Supplementary information

Artificial enzymes for the enantioselective Michael-type addition of thiols combining basic catalysis with two- and three-pronged oxyanion hole mimics

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(10) Gaussian 98 (Revision A.1.0), Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian, Inc*., Pittsburgh PA, **1998**.

Cartesian atomic coordinates of *s-trans* acrolein:

C	1.76063	0.14126	0.00018
C	0.56164	-0.45042	-0.00049
C	-0.67345	0.34986	-0.00035
O	-1.79567	-0.12068	0.00043
H	2.68691	-0.42386	0.00105
H	1.85096	1.22537	0.00076
H	0.44578	-1.53054	-0.00035
H	-0.51118	1.45018	-0.00094

Cartesian atomic coordinates of methyl mercaptane:

C	1.16348	0.01983	0.00000
H	1.52960	-1.00823	-0.00069

H	1.53248	0.52402	-0.89434
H	1.53243	0.52276	0.89506
S	-0.66639	-0.08720	-0.00000
H	-0.91313	1.23770	0.00004

Cartesian atomic coordinates of ammonia:

N	-0.00032	0.00000	-0.12070
H	0.46884	-0.80883	0.28130
H	0.46813	0.80923	0.28130
H	-0.93475	-0.00041	0.28226

Cartesian atomic coordinates of trimethylamine:

N	-0.00018	-0.00025	-0.37795
C	0.33626	1.34484	0.06168
H	0.36694	1.44996	1.16358
H	1.31771	1.62946	-0.32954
H	-0.40053	2.05666	-0.32262
C	0.99724	-0.96343	0.06172
H	1.97959	-0.68788	-0.33367
H	1.08241	-1.03270	1.16357
H	0.74633	-1.95825	-0.31839
C	-1.33334	-0.38139	0.06178
H	-1.58357	-1.37366	-0.32544
H	-2.06958	0.32881	-0.32654
H	-1.43898	-0.41070	1.16363

Cartesian atomic coordinates of the proton-switch 1,2 addition:

S	1.93330	-0.00680	-0.39111
C	0.05481	-1.10459	-0.97419
C	-1.18719	-0.43164	-0.80063
C	-2.00052	-0.62210	0.36776
N	-0.18550	2.11525	-0.06704
O	-3.09174	-0.09587	0.60065
H	0.78939	1.63927	-0.14318
H	0.26389	-1.93555	-0.30270
H	0.39138	-1.29870	-1.98777
H	-1.65551	0.05009	-1.66015

H	-1.53837	-1.30479	1.12835
C	1.90445	-0.48975	1.37893
H	2.22459	-1.52837	1.49049
H	2.59043	0.14590	1.94340
H	0.89705	-0.38877	1.79836
H	-0.30757	2.85622	-0.75562
H	-0.37847	2.46586	0.86997
H	-0.80657	1.25637	-0.29064

Cartesian atomic coordinates of the proton-switch 1,4 addition:

S	1.84003	0.17330	-0.43794
C	0.16629	-1.70993	-0.63468
C	-1.08666	-1.12697	-0.62567
C	-1.71277	-0.71588	0.57810
N	-0.75150	1.90583	-0.60712
O	-2.46683	0.28848	0.67528
H	0.19075	1.31355	-0.58665
H	0.56011	-2.17203	0.26581
H	0.62553	-2.03850	-1.55829
H	-1.48207	-0.70643	-1.54938
H	-1.47980	-1.29595	1.49244
C	1.78928	0.17111	1.39510
H	2.49278	-0.56377	1.79471
H	2.06279	1.15372	1.78992
H	0.78395	-0.07680	1.76283
H	-0.96954	2.13813	-1.57525
H	-0.61013	2.77262	-0.08918
H	-1.55670	1.34398	-0.16936

Cartesian atomic coordinates of the proton-slide (catalyzed by trimethylamine):

S	1.87272	-0.55644	-0.73371
C	1.70860	1.62973	-0.24587
C	0.53626	1.94209	0.47299
C	-0.64693	2.27360	-0.20844
N	-1.18402	-1.08205	-0.03280
O	-1.81550	2.32245	0.25293
H	-0.21135	-0.68864	-0.24941
H	1.76624	1.97713	-1.27469

H	2.66853	1.66050	0.26099
H	0.49209	1.77426	1.54638
H	-0.49768	2.48729	-1.29367
C	2.46121	-1.06148	0.92563
H	1.89557	-0.55229	1.71401
H	2.34932	-2.14162	1.05310
H	3.51977	-0.81648	1.04707
C	-1.61935	-0.61202	1.31876
H	-0.85201	-0.88447	2.04399
H	-1.75772	0.47304	1.28011
H	-2.55766	-1.11193	1.57117
C	-0.99582	-2.55834	-0.07776
H	-0.27879	-2.84779	0.69055
H	-1.95421	-3.04881	0.10095
H	-0.60371	-2.83409	-1.05674
C	-2.12565	-0.61614	-1.09568
H	-3.06331	-1.16768	-0.99844
H	-2.29894	0.45193	-0.95782
H	-1.67745	-0.81722	-2.06973

Cartesian atomic coordinates of the transition-state structure found for the addition of methyl mercaptane to the lactam **1** catalyzed by receptor **13**, leading to the *S* enantiomer of the product:

C	-0.14300	3.81014	0.89604
C	0.76320	4.68178	1.51196
C	2.12842	4.40389	1.56347
C	2.62098	3.22370	0.97060
C	1.70954	2.34885	0.34279
C	0.30678	2.62101	0.30421
C	4.05459	2.88834	0.98110
C	4.38375	1.53799	0.44614
C	3.37843	0.76046	-0.13721
O	2.08803	1.20603	-0.30880
C	5.68241	1.02257	0.52283
C	5.96640	-0.23843	0.02585
C	4.96199	-1.02627	-0.54751
C	3.64861	-0.54580	-0.62309
O	4.91326	3.64809	1.39631
N	-0.53242	1.69449	-0.32971
C	-1.86647	1.85429	-0.65357

O	-2.62350	2.76504	-0.23698
N	-2.28986	0.83241	-1.49786
C	-3.69697	0.68188	-1.88348
C	-4.53269	0.27064	-0.63061
C	-6.00010	0.11271	-0.95709
C	-6.54359	1.39714	-1.56718
C	-5.77000	1.78112	-2.81939
C	-4.29980	1.97884	-2.51410
C	5.27537	-2.37853	-1.07603
C	4.25102	-2.96731	-2.01998
C	2.82373	-2.64139	-1.64197
N	2.59560	-1.36878	-1.15155
O	1.92624	-3.51321	-1.75310
O	6.29718	-2.97616	-0.79823
H	-1.20010	4.02011	0.85531
H	0.38649	5.59080	1.96104
H	2.81323	5.08840	2.04807
H	6.47621	1.62909	0.97739
H	6.98897	-0.63275	0.08523
H	-0.16235	0.75302	-0.54812
H	-1.61163	0.10950	-1.72199
H	-3.74094	-0.12827	-2.61740
H	-4.33641	1.01981	0.14780
H	-6.57628	-0.14187	-0.04474
H	-6.15804	-0.72757	-1.66603
H	-6.49364	2.21862	-0.82443
H	-7.61664	1.26742	-1.80644
H	-6.18730	2.71328	-3.24654
H	-5.90049	1.00549	-3.60068
H	-3.72800	2.20871	-3.42551
H	-4.12159	2.78743	-1.79247
H	4.38292	-4.06703	-2.10625
H	4.44829	-2.57151	-3.03904
H	1.58430	-1.09953	-1.08386
S	-3.88408	-2.60807	2.53243
C	-4.14818	-1.31832	3.82110
H	-3.60485	-1.57978	4.72883
H	-3.82183	-0.33716	3.47513
H	-5.21177	-1.27672	4.05412
C	-1.65027	-2.13307	2.20286

C	-1.32699	-1.25665	1.11187
C	-0.61007	-1.72493	-0.02323
O	-0.09378	-0.90762	-0.92329
N	-0.43006	-3.06550	-0.22964
C	-1.07027	-3.51204	2.14409
C	-0.98037	-4.05986	0.72121
H	-1.62772	-1.67991	3.19609
H	-1.31451	-0.19046	1.28260
H	0.31205	-3.33336	-0.89640
H	-1.66300	-4.21330	2.76684
H	-0.06239	-3.47751	2.60920
H	-1.98540	-4.35409	0.35493
H	-0.35242	-4.97117	0.69156
N	-3.96722	-1.07307	-0.11598
H	-4.34816	-1.44702	0.79797
H	-4.07755	-1.81000	-0.81467
H	-2.93467	-0.99427	0.11965

Cartesian atomic coordinates of the transition-state structure found for the addition of methyl mercaptane to the lactam **1** catalyzed by receptor **13**, leading to the *R* enantiomer of the product:

