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An Asymmetric Synthesis of a Chiral Sulfone Acid with Concomitant Hydrolysis and Oxidation to Enable the Preparation of a Glucokinase Activator

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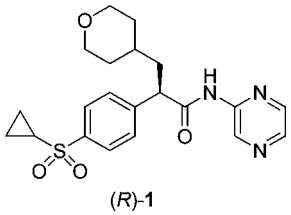
ABSTRACT: This contribution describes the demonstration of an asymmetric synthesis of a glucokinase activator via protonation of the enolate generated from an alkylaryl ketene and (*R*)-pantolactone. Additionally, a one-pot hydrolysis/oxidation protocol with lithium hydroperoxide was developed to afford a chiral sulfone acid without degradation of the labile stereocenter.

INTRODUCTION

It is estimated that 346 million people worldwide have diabetes, and the World Health Organization (WHO) anticipates that diabetes deaths will double between 2005 and 2030.[1] Of the three types of diabetes, type 2 is the most common form and is characterized by the body's inability to control glucose.[2] The glucose-phosphorylating enzyme, glucokinase, has been identified as a promising drug target for type 2 diabetes and has led to the development of several glucokinase activators.[3]

The glucokinase activator (GKA), (*R*)-**1** (Figure 1), was developed as a potential therapeutic agent for the treatment of type 2 diabetes. It was designed to lower blood glucose levels by increasing the uptake of glucose in the liver and increasing insulin secretion from the pancreas. Herein, we describe the demonstration of an asymmetric synthesis of glucokinase activator (*R*)-**1** via protonation of the enolate generated from an alkylaryl ketene and (*R*)-pantolactone[4] followed by concomitant hydrolysis and oxidation.



(*R*)-**1**

Figure 1. Glucokinase activator (*R*)-**1**.

RESULTS AND DISCUSSION

The goal of this research was to demonstrate a cost-effective, asymmetric synthesis of glucokinase activator (*R*)-**1** with the potential for scale-up. Previous quantities of the active pharmaceutical ingredient (API), (*R*)-**1**, had been prepared via a synthesis devised by Prosidion Ltd. that utilized an enantioselective hydrogenation to set the labile chiral center (Scheme 1).[5] In order to convert (*E*)-acrylic acid **2** to chiral sulfone acid (*R*)-**3**, 750 psig (5171 kPa) of hydrogen and a substrate to catalyst ratio (s/c) of 2000 to 1 was required. Sulfone acid (*R*)-**3** was obtained in 86% ee and was upgraded to >99% ee via recrystallization. A charcoal-absorbent treatment was required to remove residual rhodium, which led to significant yield loss.

Since it had been reported that pantolactone adds to ketenes to yield esters with high stereoselectivity[6−8] and the reagent is readily available,[9] we investigated its utilization in the asymmetric synthesis of glucokinase activator (*R*)-**1**. We chose to target the synthesis of (*R*)-**3** and utilize the amide coupling conditions as described by Prosidion.[5] To that end, chiral sulfone acid (*R*)-**3** would be generated from the addition of (*R*)-pantolactone to the ketene produced from racemic sulfide acid **5** and subsequent hydrolysis and oxidation of ester **4** (Figure 2).

To investigate this approach, an efficient synthesis of racemic sulfide acid **5** was developed from sulfide α-ketoester **7**[10] (Scheme 2). Wittig olefination of **7** with the ylide generated from phosphonium iodide **8** and lithium hexamethyldisilazide (LiHMDS) gave sulfide acrylic esters **9** as a 55:45 mixture of *E*:*Z* isomers, which contained residual triphenylphosphine oxide that could be removed in the subsequent step. Hydrolysis of the (*E*/*Z*)-sulfide acrylic esters, **9**, cleanly gave the (*E*/*Z*)-sulfide acrylic acids **10** in a 89% yield.[11]

