JOC The Journal of Organic Chemistry

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Unusual Deoxidative Coupling Reaction of β-Sulfinyl Esters with Benzylic Trimethylammonium Salts

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Cite This: J. Org. Chem. 2021, 86, 7806−7812 Read Online

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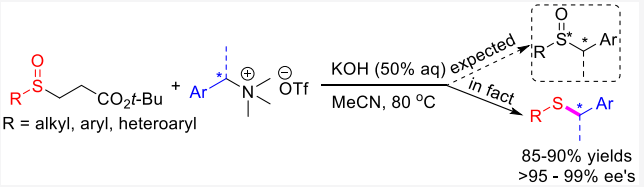
ABSTRACT: A KOH-promoted unusual deoxidative coupling reaction of β-sulfinyl esters with benzylic trimethylammonium salts to produce thioethers is discovered for the first time. If quaternary ammonium salts synthesized from enantiomerically enriched amines are adopted, highly enantiomerically enriched benzyl thioethers (>95−99% ee) with configurations opposite to those of the enantiomerically enriched amines are obtained.

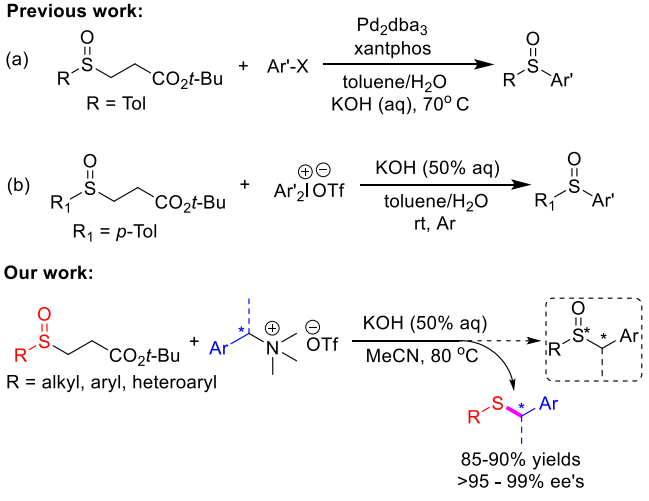


With more and more new bioactive organosulfur compounds being discovered and used in the clinic, organosulfur chemistry, especially chiral organosulfur chemistry, is developing rapidly.[1,2] Sulfinate anions (RSO^-),[3−5] a class of new reactive organosulfur intermediates, have recently displayed valuable applications in enantioselective reactions and cross-coupling reactions.

Sulfinate anions (RSO^-) could react with halogenated aryl groups to form diaryl sulfoxides under the catalysis of palladium (Scheme 1a).[6] The transition-metal-free arylation reaction of diaryliodonium salts and sulfenate anions generated from β-sulfinyl esters was developed by Bolm's group in 2018 (Scheme 1b).[7] In this process, the diaryl sulfoxides were also formed under mild reaction conditions.

As part of our ongoing research on organosulfur chemistry,[8,9] we tried to explore the reaction between sulfinate anions (RSO^-) and benzyl quaternary ammonium salts to synthesize chiral benzylic sulfoxides under reaction conditions similar to those of Bolm's protocol and Poli's method.[6,7] However, we found that the products were not the expected benzylic sulfoxides but instead thioethers, which is an interesting unusual new reaction. In this context, we wish to report the unusual deoxidative coupling reaction of β-sulfinyl esters with benzylic trimethylammonium salts (Scheme 1).

Scheme 1. Reaction of Some Sulfinate Anions with Electrophiles

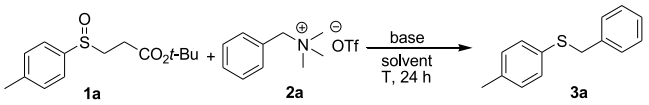


First, 3-(toluene-4-sulfinyl)-propionic acid *tert*-butyl esters and benzyl quaternary ammonium salts[10−12] were used as template substrates for a preliminary reactivity exploration and condition optimization (Table 1). In the beginning, the reaction in toluene with Cs_2CO_3 as the base went well, and the target product was obtained with a yield of 60% (Table 1, entry 1). When exploring the effect of the catalyst on the reaction, we found that the reaction with a transition-metal catalyst or without a catalyst made little difference (Table 1, entries 2−4). Then, the effects of various bases on the reaction were further explored (Table 1, entries 1 and 5−7). The results show that the reaction could proceed smoothly under weaker bases such as Cs_2CO_3 and K_2CO_3, but strong bases such as ^{t}BuOK and KOH gave higher yields (Table 1, entries 6 and 7 vs 1 and 5, respectively). Solvent screening demonstrated that acetonitrile achieved the best result under the reaction conditions (Table 1, entries 7−12). Increasing the temperature to 80 °C greatly promoted the reaction, affording a highest yield of 90% (Table 1, entries 12−14). Since the boiling point of acetonitrile is 81.6 °C, no higher temperature was tested.

