Supplementary Material

Application of Polyamines and Amino Acid Derivatives Based on 2-Azabicycloalkane Backbone in a Stereoselective Aldol Reaction

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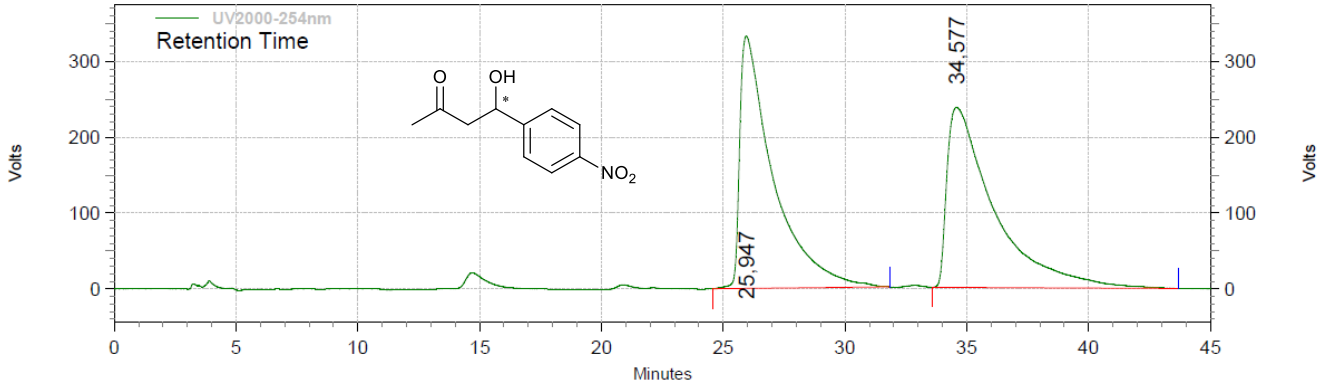
1. General Information

All commercial reagents were purchased and used without further purification. All reactions were carried out in flame-dried glassware with magnetic stirring. Schmelzpunkt Bestimmer Apotec melting point apparatus (WEPA Apothekenbedarf GmbH & Co. KG., Hillscheid, Germany) was used for the determination of melting points in a standard open capillary. ^{1}H and ^{13}C NMR spectra were recorded on Jeol 400yh (Jeol Ltd., Tokyo, Japan), Bruker Avance III 500, and Bruker Avance II 600 spectrometers (Bruker, Billerica, MA, USA). The residual ^{1}H or ^{13}C signals of the solvent ($CDCl_3$, MeOH-d_4) were used as references. Multiplicity of chemical shift are reported as s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet and br = broad. Chemical shifts are given in ppm, and coupling constants are expressed in Hz. The spectra are shown in Supplementary Material. High-resolution mass spectra were recorded using electrospray ionization mode on a Waters LCT Premier XE TOF spectrometer (Waters Corporation, Milford, MA, USA). Infrared spectra were measured in a 4000–400 cm^{-1} range on a Perkin Elmer 2000 FTIR instrument (PerkinElmer, Waltham, MA, USA). Optical rotations were determined with an automatic polarimeter Model AA-5 (OpticalActivity, Ltd., Ramsey, UK); $[\alpha]^{20}_{D}$ values are expressed in 10^{-1} deg cm^2 g^{-1}. Silica gel 60 (60–200 μm, 70–230 mesh) was used for column chromatography, and precoated plates precoated with the same adsorbent were applied for thin-layer chromatography. Diastereomeric ratio and enantiomeric excess were determined by high performance liquid chromatography (HPLC) with chiral columns (Chiralpak ASH and ADH).

2. Copies of HPLC Chromatograms

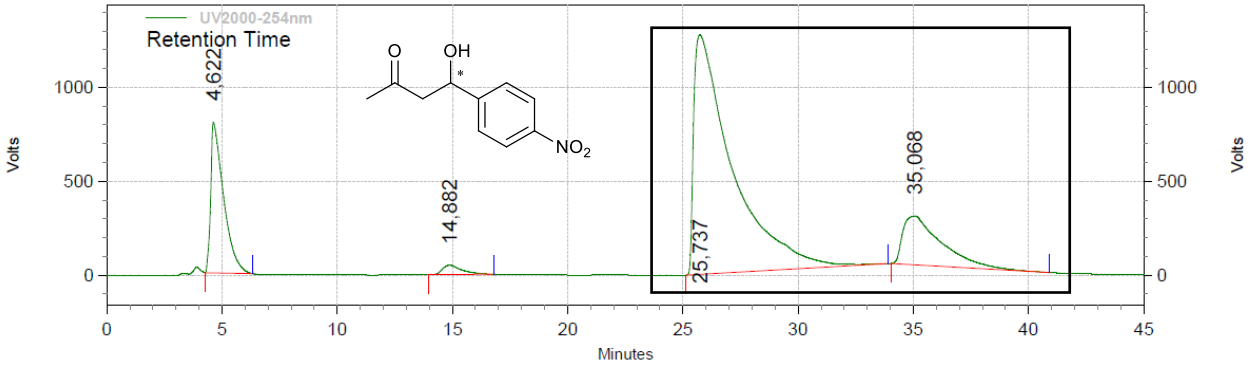
Racemic mixture
Chiralpak AS-H, hexane/isopropanol 85:15, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
25,947	31662683	49,83	332746	58,35
34,577	31884766	50,17	237467	41,65

L-Proline, entry 1 in Table 1.