The hydrogenation of (*E*/*Z*)-sulfide acrylic acids **10** to yield sulfide acid **5** proved to be challenging and required less than ideal substrate-to-catalyst loadings (Scheme 3, Table 1).[12] Pd/C required a 3:1 s/c, 150 psig (1034 kPa), and 75 °C to completely consume **10** (entries 1 and 2). Wilkinson's catalyst, ($RuCl(PPh_3)_3$), (entries 3 and 4) and [Rh(dippf)(cod)]BF_4 (entries 5−8) were found to be effective at reducing the olefin without being sufficiently poisoned; however, at least one equivalent of triethylamine was necessary to suppress hydrogenation of the cyclopropyl moiety to give **11** (Scheme 3).[12] Using preformed [Rh(dippf)(cod)]BF_4 at a 200:1 s/c, **5** was obtained in a 84% yield after recrystallization on a 100-g scale

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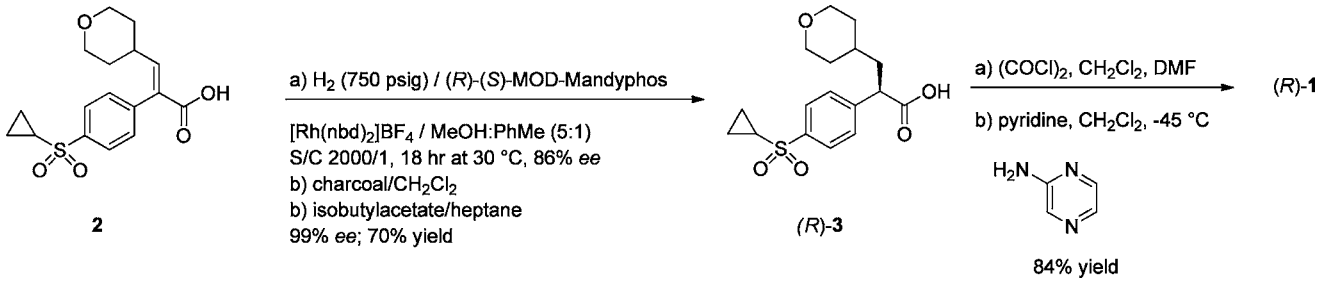
Scheme 1. Prosidion's synthesis of (*R*)-1



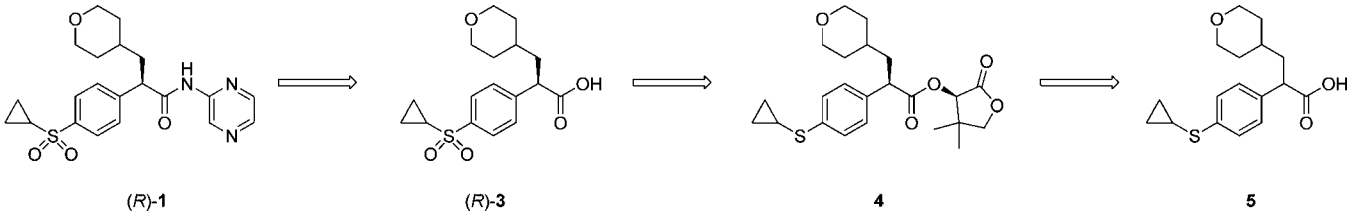
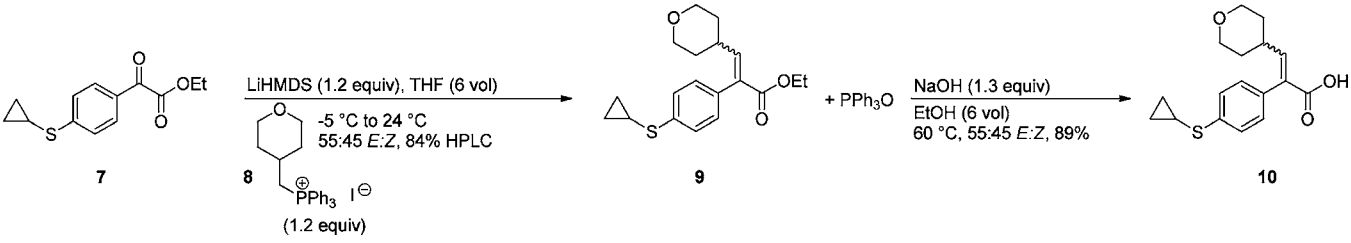


Figure 2. Retrosynthetic analysis of glucokinase activator (*R*)-**1**.