Received: March 15, 2021
Published: May 17, 2021

https://doi.org/10.1021/acs.joc.1c00615
J. Org. Chem. 2021, 86, 7806−7812

Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	base	solvent	temperature (°C)[c]	yield (%)[b]
1		Cs_2CO_3	toluene	60	60
2	CuI	Cs_2CO_3	toluene	60	65
3	$NiCl_2$	Cs_2CO_3	toluene	60	60
4	$Pd(OAc)_2$	Cs_2CO_3	toluene	60	69
5		K_2CO_3	toluene	60	63
6		*t*-BuOK	toluene	60	76
7		KOH	toluene	60	80
8		KOH	DMSO	60	88
9		KOH	THF	60	79
10		KOH	DMF	60	82
11		KOH	dioxane	60	81
12		KOH	MeCN	60	86
13		KOH	MeCN	40	57
14		KOH	MeCN	80	90

[a]Unless otherwise specified, perform the reaction with **1a** (1.0 mmol) and **2a** (1.2 mmol) under closed conditions in a test tube with a sleeve rubber stopper. For entries 1−6, perform the reaction with Cs_2CO_3, K_2CO_3, or *t*-BuOK (4 equiv). For entries 7−14, perform the reaction with a KOH (50% aqueous, 20.0 equiv) and solvent (5 mL). [b]Isolated yield. [c]Oil bath.

With the optimized reaction conditions in hand, various benzylic quaternary ammonium salts, 3-(toluene-4-sulfinyl)-propionic acid, and *tert*-butyl ester were investigated. The outcomes of these transformations are shown in Table 2. The various benzylic quaternary ammonium salts were tested with different substituted groups, leading to a transformation into the desired products in 85−90% yields (**3a**−**3l**). In addition, compound **3j** could be used in the synthesis of drug intermediates and material intermediates 2-(4-chloro-3-methyl-2-pyridylmethylthio)-1*H*-benzimidazole.

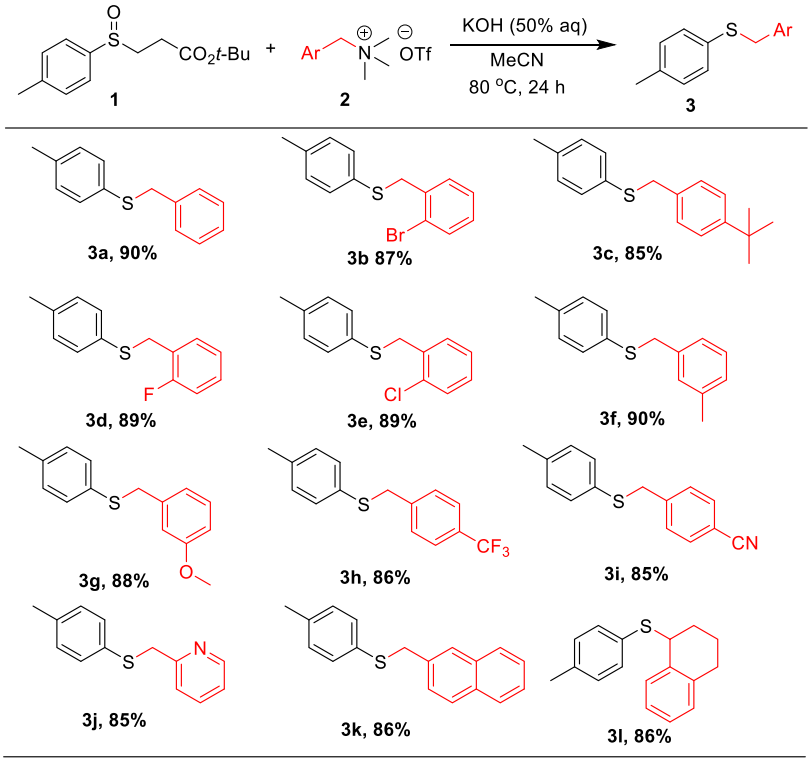
To show that this protocol was applicable to a wider range of substrates, various *β*-sulfinyl esters were evaluated (Table 3). The transformation was performed and provided the corresponding products in 85%−89% yields (**3m**−**3w**).

