Supporting Information

C_2-Symmetric pyrrolidine-derived squaramides as recyclable organocatalysts for asymmetric Michael reactions

*A.S. Kucherenko[a], V.G. Lisnyak[a], A.A. Kostenko[a,b], S.V. Kochetkov[a] and S.G. Zlotin[a]**

[a]N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky Prospect, 119991 Moscow, Russia.

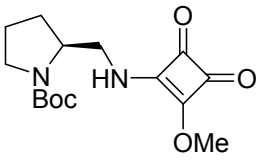
[b]D. I. Mendeleev University of Chemical Technology, 9 Miusskaya Square, 125047 Moscow, Russia

Email: zlotin@ioc.ac.ru

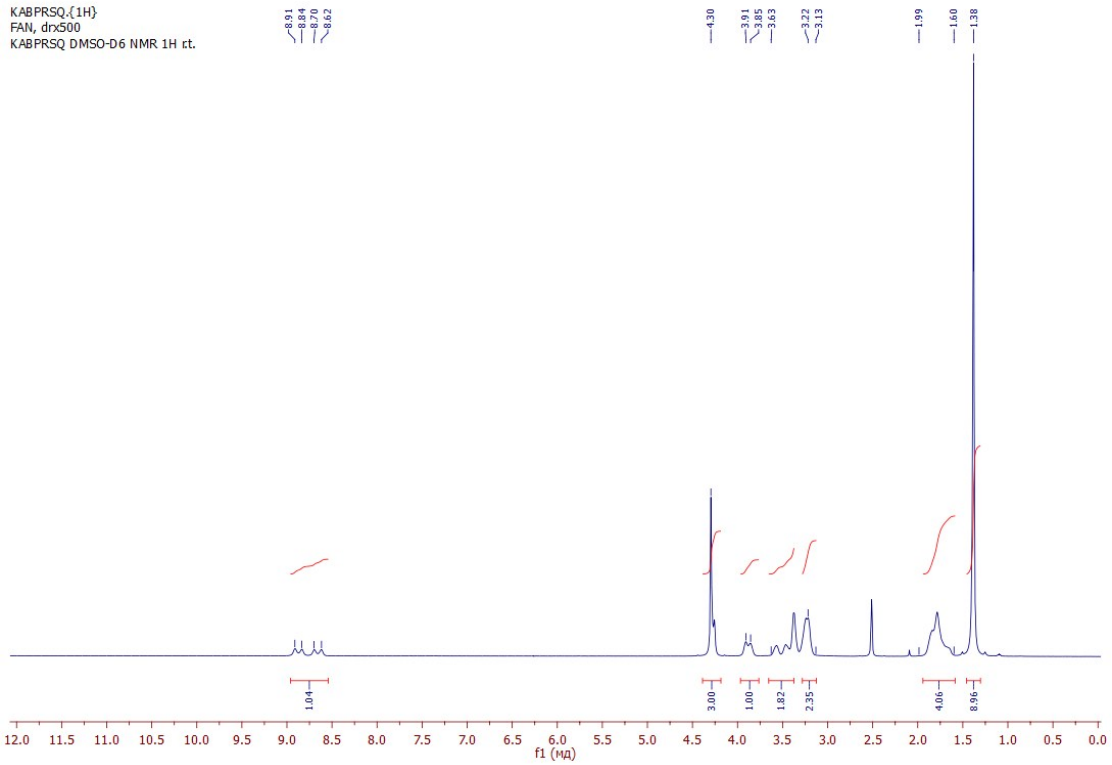
Table of Contents

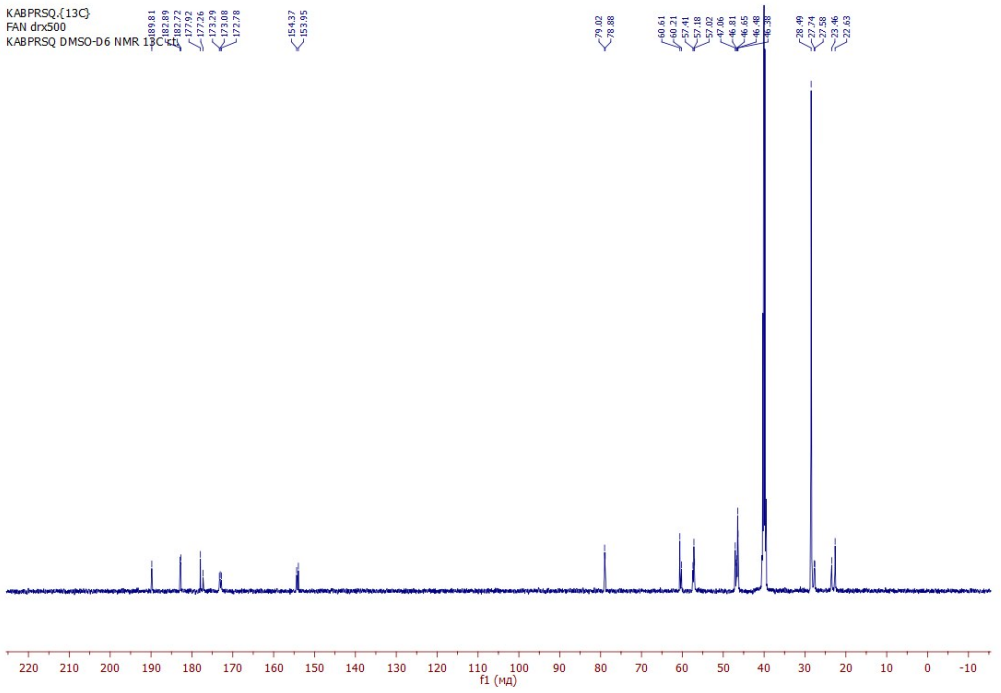
1. NMR DATA FOR NOVEL COMPOUNDS

***tert*-Butyl (*S*)-2-(((2-methoxy-3,4-dioxocyclobut-1-en-1-yl)amino)methyl)pyrrolidine-1-carboxylate ((*S*)-6)**

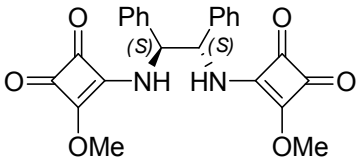


(*S*)-**6**

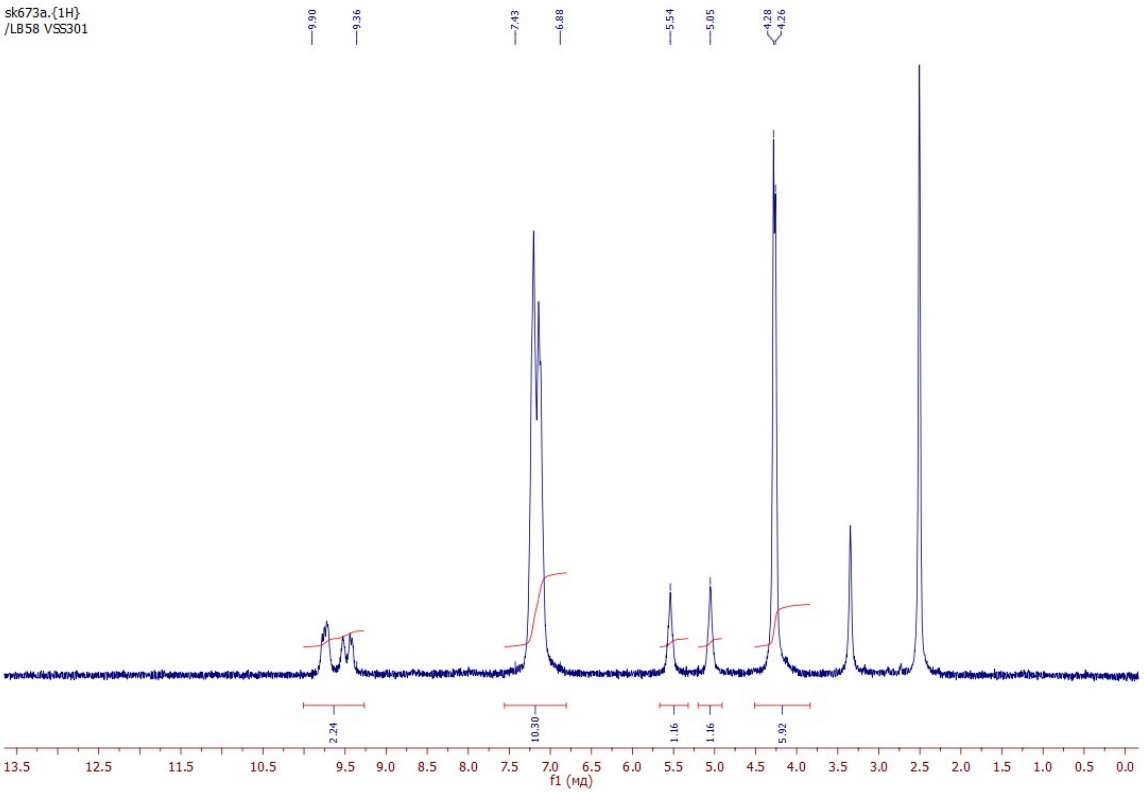


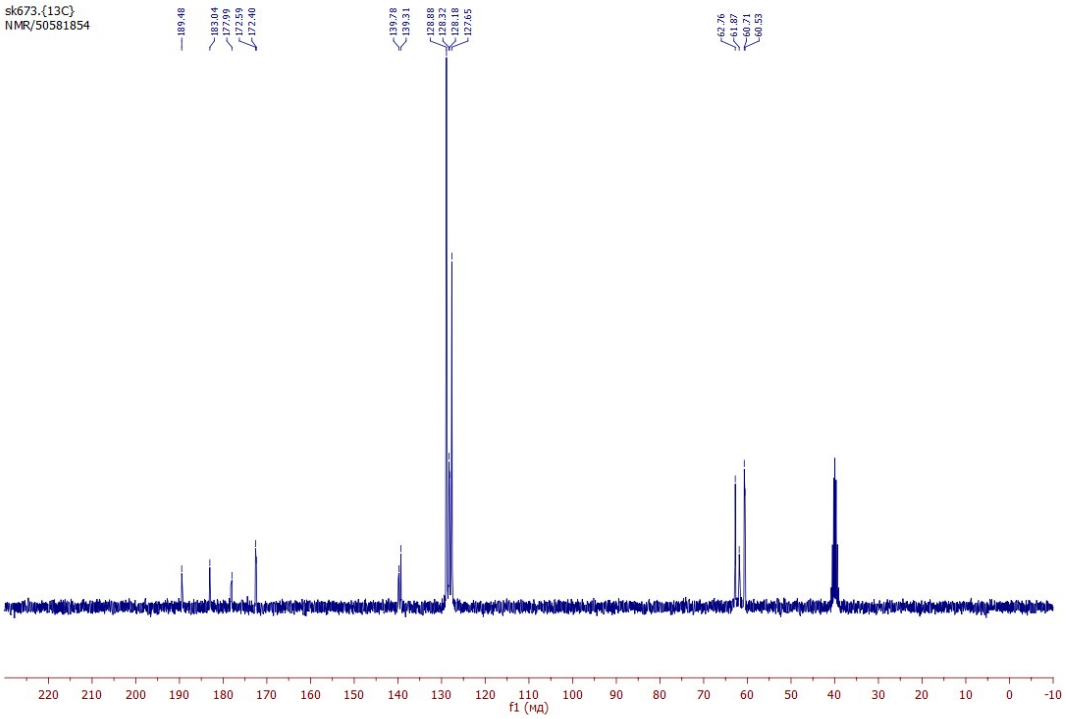


4,4'-(((1*S*,2*S*)-1,2-Diphenylethane-1,2-diyl)bis(azanediyl))bis(3-methoxycyclobut-3-ene-1,2-dione) ((*S*,*S*)-8)

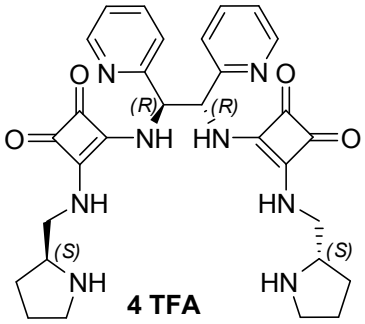


(*S*,*S*)-**8**

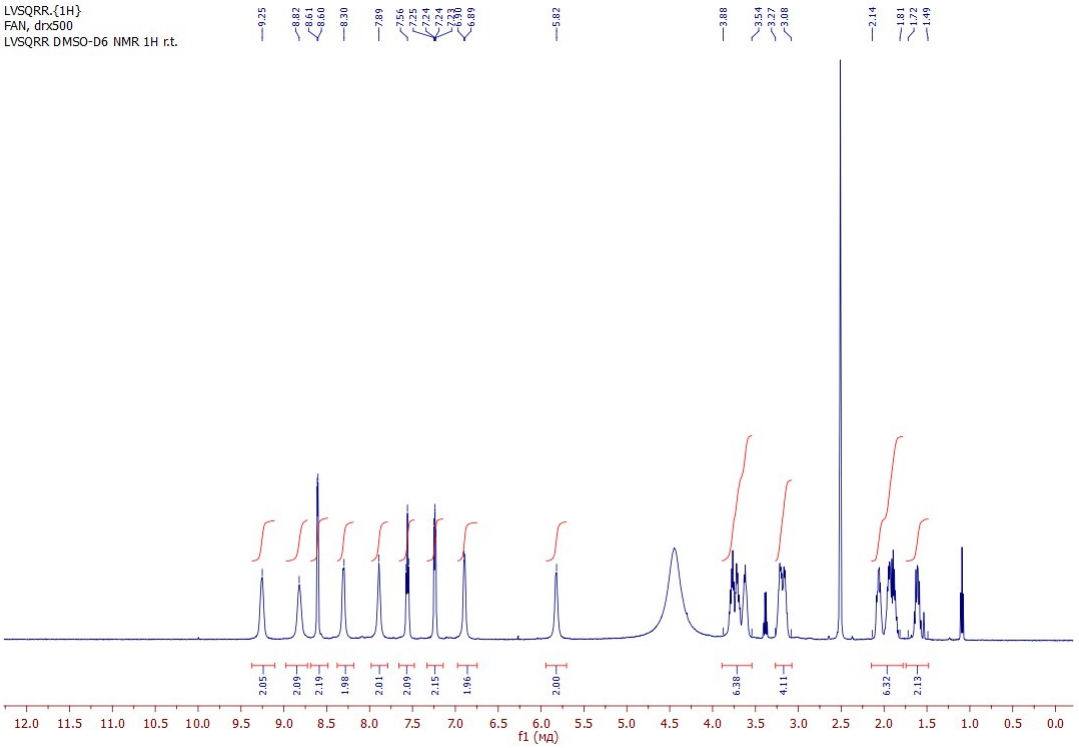


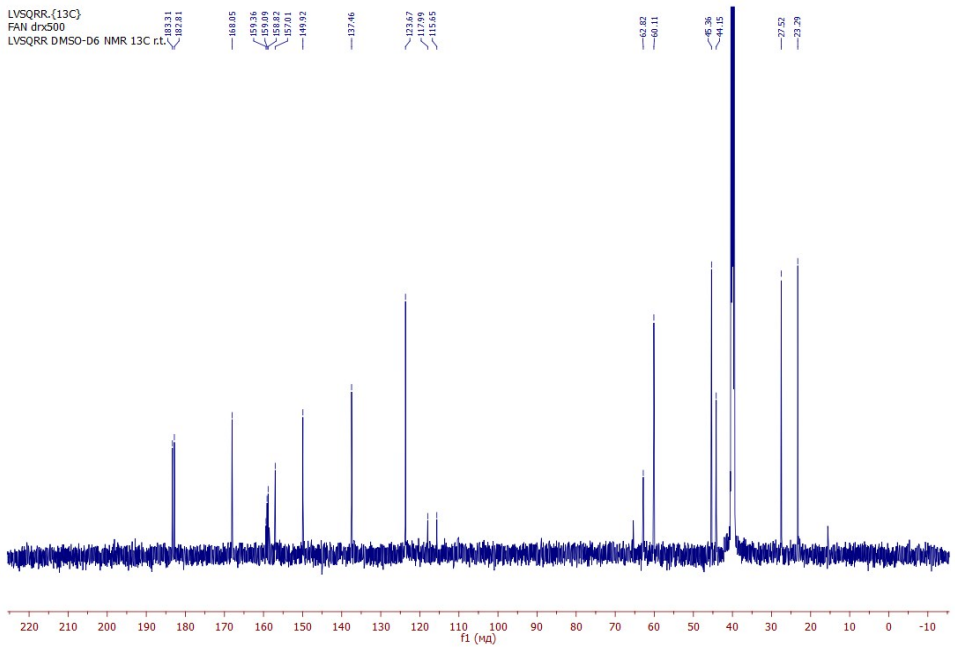


4,4'-(((1*R*,2*R*)-1,2-Di(pyridin-2-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-((((*S*)-pyrrolidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione) tetrafluoroacetate (1)

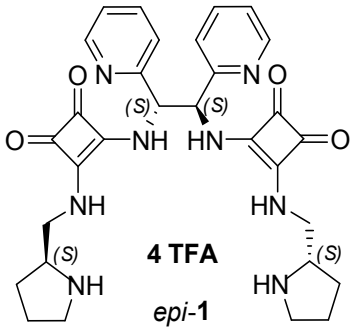


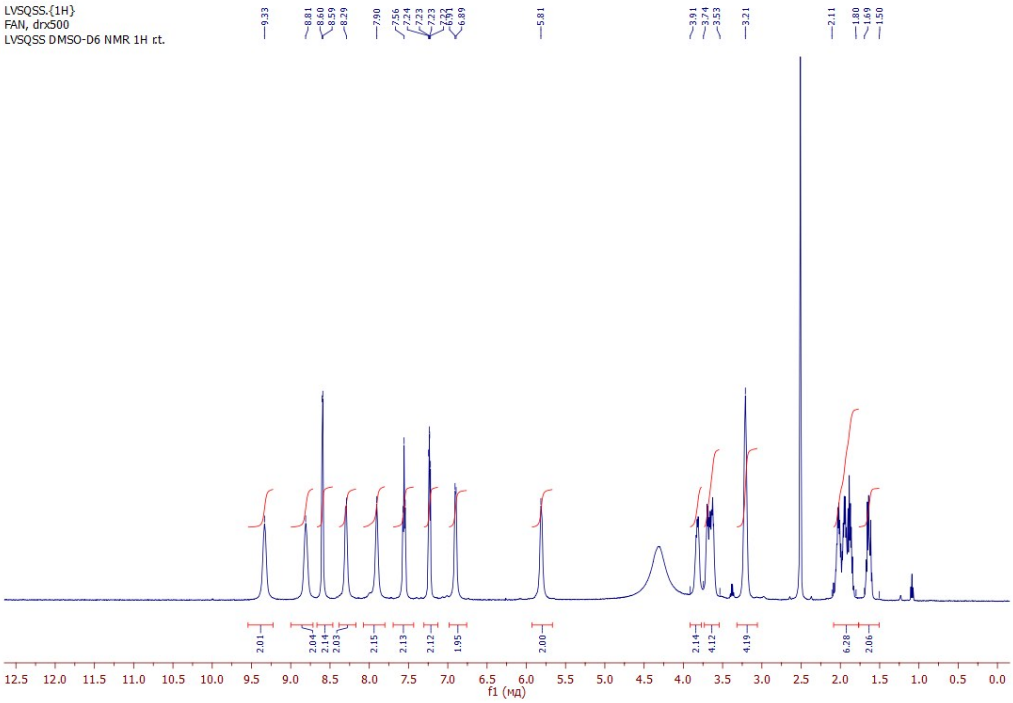
1

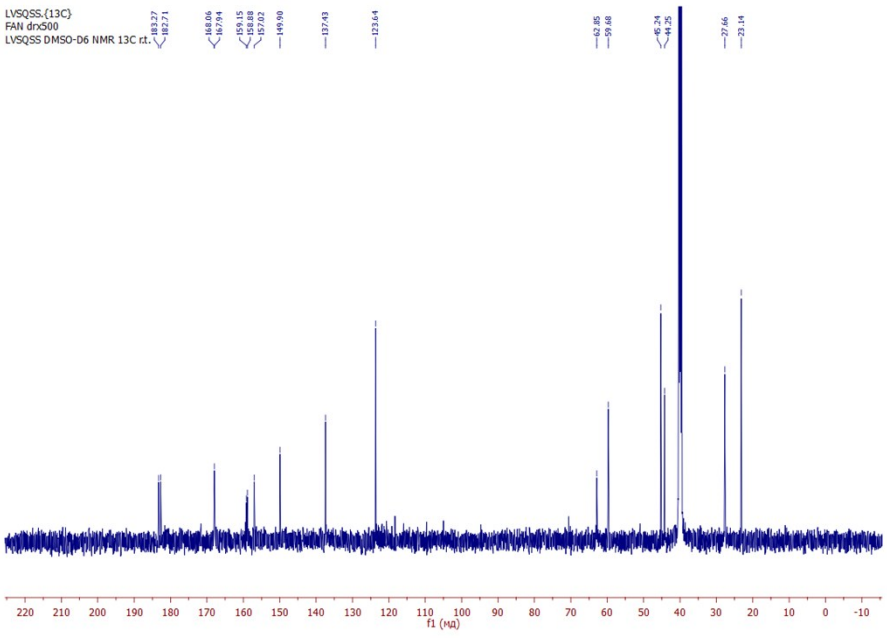




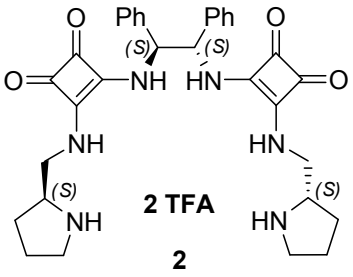
4,4'-(((1*S*,2*S*)-1,2-di(pyridin-2-yl)ethane-1,2-diyl)bis(azanediyl))bis(3-((((*S*)-pyrrolidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione) tetrafluoroacetate (*epi*-1)



