Supporting Information

Synthesis of Esomeprazole and Related Proton Pump Inhibitors through Iron-Catalyzed Enantioselective Sulfoxidation

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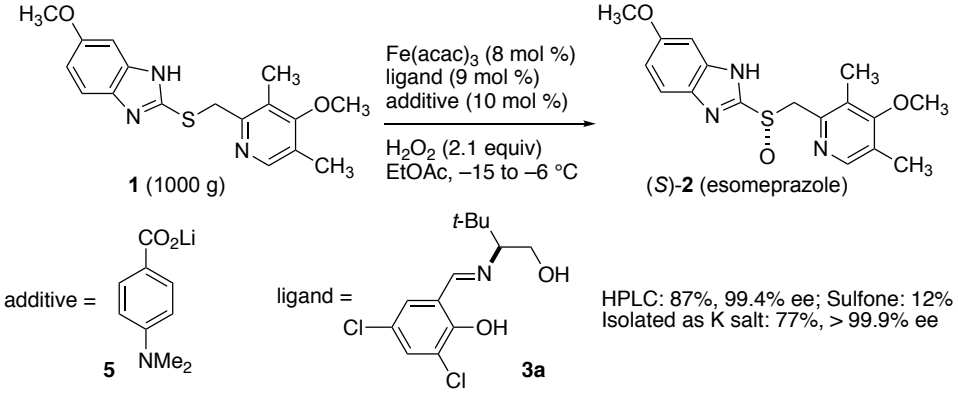
1. Materials and methods

The reaction on 1 kg scale was performed in a 30 L or 100 L glass-lined reactor fitted with a mechanical stirrer, under a nitrogen atmosphere. The reactions on small scale were performed in Schenk tubes or side-arm test tubes fitter with a stirring bar; similar results were obtained when the reaction was performed under inert gas and under air. Analytical thin-layer chromatography was performed on glass plates coated with 0.25 mm 230–400 mesh silica gel containing a fluorescent indicator (Merck). Flash silica gel column chromatography was performed on silica gel 60N (Kanto, spherical and neutral, 140–325 mesh) or wakogel C-200 (Fujifilm Wako Pure Chemical Co., 75-150 mesh), as described by Still.[1] HPLC analysis was performed on a Shimadzu Prominence, equipped with Daicel CHIRALPAK IC 4.6 x 250 mm (5 μm) column or Daicel CHIRALPAK IA 4.6 x 250 mm (5 μm) column and Agilent ZORBAX SB-C8 4.6 x 150 mm (5 μm) column. Optical rotation was measured on HORIBA SEPA-500. NMR spectra were measured on JEOL ECX-400 or Bruker AVANCE III HD400 and reported in parts per million from tetramethylsilane. ^{1}H NMR spectra in $CDCl_3$ or DMSO-d_6 were referenced internally to tetramethylsilane as a standard, and ^{13}C NMR spectra to the solvent resonance. Mass spectra were measured on Waters SQ Detector. Melting point was measured on Buchi M-565. Reaction calorimetry was performed with a RC1 calorimeter. PXRD was measured on Rigaku MiniFlex300.

Unless otherwise noted, materials were purchased from Tokyo Chemical Industry Co., Aldrich Inc., and other commercial suppliers and used as received. Reagent grade ethyl acetate was used without further purification. Sulfide **1** was purchased and the sulfide substrates in Figure 1b were purchased or prepared according to a modified literature method.[2] *N*-methylated sulfide **11** was prepared according to the literature,[3] as an inseparable 1:1 mixture of *N*-methylated isomers. $Fe(acac)_3$ from various commercial suppliers gave similar results. Aqueous hydrogen peroxide (30.0–35.5%) was purchased from KANTO CHEMICAL CO., INC. or Fujifilm Wako Pure Chemical Co., and stored at 5 °C. Lithium 4-dimethylaminobenzoate was prepared according to the literature.[4] The chiral Schiff bases were prepared according to the literature[5] and purified by recrystallization.

2. Iron-Catalyzed Synthesis of Esomeprazole

Reaction on 1 kg Scale (Figure 1a)



In a 30 L glass-lined reactor fitted with a mechanical stirrer, under a nitrogen atmosphere chiral Schiff base **3a** (79.3 g, 273 mmol) and iron(III) acetylacetonate (85.8 g, 243 mmol) were dissolved in ethyl acetate (1.80 kg) at 25 °C, and the mixture was stirred for 30 min. Lithium 4-dimethylaminobenzoate (**5**, 51.9 g, 304 mmol) and ethyl acetate (0.90 kg) were added and the resulting suspension was stirred for 30 min at 25 °C; next, sulfide **1** (1.00 kg, 3.04 mol) and ethyl acetate (6.30 kg) were added, stirred for 30 min at 25 °C, then the suspension was cooled to –15 °C. Aqueous hydrogen peroxide (35%, 613 g, 6.38 mol) was added over 6 h, and the reaction mixture was stirred for an additional 5 h at –13 to –14 °C. The reaction progress was monitored by HPLC; at the end of the reaction, the sulfoxide was formed in 87% yield and 99.4% ee, with 12% of the sulfone, and 0.2% of the sulfide **1**. After aqueous workup, KOH (178 g, 3.04 mol) in methanol (2.45 kg) was added to the organic phase, stirred overnight, and esomeprazole potassium salt dimethanol solvate was obtained upon cooling to –10 °C as an off-white solid (1.04 kg, 2.32 mol, 77% yield, >99.9% ee). The product data was in good agreement with the literature.[6,7,8]

Mp 119-122 °C; $[\alpha]_D^{20}$ = +28.7 (c = 1%, H_2O); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.22 (s, 1H), 7.31 (d, J = 8.4 Hz, 1H), 6.96 (d, J = 2.4 Hz, 1H), 6.54 (dd, J = 8.8, 2.4 Hz, 1H), 4.77 (d, J = 12.8 Hz, 1H), 4.36 (d, J = 12.8 Hz, 1H), 4.23 (br s, 2H), 3.72 (s, 3H), 3.69 (s, 3H), 3.17 (s, 6H), 2.23 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.3, 162.2, 153.4, 152.2, 148.9, 147.0, 141.7, 126.4, 124.7, 117.4, 108.7, 99.4, 59.6, 59.1, 55.2, 48.6, 12.9, 11.3; ESI-MS m/z: 384.27 ($M+K^+$).

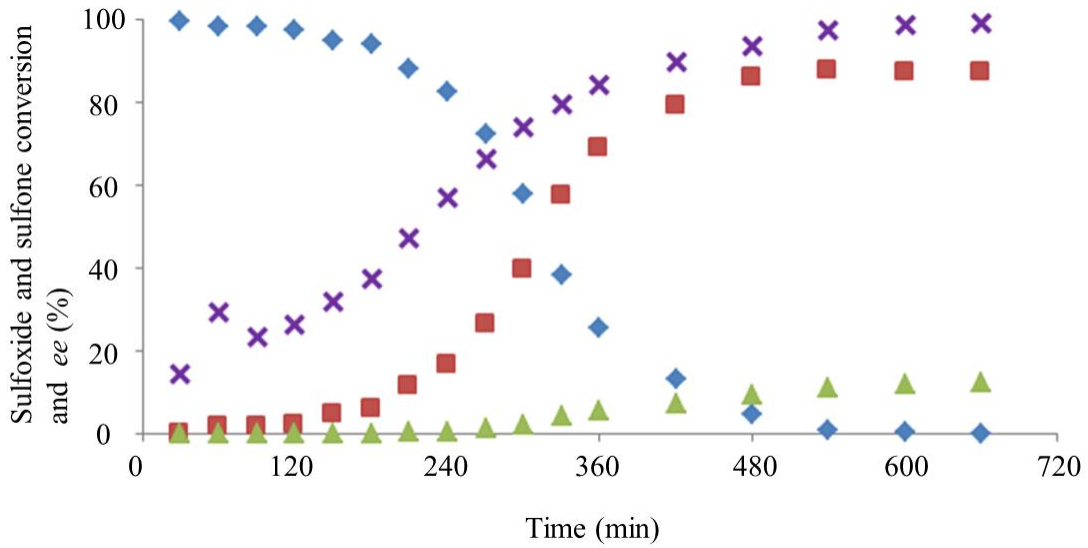


***Figure S1*. Time course of the enantioselective oxidation of 1 (1 kg scale). The HPLC conversion of 1 (◆) to sulfoxide (■) and sulfone (▲) and *ee* (×) are represented.**

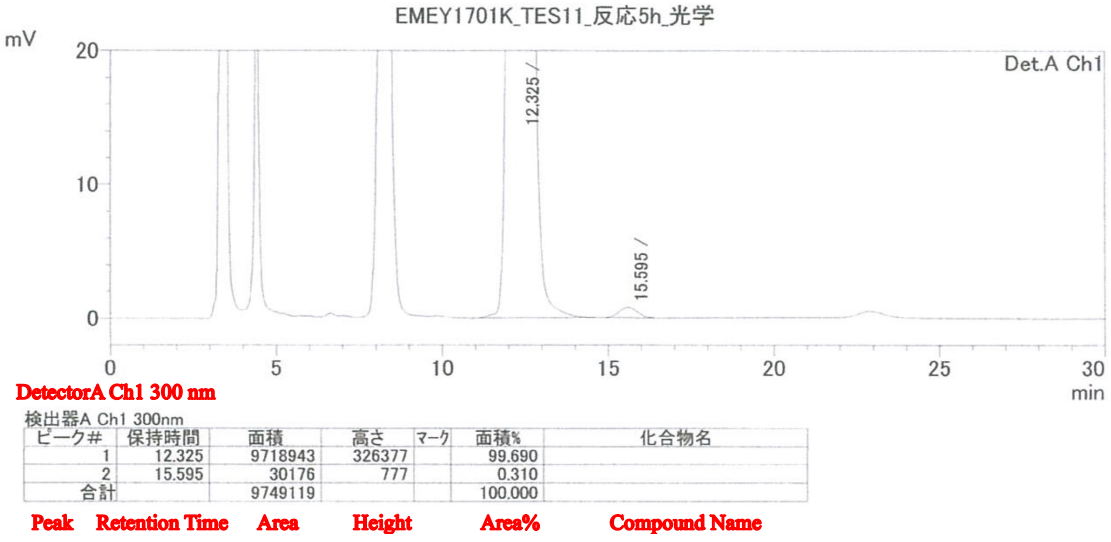
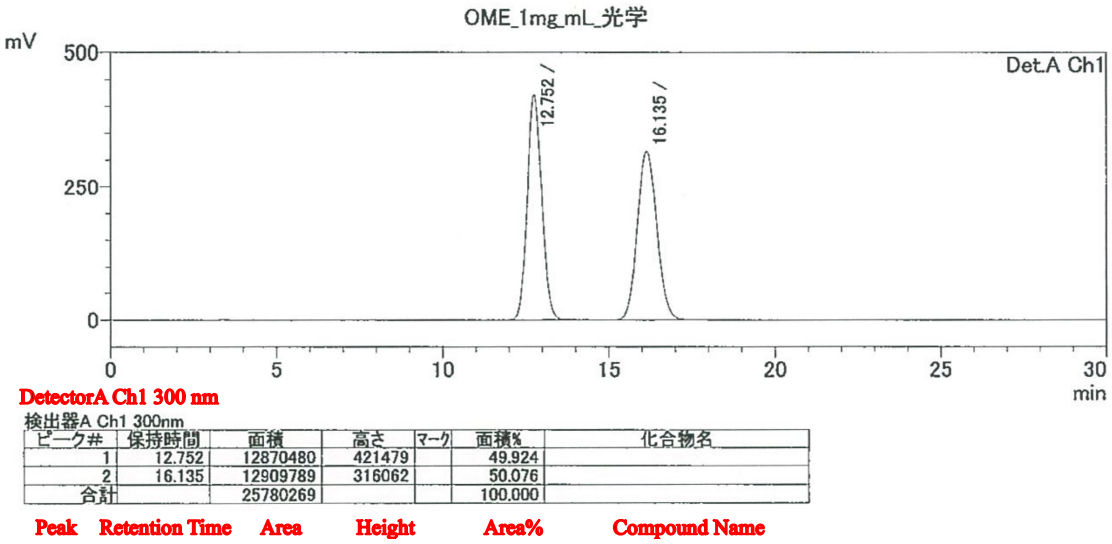


