Synthesis of interesting β-nitrohydrazides through thiourea organocatalysed aza-Michael addition

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ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

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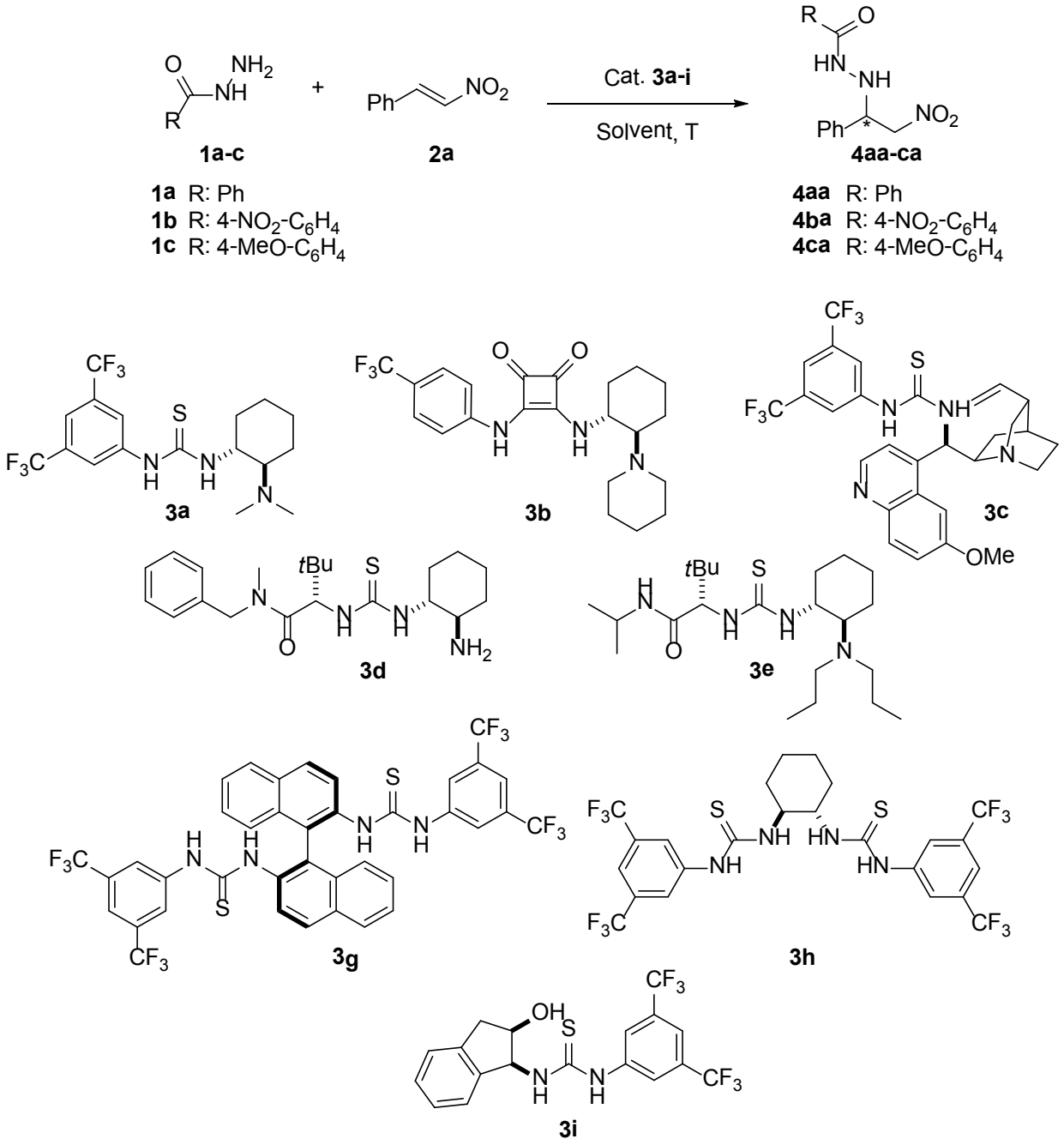
General experimental methods. Purification of reaction products was carried out by flash chromatography using silical-gel (0.063-0.200 mm). Analytical thin layer chromatography was performed on 0.25 mm silical gel 60-F plates. ESI ionization method and mass analyser type MicroTof-Q were used for the HRMS measurements. ^{1}H-NMR spectra were recorded at 300 MHz and 400 MHz; ^{13}C-NMR spectra were recorded at 75 MHz and 100 MHz; CD_3CN, $CDCl_3$, CD_2Cl_2, THF-d_8 and CD_3COCD_3 as the solvent. Chemical shifts were reported in the δ scale relative to residual CH_3CN (1.94 ppm), $CHCl_3$ (7.26 ppm), CH_2Cl_2 (5.32 ppm), THF (1.73 ppm) and CH_3COCH_3 (2.05 ppm) for ^{1}H-NMR and to the central line of $CDCl_3$ (77 ppm), CD_2Cl_2 (53.8 ppm), THF-d_8 (25.3 ppm) and CD_3COCD_3 (30.8 ppm) for ^{13}C-NMR.

Materials. All commercially available solvents and reagents were used as received. Nitroalkenes **2k**[1] and **2l**[1] have been synthesised following the described method in the literature. The NMR spectra (^{1}H-NMR and APT) for nitroalkenes **2k**[1] and **2l**[2] are consistent with values previously reported in the literature.

[1] S. E. Denmark and L. R. Marcin, *J. Org. Chem.*, 1993, **58**, 3850.
[2] E. C. Taylor and B. Liu,. *J. Org. Chem.*, 2003, **68**, 9938.

Screening of Catalysts and Study of the Reaction Conditions

Scheme S1. Organocatalytic enantioselective aza-Michael addition reaction of hydrazine **1** to nitrostyrene **2a**.



In an initial screening of solvents at room temperature (Table S1, entries 1-7), CH_3CN (entry 3) and EtOAc (entry 7) were identified as the solvents of choice for further variations, since they led to the highest values of enantiomeric ratio. Although we also continued with EtOAc in the ensuing screenings, we finally decided to proceed with CH_3CN because slightly better results were rendered for similar conditions. It was found that lowering the temperature to 5 or –27 °C improved enantiomeric ratios were achieved, although longer reaction

times were required (entries 8 and 11). Decreasing the catalyst loading until 10 or 5 mol% (entries 13 and 14), and increasing the concentration of the reaction mixture had a positive effect on the enantioselectivity without altering the final good yield. Unfortunately, experiments made lowering further the temperature to –35 °C afforded poorer enantioselectivities and yields (entries 15 and 16). Finally, the combination of 10 mol% of catalyst **3a** cooling down the reaction mixture to –27 °C in 0.25 mL of solvent, led to a slight increase in the asymmetric induction as well as in the yield, providing the best reaction conditions (entry 13).

Table S1. aza-Michael addition reaction of hydrazine **1** to nitrostyrene **2a** catalysed by thiourea **3a**.[a]

Entry	Solvent (mL)	**3a** (mol%)	T (ºC)	Time (h)	Yield (%)[b]	e.r.[c]
1	Toluene (0.5)	20	r.t.	72	12	56:44
2	Xylene (0.5)	20	r.t.	48	24	55:45
3	CH_3CN (0.5)	20	r.t.	48	>95	75:25
4	$CHCl_3$ (0.5)	20	r.t.	72	33	52:48
5	CH_2Cl_2 (0.5)	20	r.t.	48	70	55:45
6	THF (0.5)	20	r.t.	78	91	55:45
7	EtOAc (0.5)	20	r.t.	20	79	65:35
8	CH_3CN (0.5)	20	5	84	87	77:23
9	CH_3CN (0.5)	10	5	40	>95	67:33
10	CH_3CN (0.25)	10	5	42	>95	80:20
11	CH_3CN (0.5)	20	–27	93	91	82:18
12	CH_3CN (0.5)	10	–27	72	88	82:18
13	CH_3CN (0.25)	10	–27	84	>95	88:12
14	CH_3CN (0.25)	5	–27	72	79	86:14
15	CH_3CN (0.5)	20	–35	48	12	70:30
16	CH_3CN (0.25)	10	–35	120	27	75:25

[a] Experimental conditions: To a solution of thiourea **3a** and nitrostyrene **2a** (0.1 mmol) in solvent, hydrazide **1b** (0.1 mmol) was added at the indicated temperature. After a reasonable reaction time, product **4ba** was isolated by flash chromatography (Hex:EtOAc, 7:3). [b] Isolated yield. [c] Determined by chiral HPLC analysis (Chiralpak IC, 80:20 Hex:EtOAc, 1 mL/min).

We have also explored different conditions with thioureas **3b-e** (Table S2) and **3g-i** (Table S3) before to discard these catalysts as suitable ones for developing this reaction.

Table S2. aza-Michael addition reaction of hydrazine **1** to nitrostyrene **2a** catalysed by thiourea **3a-e**.[a]

Entry	Cat. (mol%)	Hydraz.	Solvent (mL)	T (ºC)	Time (h)	Yield (%)[b]	e.r.[c]
1[d]	**3b** (20)	**1b**	CH_3CN (0.25)	r.t.	18	60	52:48
2[d]	**3c** (20)	**1b**	CH_3CN (0.25)	r.t.	18	60	65:35
3	**3d** (20)	**1b**	CH_3CN (0.5)	r.t.	48	76	52:48
4	**3e** (20)	**1b**	CH_3CN (0.5)	r.t.	48	74	53:47
5	**3a** (20)	**1a**	CH_3CN (0.5)	r.t.	20	63	52:48
6	**3a** (20)	**1c**	CH_3CN (0.5)	r.t.	20	86	54:46
7	**3a** (20)	**1b**	EtOAc (0.5)	5	91	67	69:31
8	**3a** (30)	**1b**	EtOAc (0.5)	5	85	76	74:26
9	**3a** (20)	**1b**	EtOAc (0.5)	–27	113	33	81:19
10	**3a** (30)	**1b**	EtOAc (0.5)	–27	109	52	80:20
11	**3a** (30)	**1b**	CH_3CN (0.5)	5	84	79	64:36
12	**3a** (30)	**1b**	CH_3CN (0.5)	–27	92	97	82:18
13	**3a** (2.5)	**1b**	CH_3CN (0.25)	–27	72	70	82:18
14	**3a** (10)	**1b**	CH_3CN (0.25)/EtOAc (0.25)	–27	72	61	81:19
15	**3a** (20)	**1b**	CH_3CN (0.25)/EtOAc (0.25)	–27	73	80	82:18
16	**3a** (10)	**1b**	CH_3CN (0.225)/EtOAc (0.025)	–27	76	<95	86:14
17	**3a** (20)	**1b**	CH_3CN (0.450)/EtOAc (0.050)	–27	76	48	86:14

[a] Experimental conditions: To a solution of thiourea **3a-e** and nitrostyrene **2a** (0.1 mmol) in the corresponding solvent, hydrazide **1a-c** (0.1 mmol) was added at the corresponding temperature. After a reasonable reaction time, final product was isolated by flash chromatography (Hex:EtOAc, 7:3). [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Reaction performed using 0.05 mmol of nitroalkenes.

Table S3. aza-Michael addition reaction of hydrazine **1** to nitrostyrene **2a** catalysed by thiourea **3g-i**.[a]

Entry	Cat.	Hydraz.	Solvent	Time (h)	Yield (%)[b]	e.r.[c]
1	**3g**	**1a**	Toluene	24	62	56:44
2	**3g**	**1a**	$CHCl_3$	24	68	56:44
3	**3g**	**1a**	THF	24	47	52:48
4	**3g**	**1a**	CH_3CN	48	46	56:44
5	**3g**	**1a**	Xylene	48	49	57:43
6	**3g**	**1b**	CH_3CN	40	15	62:38
7	**3g**	**1b**	Toluene	72	22	52:48
8	**3g**	**1b**	$CHCl_3$	72	36	56:44
9	**3g**	**1b**	THF	72	42	56:44
10	**3g**	**1b**	CH_3CN	72	45	61:39
11	**3g**	**1b**	Xylene	72	32	56:44
12	**3g**	**1c**	Toluene	24	63	57:43
13	**3g**	**1c**	$CHCl_3$	24	66	56:44
14	**3g**	**1c**	THF	72	64	52:48
15	**3g**	**1c**	CH_3CN	72	63	55:45
16	**3g**	**1c**	Xylene	72	42	58:42
17	**3h**	**1b**	CH_3CN	40	39	53:47
18	**3i**	**1b**	CH_3CN	42	27	57:43

[a] Experimental conditions: To a solution of thiourea **3g-i** (20 mol%) and nitrostyrene **2a** (0.1 mmol) in the corresponding solvent (0.5 mL), hydrazide **1a-c** (0.1 mmol) was added at room temperature. After a reasonable reaction time, final products were isolated by flash chromatography (Hex:EtOAc, 7:3). [b] Isolated yield. [c] Determined by chiral HPLC analysis.

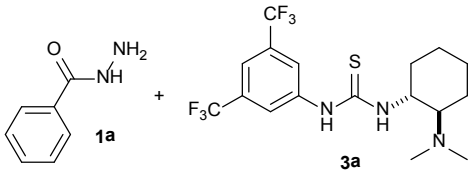
The background reaction at room temperature was found to be very high for the three hydrazides (Table S4, entries 1,2 and 4). However, at the temperature for best reaction conditions, the background is clearly minor (entry 5). Moreover, since the catalysed reaction is faster than the background one (compare entry 6 with 5), no competition between both routes should be expected at –27 ºC.

