solution and extracted with three portions of ether. The combined organic layers were dried (Na_2SO_4) and evaporated to give 0.029 g (68%) of pure (±)-**1b**: NMR ($CDCl_3$) δ 4.77 (br s, 1), 3.53 (dd, 1, J = 9, 4 Hz), 3.17 (d, 1, J = 12 Hz), 3.00–2.63 (m, 1), 2.27 (s, 3), 2.2–1.1 (m, 14); ^{13}C NMR ($CDCl_3$) δ 78.0 (C-7), 61.4 (C-1), 56.1 (C-3), 46.4 (N-Me), 37.4 (2 carbons), 36.9, 32.7, 24.3, 23,4, 21.1; IR ($CDCl_3$) 3230, 2940, 2860, 2800, 1455, 1265, 1160, 1065, 1020 cm^{-1}. The ^1H NMR and IR data correspond closely to those previously reported.[2a]

***trans*- and *cis*-Hexahydro-1-indanone (13 and 14).** $MeAlCl_2$ (1 mL of 1.4 M in hexane, 1.4 mmol) was added to a solution of aldehyde **4** (0.234 g, 1.69 mmol) in 20 mL of CH_2Cl_2 at 0 °C under nitrogen. The solution was stirred for 5 min at 0 °C and 1.5 h at 20 °C. The reaction mixture was poured into water and treated with 10% HCl to dissolve the precipitate. The mixture was extracted with three portions of CH_2Cl_2, which were combined, dried ($MgSO_4$), and evaporated to give 0.181 g of a brown oil. Chromatography on silica gel (9:1 hexane–ether) gave 0.121 g (52%) of a ≈3.5:1 mixture of **13** and **14** as determined by GC analysis and ^{13}C NMR spectroscopy: NMR ($CDCl_3$) δ 0.7–2.5 (m, 14); ^{13}C NMR ($CDCl_3$) δ **13** 217.9, 55.4, 43.2, 36.9, 32.5, 27.6, 25.8, 25.5, 24.9; **14** 49.3, 34.7, 28.1, 23.9, 22.8, 22.4, three carbons were not observed; IR (neat) 2930, 2850, 1740, 1450, 1085 cm^{-1}; GC (9 ft; $^1/_4$ in.; 10% Carbowax 20 M on Chromosorb PNAW 60/80, 50 mL/min, 150 °C) t_R 20.9 (**13**) and 21.9 (**14**) min, partially overlapping. The ^{13}C NMR data are identical with those previously reported.[17]

An identical reaction was carried out at −20 °C and monitored by GC. Ketones **13** and **14** were formed as a ≈12:1 mixture. The reaction was worked up after 8 h, at which time it was 90% complete.

Acknowledgment. We are grateful to the National Institues of Health for financial support. The 500-MHz spectrometer was purchased with funds provided by NIH Grant GM 20168. C.P.C-M. gratefully acknowledges a fellowship support from CONICIT (Venezuela).

Registry No. (±)-**1a**, 82227-98-3; (±)-**1a**·HCl, 89398-21-0; (±)-**1b**, 89460-82-2; (±)-**2**, 89398-19-6; **4**, 60416-25-3; (±)-**5**, 89398-16-3; (±)-**6**, 89414-11-9; (*E*)-**7**, 89398-17-4; (*Z*)-**7**, 89398-24-3; **8**, 89398-18-5; (±)-**9**, 89398-20-9; (±)-**13**, 89398-22-1; (±)-**14**, 89398-23-2; methylenecyclohexane, 1192-37-6; methyl α-chloroacrylate, 80-63-7.

Asymmetric Diels–Alder Reactions with Sulfines Derived from Proline

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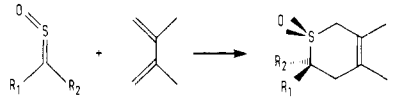
Received September 13, 1983

The synthesis of a variety of sulfines **8** derived from *S*-proline, utilizing the reaction of α-silyl carbanions with sulfur dioxide, is described. Reaction of the thus prepared sulfines **8** with 2,3-dimethyl-1,3-butadiene gave dihydrothiopyran *S*-oxides **9**. During these cycloaddition reactions asymmetric inductions up to 40% were observed. From one pure diastereomeric form of cycloadduct **9d** an X-ray analysis was carried out in order to provide insight in the steric course of the cycloaddition reaction.