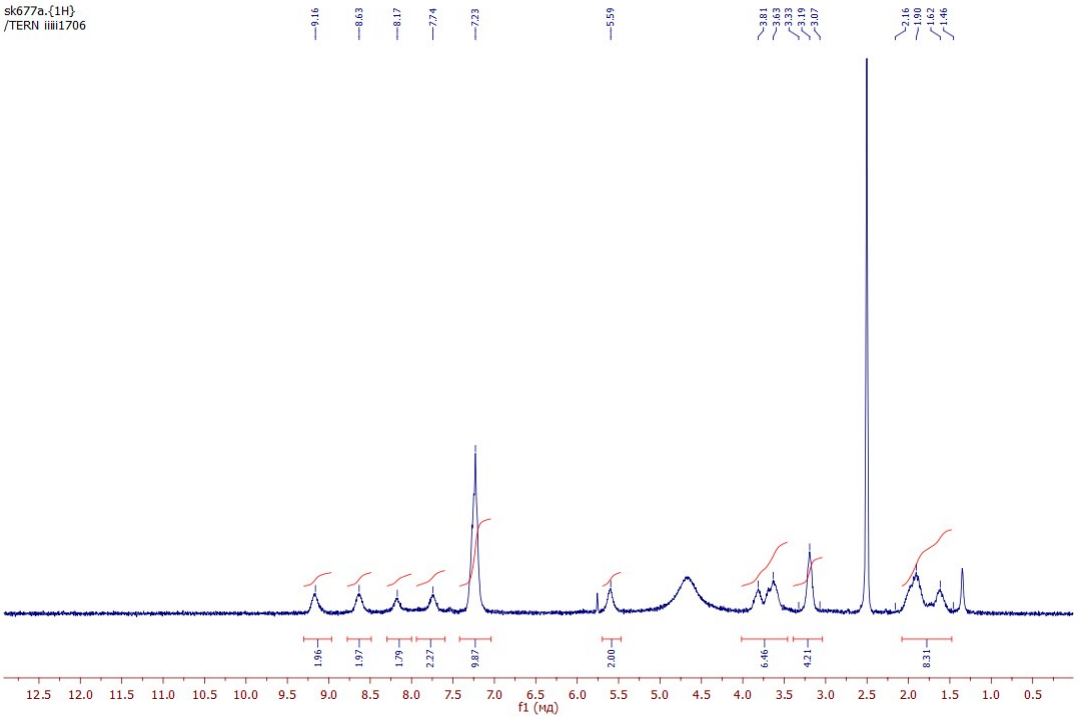


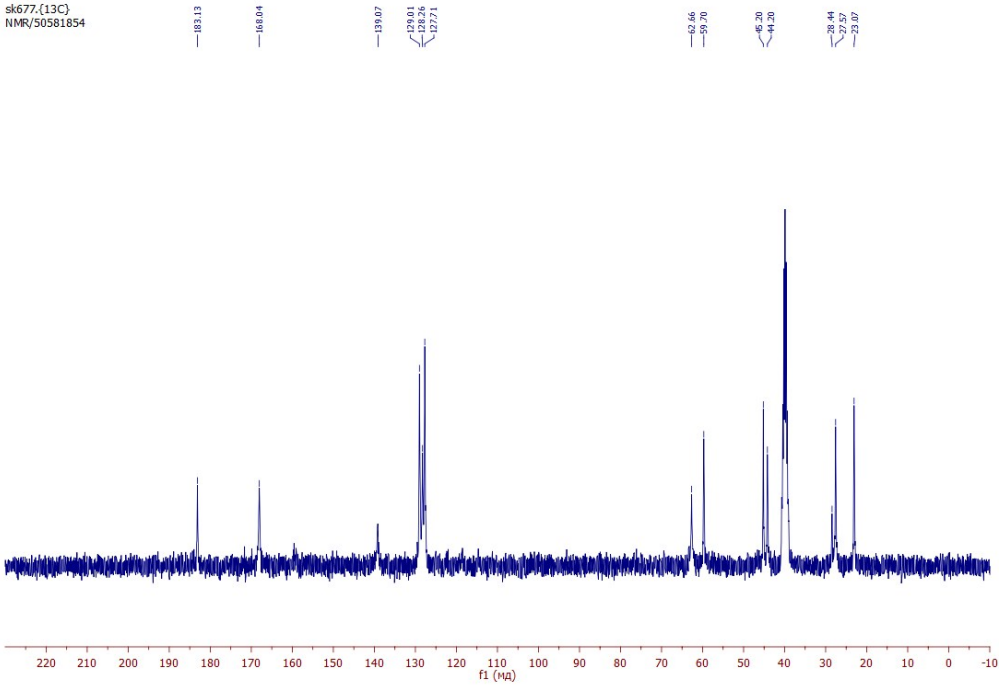


(2*S*,2'*S*)-2,2'-((((((1*S*,2*S*)-1,2-Diphenylethane-1,2-diyl)bis(azanediyl))bis(3,4-dioxocyclobut-1-ene-2,1-diyl))bis(azanediyl))bis(methylene))bis(pyrrolidin-1-ium) bistrifluoroacetate (2)

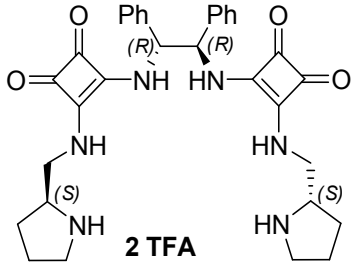


2

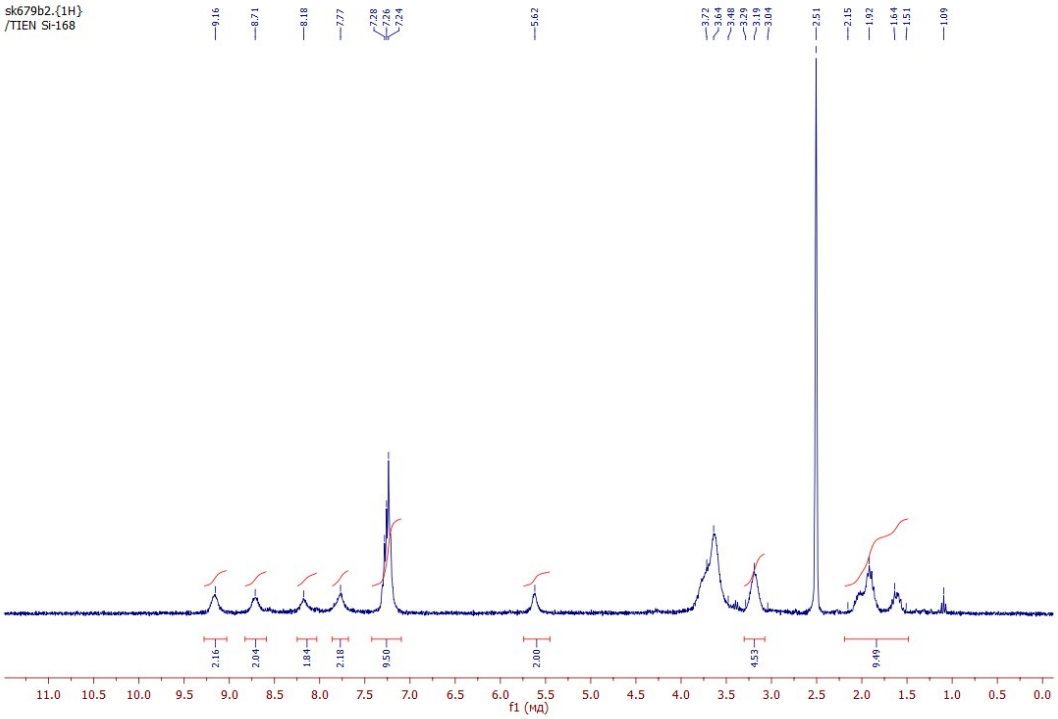


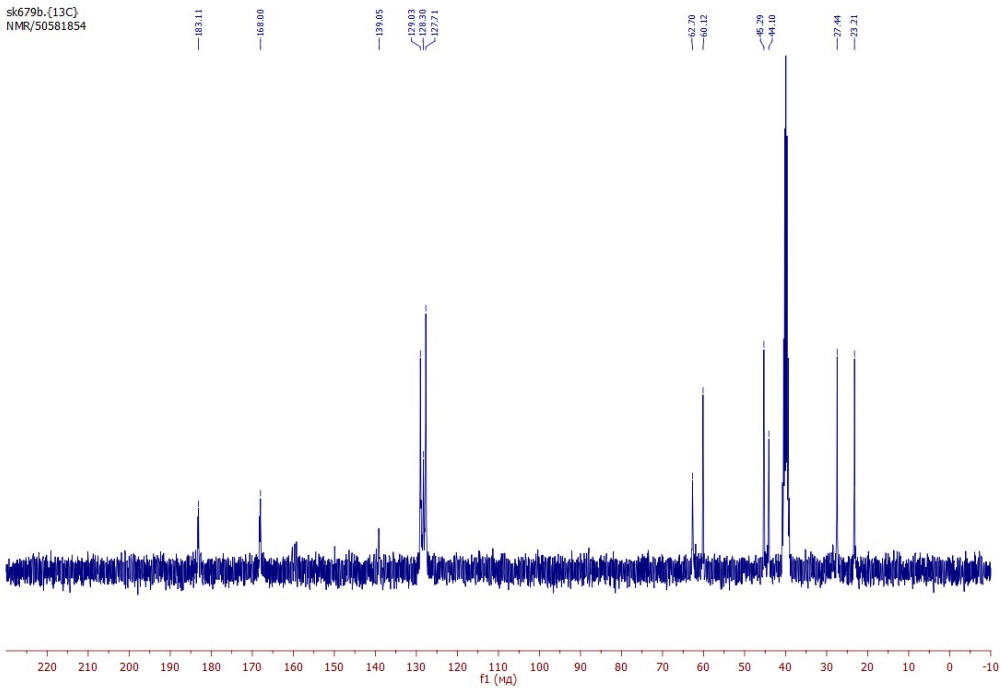


(2*S*,2'*S*)-2,2'-((((((1*R*,2*R*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))bis(3,4-dioxocyclobut-1-ene-2,1-diyl))bis(azanediyl))bis(methylene))bis(pyrrolidin-1-ium) bistrifluoroacetate (*epi*-2)

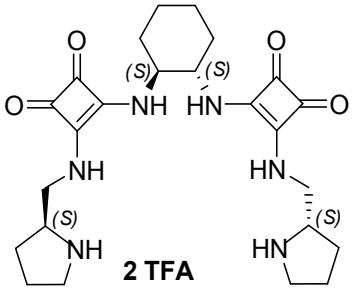


epi-**2**

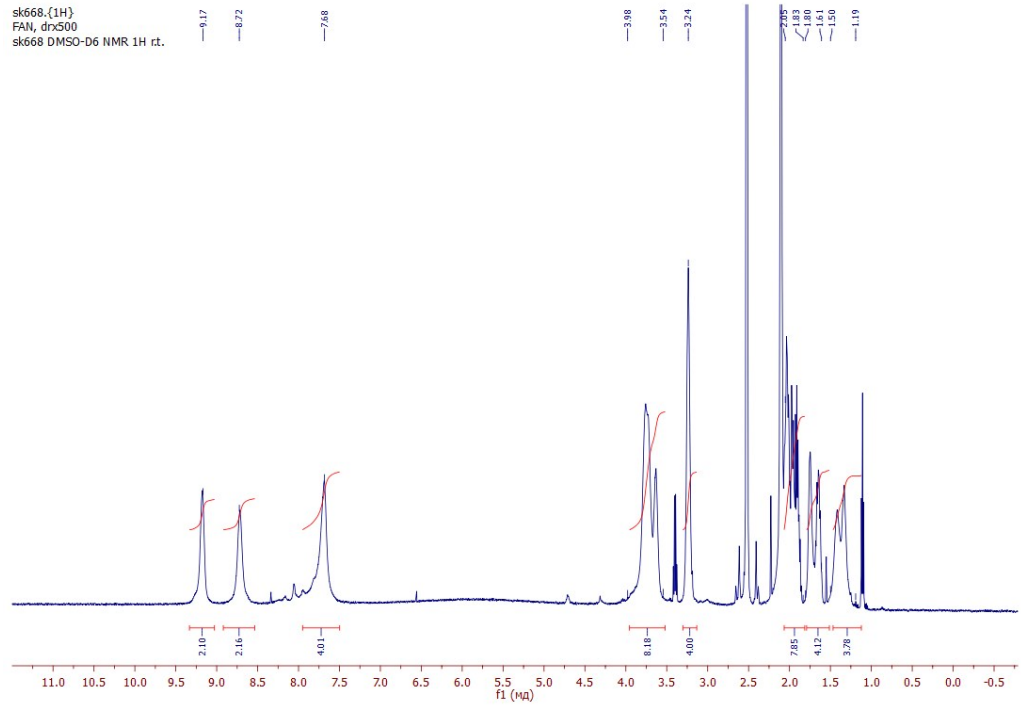


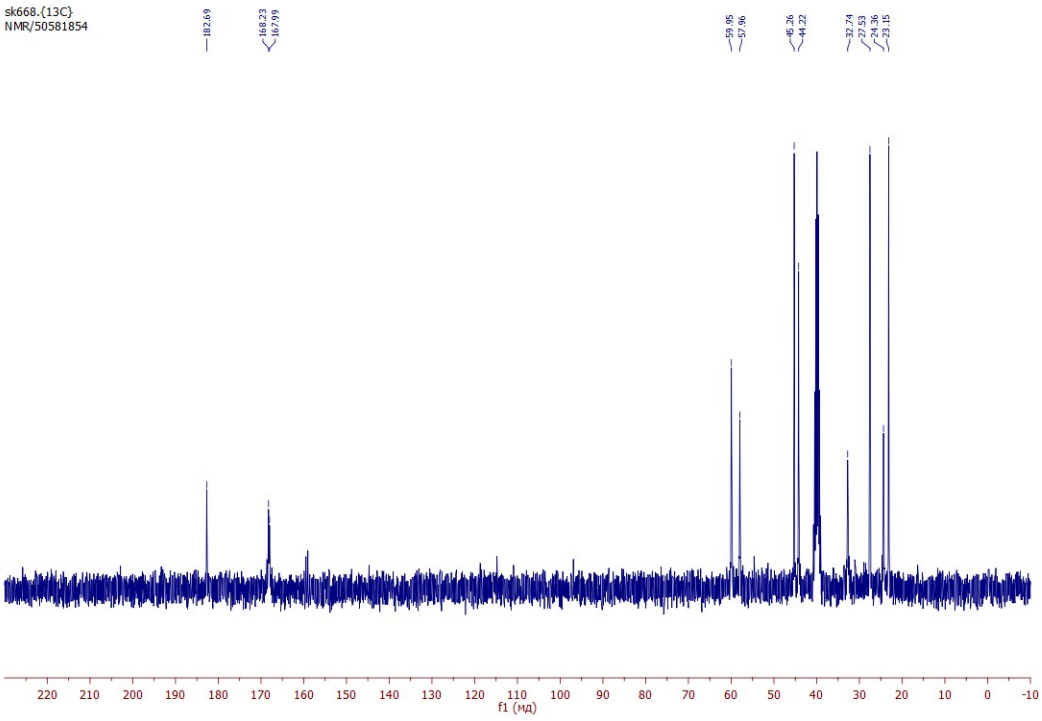


4,4'-(((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(azanediyl))bis(3-((((*S*)-pyrrolidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione) bistrifluoroacetate (3)

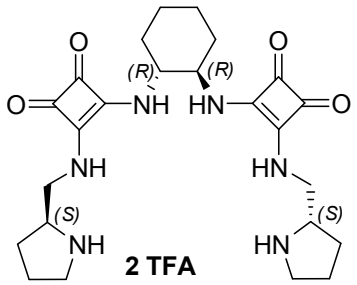


3

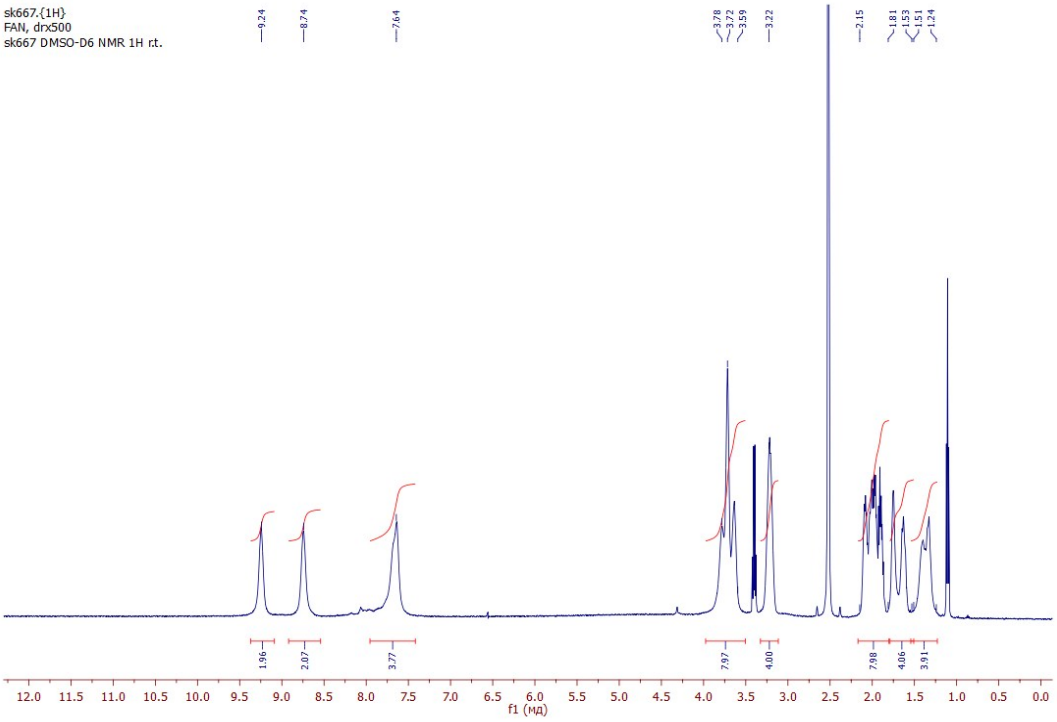


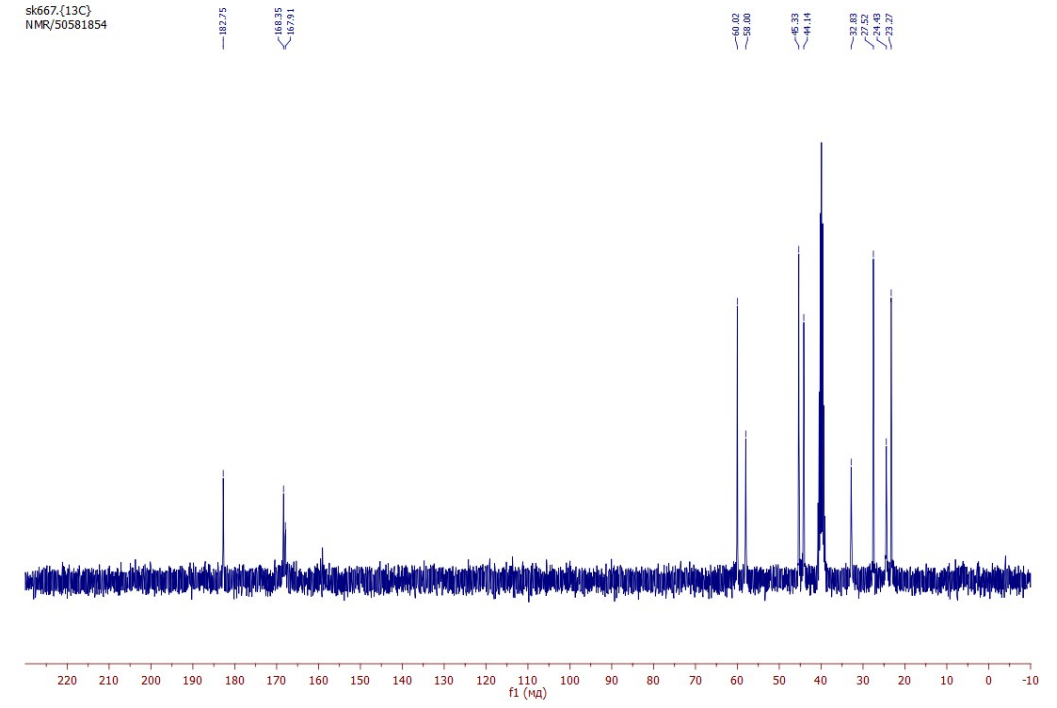


4,4'-(((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(azanediyl))bis(3-((((*S*)-pyrrolidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione) bistrifluoroacetate (*epi*-3)

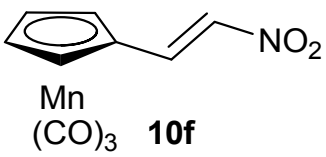


epi-**3**

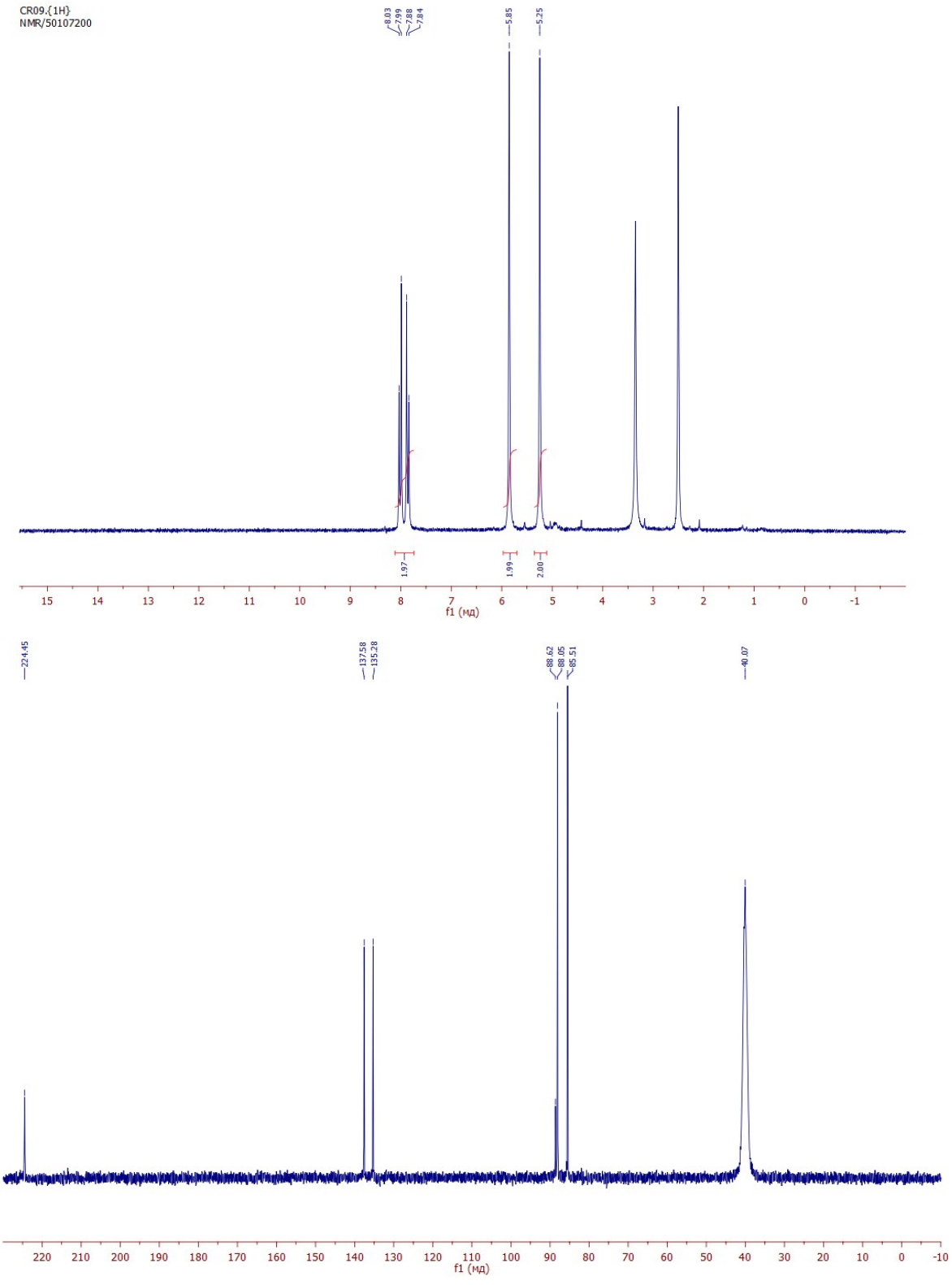




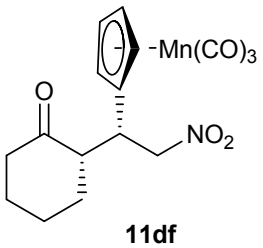
(*E*)-(2-nitrovinyl)cymantrene (10f)