Table S4. Background reaction for the aza-Michael addition reaction of hydrazines **1** to nitrostyrene **2a**.[a]

Entry	Hydraz.	Solvent (mL)	T (ºC)	Time (days)	Yield (%)[b]	er (%)[c]
1	**1a**	CH_2Cl_2 (0.5)	r.t.	8	94	_
2	**1b**	CH_2Cl_2 (0.5)	r.t.	8	68	_
3[d]	**1b**	CH_2Cl_2 (0.5)	r.t.	48 h	70	55:45
4	**1c**	CH_2Cl_2 (0.5)	r.t.	8	91	_
5[e]	**1b**	CH_3CN (0.25)	–27	7	18	_
6[e,f]	**1b**	CH_3CN (0.25)	–27	84 h	>95	88:12

[a] Experimental conditions: To a solution of nitrostyrene **2a** (0.1 mmol) in the corresponding solvent, hydrazide **1a-c** (0.15 mmol) was added at the indicated temperature. After a reasonable reaction time, final products were isolated by flash chromatography (Hex:EtOAc, 7:3). Reactions performed in absence of catalyst. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Reaction performed in the presence of 20 mol% of catalyst **3a**. [e] 1 equiv. of hydrazide. [f] Reaction performed in the presence of 10 mol% of catalyst **3a**.

^{1}H-RMN EXPERIMENTS



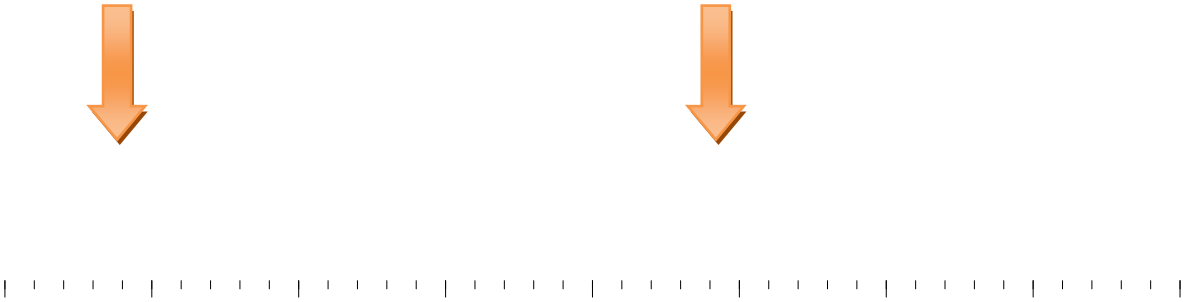
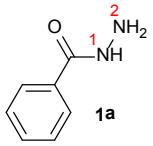


Figure S1. ^{1}H-NMR experiment performed in CD_3CN with thiourea **3a** and hydrazide **1a** (400 MHz).



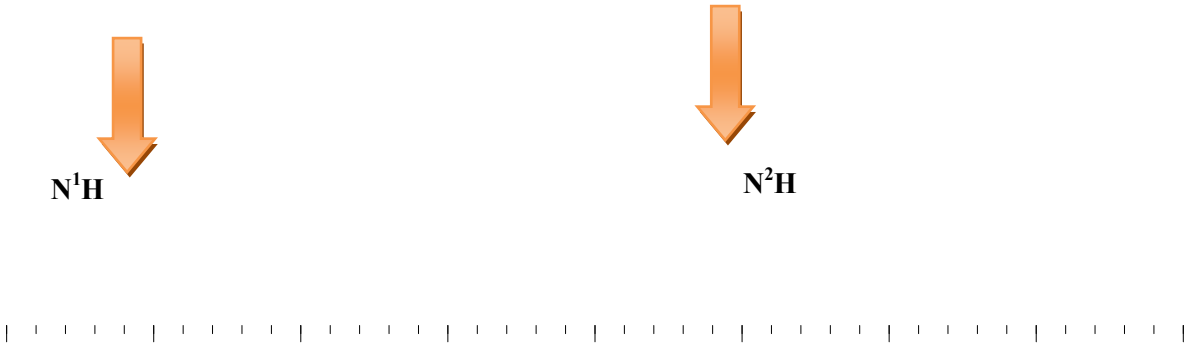
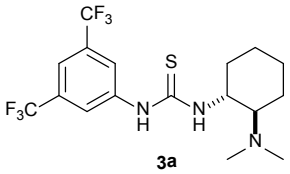


Figure S2. ^{1}H-NMR experiment performed in CD_3CN with hydrazide **1a** (400 MHz).

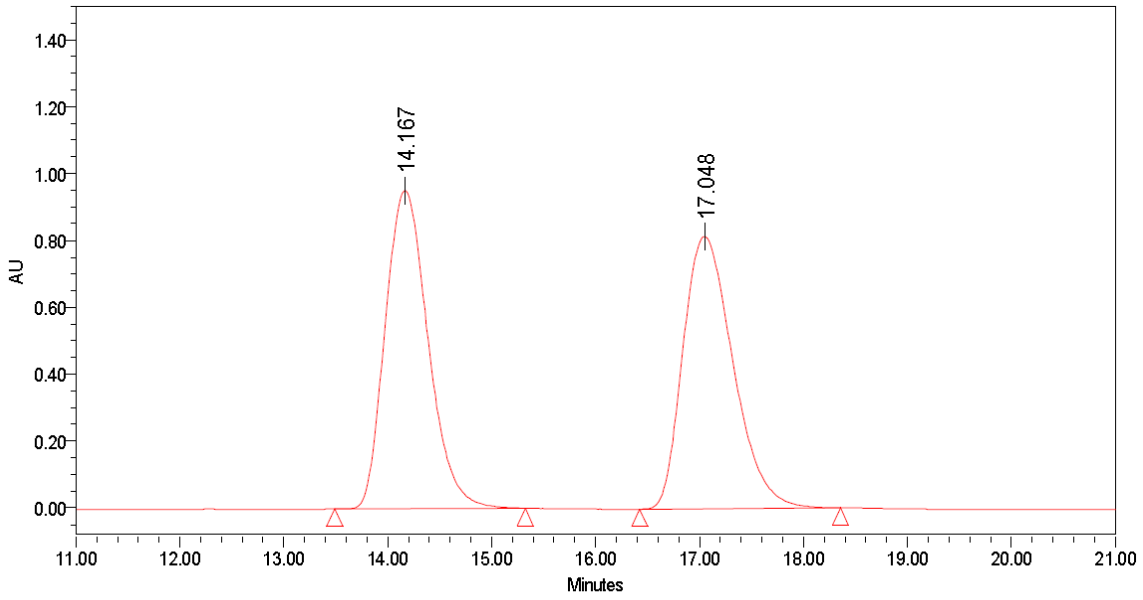


3a

Figure S3. ^{1}H-NMR experiment performed in CD_3CN with thiourea **3a** (400 MHz).

In order, to support if a deprotonation occurs between the hydrazide **1b** and the catalyst **3a**, we performed the same ^{1}H-NMR experiments (Figures S1-3) for the less acidic hydrazide **1a** (compared with hydrazide **1b**). First, catalyst **3a** (0.01 mmol), and hydrazide **1a** (0.01 mmol) in CD_3CN (0.5 mL) were analysed separately in two NMR tubes at room temperature (Figures S2 and S3). Subsequently, a mixture of both, catalyst **3a** and hydrazide **1a** in the same concentration in CD_3CN, was analysed by ^{1}H-NMR (Figure S1). Interestingly, the signal belonging to the $N^{1}H$ disappears becoming a very broad singlet in the base line of the spectrum and $N^{2}H$ of the hydrazide does not disappear but it becomes a broader singlet. This fact will support a possible interaction between the NH's of the hydrazide and the catalyst more than a deprotonation, since in this case the deprotonation using hydrazide **1a** is clearly less favourable but the signals do not remain unaltered.

HPLC CROMATOGRAMS OF COMPOUNDS 4ba-bl



Processed Channel: PDA 258.8 nm

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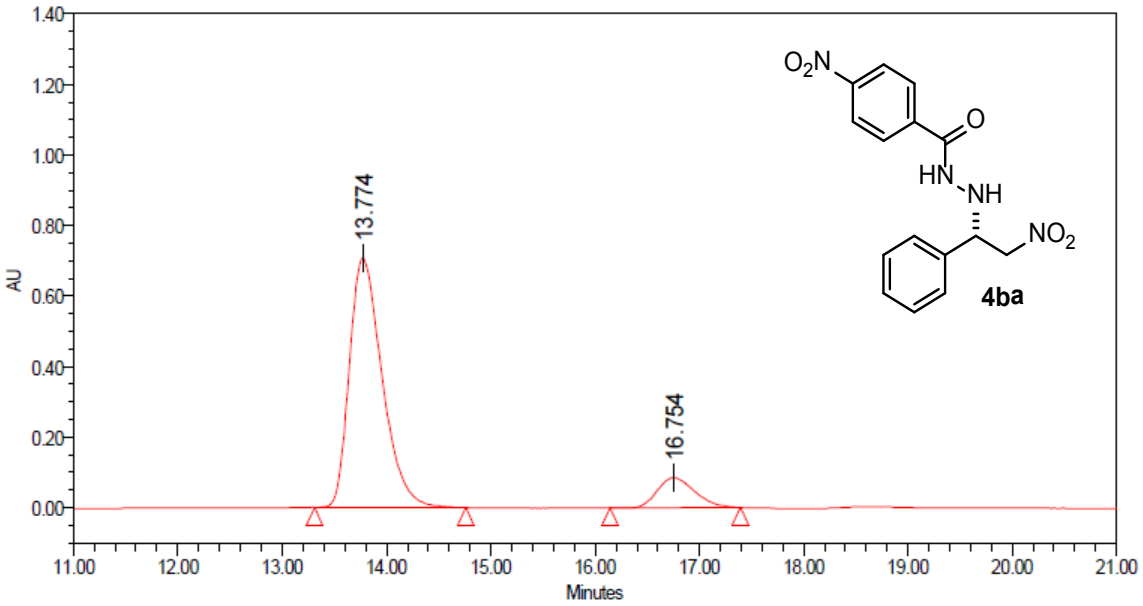
1	PDA 258.8 nm	14.167	27281313	50.03	952005
2	PDA 258.8 nm	17.048	27247520	49.97	814501

Figure S4. Racemic mixture of **4ba**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



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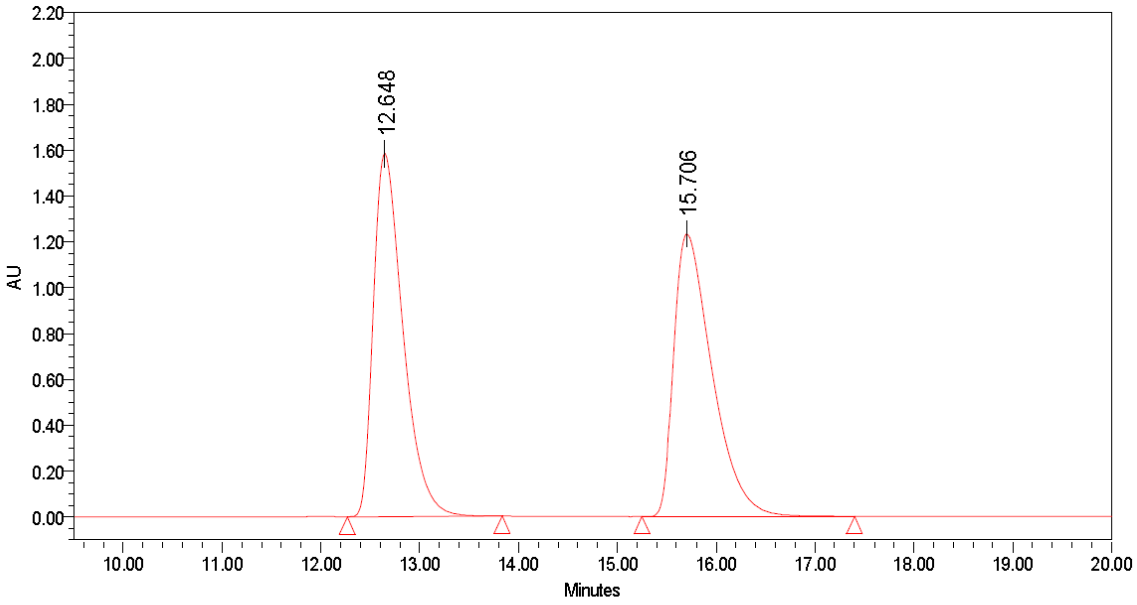
1	PDA 258.8 nm	13.774	15429883	87.78	706798
2	PDA 258.8 nm	16.754	2147592	12.22	85677

Figure S5. Chiral sample of compound (*S*)-**4ba**.



