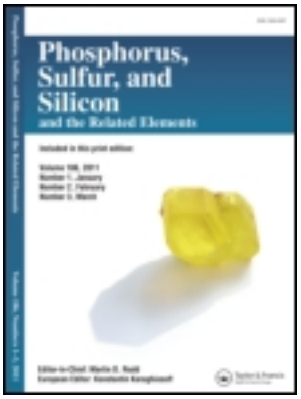

Phosphorus, Sulfur, and Silicon and the Related Elements

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One-Pot Synthesis and Asymmetric Oxidation of 2-Nitro-4-(Trifluoromethyl)Benzene Containing Sulfides

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ONE-POT SYNTHESIS AND ASYMMETRIC OXIDATION OF 2-NITRO-4-(TRIFLUOROMETHYL)BENZENE CONTAINING SULFIDES

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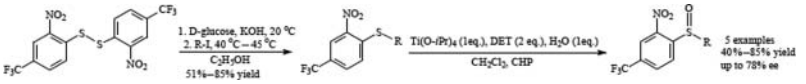
GRAPHICAL ABSTRACT



Abstract *An efficient one-pot method for the preparation of 2-nitro-4-(trifluoromethyl)benzene containing sulfides from 1,1′-disulfanediylbis[2-nitro-4-(trifluoromethyl)benzene] is proposed. The corresponding enantiomerically enriched sulfoxides with up to 78% enantiomeric excess are prepared by the asymmetric oxidation of sulfides using a modified Sharpless method. The yield of sulfoxides is shown to decrease with an increase in the bulk of the aliphatic group and with a decrease of the inductive effect of the hydrocarbonic moiety on the sulfur atom.*

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords Fluorinated sulfides; fluorinated sulfoxides; asymmetric sulfoxidation; Sharpless method

INTRODUCTION

The interest in chiral sulfoxides is due to their employment in asymmetric synthesis[1] and enantioselective catalysis as ligands.[2] The increasing use of chiral sulfur ligands in asymmetric catalysis has been published in recent reviews.[3] Nonracemic sulfoxides are also employed in enantioselective organocatalysis.[4] The next aspect of enantiomerically enriched sulfoxides employment is related to their high biological activity.[5] It should be

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noted that in the last years, nonracemic compounds are widely used in pharmaceutical industry,[6] among them are sulfinyl derivatives, that play an essential role.[7]

Fluorinated sulfoxides are of special interest. The introduction of a trifluoromethyl group allows one not only to retain high pharmacological activity of sulfoxides but also to increase considerably the solubility in nonpolar solvents and lipids, which obviously increases the speed of absorption and plays a key role in the compound's transportation in vivo.[8] Fluoro-containing sulfoxides remain an insufficiently explored class of compounds inspite of the shown interest of the researchers[9] and the fact that some fluorinated substrates have already been employed as insecticides,[10] gastric acid secretion inhibitors,[11] and antileishmanial preparations.[12] Among the methods for preparation of enantiomerically enriched sulfoxides (separation of a racemic mixture,[13] transformation of a reagent from the chiral pool,[14] enzymatic systems,[15] or the use of chiral catalyst for enantioselective synthesis[16]), there is a simple and universal method of approach, based on the enantioselective oxidation of the corresponding prochiral sulfides with the use of catalytic systems.

According to the literature data,[17] the Sharpless method modified by Kagan allows one to carry out the enantioselective oxidation of alkyl aryl sulfides in good yields and high enantiomeric excess (ee).