***Figure S2*. Chiral HPLC chart of the reaction mixture after 5 h reaction. English translation is provided in red.**



ピーク#	保持時間	面積	高さ	マーク	面積%	化合物名
1	12.752	12870480	421479		49.924	
2	16.135	12909789	316062		50.076	
合計		25780269			100.000	

Peak Retention Time Area Height Area% Compound Name

***Figure S3*. Chiral HPLC chart of omeprazole (racemic mixture of sulfoxide 2). English translation is provided in red.**

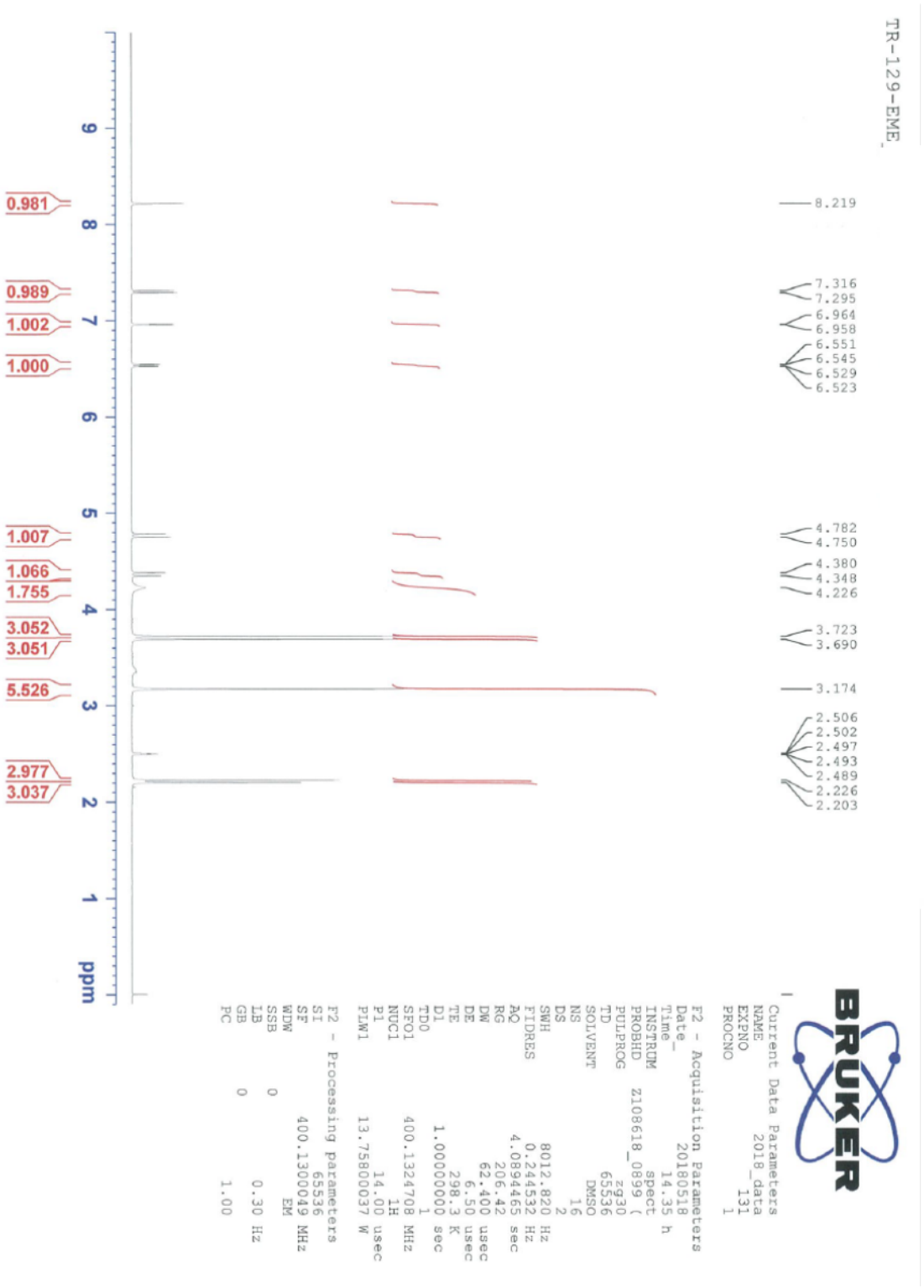


Figure S4. **^{1}H NMR chart of esomeprazole potassium salt dimethanol solvate.**

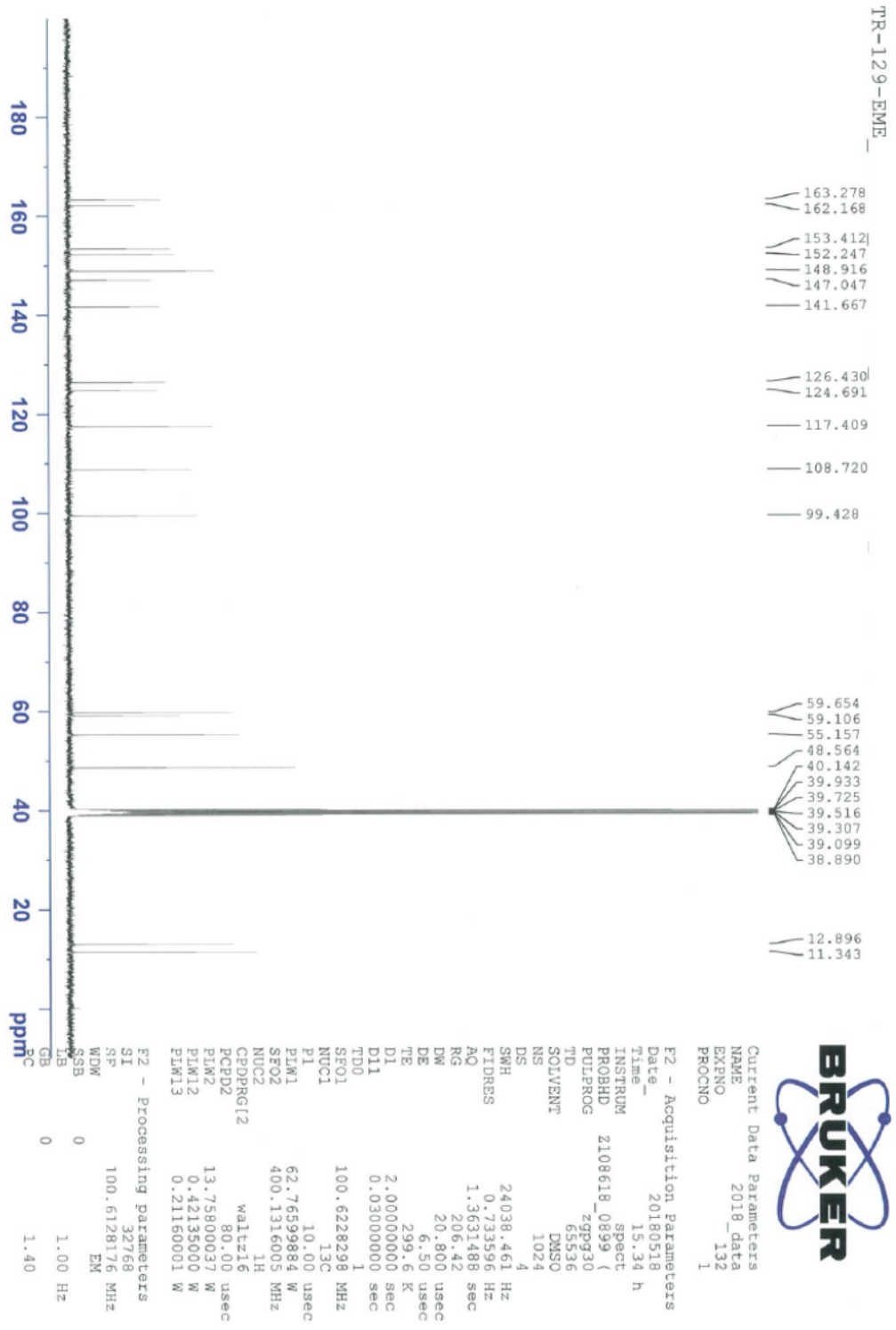


Figure S5. **^{13}C NMR chart of esomeprazole potassium salt dimethanol solvate.**

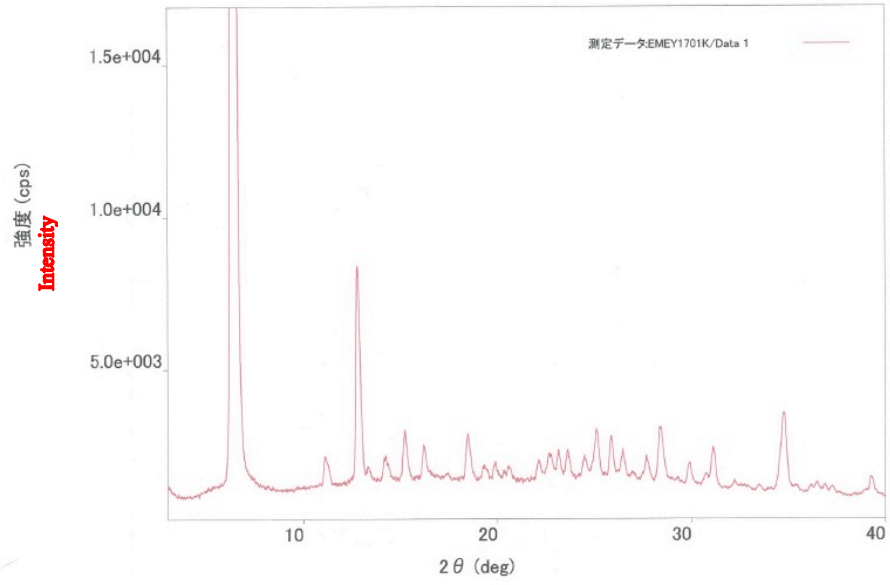
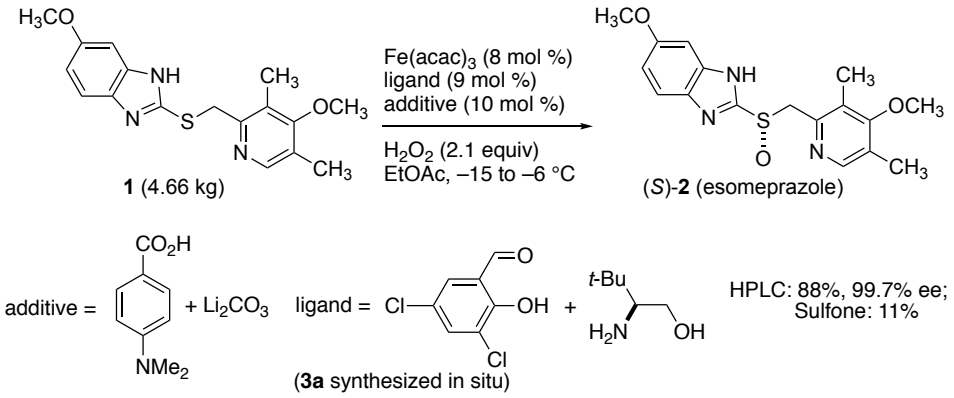


***Figure S6*. PXRD chart of esomeprazole potassium salt dimethanol solvate. English translation is provided in red.**

Reaction on 4.66 kg Scale with *In Situ*-Generated Ligand and Additive (Figure 1a)