Processed Channel: PDA 260.0 nm

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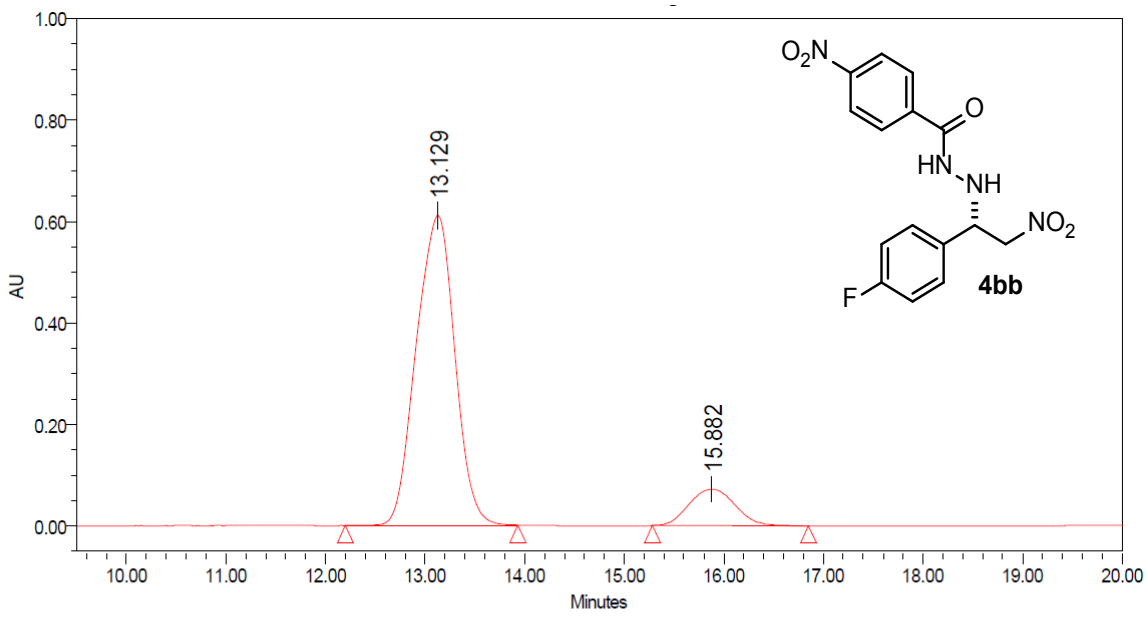
1	PDA 260.0 nm	12.648	33095830	49.94	1583528
2	PDA 260.0 nm	15.706	33181412	50.06	1232497

Figure S6. Racemic mixture of **4bb**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



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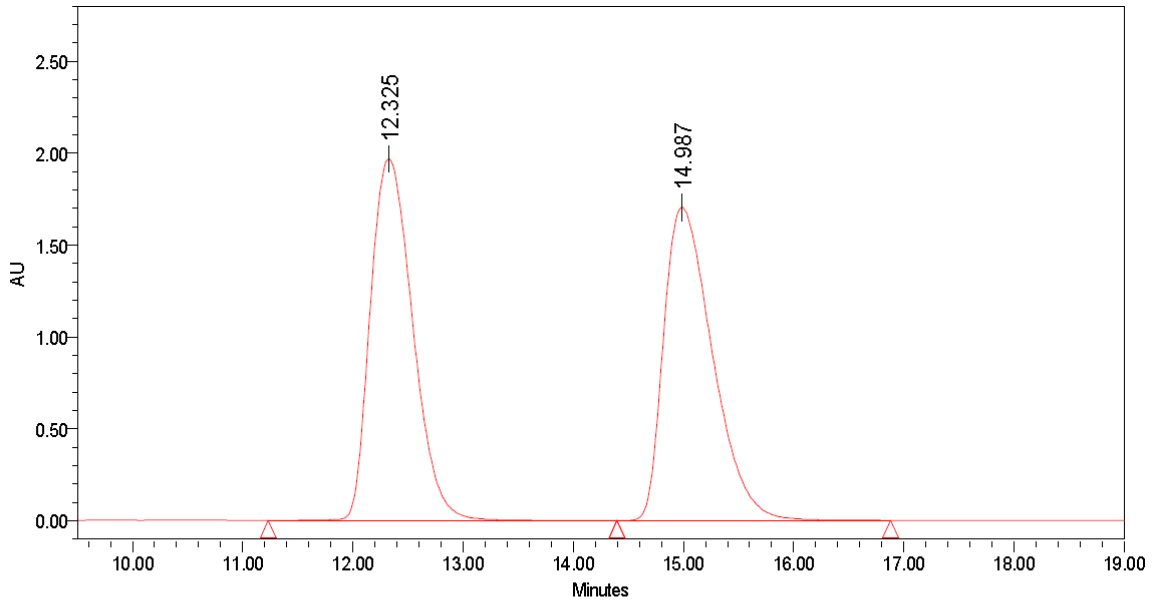
1	PDA 260.0 nm	13.129	16481791	87.85	610743
2	PDA 260.0 nm	15.882	2279291	12.15	71775

Figure S7. Chiral sample of compound (*S*)-**4bb**.



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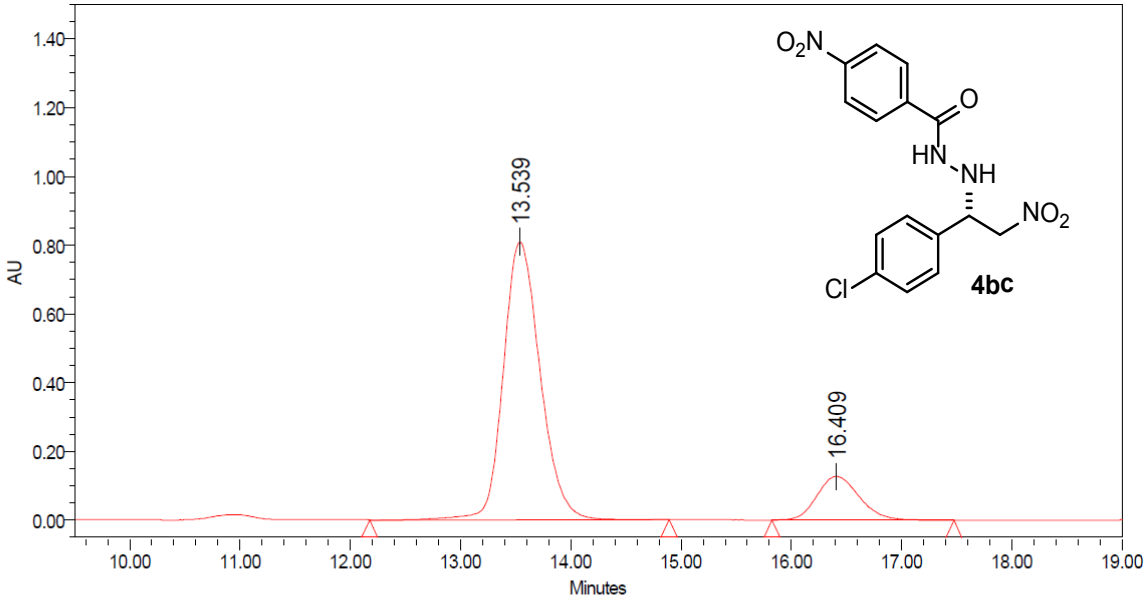
1	PDA 258.8 nm	12.325	52585626	50.08	1969868
2	PDA 258.8 nm	14.987	52409891	49.92	1705808

Figure S8. Racemic mixture of **4bc**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



Processed Channel: PDA 258.8 nm

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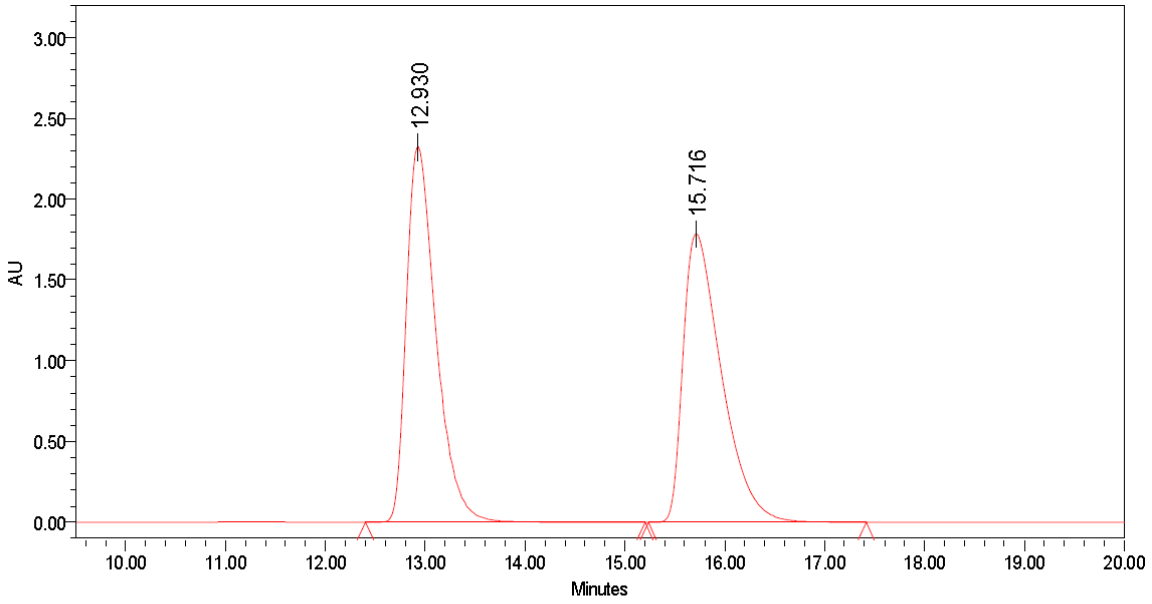
1	PDA 258.8 nm	13.539	18732559	84.86	808404
2	PDA 258.8 nm	16.409	3341180	15.14	126918

Figure S9. Chiral sample of compound (*S*)-**4bc**.



Processed Channel: PDA 258.8 nm

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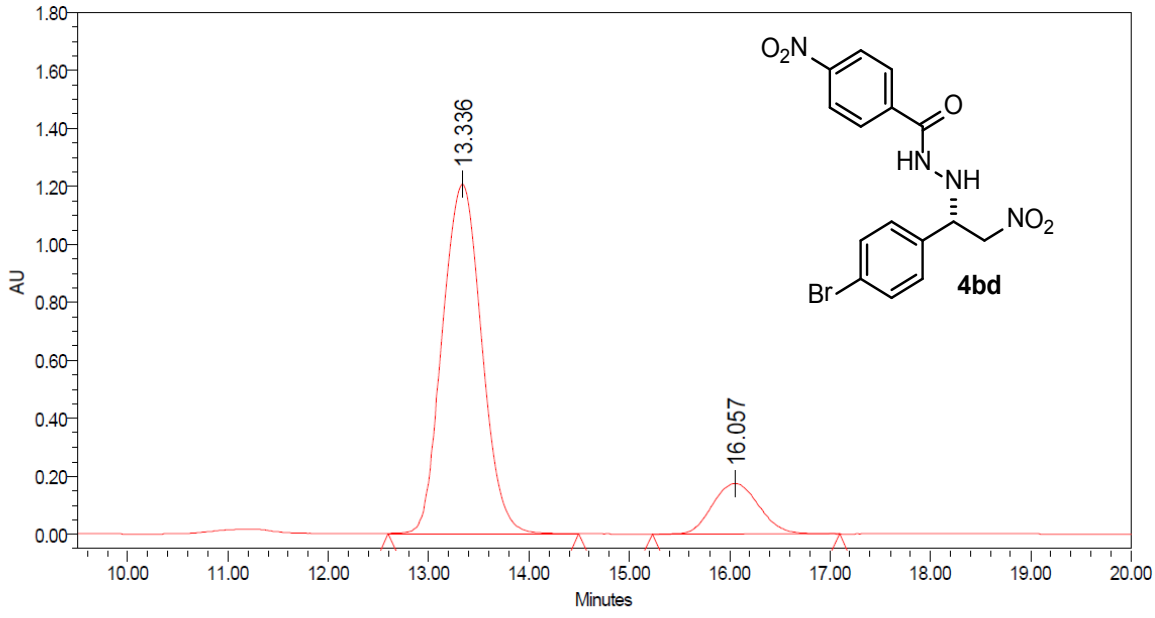
1	PDA 258.8 nm	12.930	47902806	50.03	2326800
2	PDA 258.8 nm	15.716	47853605	49.97	1787406

Figure S10. Racemic mixture of **4bd**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



Processed Channel: PDA 258.8 nm

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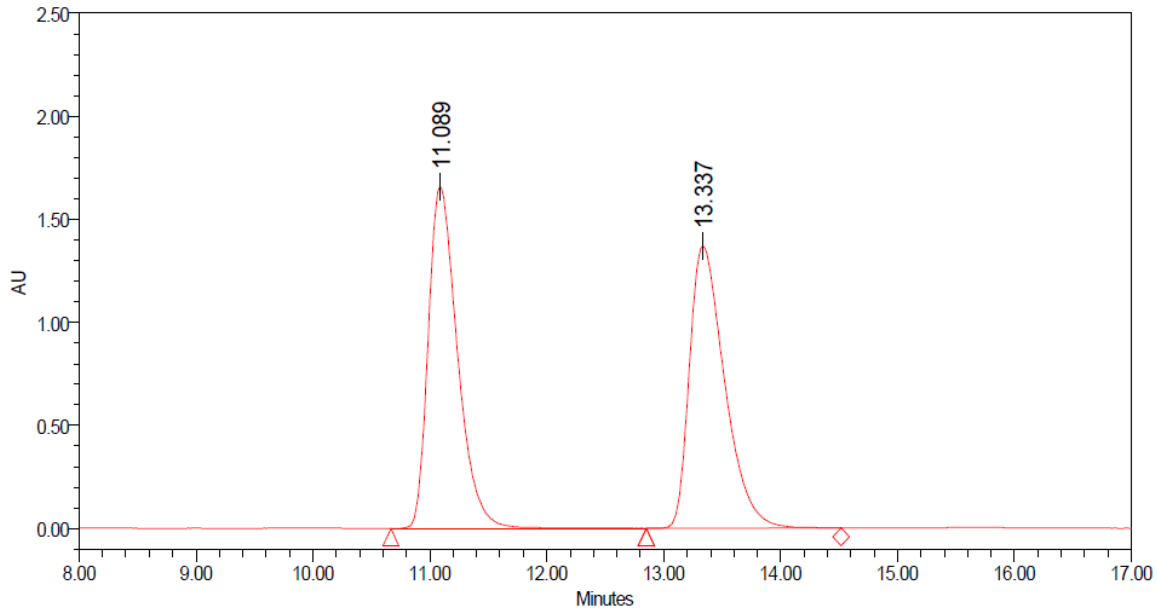
1	PDA 258.8 nm	13.336	32888243	85.52	1205292
2	PDA 258.8 nm	16.057	5566538	14.48	174056

Figure S11. Chiral sample of compound (*S*)-**4bd**.