Sulfines (thione *S*-oxides) are sulfur-centered heterocumulenes that can undergo a variety of cycloaddition reactions,[2] e.g., with carbon 1,3-dienes, heterodienes, diazo compounds, nitrile oxides, and nitrilimines. The Diels–Alder type reactions with 1,3-butadienes lead to dihydrothiopyran *S*-oxides (Scheme I). An interesting feature of this cycloaddition is that geometrically isomeric sulfines

Scheme I



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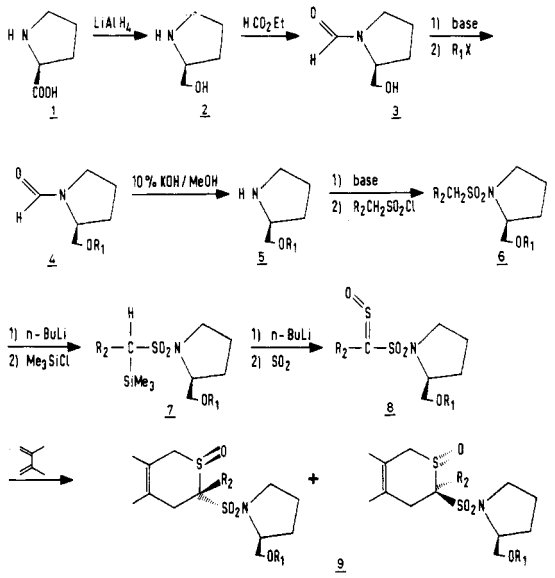
Scheme II



produce cycloadducts in which the stereochemical relationship present in the sulfine is predominantly retained.[2,3] The dienophilicity of sulfines is strongly dependent on the substituents. As expected, sterically filled substituents have a retarding effect, while electron-withdrawing functions enhance the reactivity.[2] During the cycloaddition reaction with sulfines having unequal substituents ($R_1 \neq R_2$) two chiral centers are formed, in other words the sulfine carbon and sulfur atoms both are prochiral centers.

The aim of this investigation is to study the extent of asymmetric induction of the Diels–Alder reaction with sulfines bearing a chiral substituent. In the literature asymmetric Diels–Alder reactions have been reported with chiral olefinic dienophiles,[4] chiral dienes,[5] and chiral Lewis acid catalysts.[6] In a recent paper we described our results with 10-chloro-10-sulfinylcamphor and sulfoximino substituted sulfines as chiral sulfines.[7] In these cases complete asymmetric inductions were observed.

Naturally occurring amino acids are frequently used as chiral inductor in asymmetric synthesis.[8] Therefore, it is of interest to design a sulfine having a substituent derived from an amino acid. For this purpose we chose *S*-proline as it is relatively cheap, it can readily be modified, and it has an excellent reputation in asymmetric synthesis.[8,9]

For the purpose of incorporating proline or a congener in a sulfine molecule the following aspects need to be taken into account. The modified Peterson reaction, i.e., al-

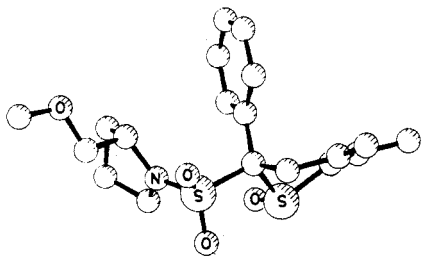


Figure 1.

kylidenation of sulfur dioxide using α-silyl carbanions,[10] offers the best prospects for the synthesis of the desired sulfines. Therefore, a suitable active methylene function is required in the precursor for the sulfine. Furthermore, in order to ensure sufficient dienophilicity of the sulfine, it must bear an appropriate electron-withdrawing substituent. To serve this purpose a sulfonyl group was chosen as activating substituent for the methylene group as well as connecting function with the proline derivative. In essence, the sulfine precursors are then sulfonyl pyrrolidines which are readily accessible from appropriately modified proline and a variety of sulfonyl chlorides (Scheme II). Proline was converted into (alkoxymethyl)pyrrolidines **5** by the sequence of reactions outlined in Scheme II. The ether function was introduced in the N-protected prolinol[11] (reaction of **3** with sodium hydride and methyl iodide, benzyl bromide, and 2,4,6-trimethylbenzyl chloride, respectively; in the case of the trityl ether pyridine was used as the base). Sulfonylation of **5** was carried out with chloromethanesulfonyl chloride,[12,13] phenylmethanesulfonyl chloride, and ethanesulfonyl chloride in the presence of triethylamine (solvent tetrahydrofuran).

Silylation of the active methylene compounds **6** was performed by deprotonation with *n*-butyllithium and subsequent treatment with trimethylsilyl chloride. The required α-silyl carbanions were obtained by deprotonation of **7** with *n*-butyllithium. The carbanions were then added to an excess of sulfur dioxide dissolved in tetrahydrofuran at −78 °C. In this manner the sulfines **8a–c,i–m** were obtained in solution. These sulfines are all very sensitive toward hydrolysis.[14] Upon contact with water they easily hydrolyze to the corresponding methylene compounds **6**. The sulfines **8d–f** enjoy a much greater stability, they could be isolated by the usual aqueous workup and subsequent chromatography. However, during the purification considerable loss of material had to be accepted.