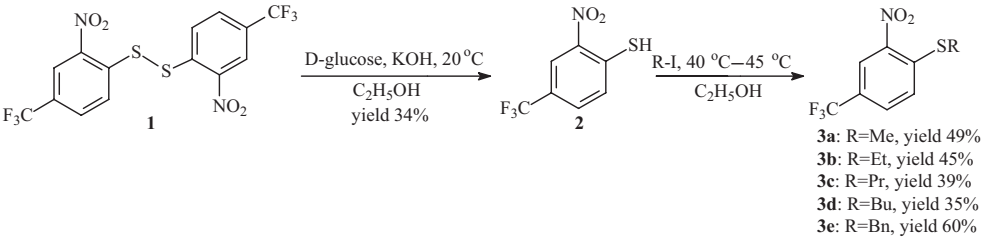
Preparation of thioethers (the initial substrates for oxidation) is also an important problem of modern organic chemistry. It is related not only to the fact that sulfides are the main intermediates in the synthesis of sulfoxides, but also to the role in bio-organic and medicinal chemistry.[18] There are a number of methods for the preparation of sulfides[19] but a general one is the condensation of a metal alkyl or aryl thiolate with an alkyl halide in the presence of a strong base.[20] Among the shortcomings of this method, a special attention should be focused on the heat of the reaction mixture, as in the case of thiol, instability can result in the formation of undesirable products such as disulfides and resins. The instability of the initial thiol also causes complications in its use in synthesis.

In the present work, we have compared a general method of approach to the synthesis of 2-nitro-4-(trifluoromethyl)benzene containing sulfides by the use of thiol and our one-pot method based on the reduction of the corresponding disulfide. As an available and selective reducing agent, we have chosen glucose, the use of which has been published earlier in analogous reactions.[21] In addition, here we report the asymmetric oxidation of the sulfides in the presence of a modified Sharpless system.

RESULTS AND DISCUSSION

The synthesis of 2-nitro-4-(trifluoromethyl)benzenethiol (**2**) began with the addition of an alcoholic solution of KOH to an alcoholic suspension of the initial commercially available and convenient in use disulfide **1** and glucose at room temperature (Scheme 1).

Under these conditions, thiol **2** was obtained in 34% yield. The selection of glucose as a reducing agent is related to its availability and the selectivity of the reduction (under these conditions a nitro group is not reduced to an amino group). It should be noted that a temperature increase leads to a considerable decrease of the conversion of disulfide and thiol yield. Earlier it has been proposed to use aqueous alcoholic solutions in the analogous reactions.[21] However, it leads to complications in thiol extraction, and therefore, it is useful to apply anhydrous ethanol as a solvent.

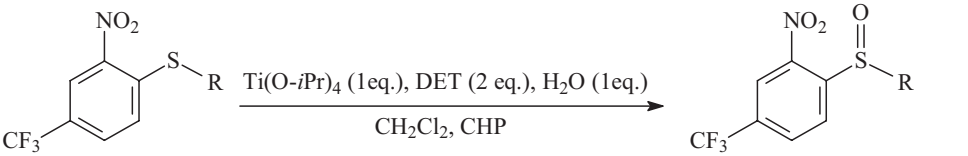


Scheme 1

Then, following the general procedure, to an alcoholic solution of **2** in the presence of a strong base (KOH) alkyl iodide was added. The yield and conversion were insufficient at room temperature, but on heating up to 40 °C–45 °C, we succeeded to obtain sulfides in 35%–60% yield.

A one-pot method is shorter and more efficient by omitting the stage of thiol extraction, the work with which is difficult enough (air oxidation by oxygen already occurred upon gentle heating, and instability was observed under the conditions of column chromatography). Glucose and the products of its oxidation do not prevent the main reaction (presumably, the oxidized product is a lactone, it has not isolated). The only required condition for good yields is an accurate adjustment of temperature (40 °C–45 °C), because on heating above 55 °C–60 °C the sulfides are unstable. In addition, the conduction of the reaction in one stage allowed a reduction in the time of the synthesis to only 15–20 min. All sulfides were isolated by column chromatography. Sulfide **3d** was crystallized from diethyl ether/hexane and unambiguously characterized by means of X-ray experiments (see Figure S1; supplemental materials).

The corresponding sulfoxides **4a–e** in yields 40%–85% and ee 11%–78% (Scheme 2) were obtained by asymmetric oxidation. The Sharpless method modified by Kagan was chosen as the catalytic system.