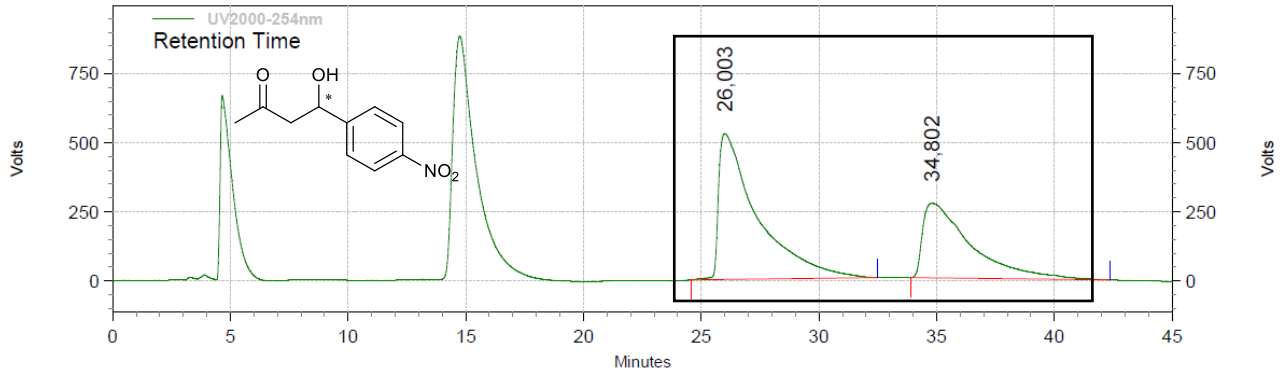
10% mol of L-proline, in acetone at RT
Chiralpak AS-H, hexane/isopropanol 85:15, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
4,622	31136529	14,69	802669	33,61
14,882	2868562	1,35	49269	2,06
25,737	147501851	69,59	1276016	53,43
35,068	30446184	14,36	260415	10,90

Compound **4**, entry 2 in Table 1.

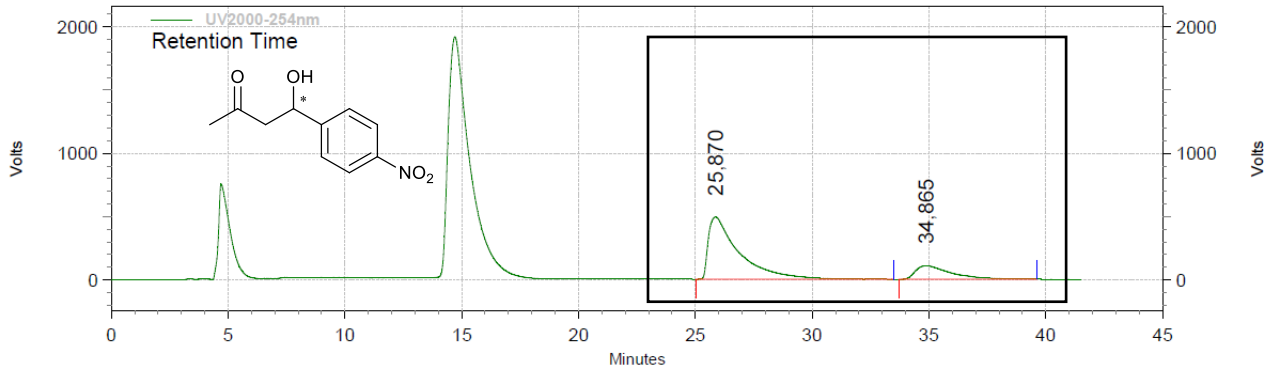
10% mol of cat **4**, in acetone at RT
Chiralpak AS-H, hexane/isopropanol 85:15, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
26,003	60434036	61,24	527900	66,13
34,802	38251800	38,76	270366	33,87

Compound **9**, entry 4 in Table 1.

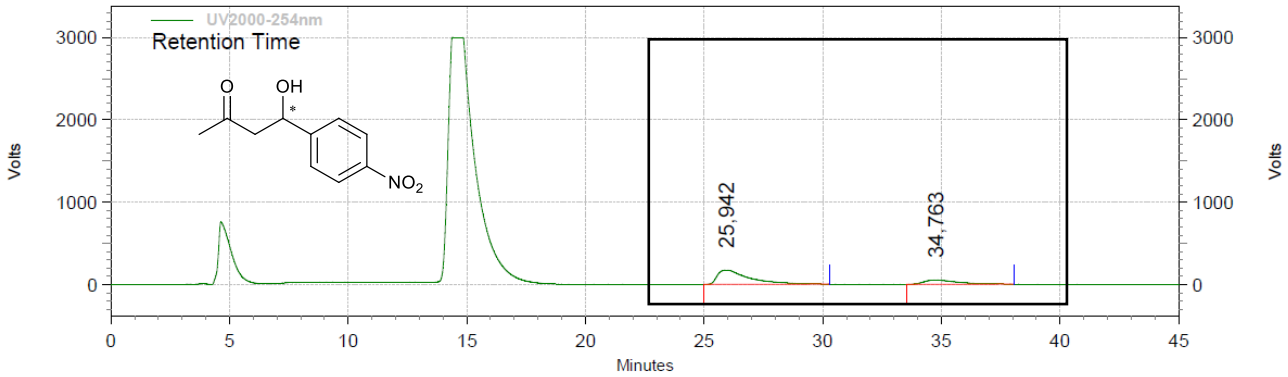
10% mol of cat **9**, in acetone at RT
Chiralpak AS-H, hexane/isopropanol 85:15, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
25,870	45181056	79,86	492286	82,23
34,865	11393450	20,14	106380	17,77