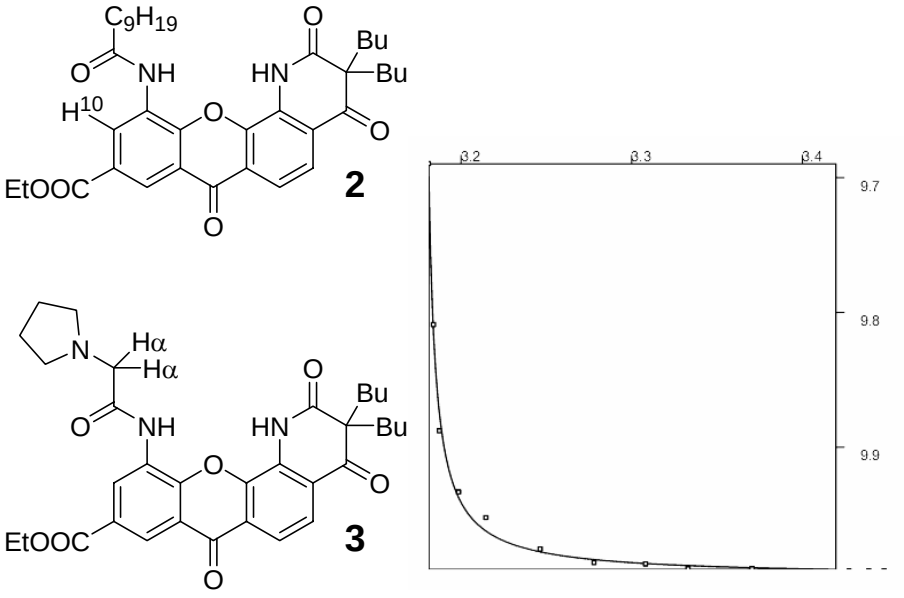
C	0.72067	4.12926	0.72947
C	1.82892	4.87228	1.15452
C	3.09333	4.29789	1.28193
C	3.26958	2.93336	0.97684
C	2.15339	2.18443	0.55018
C	0.85564	2.76805	0.41870
C	4.58608	2.27821	1.06184
C	4.64260	0.91949	0.45396
C	3.45784	0.29223	0.05745
O	2.21471	0.85116	0.24670
C	5.85897	0.25433	0.26353
C	5.88492	-1.00682	-0.30793
C	4.70227	-1.63572	-0.71449
C	3.46939	-0.99578	-0.53960
O	5.55873	2.80007	1.57934
N	-0.19524	1.96329	-0.03983
C	-1.43772	2.38708	-0.47465
O	-1.95810	3.50561	-0.27642
N	-2.08388	1.36111	-1.16690

C	-3.46671	1.53521	-1.58090
C	-3.66508	1.52402	-3.12810
C	-5.13381	1.70994	-3.45986
C	-6.00236	0.65310	-2.79187
C	-5.80519	0.63433	-1.28062
C	-4.34430	0.40468	-0.96957
C	4.73970	-2.98692	-1.32853
C	3.51053	-3.39165	-2.10984
C	2.20930	-2.87633	-1.53715
N	2.24467	-1.63575	-0.93062
O	1.17069	-3.58071	-1.60780
O	5.70215	-3.72511	-1.23936
H	-0.25629	4.57278	0.61718
H	1.69340	5.91996	1.38689
H	3.93864	4.88983	1.60943
H	6.79227	0.73942	0.57648
H	6.84204	-1.52644	-0.44388
H	-0.04225	0.94741	-0.15137
H	-1.57010	0.49484	-1.31605
H	-3.76684	2.50836	-1.18178
H	-3.28091	0.57273	-3.53217
H	-5.27586	1.67064	-4.55712
H	-5.46510	2.72122	-3.14870
H	-5.77230	-0.34675	-3.21198
H	-7.06887	0.83978	-3.02268
H	-6.43546	-0.15844	-0.82933
H	-6.15425	1.59330	-0.84423
N	-4.09272	0.36237	0.54770
H	-3.99594	-0.57116	-1.33791
H	3.46545	-4.49633	-2.22077
H	3.61544	-3.00233	-3.14517
H	1.30155	-1.20101	-0.76844
S	-4.48090	-2.07808	2.38866
C	-4.83352	-1.31108	4.02566
H	-4.43104	-1.93392	4.82369
H	-4.40833	-0.30922	4.10033
H	-5.91448	-1.24670	4.14790
C	-2.23509	-1.83195	2.42989
C	-1.66095	-0.94365	1.44412
C	-0.98175	-1.46715	0.30985

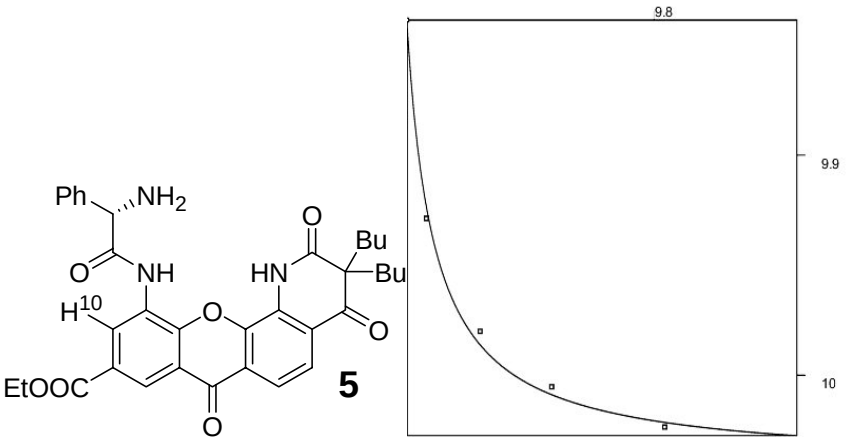
O	-0.28698	-0.70666	-0.51634
N	-1.02993	-2.80157	0.01820
C	-1.81078	-3.26679	2.33626
C	-1.75283	-3.75548	0.89117
H	-2.25706	-1.44295	3.45143
H	-1.39074	0.06302	1.73569
H	-0.34710	-3.14854	-0.67536
H	-2.49244	-3.92264	2.91464
H	-0.81652	-3.36408	2.82105
H	-2.77751	-3.88298	0.48430
H	-1.25849	-4.74420	0.83013
H	-4.22850	1.27900	0.97544
H	-3.09149	0.03120	0.71913
H	-4.63048	-0.37955	1.07058
H	-3.05421	2.33047	-3.55816

Graphic plots for competitive titration: vs. receptor **2**: $CDCl_3$ at 298 K, [receptor] = 0.005 M

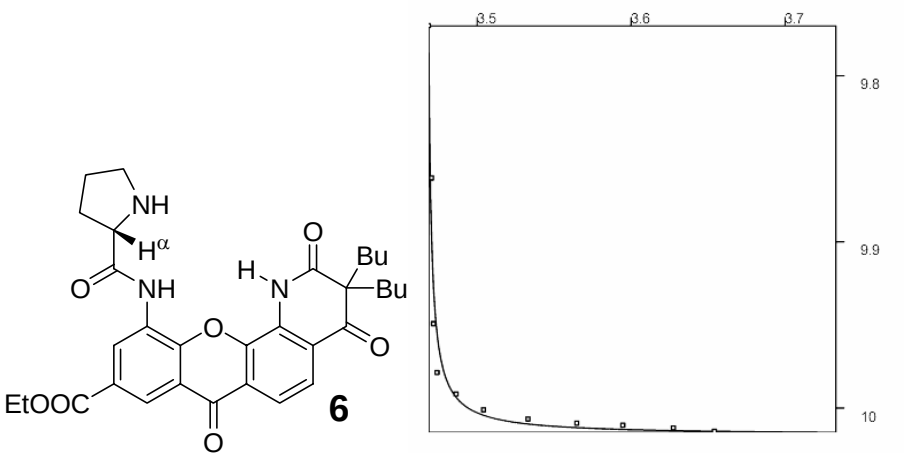
Competitive titration between receptors **3** and **2** *(receptor* **3** *Hα: δ_{free} = 3.1811 ppm.; $\delta_{complex}$ = 3.4477 ppm.; receptor* **2** *H–10: δ_{free} = 9.8622 ppm.; $\delta_{complex}$ = 10.020 ppm.).*



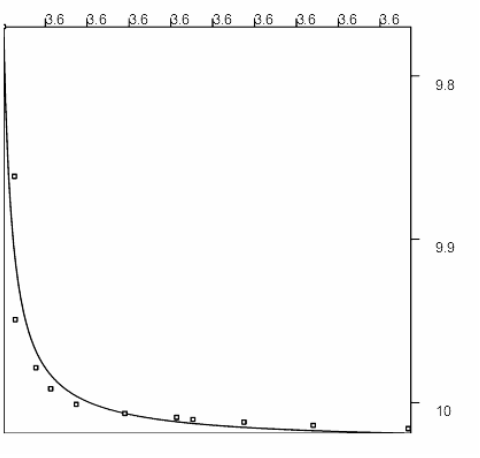
Competitive titration between receptors **5** and **2** *(receptor* **5** *H-10: δ_{free} = 9.7156 ppm.; $\delta_{complex}$ = 9.8489 ppm.; receptor* **2** *H-10: δ_{free} = 9.8623 ppm., $\delta_{complex}$ = 10.024 ppm.).*