Scheme 2. Synthesis of (*E*/*Z*)-sulfide acrylic acids 10



Scheme 3. Hydrogenation of (*E*/*Z*)-sulfide acrylic acids 10

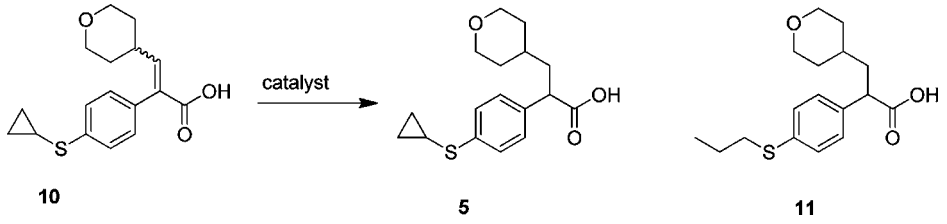


Table 1. Hydrogenation of (*E*/*Z*)-sulfide acrylic acids 10 to yield racemic sulfide acid 5

entry	catalyst	pressure (psig H_2)	temp (°C)	time (h)	conversion/yield
1	5% Pd/C Degussa type (8:1 s/c)	150	75	12	1:1 mixture of **10**:**5** by ^{1}H NMR
2	5% Pd/C Degussa type (3:1 s/c)	150	75	12	100% conversion by ^{1}H NMR
3	$RhCl(PPh_3)_3$ (30:1 s/c)	50	50	24	1:0.55 mixture of **5**:**11** by ^{1}H NMR
4[a]	$RhCl(PPh_3)_3$ (30:1 s/c)	50	50	18	100% conversion by ^{1}H NMR
5[b,c]	$[Rh(dippf)(cod)]BF_4$ (200:1 s/c)	50	24	24	84% isolated yield
6[b]	0.1 mol % Rh with dippf ligand prepared from $[Rh(cod)_2]CF_3SO_3$	50	24	16	100% by HPLC
7[b]	0.1 mol % Rh with dippf ligand prepared from $[Rh(nbd)Cl]_2$	50	24	16	100% by HPLC
8[b]	0.1 mol % Rh with dippf ligand prepared from $[Rh(cod)_2]BF_4$	50	24	16	100% by HPLC

[a]3.0 equiv of TEA. [b]1.0 equiv of TEA. [c]EtOH was utilized as the reaction solvent. Entries 1–4 and 6–8 were conducted in MeOH.

(entry 5). The substrate-to-catalyst loading was further improved to 1000:1 via the in situ preparation of the catalyst in MeOH with 1.0 equiv of triethylamine at 24 °C and 50 psig (345 kPa) (entries 6–8).

With **5** in hand, the selectivity of the protonation of the enolate generated from the sulfide alkylaryl ketene **13** and (*R*)-pantolactone (**6**) could be evaluated. Treatment of **5** with oxalyl chloride and catalytic DMF in toluene generated the acid chloride **12** (Scheme 4). The reaction solution was cooled to 0 °C, and 3 equiv of dimethylethylamine[6] was added to generate **13**. Addition of a solution of **6** in toluene to **13** at −78 °C generated sulfide ester **4** in 98% yield and 88% de as determined by HPLC. Additionally, it was shown that changing the reaction solvent to THF (instead of toluene) gave sulfide