3a: R=Me,
3b: R=Et,
3c: R=Pr,
3d: R=Bu,
3e: R=Bn,

4a: R=Me, yield 60%, ee 20%;
4b: R=Et, yield 52%, ee 68%;
4c: R=Pr, yield 47%, ee 62%;
4d: R=Bu, yield 40%, ee 11%;
4e: R=Bn, yield 85%, ee 78%.

Scheme 2

Oxidation proceeded at room temperature for 1–2 h in anhydrous dichloromethane in the presence of Sharpless modified reagent.[17] At low temperatures, reaction did not proceed. The oxidizer was a solution of cumene hydroperoxide (CHP) in cumene. The yield of sulfoxides increased with transition from a C_4H_9-moiety at sulfur atom to a CH_3-group one and further to a benzene-moiety. Sulfoxide with the benzene-moiety (**4e**) is

Table 1 Crystal data and data collection parameters

Compound	**3d**	**4a**	**4d**
Empirical formula	$C_{11}H_{12}F_3NO_2S$	$C_8H_6F_3NO_3S$	$C_{11}H_{12}F_3NO_3S$
Formula weight	279.28	253.20	295.28
Temperature (K)	130(2)	295(2)	136(2)
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	P-1	$P2_1/n$	$P2_1/n$
a(Å)	12.0506(6)	5.6927(4)	14.8786(17)
b(Å)	13.6622(11)	5.6294(6)	5.3901(6)
c(Å)	15.7467(13)	30.660(3)	16.5318(19)
α (°)	80.205(7)	90	90
β (°)	74.194(6)	92.994(7)	96.722(9)
Γ (°)	84.277(5)	90	90
Volume (Å^3)	2454.2(3)	981.19(16)	1316.7(3)
Z	8	4	4
Calculated density (g/cm^3)	1.512	1.714	1.490
Absorption coefficient (mm^{-1})	0.295	0.367	0.285
F (000)	1152	512	608
Crystal size (mm)	0.41 × 0.18 × 0.08	0.46 × 0.25 × 0.07	0.46 × 0.19 × 0.02
Crystal color/shape	Yellow prism	Yellow plate	Yellow plate
θ Range for data collection (°)	2.63–28.28	2.66–26.37	3.49–26.38
Completeness (%)	96.2	97.5	98.4
Reflections collected	24155	4624	6540
Independent reflections (R_{int})	11698 (0.0361)	1940 (0.0573)	2650 (0.0657)
Observed reflections [$I > 2\sigma(I)$]	6082	954	1199
Refinement method	Full-matrix least-squares on F^2		
Data/restrains/parameters	11698/72/706	1940/0/145	2650/0/172
Goodness of fit on F^2	1.004	1.000	0.961
R_1 (all data)	0.0973	0.1507	0.1157
wR_2 (all data)	0.0583	0.1153	0.0630
R_1 [$I > [2\sigma(I)]$]	0.0387	0.0605	0.0440
wR_2 [$I > [2\sigma(I)]$]	0.0542	0.1003	0.0581
Largest peak and hole (eÅ^{-3})	0.339 and –0.346	0.210 and –0.263	0.302 and –0.313

obtained in the most yield and enantiomeric excess. A total dependence of enantiomeric excess on the length of hydrocarbonic group was not observed that is typical for analogous reactions. All sulfoxides were isolated by column chromatography; sulfoxides **4a**,**d** were crystallized from diethyl ether/hexane and unambiguously characterized by means of X-ray experiments (see Figures S2 and S3, supplemental information; Table 1). Bond lengths and

Table 2 Selected X-ray determined bond lengths (in Å) and angles (in °)