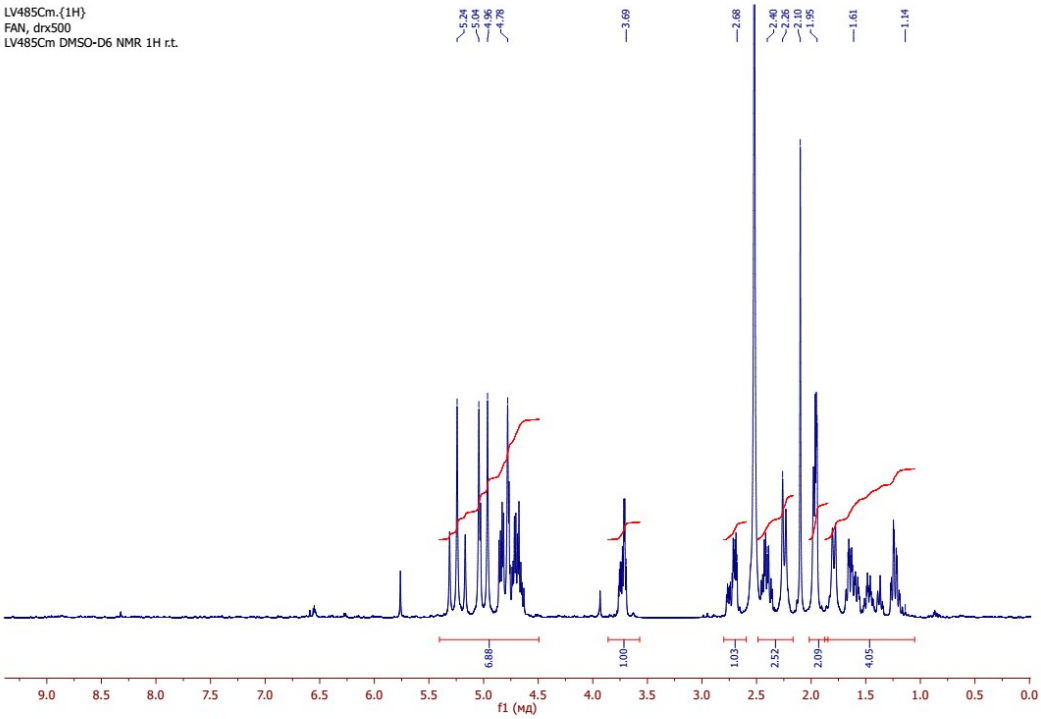
10f

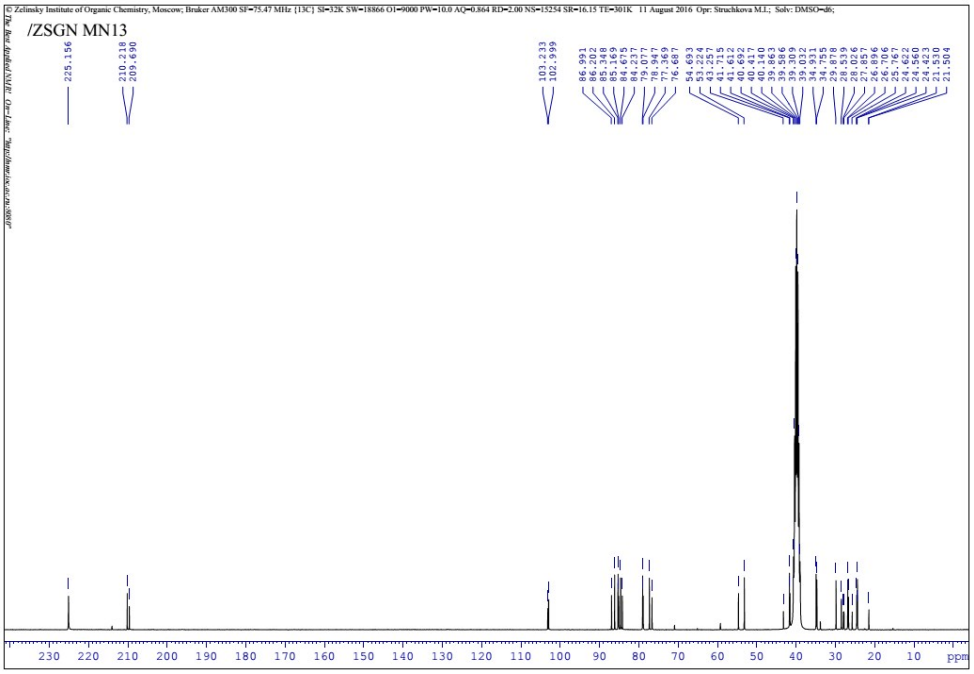


(*S*)-2-((*R*)-1-(cymantrenyl-3-yl)-2-nitroethyl)cyclohexanone (11df)



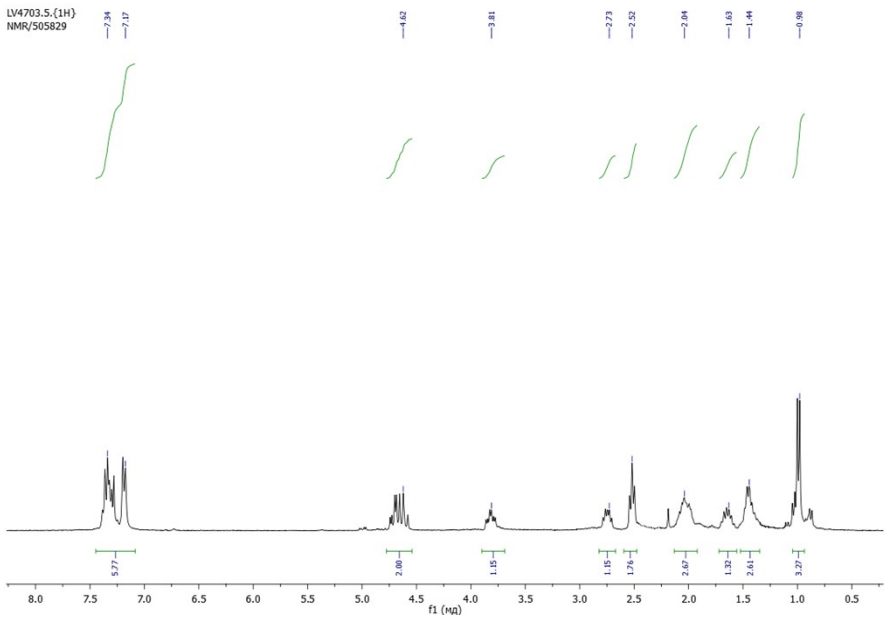
11df



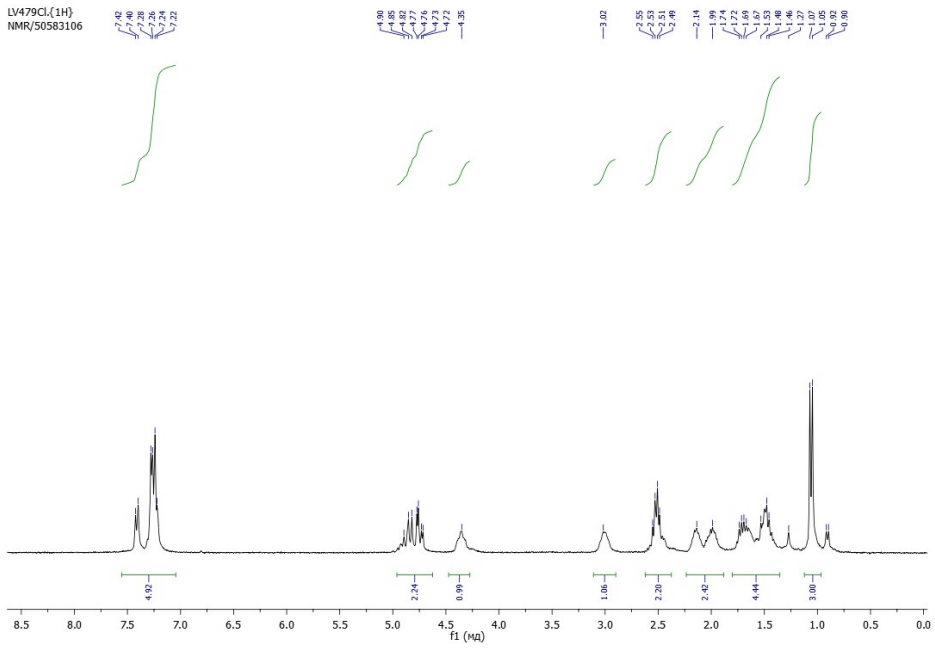


2. ^{1}H NMR data for known compounds 11 and 13 (for structural formulas see Section 3)

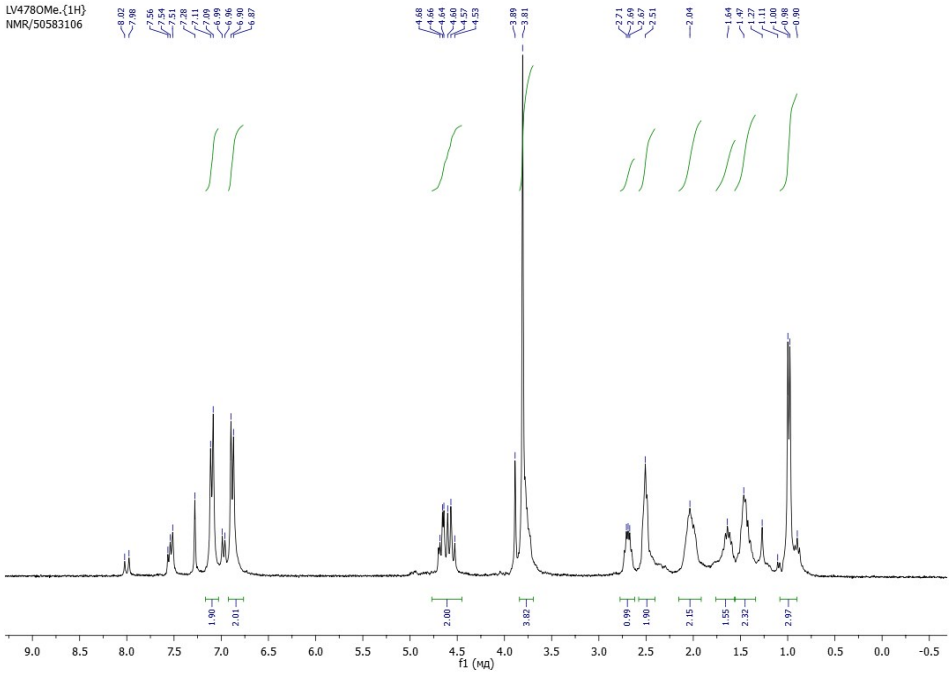
(2*S*,4*S*)-4-Methyl-2-((*R*)-2-nitro-1-phenylethyl)cyclohexan-1-one (11aa): ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98 (d, 3H, *J* = 6.6 Hz), 1.35−1.48 (m, 2H), 1.56−1.66 (m, 1H), 1.90−2.15 (m, 2H,), 2.50 (t, 2H, *J* = 6.59 Hz), 2.69−2.80 (m, 1H), 3.76−3.84 (m, 1H), 4.56−4.73 (m, 2H), 7.17−7.18 (m, 2H), 7.26−7.40 (m, 3H).



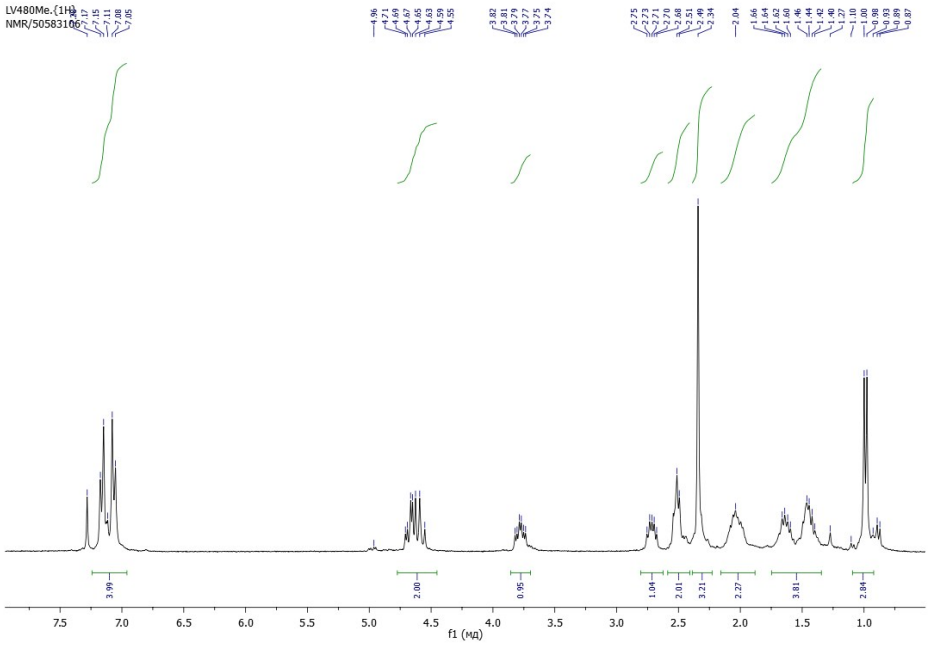
(2*S*,4*S*)-2-((*R*)-1-(2-Chlorophenyl)-2-nitroethyl)-4-methylcyclohexan-1-one (11ab): ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (d, 3H, *J* = 6.8 Hz), 1.41−1.56 (m, 2H), 1.65−1.74 (m, 1H), 1.92−2.03 (m, 1H), 2.08−2.17 (m, 1H), 2.46−2.53 (m, 2H), 2.94−3.03 (m, 1H), 4.30−4.38 (m, 1H), 4.70−4.88 (m, 2H), 7.20−7.28 (m, 3H), 7.37−7.46 (m, 1H).


LV479Cl.{1H}
NMR/50583106
7.42
7.40
7.38
7.26
7.24
7.22
4.90
4.85
4.82
4.77
4.76
4.73
4.72
4.35
3.02
2.55
2.53
2.51
2.49
2.14
1.99
1.74
1.72
1.69
1.67
1.53
1.48
1.46
1.27
1.07
1.05
0.92
0.90
4.92
2.24
0.99
1.08
2.20
2.42
4.44
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (мд)

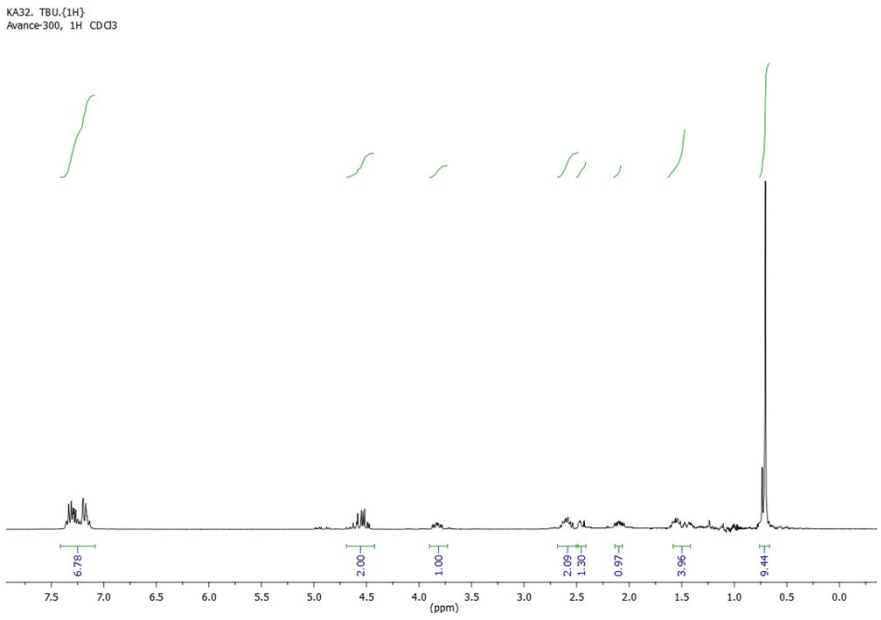
(2*S*,4*S*)-2-((*R*)-1-(4-Methoxyphenyl)-2-nitroethyl)-4-methylcyclohexan-1-one (11ac): ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98 (d, 3H, *J* = 6.8 Hz), 1.37–1.50 (m, 2H), 1.56–1.66 (m, 1H), 1.93–2.08 (m, 2H), 2.46–2.51 (m, 2H), 2.63–2.71 (m, 2H), 3.70–3.79 (m, 4H), 4.53–4.68 (m, 2H), 6.87–6.90 (m, 2H), 7.05–7.11 (m, 1H).



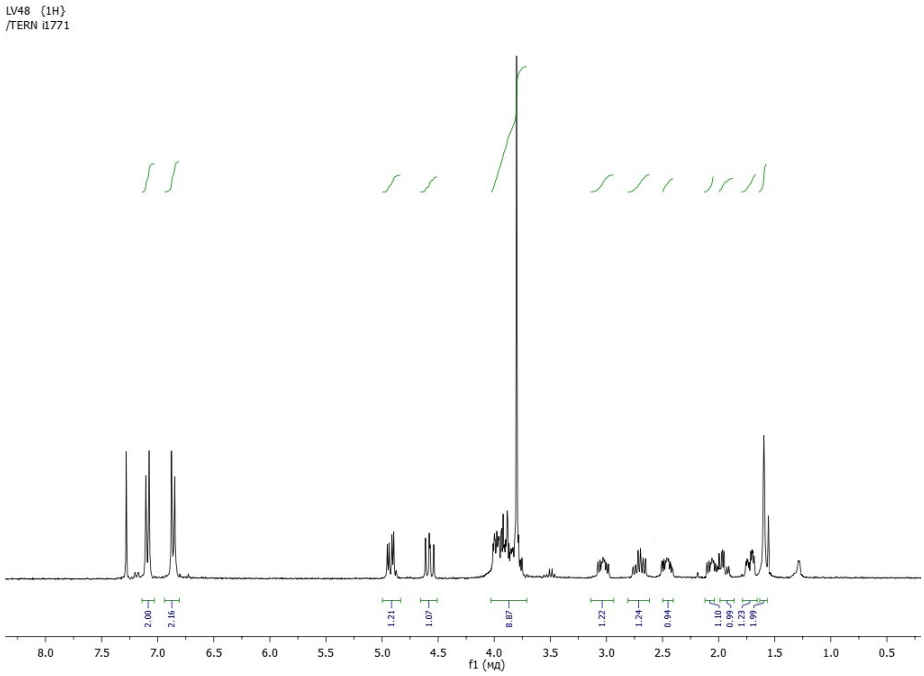
(2*S*,4*S*)-4-Methyl-2-((*R*)-2-nitro-1-(p-tolyl)ethyl)cyclohexan-1-one (11ad): ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (d, 3H, *J* = 6.6 Hz), 1.40–1.51 (m, 1H), 1.57–1.67 (m, 1H), 1.93–2.10 (m, 2H), 2.32 (s, 3H), 2.48–2.52 (m, 2H), 2.66 – 2.74 (m, 1H), 3.72 – 3.80 (m, 1H), 4.53–4.69 (m, 2H), 7.03–7.17 (m, 4H).



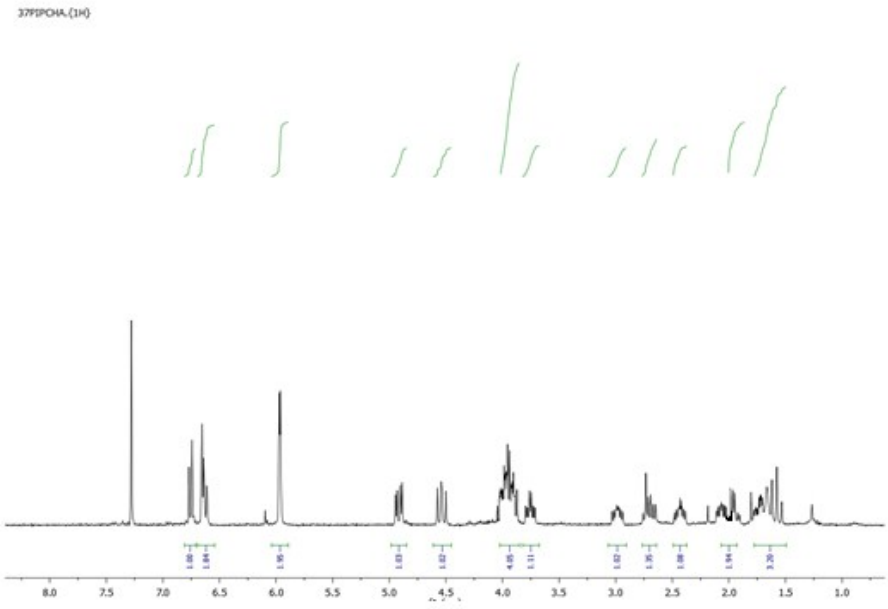
(2*S*,4*S*)-4-(*tert*-Butyl)-2-((*R*)-2-nitro-1-phenylethyl)cyclohexan-1-one (11ba): ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.73 (s, 9H), 1.32-1.65 (m, 4H), 2.03-2.15 (m, 1H), 2.43-2.50 (m, 1H), 2.54-2.70 (m, 2H), 3.78-3.90 (m, 1H), 4.49-4.64 (m, 2H), 7.18-7.21 (m, 2H), 7.28-7.38 (m, 3H).