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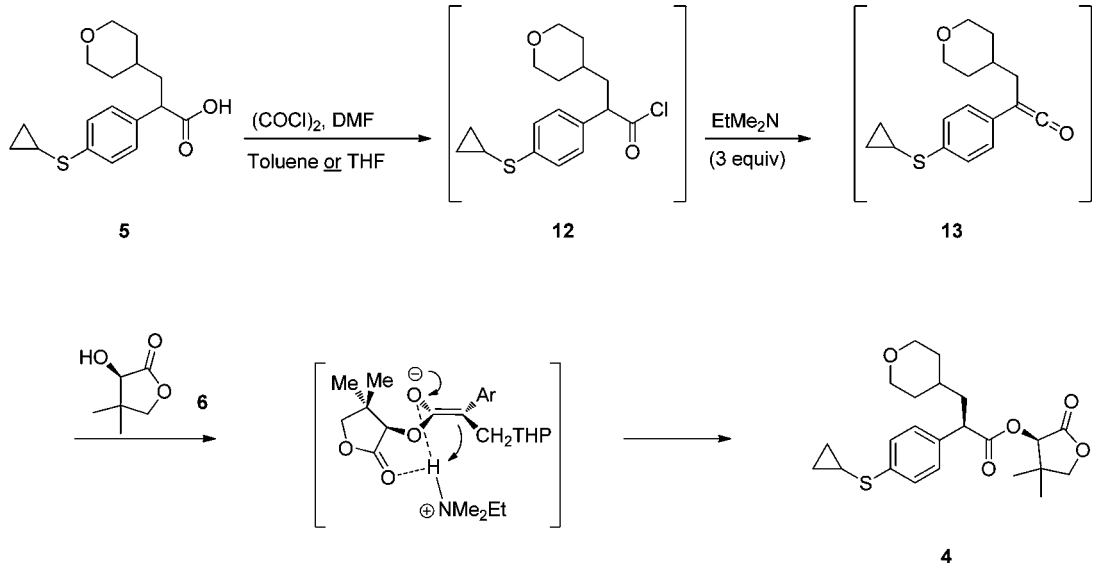
Scheme 4. Addition of (*R*)-pantolactone (6) to the ketene (13) generated from racemic sulfide acid 5



ester **4** with 82% de, whereas changing the reaction temperature from −78 °C in toluene to −50 °C, −20 °C, or 0 °C also led to a decrease in diastereoselectivity (82%, 80%, and 74% de, respectively) (Table 2).

Table 2. Diastereoselectivity of the protonation of the enolate generated from 13 and 6

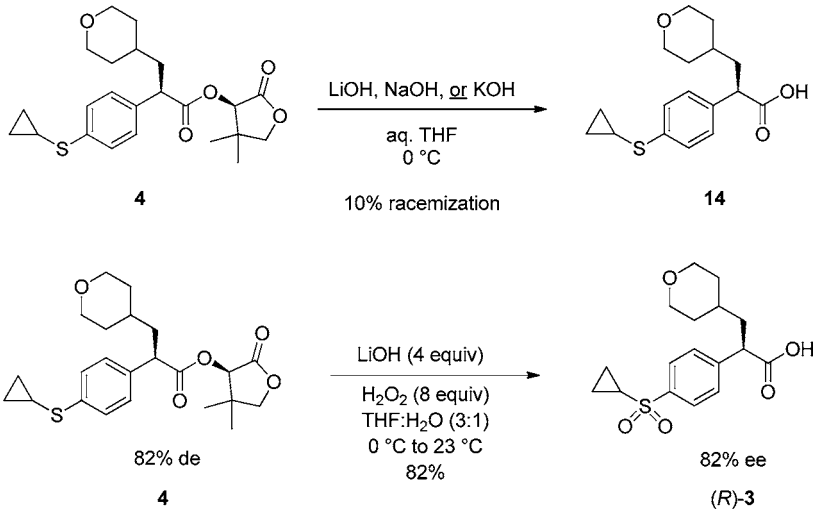
solvent	temperature (°C)	yield (%)	de (%)
THF	−78	60	82
toluene	−78	98	88
toluene	−50	96	82
toluene	−20 to −15	90	80
toluene	0 to 3	99	74

Sulfide ester **4** required an ester hydrolysis and sulfide to sulfone oxidation that avoided stereochemical erosion to prepare chiral sulfone acid (*R*)-**3**. To minimize chiral degradation, the ester was hydrolyzed before oxidizing the sulfide to the sulfone since the α-proton is less acidic in the sulfide oxidation state. The hydrolysis of **4** to chiral sulfide acid **14** was initially investigated with hydroxide sources (LiOH, NaOH, or KOH in THF/H_2O) (Scheme 5). Comparison of the diastereomeric and enantiomeric excess data indicated that ~10% erosion of the stereocenter was occurring under these conditions. Surprisingly, upon exposure of **4** to lithium hydroperoxide,[13] oxidation of the sulfide to the sulfoxide and sulfone was observed in addition to the desired hydrolysis. Furthermore, a more concentrated reaction (5−7 vols) with 4 equiv of LiOH and 8 equiv of H_2O_2 enabled complete hydrolysis with concomitant oxidation to yield sulfone acid (*R*)-**3** without erosion of the stereocenter.