This deoxidative coupling reaction also provided an excellent stereospecific synthesis of enantioenriched benzylic thioethers with am inverse absolute configuration (Table 4). Importantly, no racemization occurred during this coupling reaction. The products **5a** and **5b** have nearly the same enantiomeric purities as those of the starting (*R*)- and (*S*)-benzylic amines **4a** and **4b**, respectively. By comparing our corresponding products as well as the reported optical rotation[21] and HPLC elution order of the highly enantiomerically enriched product, the absolute configuration of our product was determined. The obtained target product had a configuration opposite to that of the highly enantiomerically enriched benzyltrimethylammonium triflate, suggesting that the reaction occurred through an S_N2-type Walden inversion.[12−14]

To check the effectiveness of the synthesis method, a gram-scale reaction was carried out (Scheme 2). The 10 mmol scale reaction gave the targeted product with a yield of 81%.

To explore the reaction mechanism, we conducted a few control experiments (Scheme 3). First, experiments based on

Table 2. Scope of Benzyl Quaternary Ammonium Salts[a]



[a]Reaction conditions are as follows: **1a** (1 mmol), **2** (1.2 mmol, 1.2 equiv), and KOH (50% aqueous, 20.0 equiv) in MeCN (5 mL) at 80 °C under air for 24 h.

https://doi.org/10.1021/acs.joc.1c00615
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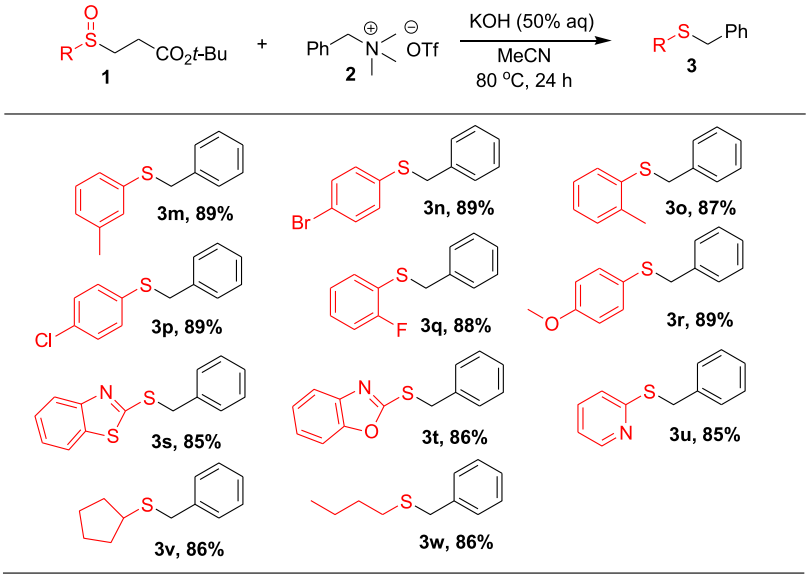
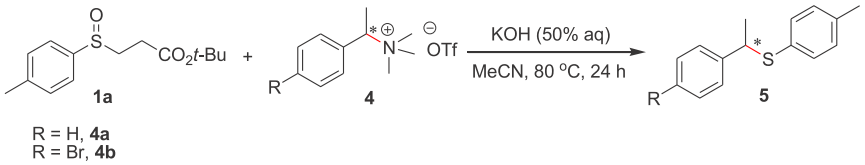
Table 3. Scope of β-Sulfinyl Esters[a]



[a]Reaction conditions are as follows: **1** (1 mmol), **2a** (1.2 mmol, 1.2 equiv), and KOH (50% aqueous, 20.0 equiv) in MeCN (5 mL) at 80 °C under air for 24 h.

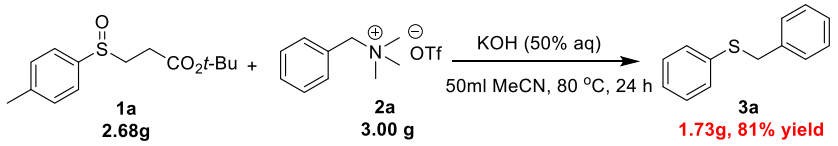
Table 4. Scope of the Reaction of Enantioenriched Benzylic Ammonium Salts with β-Sulfinyl Esters[a]



entry	4[b]	product 5	yield (%)	ee (%)
1	*rac*-**4a**	*rac*-**5a**	85	
2	(*R*)-**4a**	(*S*)-**5a**	85	95
3	(*S*)-**4a**	(*R*)-**5a**	85	95
4	*rac*-**4b**	*rac*-**5b**	87	
5	(*R*)-**4b**	(*S*)-**5b**	88	96
6	(*S*)-**4b**	(*R*)-**5b**	86	99

[a]Reaction conditions are as follows: **1a** (1 mmol), **4** (1.2 mmol, 1.2 equiv), and KOH (50% aqueous, 20.0 equiv) in MeCN (5 mL) at 80 °C under air for 24 h. [b]The enantiopurities of (*R*)- and (*S*)-1-phenylethylamine, (*R*)- and (*S*)-1-(4-bromophenyl)ethan-1-amine, the starting enantioenriched benzylic amines for the preparation of enantioenriched benzylic ammonium salts (*R*)- and (*S*)-**4a**, and (*R*)- and (*S*)-**4b** are >95%, > 95%, > 96%, and >99% ee, respectively.