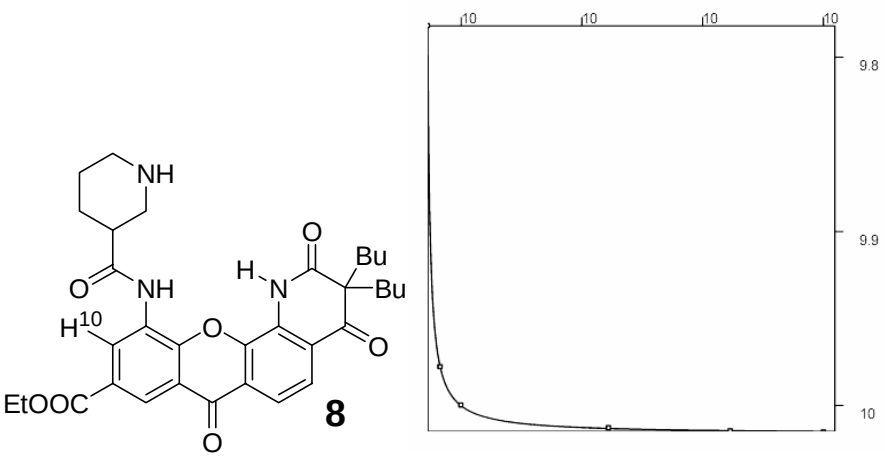
Competitive titration between receptors **6** and **2**; *(receptor* **6** *Hα:* δ_{free} *= 3.6399 ppm.;* $\delta_{complex}$ *= 3.5426 ppm.; receptor* **2** *H-10:* δ_{free} *= 9.8631 ppm.,* $\delta_{complex}$ *= 10.019 ppm.).*



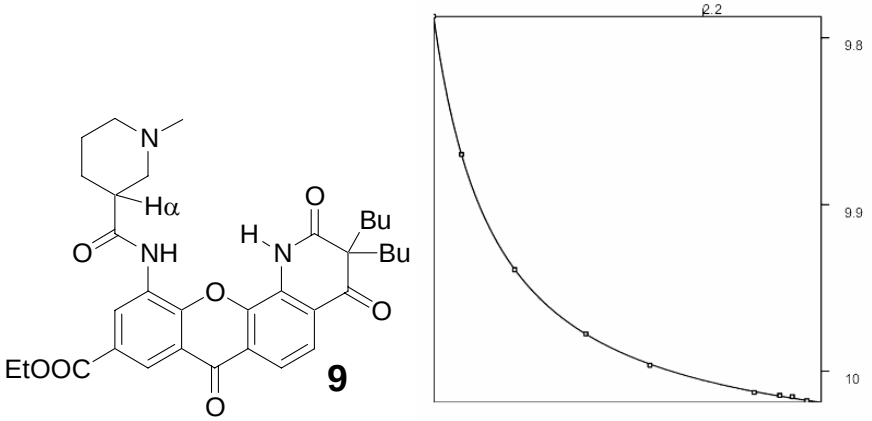
Competitive titration between receptors **7** and **2** *(receptor* **7** *Hα:* δ_{free} *= 3.4686 ppm.;* $\delta_{complex}$ *= 3.7331 ppm.; receptor* **2** *H–10:* δ_{free} *= 9.8624 ppm.;* $\delta_{complex}$ *= 10.019 ppm.).*



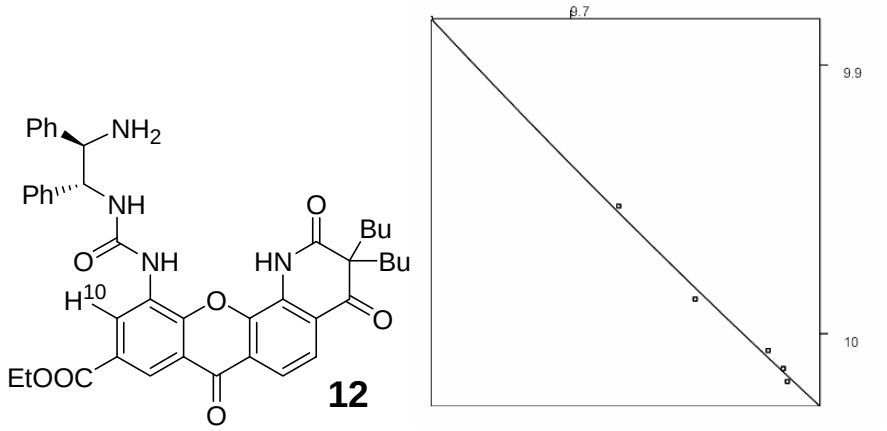
Competitive titration between receptors **8** and **2** *(receptor* **8** *H–10: δ_{free} = 10.3230 ppm.; $\delta_{complex}$ = 10.0150 ppm.; receptor* **2** *H–10: δ_{free} = 9.8623 ppm.; $\delta_{complex}$ = 10.019 ppm.).*



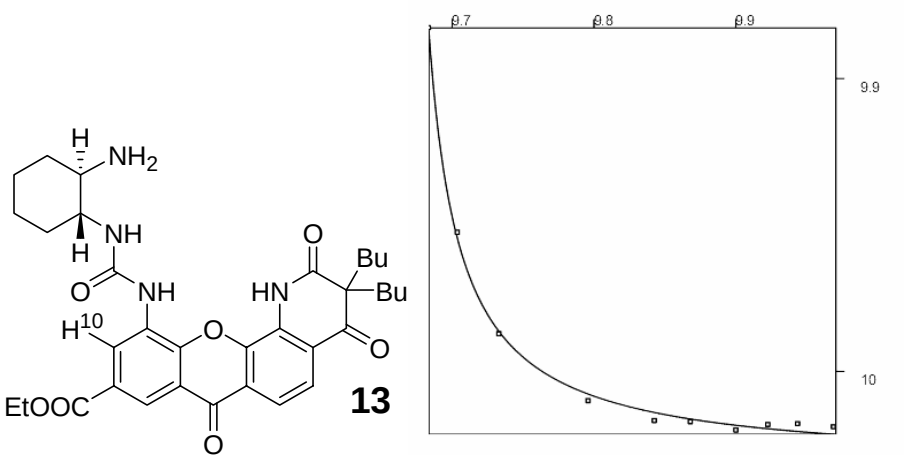
Competitive titration between receptors **9** and **2** *(receptor* **9** *Hα: δ_{free} = 2.2742 ppm.; $\delta_{complex}$ = 2.1675 ppm.; receptor* **2** *H–10: δ_{free} = 9.8623 ppm.; $\delta_{complex}$ = 10.019 ppm.).*



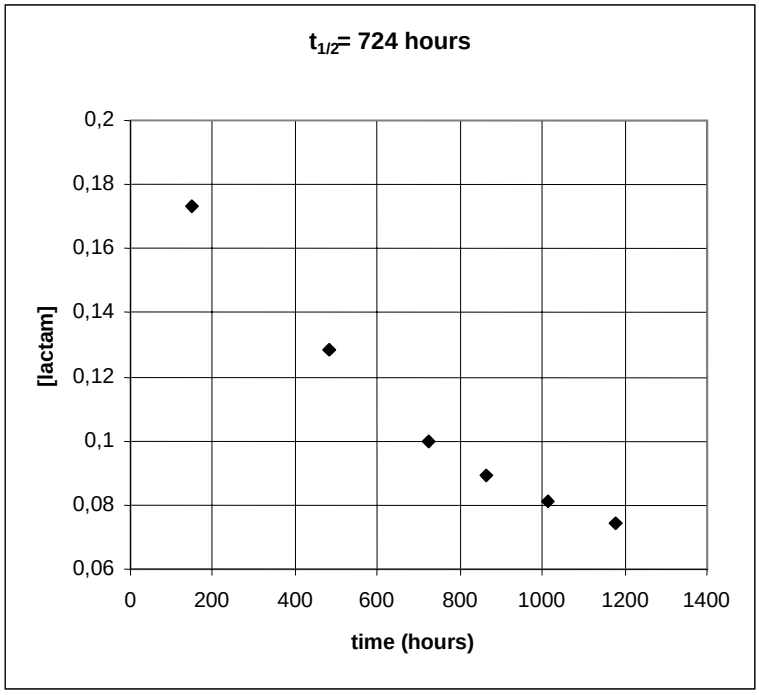
Competitive titration between receptors **12** and **2** (*receptor* **12** *H-10:* δ_{free} *= 9.6585 ppm.;* $\delta_{complex}$ *= 9.7738 ppm.; receptor* **2** *H–10:* δ_{free} *= 9.8626 ppm.,* $\delta_{complex}$ *= 10.024 ppm.).*