Processed Channel: PDA 258.8 nm

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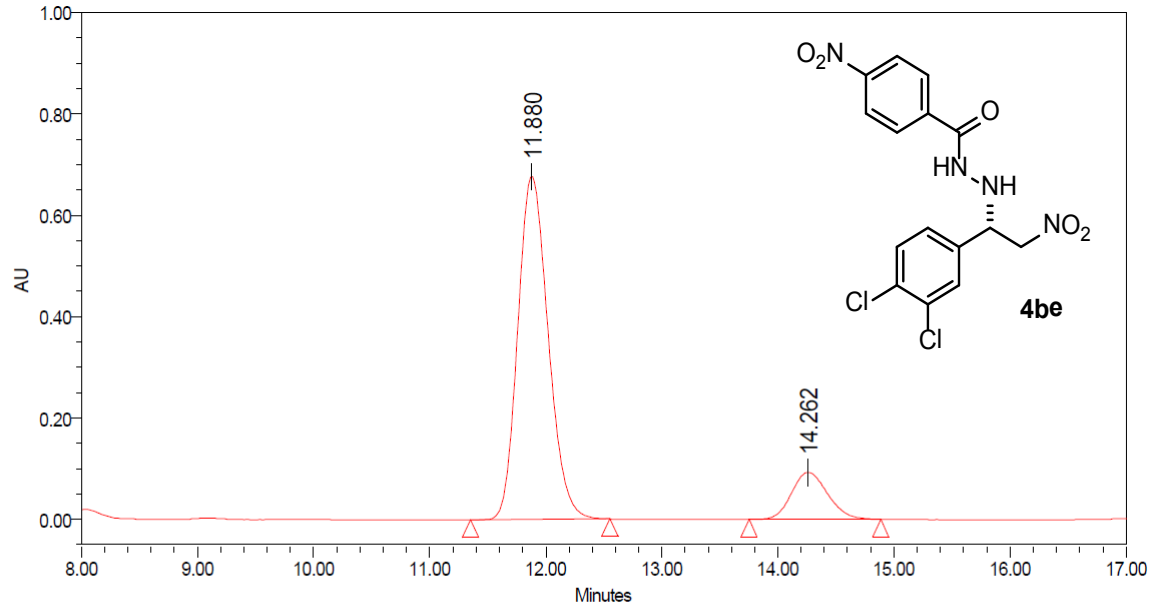
1	PDA 258.8 nm	11.089	28782672	50.08	1661031
2	PDA 258.8 nm	13.337	28690952	49.92	1371165

Figure S12. Racemic mixture of **4be**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



Processed Channel: PDA 258.8 nm

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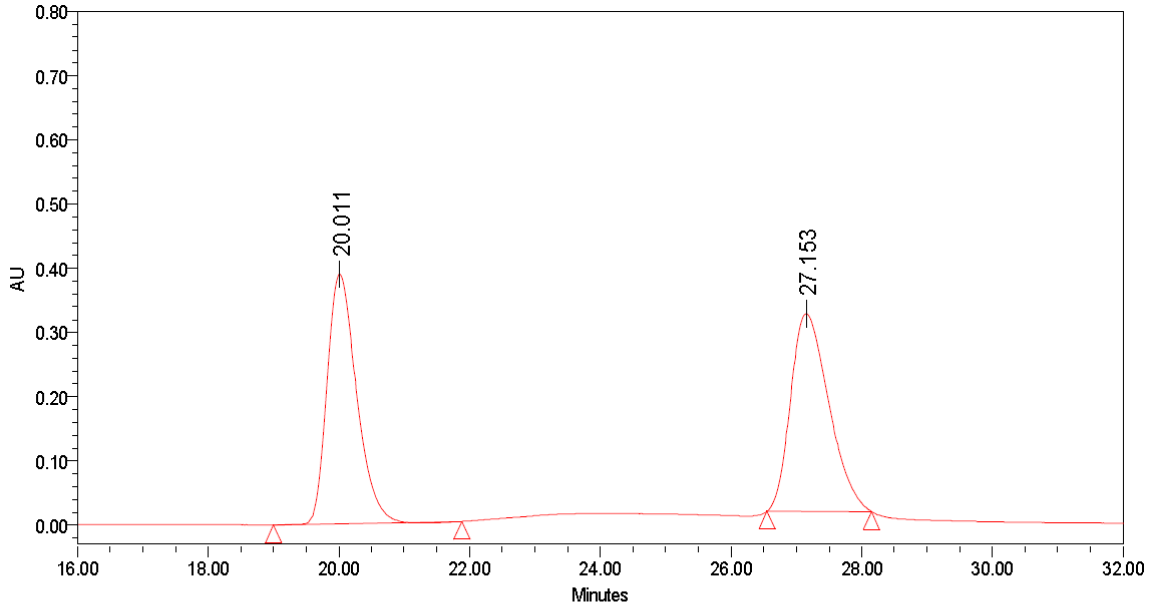
2	PDA 258.8 nm	14.262	1996160	14.02	92786

Figure S13. Chiral sample of compound (*S*)-**4be**.



Processed Channel: PDA 260.0 nm

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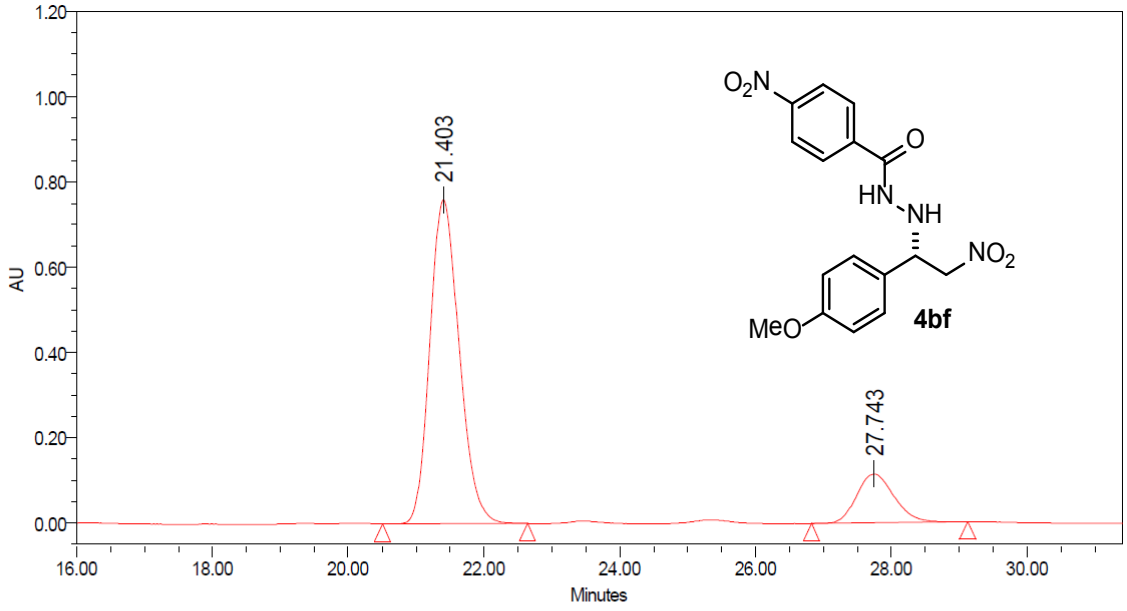
2	PDA 260.0 nm	27.153	12529288	50.70	308138

Figure S14. Racemic mixture of **4bf**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



Processed Channel: PDA 260.0 nm

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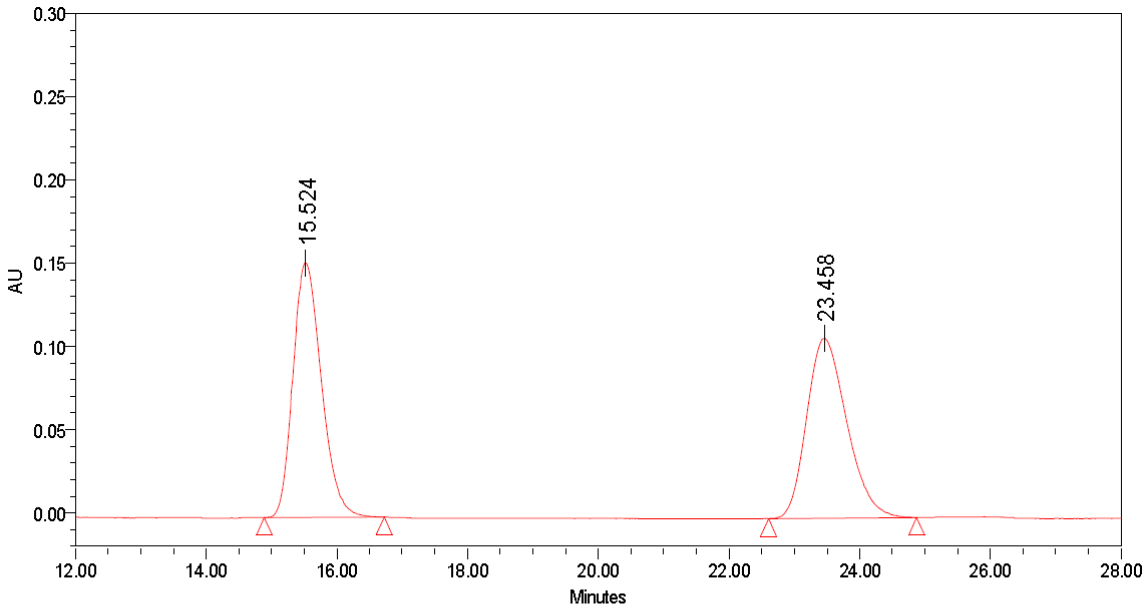
2	PDA 260.0 nm	27.743	4378976	16.11	114409

Figure S15. Chiral sample of compound (*S*)-**4bf**.



Processed Channel: PDA 262.4 nm

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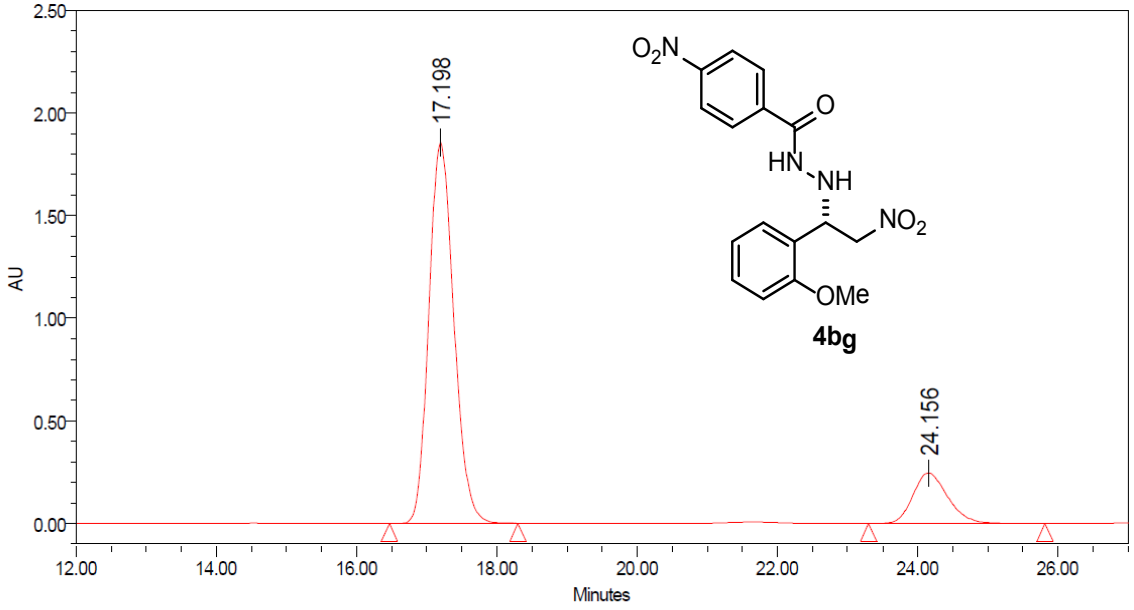
1	PDA 262.4 nm	15.524	4643265	50.20	153044
2	PDA 262.4 nm	23.458	4607086	49.80	108001

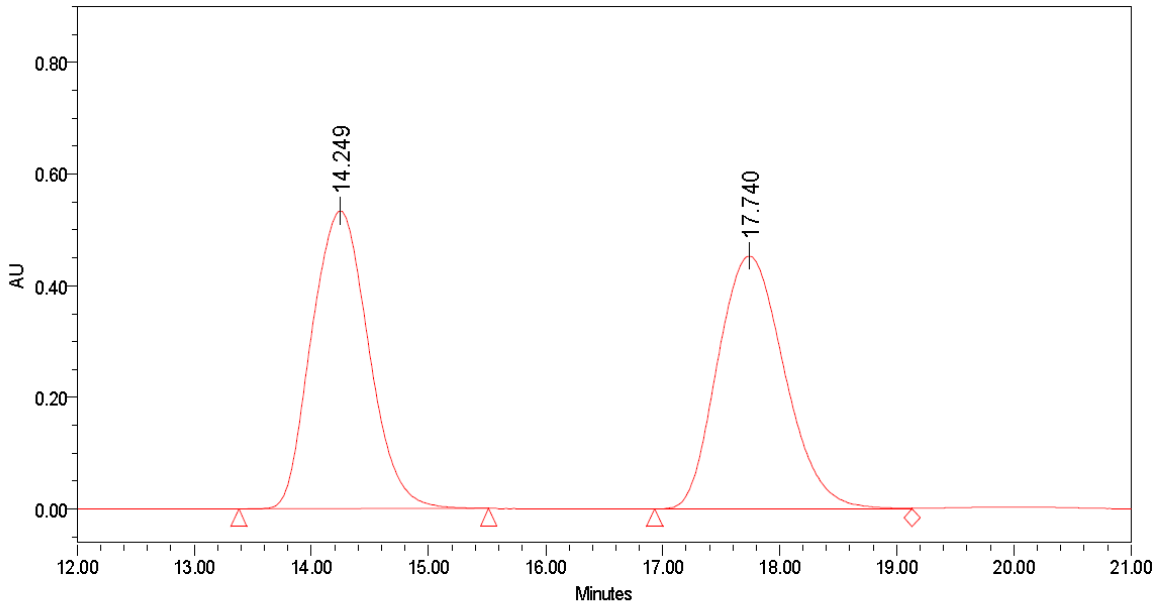
Figure S16. Racemic mixture of **4bg**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