From the ^{1}H NMR spectra of the sulfines **8d–f** it was concluded that these compounds have the *E* geometry; the ortho protons of the phenyl ring in these sulfines absorb at lower field than the remaining aromatic protons. This is due to the anisotropic deshielding effect of the S=O moiety which is directed toward the phenyl substituent.[2] By extrapolation it is assumed that the other sulfines **8a–c** and **8i–m** also possess the *E* geometry.[15]

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(15) The ratio of geometrical isomers during this synthesis of sulfines by the modified Peterson reaction is determined by the relative bulkiness of the substituents at the sulfine carbon atom. In the case of sulfonyl substituted sulfines we invariably obtained *E* sulfines.[14b]

Table I. Thiopyran *S*-Oxides 9 by Cycloaddition of 2,3-Dimethyl-1,3-butadiene and Sulfines Derived from Proline

starting materials	R_1	R_2	silyl compd	yield, %	de, %	cycloadduct	T, °C	yield, %[a]	de, % determined by ^{1}H NMR	de, % determined by HPLC
6a	CH_3	Cl	7a	83.3	28	9a	78	57.5	21.4	22.2
6b	CH_2Ph	Cl	7b	81.3	36	9b	78	44.5	35.6	38.4
6c	CH_2Mes	Cl	7c	90.7	34	9c	78	44.1	38.0	40.8
6d	CH_3	Ph	7d	89.3	16	9d	25	90.0[b]	15.6	15.4
6e	CH_2Ph	Ph	7e	89.0	10	9e	25	95.1[b]	10.5	
6f	CH_2Mes	Ph	7f	78.1	10	9f	25	70.0[b]	19.5	21.8
6i	CPh_3	Ph	7i	55.0	0	9i	25	24.6	0	
6j	CH_3	CH_3	7j	74.8	0	9j	78	45.0	5.4	
6k	CH_2Ph	CH_3	7k	77.6	0	9k	78	41.5	3.4	2.4
6l	CH_3	CH_2Ph	7l	68.9	40	9l	78	45.8	34.0	
6m	CH_2Ph	CH_2Ph	7m	86.0	60	9m	78	23.6	36.4	

[a] Determined starting from 7 based on silyl compound 7 (without isolation of sulfine 8). [b] Based on isolated sulfine 8.

All the sulfines 8, either prepared in situ or isolated, were subjected to a Diels–Alder reaction with 2,3-dimethyl-1,3-butadiene giving the expected cycloadducts **9**. In the cases of in situ prepared sulfines (**8a–c,i–m**) the adduct was accompanied by some 3,4-dimethylsulfolene[16] arising from dimethylbutadiene and the excess of sulfur dioxide. This byproduct sometimes hampered the isolation of the cycloadducts **9**.

The thiopyran *S*-oxides **9** were all obtained as mixtures of diastereomers. The differences in physical properties of the diastereomers are apparently small as separation by chromatography could not be accomplished. In one case, viz. **9d**, one of the diasteromers was separated by fractional crystallization (vide infra).

The ratio of diastereomers[17] was determined by analytical HPLC using an ultraviolet detector. To avoid any errors due to differences in extinction coefficients of the stereoisomers, the analyses were performed at several wavelengths. No deviations in diastereomeric ratios were found, however. The ratio of diastereomers was also determined by means of ^{1}H NMR analysis using (optically active)[18] shift reagents. Within the limits of accuracy the diastereomeric excess values are the same as those found with the HPLC method. The data are compiled in Table I. The cycloaddition of **9b** was carried out at two different temperatures, viz. 25 and −78 °C. The lower temperature experiment gave a higher asymmetric induction (36% at −78 °C vs. 25% at 25 °C). As mentioned above one of the diastereomeric cycloadducts **9d**, namely the predominant one, could be separated by careful crystallization. In order to gain insight in the steric course of the cycloaddition reaction the structure of this crystalline single diastereomer of **9d** was determined by X-ray analysis[19] (Figure 1). As expected[2,3] this analysis shows that the stereochemical relationship (*E* geometry) present in the sulfine is retained in the cycloadduct. From the absolute configurations of the sulfoxide (*S*) and of C_2 (*R*) it can readily be reconstructed that the predominant diastereomeric cycloadduct **9d** originates from an approach of the diene to the $C_{si}S_{si}$ face of the sulfine.

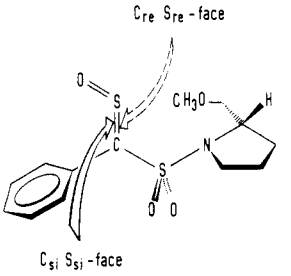

Figure 2.