Scheme 2. Gram-Scale Reaction



radical trapping using 3 equiv of TEMPO were carried out to suppress this transformation. The results showed that this transformation did not undergo a free -adical-type reaction. Second, benzyl chloride was investigated under the standard conditions, giving the product **3a** in an 80% yield. This work showed that the benzyl quaternary ammonium salts did not play any role in the deoxygenation reduction of this reaction. Third, in the absence of benzyl quaternary ammonium salts, **1a** produced products **6** (10% yield) and **7** (90% yield) under the standard conditions. Both **6** and **7** were isolated and characterized by NMR (See the Supporting Information).

Based on the above experimental results, we propose a plausible mechanism (Scheme 4). At the outset of the reaction, the base KOH-mediated sulfinate **8** was formed via the retro-Michael Aaddition of the deprotonated β-sulfinyl esters **1**. The oxygen-Michael addition of **8′**, the tautomer **8** ,and *tert*-butyl acrylate produced the oxygen-Michael addition product **6**.[15,16] Intermediate **6** aptly carried out disproportionation and turned into diaryl disulfide **7** and the unstable intermediate **9**, which was decomposed by KOH. In the presence of KOH, intermediate **7** produced RS^- **10** and RSOH **11**, which was turned into **8′**. The negatively charged RS^- **10** attacked the

https://doi.org/10.1021/acs.joc.1c00615
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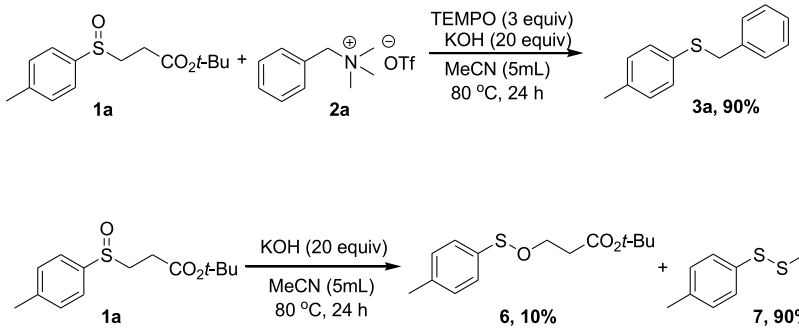
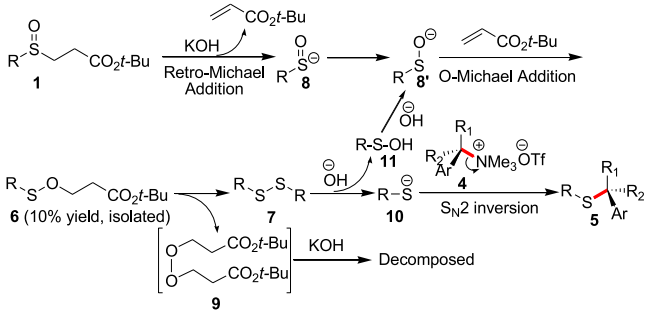
Scheme 3. Control Experiments



Scheme 4. A Plausible Mechanism



benzyl quaternary ammonium salt **4** via an S_N2 nucleophilic substitution to afford the desired highly enantiopure thioether product **5** with the reverse configuration.

In summary, we have developed an unusual deoxidative coupling reaction of β-sulfinyl esters with benzylic trimethylammonium salts. This protocol achieves the products of thioethers with excellent yields. In addition, when enantiomerically pure benzyl quaternary ammonium salts are used as reactants, chiral benzyl thioethers with S_N2-type reverse configurations were obtained with extremely high enantiopurities.

EXPERIMENTAL SECTION

General Information. The test tube used was dried in an electric oven at 110 °C. Chemicals were purchased from Aladdin, Adamas, Aldrich, Alfa Aesar, and Kelong Chemical Co. and used as received unless other mentioned. Petroleum ether (PE) refers to the fraction that boils in the 60−90 °C range. Unless otherwise stated, there was no further purification of the commercial supplier's products. ^{1}H NMR spectra were recorded on a Bruker Avance III 400 MHz instrument. ^{1}H NMR data are reported in δ units (ppm) and were measured relative to the signals for either residual chloroform (7.26 ppm) or residual acetone (2.05 ppm) in the deuterated solvent unless otherwise stated. ^{13}C {^{1}H} NMR spectra are reported in (ppm) relative to deuterated chloroform (77.2 ppm) unless otherwise stated, and all were obtained with ^{1}H decoupling. Mass spectral data of the products were collected by a GC-MS analysis with a QP-2010 SE instrument. All chiral HPLC analyses were performed on an LC3000 I-type high-performance liquid chromatograph (Beijing Gangchen Technology Co., Ltd.) with Daicel Chiralcel OD-H, Chiralcel OJ-H, Chiralpak AD-H, and Chiralpak AS-H chiral columns (4.6 mm × 250 mm × 5 μm) using *n*-hexane/isopropanol as the mobile phase, and the UV detection was monitored at 254 nm. Optical rotations were measured on a Autopol IV polarimeter with a sodium lamp at λ = 589 nm and reported as $[\alpha]_D$T (c in grams per 100 mL, solvent). Quaternary ammonium triflates and β-sulfinyl esters were prepared according to literature methods.[14,17]