Processed Channel: PDA 262.4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 262.4 nm	17.198	45955714	84.45	1855358
2	PDA 262.4 nm	24.156	8464751	15.55	246044

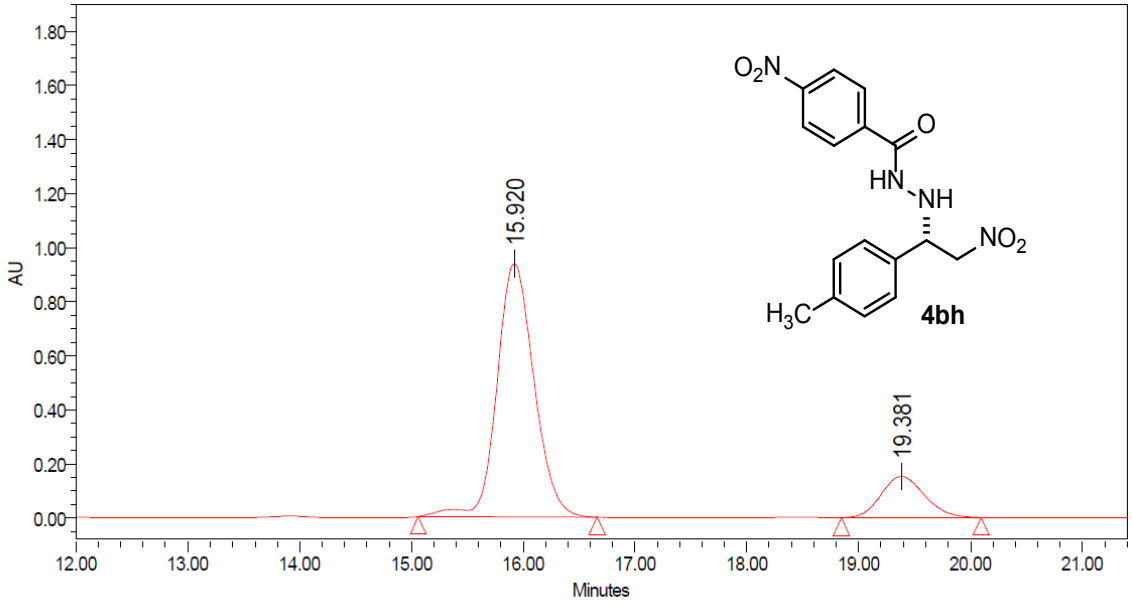
Figure S17. Chiral sample of compound (*S*)-**4bg**.



Processed Channel: PDA 260.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 260.0 nm	14.249	17979659	50.08	533388
2	PDA 260.0 nm	17.740	17924412	49.92	452351

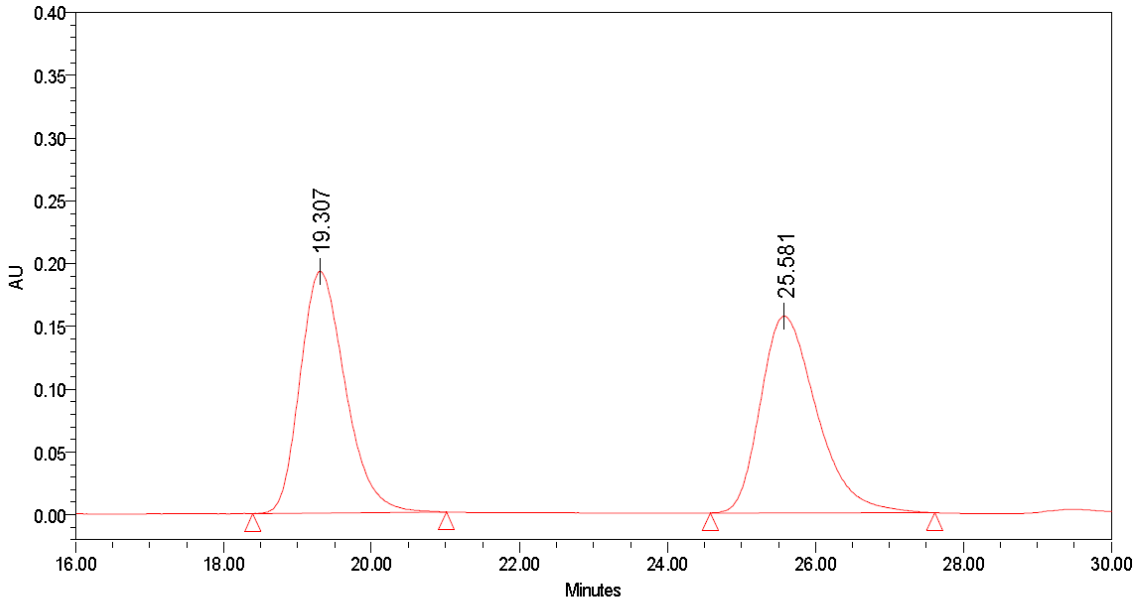
Figure S18. Racemic mixture of **4bh**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



Processed Channel: PDA 260.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 260.0 nm	15.920	21672667	84.16	938517
2	PDA 260.0 nm	19.381	4077907	15.84	152398

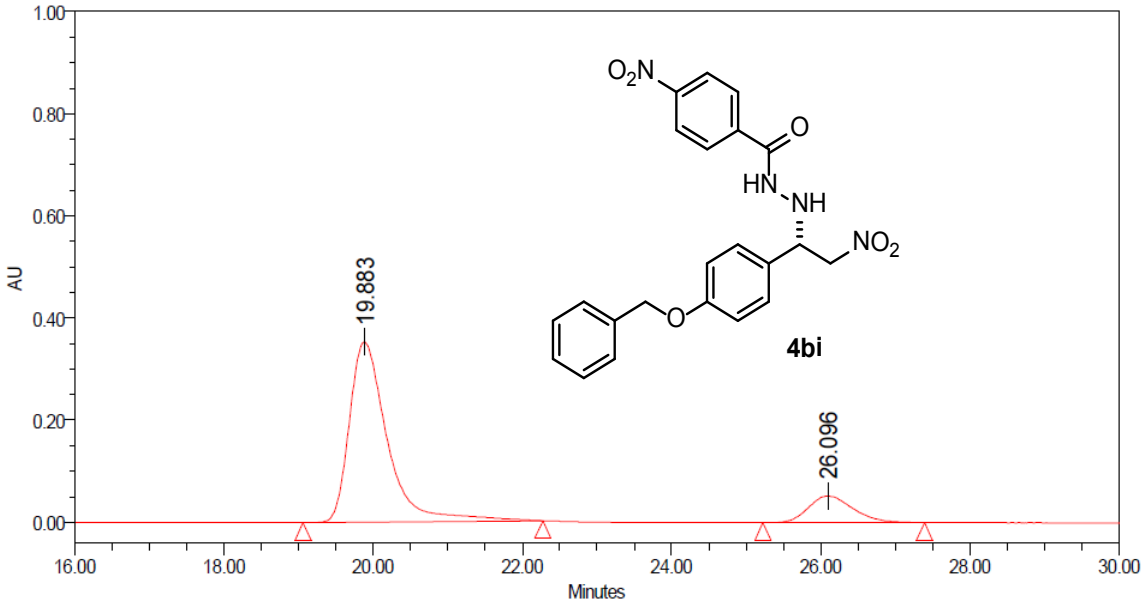
Figure S19. Chiral sample of compound (*S*)-**4bh**.



Processed Channel: PDA 260.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 260.0 nm	19.307	8157594	49.62	192515
2	PDA 260.0 nm	25.581	8282091	50.38	156721

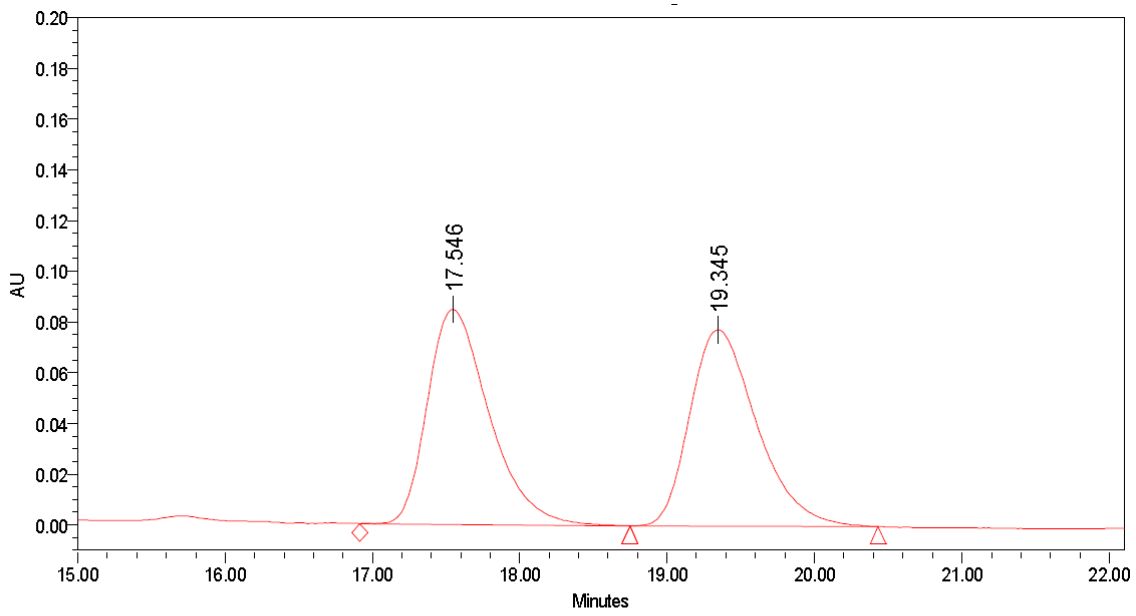
Figure S20. Racemic mixture of **4bi**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



Processed Channel: PDA 260.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 260.0 nm	19.883	12519017	85.15	353337
2	PDA 260.0 nm	26.096	2183052	14.85	52205

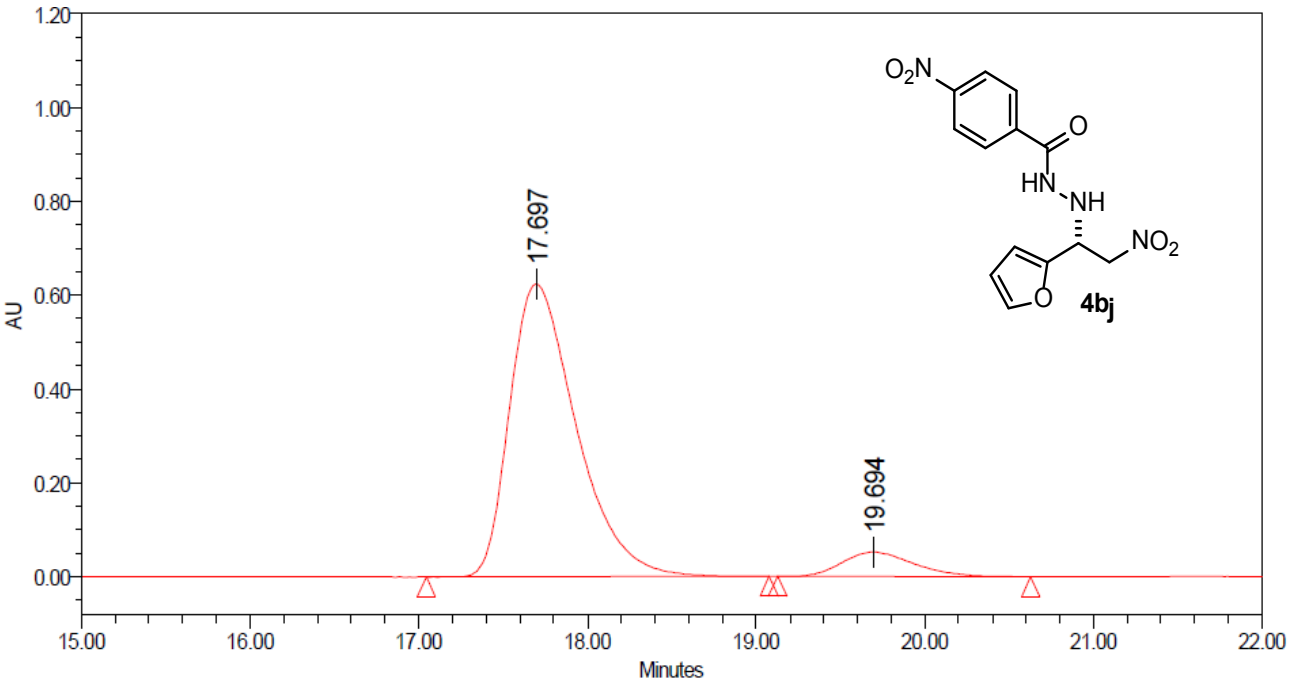
Figure S21. Chiral sample of compound (*S*)-**4bi**.