Compound		S–C_{Ar}	S–C_{Alk}	S–O	C_{Alk}–S–C_{Ar}	C_{Ar}–S–O
3d	1	1.7496 (19)	1.8147 (18)	—	103.33 (8)	—
	2	1.7530 (18)	1.8064 (18)	—	103.18 (8)	—
	3	1.7470 (18)	1.8083 (18)	—	103.17 (9)	—
	4	1.7521 (18)	1.8130 (18)	—	103.18 (9)	—
4a		1.818 (4)	1.782 (4)	1.484 (3)	96.38 (19)	104.20 (18)
4d		1.815 (2)	1.809 (2)	1.4948 (18)	95.17 (12)	105.16 (11)

angles for S-contained moieties of **3d**, **4a**, and **4d** (Table 2) are typical for these classes of compounds.[22]

CONCLUSION

In conclusion, the efficient one-pot synthesis of 2-nitro-4-(trifluoromethyl)benzene containing sulfides has been achieved starting from the corresponding disulfide. We have proposed to use disulfide in the synthesis of sulfides as initial substrate. As a result of the enantioselective Sharpless oxidation, the enantiomerically enriched 2-nitro-4-(trifluoromethyl)benzene containing sulfoxides have been obtained. The yield of sulfoxides is shown to decreases with an increase in the bulk of aliphatic moiety and with a decrease of the inductive effect of the hydrocarbonic group on the sulfur atom.

EXPERIMENTAL

General Experimental Procedures

All reactions were performed with magnetic stirring using freshly distilled solvents unless otherwise indicated. All reactions of oxidation (with $Ti(O\text{-}iPr)_4$) were performed under an atmosphere of argon. Dichloromethane and ethanol were distilled from calcium hydride. All other commercially available reagents were used as received unless otherwise specified. All reactions were monitored by thin layer chromatography (TLC) using MERCK precoated silica gel 60 F254 and diethyl ether/hexane mixtures as eluents; the TLC spots were visualized with $KMnO_4/H_2SO_4$ solution. Column chromatography was carried out using Merck type 9385 silica gel and diethyl ether/hexane mixtures as eluents.

Proton magnetic resonance spectra were recorded on a Bruker Avance 300 spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) and are referenced to the residual nondeuterated solvent peak (7.26 ppm for $CHCl_3$ of $CDCl_3$). Coupling constants (J) are reported in hertz. Data are reported as follows: s, singlet; d, doublet; t, triplet; m, multiplet; and dd, double doublet. Carbon magnetic resonance spectra were recorded on a Bruker Avance 300 spectrometer operating at 75 MHz. Chemical shifts (δ) are reported in ppm and are referenced to the deuterated solvent peak (77.0 ppm for ^{13}C of $CDCl_3$). Fluorine magnetic resonance spectra were recorded on a Bruker Avance 300 spectrometer operating at 282 MHz. Chemical shifts (δ) are reported (trifluoroacetic acid as the internal standard). Melting points were determined using a Gallenkamp-Sanyo apparatus. Optical rotations were measured using a Kruss P3002RS polarimeter with a 10 cm cell and are reported as follows: $[\alpha]_D^{t^\circ C}$ (concentration in g/10 mL, solvent). Elemental analyses were performed using an automatic analyzer EA 1110 CHNS-O. All the ee of sulfoxides were measured by chiral high-performance liquid chromatography analysis: Chiralcel OD-H and Chiralcel OJ-H columns using a Surveyor LC with a UV detector.

X-Ray Structure Data Collection and Refinement

X-ray intensity data were collected with an Xcalibur 3 diffractometer with a CCD detector using Mo-$K\alpha$ ($\lambda = 0.71069$ Å) radiation. Crystal data and data collection parameters are summarized in Table 1 (supplemental materials). The unit cell parameters were refined using all collected spots after the integration process. The data were not corrected for absorption. The structures were solved by direct methods using SHELX97.[23] All the

structures were refined by full-matrix least-squares on F^2 using SHELX97. All the non-hydrogen atoms were refined with anisotropic temperature factors. The hydrogen atoms were calculated with AFIX and were included in the refinement with a common isotropic temperature factor. Crystallographic data for the structure of compounds **3d**, **4a**, and **4d** have been deposited with the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication numbers CCDC 803705, 803707, and 803706. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (E-mail deposit@ccdc.cam.ac.uk).