In a 100 L glass-lined reactor fitted with a mechanical stirrer, under a nitrogen atmosphere (*S*)-*tert*-leucinol (159.1 g, 1.36 mol), 3,5-dichlorosalicylaldehyde (272.9 g, 1.43 mol), lithium carbonate (104.5 g, 1.42 mol), 4-dimethylaminobenzoic acid (233.7 g, 1.42 mol), and iron(III) acetylacetonate (399.7 g, 1.13 mol) were added to ethyl acetate (37.7 kg) at 25 °C, and the resulting suspension was stirred for 60 min. Sulfide **1** (4.66 kg, 14.1 mol) and ethyl acetate (4.19 kg) were added at 25 °C, then the suspension was cooled to –15 °C. Aqueous hydrogen peroxide (35%, 2.85 kg, 29.7 mol) was added over 10 h, and the reaction mixture was stirred for an additional 14 h

at –13 to –9 °C. The reaction progress was monitored by HPLC; at the end of the reaction, the sulfoxide was formed in 88% yield and 99.7% ee, with 11% of the sulfone, and 0.2% of the sulfide **1**. After aqueous workup, KOH (830 g, 14.1 mol) in methanol (11.4 kg) was added to the organic phase, stirred overnight, and esomeprazole potassium salt dimethanol solvate was obtained upon cooling to –10 °C as an off white-solid (5.00 kg, 11.2 mol, 79% yield, >99.9% ee). The product data was in good agreement with the literature.[6,7,8]

Mp 118-123 °C; $[\alpha]_D^{20}$ = +27.2 (c = 1%, H_2O); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.22 (s, 1H), 7.31 (d, J = 8.8 Hz, 1H,), 6.97 (d, J = 2.4 Hz, 1H), 6.54 (dd, J = 8.8, 2.8 Hz, 1H), 4.76 (d, J = 12.8 Hz, 1H), 4.37 (d, J = 13.2 Hz, 1H), 4.30 (br s, 2H), 3.72 (s, 3H), 3.69 (s, 3H), 3.18 (s, 6H), 2.22 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.3, 162.1, 153.5, 152.2, 149.0, 147.0, 141.6, 126.5, 124.8, 117.4, 108.8, 99.4, 59.7, 59.2, 55.2, 48.6, 12.9, 11.4; ESI-MS *m/z*: 384.28 ($M+K^+$).

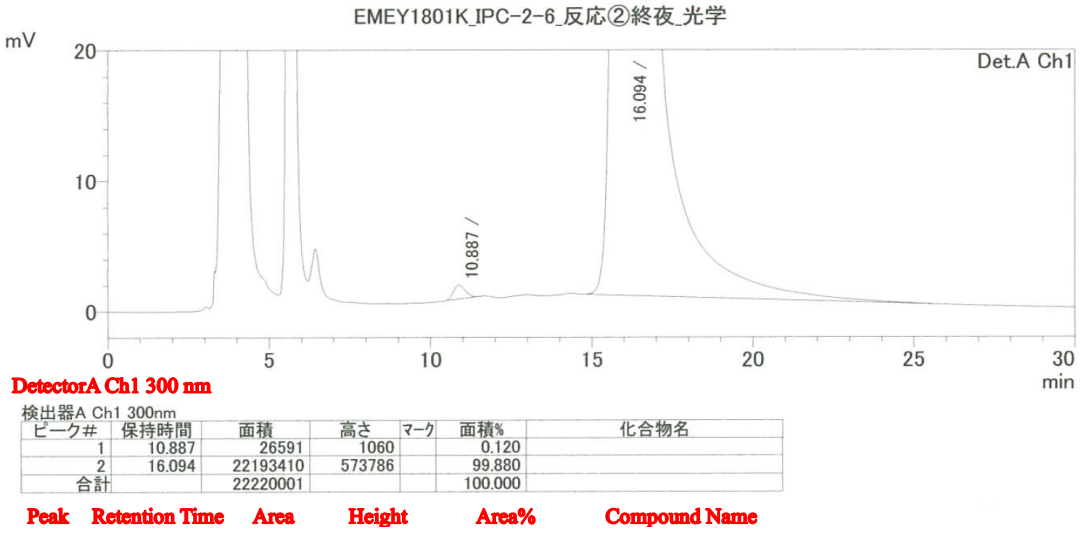
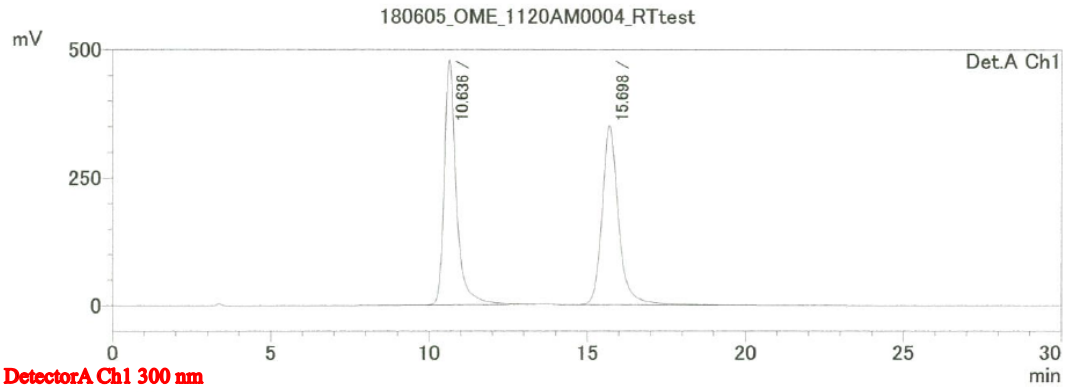


***Figure S7*. Chiral HPLC chart of the reaction mixture after 14 h reaction. English translation is provided in red.**



DetectorA Ch1 300 nm

検出器A Ch1 300nm

ピーク#	保持時間	面積	高さ	マーク	面積%	化合物名
1	10.636	12720745	478242		49.995	
2	15.698	12723442	349248		50.005	
合計		25444187			100.000	

Peak Retention Time Area Height Area% Compound Name

***Figure S8*. Chiral HPLC chart of omeprazole (racemic mixture of sulfoxide 2). English translation is provided in red.**

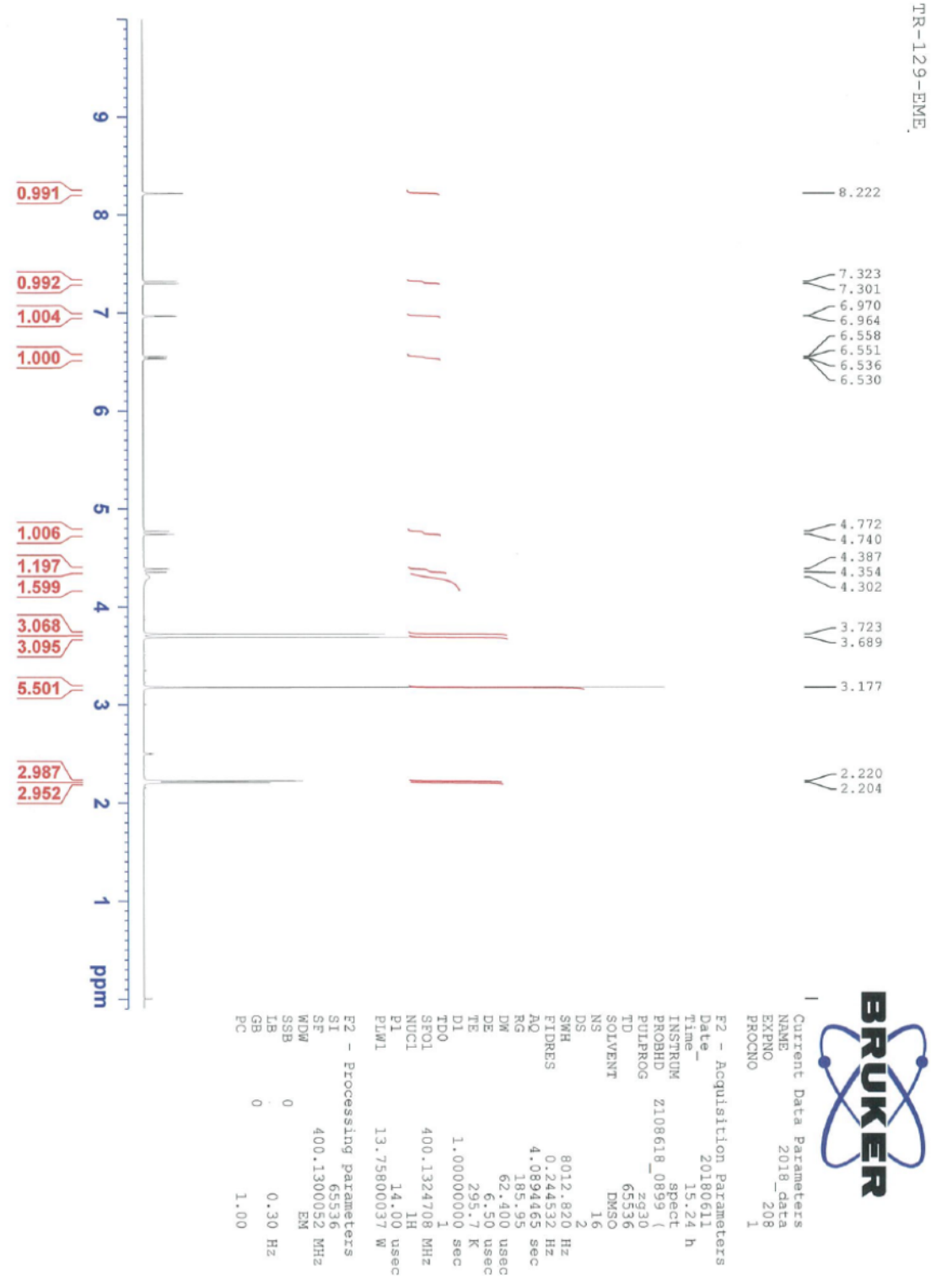


Figure S9. **^{1}H NMR chart of esomeprazole potassium salt dimethanol solvate.**