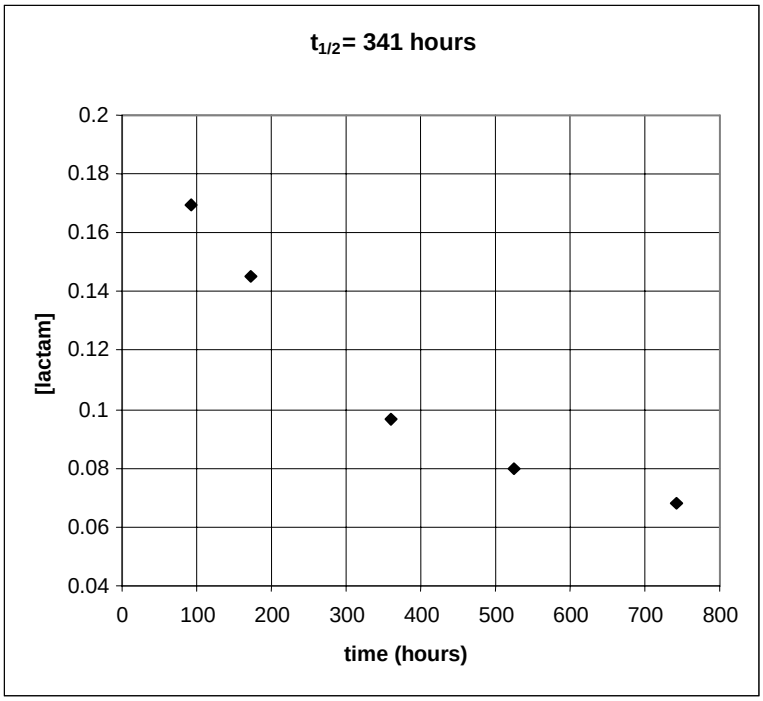
Competitive titration between receptors **13** and **2** (*receptor* **13** *H-10:* δ_{free} *= 9.6834 ppm.;* $\delta_{complex}$ *= 9.9707 ppm.; receptor* **2** *H–10:* δ_{free} *= 9.8622 ppm.,* $\delta_{complex}$ *= 10.024 ppm.).*



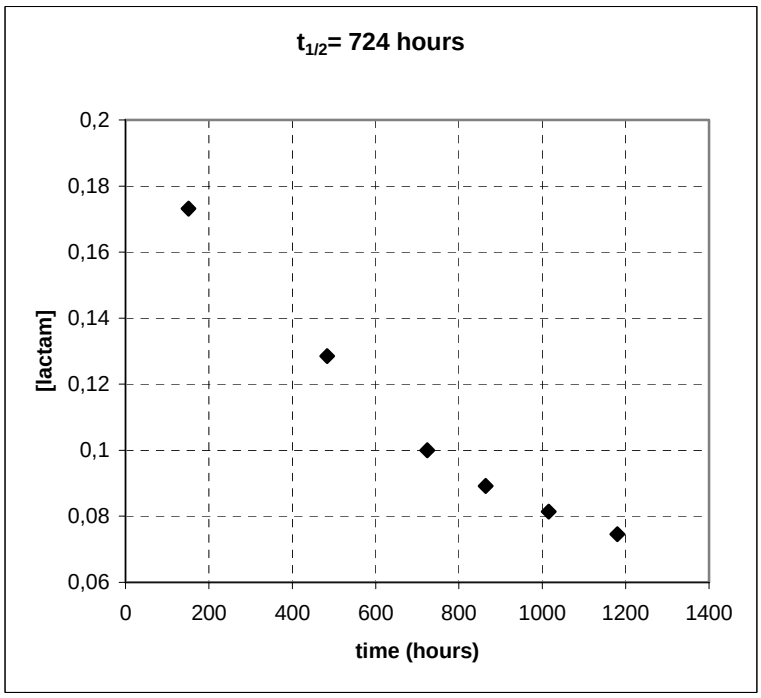
Graphic plots of the lactam concentration vs. time in kinetic experiments: Ethylmercaptane at 305 K, [lactam]= 0.2 M, [DABCO]= 0.02 M.



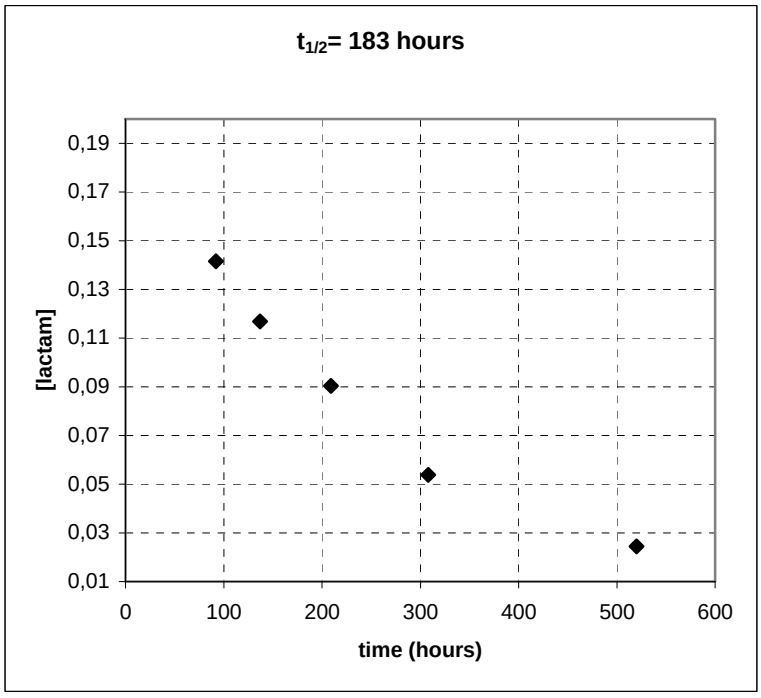
Ethylmercaptane at 305 K, [receptor **2**] = 0.02 M, [lactam] = 0.2 M, [DABCO] = 0.02 M



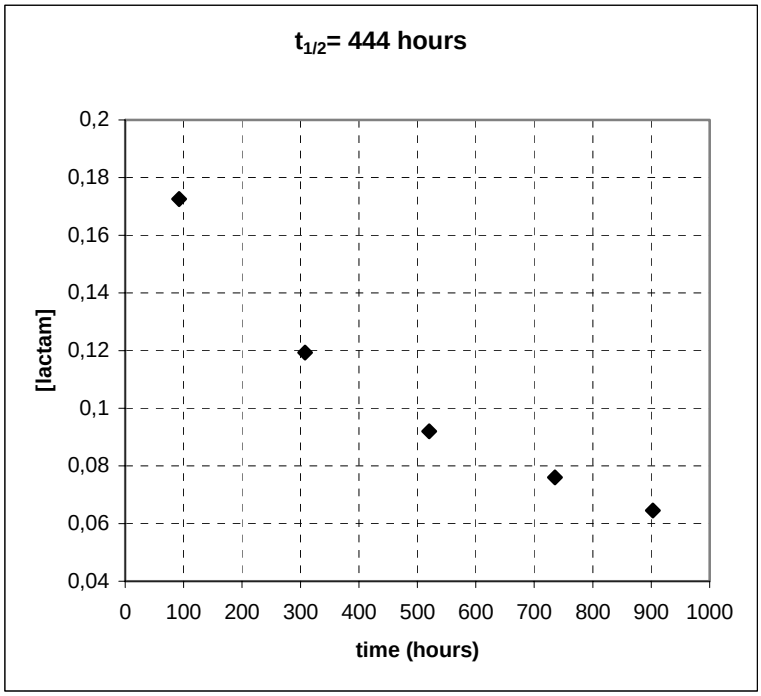
Ethylmercaptane at 305 K, [receptor **3**] = 0.02 M, [lactam] = 0.2 M



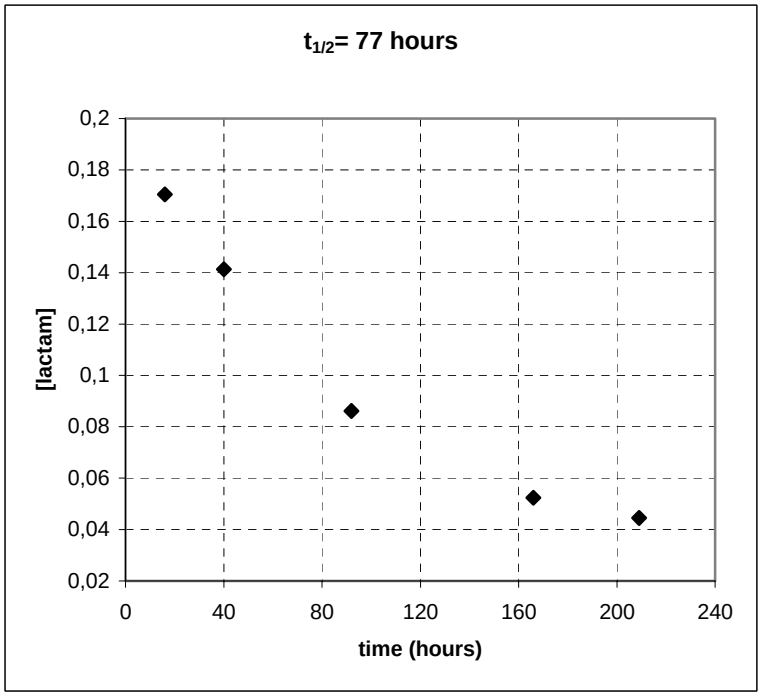
Ethylmercaptane at 305 K, [receptor **4**] = 0.02 M, [lactam] = 0.2 M