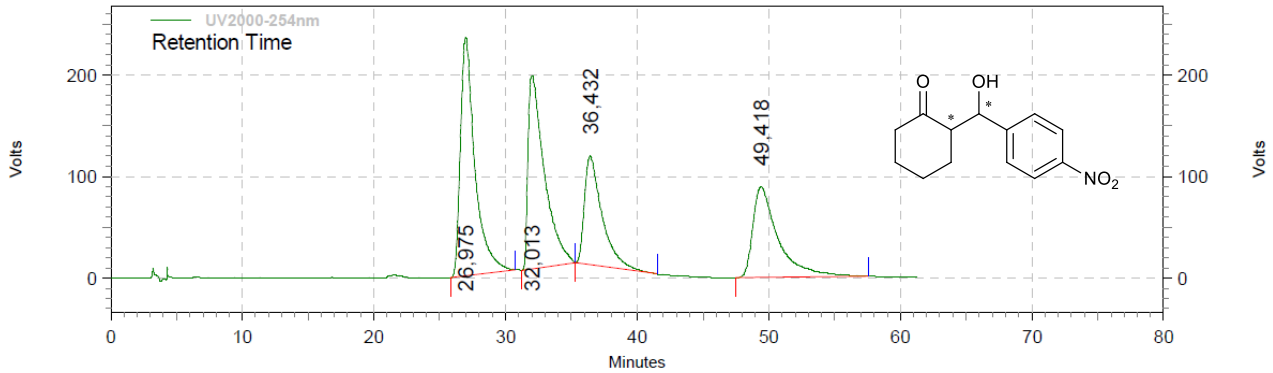
Compound **12**, entry 5 in Table 1.

10% mol of cat **12**, in acetone at RT
Chiralpak AS-H, hexane/isopropanol 85:15, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
25,942	16050395	75,91	172561	76,96
34,763	5094183	24,09	51662	23,04

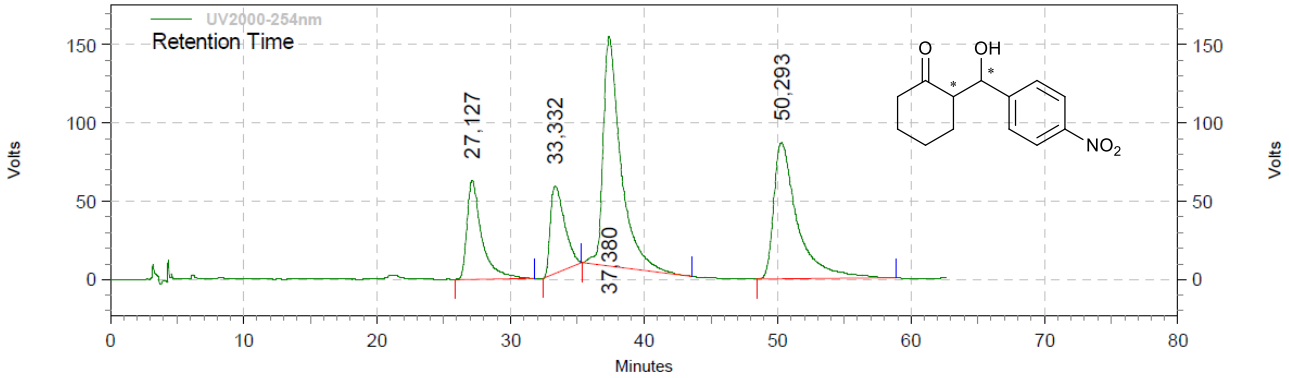
Racemic mixture
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
26,975	18019742	31,96	235088	37,88
32,013	16480261	29,23	189980	30,61
36,432	9928603	17,61	106711	17,19
49,418	11955573	21,20	88817	14,31

Compound **4**, entry 7 in Table 1.

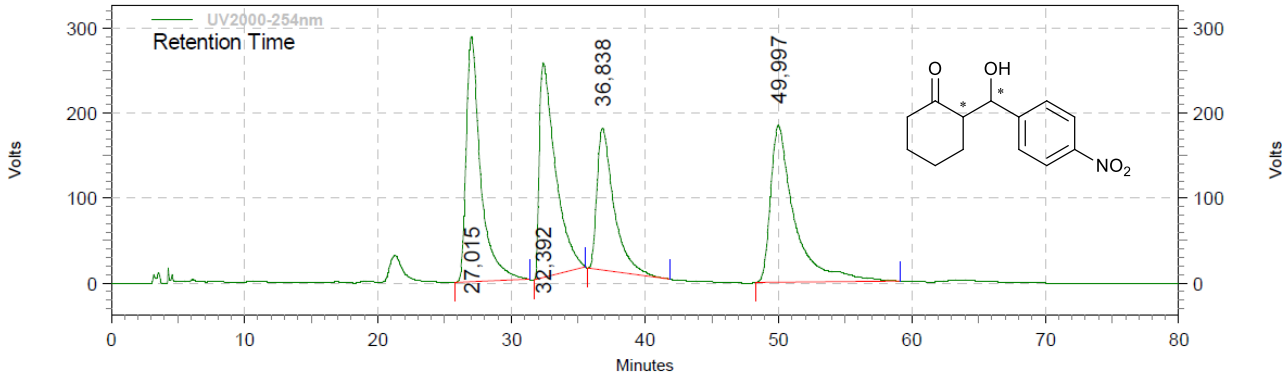
10% mol of cat **4**, in $CHCl_3$ at RT
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
27,127	4883342	14,66	63169	17,90
33,332	4148033	12,45	55886	15,83
37,380	13476359	40,45	146968	41,64
50,293	10806146	32,44	86938	24,63

Compound **6**, entry 8 in Table 1.