2-Nitro-4-(Trifluoromethyl)Benzenethiol (2)

To a solution of **1** (444 mg, 1 mmol) in EtOH (10 mL) a solution of α-D-glucose (540 mg in EtOH, 5 mL, 3 mmol) was added at 55 °C. The mixture was stirred at 55 °C for 10 min, the temperature was then adjusted to 20 °C, and a solution of KOH (168 mg in EtOH, 7 mL, 3 mmol) was added. After 10 min at 20 °C, the conversion of disulfide was 92%. The solvent was removed in vacuo and the product was purified on silica. Purification afforded **2** as a yellowish solid (152 mg, 34%). mp 35 °C–36 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.26 (s, 1H, SH), 7.61 (d, $J = 8.4$ Hz, 1H), 7.70 (d, $J = 8.4$ Hz, 1H), 8.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 121.9 (dd, $J_{C,F} = 272.1$ Hz), 123.7 (dd, $J_{C,F} = 4.9$ Hz), 126.9 (dd, $J_{C,F} = 103.54$ Hz), 129.7 (dd, $J_{C,F} = 4.9$ Hz), 132.8 (d, $J_{C,F} = 4.9$ Hz), 144.1, 146.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.9 (s). Anal. Calcd. for $C_7H_4F_3NO_2S$: C, 37.67; H, 1.81; N, 6.28; O, 14.34; S, 14.37. Found: C, 37.59; H, 1.97; N, 6.10; O, 14.22; S, 14.30.

General Procedure for Synthesis of Sulfides (Two Step)

To a solution of **2** (223 mg, 1 mmol) in EtOH (5 mL) a solution of KOH (56 mg in EtOH, 3 mL, 1 mmol) was added at 20 °C. The mixture was stirred at 20 °C for 10 min, the temperature was then adjusted to 40 °C–45 °C, and a solution of alkyl iodide (1 mmol in EtOH, 5 mL) was added. After 20 min at 40 °C–45 °C, the solvent was removed in vacuo and the products were purified on silica using 50:1 hexane/diethyl ether. Purification afforded sulfides. The yields of all sulfides are shown in Scheme 1.

General Procedure for Synthesis of Sulfides (One Pot)

To a solution of **1** (444 mg, 1 mmol) in EtOH (10 mL) a solution of α-D-glucose (540 mg in EtOH, 5 mL, 3 mmol) was added at 55 °C. The mixture was stirred at 55 °C for 10 min, the temperature was then adjusted to 20 °C and a solution of KOH (168 mg in EtOH, 7 mL, 3 mmol) was added. Then a solution of alkyl iodide (2 mmol in EtOH, 5 mL) was added and the temperature was adjusted to 40 °C–45 °C. After 10 min at 40 °C–45 °C the solvent was removed in vacuo and the products were purified on silica using 50:1 hexane/diethyl ether. Purification afforded sulfides.

1-(Methylsulfanyl)-2-Nitro-4-(Trifluoromethyl)Benzene 3a. Yellowish solid[24]: mp 85 °C–86 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.59 (s, 3H), 7.54 (d, $J = 7.8$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.1, 122.9 (dd, $J_{C,F} = 272.1$ Hz), 123.5 (dd, $J_{C,F} = 3.6$ Hz), 126.4 (d, $J_{C,F} = 3.6$ Hz), 127.1 (dd, $J_{C,F} = 103.55$ Hz), 129.7 (dd, $J_{C,F} = 3.6$ Hz), 142.8, 144.8; ^{19}F NMR (282 MHz, $CDCl_3$)

δ −62.6 (s). Anal. Calcd. for $C_8H_6F_3NO_2S$: C, 40.51; H, 2.55; N, 5.90; O, 13.49; S, 13.52. Found: C, 40.60; H, 2.66; N, 5.78; O, 13.28; S, 13.40.