Processed Channel: PDA 258.8 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 258.8 nm	17.546	2471201	50.32	84916
2	PDA 258.8 nm	19.345	2439618	49.68	77441

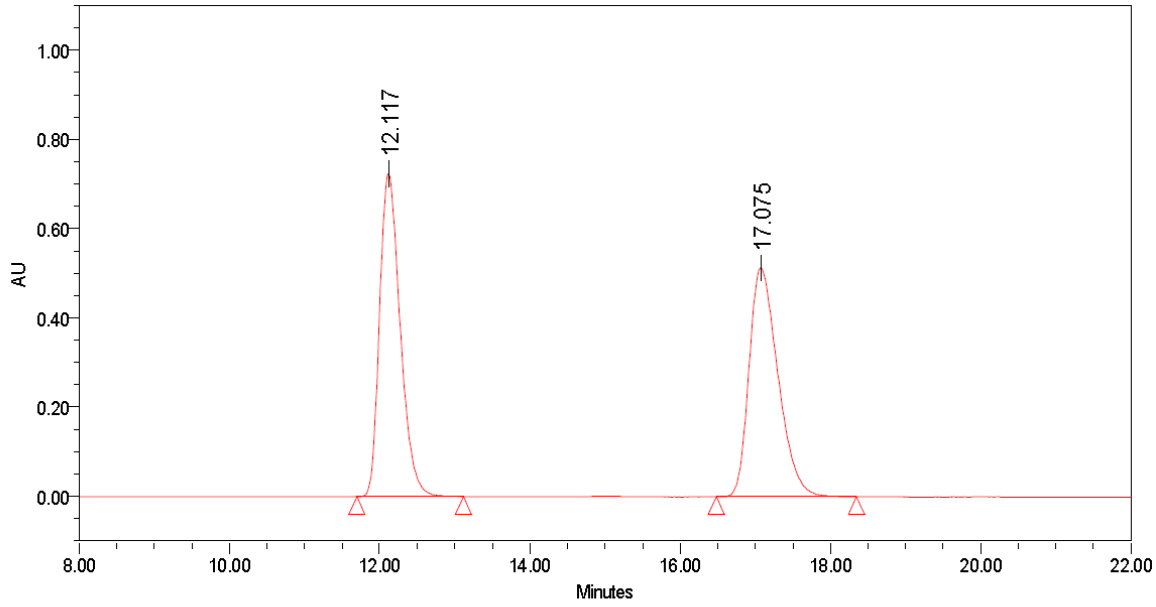
Figure S22. Racemic mixture of **4bj**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



Processed Channel: PDA 258.8 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 258.8 nm	17.697	17159347	91.70	625003
2	PDA 258.8 nm	19.694	1552558	8.30	52253

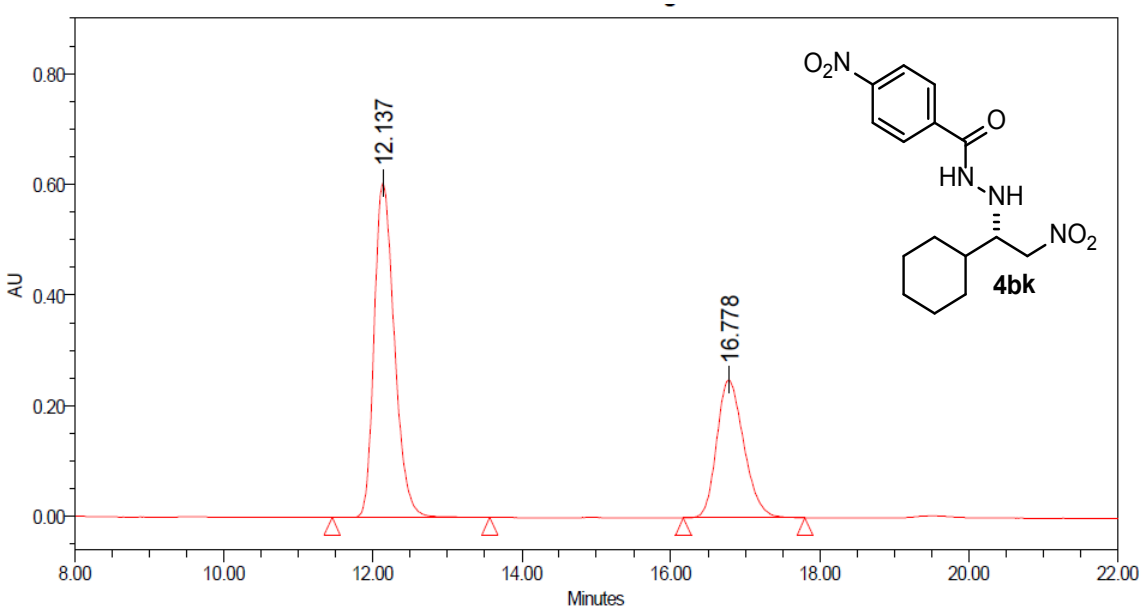
Figure S23. Chiral sample of compound (*S*)-**4bj**.



Processed Channel: PDA 258.8 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 258.8 nm	12.117	13751895	50.05	724094
2	PDA 258.8 nm	17.075	13726466	49.95	512952

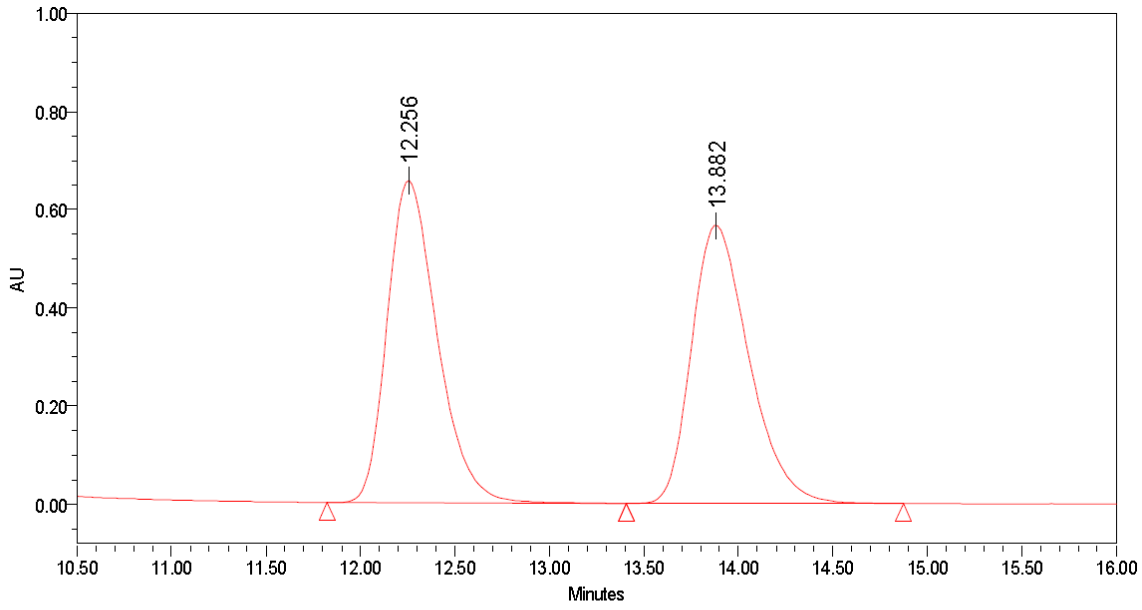
Figure S24. Racemic mixture of **4bk**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



Processed Channel: PDA 258.8 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 258.8 nm	12.137	11386921	64.37	604942
2	PDA 258.8 nm	16.778	6302012	35.63	249410

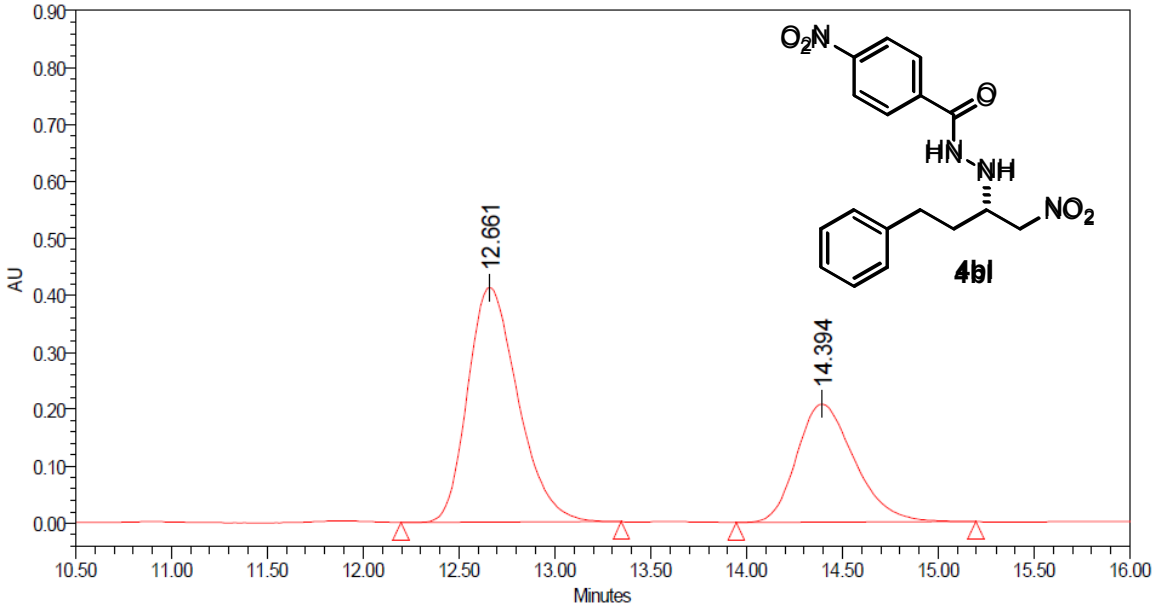
Figure S25. Chiral sample of compound (*S*)-**4bk**.



Processed Channel: PDA 258.8 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 258.8 nm	12.256	12056055	50.16	656886
2	PDA 258.8 nm	13.882	11977637	49.84	566832

Figure S26. Racemic mixture of **4bl**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).



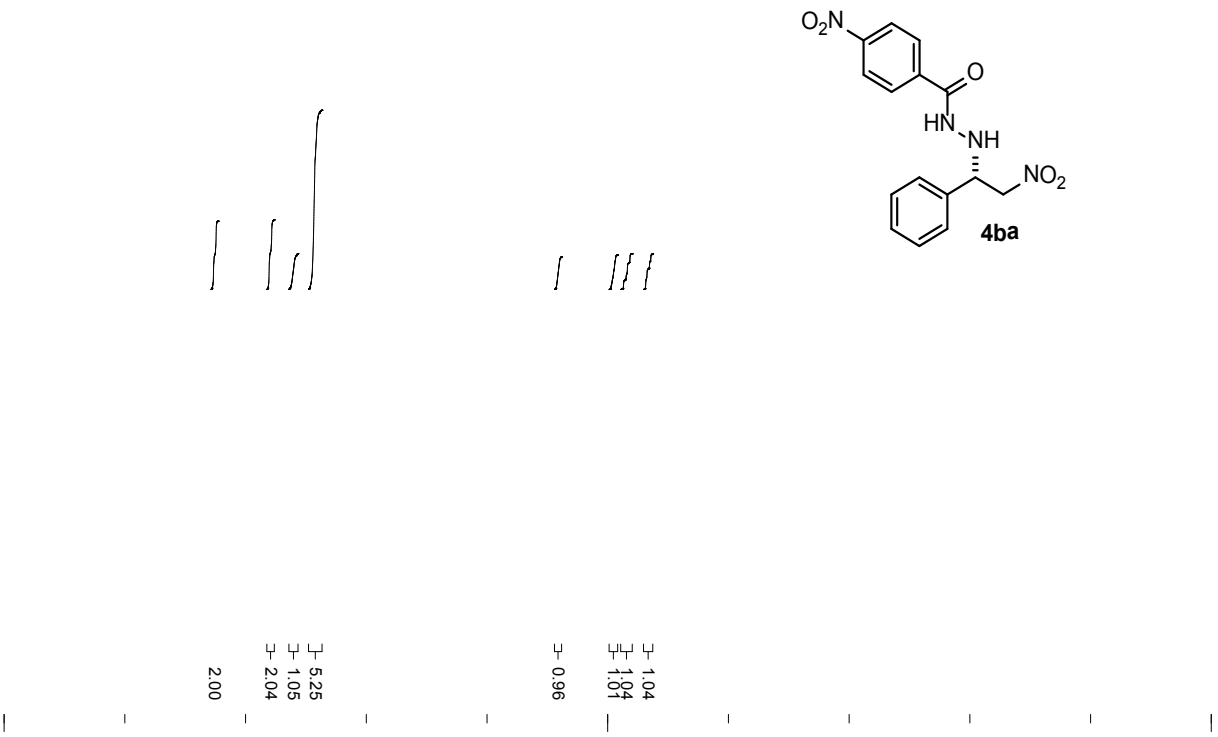
Processed Channel: PDA 258.8 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 258.8 nm	12.661	7517318	63.36	412648
2	PDA 258.8 nm	14.394	4347250	36.64	207456

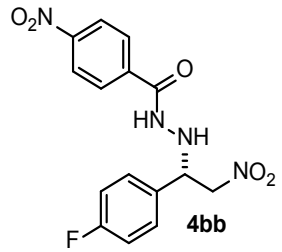
Figure S27. Chiral sample of compound (*S*)-**4bl**.