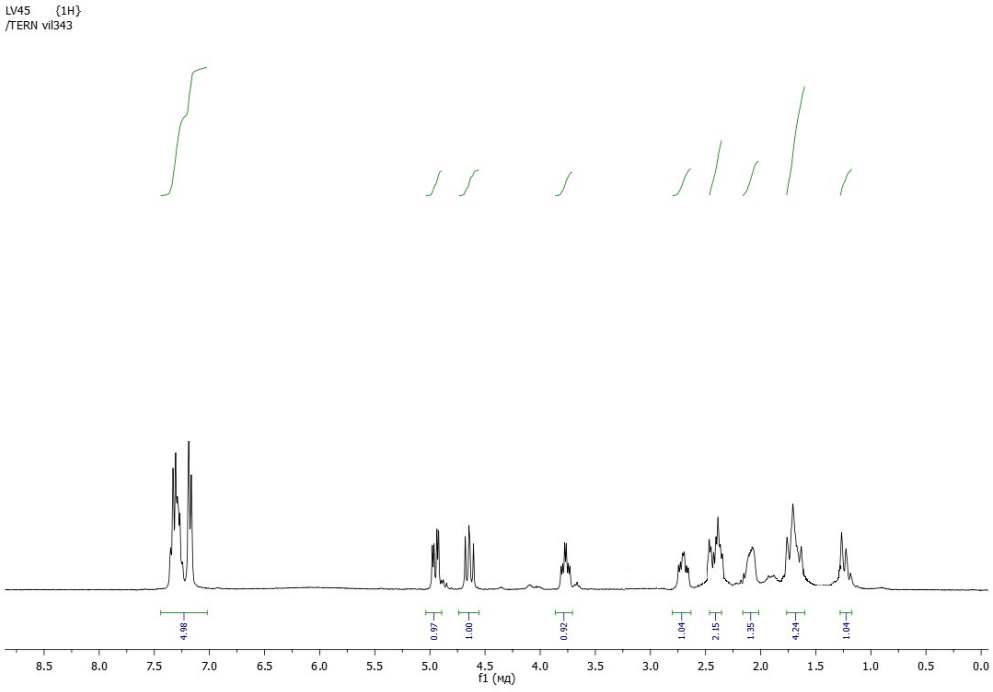
(*S*)-7-((*R*)-1-(4-Methoxyphenyl)-2-nitroethyl)-1,4-dioxaspiro[4.5]decan-8-one (11cc): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.08 (d, 2H, *J* = 8.7 Hz), 6.85 (d, 2H, *J* = 8.7 Hz), 4.93-4.89 (dd, 1H, *J* = 12.3 Hz, 4.8 Hz), 4.58 - 4.54 (dd, 1H, *J* = 12.3 Hz, 9.9 Hz), 4.0-3.83 (m, 4H), 3.79 (s, 3H), 3.0 - 2.9 (m, 1H), 2.72 - 2.66 (dt, 1H, *J* = 13.8 Hz, 6.4 Hz), 2.48-2.44 (m, 1H), 2.07-1.92 (m, 2H), 1.72-1.68 (m, 1H), 1.57-1.51 (m, 2H).


LV48 {1H}
/TERN il771
2.00
2.16
1.21
1.07
8.87
1.22
1.24
0.94
1.10
0.99
1.23
1.98
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (мд)

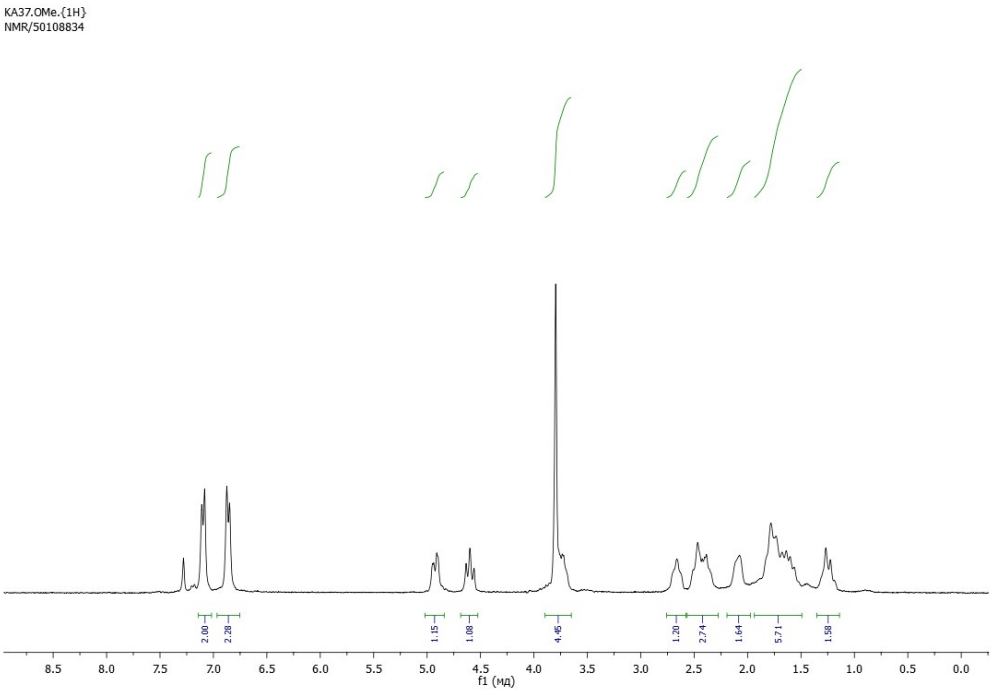
(*S*)-7-((*R*)-1-(Benzo[d][1,3]dioxol-5-yl)-2-nitroethyl)-1,4-dioxaspiro[4.5]decan-8-one (11ce): ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.8 (d, 1H, *J* = 8.0 Hz,), 6.6 - 6.63 (m, 2H), 5.99 (m, 2H,), 4.94-4.89 (dd, 1H, *J* = 12.4 Hz, 4.5 Hz), 4.57-4.53 (dd, 1H, *J* = 12.4 Hz, 10.1 Hz), 4.02-3.88 (m, 4H), 3.80-3.70 (dt, 1H, *J* = 10.1 Hz, 4.7 Hz), 3.02-2.97 (m, 1H), 2.74-2.68 (dt, 1H, *J* = 13.5 Hz, 6.4 Hz), 2.49-2.45 (m, 1H), 2.07-2.04 (m, 1H), 2.0-1.9 (dt, 1H, *J* = 13.3 Hz, 5.2 Hz), 1.77-1.73 (m, 1H), 1.59 (m, 1H).



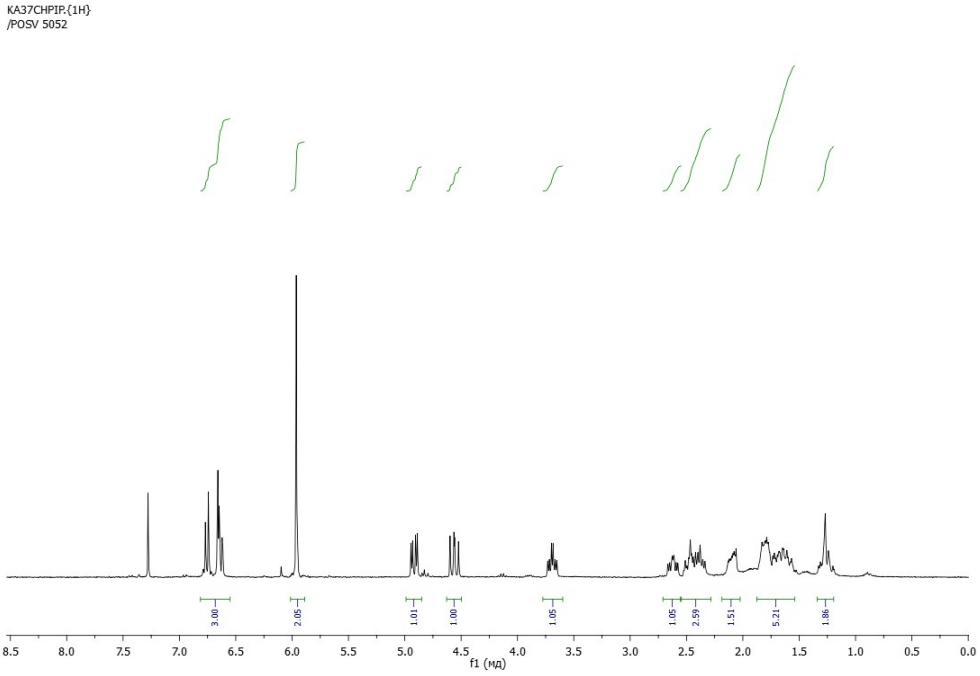
(*S*)-2-((*R*)-2-Nitro-1-phenylethyl)cyclohexan-1-one (11da): ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.29 -7.37 (m, 3H), 7.19 (d, *J* = 6.6 Hz, 2H), 4.97 (dd, *J* = 4.5, 12.5 Hz, 1H), 4.65 (dd, *J* = 10, 12.4 Hz, 1H), 3.78 (dt, *J* = 4.5, 10.0 Hz, 1H), 2.67-2.76 (m, 1H), 2.36-2.52 (m, 2H), 2.08-2.13 (m, 1H), 1.61-1.82 (m, 4H), 1.24-1.32 (m, 1H).



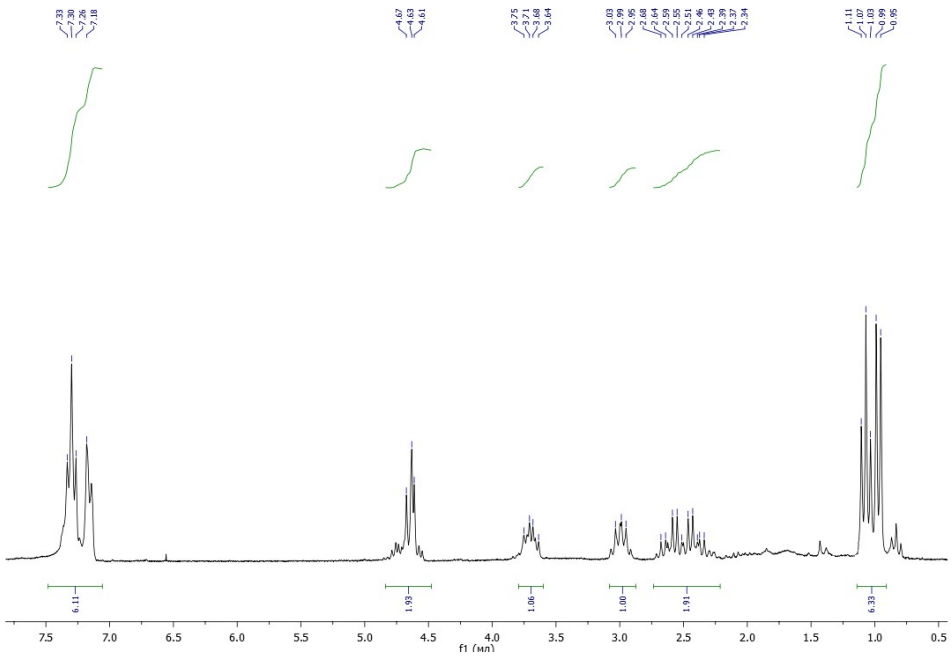
(*S*)-2-((*R*)-1-(4-Methoxyphenyl)-2-nitroethyl)cyclohexan-1-one (11dc): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.06 (d, *J* = 8.3 Hz, 2H), 6.82 (d, *J* = 8.9 Hz, 2H), 4.94 (dd, *J* = 4.5, 12.2 Hz, 1H), 4.56 (dd, *J* = 10.2, 12.3 Hz, 1H), 3.75 (s, 3H), 3.72 (m, 1H), 2.65–2.63(m, 1H), 2.54–2.43 (m, 1H), 2.44–2.36 (m, 1H), 2.13–2.06 (m, 1H), 1.82–1.57 (m, 4H), 1.27–1.20 (m, 1H).



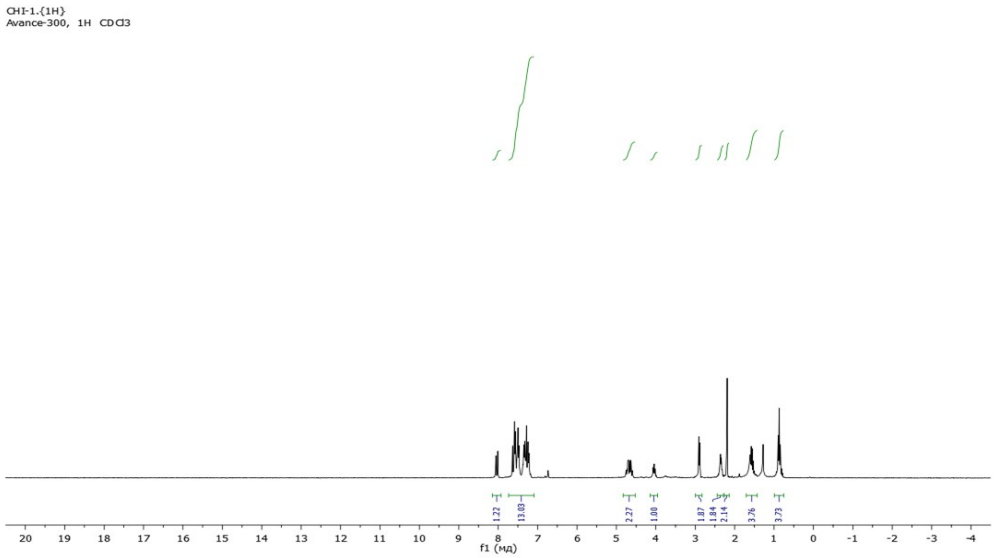
(*S*)-2-((*R*)-1-(Benzo[d][1,3]dioxol-5-yl)-2-nitroethyl)cyclohexan-1-one (11de): ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.19–1.22 (m, 1H), 1.56–1.69 (m, 2H), 1.78 (m, 2H), 2.06 (m, 1H), 2.33–2.48 (m, 2H), 2.58–2.62 (m, 1H), 3.65–3.68 (m, 1H), 4.54 (t, *J* = 11.0 Hz, 1H), 4.89 (dd, *J* = 2.8, 12.0 Hz, 1H), 5.94 (s, 2H), 6.61 (d, *J* = 7.6 Hz, 1H), 6.64 (s, 1H), 6.73 (d, *J* = 7.6 Hz, 1H).



(4*S*,5*R*)-4-Methyl-6-nitro-5-phenylhexan-3-one (**13a**)**:** ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.95 (d, 3H, *J* = 7.0 Hz), 1.09 (t, 3H, *J* = 7.5 Hz), 2.43 (dq, 1H, *J* = 7.5, 18.0 Hz), 2.64 (dq, 1H, *J* = 7.0, 18.0 Hz), 2.98 - 3.06 (m, 1H), 3.74 (m, 1H), 4.62 (m, 1H), 4.70 (m, 1H), 7.18 –7.21 (m, 2H), 7.30–7.40 (m, 3H).

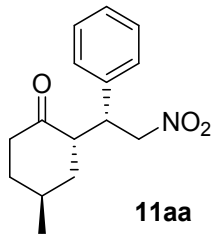


(*R*)-1-Nitro-2-phenylheptan-4-one (13b):^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.6 Hz), 1.58 (m, 4H,), 2.20 (m, 2H,), 2.39 (m, 2H), 4.10 (m, 1H), 4.60 (m, 2H), 7.18–7.37 (m, 5H).



3. HPLC DATA

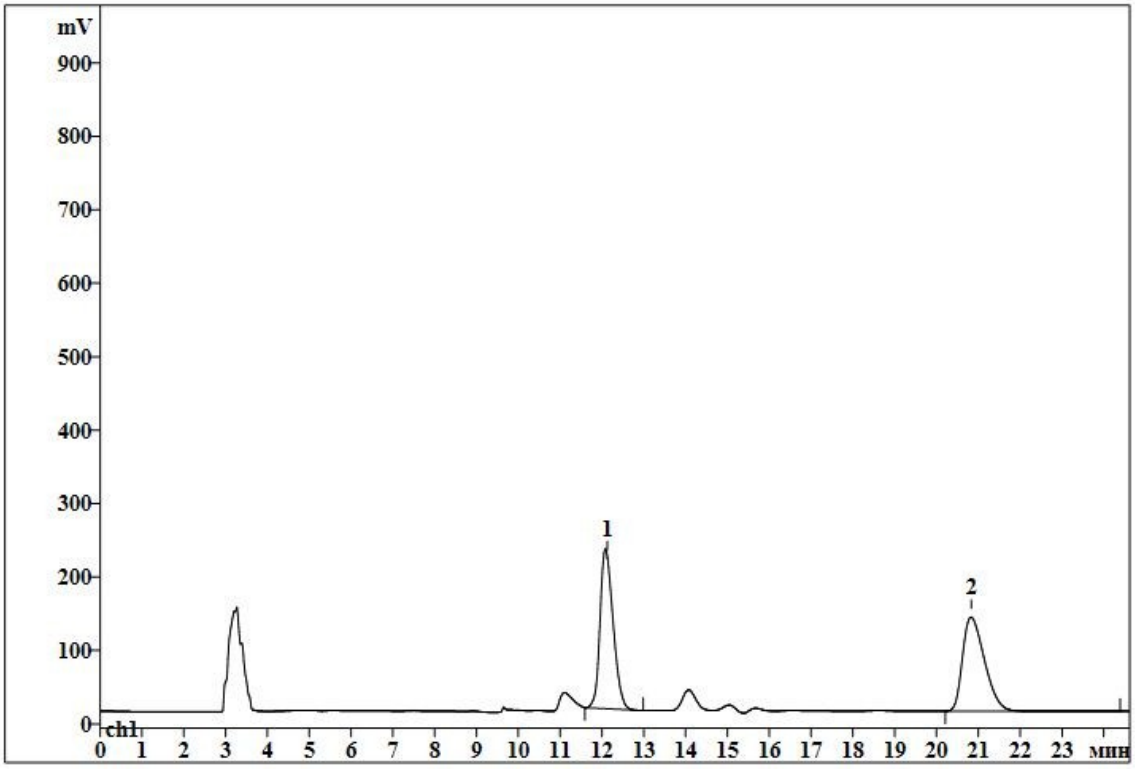
(2*S*,4*S*)-4-methyl-2-((*R*)-2-nitro-1-phenylethyl)cyclohexan-1-one (11aa).



11aa

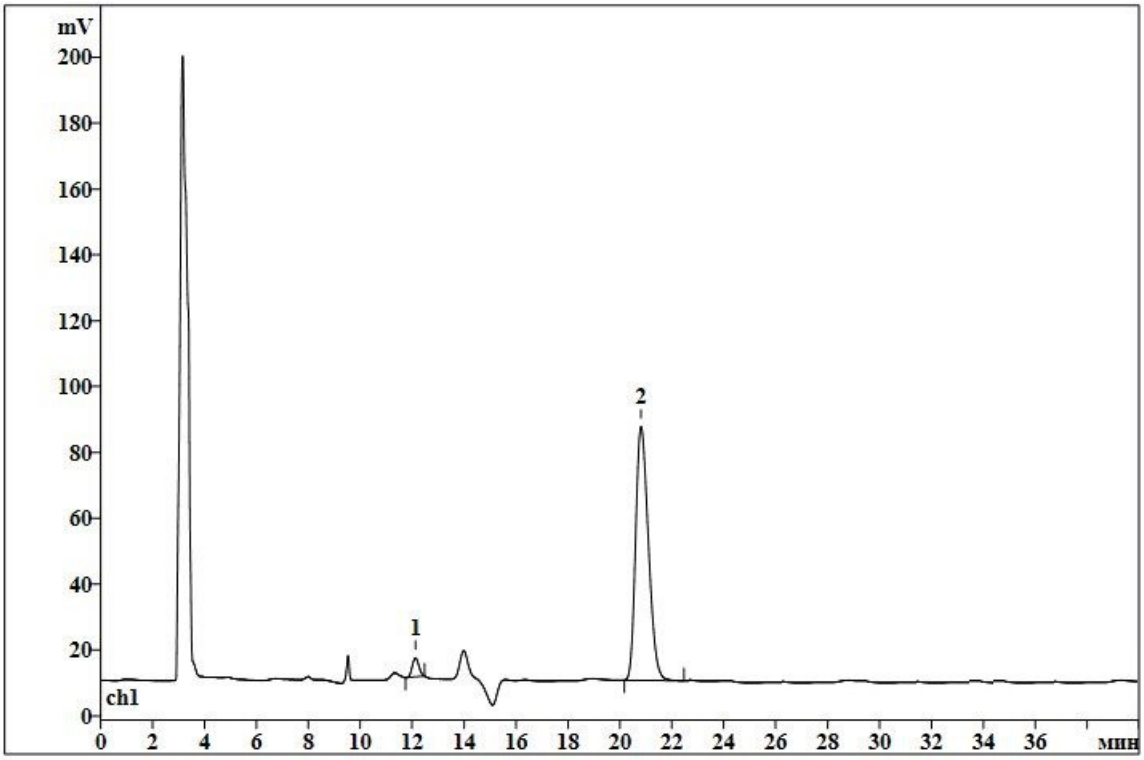
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ =220 nm), t_R = 12.1 min (minor), t_R = 20.8 min (major).