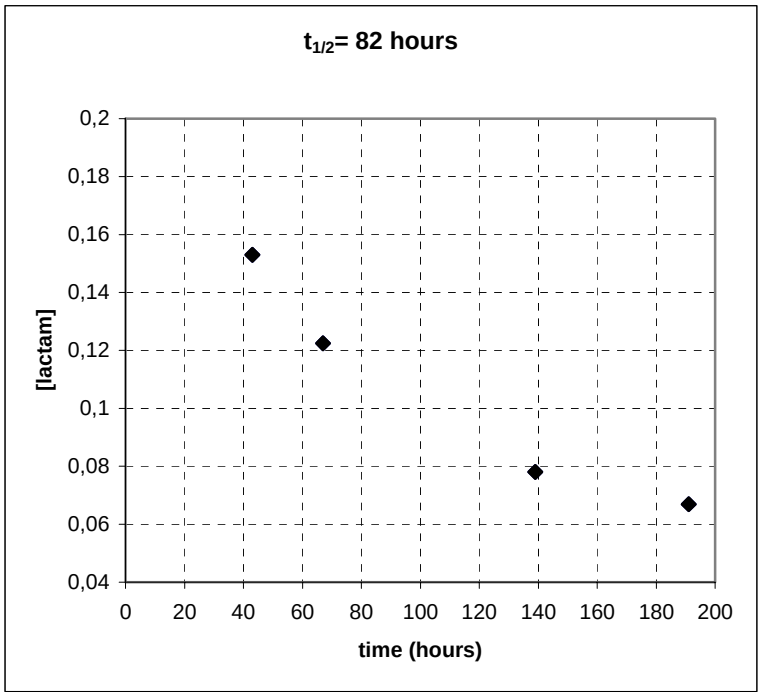
Ethylmercaptane at 305 K, [receptor **5**] = 0.02 M, [lactam] = 0.2 M



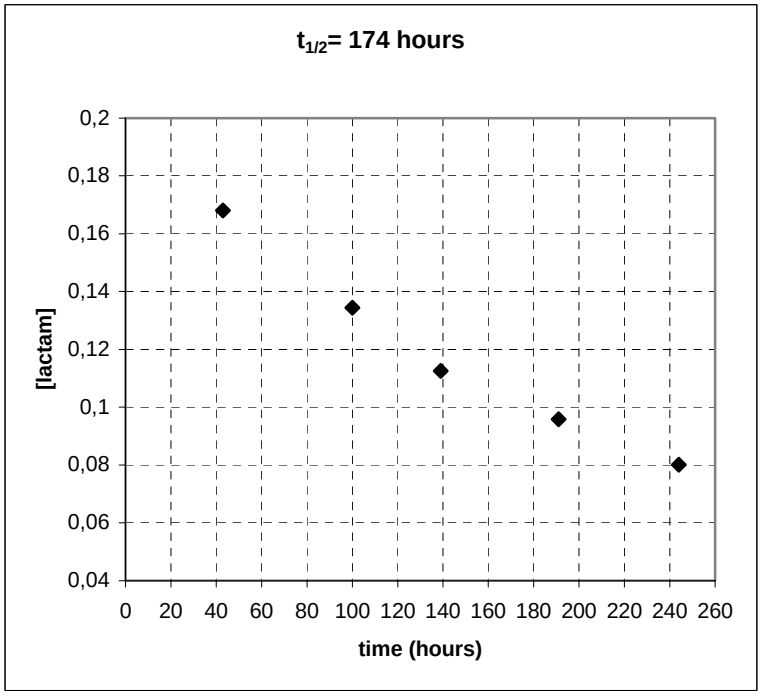
Ethylmercaptane at 305 K, [receptor **6**] = 0.02 M, [lactam] = 0.2 M



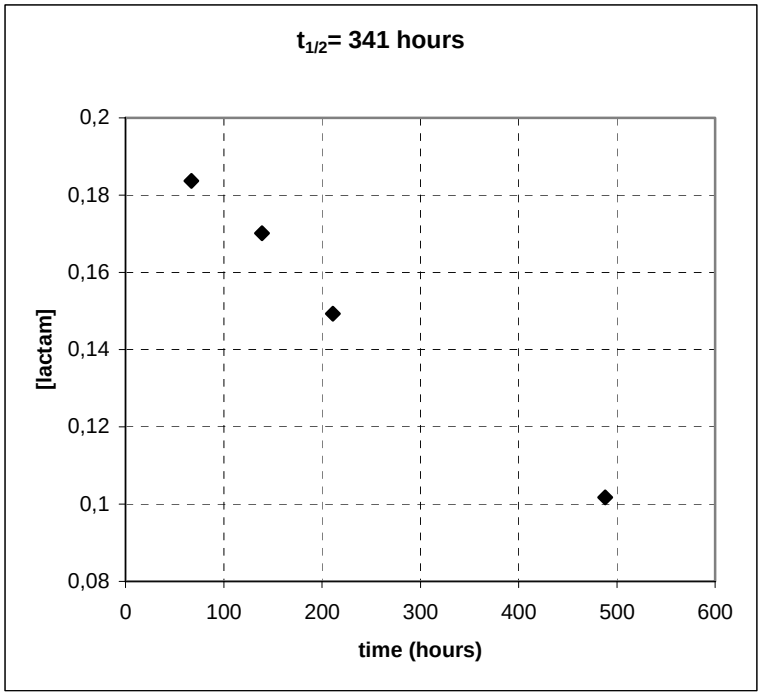
Ethylmercaptane at 305 K, [receptor D-**6**] = 0.02 M, [lactam] = 0.2 M



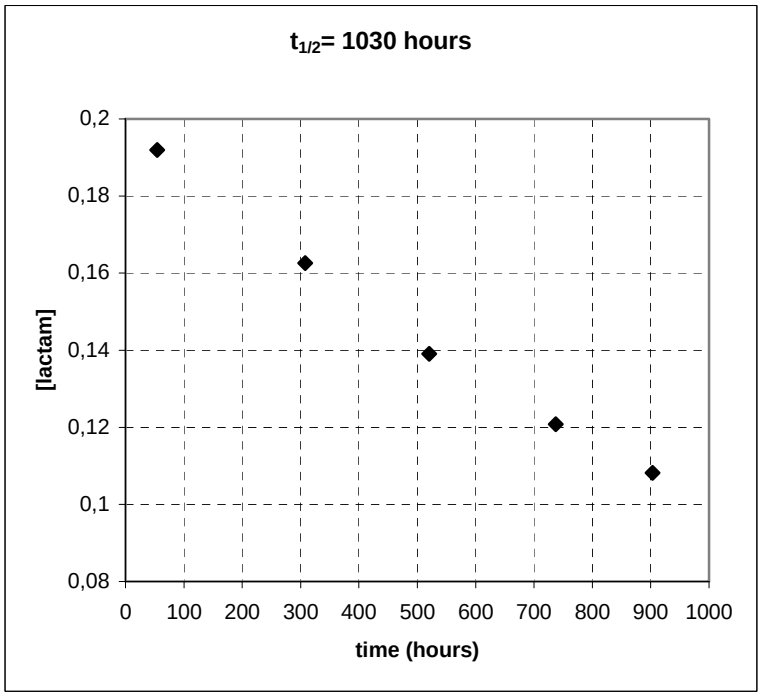
Ethylmercaptane at 305 K, [receptor D-**6**] = 0.01 M, [lactam] = 0.2 M



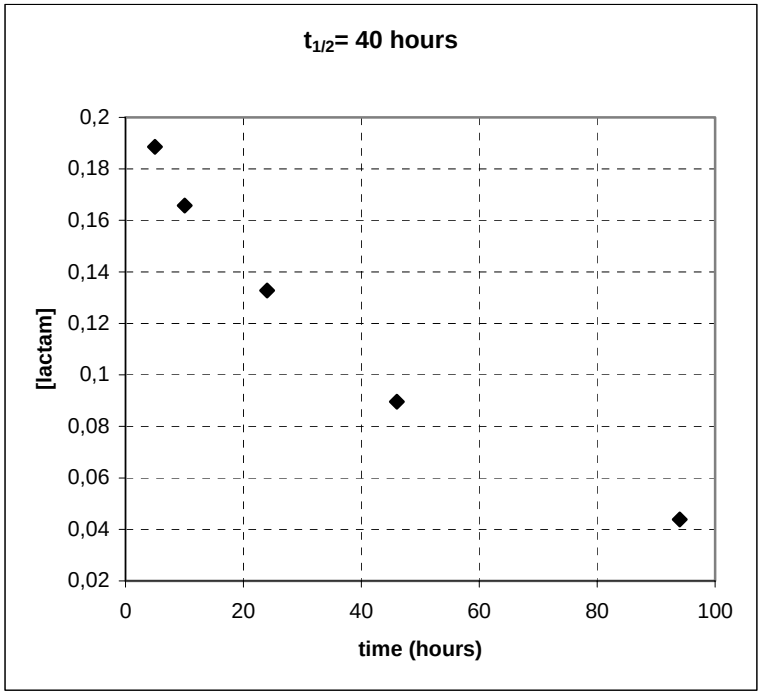
Ethylmercaptane at 305 K, [receptor D-**6**] = 0.005 M, [lactam] = 0.2 M