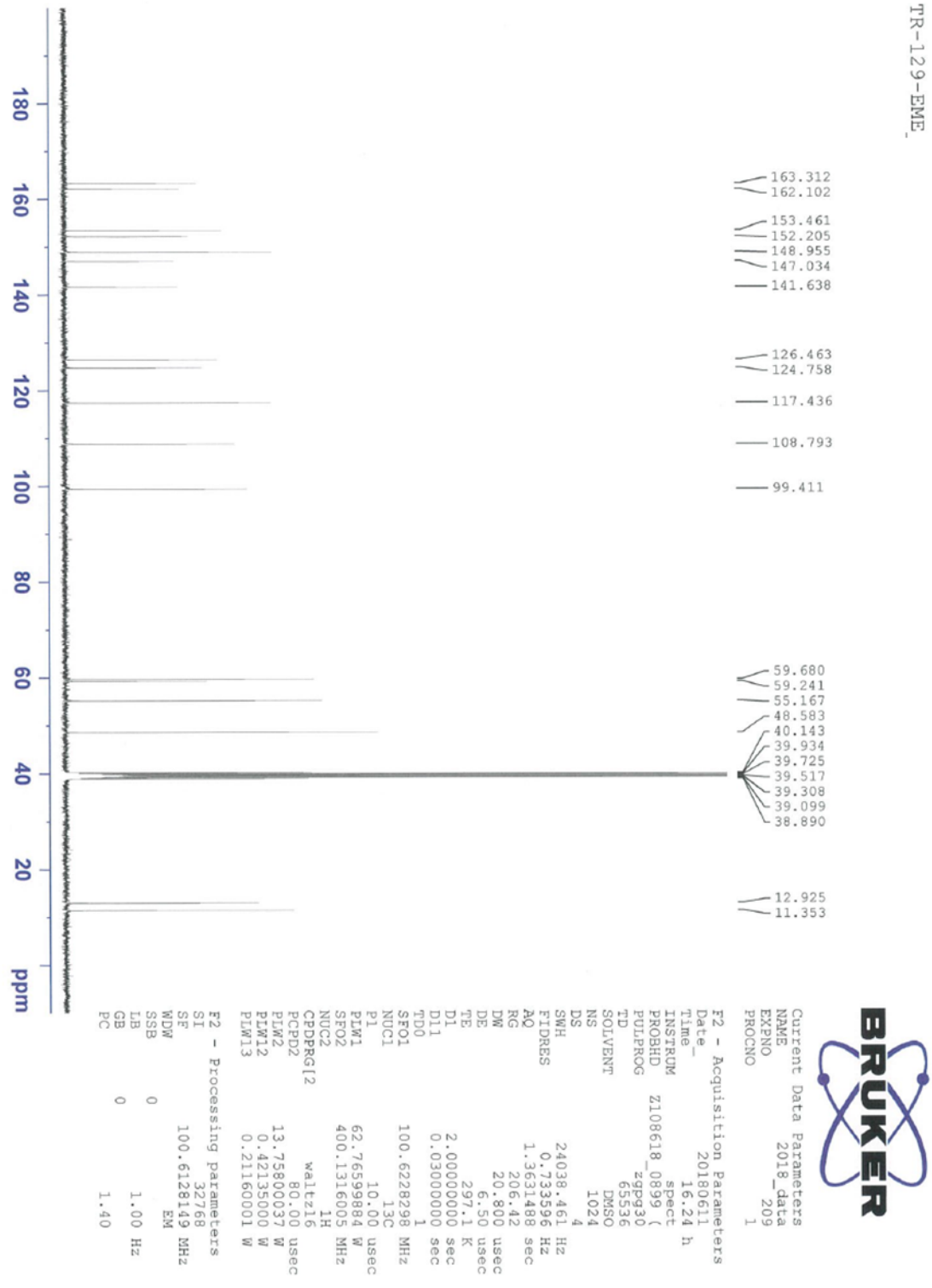


Figure S10. **^{13}C NMR chart of esomeprazole potassium salt dimethanol solvate.**

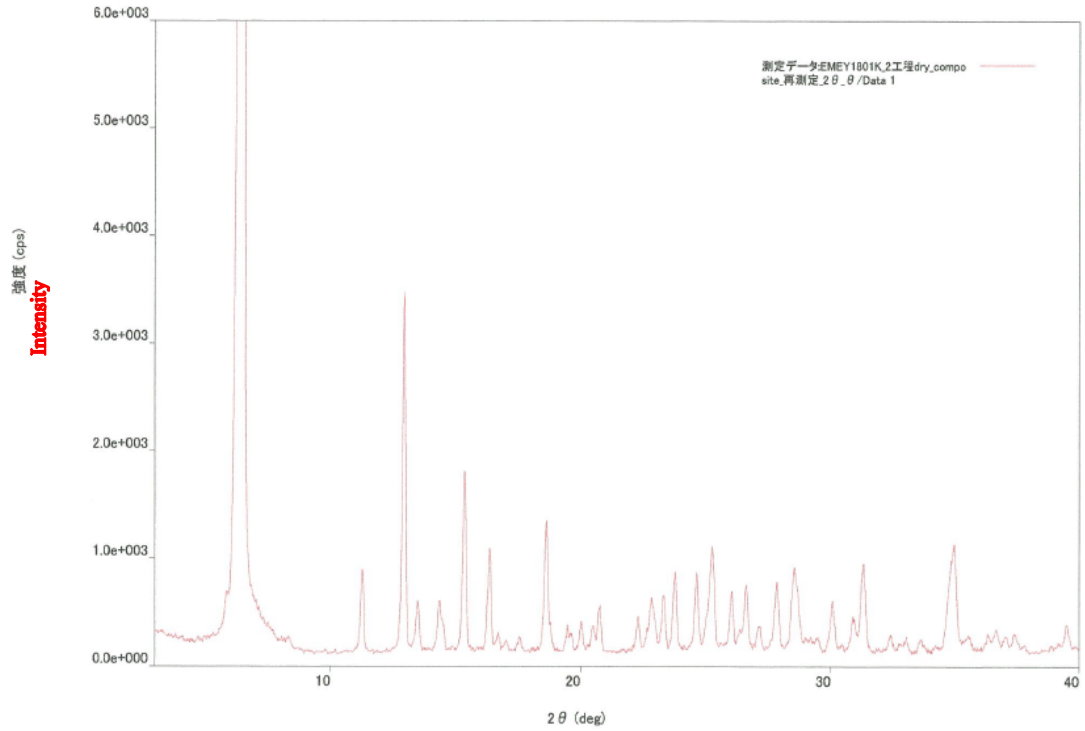


***Figure S11*. PXRD chart of esomeprazole potassium salt dimethanol solvate. English translation is provided in red.**

Representative Procedure for Optimization Studies (Table 4, entry 8)

In a Schenck tube, chiral Schiff base **3a** (79 mg, 273 μmol) and iron(III) acetylacetonate (32 mg, 91 μmol) were dissolved in ethyl acetate (0.6 mL) at 25 °C, and the mixture was stirred for 30 min. Lithium 4-dimethylaminobenzoate (**5**, 7.7 mg, 45.0 μmol) and ethyl acetate (0.3 mL) were added and the resulting suspension was stirred for 2 h at 25 °C; next, sulfide **1** (0.30 g, 911 μmol) and ethyl acetate (0.9 mL) were added, stirred for 30 min at 25 °C, then the suspension was cooled to –5 °C. Aqueous hydrogen peroxide (30%, 186 μL, 1.82 mmol) was slowly added over 2 min, and the reaction mixture was stirred for an additional 4.5 h at –5 °C. The reaction mixture was analyzed by HPLC, to reveal that the sulfoxide **2** was formed in 83% yield and 96% ee, with 12% of the sulfone, and 5% of the sulfide **1**.

3. Iron-Catalyzed Synthesis of (*S*)-Lansoprazole, (*S*)-Rabeprazole, and (*S*)-Pantoprazole (Figure 1b)

Representative Procedure: Synthesis of (*S*)-Lansoprazole

In a test tube fitted with a side arm, chiral Schiff base **3a** (234 mg, 806 μmol), iron(III) acetylacetonate (95 mg, 269 μmol), Lithium 4-dimethylaminobenzoate (**5**, 23 mg, 134 μmol), and ethyl acetate (7.5 mL) were added, then the resulting suspension was stirred for 30 min at 25 °C; next, lansoprazole sulfide hydrate (1.00 g, 2.69 mmol) and ethyl acetate (7.5 mL) were added, then the suspension was cooled to –5 °C. Aqueous hydrogen peroxide (35%, 550 μL, 6.29 mmol) was slowly added over 2 min, and the reaction mixture was stirred for an additional 20.5 h at –5 °C. The reaction mixture was analyzed by HPLC, to reveal that (*S*)-lansoprazole was formed in 87% yield and 98% ee, with 12% of the sulfone, and 2% of the sulfide. After aqueous workup, the organic phase was concentrated under reduced pressure, and the residue was purified by flash column chromatography (hexanes/ethyl acetate = 1:2 to ethyl acetate/methanol = 3:2) to afford an analytically pure sample of the title compound.
Caution: upon standing, this compound gradually decomposed.

Compound Data

(*S*)-lansoprazole

The compound data was in good agreement with the literature.[9]

^{1}H NMR (400 MHz, DMSO-d_6): δ 13.58 (br s, 1H), 8.29 (d, J = 5.7 Hz, 1H), 7.65 (br s, 2H), 7.31 (dd, J = 6.1, 3.2 Hz, 2H), 7.10 (d, J = 5.7 Hz,1H), 4.89 (q, J = 8.8 Hz, 2H), 4.83 (d, J = 13.8 Hz, 1H), 4.75 (d, J = 13.8 Hz, 1H), 2.18 (s, 3H) ; ESI-MS *m/z*: 392.40 ($M+Na^+$).

(*S*)-rabeprazole

The compound data was in good agreement with the literature.[9]

^{1}H NMR (400 MHz, DMSO-d_6): δ 13.58 (br s, 1H), 8.22 (d, J = 5.6 Hz, 1H), 7.65 (br s, 2H), 7.32-7.29 (m, 2H), 6.96 (d, J = 5.7 Hz, 1H), 4.80 (d, J = 13.6 Hz, 1H), 4.71 (d, J = 13.6 Hz, 1H), 4.10 (t, J = 6.2 Hz, 2H), 3.48 (t, J = 6.2 Hz, 2H), 3.25 (s, 3H), 2.14 (s, 3H), 2.01–1.94 (m, 2H); ESI-MS *m/z*: 382.44 ($M+Na^+$).

(*S*)-pantoprazole

The compound data was in good agreement with the literature.[9]

$[\alpha]_D^{25}$ = –79.4 (c = 0.3%, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.77 (br s, 1H), 8.15 (d, *J* = 5.5 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.44 (s, 1H), 7.26 (s, 1H), 7.16 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.11 (d, *J* = 5.6 Hz, 1H), 4.72 (d, *J* = 13.1 Hz, 1H), 4.66 (d, *J* = 13.1 Hz, 1H), 3.90 (s, 3H), 3.77 (s, 3H); ESI-MS *m/z*: 406.36 ($M+Na^+$).