1-(Ethylsulfanyl)-2-Nitro-4-(Trifluoromethyl)Benzene 3b. Yellowish solid: mp 69 °C–70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.48 (t, J = 7.4 Hz, 3H), 3.08 (dd, J = 7.4 Hz, 2H), 7.57 (d, J = 8.3 Hz, 1H), 7.80 (d, J = 8.3 Hz, 1H), 8.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6, 26.5, 122.9 (dd, $J_{C,F}$ = 272.2 Hz), 123.5 (dd, $J_{C,F}$ = 3.6 Hz), 126.9 (d, $J_{C,F}$ = 3.6 Hz), 127.1 (dd, $J_{C,F}$ = 103.7 Hz), 129.5 (dd, $J_{C,F}$ = 3.6 Hz), 142.7, 144.88; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.5 (s). Anal. Calcd. for $C_9H_8F_3NO_2S$: C, 43.03; H, 3.21; N, 5.58; O, 12.74; S, 12.76. Found: C, 42.90; H, 3.20; N, 5.67; O, 12.68; S, 12.85.

2-Nitro-1-(Propylsulfanyl)-4-(Trifluoromethyl)Benzene 3c. Yellowish solid: mp 69 °C–70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H), 1.85 (sextet, J = 7.1 Hz, 2H), 3.02 (t, J = 7.1 Hz, 2H), 7.56 (d, J = 8.7 Hz, 1H), 7.79 (d, J = 8.7 Hz, 1H), 8.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 21.3, 34.4, 123.0 (dd, $J_{C,F}$ = 272.5 Hz), 123.5 (dd, $J_{C,F}$ = 4.9 Hz), 127.0 (d, $J_{C,F}$ = 4.9 Hz), 127.2 (dd, $J_{C,F}$ = 103.72 Hz), 129.4 (dd, $J_{C,F}$ = 4.9 Hz), 142.7, 144.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.5 (s). Anal. Calcd. for $C_{10}H_{10}F_3NO_2S$: C, 45.28; H, 3.80; N, 5.28; O, 12.06; S, 12.09. Found: C, 45.18; H, 3.88; N, 5.38; O, 12.16; S, 12.92.

1-(Butylsulfanyl)-2-Nitro-4-(Trifluoromethyl)Benzene 3d. Yellowish solid: mp 56 °C–57 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (t, J = 7.3 Hz, 3H), 1.58–1.60 (m, 2H), 1.80–1.82 (m, 2H), 3.04 (t, J = 7.3 Hz, 2H), 7.56 (d, J = 8.5 Hz, 1H), 7.79 (d, J = 8.5 Hz, 1H), 8.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 22.3, 29.7, 32.1, 122.9 (dd, $J_{C,F}$ = 274.1 Hz), 123.5 (dd, $J_{C,F}$ = 3.4 Hz), 127.0 (d, $J_{C,F}$ = 3.4 Hz), 127.1 (dd, $J_{C,F}$ = 103.74 Hz), 129.4 (dd, $J_{C,F}$ = 3.4 Hz), 142.8, 144.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.6 (s). Anal. Calcd. for $C_{11}H_{12}F_3NO_2S$: C, 47.31; H, 4.33; N, 5.02; O, 11.46; S, 11.48. Found: C, 47.22; H, 4.40; N, 5.21; O, 11.52; S, 11.58.

1-(Benzylsulfanyl)-2-Nitro-4-(Trifluoromethyl)Benzene 3e. Yellowish solid: mp 132 °C–133 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.29 (s, 2H), 7.33–7.51 (m, 5H), 7.62 (d, J = 8.7 Hz, 1H), 7.77 (d, J = 8.7 Hz, 1H), 8.54 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.6, 123.5 (dd, $J_{C,F}$ = 3.5 Hz), 122.9 (dd, $J_{C,F}$ = 272.1 Hz), 127.1 (dd, $J_{C,F}$ = 103.74 Hz), 127.3 (d, $J_{C,F}$ = 3.5 Hz), 128.1, 129.0, 129.0, 129.6 (dd, $J_{C,F}$ = 3.5 Hz), 134.1, 143.0, 145.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.6 (s). Anal. Calcd. for $C_{14}H_{10}F_3NO_2S$: C, 53.67; H, 3.22; N, 4.47; O, 10.21; S, 10.23. Found: C, 53.78; H, 3.18; N, 4.58; O, 10.36; S, 10.15.