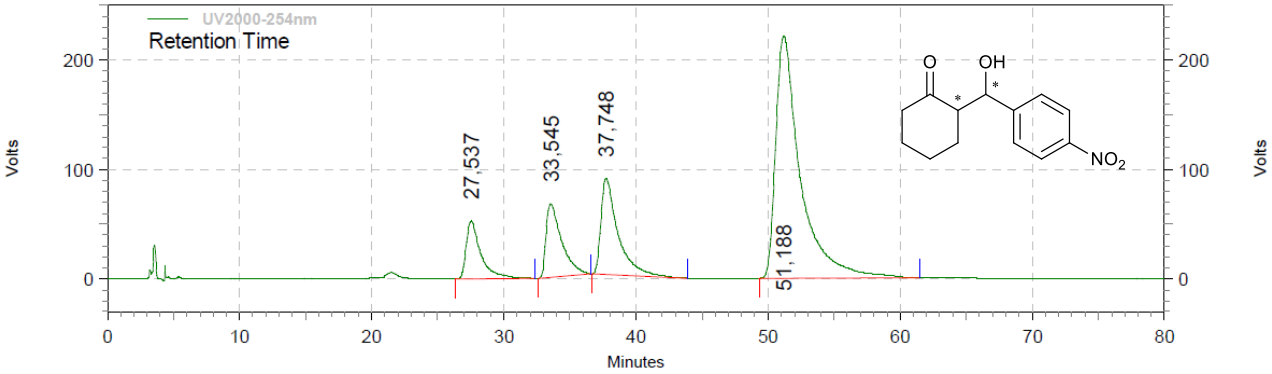
10% mol of cat **6**, in $CHCl_3$ at RT
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
27,015	21720497	26,87	288765	32,31
32,392	21168546	26,19	252484	28,25
36,838	14761002	18,26	167249	18,71
49,997	23191765	28,69	185290	20,73

Compound **9**, entry 10 in Table 1.

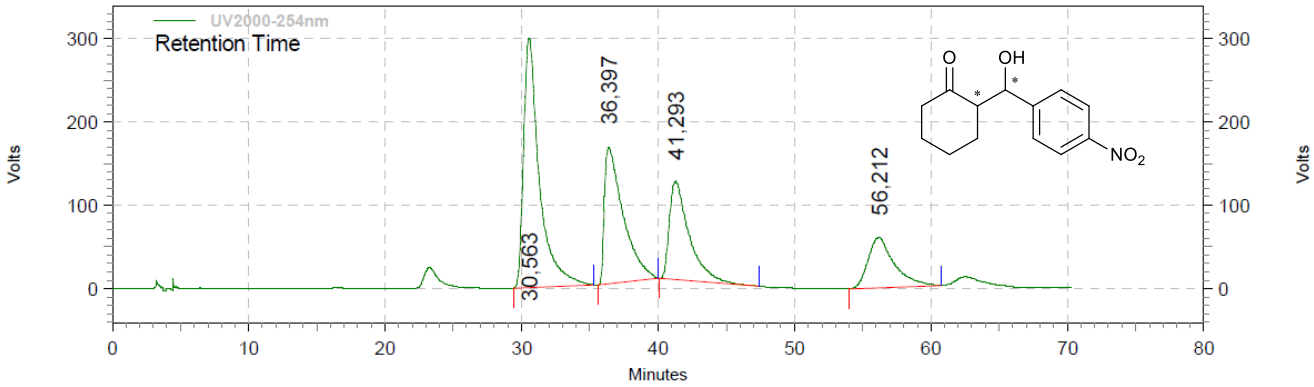
10% mol of cat **9**, in $CHCl_3$ at RT
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
27,537	4082268	8,82	52729	12,27
33,545	5547946	11,98	67205	15,64
37,748	7919310	17,10	87997	20,48
51,188	28753002	62,10	221643	51,60

Compound **11**, entry 12 in Table 1.

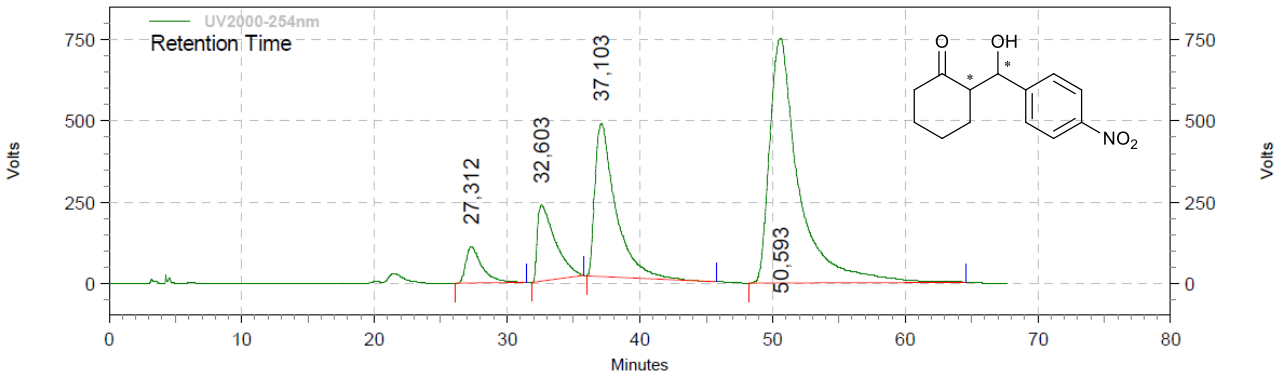
10% mol of cat **11**, in $CHCl_3$ at RT
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
30,563	24042476	40,31	299711	46,66
36,397	15693276	26,31	164310	25,58
41,293	11915135	19,98	118013	18,37
56,212	7992036	13,40	60275	9,38

Compound **12**, entry 13 in Table 1.