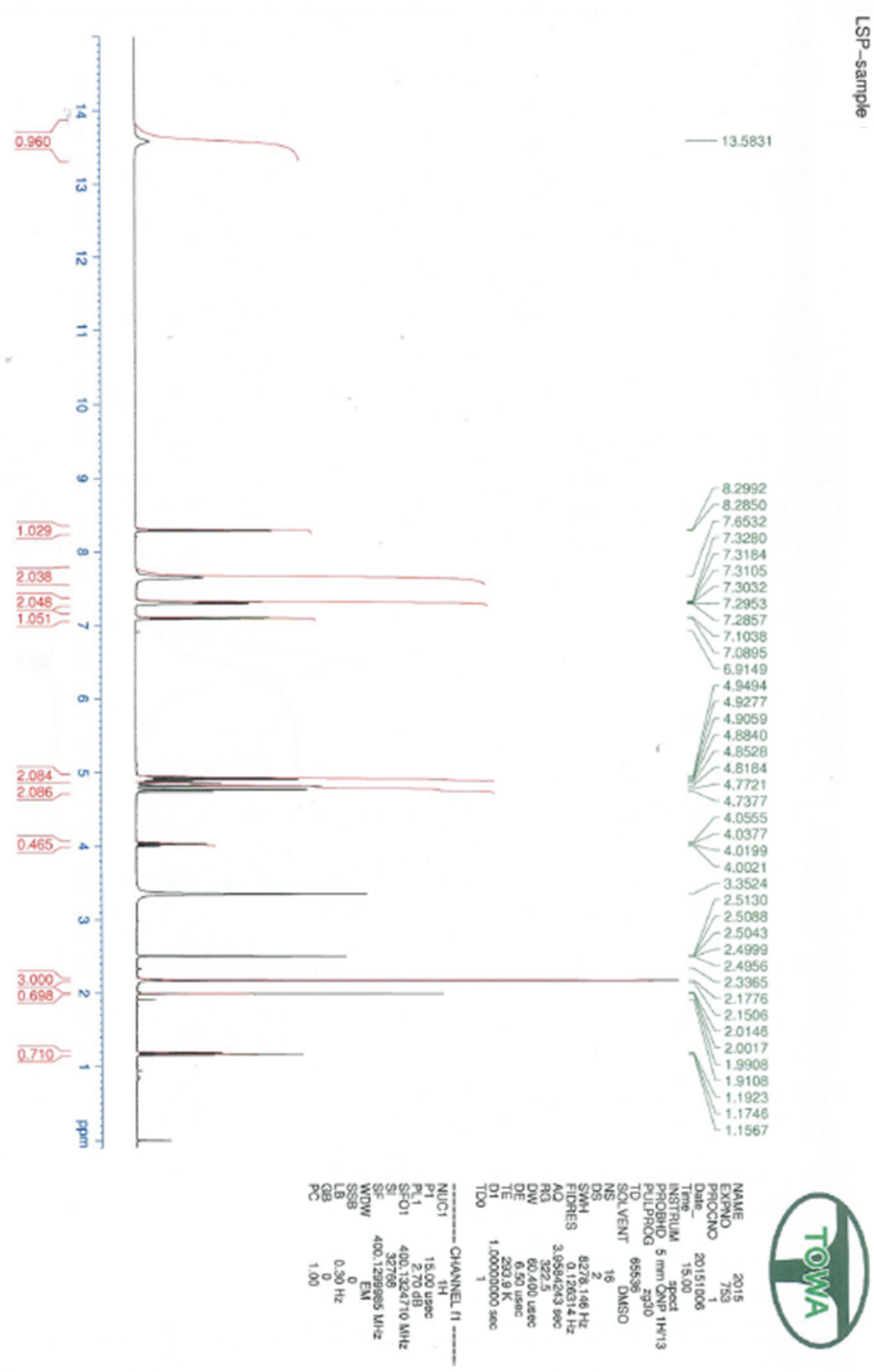


***Figure S12*. ^{1}H NMR chart of (*S*)-lansoprazole.**

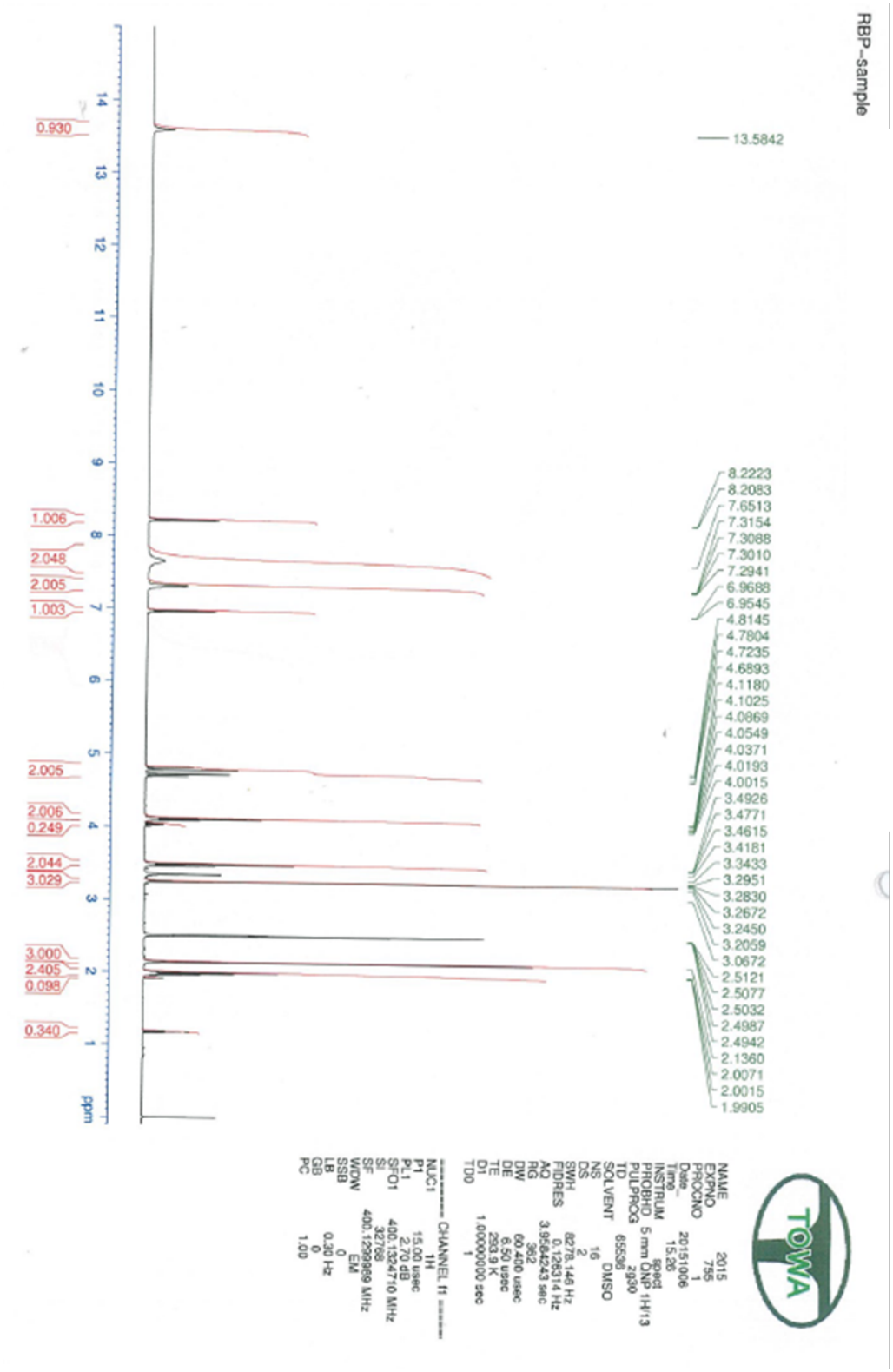


***Figure S13*. ^{1}H NMR chart of (*S*)-rabeprazole.**

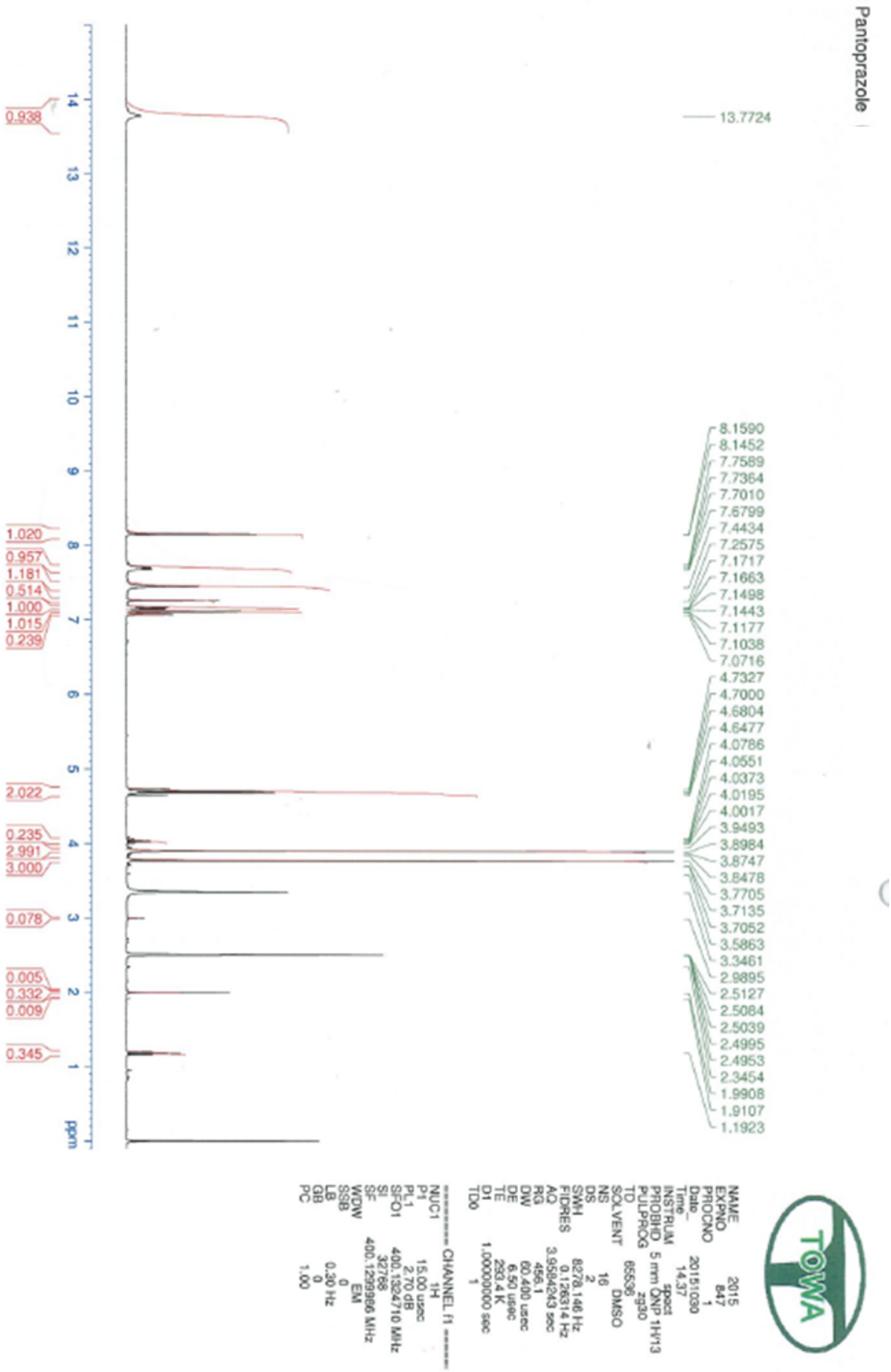
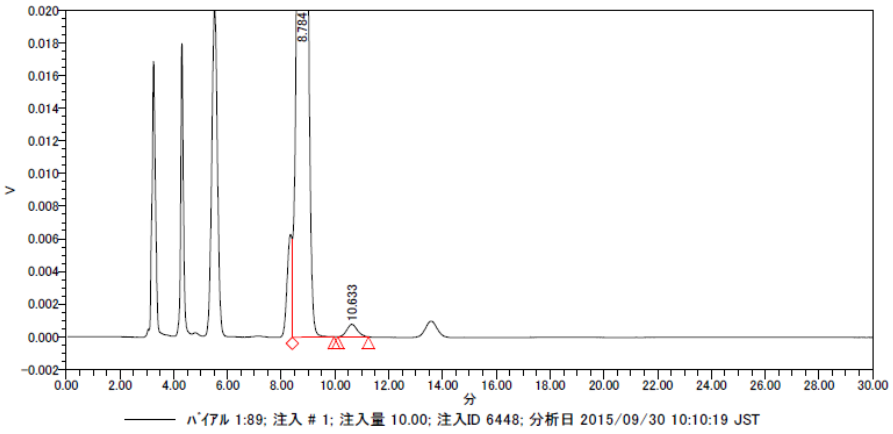


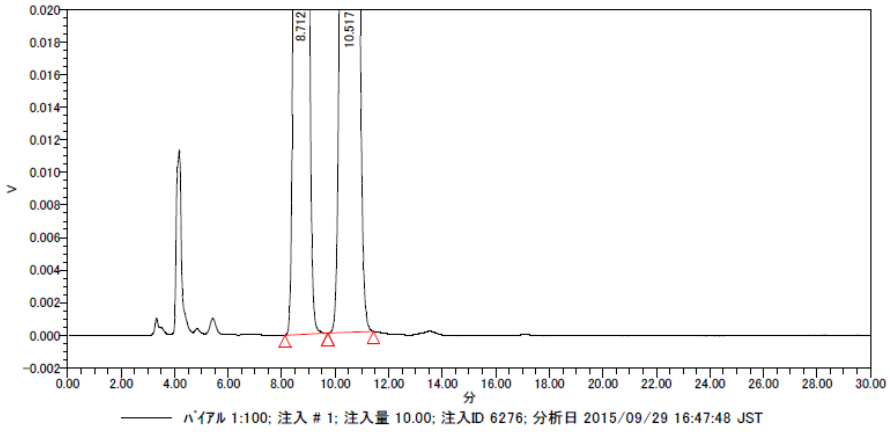
***Figure S14*. ^{1}H NMR chart of (*S*)-pantoprazole.**