***rac*-11aa**



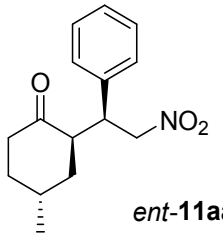
No	Retention мин	Area mV*сек	Area %	Name
1	12.13	4727.86	50.25	
2	20.82	4679.94	49.75	
2	24.62	9407.80	100.00	

11aa



No	Retention мин	Area mV*сек	Area %	Name
1	12.12	100.51	3.68	
2	20.81	2629.78	96.32	
2	22.89	2730.28	100.00	

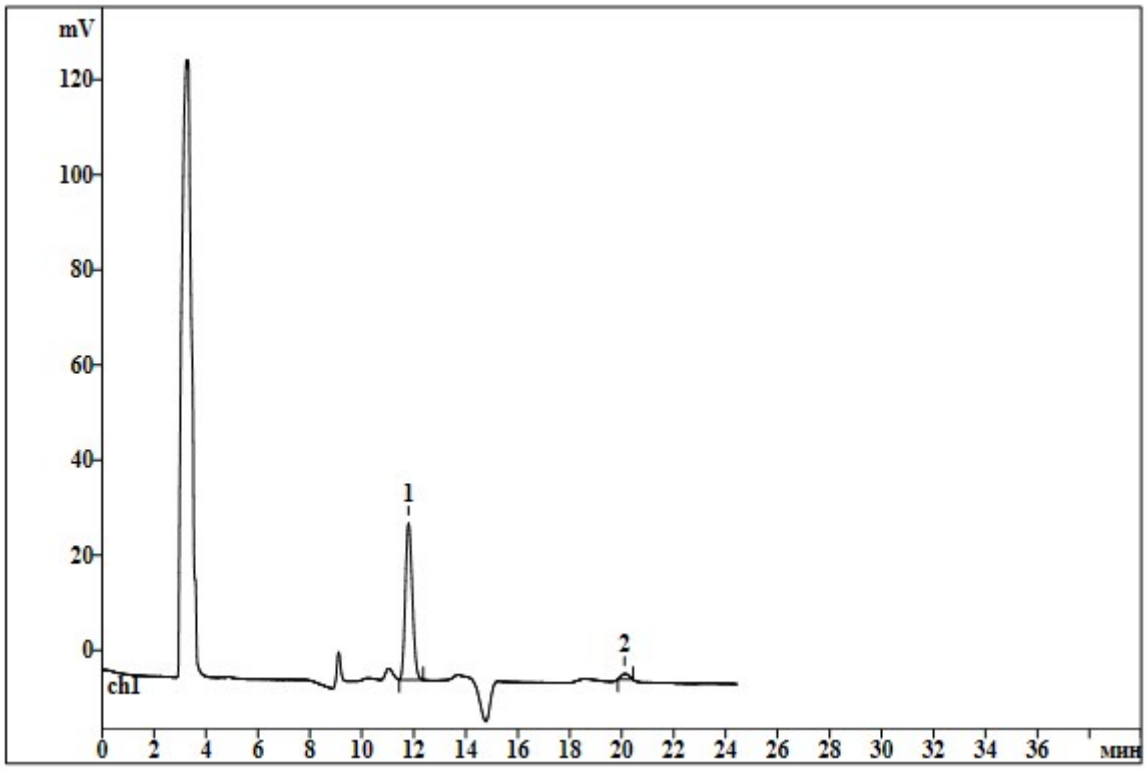
(2*R*,4*R*)-4-methyl-2-((*S*)-2-nitro-1-phenylethyl)cyclohexan-1-one (*ent*-11aa).



ent-**11aa**

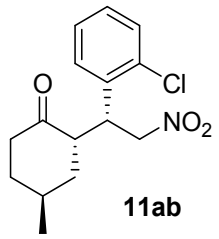
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ =220 nm), t_R = 12.1 min (major), t_R = 20.8 min (minor).

***ent*-11aa**



No	Retention мин	Area mV*сек	Area Name %
1	11.79	615.17	96.18
2	20.1	24.43	3.82
2	24.44	639.60	100.00

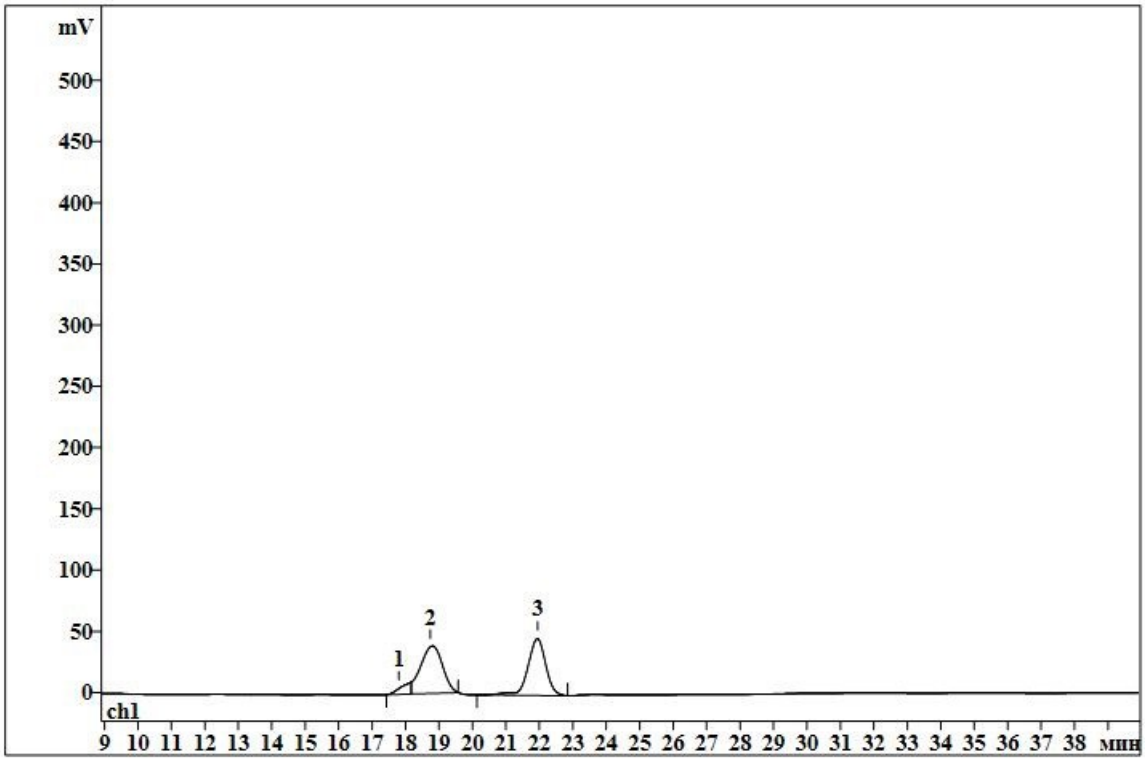
(2*S*,4*S*)-2-((*R*)-1-(2-chlorophenyl)-2-nitroethyl)-4-methylcyclohexan-1-one (11ab).



11ab

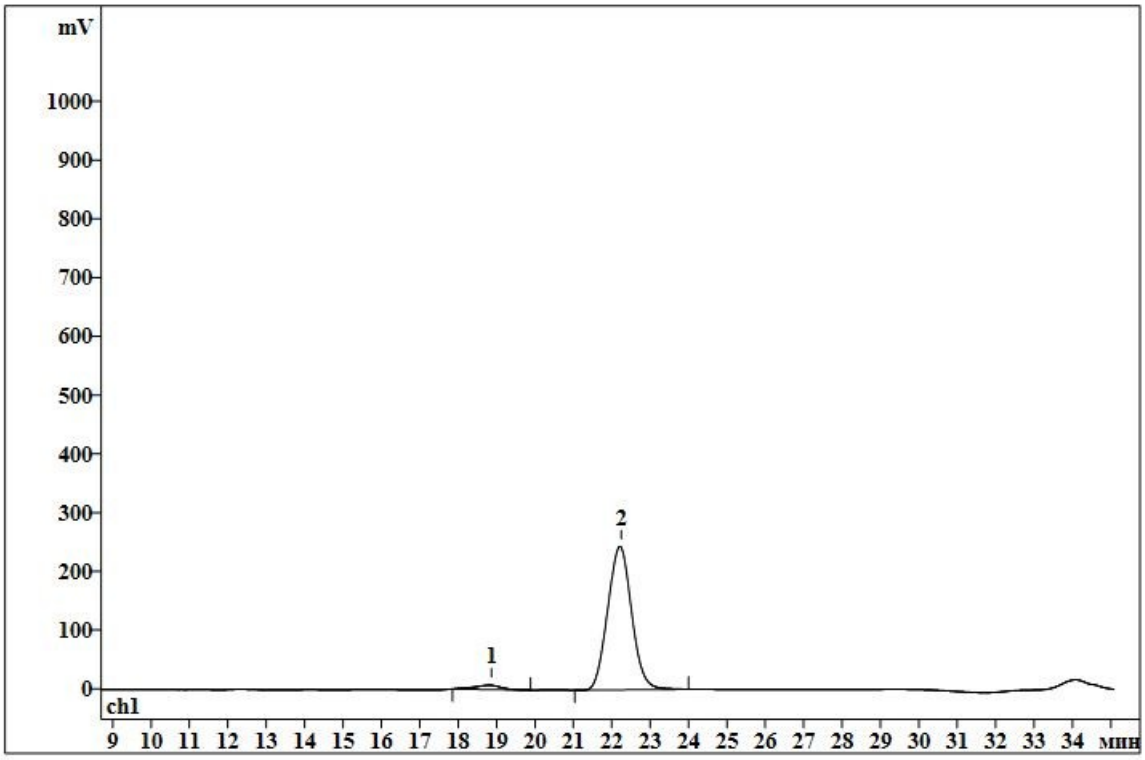
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ =220 nm), t_R = 18.8 min (minor), t_R = 21.9 min (major).

***rac*-11ab**



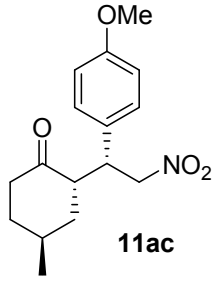
No	Retention мин	Area mV*сек	Area %	Name
1	17.79	206.50	5.57	
2	18.74	1764.16	47.61	
3	21.94	1734.88	46.82	
3	31.28	3705.54	100.00	

11ab



No	Retention мин	Area mV*сек	Area %	Name
1	18.87	347.00	3.17	
2	22.25	10601.95	96.83	
2	35.09	10948.95	100.00	

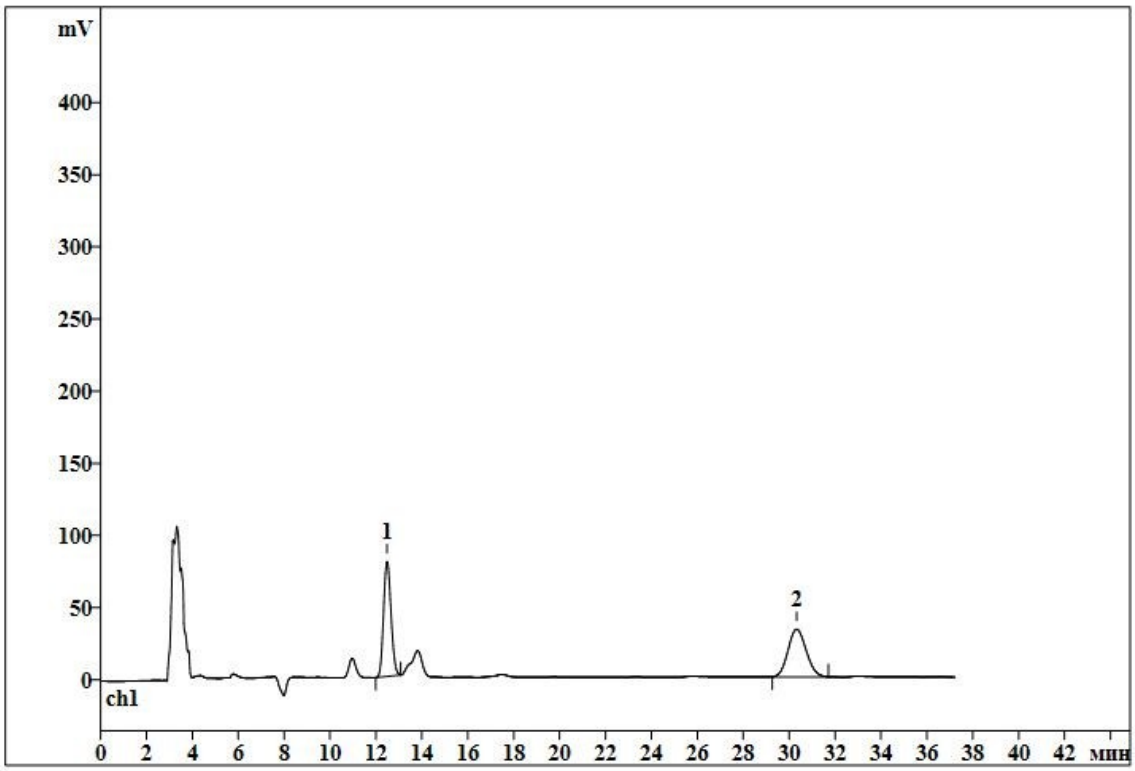
(2*S*,4*S*)-2-((*R*)-1-(4-methoxyphenyl)-2-nitroethyl)-4-methylcyclohexan-1-one (11ac).



11ac

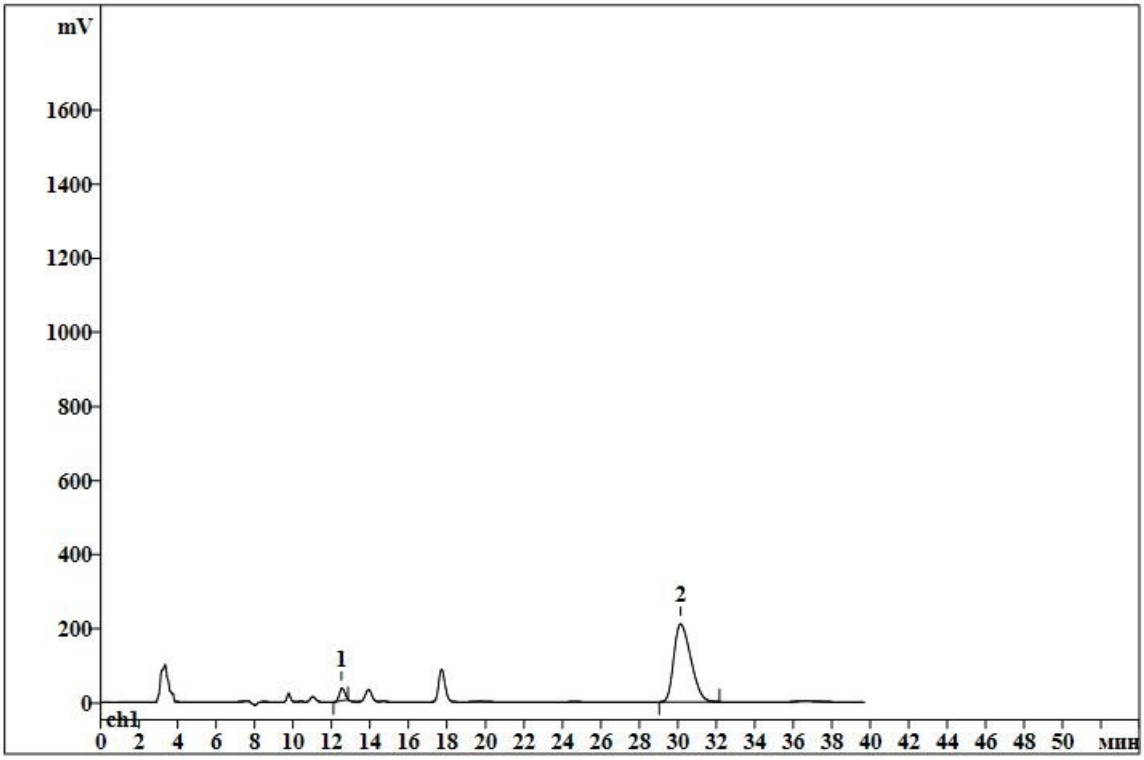
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ =220 nm), t_R = 12.5 min (minor), t_R = 30.3 min (major).

***rac*-11ac**



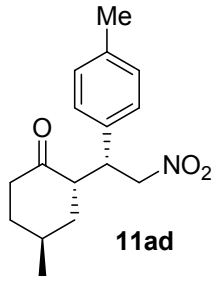
No	Retention мин	Area mV*сек	Area %	Name
1	12.48	1805.14	49.89	
2	30.32	1813.30	50.11	
2	37.22	3618.44	100.00	

11ac



No	Retention мин	Area mV*сек	Area %	Name
1	12.54	646.94	4.75	
2	30.14	12978.23	95.25	
2	39.69	13625.16	100.00	

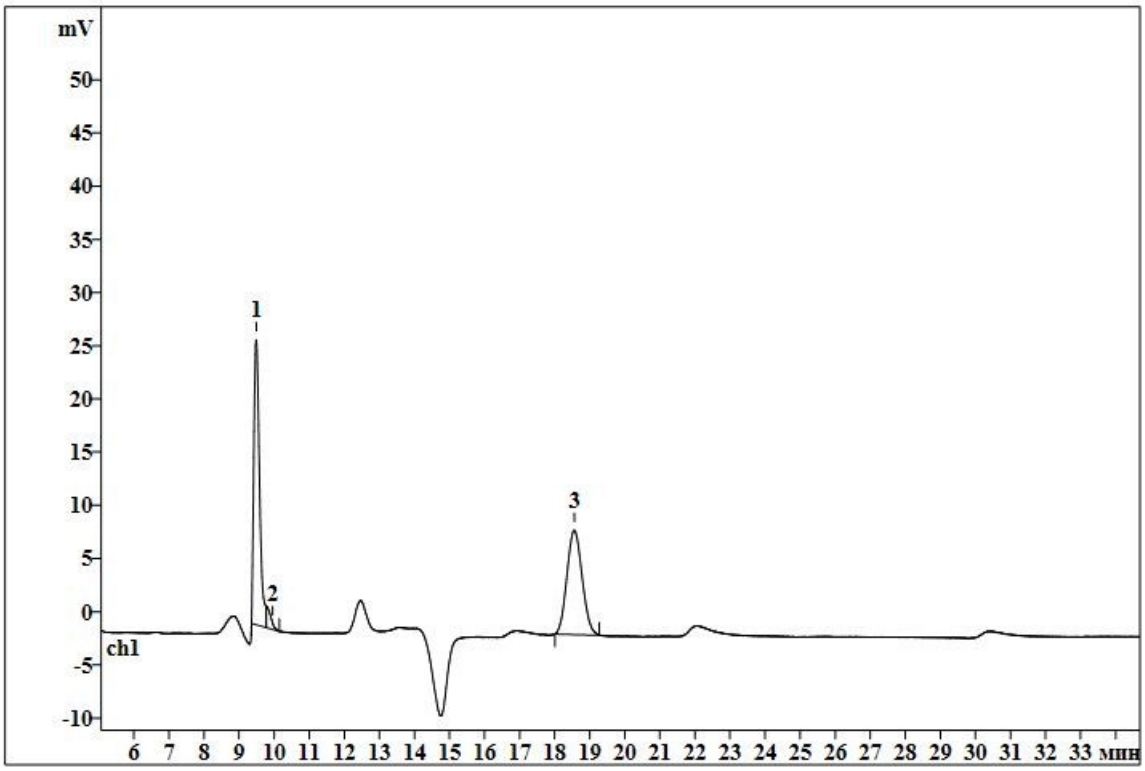
(2*S*,4*S*)-4-methyl-2-((*R*)-2-nitro-1-(p-tolyl)ethyl)cyclohexan-1-one (11ad).



11ad

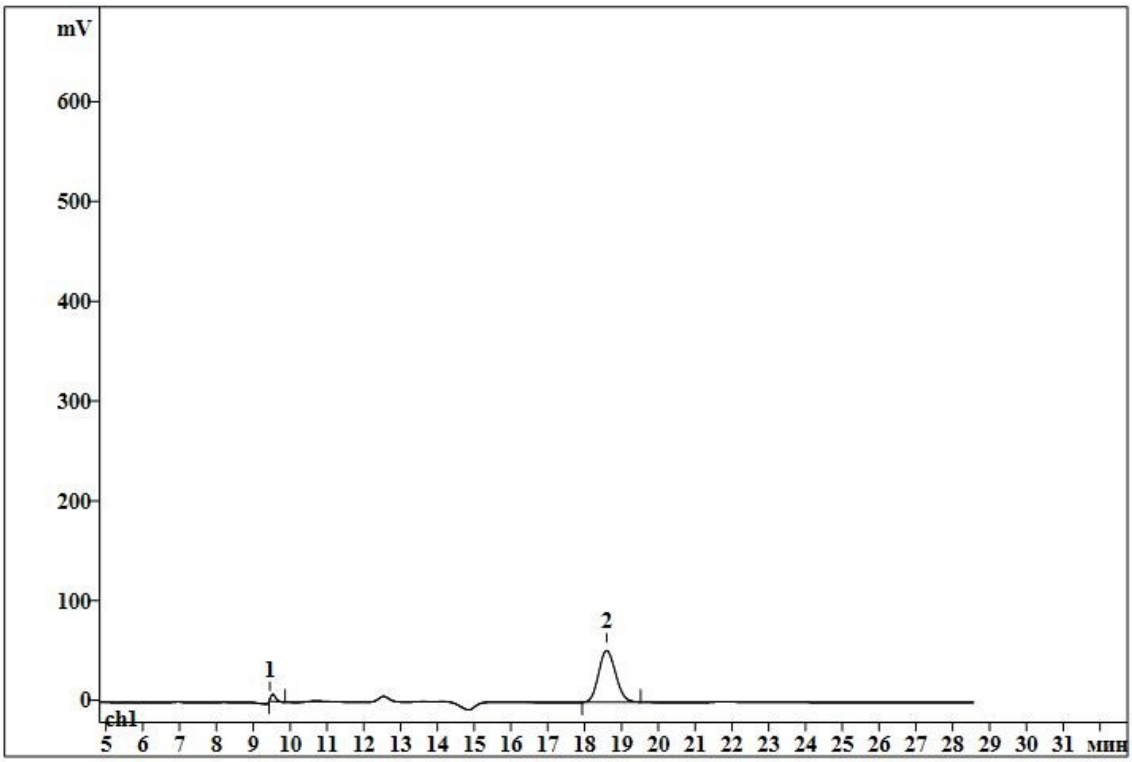
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ =220 nm), t_R = 9.5 min (minor), t_R = 18.6 min (major).