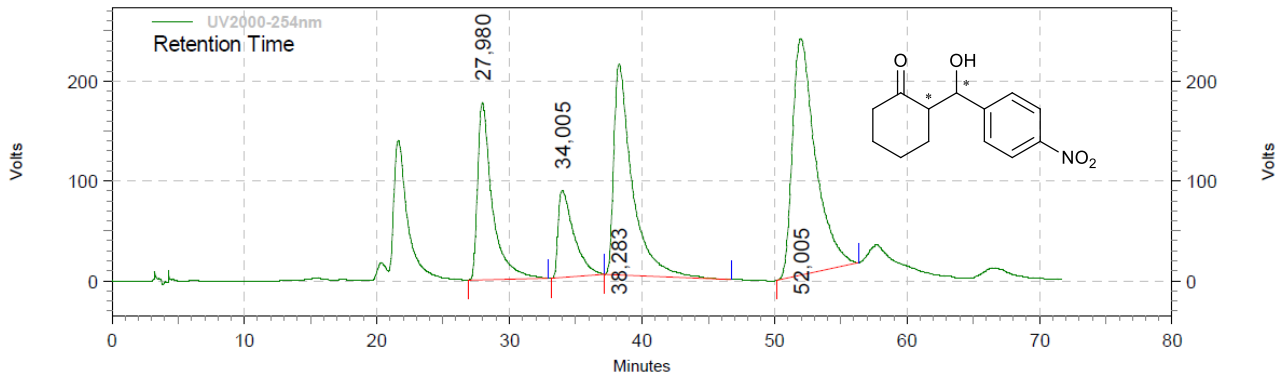
10% mol of cat **12**, in $CHCl_3$ at RT
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
27,312	9488431	4,81	111311	7,11
32,603	21918533	11,12	234077	14,94
37,103	51059117	25,90	469625	29,98
50,593	114698791	58,17	751363	47,97

Compound **6**, entry 17 in Table 1.

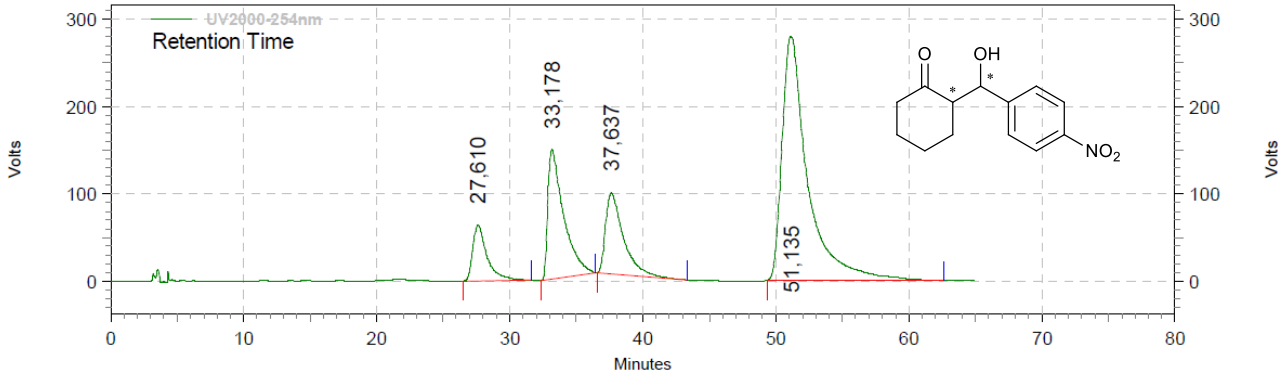
10% mol of cat **6**, 20% mol HOAc, in brine at RT
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
27,980	13634118	19,54	177659	24,90
34,005	7180173	10,29	87492	12,26
38,283	20352550	29,17	211439	29,64
52,005	28593847	40,99	236883	33,20

Compound **9**, entry 19 in Table 1.

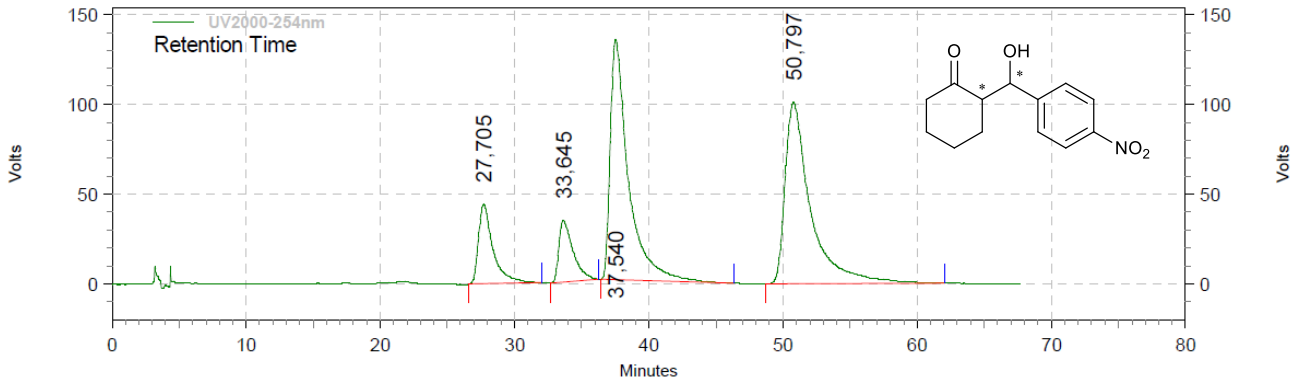
10% mol of cat **9**, 20% mol HOAc, in brine at RT
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
27,610	4828495	7,60	64233	10,97
33,178	12317926	19,39	148056	25,29
37,637	8650584	13,62	92998	15,88
51,135	37739298	59,40	280253	47,86

Compound **11**, entry 21 in Table 1.