General Procedure for the Preparation of β-Sulfinyl Esters. β-Sulfinyl esters were prepared according to literature methods.[17]

General Procedure for the Deoxidative Coupling of β-Sulfinyl Esters (3a−3w, 5a, and 5b). To an oven-dried 25 mL test tube with a standard ground joint equipped with a stir bar were added benzylic trimethylammonium triflate (enantioenriched benzylic ammonium salts) (1.2 mmol, 1.2 equiv), β-sulfinyl esters (1 mmol, 1 equiv), KOH (50% aqueous, 20 mmol, 20 equvalents), and acetonitrile (5.0 mL). The mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the reaction mixture was quenched by the addition of a saturated NaCl solution (10 mL). The reaction mixture was extracted with ethyl acetate (10 mL × 3). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated in a vacuum on a rotary evaporator. The resulting residue was purified by silica gel flash chromatography, eluting with petroleum ether/EtOAc to afford the corresponding products as either a colorless or yellowish oil or a white or yellowish solid.

*Benzyl(4-tolyl)sulfide (**3a**).*[18] Colorless oil, 90% yield, 241.3 mg, R_f = 0.3, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.08 (m, 7H), 6.96 (d, J = 7.9 Hz, 2H), 3.96 (s, 2H), 2.20 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.82, 136.59, 132.50, 130.74, 129.63, 128.86, 128.45, 127.09, 39.82, 21.07; GCMS (EI) m/z (%) 214.00 (46) $[M]^+$, 123.00 (5), 91.00 (100), 77.00 (5) 65 (20).

*(2-Bromobenzyl)(4-tolyl)sulfide (**3b**).*[19] Yellowish oil, 87% yield, 255.1 mg, R_f = 0.33, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.7 Hz, 1H), 7.18−7.05 (m, 4H), 7.04−6.96 (m, 3H), 4.08 (s, 2H), 2.23 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.18, 137.05, 132.97, 131.86, 131.58, 130.78, 129.68, 128.71, 127.34, 124.54, 40.45, 21.11.

*(4-tert-Butylbenzyl)(4-methylphenyl)sulfide (**3c**).*[20] White solid, 85% yield, 229.9 mg, R_f = 0.35, in PE, mp 57−65 °C. ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dt, J = 8.3, 5.9 Hz, 6H), 6.99 (d, J = 8.0 Hz, 2H), 3.99 (s, 2H), 2.23 (s, 3H), 1.22 (s, 9H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.07, 136.32, 134.60, 133.06, 130.23, 129.62, 128.51, 125.44, 39.24, 34.51, 31.37, 21.06.

*(2-Fluorobenzyl)(4-tolyl)sulfide (**3d**).*[21] Yellowish oil, 89% yield, 206.8 mg, R_f = 0.33, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.17 (m, 4H), 7.11−6.99 (m, 4H), 4.10 (s, 2H), 2.33 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.77 (d, J = 247.0 Hz), 136.99, 131.85, 131.39, 130.88 (d, J = 3.9 Hz), 129.65, 128.83 (d, J = 8.2 Hz), 125.17 (d, J = 14.8 Hz), 123.97 (d, J = 3.8 Hz), 115.36 (d, J = 21.8 Hz), 32.93 (d, J = 3.1 Hz), 21.09.

*(2-Chlorobenzyl)(4-tolyl)sulfide (**3e**).*[19] Yellowish oil, 89% yield, 221.4 mg, R_f = 0.29, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.25 (m, 1H), 7.17−6.96 (m, 7H), 4.08 (s, 2H), 2.23 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.03, 135.55, 134.05, 131.90, 131.55, 130.75, 129.67, 129.64, 128.49, 126.69, 37.73, 21.10.

*(3-Methylbenzyl)(4-tolyl)sulfide (**3f**).*[22] Colorless oil, 90% yield, 205.5 mg, R_f = 0.24, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16−7.04 (m, 3H), 7.04−6.92 (m, 5H), 3.95 (s, 2H), 2.22 (s, 6H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 138.11, 137.60, 136.48, 132.77, 130.56, 129.62, 128.35, 127.89, 125.90, 39.76, 21.38, 21.07.