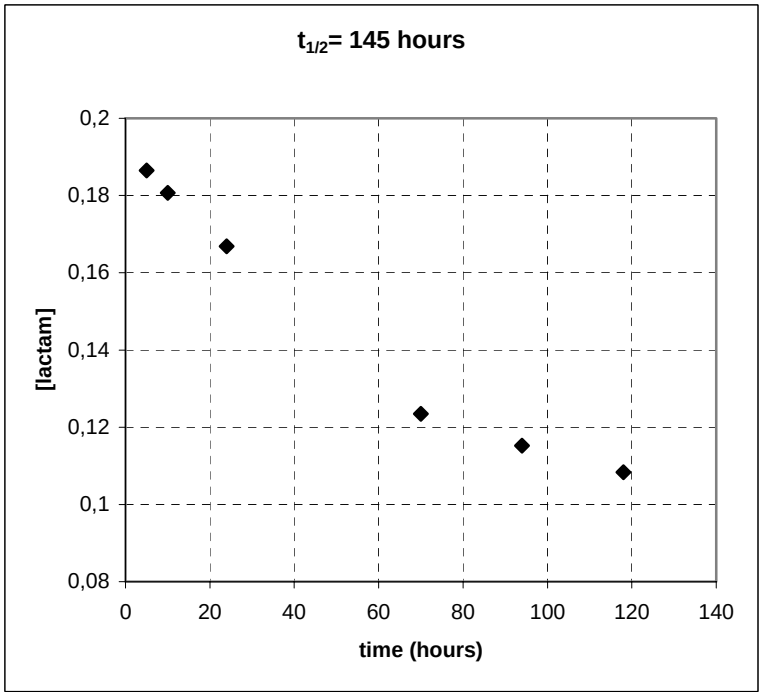
Ethylmercaptane at 305 K, [receptor **7**] = 0.02 M, [lactam] = 0.2 M



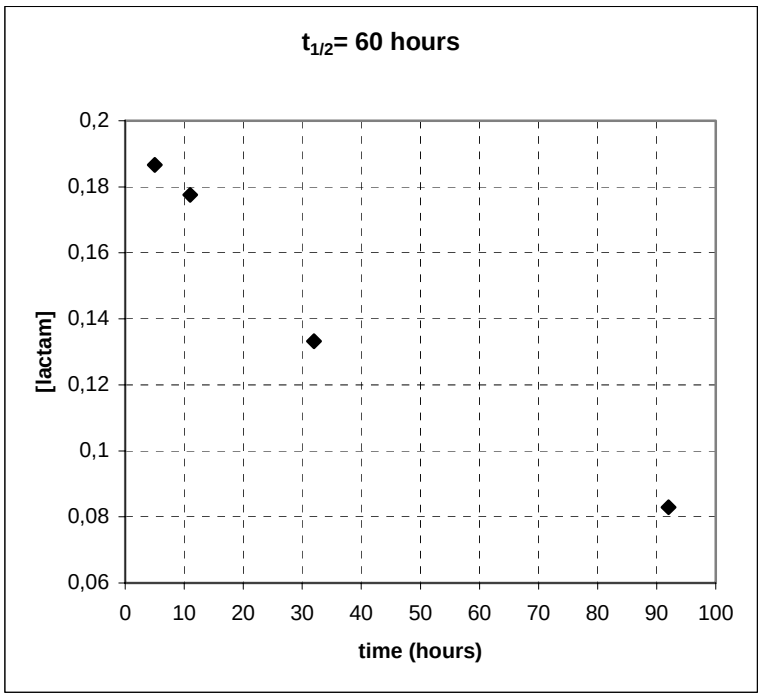
Ethylmercaptane at 305 K, [receptor **8**] = 0.02 M, [lactam] = 0.2 M



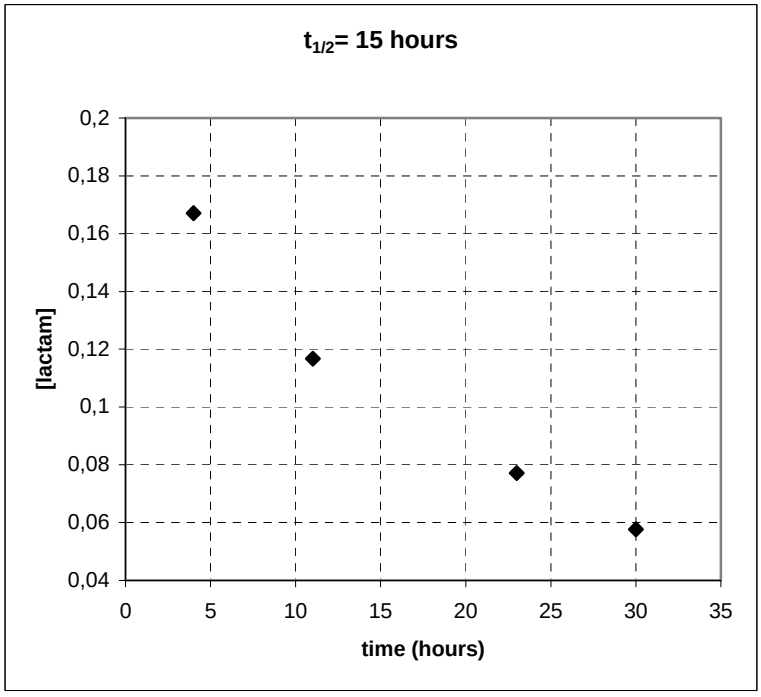
Ethylmercaptane at 305 K, [receptor **9**] = 0.02 M, [lactam] = 0.2 M



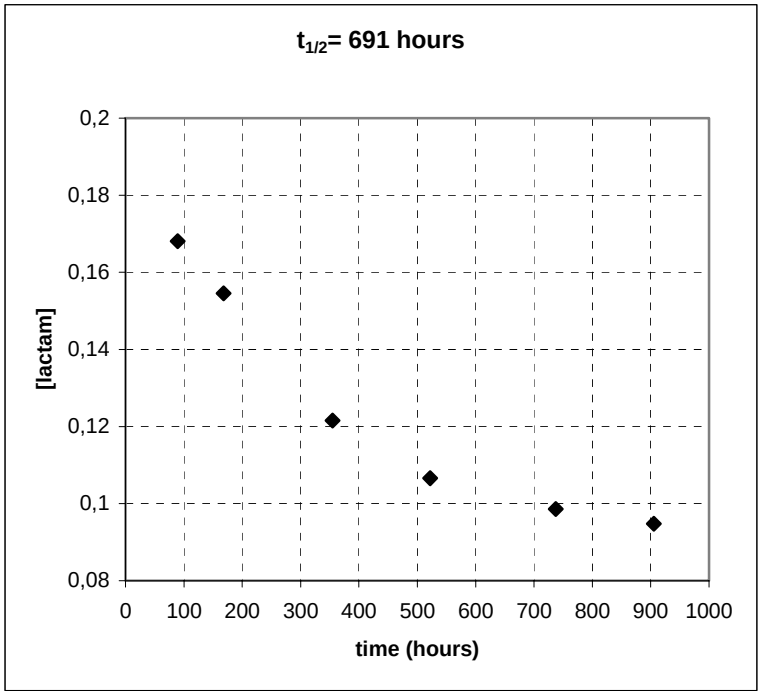
Ethylmercaptane at 305 K, [receptor **10**] = 0.02M, [lactam] = 0.2M



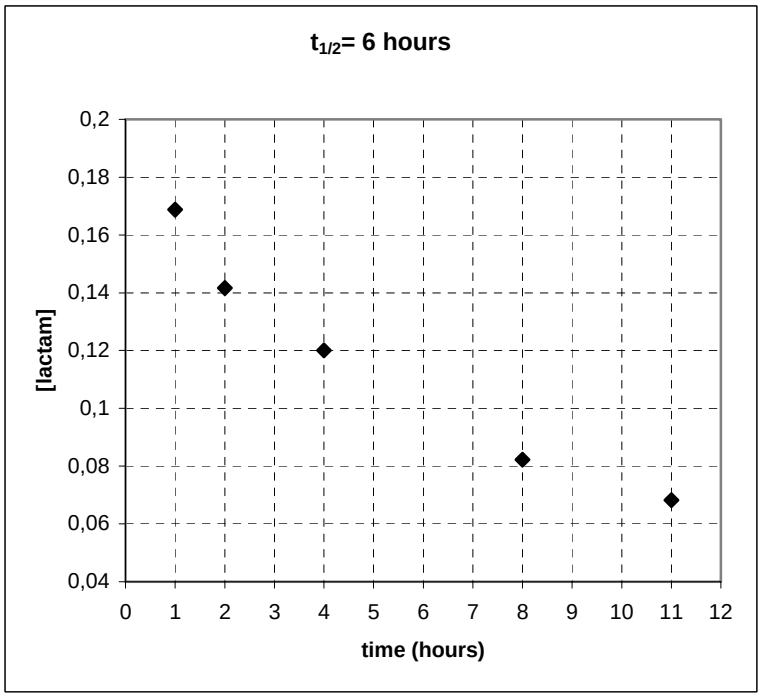
Ethylmercaptane at 305 K, [receptor **11**] = 0.02 M, [lactam] = 0.2M