General Procedure for Synthesis of Sulfoxides

(–)-Diethyl-D-tartrate (1 mmol), titanium tetraisopropoxide (2 mmol), and water (1 mmol) were added to a solution of sulfide (1 mmol) in dichloromethane (10 mL) at room temperature. The mixture was stirred for 30 min and CHP (84% in cumene, 1 mmol) was added. After 6 h, the solvent was removed in vacuo and the products were purified on silica using 50:5 hexane/diethyl ether. Purification afforded sulfoxides. The yields of all sulfoxides are shown in Scheme 2.

1-(Methylsulfinyl)-2-Nitro-4-(Trifluoromethyl)Benzene 4a. Yellowish solid: mp 109 °C–110 °C; $[\alpha]_D^{25}$ = +37.5 (*c* 0.45, *n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.00 (s, 3H), 8.26 (d, J = 8.2 Hz, 1H), 8.55–8.63 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.8, 122.3 (dd, $J_{C,F}$ = 273.5), 122.4 (d, $J_{C,F}$ = 3.4 Hz), 127.6, 132.1 (d, $J_{C,F}$ = 3.4 Hz), 133.4 (dd, $J_{C,F}$ = 35.1 Hz), 145.1, 146.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.9 (s). Anal. Calcd. for $C_8H_6F_3NO_3S$: C, 37.95; H, 2.39; N, 5.53; O, 18.96; S, 12.66. Found: C, 37.84; H, 2.45;

N, 5.50; O, 18.88; S, 12.78. Chiralcel OD-H column at λ 254 nm, *n*-hexane/2-propanol (85:15) as eluent, and a flow rate of 1.0 mL/min: $t_{maj} = 20.58$, $t_{min} = 12.56$ min, ee = 20%.

1-(Ethylsulfinyl)-2-Nitro-4-(Trifluoromethyl)Benzene 4b. Yellowish solid: mp 55 °C–56 °C; $[\alpha]_D^{25} = +152.9$ (*c* 0.35, *n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (t, $J = 6.9$ Hz, 3H), 2.84–2.98 (m, 1H), 3.25–3.41 (m, 1H), 8.22 (d, $J = 8.2$ Hz, 1H), 8.48 (d, $J = 8.2$ Hz, 1H), 8.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.9, 49.7, 122.0 (dd, $J_{C,F} = 272.8$), 122.6 (d, $J_{C,F} = 4.9$ Hz), 128.6, 131.5 (d, $J_{C,F} = 4.9$ Hz), 133.3 (dd, $J_{C,F} = 35.3$ Hz), 145.0, 146.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.9 (s). Anal. Calcd. for $C_9H_8F_3NO_3S$: C, 40.45; H, 3.02; N, 5.24; O, 17.96; S, 12.00. Found: C, 40.53; H, 3.12; N, 5.18; O, 17.99; S, 12.11. Chiralcel OD-H column at λ 254 nm, *n*-hexane/2-propanol (85:15) as eluent, and a flow rate of 1.0 mL/min: $t_{maj} = 18.59$, $t_{min} = 10.10$ min, ee = 68%.