*(3-Methoxybenzyl)(4-tolyl)sulfide (**3g**).*[21] Yellowish oil, 88% yield, 215.1 mg, R_f = 0.3, 5% ethyl acetate, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17−7.07 (m, 3H), 6.98 (d, J = 7.9 Hz, 2H), 6.72 (ddd, J =

https://doi.org/10.1021/acs.joc.1c00615
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13.9, 10.6, 5.0 Hz, 3H), 3.96 (s, 2H), 3.67 (s, 3H), 2.22 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.65, 139.39, 136.60, 132.53, 130.74, 129.65, 129.44, 121.22, 114.19, 112.91, 55.18, 39.84, 21.07.

(4-Trifluoromethyl)(4-tolyl)sulfide (**3h**).[23] White solid, 86% yield, 242.8 mg, R_f = 0.35, in PE, mp 77−82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 7.18−7.07 (m, 2H), 6.99 (d, J = 8.0 Hz, 2H), 3.99 (s, 2H), 2.23 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.18 (d, J = 1.3 Hz), 137.20, 131.45, 131.30, 129.77, 129.28 (d, J = 32.7 Hz), 129.09, 125.36 (q, J = 3.8 Hz), 124.17 (d, J = 272.1 Hz), 39.56, 21.07.

(4-Cyanobenzyl)(4-methylphenyl)sulfide (**3i**).[24] Yellowish solid, 85% yield, 203.4 mg, R_f = 0.18, 5% ethyl acetate, in PE, mp 65−71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.3 Hz, 2H), 7.13 (dd, J = 73.0, 20.1 Hz, 6H), 3.96 (s, 2H), 2.23 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.76, 137.56, 132.20, 131.74, 130.81, 129.83, 129.52, 118.82, 110.85, 39.90, 21.09.

2-(4-Methylphenyl)thiomethyl-pyridine (**3j**).[25] Brown oil, 85% yield, 182.8 mg, R_f = 0.13, 10% ethyl acetate, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 7.50 (td, J = 7.7, 1.8 Hz, 1H), 7.23−7.12 (m, 3H), 7.09−6.93 (m, 3H), 4.14 (s, 2H), 2.21(s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.95, 149.35, 136.60, 136.56, 131.95, 130.53, 129.67, 123.01, 121.98, 41.29, 21.04.

(Naphthalen-2-ylmethyl)(4-tolyl)thioether (**3k**).[26] Yellowish oil, 86% yield, 227.4 mg, R_f = 0.23, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.5 Hz, 1H), 7.78 (dd, J = 8.3, 1.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.44 (dddd, J = 20.3, 8.0, 6.8, 1.3 Hz, 2H), 7.28−7.11 (m, 4H), 6.99 (d, J = 7.9 Hz, 2H), 4.43 (s, 2H), 2.23 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 136.79, 133.99, 133.13, 132.85, 131.50, 131.13, 129.68, 128.81, 128.20, 127.33, 126.21, 125.82, 125.27, 124.00, 37.98, 21.11.

1,2,3,4-Tetrahydro-1-(4-methylphenylthio)naphthalene (**3l**).[13] Colorless oil, 86% yield, 230.6 mg, R_f = 0.25, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.26 (m, 3H), 7.08−6.95 (m, 5H), 4.40 (t, J = 4.1 Hz, 1H), 2.81−2.57 (m, 2H), 2.26 (s, 3H), 2.20−2.06 (m, 1H), 1.98−1.78 (m, 2H), 1.71−1.59 (m, 1H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.60, 137.32, 135.76, 132.82, 132.38, 130.58, 129.78, 129.28, 127.05, 125.72, 48.27, 29.21, 28.49, 21.20, 18.62.

Benzyl(3-tolyl)sulfide (**3m**).[27] Yellowish oil, 89% yield, 190.8 mg, R_f = 0.25, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−6.98 (m, 8H), 6.91 (s, 1H), 4.02 (s, 2H), 2.20 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 138.61, 137.56, 136.19, 130.42, 128.88, 128.71, 128.49, 127.20, 127.17, 126.70, 39.03, 21.34.

Benzyl(4-bromophenyl)sulfide (**3n**).[18] White solid, 89% yield, 248.4 mg, R_f = 0.38, in PE, 53−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.12 (m, 7H), 7.06 (d, J = 8.5 Hz, 2H), 4.00 (s, 2H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.06, 135.45, 131.88, 131.51, 128.81, 128.59, 127.36, 120.35, 39.11.

Benzyl(2-tolyl)sulfide (**3o**).[28] Colorless oil, 87% yield, 186.5 mg, R_f = 0.25, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−6.96 (m, 9H), 3.99 (s, 2H), 2.23 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.97, 137.31, 135.79, 130.08, 129.01, 128.90, 128.52, 127.22, 126.44, 126.15, 38.36, 20.33.