***rac*-11ad**



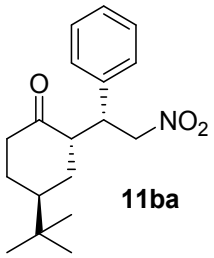
No	Retention мин	Area mV*сек	Area %	Name
1	9.482	301.95	49.10	
2	9.956	17.76	2.89	
3	18.55	295.21	48.01	
3	41.95	614.92	100.00	

11ad



No	Retention мин	Area mV*сек	Area %	Name
1	9.445	68.41	3.95	
2	18.6	1662.37	96.05	
2	28.57	1730.77	100.00	

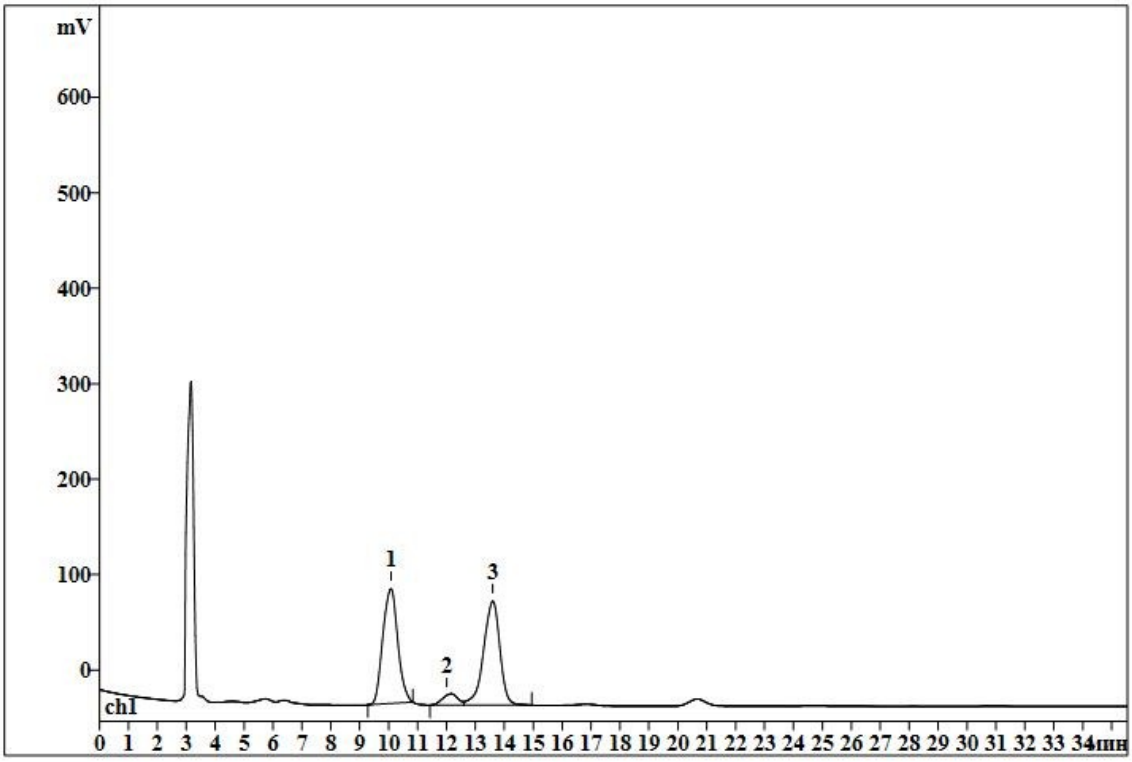
(2*S*,4*S*)-4-(tert-butyl)-2-((*R*)-2-nitro-1-phenylethyl)cyclohexan-1-one (11ba).



11ba

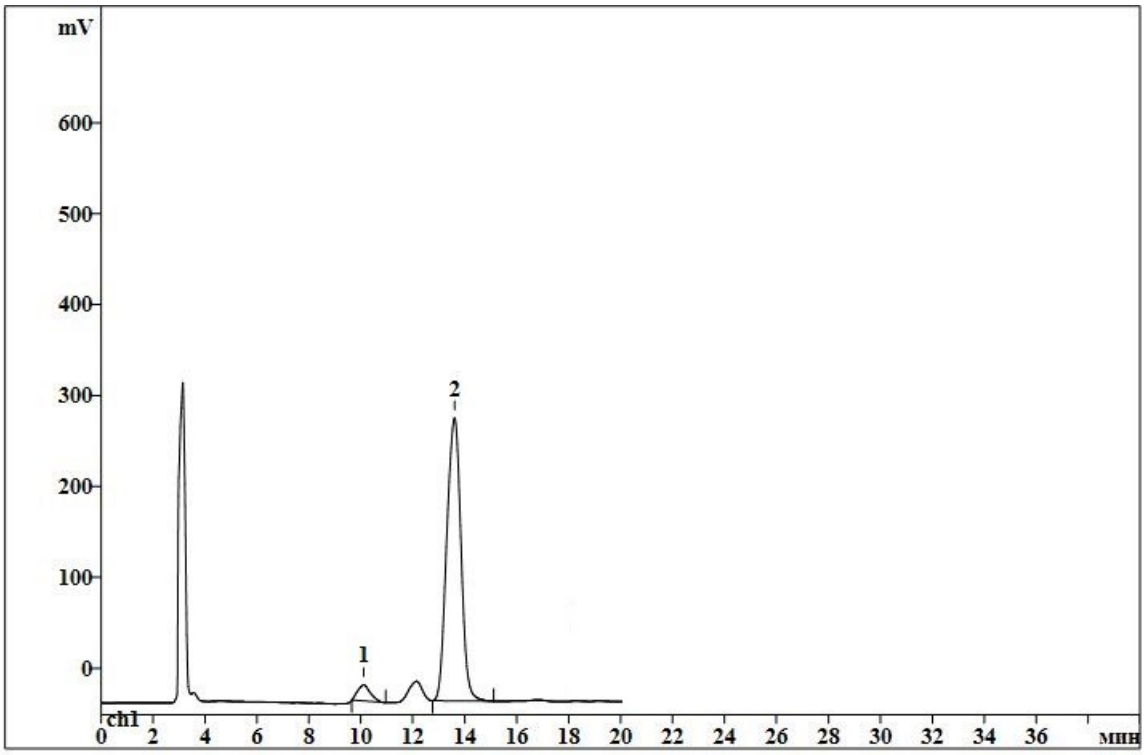
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ =220 nm), t_R = 10.1 min (minor), t_R = 13.6 min (major).

***rac*-11ba**



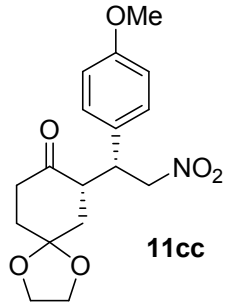
No	Retention мин	Area mV*сек	Area %	Name
1	10.07	4321.82	47.75	
2	12.01	436.92	4.83	
3	13.6	4292.71	47.43	
3	35.56	9051.45	100.00	

11ba



No	Retention мин	Area mV*сек	Area %	Name
1	10.11	595.22	4.80	
2	13.6	11812.57	95.20	
2	18.28	12407.79	100.00	

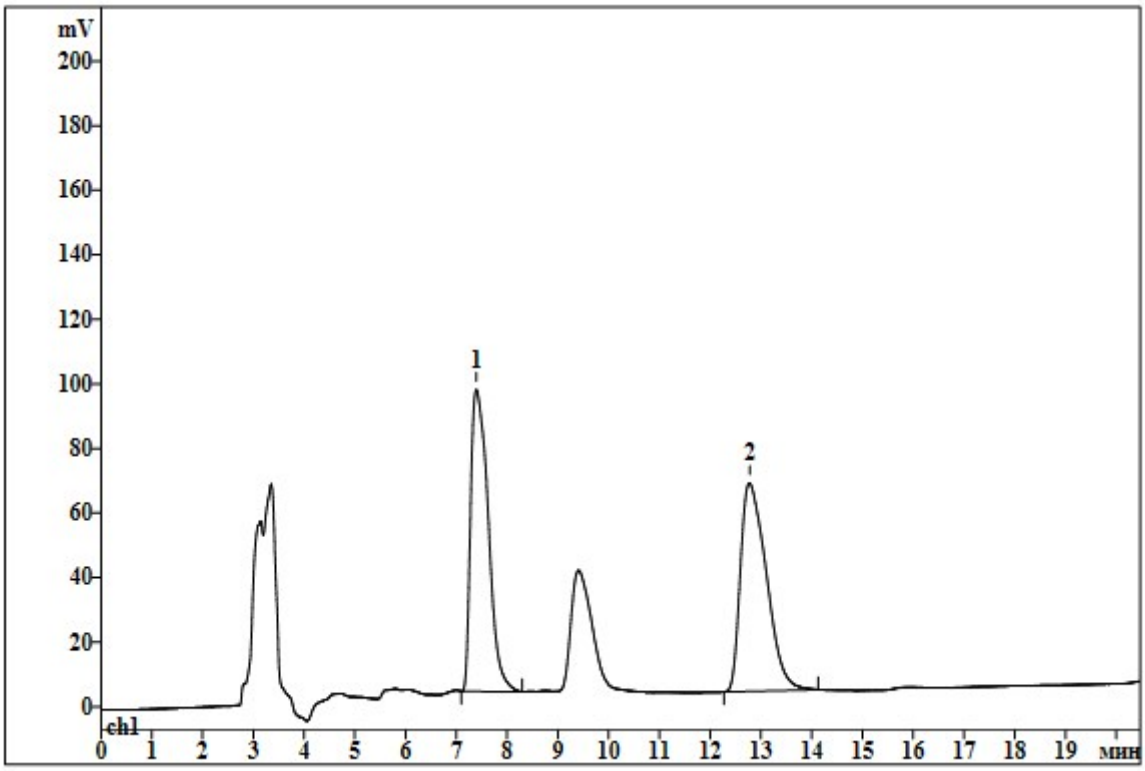
(*S*)-7-((*R*)-1-(4-methoxyphenyl)-2-nitroethyl)-1,4-dioxaspiro[4.5]decan-8-one (11cc).



11cc

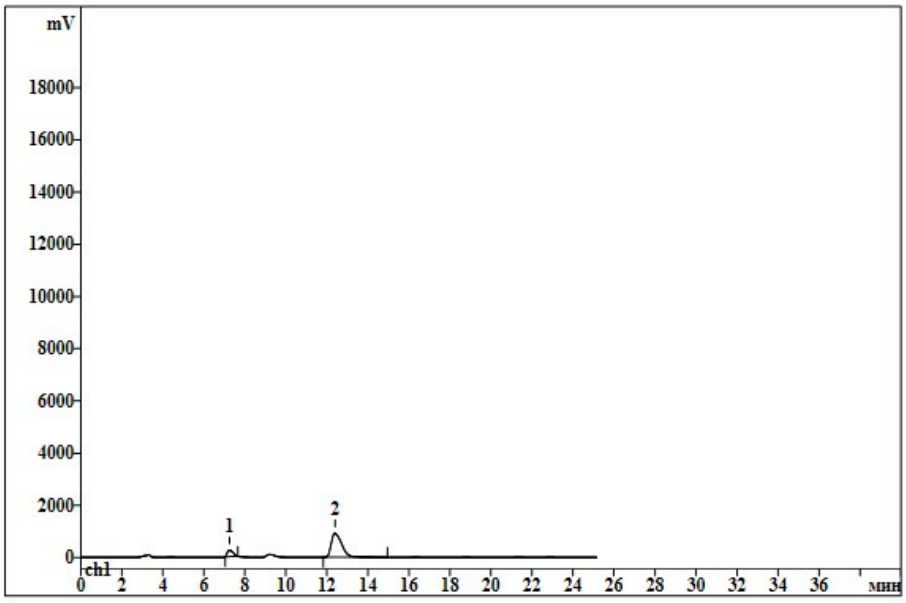
HPLC (CHIRALPAK AD-H, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ =220 nm), t_R = 7.4 min (minor), t_R = 12.8 min (major).

***rac*-11cc**



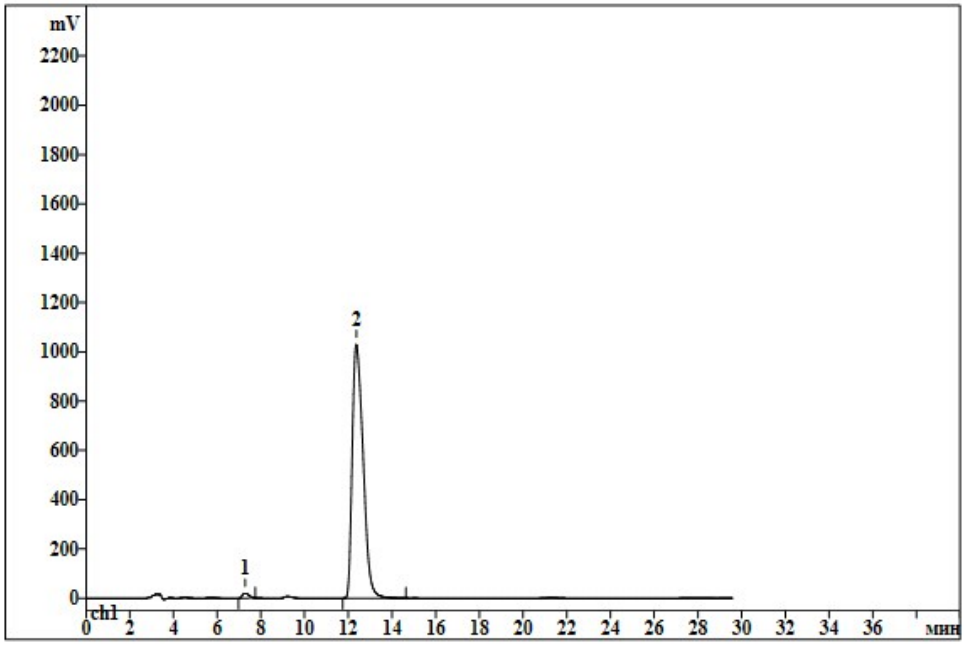
No	Retention мин	Area mV*сек	Area %	Name
1	7.393	2257.69	49.60	
2	12.77	2294.32	50.40	
2	20.48	4552.00	100.00	

11cc



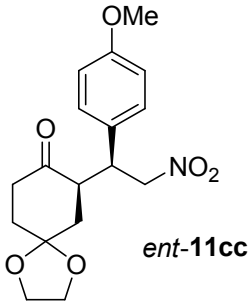
No	Retention мин	Area mV*сек	Area %	Name
1	7.25	4745.52	12.67	
2	12.39	32694.76	87.33	
2	15.06	37440.28	100.00	

11cc after recrystallization



No	Retention мин	Area mV*сек	Area %	Name
1	7.275	415.49	1.15	
2	12.36	35687.73	98.85	
2	29.59	36103.22	100.00	

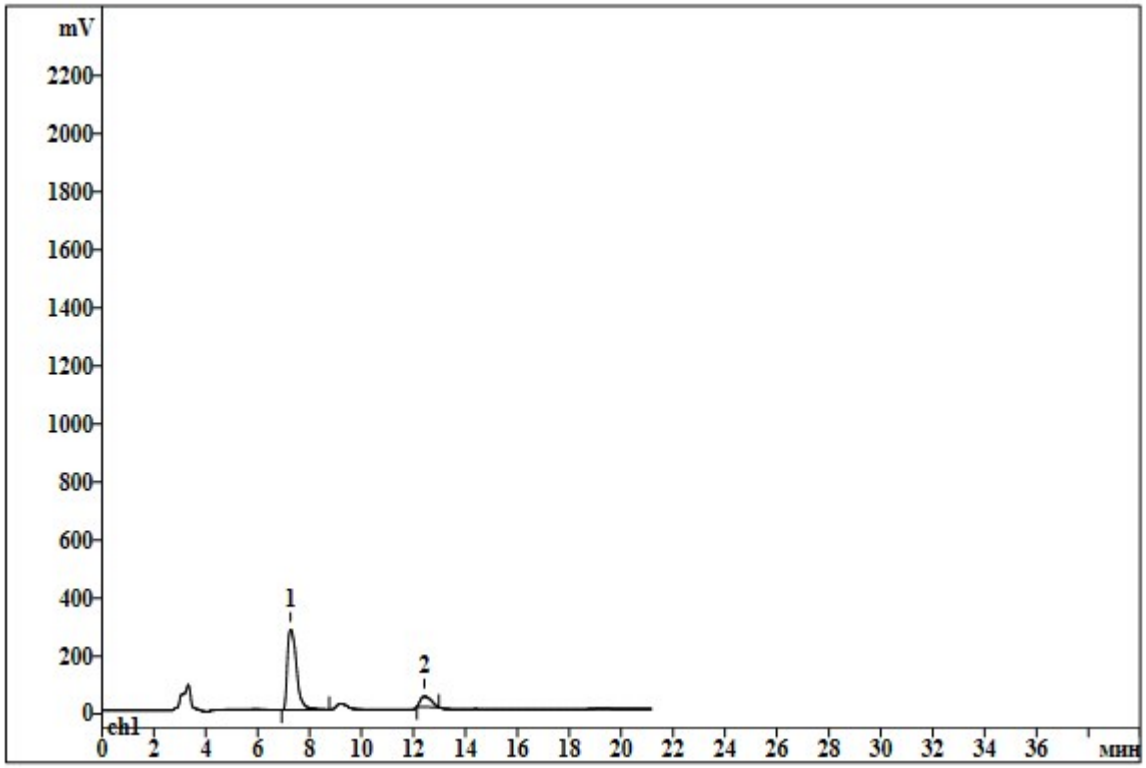
(*R*)-7-((*S*)-1-(4-methoxyphenyl)-2-nitroethyl)-1,4-dioxaspiro[4.5]decan-8-one (*ent*-11cc).



ent-**11cc**

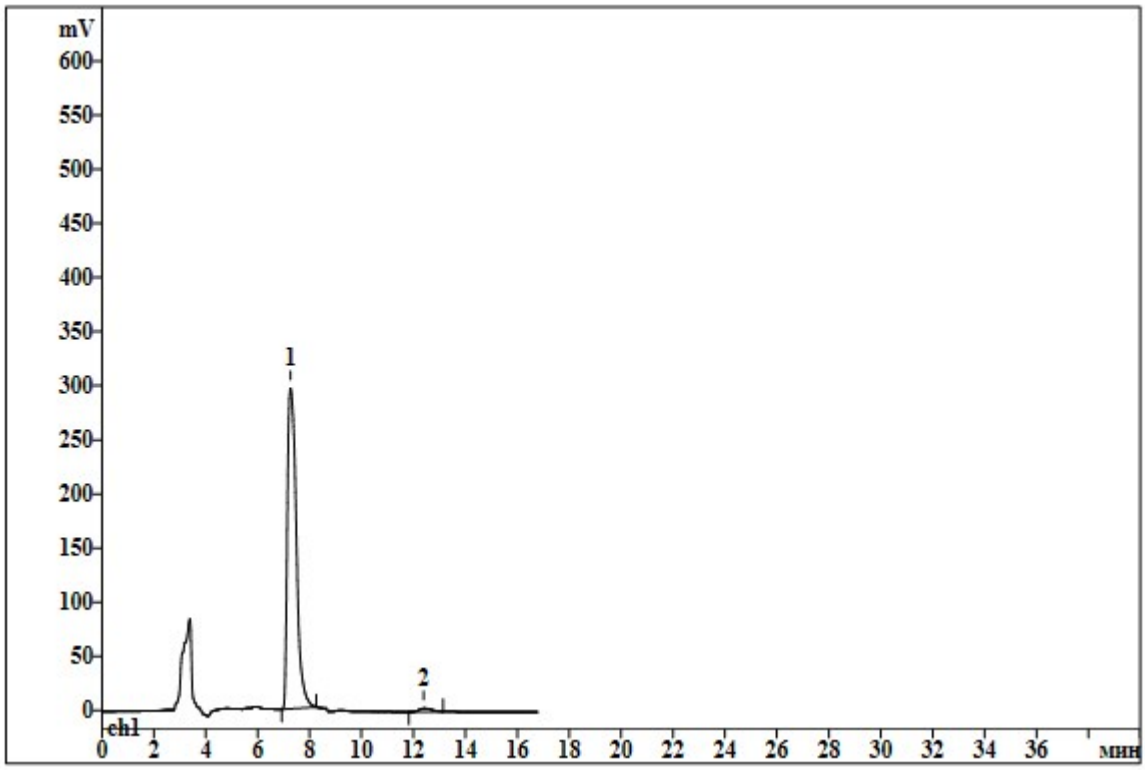
HPLC (CHIRALPAK AD-H, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ =220 nm), t_R = 7.4 min (major), t_R = 12.8 min (minor).