We hypothesize that intermediate peracids derived from sulfide ester **4** and pantolactone are the active oxidants generated under the lithium hydroperoxide conditions. To test this theory, sulfide acid **5** was exposed to the lithium hydroperoxide reaction conditions, and <20% oxidation to sulfone **3** was observed.

In preparation for a multikilogram campaign,[14] continuous processing was evaluated as an option to avoid the expensive

Scheme 5. Hydrolysis and concomitant oxidation of sulfide ester 4



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cryogenic conditions required to obtain selectivity in the protonation of the enolate generated from the sulfide alkylaryl ketene (**13**) and (*R*)-pantolactone (**6**). Unfortunately, the insolubility of **6** in toluene proved challenging and resulted in fouling the plug flow reactors at temperatures below 0 °C. Additionally, a safety evaluation of the lithium hydroperoxide hydrolysis/oxidation protocol was conducted since a 20 °C exotherm was observed during development of the process. Heat transfer modeling of calorimetry data suggests that the lithium hydroperoxide conditions could be scaled to a half-full 2000-gal reactor with a 5 °C solution of **4** being added to the water/H_2O_2/LiOH solution over 3 h to maintain the reaction temperature below 16 °C to lessen peroxide decomposition. The robustness of the hydrolysis/oxidation procedure for long addition times was not evaluated; however, this process could be a good candidate for continuous processing as it would allow for sufficient heat removal and would limit the potential consequences of a runaway reaction.

■ CONCLUSIONS

In summary, the goal of demonstrating an asymmetric route for the synthesis of glucokinase activator (*R*)-**1** with the potential for scale-up was achieved. The ketene route is comparable in selectivity (88% de vs 86% ee) and overall cost[15] to the asymmetric hydrogenation route shown in Scheme 1. In addition, the concomitant hydrolysis and oxidation of sulfide ester **4** without degradation of the chiral center lends to the efficiency of the ketene route.

■ EXPERIMENTAL SECTION

General. HPLC conditions for diastereomeric separation of pantolactone esters **4**: Sample prep in 50:50 ACN/H_2O w/ 0.1% TFA. Column: Chiralpak AD-RH (0.46 cm ×15 cm, 5 μm). Flow rate: isocratic flow 1.0 mL/min, 45:55 H_2O/ACN w/0.1% TFA, 30 °C. UV detection at 259 nm, major t_R = 8.79 min, minor t_R = 7.35 min. HPLC for enantiomeric excess determination of sulfone carboxylic acid (*R*)-**3**: Column: ChiralPak AD-RH, (0.46 cm × 15 cm, 5 μm). Flow rate: isocratic flow, 0.6 mL/min, 30 °C. UV detection: 230 nm. Eluent: 68% H_2O/32% ACN/0.1% TFA. Run time: 15 min, major t_R = 7.75 min, minor t_R = 10.94 min. HPLC for reaction monitoring: Column: Agilent Eclipse XDB-C8 (0.46 cm ×15 cm, 3.5 μm). Flow rate: 2 mL/min, A = 0.1% H_3PO_4, B = ACN. Gradient: 95% A to 5% A over 10 min; change to 95% A over 1 min and hold for 4 min, 30 °C, UV detection: 220 nm.

*Ethyl 2-(4-(Cyclopropylthio)phenyl)-3-(tetrahydro-2H-pyran-4-yl)acrylate (**9**).* Under a nitrogen atmosphere, phosphonium iodide **8**[10] (1.46 kg, 3.00 mol) was slurried in THF (3.31 L) at 24 °C. The mixture was cooled to −5 °C, and lithium bis(trimethylsilyl)amide (3.0 L, 3.00 mol, 1.0 M in THF) was added over 1 h at 0 °C. The reaction was stirred at −5 °C for 10 min before it was warmed to 24 °C and stirred for 2.5 h. The reaction was then cooled to 5 °C, and sulfide α-ketoester 7 (625 g, 2.50 mol) in THF (625 mL) was added over 1 h. The reaction was warmed to 24 °C. After stirring 2.5 h, H_2O (2.19 L) and EtOAc (2.19 L) were added to the reaction, and the resulting biphasic mixture was stirred vigorously for 15 min. The mixture was filtered, and the solids were washed with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 2 L). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to yield 1.62 kg of **9** as a mixture of *E*:*Z* isomers (∼1:1) contaminated with triphenylphosphine oxide (84% yield by HPLC). The yellow solid was carried forward without further purification.