When it is assumed that the electrostatic interaction of the sulfone oxygen atoms and the sulfine moiety will be minimized when these functions are placed in an anti position, only rotamers about the sulfonamide bond need to be considered for the preferred approach of the diene. In a sterically controlled approach of the diene the $C_{si}S_{si}$ face (which is leading to the preferred diastereomer) must be the least hindered one, in other words, the alkoxymethyl function at the pyrrolidine ring will be opposite to the preferred $C_{si}S_{si}$ face as pictured in Figure 2. (Note that the sulfine function is the plane of the paper; $C_{si}S_{si}$ attack then refers to an approach perpendicular to this plane). Thus, through steric shielding of the $C_{re}S_{re}$ face of the sulfine by the alkoxymethyl group the asymmetric induction during this cycloaddition can be understood.

When the diastereomeric excess (de) values obtained for the three chlorosulfines **8a–c** were compared the conclusion is justified that the nature of the alkoxy substituent in the pyrrolidine moiety has only a moderate effect on the extent of the asymetric induction. The same conclusion can be drawn by comparing the induction data of the phenylsulfines **8d–f** and the benzylsulfines **8l,m**, respectively. Although shielding of one diastereotopic face of the sulfine through π-stacking of the benzyloxy or trimethylbenzyloxy is quite conceivable this effect clearly plays no significant role in the present case. The steric size of the trityloxy group (**9i**) has an unexpected influence on the induction; instead of improving the de value the induction is virtually zero.

On the basis of the above observations it is suggested that the alkoxy group turns away from the sulfine moiety, probably to escape from unfavorable interactions with the sulfine oxygen atoms. Molecular models clearly indicate that the alkoxy group can take a spatial position which causes no shielding of the sulfine at all. The methylene group at the pyrrolidine ring is then solely responsible for the steric differentiation of the diastereotopic faces of the sulfine function.

The results presented here also suggest that better asymmetric induction may be expected when the inducing

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(17) The product mixture consists of two diastereomeric adducts only, both derived from the *E* sulfine. The alternative that these two products arise from isomerized sulfine with complete asymmetric induction during the subsequent cycloaddition for each geometrical isomer seems highly unlikely.

(18) Although the ratio of diastereomers can be determined by nonoptically active shift reagents, in this case optically active shift reagents gave better results.

(19) The details of this analysis are published elsewhere: Haltiwanger, R. C.; Beurskens, P. T.; Porskamp, P. A. T. W.; van den Broek, L. A. G. M.; Zwanenburg, B. *J. Crystallogr. Spectrosc. Res.*, submitted for publication.

chiral center is in closer proximity of the sulfine group.

It should be noted that the Diels–Alder reacitons in this study were carried out without a Lewis acid catalyst.[20]

It is of interest to compare the asymmetric induction during the Diels–Alder reaction with that during the silylation of the sulfonamides **6**. The diastereomeric ratios of the silyl compounds **7** were determined by means of ^1H NMR; the de values are listed in Table I. The asymmetric induction data obtained for the silylation and the cycloaddition show a remarkable parallel. In fact, when the silylation proceeds with an appreciable induction the same is found for the cycloaddition despite the fact that we are dealing with entirely different diastereoselection processes.

Experimental Section

Melting points were determined on a Koffler hotstage and are uncorrected. ^1H NMR spectra were recorded at 90 MHz using a Varian EM 390 instrument with Me_4Si as internal standard. IR spectra were taken on a Perkin Elmer 257 Grating Spectrometer. The combustion analyses were performed in the Microanalytical Department of our laboratory by J. Diersmann. Mass spectra were recorded on a Varian SM1B mass spectrometer or a Finnigan 3100 GC/MS. The *n*-BuLi used was a stock solution in hexane. THF was distilled twice from CaH_2 before use. All reactions in which carbanions are used are carried out under nitrogen. The HPLC analyses were performed using a "SP-8700 solvent delivery system" instrument equiped with a "SP-8400 variable wavelength" detector. The following columns were used: A Chrompack LiChrosorb Si-60-10 and a Chrompack LiChrosorb 10-RP-18 column (25 cm). For the ^1H NMR analyses of the diastereomeric product mixtures the following shift reagents were used: $Pr(C_{14}H_{14}F_7O_2)_3$, tris[3-((heptafluoropropyl)hydroxymethylene)-α-camphorato]praseodymium(III) [Pr(hfc)$_3$]; $Yb(C_{12}H_{14}F_3O_2)_3$, tris[3-((trifluoromethyl)hydroxymethylene)-α-camphorato]ytterbium(III) [Yb(tfc)$_3$]; and $Yb(C_{14}H_{14}F_7O_2)_3$, tris[3-((heptafluropropyl)hydroxymethylene)-α-camphorato]ytterbium(III) [Yb(hfc)$_3$].