Ethylmercaptane at 305 K, [receptor **12**] = 0.02 M, [lactam] = 0.2M

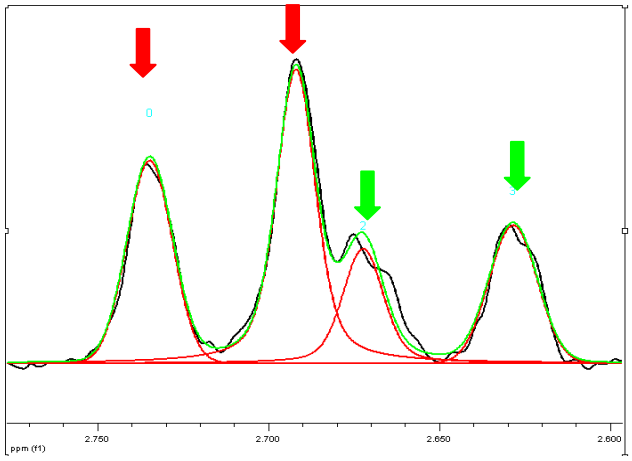


Ethylmercaptane at 305 K, [receptor **13**] = 0.02 M, [lactam] = 0.2M

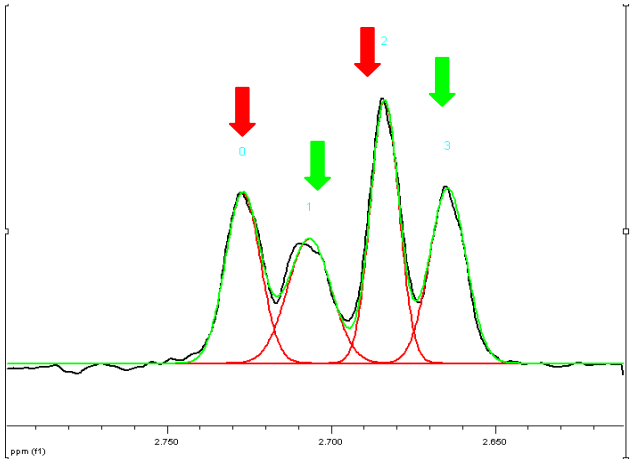


Enantiomer ratio induced by the receptors measured at the half-life time of the reaction. Integration was performed by Gaussian deconvolution of the signals. The *R* enantiomer signal is shown in red and that of the *S* enantiomer in green. The chiral-shift reagent **14** was used.

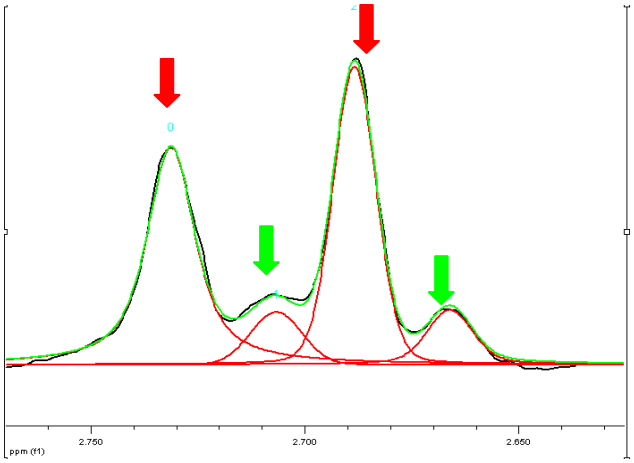
Receptor **4**:



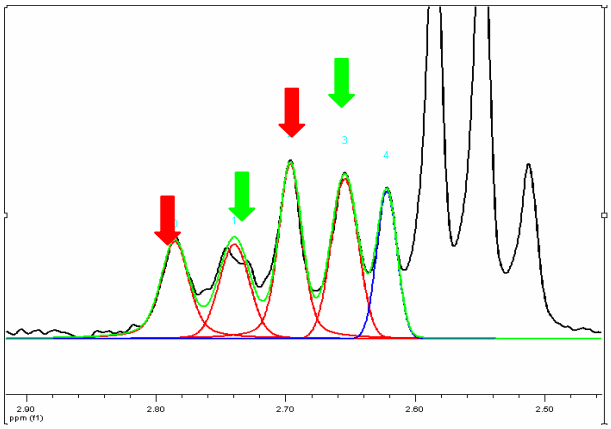
Receptor **5**:



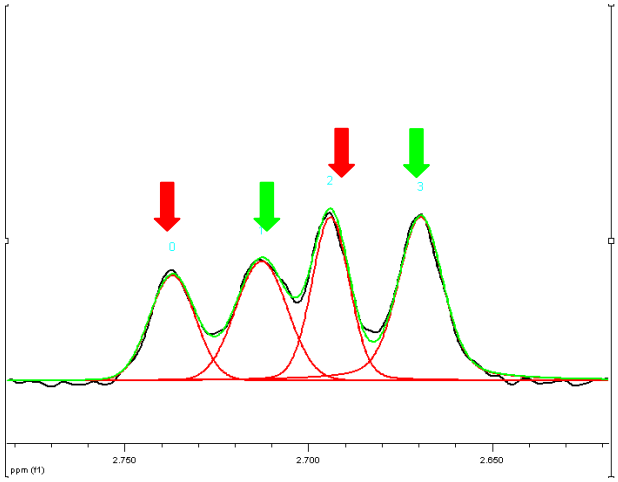
Receptor **6**:



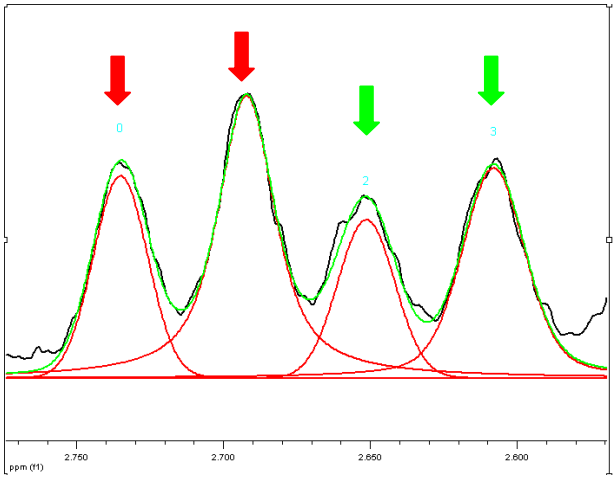
Receptor **7**:



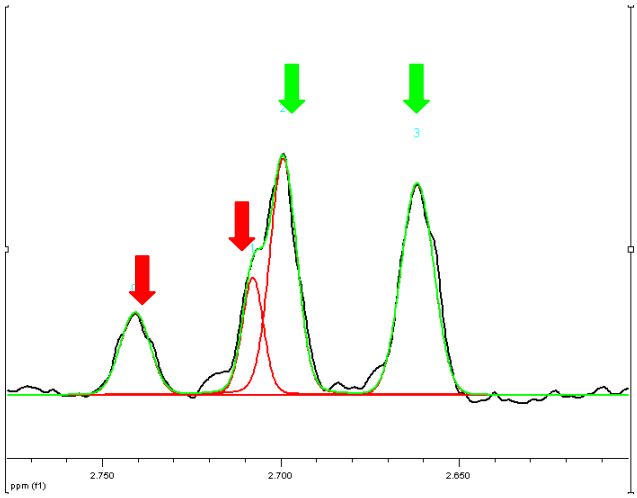
Receptor **11**:



Receptor **12**:

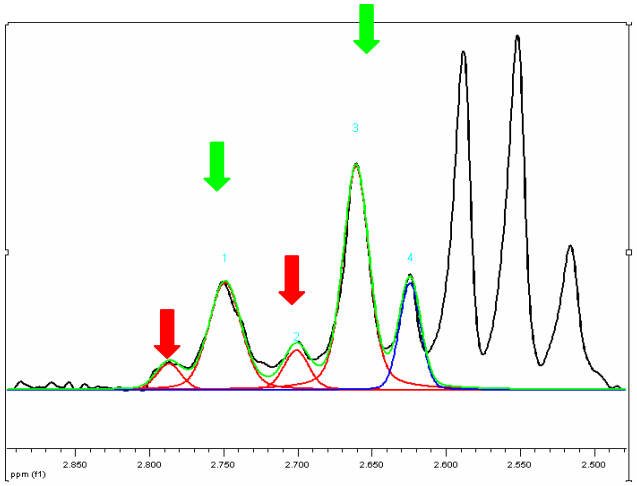


Receptor **13**:

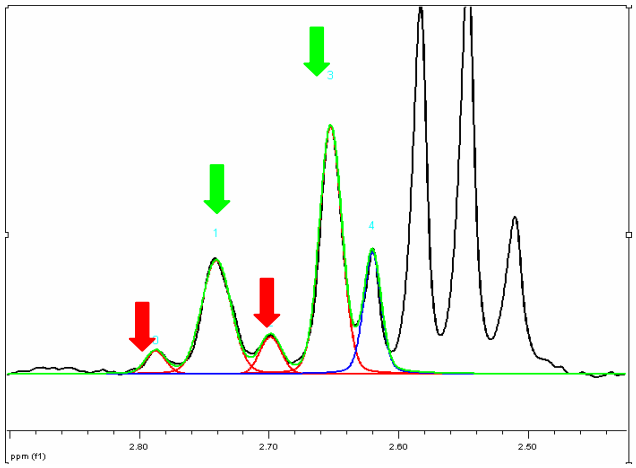


Enantiomer ratio induced by the receptor **D-6** measured at different times and different concentrations of the receptor. The *R* enantiomer signal is shown in red and that of the *S* enantiomer in green. The chiral-shift reagent **14** was used.