*2-(4-(Cyclopropylthio)phenyl)-3-(tetrahydro-2H-pyran-4-yl)acrylic Acid (**10**).* Under a nitrogen atmosphere at 24 °C, crude (*E*/*Z*)-sulfide acrylic ethyl esters **9** with triphenylphosphine oxide (350 g of crude, 152 g (0.46 mol) of **9** as determined by HPLC), were combined with EtOH (903 mL) and 2 M aqueous NaOH (294 mL, 0.59 mol). The solution was heated at 60 °C for 2.5 h until the content of the ethyl ester was <2% by HPLC. The solution was cooled to 24 °C, and EtOH was removed via concentration in vacuo at 60 °C to afford a brown slurry. H_2O (900 mL) was added, and the mixture was stirred for 30 min. The mixture was filtered, and the cake was washed with H_2O (250 mL). MTBE (250 mL) was then added to the aqueous mother liquor, followed by 1 M HCl (600 mL). The biphasic mixture was stirred for 15 min, and then the layers were separated. The aqueous layer was back extracted with MTBE (2 × 250 mL), and the combined organic layers were dried over Na_2SO_4. Concentration in vacuo at 45 °C gave 174 g of a yellow solid of 2-(4-(cyclopropylthio)phenyl)-3-(tetrahydro-2*H*-pyran-4-yl)acrylic acid **10** as a mixture of *E*- and *Z*-isomers that contained a trace amount of triphenylphosphine oxide. To further remove the triphenylphosphine oxide, the solid was dissolved in 2 M NaOH (2 L) and CH_2Cl_2 (1.5 L). The layers were separated, and the aqueous layer was washed with additional CH_2Cl_2 (1.5 L). MTBE (1 L) followed by 1 M HCl (600 mL) was added to the aqueous layer. The layers were separated, and the aqueous layer was extracted with MTBE (1 L). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to yield 124 g (89%) of a white solid of **10** as a mixture of *E*- and *Z*-isomers. ^{1}H NMR ($CDCl_3$, 400 mHz) *E*-**10** δ 0.68−0.73 (m, 2H), 1.07−1.11 (m, 2H), 1.46−1.51 (m, 2H), 1.52−1.59 (m, 2H), 2.13−2.18 (m, 1H), 2.42 (qt, 1H, *J* = 4.2, 10.8 Hz), 3.30 (td, 2H, *J* = 2.0, 11.7 Hz), 3.92 (ddd, 2H, *J* = 1.9, 4.2, 11.7 Hz), 6.94 (d, 1H, *J* = 10.2 Hz), 7.08 (d, 2H, *J* = 8.2 Hz), 7.36 (d, 2H, *J* = 8.0 Hz), 11.70 (br s, 2H). ^{13}C NMR ($CDCl_3$, 100 mHz) 8.5, 11.7, 31.4, 35.6, 66.7, 125.8, 129.8, 131.0, 132.1, 138.9, 149.9, 172.2. ^{1}H NMR ($CDCl_3$, 400 mHz) *Z*-**10** δ 0.65−0.69 (m, 1H), 1.02−1.07 (m, 1H), 1.59−1.65 (m, 1H), 1.71 (ddd, 1H, *J* = 1.3, 3.5, 12.8 Hz), 2.16−2.21 (m, 1H), 3.14 (qt, 1H, *J* = 4.0, 11.1 Hz), 3.48 (td, 1H, *J* = 1.8, 11.7 Hz), 3.99 (ddd, 1H, *J* = 1.4, 4.2, 11.5 Hz), 6.04 (d, 1H, *J* = 9.8 Hz), 7.25 (d, 1H, *J* = 8.3 Hz), 7.31 (d, 1H, *J* = 8.3 Hz), 11.70 (br s, 2H). ^{13}C NMR ($CDCl_3$, 100 mHz) δ 8.5, 11.9, 32.1, 36.1, 67.2, 126.1, 128.1, 132.5, 134.3, 138.8, 146.2, 172.7.