(*S*)-(−)-1-Formyl-2-(methoxymethyl)pyrrolidine (4a). To a suspension of NaH (9.8 g, 0.40 mol) in THF (500 mL) was added (*S*)-(−)-1-formyl-2-(hydroxymethyl)pyrrolidine[11] (35.1 g, 0.27 mol) at room temperature under N_2. Under vigorous stirring MeI (61.5 g, 0.43 mol) dissolved in THF (45 mL) was gradually added. After refluxing for 1.5 h the suspension was poured into a saturated aqueous NaCl solution. The aqueous layer was extracted twice with CH_2Cl_2 (100 mL). After drying of the combined organic layers with $MgSO_4$ the solution was concentrated. The crude product **4a** was purified by distillation under reduced pressure, bp 72–73 °C (0.6 torr) [lit.[11] 67 °C (0.26 torr)]; yield, 25.9 g (67.0%). The spectroscopic data were in agreement with those reported in the literature.[11]

Similarly (*S*)-(−)-2-((benzyloxy)methyl)-1-formylpyrrolidine (**4b**) and (S)-(−)-2-(((2,4,6-trimethylbenzyl)oxy)methyl)-1-formylpyrrolidine (**4c**) were prepared. See the paragraph at the end of the paper about supplementary material, concerning characteristics for compounds **4b** and **4c**.

(*S*)-(−)-1-Formyl-2-(((triphenylmethyl)oxy)methyl)pyrrolidine (4d). To a solution of S-(−)-1-formyl-2-(hydroxymethyl)pyrrolidine **3** (12.0 g, 93 mmol) in dry pyridine (0.5 L) was added triphenylmethyl chloride (25 g, 93 mmol) at room temperature. After refluxing for 1.5 h the exces of pyridine was evaporated under reduced pressure. The residue was washed with diluted aqueous HCl. The crude product **4d** was purified by chromatography (silica gel, ethyl acetate): yield, 30 g (86.9%); IR (NaCl) 1655 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.37–2.10 (m, 4 H, $-CH_2CH_2-$), 2.90–4.00 (m, 5 H, $-CH_2-N$, $-CH_2-O$, H–C–N), 6.93–7.57 (m, 15 H, Ar), 8.13 and 8.37 (s, 1 H, HC=O); $[\alpha]^{20}_D$ −22.1 (*c* 1.00, $CHCl_3$); MS, *m/e* 371.1859 (M^+); calcd for $C_{25}H_{25}O_2N$, 371.1885.

(20) In the literature, however, the best asymmetric [4 + 2] cycloadditions are always performed with the aid of a Lewis acid catalyst.[4,5] Unfortunately, sulfines show a limited stability in the presence of Lewis acid catalysts.

(*S*)-(+)-2-(Methoxymethyl)pyrrolidine (5a). The procedure as given in the literature[11] was followed. When **4a** (25 g, 0.18 mol) was used as starting material 14.2 g (68%) of **5a** was obtained after distillation, bp 34–35 °C (32 torr) [lit.[11] 62 °C (40 torr)]. The spectroscopic data were in agreement with those reported in the literature.[11]

Following the same procedure (S)-(−)-2-((Benzyloxy)methyl)-pyrrolidine (**5b**) (*S*)-(+)-2-[((2,4,6-Trimethylbenzyl)oxy)-methyl]pyrrolidine (**5c**), and (*S*)-2-[(Triphenylmethoxy)-methyl]pyrrolidine (**5d**) were prepared. See the paragraph at the end of the paper about supplementary material concerning characteristics for compounds **5b–d**.

(*S*)-(−)-1-((Chloromethyl)sulfonyl)-2-(methoxymethyl)-pyrrolidine (6a). To a solution of **5a** (7.0 g, 61 mmol) and triethylamine (8.6 g) in THF (125 mL) was added at 0 °C and under nitrogen chloromethanesulfonyl chloride (9.1 g, 61 mmol) dissolved in THF (10 mL). After stirring for 2 h at room temperature the reaction mixture was poured into a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with $CHCl_3$ (50 mL). After drying with $MgSO_4$ the combined organic layers were concentrated and the residue was distilled under reduced pressure: bp 124–125 °C (0.8 torr); yield, 6.84 g (49.4%); IR (NaCl) 1160, 1345 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ 1.58–2.27 (m, 4 H, $-CH_2CH_2-$), 3.13–3.82 (m, 4 H, $-CH_2-N$, $-CH_2-O$), 3.37 (s, 3 H, OCH_3), 4.00–4.33 (m, 1 H, H–C–N), 4.66 and 4.73 (AB q, 2 H, J = 12 Hz, CH_2Cl); $[\alpha]^{20}D$ −12.8 (*c* 1.10, $CHCl_3$); MS, *m/e* 182.0015 ($M^+ - CH_2OCH_3$); calcd for $C_5H_9O_2NSCl$, 182.0043.

In the same manner **6b-k** were prepared. See the paragraph at the end of the paper about supplementary material concerning characteristics for compounds **6b–k**.