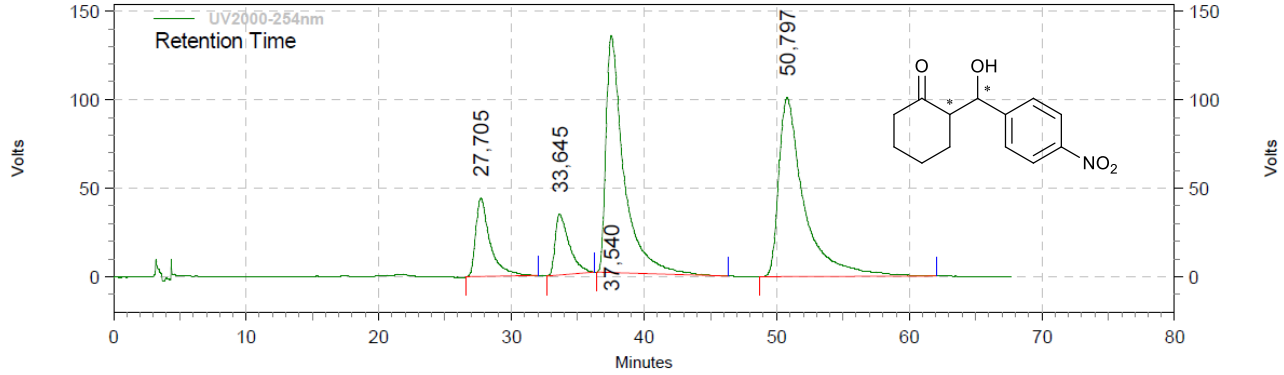
10% mol of cat **11**, 20% mol HOAc, in brine at RT
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



Retention Time	Area	Area %	Height	Height %
27,705	3361346	10,51	44262	14,12
33,645	2525043	7,90	34119	10,88
37,540	12613926	39,46	133951	42,73
50,797	13468111	42,13	101172	32,27

Compound **11**, entry 21 in Table 1.

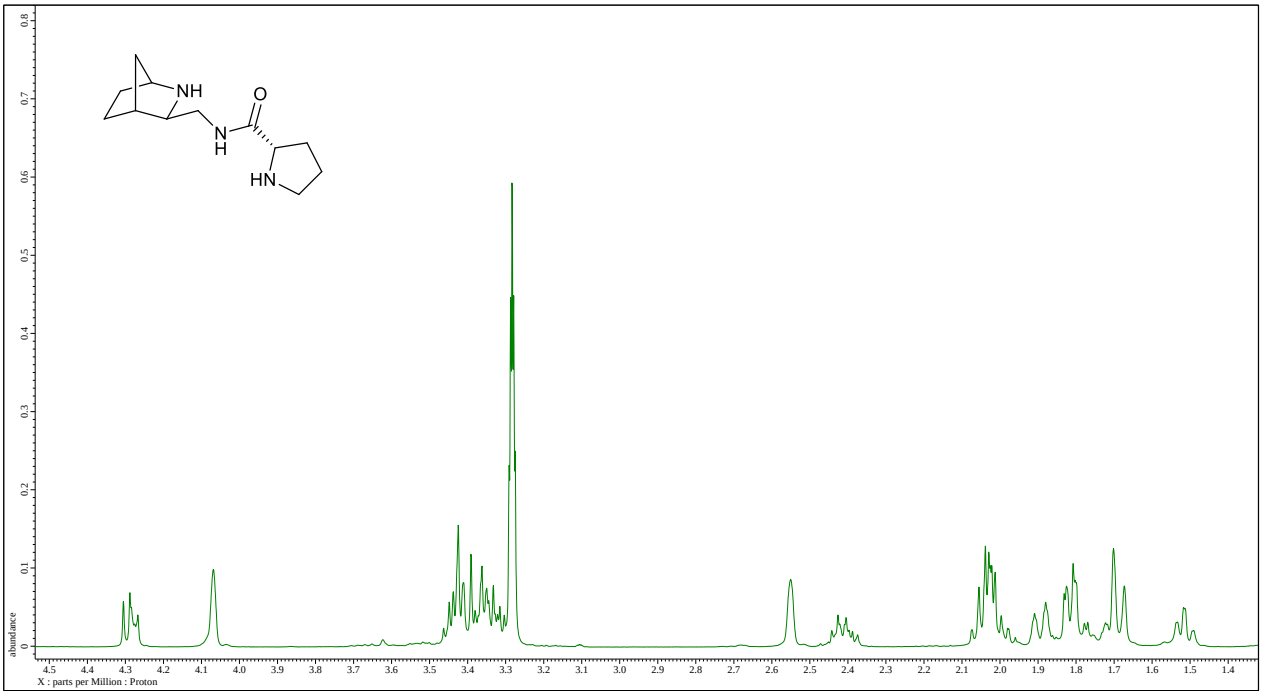
10% mol of cat **11**, 20% mol HOAc, in brine at RT
Chiralpak AD-H, hexane/isopropanol 95:5, λ = 254 nm, 1.0 ml/min