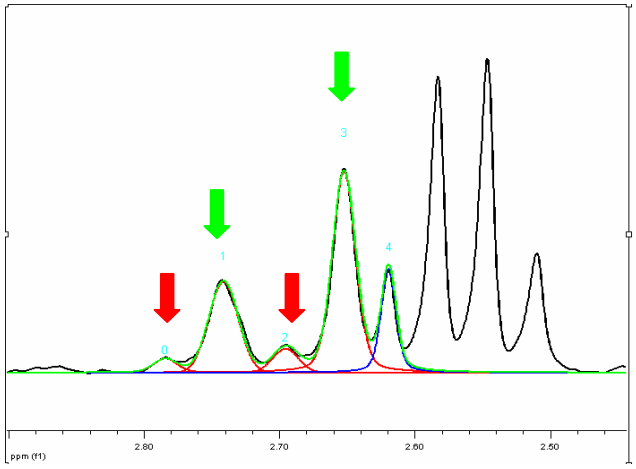
[receptor]: 0.02 M; 43 hours:



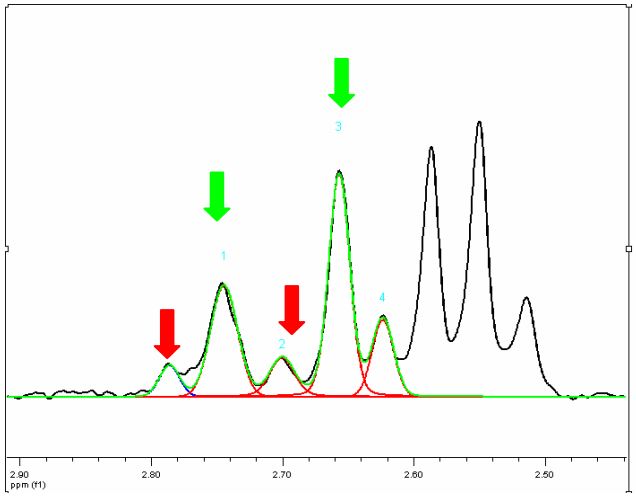
[receptor]: 0.02 M; 67 hours:



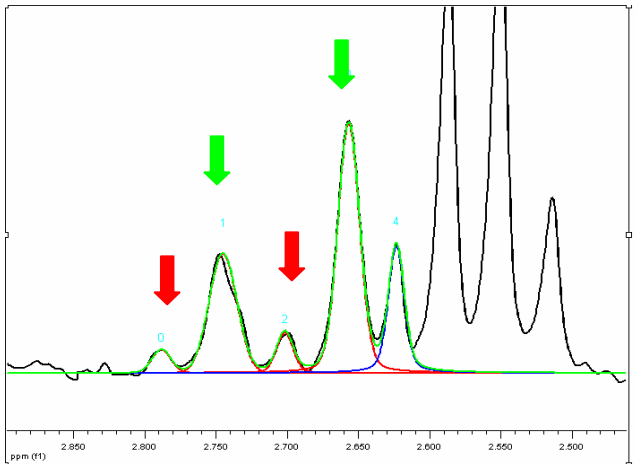
[receptor]: 0.02 M; 139 hours:



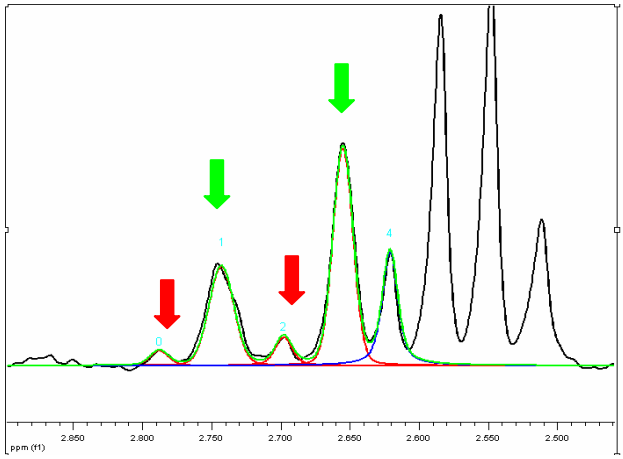
[receptor]: 0.02 M; 650 hours:



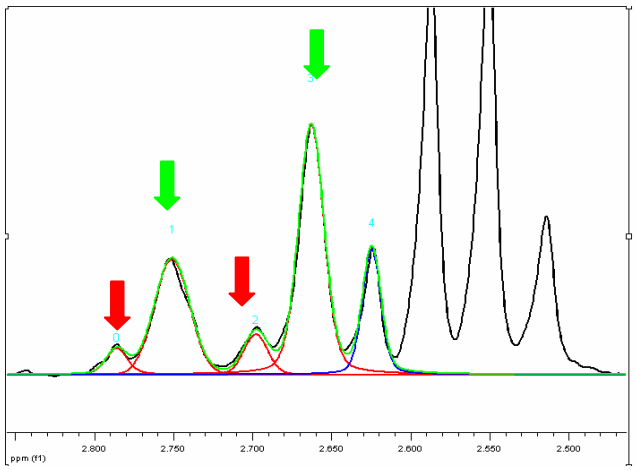
[receptor]: 0.01 M; 43 hours:



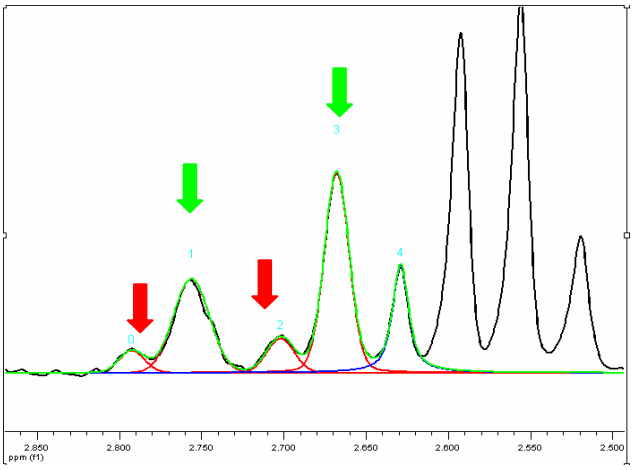
[receptor]: 0.01 M; 139 hours:



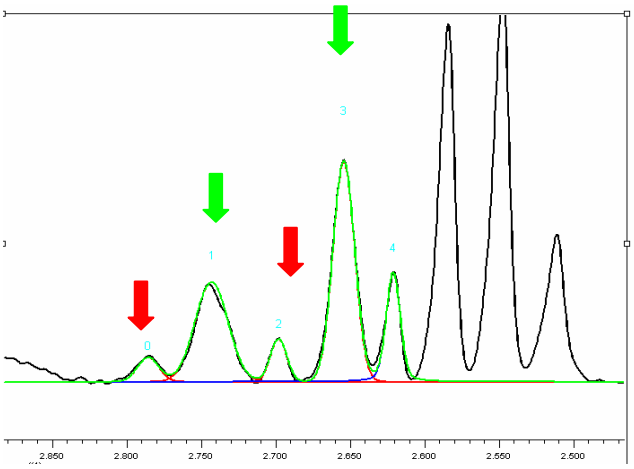
[receptor]: 0.01 M; 191 hours:



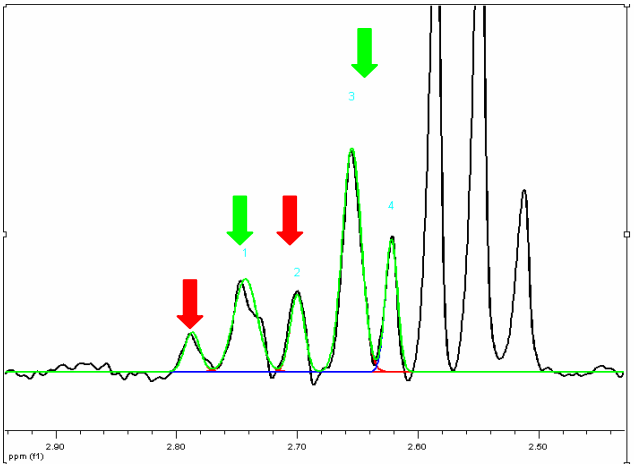
[receptor]: 0.01 M; 672 hours:



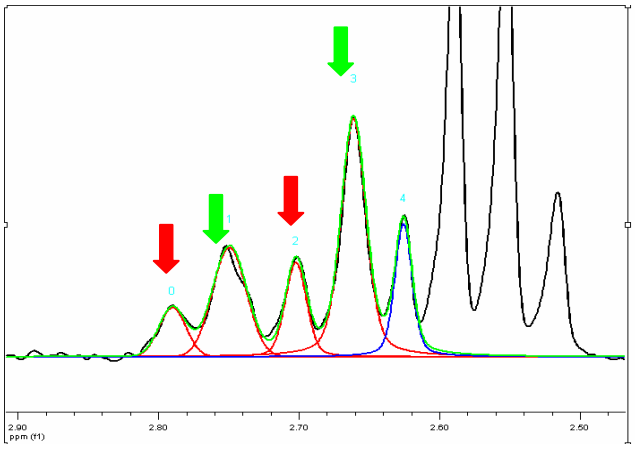
[receptor]: 0.005 M; 139 hours:



[receptor]: 0.005 M; 211 hours:



[receptor]: 0.005 M; 488 hours:



Circular dichroism spectrum of compound **15** obtained from the reaction catalyzed by the receptor **D-6**. Solvent: ethanol; T = 293 K; λ = 218 nm; ε = -1.1, corrected taking into account the enantiomeric excess of the product.