Benzyl(4-chlorophenyl)sulfide (**3p**).[18] White solid, 89% yield, 208.9 mg, R_f = 0.35, in PE, mp 45−48 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.10 (m, 9H), 4.00 (s, 2H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.14, 134.69, 132.50, 131.45, 128.97, 128.82, 128.57, 127.33, 39.34.

Benzyl(2-fluorophenyl)sulfide (**3q**).[24] Yellowish oil, 88% yield, 192.1 mg, R_f = 0.35, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.07 (m, 7H), 6.95 (ddd, J = 7.9, 7.5, 4.8 Hz, 2H), 4.02 (s, 2H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.72 (d, J = 245.6 Hz), 137.23, 133.05 (d, J = 1.8 Hz), 128.86, 128.80, 128.48, 127.27, 124.35 (d, J = 3.8 Hz), 122.76 (d, J = 17.8 Hz), 115.62 (d, J = 22.6 Hz), 38.43 (d, J = 2.9 Hz).

Benzyl(4-methoxyphenyl)sulfide (**3r**).[18] White solid, 89% yield, 204.9 mg, R_f = 0.4, 5% ethyl acetate, in PE, mp 42−45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.05 (m, 7H), 6.75−6.66 (m, 2H), 3.90 (s, 2H), 3.69 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.23, 138.15, 134.10, 128.91, 128.38, 127.00, 126.10, 114.45, 55.32, 41.25.

2-(Benzylthio)benzo[d]thiazole (**3s**).[29] Yellowish oil, 85% yield, 218.8 mg, R_f = 0.4, 5% ethyl acetate, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.1 Hz, 1H), 7.69−7.62 (m, 1H), 7.42−7.13 (m, 7H), 4.52 (s, 2H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.44, 153.18, 136.20, 135.36, 129.17, 128.74, 127.79, 126.09, 124.32, 121.59, 121.04, 37.75.

2-(Benzylthio)benzo[d]oxazole (**3t**).[30] White solid, 86% yield, 207.5 mg, R_f = 0.3, 5% ethyl acetate, in PE, mp 42−47 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.52 (m, 1H), 7.40−7.33 (m, 3H), 7.28−7.13 (m, 5H), 4.48 (s, 2H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.56, 151.91, 141.95, 135.87, 129.11, 128.80, 127.95, 124.34, 123.97, 118.51, 109.93, 36.60.

3-(Benzylthio)pyridine (**3u**).[24] Yellowish oil, 85% yield, 171.1 mg, R_f = 0.18, 5% ethyl acetate, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 7.41−7.27 (m, 3H), 7.26−7.03 (m, 4H), 6.89 (ddd, J = 7.4, 4.9, 1.0 Hz, 1H), 4.36 (s, 2H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.85, 149.44, 138.01, 135.99, 129.00, 128.52, 127.12, 122.11, 119.62, 34.46.

Benzyl(cyclopentyl)sulfide (**3v**).[31] Yellowish oil, 86% yield, 173.1 mg, R_f = 0.37, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.09 (m, 5H), 3.66 (s, 2H), 2.93−2.83 (m, 1H), 1.93−1.32 (m, 8H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 138.94, 128.79, 128.45, 126.80, 43.06, 36.47, 33.56, 24.94.

Benzyl(butyl)sulfide (**3w**).[32] Colorless oil, 86% yield, 155.1 mg, R_f = 0.35, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.08 (m, 5H), 3.60 (s, 2H), 2.38−2.23 (m, 2H), 1.51−1.39 (m, 2H), 1.34−1.19 (m, 2H), 0.79 (t, J = 7.3 Hz, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 138.70, 128.84, 128.45, 126.87, 36.31, 31.34, 31.08, 22.01, 13.70.

*(1-Phenylethyl)(4-tolyl)sulfide (rac-***5a**).[13] Yellowish oil, 85% yield, 194.1 mg, R_f = 0.25, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.07 (m, 7H), 6.95 (d, J = 7.9 Hz, 2H), 4.19 (q, J = 7.0 Hz, 1H), 2.21 (s, 3H), 1.53 (d, J = 7.0 Hz, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.39, 137.38, 133.23, 131.30, 129.48, 128.36, 127.33, 127.07, 48.40, 22.21, 21.13; HPLC Chiralcel OJ-H column, λ= 254 nm, hexane/isopropanol = 90:10, 1.0 mL/min flow rate, t_R(major) = 8.14 min, t_R(major) = 16.69 min.