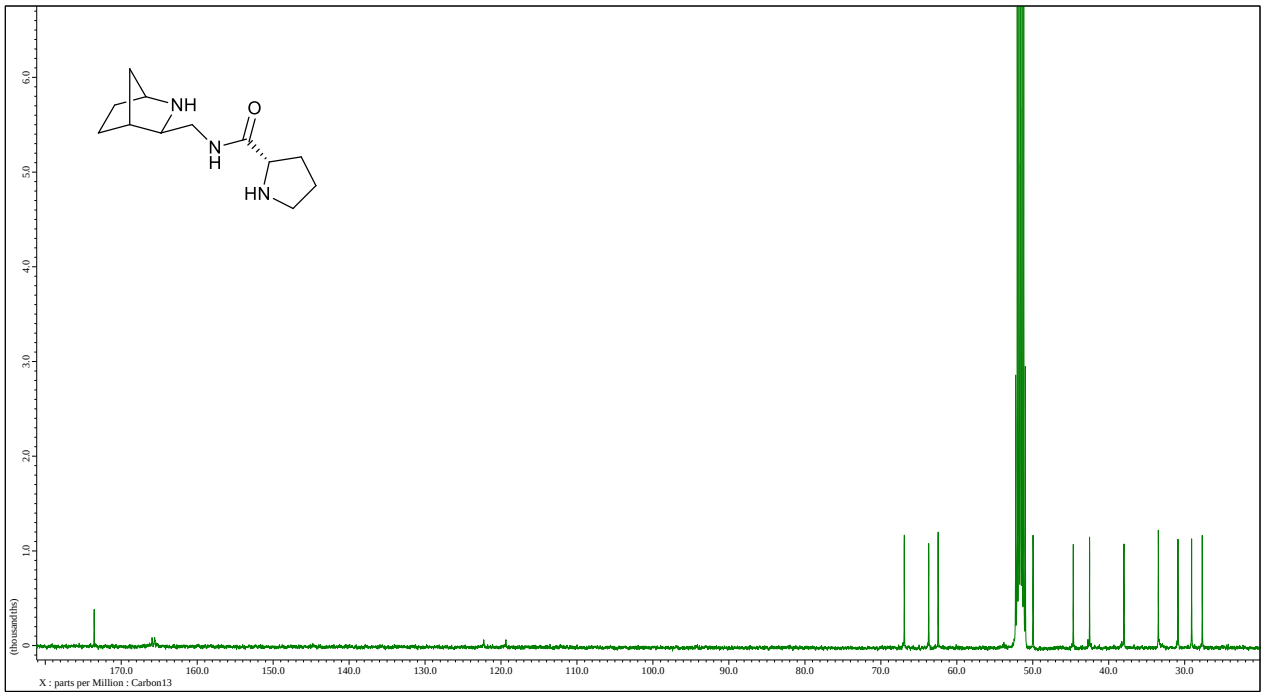
Retention Time	Area	Area %	Height	Height %
27,705	3361346	10,51	44262	14,12
33,645	2525043	7,90	34119	10,88
37,540	12613926	39,46	133951	42,73
50,797	13468111	42,13	101172	32,27

3. NMR Spectra of Catalysts **8** and **12**

*N-((1S,3R,4R)-2-azabicyclo[2.2.1]heptan-3-ylmethyl)pyrrolidine-2-carboxamide (**8**)*



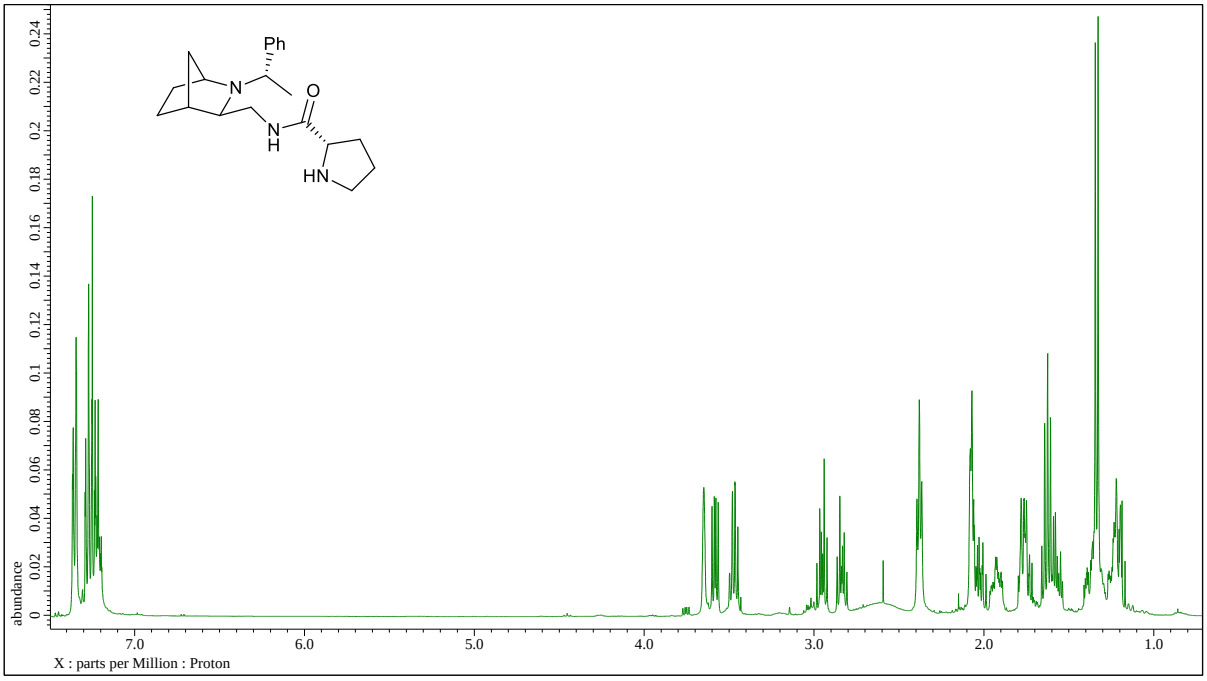
^{1}H NMR spectrum of *N*-((1*S*,3*R*,4*R*)-2-azabicyclo[2.2.1]heptan-3-ylmethyl)pyrrolidine-2-carboxamide (**8**)