***ent*-11cc**



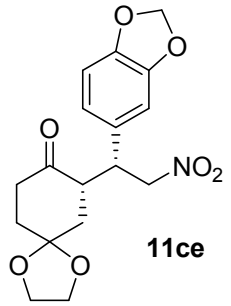
No	Retention мин	Area mV*сек	Area %	Name
1	7.268	6796.58	86.53	
2	12.43	1057.68	13.47	
2	21.17	7854.26	100.00	

***ent*-11cc after recrystallization**



No	Retention мин	Area mV*сек	Area %	Name
1	7.262	7104.27	98.64	
2	12.41	97.66	1.36	
2	16.79	7201.93	100.00	

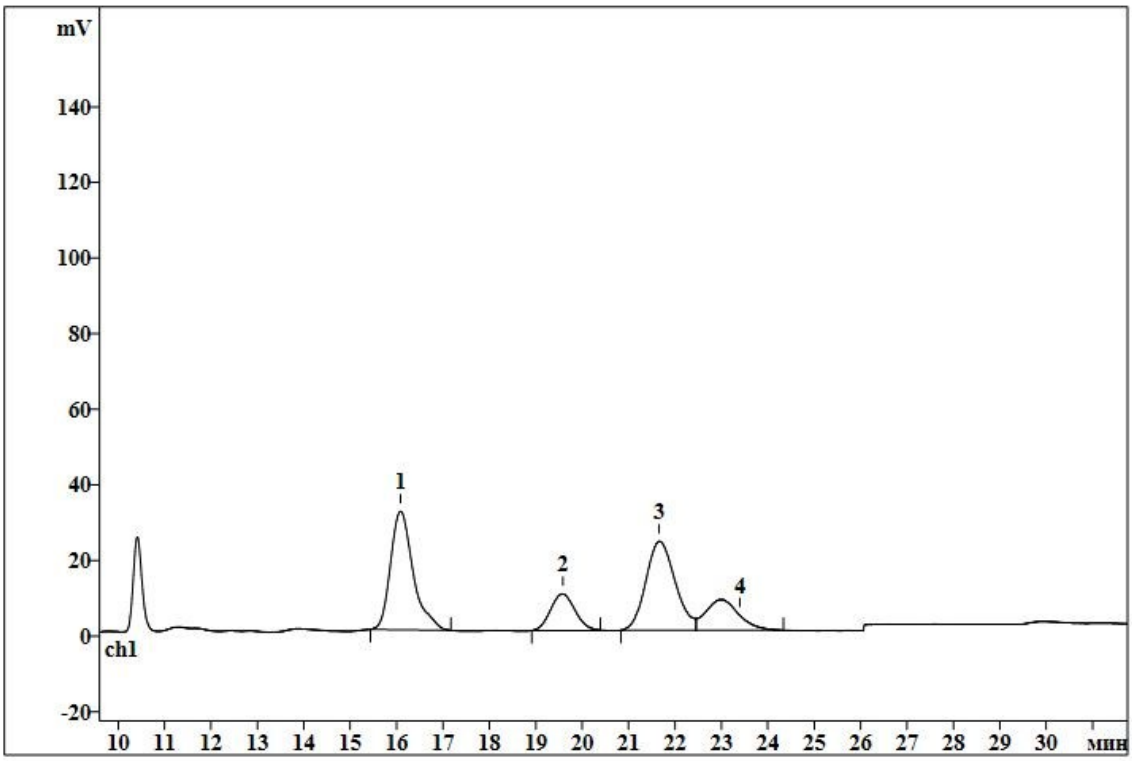
(*S*)-7-((*R*)-1-(benzo[d][1,3]dioxol-5-yl)-2-nitroethyl)-1,4-dioxaspiro[4.5]decan-8-one (11ce).



11ce

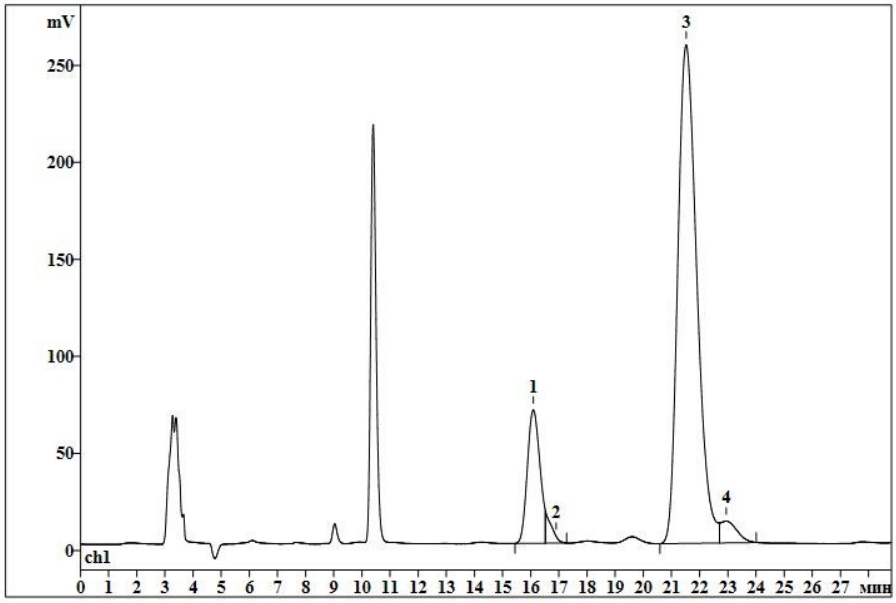
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 60/40, flow rate = 1.0 mL/min, λ =220 nm), t_R = 16.0 min (minor), t_R = 21.7 min (major).

***rac*-11ce**



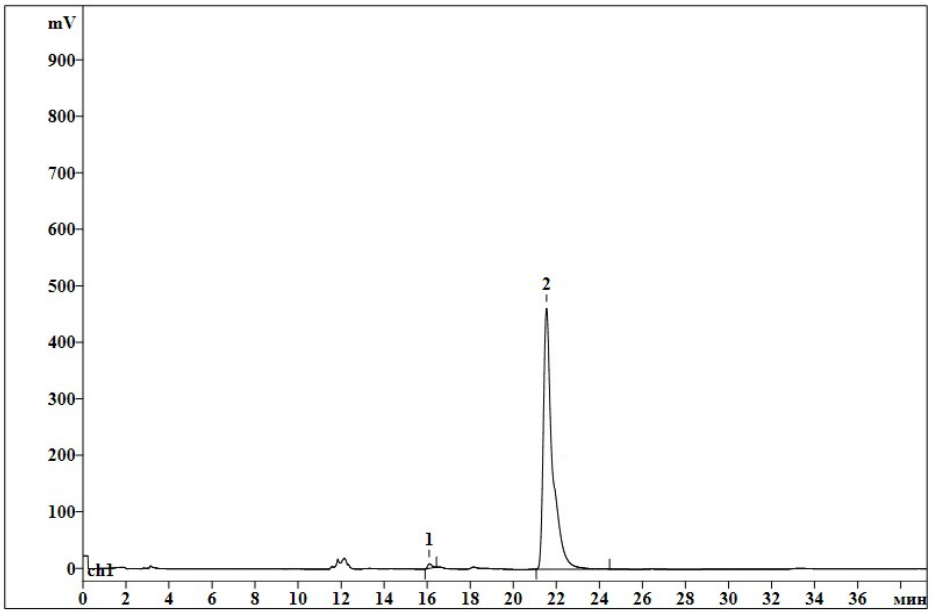
No	Retention мин	Area mV*сек	Area %	Name
1	16.08	1064.67	37.22	
2	19.57	351.75	12.30	
3	21.66	1040.04	36.36	
4	23.39	404.10	14.13	
4	31.78	2860.56	100.00	

11ce



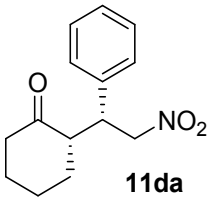
No	Retention мин	Area mV*сек	Area %	Name
1	16.09	2137.41	14.34	
2	16.89	239.41	1.61	
3	21.52	12068.31	80.99	
4	22.94	455.68	3.06	
4	28.82	14900.82	100.00	

11ce after recrystallization



No	Retention мин	Area mV*сек	Area %	Name
1	16.1	104.77	0.70	
2	21.54	14922.39	99.30	
2	39.23	15027.15	100.00	

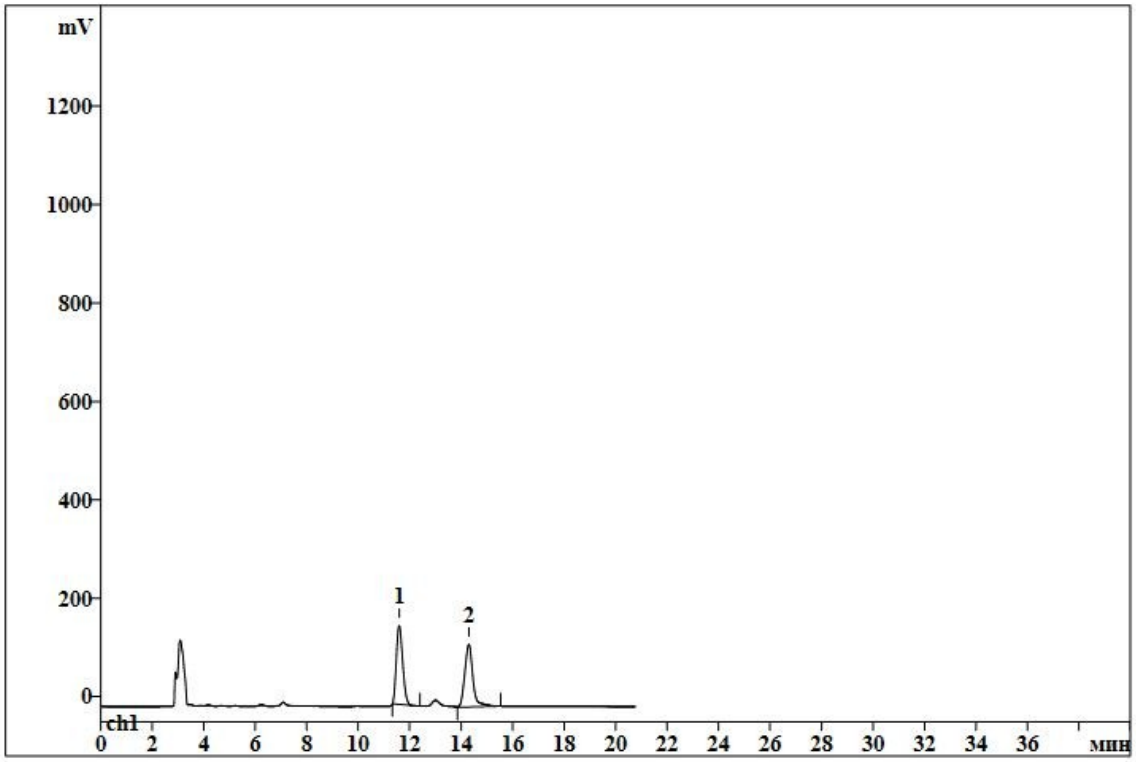
(*S*)-2-((*R*)-2-nitro-1-phenylethyl)cyclohexan-1-one (11da).



11da

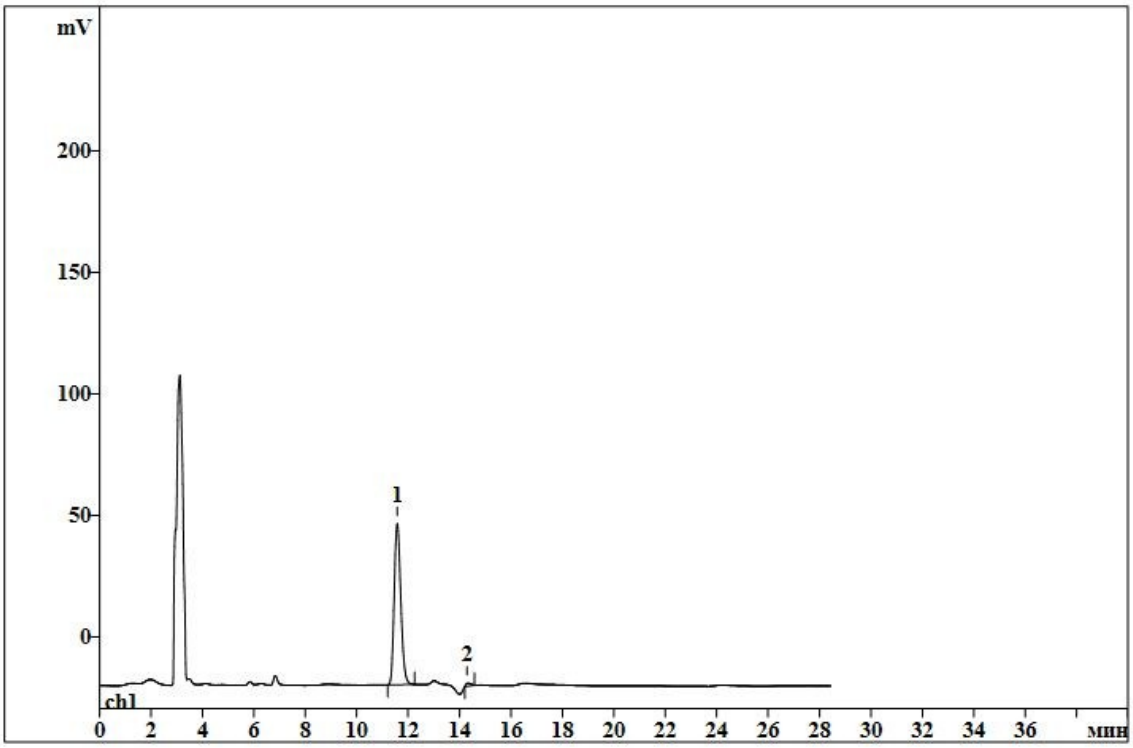
HPLC (CHIRALPAK AD-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ =220 nm), t_R = 11.6 min (minor), t_R = 14.3 min (major).

***rac*-11da**



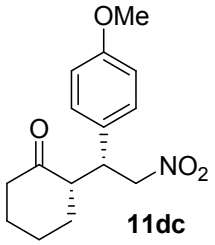
No	Retention мин	Area mV*сек	Area %	Name
1	11.59	2737.92	49.79	
2	14.3	2761.24	50.21	
2	20.77	5499.16	100.00	

11da



No	Retention мин	Area mV*сек	Area %	Name
1	11.57	1181.92	98.69	
2	14.28	15.70	1.31	
2	28.44	1197.62	100.00	

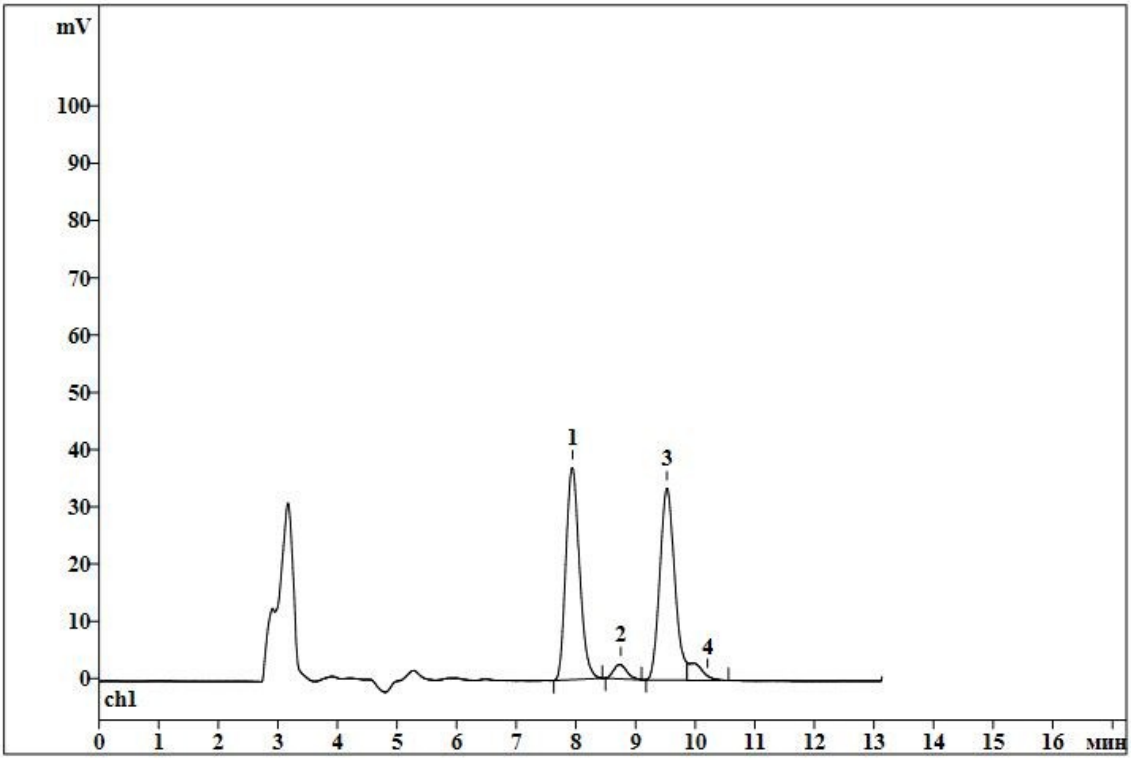
(*S*)-2-((*R*)-1-(4-methoxyphenyl)-2-nitroethyl)cyclohexan-1-one (11dc).



11dc

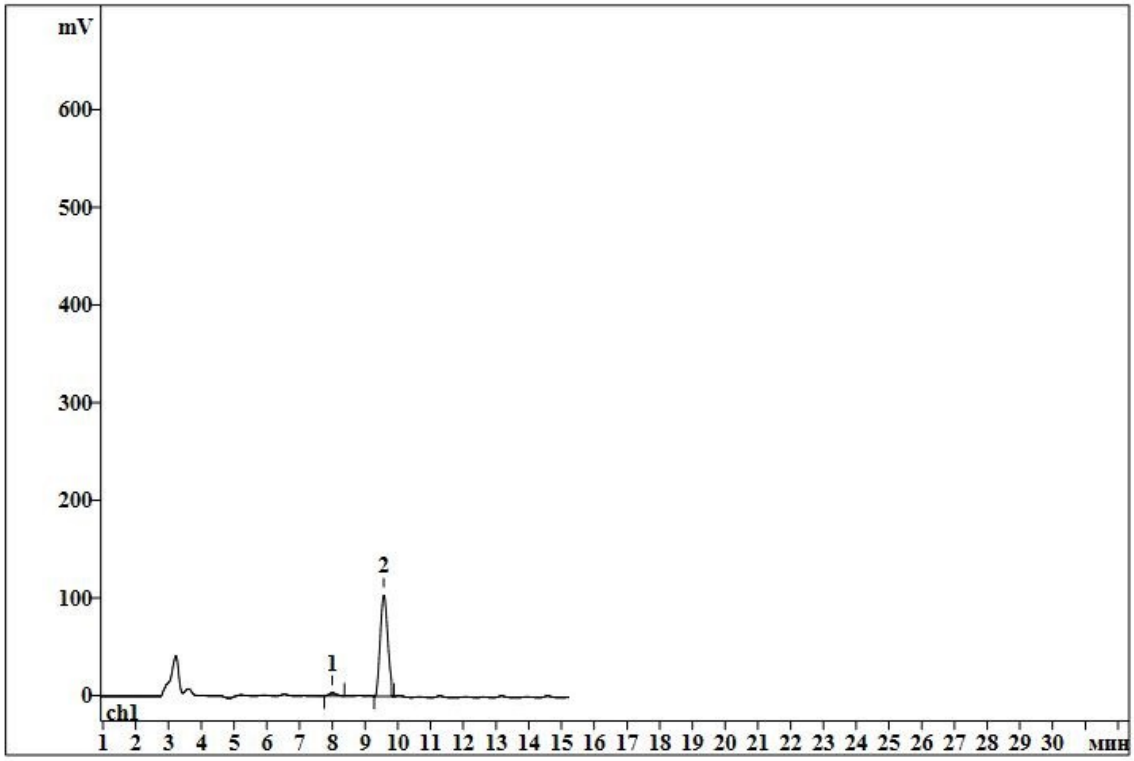
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ =220 nm), t_R = 7.9 min (minor), t_R = 9.5 min (major).

***rac*-11dc**



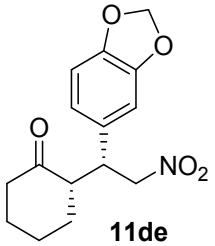
No	Retention мин	Area mV*сек	Area %	Name
1	7.936	587.29	46.58	
2	8.74	38.35	3.04	
3	9.526	582.82	46.23	
4	10.21	52.27	4.15	
4	13.13	1260.74	100.00	

11dc



No	Retention мин	Area mV*сек	Area %	Name
1	7.999	48.00	2.84	
2	9.573	1642.85	97.16	
2	10.38	1690.85	100.00	

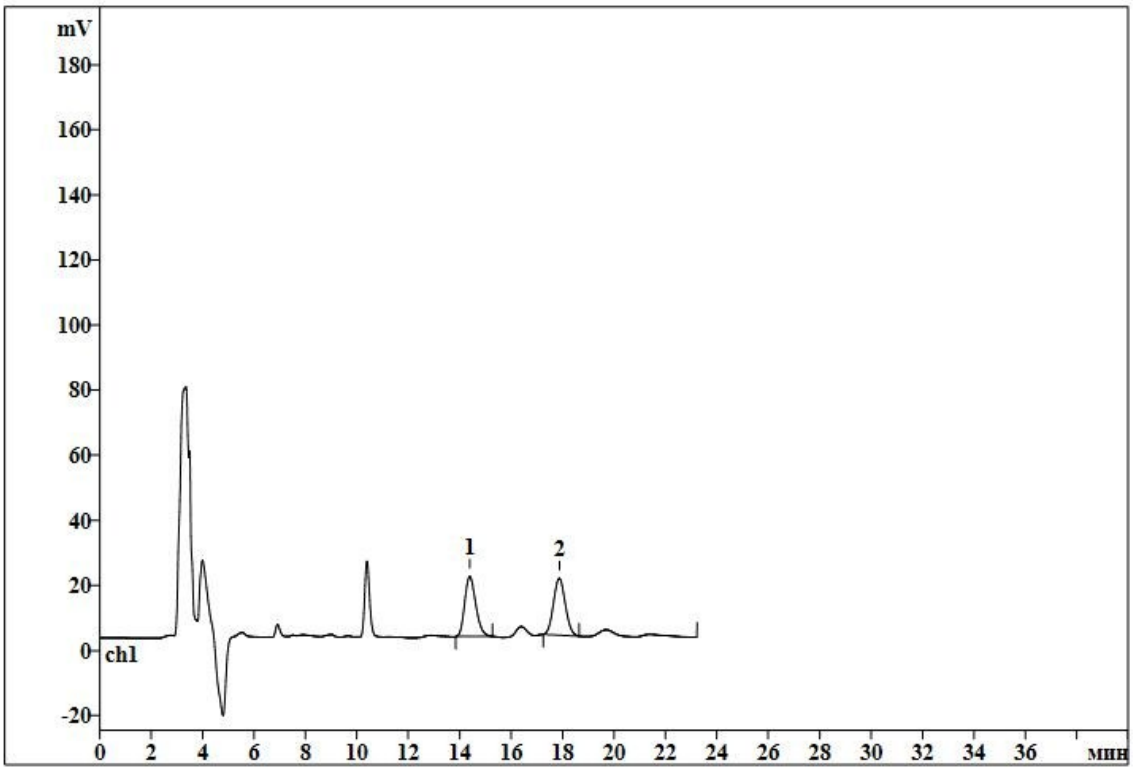
(*S*)-2-((*R*)-1-(benzo[d][1,3]dioxol-5-yl)-2-nitroethyl)cyclohexan-1-one (11de).