	名前	保持時間	面積	%面積	分離度
1		8.784	1702881	98.80	
2		10.633	20725	1.20	2.921583e+000

Name Retention Time Area Area% Resolution

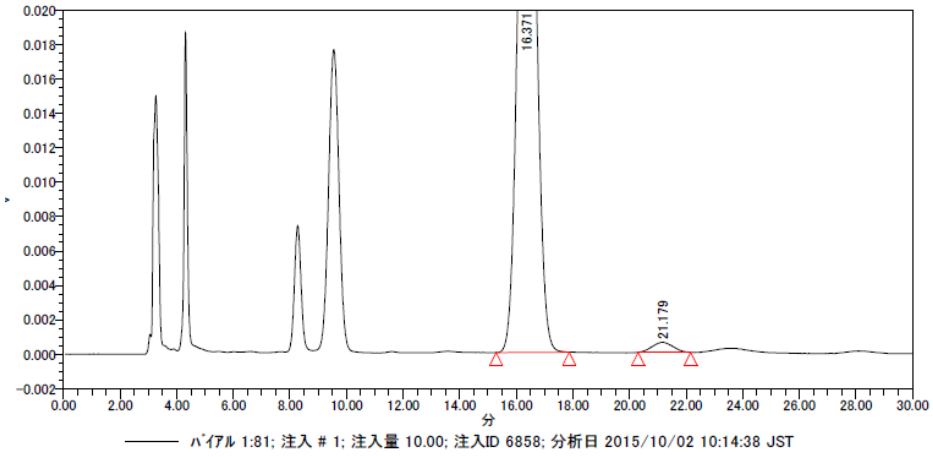
Figure S15. **Chiral HPLC chart of the lansoprazole reaction mixture after 20.5 h reaction. English translation is provided in red.**



	名前	保持時間	面積	%面積	分離度
1		8.712	6039649	49.83	
2		10.517	6080591	50.17	2.856956e+000

Name Retention Time Area Area% Resolution

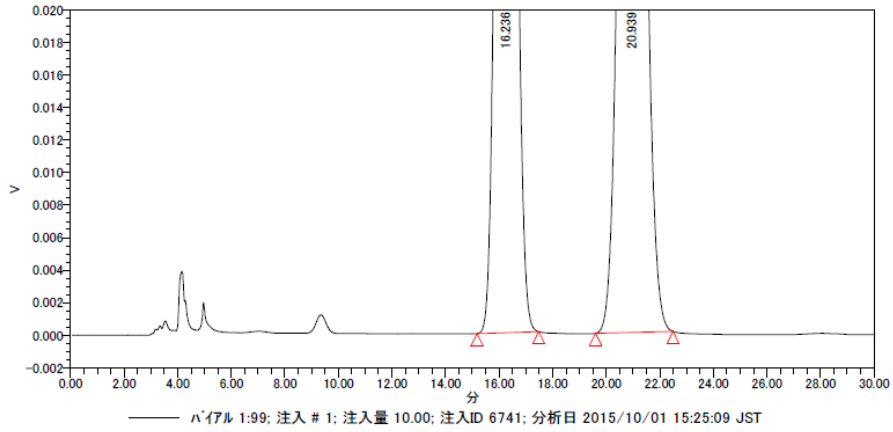
Figure S16. **Chiral HPLC chart of lansoprazole (racemic mixture of sulfoxide). English translation is provided in red.**



	名前	保持時間	面積	%面積	分離度
1		16.371	1843089	98.39	
2		21.179	30183	1.61	3.854855e+000

Name Retention Time Area Area% Resolution

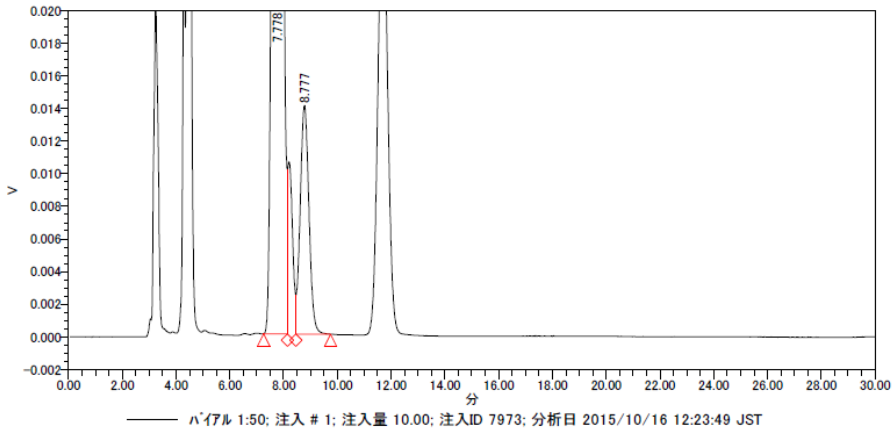
***Figure S17*. Chiral HPLC chart of the rabeprazole reaction mixture after 20.5 h reaction. English translation is provided in red.**



	名前	保持時間	面積	%面積	分離度
1		16.236	4489626	49.91	
2		20.939	4504929	50.09	3.723301e+000

Name Retention Time Area Area% Resolution

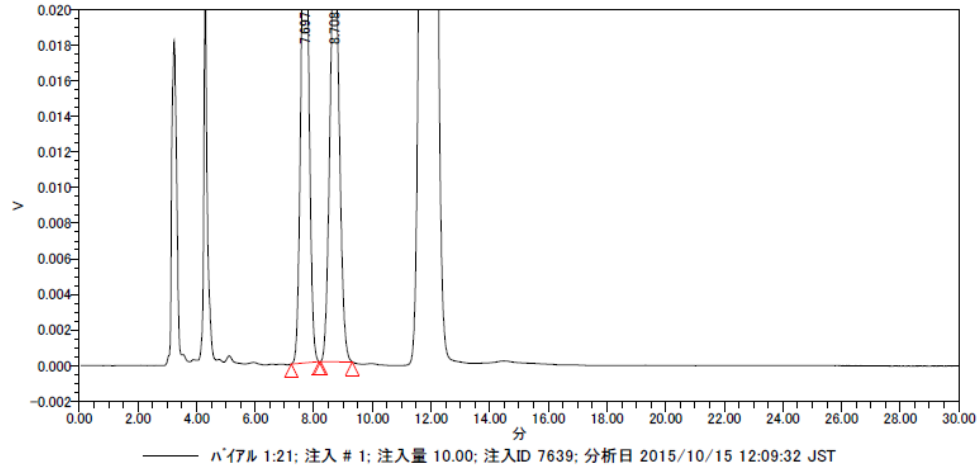
***Figure S18*. Chiral HPLC chart of rabeprazole (racemic mixture of sulfoxide). English translation is provided in red.**



	名前	保持時間	面積	%面積	分離度
1		7.778	3391323	91.39	
2		8.777	319417	8.61	1.839540e+000

Name Retention Time Area Area% Resolution

Figure S19. **Chiral HPLC chart of the pantoprazole reaction mixture after 44 h reaction. English translation is provided in red.**



	名前	保持時間	面積	%面積	分離度
1		7.697	537536	50.33	
2		8.708	530407	49.67	1.880721e+000

Name Retention Time Area Area% Resolution

Figure S20. **Chiral HPLC chart of pantoprazole (racemic mixture of sulfoxide). English translation is provided in red.**

4. Heat generation profile of the $FeCl_3$-Catalyzed Reaction (*Figure S20*)

In a RC1 calorimeter, chiral Schiff base **3a** (1.59 g, 5.48 mmol) and iron(III) chloride hydrate (1.32 g, 4.88 mmol) were dissolved in ethyl acetate (40 mL) at 25 °C, and the mixture was stirred for 30 min. Lithium 4-dimethylaminobenzoate (**5**, 1.04 g, 6.08 mmol) and ethyl acetate (20 mL) were added and the resulting suspension was stirred for 30 min at 25 °C; next, sulfide **1** (20.0 g, 60.7 mmol) and ethyl acetate (140 mL) were added, then the suspension was cooled to –10 °C. Aqueous hydrogen peroxide (35%, 12.3 g, 128 mmol) was slowly added over 2 h (green line), and then reaction mixture (viscous suspension) was additionally stirred at –10 °C. The conversion was monitored by HPLC (red plot): no induction period was observed, and after 19 h reaction the conversion was 50% (72% ee), and after 111.5 h it was 72% (73% ee). The exothermic peak at ca. 100 min observed when $Fe(acac)_3$ was used as the catalyst (Figure 2) did not appear; similar with the $Fe(acac)_3$-catalyzed reaction, the heat release peaked toward the end of the addition of hydrogen peroxide.

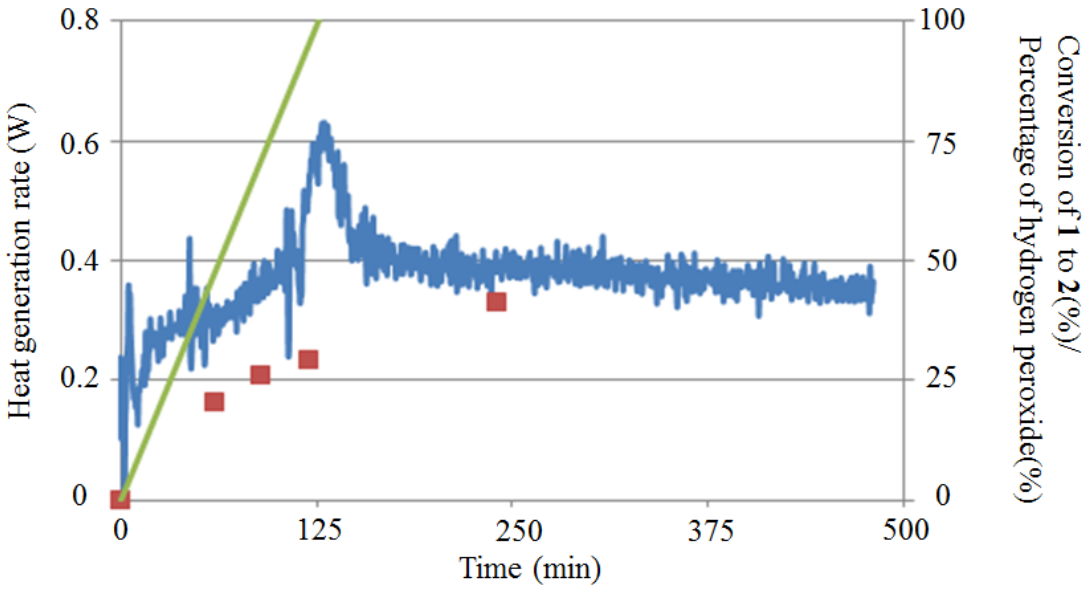


***Figure S21*. Heat generation profile of the $FeCl_3$-catalyzed reaction.** Blue line: heat generation rate (left axis); Red plot: conversion of **1** to **2**, determined by HPLC (right axis); Green line: the percentage of the total amount (2.1 equiv) of hydrogen peroxide added (right axis).

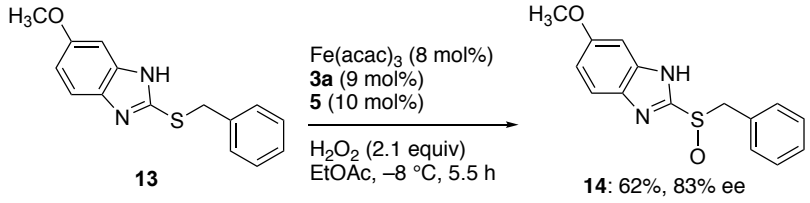
5. Iron-Catalyzed Oxidation of Benzyl Sulfide 13

Synthesis of 6-Methoxy-2-[(phenylmethyl)thio]-1*H*-benzimidazole (13)

In a four-necked flask, 1,3-dihydro-5-methoxy-2*H*-benzimidazole-2-thione (5.00 g, 27.4 mmol) was dissolved in DMF (50 mL) at 25 °C, the solution was cooled, and then benzyl bromide (4.75 g, 27.7 mmol) and potassium carbonate (5.75 g, 41.6 mmol) were added such as the temperature of the reaction mixture remained below 10 °C. The resulting suspension was stirred for 14 h at 25 °C. Water (200 mL) was added to the reaction mixture, the resulted solid was filtrated, washed with water (75 mL), and dried at 50 °C under vacuo and to afford the title compound.