*2-(4-(Cyclopropylthio)phenyl)-3-(tetrahydro-2H-pyran-4-yl)propanoic Acid (**5**).* Sulfide acrylic acid **10** (100 g, 328.5 mmol) was added to a hydrogenation bottle with EtOH (658 mL) and triethylamine (46 mL, 330 mmol). 1,1-Bis(diisopropylphosphino)ferrocene(1,5-cyclooctadiene)rhodium(I)-tetrafluoroborate (1.18 g, 1.64 mmol) was added, and the bottle was purged with nitrogen, followed by hydrogen at 24 °C. After the solution stirred for 24 h at 50 psig, the reaction pH was adjusted to 4 with 5 N HCl and treated with 100 mesh DARCO (50 g) for 2 h at 50 °C. The mixture was then filtered, and the filtrate was concentrated to 400 mL. After stirring at 23 °C for 12 h, a suspension was obtained. H_2O (450 mL) was added over 30 min, and the resulting thick suspension was heated to 70 °C. The resulting solution was allowed to cool to 24 °C. The solids were filtered and rinsed with 30% EtOH/H_2O (500 mL) to yield 84.5 g (84%) of **5** as a tan solid. ^{1}H

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NMR ($CDCl_3$, 400 mHz) δ 0.66 (dt, 2H, J = 4.8, 6.4 Hz), 1.04 (dt, 2H, J = 4.8, 6.4 Hz), 1.23−1.33 (m, 2H), 1.37−1.45 (m, 1H), 1.54−1.62 (m, 2H), 1.71 (ddd (app dt), 1H, J = 6.8, 14 Hz), 1.98 (ddd (app dt), 1H, J = 7.2, 14.0 Hz), 2.14 (tt, 1H, J = 4.4, 7.6 Hz), 3.25−3.32 (m, 2H), 3.62 (dd (app t), 1H, J = 6.8 Hz), 3.91−3.93 (m, 2H), 7.21 (d, 2H, J = 8.4 Hz), 7.25 (d, 2H, J = 8.4 Hz), 11.4−11.6 (br s, 1H). ^{13}C NMR ($CDCl_3$, 100 mHz) δ 8.5, 11.9, 32.4, 32.5, 32.9, 29.9, 47.7, 67.6, 67.7, 126.6, 128.3, 135.0, 138.3, 179.2. IR (film) 3100−2700 (br s), 2990, 2934, 1710, 1491, 1435, 1275, 1223, 1171, 1127, 1119, 1104, 1086, 1074, 1026, 1011, 978, 881, 859, 747 cm^{-1}. HRMS (EI$^+$) calcd for $C_{17}H_{22}O_3S$ 306.12897, found 306.12858.