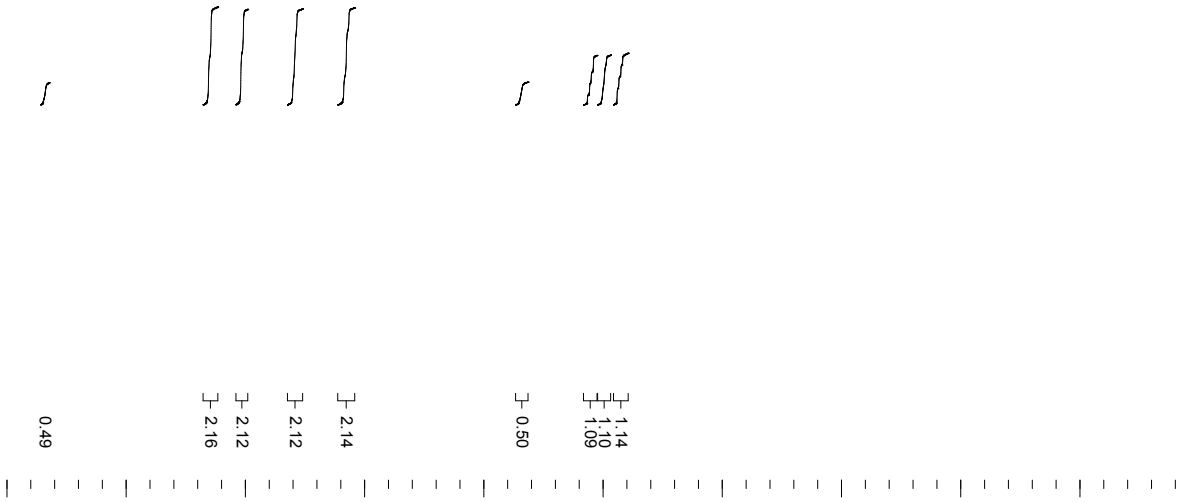
NMR SPECTRA OF COMPOUNDS 4ba-bl

(*S*)-4-Nitro-*N*′-(2-nitro-1-phenylethyl)benzohydrazide (4ba)

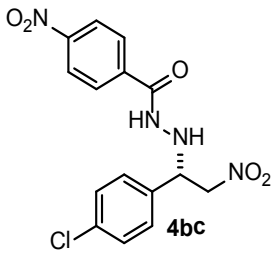


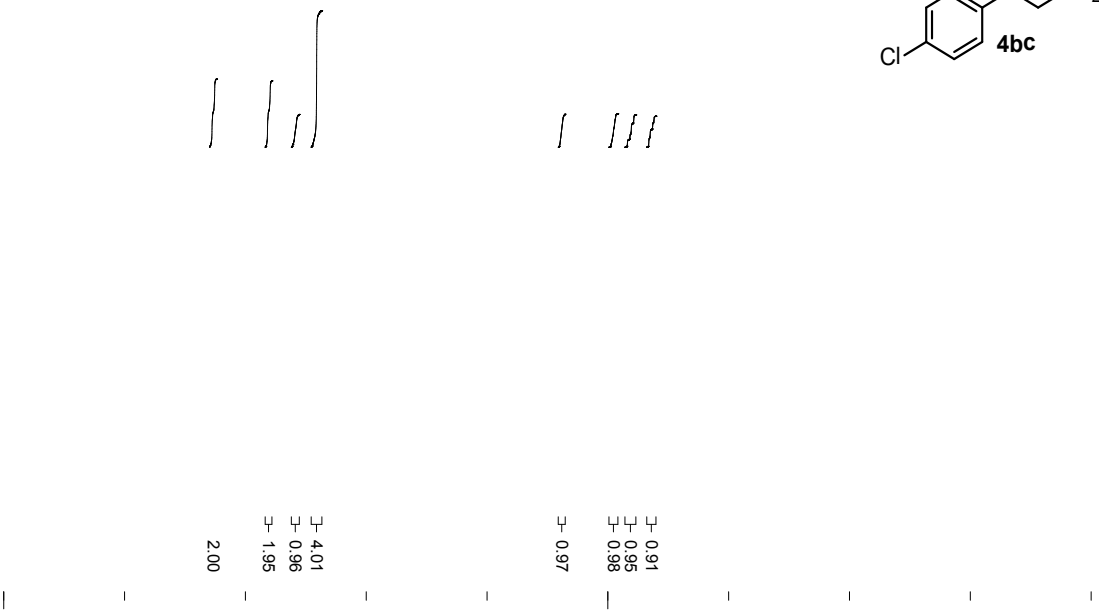
(*S*)-*N'*-(1-(4-Fluorophenyl)-2-nitroethyl)-4-nitrobenzohydrazide (4bb)



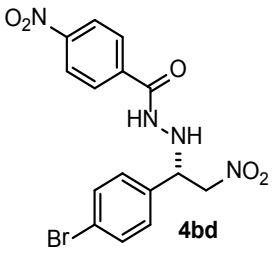


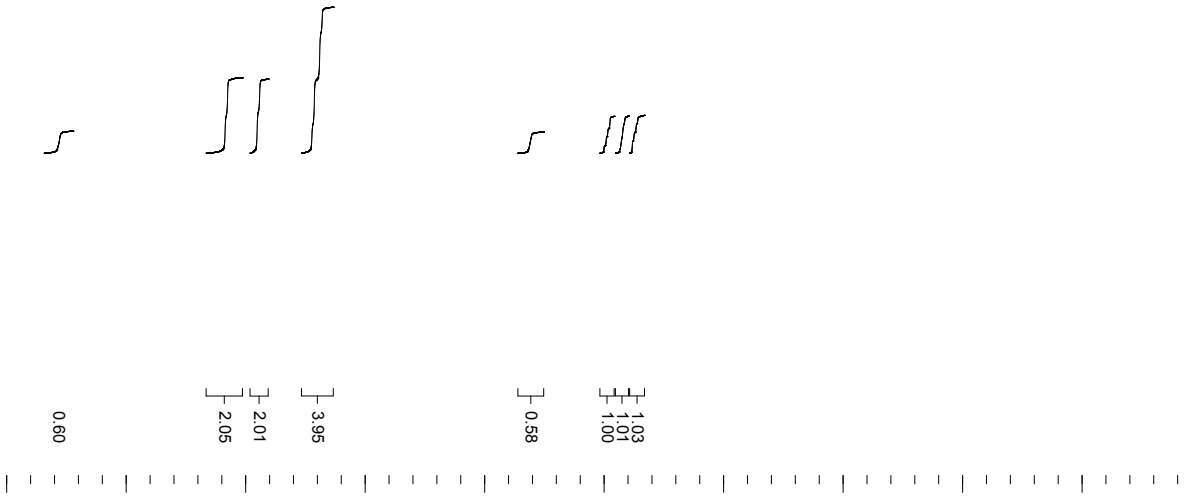
(*S*)-*N′*-(1-(4-Chlorophenyl)-2-nitroethyl)-4-nitrobenzohydrazide (4bc)



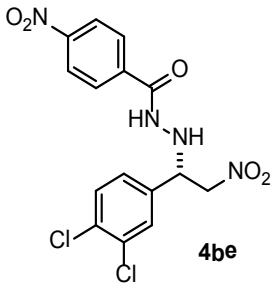


(*S*)-*N'*-(1-(4-Bromophenyl)-2-nitroethyl)4-nitrobenzohydrazide (4bd)

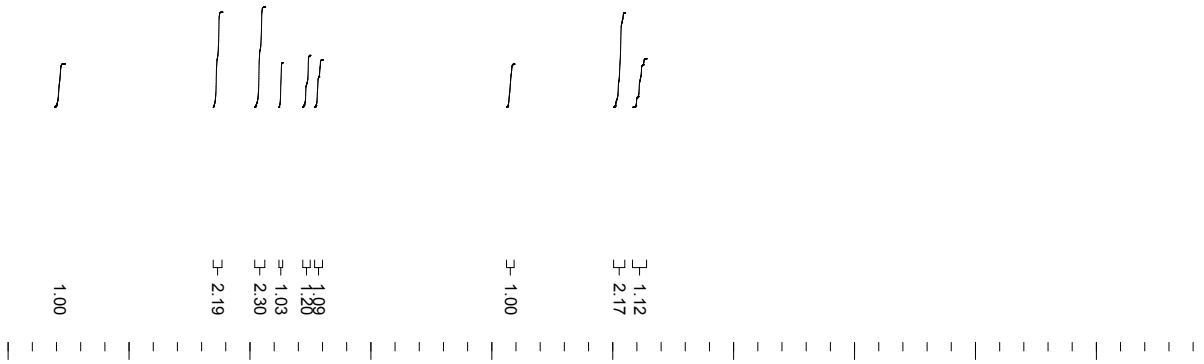




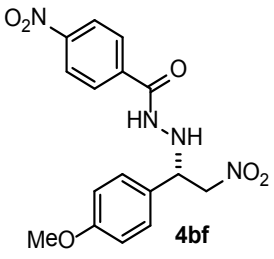
(*S*)-*N'*-(1-(3,4-Dichlorophenyl)-2-nitroethyl)-4-nitrobenzohydrazide (4be)

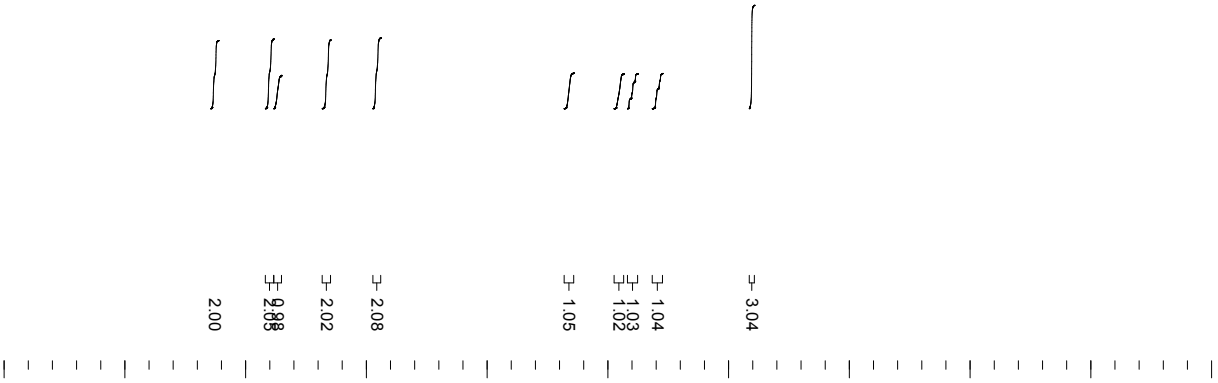


4be

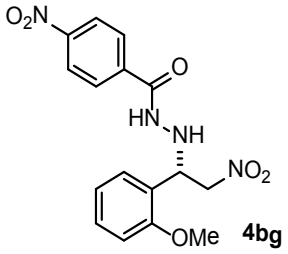


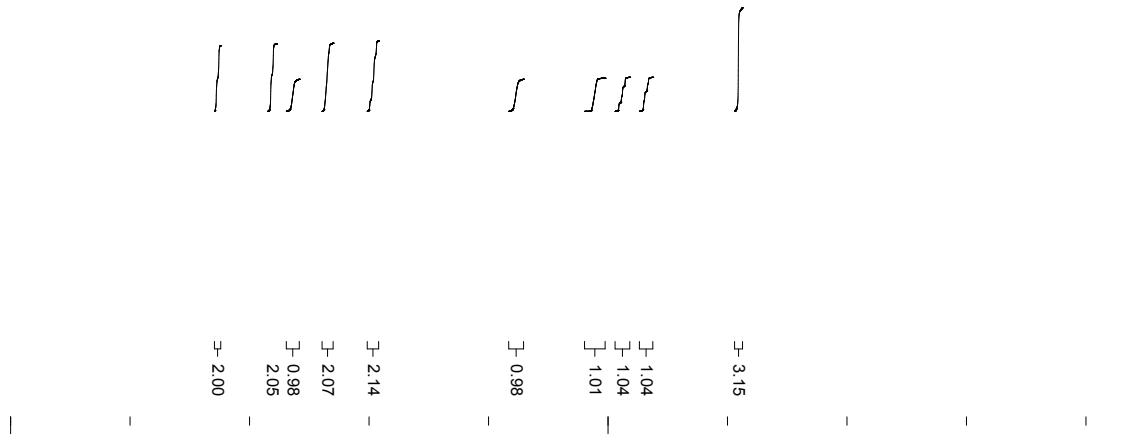
(*S*)-*N'*-(1-(4-Methoxyphenyl)-2-nitroethyl)-4-nitrobenzohydrazide (4bf)



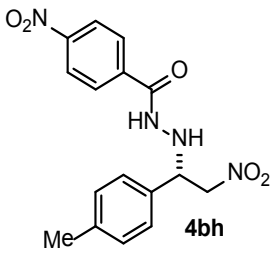


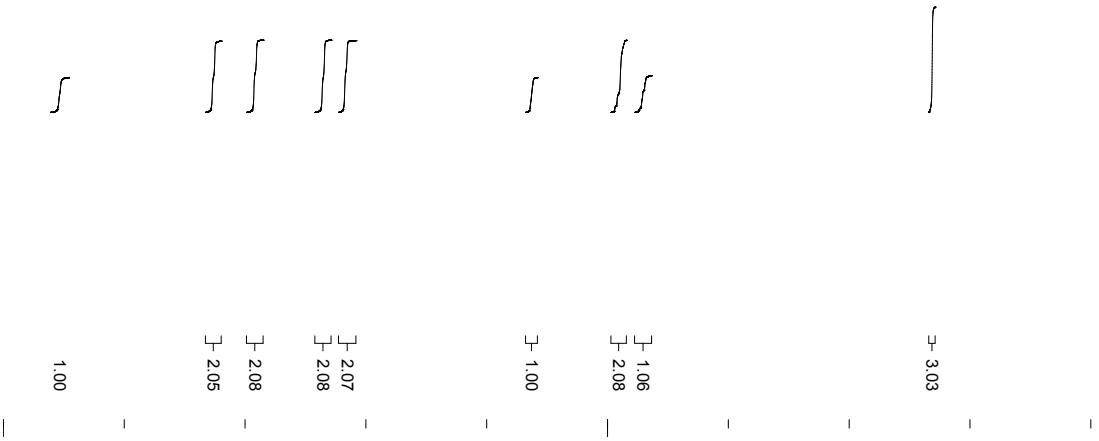
(*S*)-*N'*-(1-(2-Methoxyphenyl)-2-nitroethyl)-4-nitrobenzohydrazide (4bg)