11de

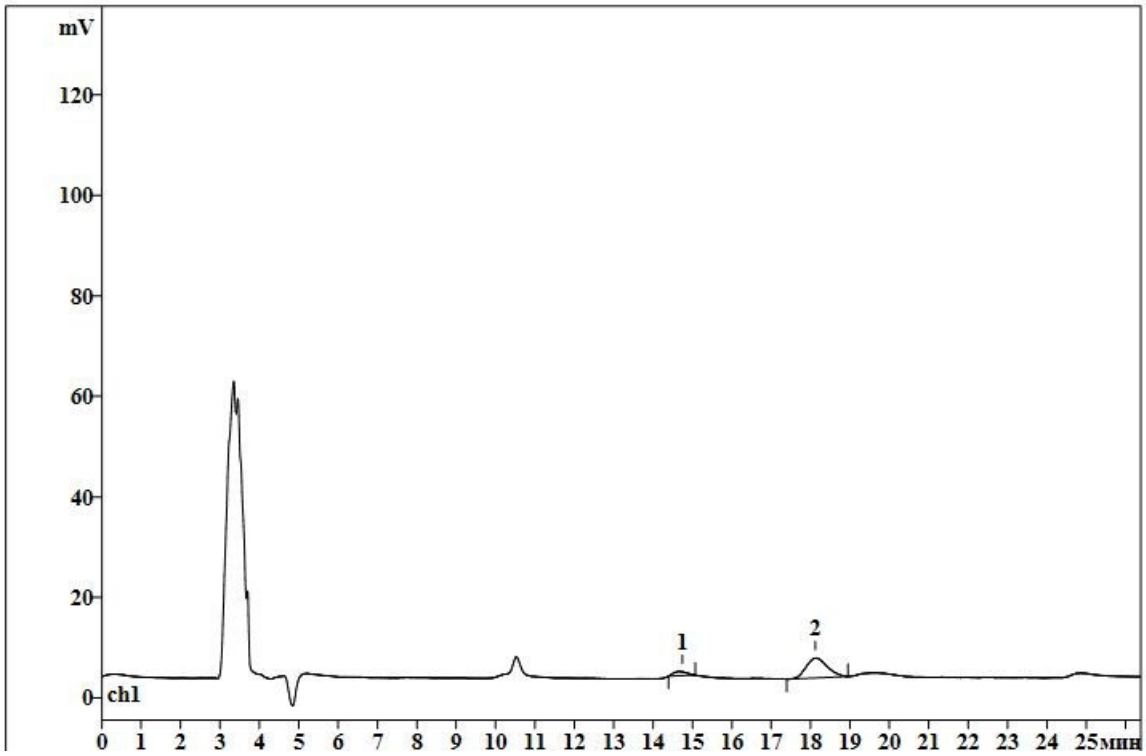
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 60/40, flow rate = 1.0 mL/min, λ =220 nm), t_R = 14.4 min (minor), t_R = 17.9 min (major).

***rac*-11de**



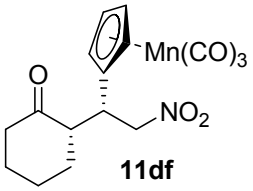
No	Retention мин	Area mV*сек	Area %	Name
1	14.39	555.06	49.91	
2	17.87	556.95	50.09	
2	23.23	1112.01	100.00	

11de



No	Retention мин	Area mV*сек	Area %	Name
1	14.74	20.26	12.18	
2	18.13	146.10	87.82	
2	26.39	166.36	100.00	

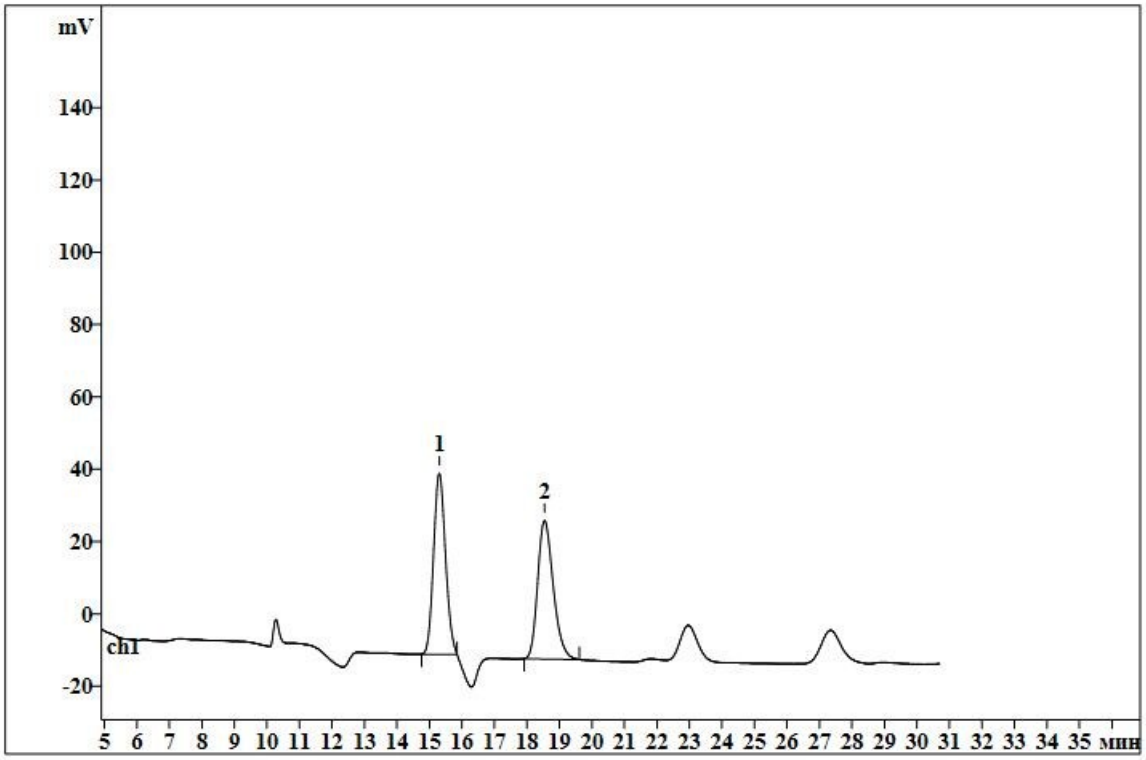
(*S*)-2-((*R*)-1-(4-cymantrenyl)-2-nitroethyl)cyclohexan-1-one (11df).



11df

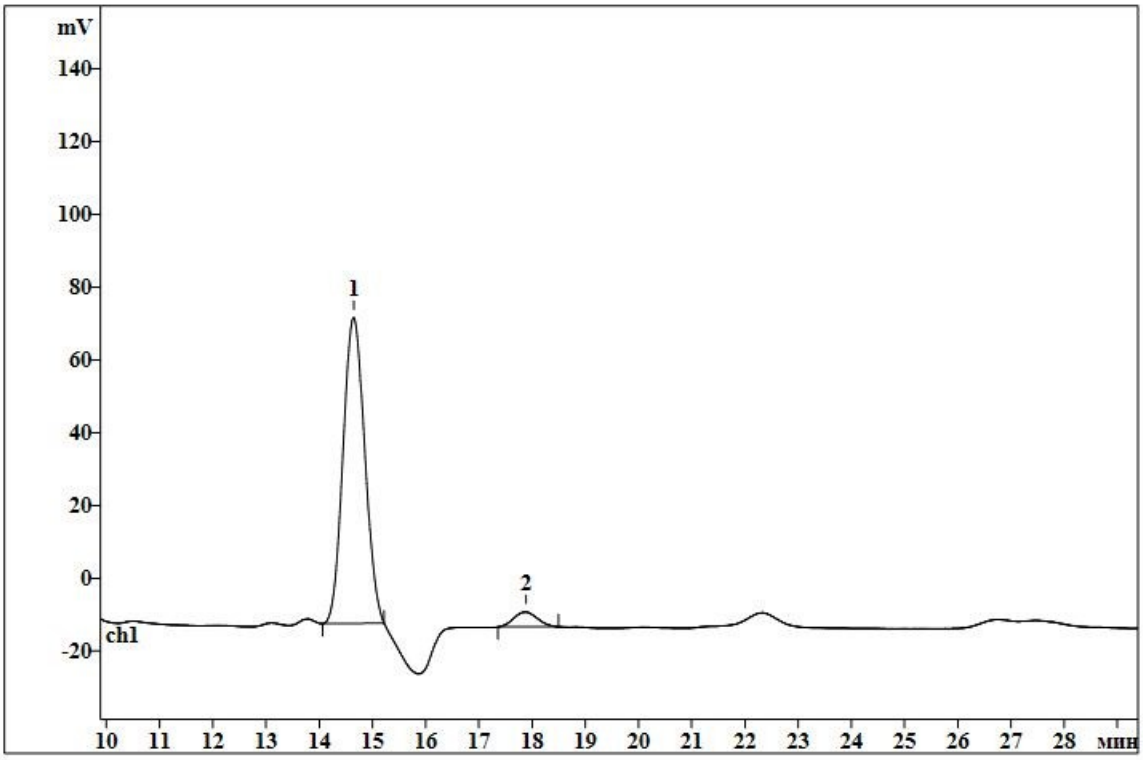
HPLC (CHIRALPAK AS-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ =220 nm), t_R = 15.3 min (major), t_R = 18.5 min (minor).

***rac*-11df**



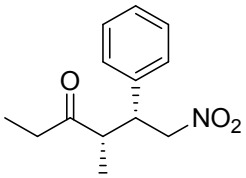
No	Retention мин	Area mV*сек	Area %	Name
1	15.3	1275.04	49.92	
2	18.54	1279.17	50.08	
2	30.7	2554.21	100.00	

11df



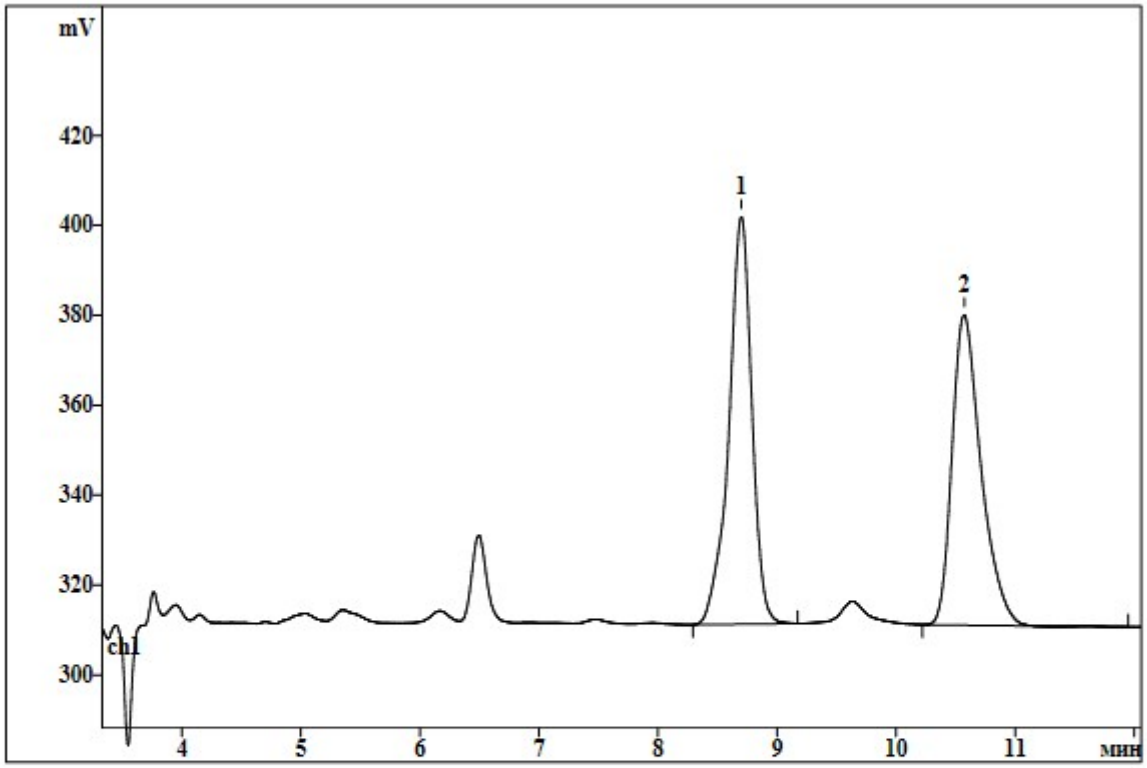
No	Retention мин	Area mV*сек	Area %	Name
1	14.64	2379.14	94.90	
2	17.88	127.76	5.10	
2	29.41	2506.90	100.00	

(4S,5R)-4-methyl-6-nitro-5-phenylhexan-3-one (**13a**).



HPLC (CHIRALPAK OD-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ =220 nm), t_R = 8.7 min (major), t_R = 10.6 min (minor).

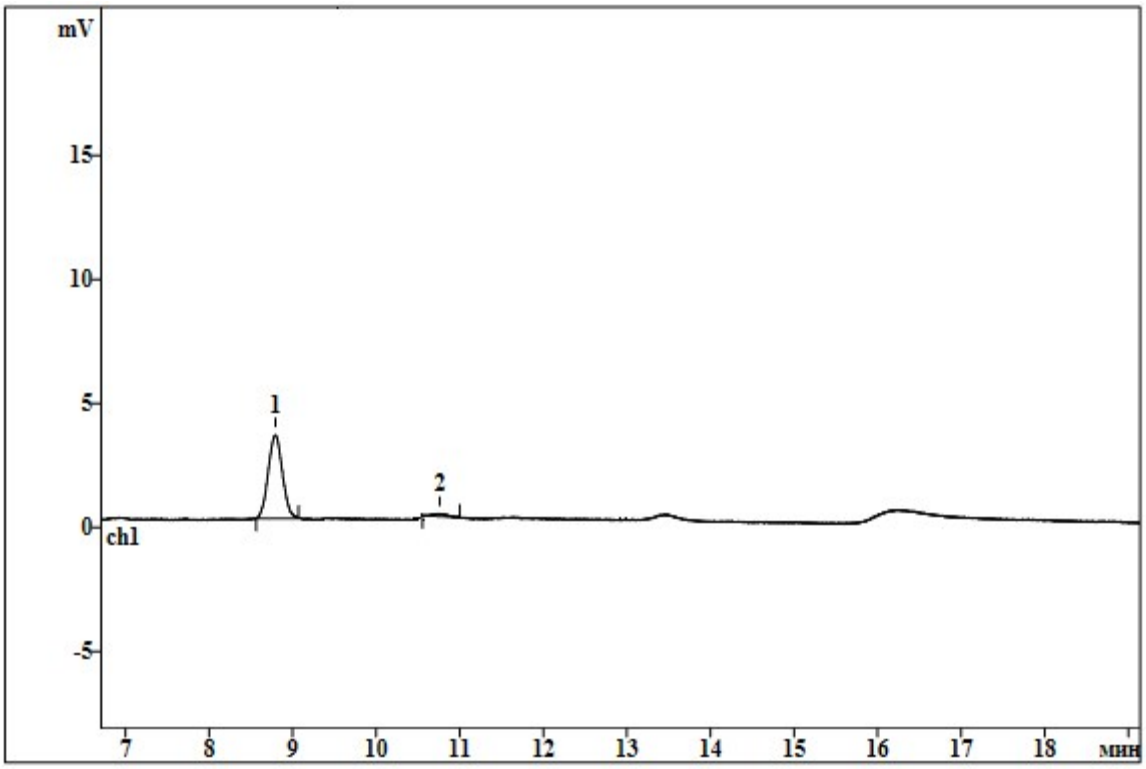
***rac*-13a**



RESULTS
Quantitation method: Нормировка отклика
Standard component: Нет

No	Retention мин	Area mV*сек	Area %	Name
1	8.698	1217.01	51.02	
2	10.57	1168.50	48.98	
2	19.98	2385.51	100.00	

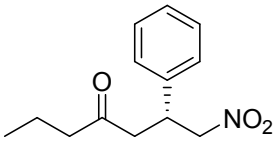
13a



RESULTS
Quantitation method: Нормировка отклика
Standard component: Нет

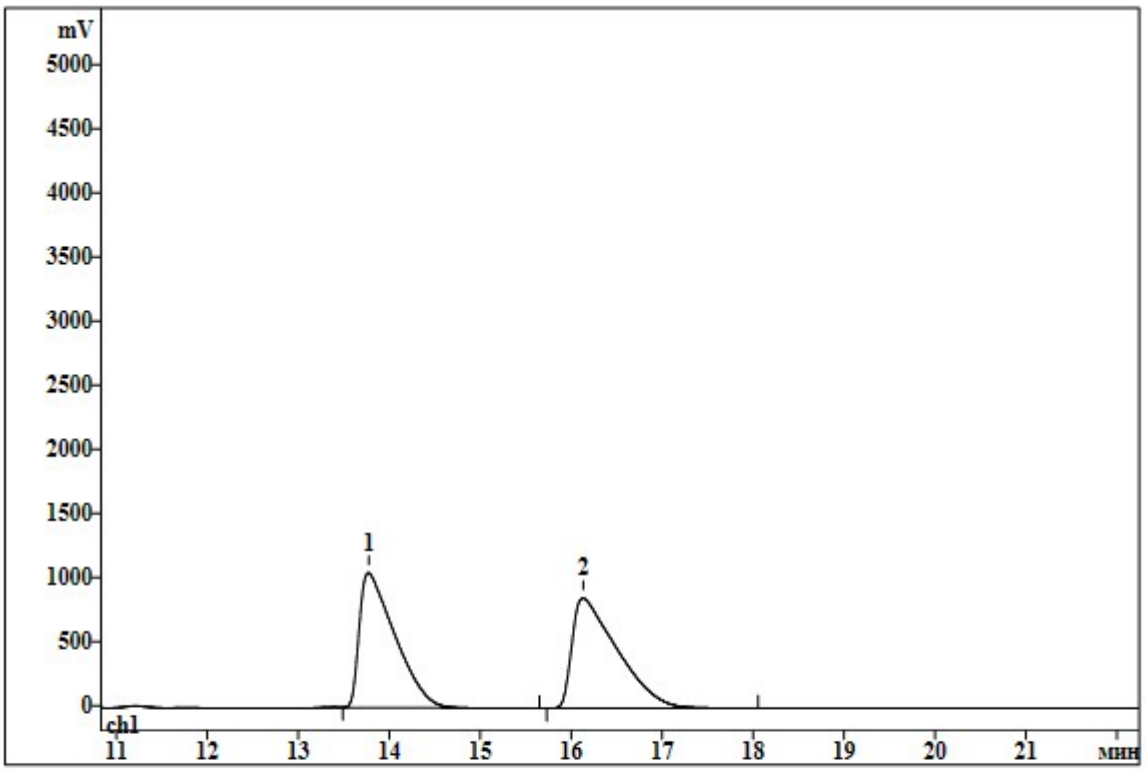
No	Retention мин	Area mV*сек	Area %	Name
1	8.792	39.63	97.31	
2	10.77	1.09	2.69	
2	40	40.73	100.00	

(R)-1-nitro-2-phenylheptan-4-one (13b).



HPLC (CHIRALPAK OD-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ =220 nm), t_R = 13.8 min (major), t_R = 16.1 min (minor).

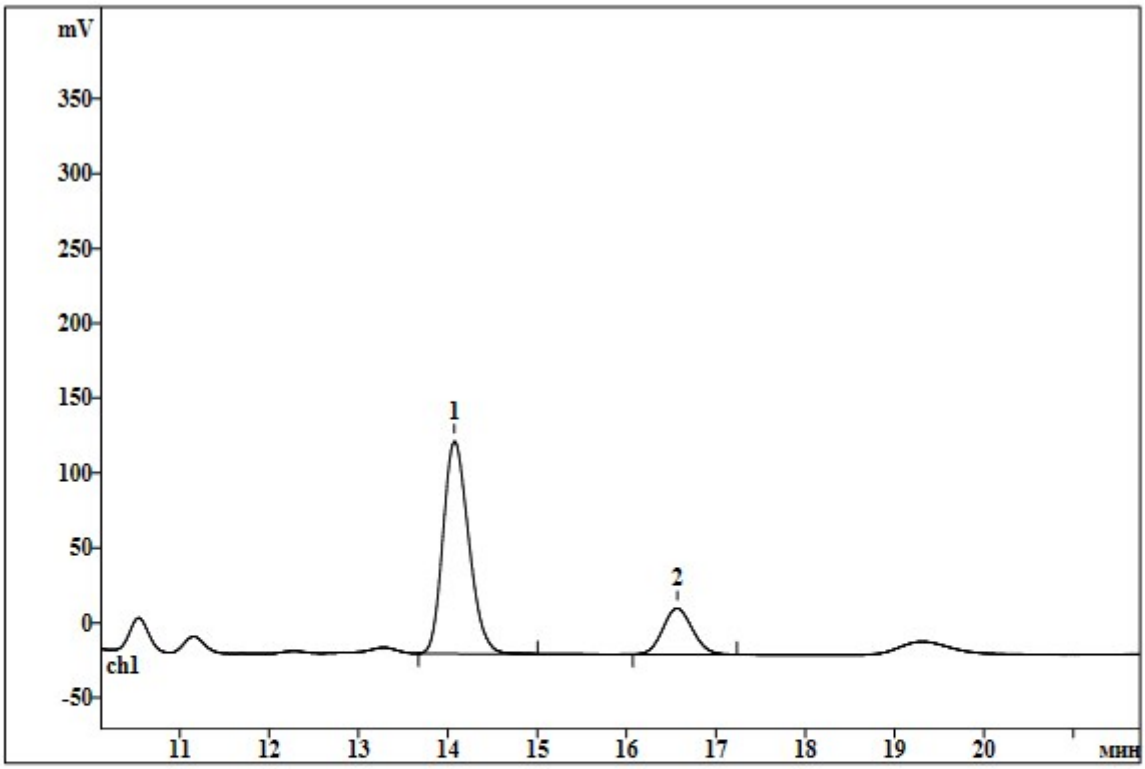
***rac*-13b**



RESULTS
Quantitation method: Нормировка отклика
Standard component: Нет

No	Retention мин	Area mV*сек	Area %	Name
1	13.77	28543.41	49.05	
2	16.13	29653.40	50.95	
2	24.95	58196.81	100.00	

13b



RESULTS
Quantitation method: Нормировка отклика
Standard component: Нет

No	Retention мин	Area mV*сек	Area %	Name
1	14.07	2841.25	80.01	
2	16.57	709.92	19.99	
2	59.76	3551.16	100.00	