*(R)-((R)-4,4-dimethyl-2-oxotetrahydrofuran-3-yl)-2-(4-(cyclopropylthio)phenyl)-3-(tetrahydro-2H-pyran-4-yl)-propanoate (**4**).* Following a procedure reported in the literature,[7] to a solution of sulfide acid **5** (2.34 g, 7.64 mmol) in toluene (46 mL) and DMF (10 μL) under a nitrogen atmosphere was added oxalyl chloride (0.80 mL, 9.16 mmol). The solution was stirred at 24 °C for 3 h, and then it was cooled to 0 °C. Dimethylethylamine (2.49 mL, 22.91 mmol) was added dropwise, and the solution was allowed to warm to 24 °C and stir for 2 h. The solution was cooled to −69 °C, and a solution of (*R*)-pantolactone **6** (1.20 g, 9.16 mmol) in toluene (37 mL) was added at such a rate to maintain the solution temperature <−60 °C. The solution was allowed to stir and warm to 24 °C slowly over 12 h. The reaction was quenched with H_2O, and the aqueous layer was separated. The organic layer was washed with saturated $NaHCO_3$ and brine, and the aqueous layer was back extracted with EtOAc (2×). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to give 3.14 g (98%) of **4** as a colorless oil with 88% de as determined by chiral HPLC. ^{1}H NMR ($CDCl_3$, 400 mHz) δ 0.62−0.66 (m, 2H), 0.98 (s, 3H), 1.01−1.05 (m, 2H), 1.09 (s, 3H), 1.23−1.34 (m, 2H), 1.42−1.53 (m, 1H), 1.58−1.62 (m, 2H), 1.77 (ddd (app dt), 1H, J = 7.2, 14.4 Hz), 2.05 (ddd, 1H, J = 6.8, 8.0, 14.0 Hz), 2.13 (dddd (app tt), 2H, J = 4.4, 7.2 Hz), 3.28 (ddd (app dt), 2H, J = 2.0, 11.6 Hz), 3.78 (dd, (app t), 1H, J = 8.0 Hz), 3.87−3.90 (m, 2H), 3.94−3.99 (m, 2H), 5.28 (s, 1H), 7.22 (d, 2H, J = 8.4 Hz), 7.29 (d, 2H, J = 8.4 Hz). ^{13}C NMR ($CDCl_3$, 100 mHz) δ 8.5, 11.9, 19.8, 23.0, 32.6, 32.7, 32.9, 39.9, 40.2, 47.9, 67.7, 75.2, 76.0, 126.6, 128.3, 134.4, 138.3, 171.8, 172.6. IR (film) 2953, 2927, 1785, 1740, 1491, 1134, 1119, 1089, 1011, 996 cm^{-1}. HRMS (EI$^+$) calcd for $C_{23}H_{30}O_5S$ 418.18139, found 418.18161. $[\alpha]_D^{24}$ +4.58 (MeOH, c = 1.2).

*(R)-2-(4-(Cyclopropylsulfonyl)phenyl)-3-(tetrahydro-2H-pyran-4-yl)propanoic Acid ((R)-**3**).* To a 0 °C solution of lithium hydroxide (29.7 mg, 1.24 mmol), hydrogen peroxide (30%) (0.25 mL, 2.48 mmol), and H_2O (0.16 mL) was added sulfide ester **4** (0.13 g, 0.31 mmol) (82% de) in THF (0.49 mL) dropwise. The mixture was stirred at 0 °C for 2 h, and then the bath was removed and the mixture was stirred for an additional 5.5 h at 23 °C. A solution of saturated sodium sulfite (2 mL) was added to the reaction mixture followed by H_2O, MTBE, and 1.0 M HCl (10 mL) (pH approx 1). The layers were separated, and the aqueous layer was extracted with MTBE (2 × 10 mL). The combined organic layers were washed with saturated $NaHCO_3$ (3 × 5 mL). Then 1.0 M HCl was added to the combined basic aqueous layers until the pH was approximately 1. The acidic aqueous solution was extracted with MTBE, and the organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo to give 0.086 g (82%) of (*R*)-**3** as a white solid with 82% ee as determined by chiral HPLC.

^{1}H NMR (DMSO-d_6, 400 mHz) δ 0.99−1.05 (m, 2H), 1.06−1.19 (m, 4H), 1.26−1.33 (m, 1H), 1.50−1.60 (m, 2H), 1.63 (ddd, 1H, J = 7.2, 7.2, 14.0 Hz), 1.92 (ddd, 1H, J = 7.6, 7.6, 13.6 Hz), 2.82 (dddd (app tt), 1H, J = 4.8, 8.0 Hz), 3.11−3.18 (m, 2H) 3.73−3.80 (m, 3H), 7.57 (d, 2H, J = 8.4 Hz), 7.83 (d, 2H, J = 8.4 Hz), 12.54−12.60 (br s, 1H). ^{13}C NMR (DMSO-d_6, 100 mHz) δ 5.8, 32.4, 32.6, 32.8, 33.0, 48.0, 67.3, 127.9, 129.4, 139.6, 146.0, 174.6. IR (film) 3000−2600 (br s), 2916, 1718, 1316, 1294, 1272, 1223, 1190, 1149, 1130, 1089, 1071, 1037, 1015, 885, 855, 836, 822, 781, 758, 736 cm^{-1}. HRMS (EI$^+$) calcd for $C_{17}H_{22}O_5S$ 338.11879, found 338.1183. $[\alpha]_D^{24}$ −53.8 (MeOH, c = 2.8).

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Notes

The authors declare no competing financial interest.

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