Mp 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.22 (br s, 1H), 7.55 (br s, 0.5H), 7.30-7.17 (m, 6H), 6.83 (m, 1.5H), 4.45 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8, 149.8, 148.2, 144.9, 138.7, 137.1, 135.5, 129.0, 128.8, 127.7, 119.0, 112.6, 111.4, 110.7, 101.5, 94.7, 56.0, 38.0 (mixture of tautomers); ESI-MS *m/z*: 293.20 ($M+Na^+$).

Synthesis of (–)-6-methoxy-2-[(phenylmethyl)sulfinyl]-1*H*-benzimidazole (14) (Figure 3c)



In a test tube fitted with a side arm, chiral Schiff base **3a** (97 mg, 333 μmol) and iron(III) acetylacetonate (105 mg, 296 μmol) were dissolved in ethyl acetate (2.0 mL) at 25 °C, and mixture was stirred for 30 min. Lithium 4-dimethylaminobenzoate (**5**, 63 mg, 370 μmol) and ethyl acetate (1.0 mL) were added and the resulting suspension was stirred for 30 min at 25 °C; next, benzyl sulfide **13** (1.00 g, 3.70 mmol) and ethyl acetate (7.0 mL) were added, then the suspension was cooled to –9 °C. Aqueous hydrogen peroxide (35%, 660 μL, 7.77 mmol) was slowly added over 2 min, and the reaction mixture was stirred for an additional 18.5 h at –9 °C. The reaction mixture was analyzed by HPLC, to reveal that sulfoxide was formed in 71% yield and 85% ee, with 11% of the sulfone, and 18% of the sulfide. After aqueous workup, the organic

phase was concentrated under reduced pressure, and the residue was purified by flash column chromatography (hexanes/ethyl acetate = 2:1 to 1:2) to afford an analytically pure sample of the title compound.

Mp 128-130 °C; $[\alpha]_D^{20}$ = –153.8 (c = 1%, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.33 (br s, 1H), 7.67 (d, *J* = 9.2 Hz, 0.5H), 7.28-7.24 (m, 2H), 7.20-7.16 (m, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.98-6.95 (m, 1H), 6.84 (d, *J* = 2.0 Hz, 0.5H), 4.51 (d, 13.2 Hz, 1H), 4.28 (d, 13.2 Hz, 1H), 3.89 (s, 1H), 3.81 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 157.0, 152.1, 150.5, 145.2, 138.9, 135.1, 130.6, 128.9, 128.8, 121.0, 115.2, 113.8, 112.6, 102.1, 94.9, 61.7, 56.0 (mixture of tautomes); ESI-MS *m/z*: 309.22 ($M+Na^+$).