(*S*)-(−)-2-(Methoxymethyl)-1-((2-phenylethyl)sulfonyl)-pyrrolidine (6l). To a solution of **6g** (3.0 g, 15 mmol) in THF (60 mL) under N_2 was added 1.2 equiv of *n*-BuLi at −78 °C. After stirring for 1 h at room temperature benzyl bromide (4.3 g, 15 mmol) was added at −78 °C. The reaction mixture was stirred for 1 h at room temperature and subsequently poured into a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with CH_2Cl_2 (50 mL) and the combined organic layers were dried with $MgSO_4$. After evaporation of the organic solvents and chromatography (silica gel, ether) of the residue 3.64 g (83%) of **6l** was obtained: IR (NaCl) 1145, 1325 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ 1.50–2.23 (m, 4 H, $-CH_2CH_2$), 2.65–3.78 (m, 8 H, $-CH_2-O$, $-CH_2-N$, SO_2CH_2, CH_2Ph), 3.35 (s, 3 H, OCH_3), 6.85–7.57 (m, 5 H, Ar); $[\alpha]^{20}_D$ −38.7 (*c* 0.95, $CHCl_3$); MS, *m/e* 238.0891 ($M^+ - CH_2OCH_3$); calcd for $C_{12}H_{16}O_2NS$, 238.0902.

(*S*)-(−)-2-((Benzyloxy)methyl)-1-((2-phenylethyl)-sulfonyl)pyrrolidine (6m). The procedure as given for **6l** was followed. When **6h** (7.0 g, 26 mmol) was used as starting material 5.2 g (56%) of **6m** was obtained after chromatography (silica gel, diisopropyl ether). Crystallization from diisopropyl ether gave the pure product: mp 53–54.5 °C; IR (KBr) 1150, 1345 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ 1.71–2.16 (m, 4 H, $-CH_2CH_2-$), 2.91–3.73 (m, 8 H, $-CH_2-N$, $-CH_2-O$, SO_2CH_2, CH_2CH_2Ph), 3.87–4.22 (m, 1 H, H–C–N), 4.53 (s, 2 H, $O-CH_2Ph$), 6.98–7.44 (m, 10 H, Ar); $[\alpha]^{20}_D$ −47.2 (*c* 1.09, $CHCl_3$); MS, *m/e* 238 ($M^+ - CH_2OCH_2Ph$); calcd for $C_{20}H_{25}NO_3S$ 359.488. Anal. Calcd: C, 66.82; H, 7.01; N, 3.90. Found: C, 66.66, 66.47; H, 6.99, 7.04; N, 3.91, 3.98.

1-[(Chloro(trimethylsilyl)methyl)sulfonyl]-2-(methoxymethyl)pyrrolidine (7a). To a solution of **6a** (3.0 g, 13 mmol) in THF (60 mL) was added 1.2 equiv of *n*-BuLi at −78 °C under N_2. After stirring for 1.5 h at −78 °C Me_3SiCl (1.3 equiv, 25 mL) was added. At room temperature the reaction mixture was poured on a saturated aqueous NH_4Cl solution. The water layer was extracted once with CH_2Cl_2 (30 mL) and subsequently the combined organic layers were dried with $MgSO_4$. After concentration of the solution the residue was distilled under reduced pressure: bp 135 °C (0.3 torr); yield, 3.3 g (83%) of a mixture of diastereomers **7a**; IR (NaCl) 1145, 1340 (SO_2), 850, 1250 cm^{-1} ($SiMe_3$); ^1H NMR ($CDCl_3$) δ 0.30 (s, 9 H, $SiMe_3$), 1.70–2.23 (m, 4 H, $-CH_2CH_2-$), 3.20–3.93 (m, 4 H, $-CH_2-N$, $-CH_2-O$), 3.33 (s, 3 H, OCH_3), 3.93–4.37 (m, 1 H, H–C–N), 4.46 and 4.55 (s, 1 H, CHCl); MS, *m/e* 254.0410 ($M^+ - CH_2OCH_3$); calcd for $C_8H_{17}O_2NSSiCl$, 254.0438.

2-((Benzyloxy)methyl)-1-[(α-(trimethylsilyl)benzyl)-sulfonyl]pyrrolidine (7e). The procedure as given for **7a** was followed. However, the anion of **6e** was stirred for 1.5 h at room

temperature before silylation took place. When **6e** (5.0 g, 14 mmol) was used as starting material 5.2 g (89%) of **7e** was obtained: IR (NaCl) 1130, 1320 (SO_2), 850, 1250 cm^{-1} ($SiMe_3$); ^1H NMR ($CDCl_3$) δ 0.23 (s, 9 H, $SiMe_3$), 1.08–2.07 (m, 4 H, $-CH_2CH_2-$). 2.64–4.01 (m, 5 H, $-CH_2-N$, $-CH_2-O$, H–C–N), 4.07 and 4.22 (s, 1 H, $CHSiMe_3$), 4.47 (s, 2 H, CH_2Ph), 7.31 (s, 10 H, Ar).