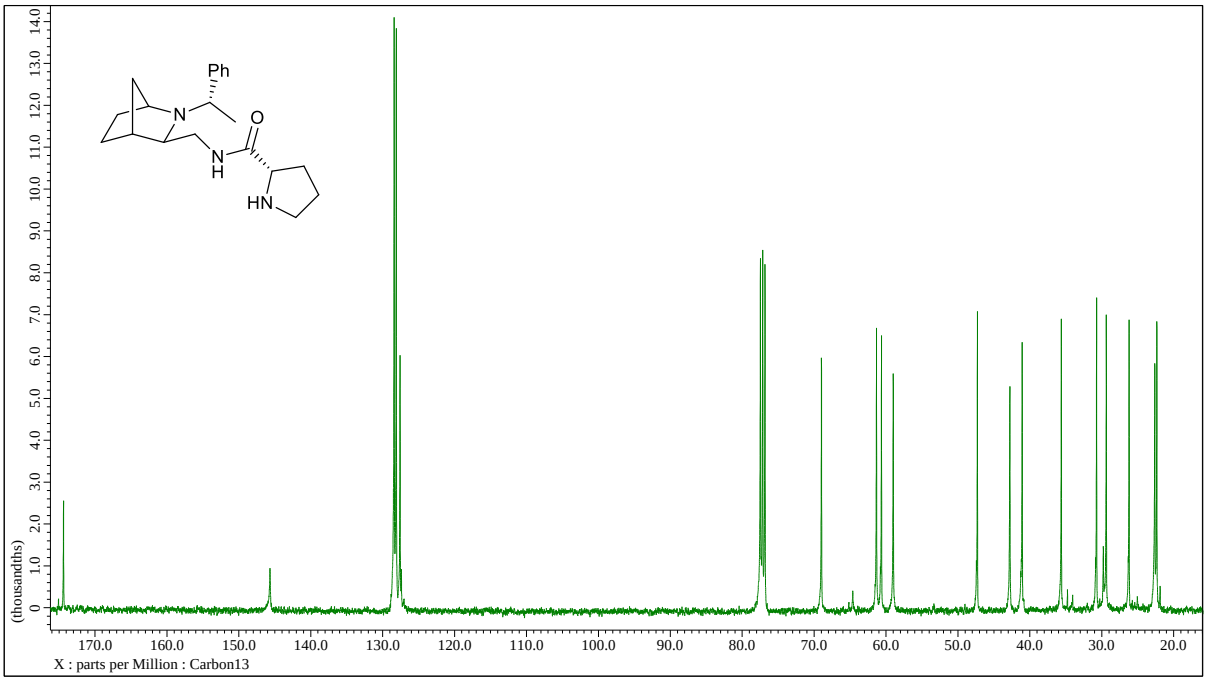
^{13}C NMR spectrum of *N*-((1*S*,3*R*,4*R*)-2-azabicyclo[2.2.1]heptan-3-ylmethyl)pyrrolidine-2-carboxamide (**8**)

Colorless crystals . Yield 84.5 mg (64%), mp. 65℃, $[\alpha]_D^{20}$ = -26.3 (c 0.0057, MeOH). ^{1}H NMR (400 MHz, MeOH-d_4): δ 1.53-1.57 (m, 1H), 1.71-1.94 (m, 6H), 2.02-2.11 (m, 3H), 2.41-2.48 (m, 1H), 2.58 (br s, 1H), 3.34-3.50 (m, 4H), 4.10 (br s, 1H), 4.30-4.34 (m, 1H) ppm. ^{13}C NMR (400 MHz, MeOH-d_4): δ 27.7, 29.1, 30.9, 33.5, 38.0, 42.5, 44.7, 50.0, 62.4, 63.7, 66.9, 173.6 ppm. HRMS (ESI$^+$, m/z): calcd for $C_{12}H_{21}N_3O$ ([M+H]$^+$) 224.1763; found 224.1758.

*N-(((1S,3R,4R)-2-(1-phenylethyl)-2-azabicyclo[2.2.1]heptan-3-yl)methyl)pyrrolidine-2-carboxamide (**12**)*



^{1}H NMR spectrum of *N*-(((1*S*,3*R*,4*R*)-2-(1-phenylethyl)-2-azabicyclo[2.2.1]heptan-3-yl)methyl)pyrrolidine-2-carboxamide (**12**)



^{13}C NMR spectrum of *N*-(((1*S*,3*R*,4*R*)-2-(1-phenylethyl)-2-azabicyclo[2.2.1]heptan-3-yl)methyl)pyrrolidine-2-carboxamide (**12**)

Yellow oil. Yield 0.39 g (62%). $[\alpha]_D^{20}$ = 42.6 (c 0.60, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ =1.19-1.26 (m, 3H), 1.29-1.41 (m, 4H), 1.54-1.66 (m, 3H), 1.71-1.78 (m, 1H), 1.99-2.08 (m, 3H), 2.38 (t, 2H, *J* = 5,6 Hz), 2.59 (br s, 1H), 2.81-2.86 (m, 1H), 2.92-2.98 (m, 1H), 3.47 (q, 1H, *J* = 6.4 Hz), 3.56-3.60 (m, 1H), 3.65 (br s, 1H), 7.19-7.36 (m, 5H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 22.3, 22.6, 26.3, 29.4, 30.7, 35.6, 41.1, 42.8, 47.3, 59.0, 60.6, 61.3, 68.9, 127.6, 128.1, 128.4, 145.7, 174.4 ppm. HRMS (ESI$^+$): calcd for $C_{20}H_{29}N_3O$ $[M+H]^+$ 328.2389; found 328.2379.