*(S)-(1-Phenylethyl) (p-tolyl) sulfide ((S)-***5a**).[13] Yellowish oil, 85% yield, 194.1 mg, R_f = 0.25, in PE; $[\alpha]_D^{28}$ = −34.7 (c = 0.03, EtOAc); HPLC Chiralcel OJ-H column, λ= 254 nm, hexane/isopropanol = 90:10; 1.0 mL/min flow rate, t_R(major) = 8.22 min, t_R(minor) = 17.13 min.

*(R)-(1-Phenylethyl) (p-tolyl) sulfide ((R)-***5a**).[13] Yellowish oil, 85% yield, 194.1 mg, R_f = 0.28, in PE; $[\alpha]_D^{28}$ = +39.4 (c = 0.03, EtOAc); HPLC, Chiralcel OJ-H column, λ= 254 nm, hexane/isopropanol = 90:10, 1.0 mL/min flow rate, t_R(minor) = 8.23 min, t_R(major) = 17.07 min.

(1-(4-Bromophenyl)ethane)(4-methylphenyl) sulfide (rac-5b). Colorless oil, 87% yield, 224.6 mg, R_f = 0.35, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.35 (m, 2H), 7.18−7.10 (m, 4H), 7.06- 7.01 (m, 2H), 4.21 (q, J = 7.0 Hz, 1H), 2.30 (s, 3H), 1.58 (d, J = 7.0 Hz, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.58, 137.70, 133.41, 131.40, 130.69, 129.57, 129.02, 120.72, 47.85, 22.03, 21.14. GCMS (EI) m/z (%) 306.00 (10) $[M]^+$, 183.00 (80), 123.03 (10), 104 (100), 91 (10), 77 (25); HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{15}H_{15}BrNaS^+$ 328.9970, found 328.9970; HPLC Chiralcel OJ-H column, λ= 254 nm, hexane/isopropanol = 99.5:0.5; 0.8 mL/min flow rate; t_R(major) = 14.20 min, t_R(major) = 15.88 min.

*(S)-(1- (4-Bromophenyl)ethane)(4-methylphenyl) sulfide ((S)-***5b**). White solid, 88% yield, 227.1 mg, R_f = 0.35, in PE, mp 49−57 °C; HPLC Chiralcel OJ-H column, λ= 254 nm, hexane/isopropanol = 99.5:0.5, 0.8 mL/min flow rate, t_R(minor) = 13.95 min, t_R(major) = 15.54 min.

*(R)-(1-(4-Bromophenyl)ethane)(4-methylphenyl) sulfide ((R)-***5b**). White solid, 86% yield, 222.0 mg, R_f = 0.38, in PE, mp 45−55 °C; HPLC Chiralcel OJ-H column, λ= 254 nm, hexane/isopropanol = 99.5:0.5, 0.8 mL/min flow rate, t_R(major) = 13.87 min, t_R(minor) = 15.57 min.

Procedure for synthesis of compound 6 and 7. To an oven-dried 25 mL test tube with standard ground joint equipped with a stir bar were added β-sulfinyl esters (1 mmol, 1 equiv), KOH (50%

https://doi.org/10.1021/acs.joc.1c00615
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aqueous, 20 mmol, 20 equiv), and acetonitrile (5.0 mL). The mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the reaction mixture was quenched by the addition of a saturated NaCl solution (10 mL). The reaction mixture was extracted with ethyl acetate (10 mL × 3). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated in a vacuum on a rotary evaporator. The resulting residue was purified by silica gel flash chromatography, eluting with petroleum ether/EtOAc to afford the corresponding products.

*2-(tert-Butoxycarbonyl)ethyl 4-methylbenzenesulfenate (**6**).* Colorless oil, 10% yield, 26.8 mg, R_f = 0.33, 5% ethyl acetate, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (dd, J = 8.4, 6.4 Hz, 2H), 7.03 (d, J = 8.0 Hz, 2H), 3.00 (t, J = 7.5 Hz, 2H), 2.43 (t, J = 7.5 Hz, 2H), 2.25 (s, 3H), 1.37 (s, 9H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.11, 135.67, 130.63, 129.91, 128.73, 79.83, 34.63, 28.92, 27.07, 20.01; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{14}H_{20}O_3SNa^+$ 291.1025, found 291.1025.

*Di(p-tolyl) disulfide (**7**).*[33] Colorless oil, 90% yield, 221.4 mg, R_f = 0.58, in PE; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.34 (m, 4H), 7.14−7.07 (m, 4H), 2.32 (s, 6H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.47, 133.92, 129.81, 128.56, 21.08.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00615.

Chiral HPLC traces of products **5a** and **5b**; ^{1}H and ^{13}C NMR spectra for compounds **3**, **5**, **6**, and **7**; and HRMS spectra for compounds **5b** and **6** (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was financially supported by the National Natural Science Foundation of China (no. 21372034) and the State Key Laboratory of Geohazard Prevention and Geoenvironment Protection (no. SKLGP2020Z003).

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