2-Nitro-1-(Propylsulfinyl)-4-(Trifluoromethyl)Benzene 4c. Yellowish solid: mp 63 °C–64 °C; $[\alpha]_D^{25} = +53.3$ (*c* 0.35, *n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (t, $J = 7.7$ Hz, 3H), 1.74–1.91 (m, 1H), 2.03–2.20 (m, 1H), 2.77–2.89 (m, 1H), 3.16–3.28 (m, 1H), 8.23 (d, $J = 9.0$ Hz, 1H), 8.52 (d, $J = 9.0$ Hz, 1H), 8.61 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 21.3, 34.4, 121.9 (dd, $J_{C,F} = 272.3$), 123.5 (d, $J_{C,F} = 4.9$ Hz), 127.0, 129.4 (d, $J_{C,F} = 4.9$ Hz), 133.2 (dd, $J_{C,F} = 35.0$ Hz), 145.0, 145.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.9 (s). Anal. Calcd. for $C_{10}H_{10}F_3NO_3S$: C, 42.70; H, 3.58; N, 4.98; O, 17.07; S, 11.40. Found: C, 42.81; H, 3.68; N, 4.89; O, 17.00; S, 11.49. Chiralcel OJ-H column at λ 254 nm, *n*-hexane/2-propanol (85:15) as eluent, and a flow rate of 1.0 mL/min: $t_{maj} = 12.19$, $t_{min} = 9.26$ min, ee = 62%.

1-(Butylsulfinyl)-2-Nitro-4-(Trifluoromethyl)Benzene 4d. Yellowish solid: mp 73 °C–74 °C; $[\alpha]_D^{25} = +20.0$ (*c* 0.3, *n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.01 (t, $J = 7.8$ Hz, 3H), 1.41–1.64 (m, 2H), 1.66–1.82 (m, 1H), 1.97–2.16 (m, 1H), 2.76–2.90 (m, 1H), 3.19–3.33 (m, 1H), 8.23 (d, $J = 9.7$ Hz, 1H), 8.52 (d, $J = 9.7$ Hz, 1H), 8.61 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 21.7, 25.1, 56.9, 122.3 (dd, $J_{C,F} = 273.8$), 122.7 (d, $J_{C,F} = 3.7$ Hz), 128.2, 131.7 (d, $J_{C,F} = 3.7$ Hz), 133.9 (dd, $J_{C,F} = 35.1$ Hz), 145.0, 146.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.9 (s). Anal. Calcd. for $C_{11}H_{12}F_3NO_3S$: C, 44.74; H, 4.10; N, 4.74; O, 16.26; S, 10.86. Found: C, 44.68; H, 4.15; N, 4.66; O, 16.34; S, 10.95. Chiralcel OD-H column at λ 254 nm, *n*-hexane/2-propanol (85:15) as eluent, and a flow rate of 1.0 mL/min: $t_{maj} = 16.06$, $t_{min} = 8.40$ min, ee = 11%.

1-(Benzylsulfinyl)-2-Nitro-4-(Trifluoromethyl)Benzene 4e. Yellowish solid: mp 125 °C–126 °C; $[\alpha]_D^{25} = +222.3$ (*c* 0.3, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.32 (d, $J = 12.8$ Hz, 2H), 7.10–7.17 (m, 2H), 7.25–7.38 (m, 3H), 7.95–8.02 (m, 2H), 8.58 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 61.9, 122.1 (dd, $J_{C,F} = 3.8$ Hz), 122.4 (dd, $J_{C,F} = 273.1$), 128.5, 128.8, 128.9, 129.4, 130.4, 131.2 (dd, $J_{C,F} = 3.8$ Hz), 134.0 (dd, $J_{C,F} = 35.0$ Hz), 145.1, 146.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.9 (s). Anal. Calcd. for $C_{14}H_{10}F_3NO_3S$: C, 51.06; H, 3.06; N, 4.25; O, 14.58; S, 9.74. Found: C, 51.12; H, 3.15; N, 4.20; O, 14.62; S, 9.78. Chiralcel OD-H column at λ 254 nm, *n*-hexane/2-propanol (85:15) as eluent, and a flow rate of 1.0 mL/min: $t_{maj} = 30.13$, $t_{min} = 15.46$ min, ee = 78%.

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