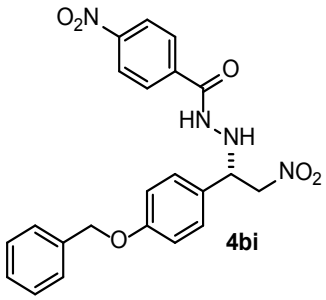


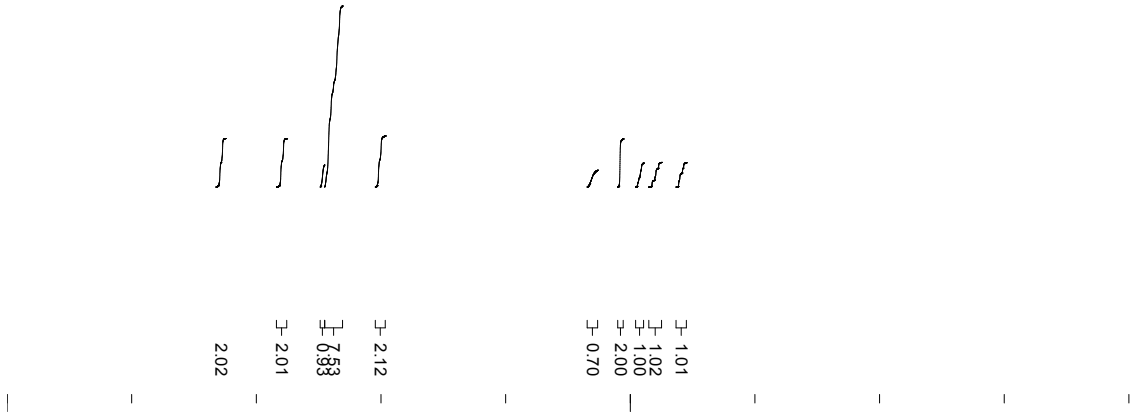
(*S*)-4-Nitro-*N*′-(2-nitro-1-p-tolylethyl)benzohydrazide (4bh)



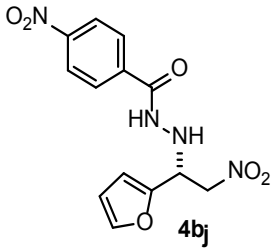


(*S*)-*N'*-(1-(4-(Benzyloxy)phenyl)-2-nitroethyl)-4-nitrobenzohydrazide (4bi)

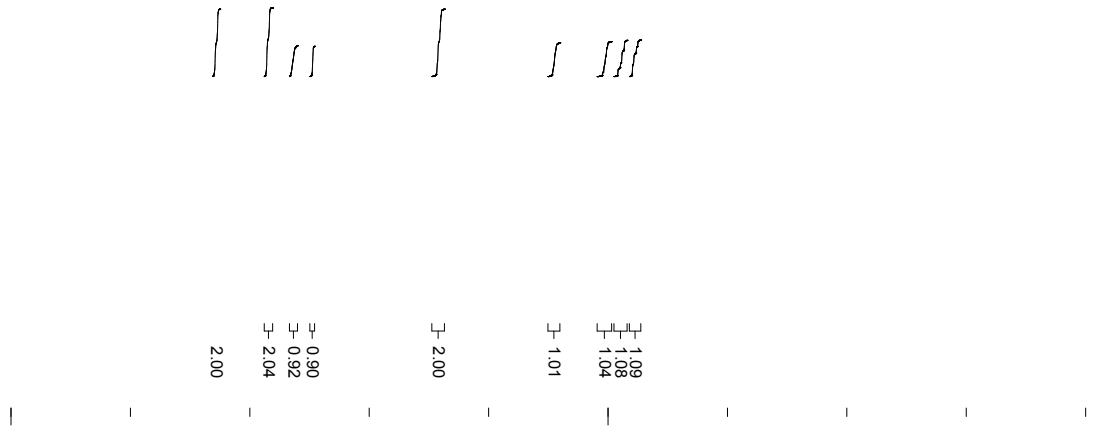




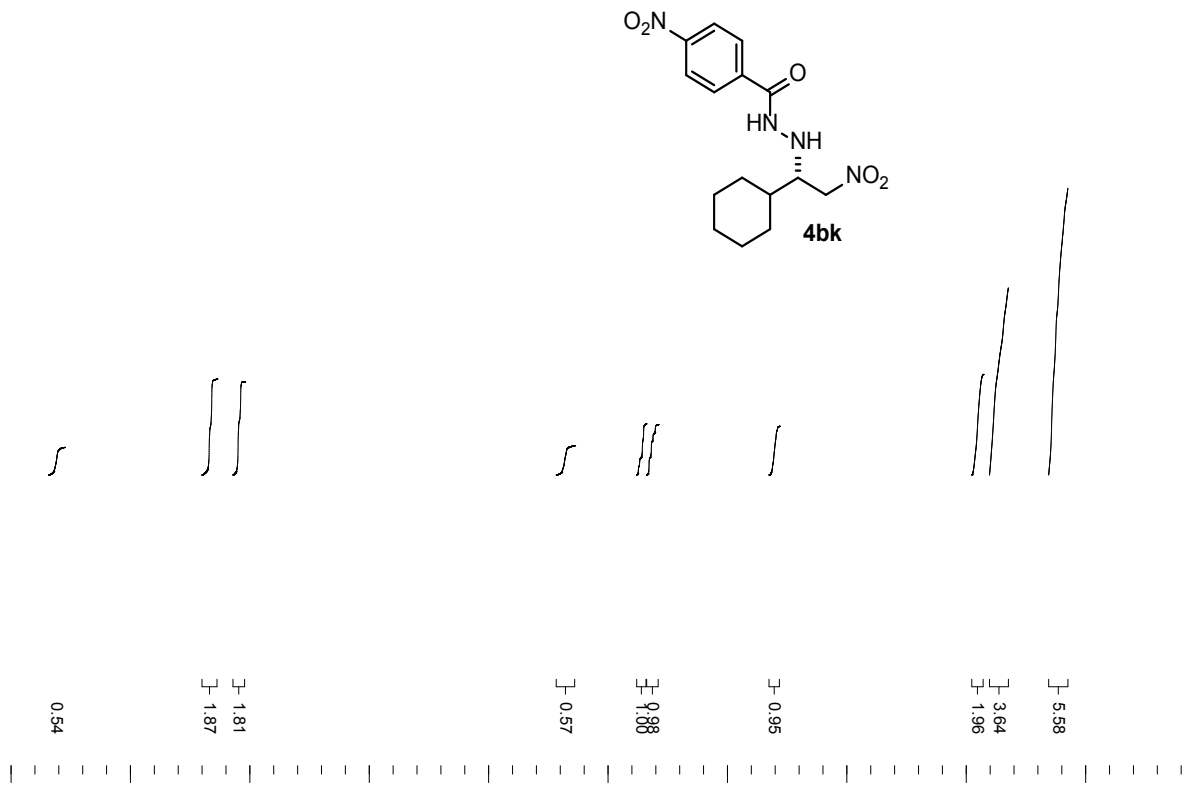
(*S*)-*N'*-(1-(Furan-2-yl)-2-nitroethyl)-4-nitrobenzohydrazide (4bj)



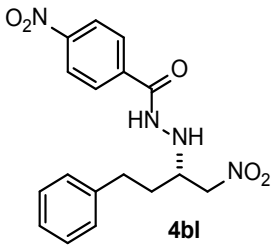
4bj



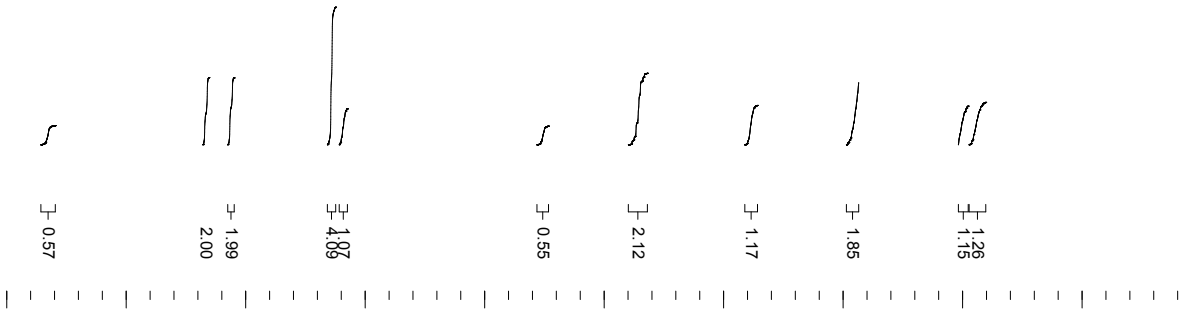
(*S*)-*N'*-(1-Cyclohexyl-2-nitroethyl)-4-nitrobenzohydrazide (4bk)



(*S*)-4-Nitro-*N*′-(1-nitro-4-phenylbutan-2-yl)benzohydrazide (4bl)

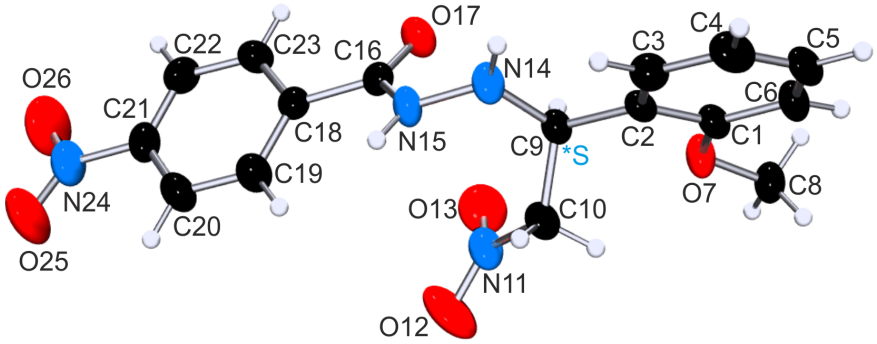


4bl

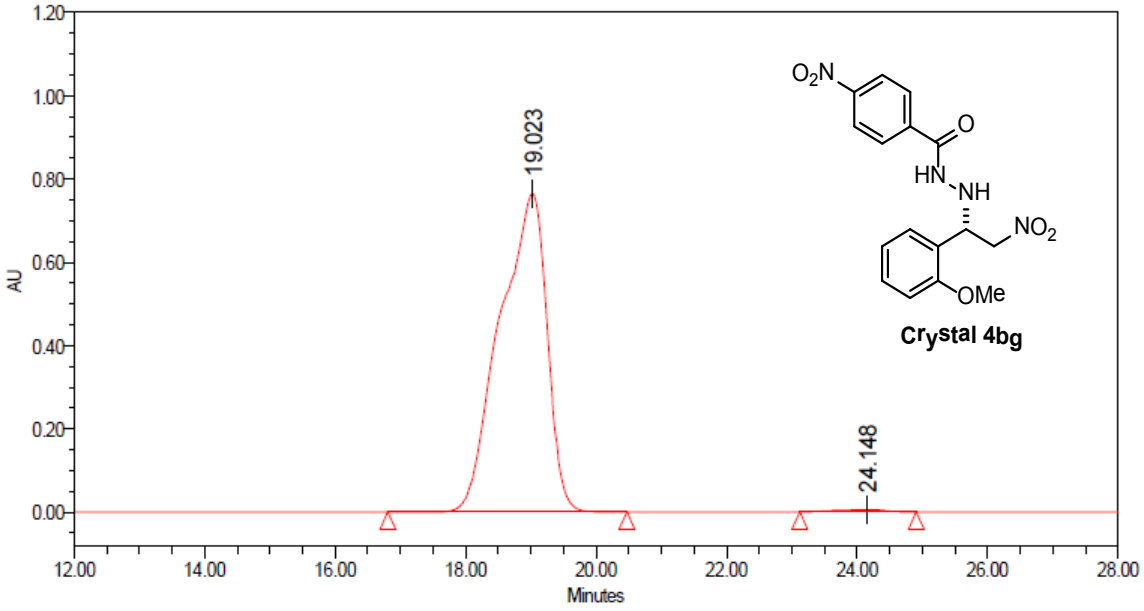


X-RAY CRYSTALLOGRAPHY

The crystals for compound **4bg** were obtained by slow evaporation of a cool AcOEt solution maintained in the fridge during two weeks. The purity of the crystals was determined by HPLC using a Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min, λ = 262.4 nm): t_{major} = 19.0 min; t_{minor} = 24.1 min. $[\alpha]_D^{25}$ = +23.4 (*c* = 0.10, acetone, 99:1 er). The e.r. of the crystals was found to be >99:1. M.p. for crystallized compound **4bg** is 140-144 ºC.



Crystal data of (*S*)-**4bg**: $[C_{16}H_{16}N_4O_6]$, monoclinic, *P21*, *a* = 5.0171(2) Å, *b* = 16.1781(6) Å, *c* = 10.3154(4) Å, *β* = 102.463(2)º, *Z* = 2, M_r = 360.33 g mol^{-1}, *V* = 817.54(5) Å^3, D_{calcd} = 1.464 g cm^{-3}, *λ*(Cu Kα) = 1.54178 Å, T = 295 K, *μ* = 0.970 mm^{-1}, 2471 reflections collected, 2342 unique, *R*1(F_o) = 0.0598 [$I > 2\sigma(I)$], *wR*2 (F_o^2) = 0.1503 (all data), GOF = 1.038. CCDC-959956.



Processed Channel: PDA 262.4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 262.4 nm	19.023	38209576	99.15	764560
2	PDA 262.4 nm	24.148	329183	0.85	6118

Figure S28. Crystal of compound (*S*)-**4bg**. Daicel Chiralpak IC column (*n*-hexane/EtOAc = 80:20, flow rate 1 mL/min).