Compounds **7b–d,f,i,l,m** were prepared as described for **7a**. **7j,k** were prepared as described for **7e**. See the paragraph at the end of the paper about supplementary material concerning characteristics for compounds **7b–d,f,i,j–l,m**.

***(E)*-[(2-(Methoxymethyl)pyrrolidinyl)sulfonyl]phenylsulfine (8d).** To a solution of **7d** (2.53 g, 7.43 mmol) in dry THF (50 mL) was added 1.2 equiv of *n*-BuLi at −78 °C under N_2. After stirring for 0.5 h at −78 °C the solution was added to a solution of an excess of SO_2 in THF (10 mL) at −78 °C. The reaction mixture was, after stirring overnight, poured into a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$ and concentrated. After chromatography (silica gel, ether) sulfine **8d** (1.0 g, 43%) was crystallized from ether: mp 98.5–99.5 °C; IR (KBr) 1150, 1350 (SO_2), 1050, 1125 cm^{-1} (C=S=O); ^1H NMR ($CDCl_3$) δ 1.37–2.14 (m, 4 H, $-CH_2CH_2-$), 2.94–3.83 (m, 5 H–C–N, $-CH_2O$, $-CH_2-N$), 3.30 (s, 3 H, OCH_3), 7.33–7.88 (m, 5 H, Ar); MS, *m/e* 315 (M^+). Anal. Calcd for $C_{13}H_{17}S_2O_4N$: C, 49.50; H, 5.43; N, 4.44. Found: C, 49.43, 49.41; H, 5.48, 5.46; N, 4.63, 4.63.

Following the same procedure sulfines **8e,f** were prepared. See the paragraph at the end of the paper about supplementary material concerning characteristics for compounds **8e,f**.

2-Chloro-3,6-dihydro-2-[(2-(methoxymethyl)pyrrolidinyl)sulfonyl]-4,5-dimethyl-2*H*-thiopyran 1-Oxide (9a). To a solution of **7a** (1.45 g, 4.84 mmol) in dry THF (50 mL) was added 1.2 equiv of *n*-BuLi at −78 °C under N_2. After stirring for 1.5 h at −78 °C the reaction mixture was added to a solution of an excess of SO_2 in THF (5 mL). A large excess of 2,3-dimethyl-1,3-butadiene was added at −78 °C. After stirring overnight in the dark, the mixture was poured into a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were concentrated after drying with $MgSO_4$. Chromatography (silica gel, diisopropyl ether) gave **9a** (0.99 g, 57%) as a mixture of diastereomers: IR (NaCl) 1155, 1340 (SO_2), 1070 cm^{-1} (S=O); ^1H NMR ($CDCl_3$) δ 1.73 (s, 6 H, 2 × CH_3C=C), 1.79–2.31 (m, 4 H, 2 × CH_2), 3.36 (s, 3 H, OCH_3), 4.19–4.57 (m, 1 H, H–C–N), 2.96–3.90 (m, 8 H, remaining protons); MS, *m/e* 355.0705 (M^+); calcd for $C_{13}H_{22}NS_2O_4Cl$, 355.0680. Determination of the de by ^1H NMR, $Yb(tfc)_3$ (OCH_3), and HPLC, RP-8, 225 nm, 2.0 mL/min, water/methanol (60:40).

Similar sulfoxides **9b,c,i–m** were prepared. See the paragraph at the end of the paper about supplementary material concerning characteristics for compounds **9b,c,i–m**.

3,6-Dihydro-4,5-dimethyl-2-[(2-(methoxymethyl)pyrrolidinyl)sulfonyl]-2-phenyl-2*H*-thiopyran 1-Oxide (9d). To a solution of **8d** (150 mg, 0.48 mmol) in CH_2Cl_2 (3 mL) was added an excess of 2,3-dimethyl-1,3-butadiene. After stirring for 1 week at room temperature in the dark cycloadduct **9d** (170 mg, 90%) was obtained after chromatography (silica gel, ether) as a mixture of diastereomers: IR (NaCl) 1145, 1330 (SO_2), 1050 cm^{-1} (S=O); ^1H NMR ($CDCl_3$) δ 1.33–2.23 (m, 4 H, $-CH_2CH_2-$), 1.54 and 1.78 (s, 6 H, 2 × CH_3) 3.21 and 3.30 (s, 3 H, OCH_3), 4.12–4.42 (m, 1 H, H–C–N), 7.32–7.57 (m, 3 H, Ar), 7.63–7.98 (m, 2 H, 2 × *o*-H), 2.72–3.93 (m, 8 H, remaining protons); MS, *m/e* 352 ($M^+ - CH_2OCH_3$). The predominant diastereomer could be obtained separately by crystallization from methanol: mp 145–146.5 °C; IR (KBr) 1145, 1330 (SO_2), 1050 cm^{-1} (S=O); ^1H NMR ($CDCl_3$) δ 1.54 and 1.78 (s, 6 H, 2 × CH_3), 1.45–2.00 (m, 4 H, $-CH_2CH_2-$), 3.21 (s, 3 H, OCH_3), 7.26–7.50 (m, 3 H, Ar), 7.63–7.93 (m, 2 H, 2 × *o*-H), 2.72–3.93 (m, 8 H, remaining protons).