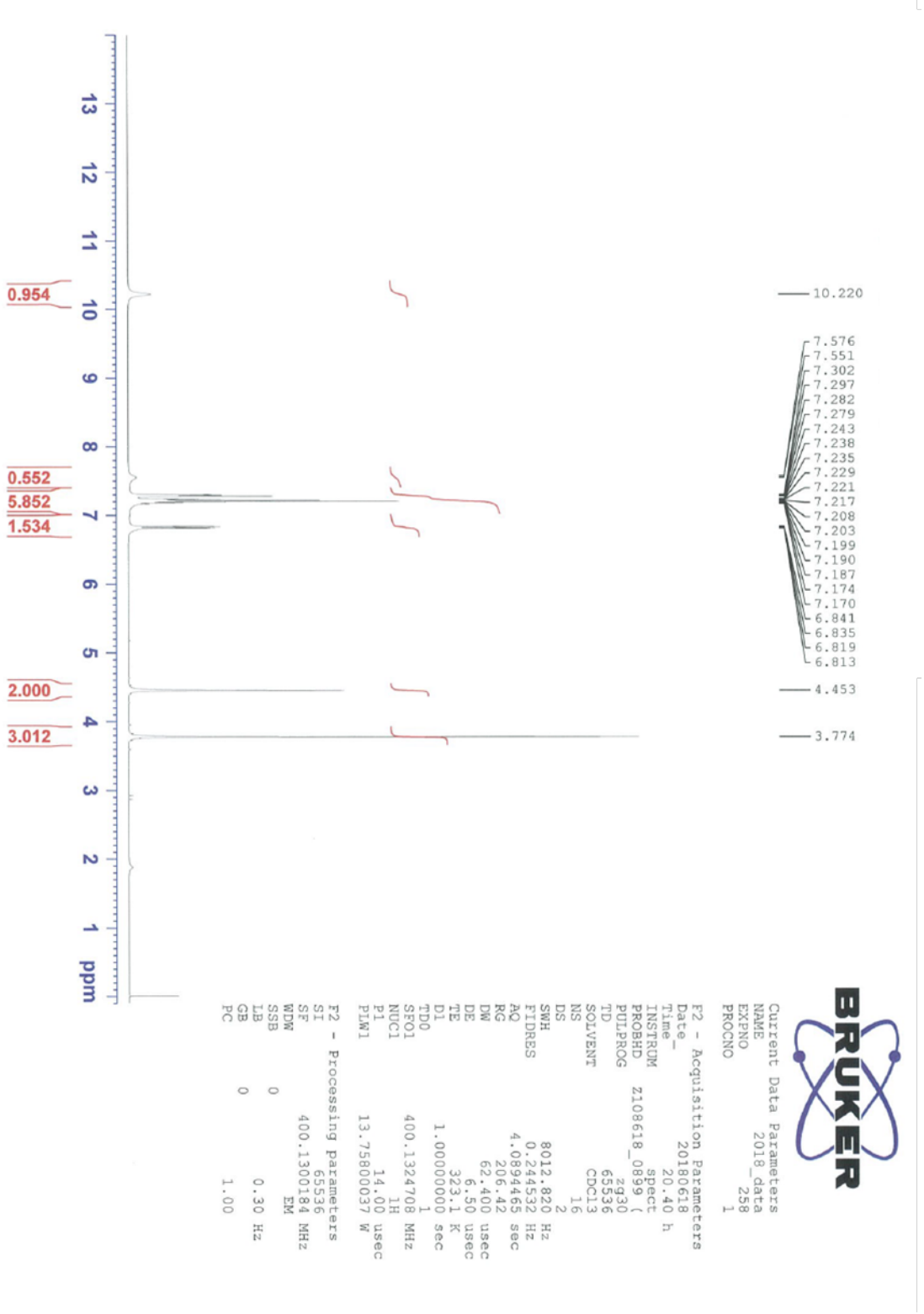


Figure S22. **^{1}H NMR chart of benzyl sulfide 13.**

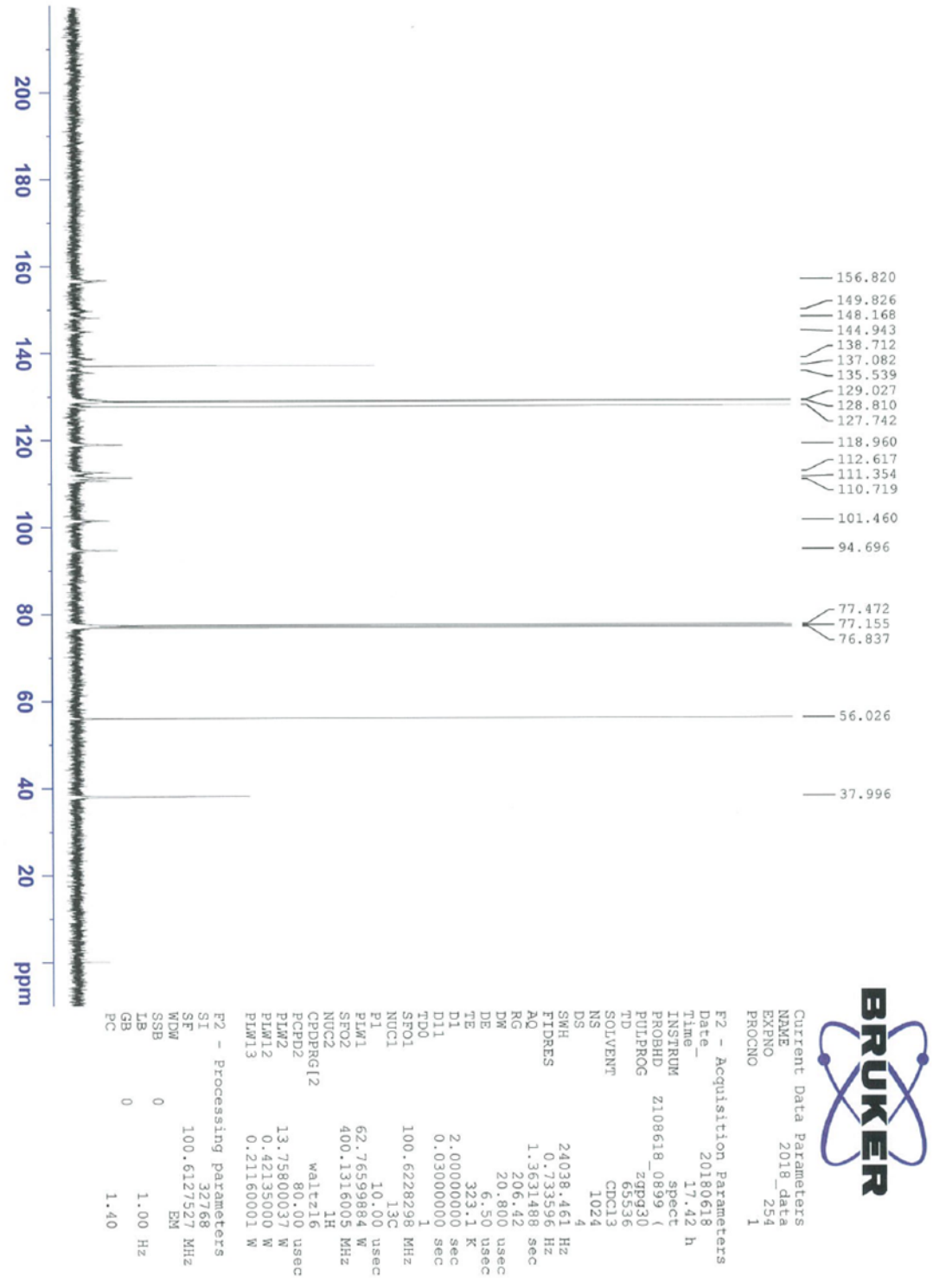


***Figure S23*. ^{13}C NMR chart of benzyl sulfide 13.**

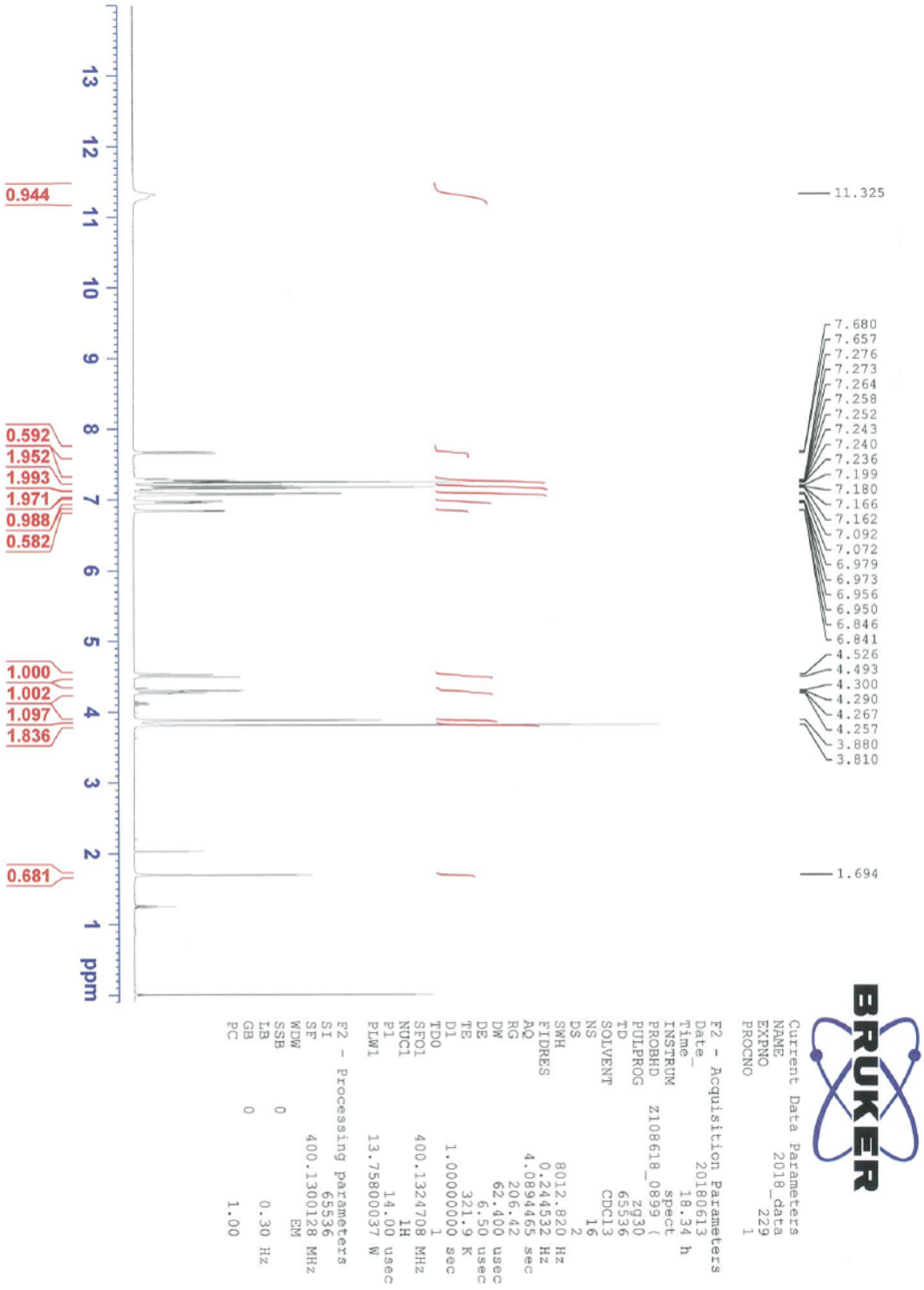


***Figure S24*. ^{1}H NMR chart of benzyl sulfoxide 14.**

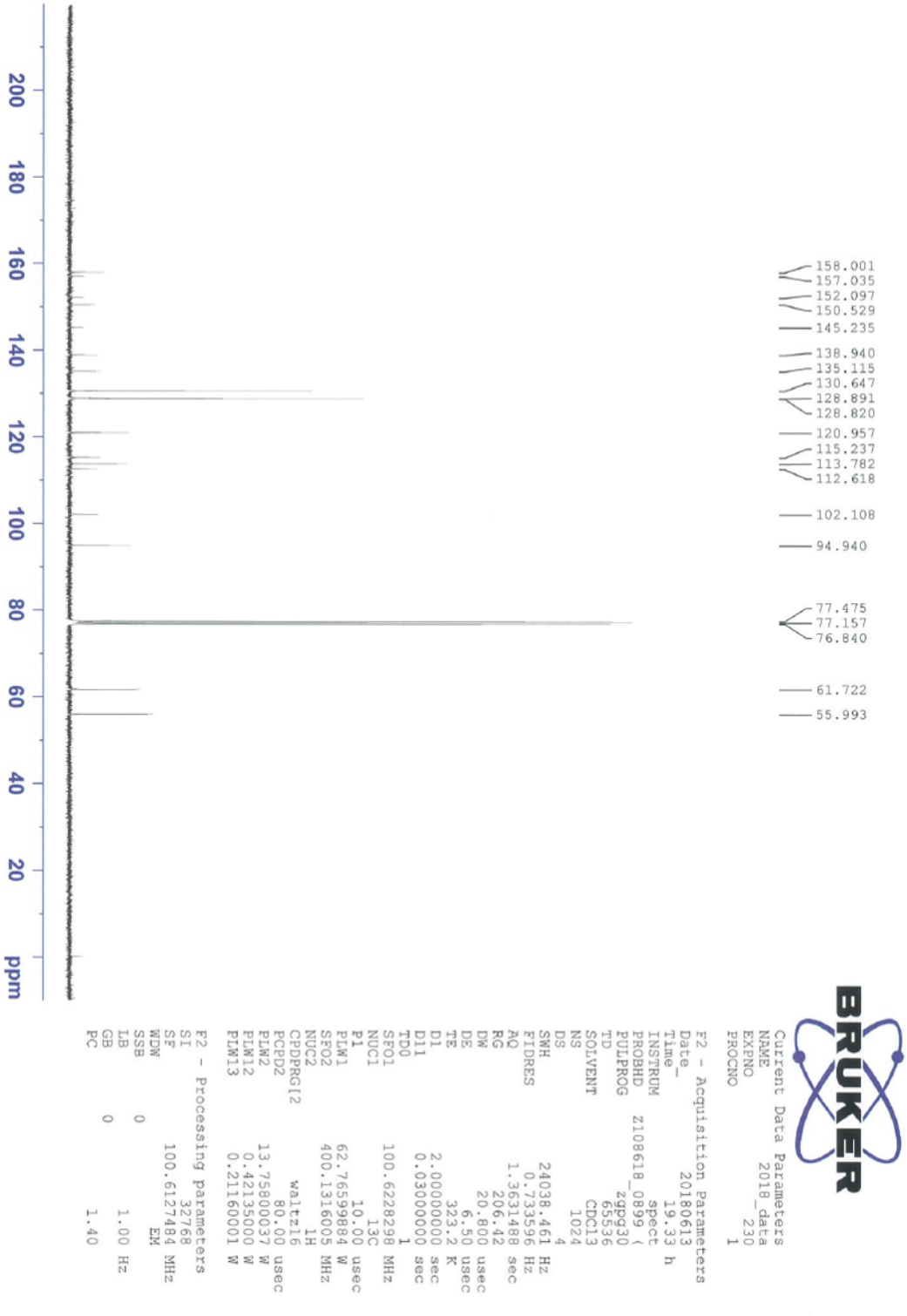
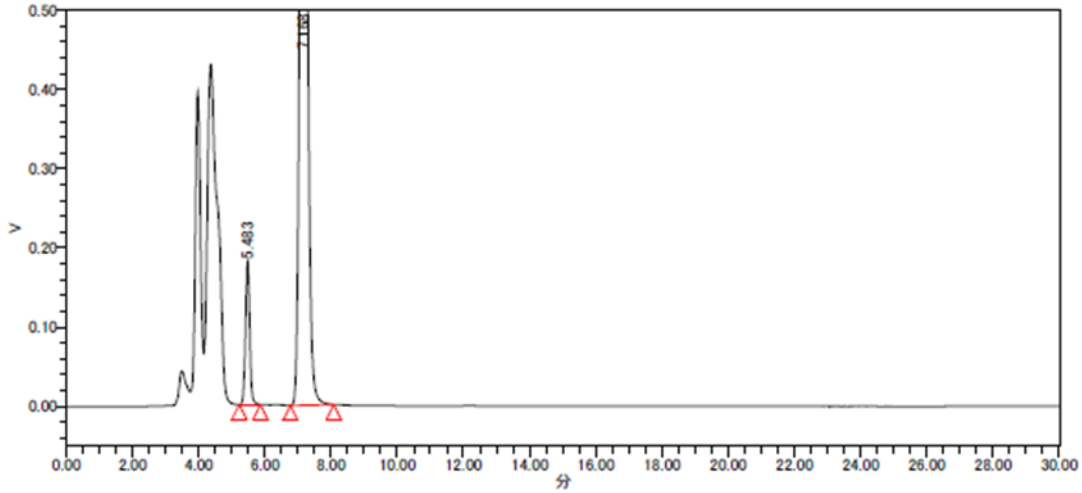


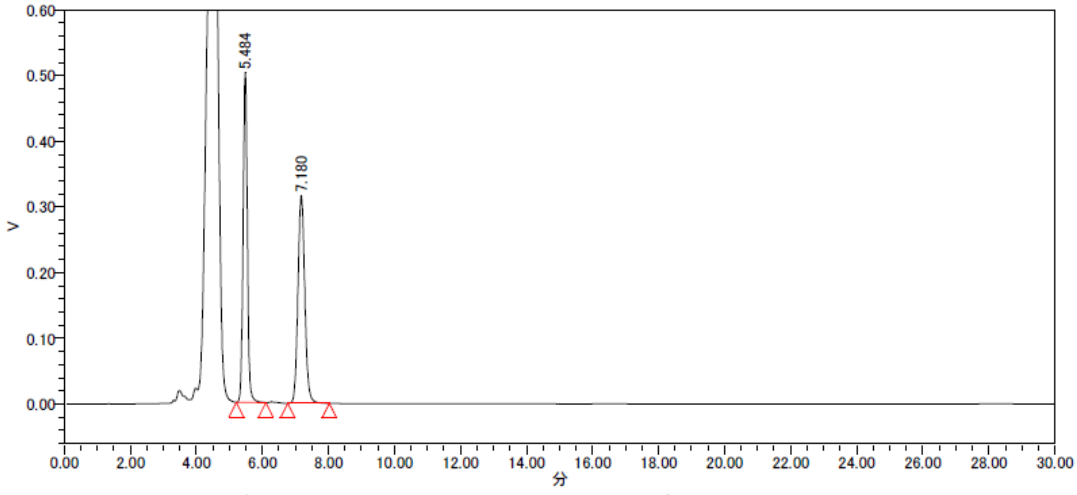
Figure S25. **^{13}C NMR chart of benzyl sulfoxide 14.**



	名前	保持時間	面積	%面積	分離度
1		5.483	1615524	7.742	
2		7.168	19252348	92.258	5.583327e+000

Name Retention Time Area Area% Resolution

Figure S26. **Chiral HPLC chart of the reaction mixture after 18.5 h reaction. English translation is provided in red.**



	名前	保持時間	面積	%面積	分離度
1		5.484	4528960	49.822	
2		7.180	4561314	50.178	5.607612e+000

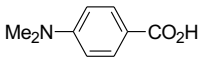
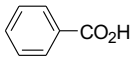
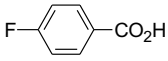
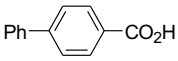
Name Retention Time Area Area% Resolution

Figure S27. **Chiral HPLC chart of benzyl sulfoxide 14 (racemic mixture). English translation is provided in red.**

Representative Procedure for Optimization Studies (*Table S1*)

In a Schenck tube, chiral Schiff base **3a** (79 mg, 273 μmol) and iron(III) acetylacetonate (32 mg, 91 μmol) were dissolved in ethyl acetate (0.6 mL) at 25 °C, and the mixture was stirred for 30 min. 4-dimethylaminobenzoic acid (7.5 mg, 45.0 μmol) and ethyl acetate (0.3 mL) were added and the resulting suspension was stirred for 30 min at 25 °C; next, sulfide **1** (0.30 g, 911 μmol) and ethyl acetate (0.9 mL) were added, stirred for 30 min at 25 °C. Aqueous hydrogen peroxide (30%, 186 μL, 1.82 mmol) was slowly added over 2 min, and the reaction mixture was stirred for an additional 0.5 h at 25 °C. The reaction mixture was analyzed by HPLC, to reveal that the sulfoxide **2** was formed in 67% yield and 69% ee, with 7% of the sulfone, and 26% of the sulfide **1**.

Table S1. Effects of addition of a benzoic acid derivative.

entry	additive	time (h)	**2** (%)	ee (%)	sulfone (%)
1		0.5	67	69	7
2		0.5	57	44	5
3		0.5	58	42	5
4		0.5	57	44	6

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