Determination of de by ^1H NMR, $Yb(tfc)_3$ (OCH_3), and HPLC, Si-60, 254 nm, 2.0 ml/min, hexane/chloroform (60:40).

Following the same procedure sulfoxides **9e,f** were prepared. See the paragraph at the end of the paper about supplementary material concerning characteristics for compounds **9e,f**.

Acknowledgment. This investigation was supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for the Advancement of Pure Research (ZWO).

Registry No. **4a**, 63126-45-4; **4b**, 89597-94-4; **4c**, 89597-95-5; **4d**, 89597-96-6; **5a**, 63126-47-6; **5b**, 89597-97-7; **5c**, 89597-98-8; **5d**, 89597-99-9; **6a**, 89598-00-5; **6b**, 89598-01-6; **6c**, 89598-02-7; **6d**, 89598-03-8; **6e**, 89598-04-9; **6f**, 89598-05-0; **6g**, 89598-06-1; **6h**, 89598-48-1; **6i**, 89598-07-2; **6j**, 89598-08-3; **6k**, 89598-09-4; **6l**, 89598-10-7; **6m**, 89598-11-8; **7a** (isomer 1), 89598-12-9; **7a** (isomer 2), 89598-13-0; **7b** (isomer 1), 89598-14-1; **7b** (isomer 2), 89598-15-2; **7c** (isomer 1), 89598-16-3; **7c** (isomer 2), 89598-17-4; **4d** (isomer 1), 89598-18-5; **7d** (isomer 2), 89598-19-6; **7e** (isomer 1), 89598-20-9; **7e** (isomer 2), 89598-21-0; **4f** (isomer 1), 89598-22-1; **7f** (isomer 2), 89598-23-2; **7i** (isomer 1), 89598-24-3; **7i** (isomer 2), 89598-25-4; **7j** (isomer 1), 89598-26-5; **7j** (isomer 2), 89598-27-6; **7k** (isomer 1), 89598-28-7; **7k** (isomer 2), 89598-29-8; **7l** (isomer 1), 89598-30-1; **7l** (isomer 2), 89598-31-2; **7m** (isomer 1), 89598-32-3; **7m** (isomer 2), 89598-33-4; **8d**, 89598-34-5; **8e**, 89598-35-6; **8f**, 89598-36-7; **9a** (isomer 1), 89598-37-8; **9a** (isomer 2), 89673-96-1; **9b** (isomer 1), 89598-38-9; **9b** (isomer 2), 89673-97-2; **9c** (isomer 1), 89598-39-0; **9c** (isomer 2), 89673-98-3; **9d** (isomer 1), 89598-40-3; **9d** (isomer 2), 89673-99-4; **9e** (isomer 1), 89598-41-4; **9e** (isomer 2), 89674-00-0; **9f** (isomer 1), 89598-42-5; **9f** (isomer 2), 89674-01-1; **9i** (isomer 1), 89598-43-6; **9i** (isomer 2), 89674-02-2; **9j** (isomer 1), 89598-44-7; **9j** (isomer 2), 89674-03-3; **9k** (isomer 1), 89598-45-8; **9k** (isomer 2), 89674-04-4; **9l** (isomer 1), 89598-46-9; **9l** (isomer 2), 89674-05-5; **9m** (isomer 1), 89598-47-0; **9m** (isomer 2), 89674-06-6; MeI, 74-88-4; Me_3SiCl, 75-77-4; (*S*)-(−)-1-formyl-2-(hydroxymethyl)pyrrolidine, 55456-46-7; triphenylmethyl chloride, 76-83-5; chloromethanesulfonyl chloride, 3518-65-8; benzyl bromide, 100-39-0; 2,3-dimethyl-1,3-butadiene, 513-81-5; 2,4,6-trimethylbenzyl chloride, 1585-16-6; phenylmethanesulfonyl chloride, 1939-99-7; methanesulfonyl chloride, 124-63-0; ethanesulfonyl chloride, 594-44-5.

Supplementary Material Available: Characteristics of compounds **4–9** which are not described in the Experimental Section (10 pages). Ordering information is given on any current masthead page.