Supplementary Material (ESI) for Organic & Biomolecular Chemistry


# Synthesis of a chiral artificial receptor with catalytic activity in Michael additions and its chiral resolution by a new methodology

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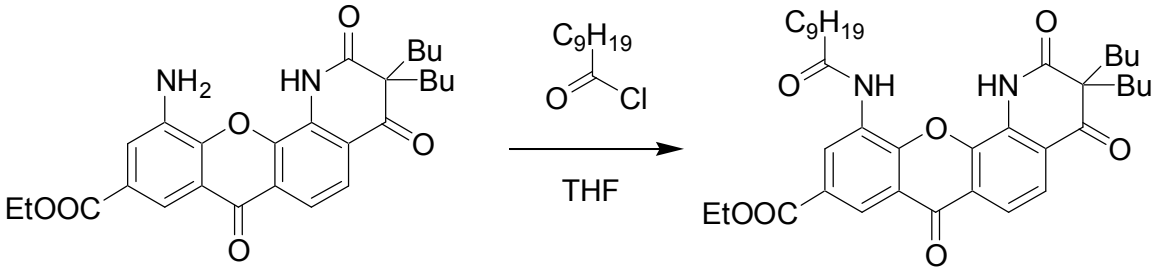
## Electronic Supplementary Information

# Preparation and physical data of receptors:

**General Remarks:** $^{1}H$ and $^{13}C$ NMR spectra were acquired on a Varian200 Mercury VX 2000 200 MHz spectrometer. Mass spectra were obtained with a Waters ZQ4000 quadrupole spectrometer, with positive electrospray ionization (3.5 KV). IR spectra were recorded on a BONEN MB-100FT IR spectrometer. Melting points were obtained with a Stuart Scientific SMP3 Apparatus. THF was distilled from sodium/benzophenone.

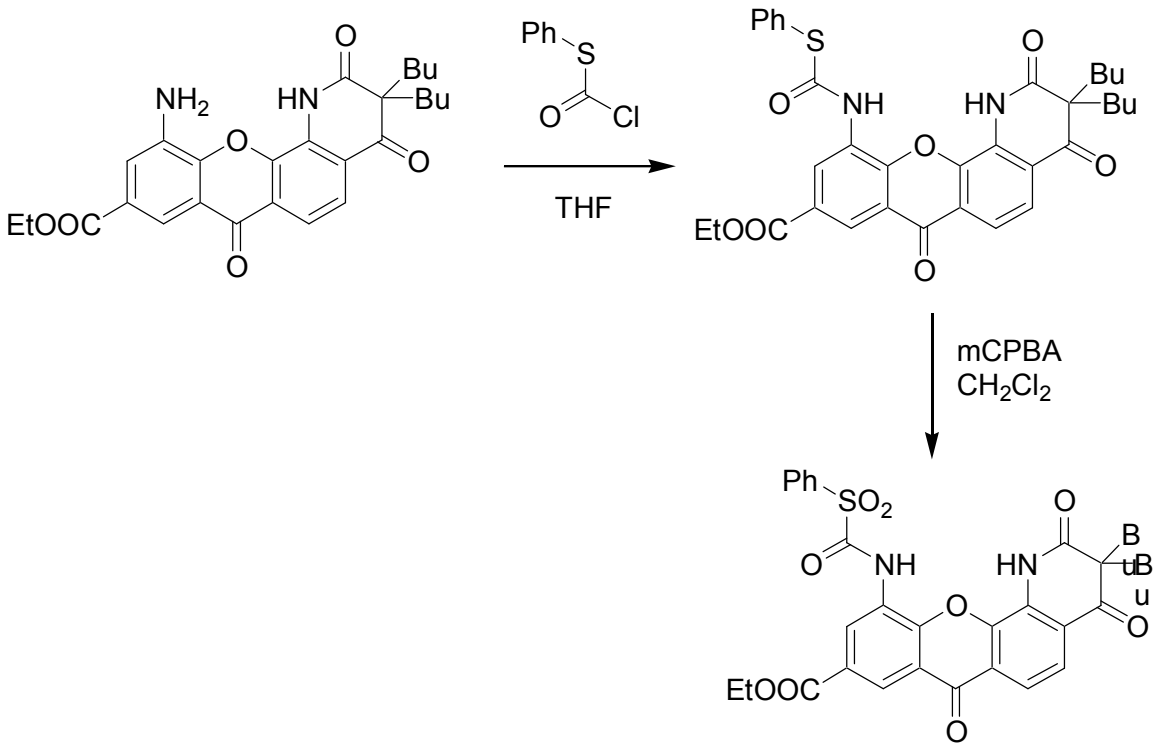
**Preparation of receptor 2:**




1 equivalent of decanoyl chloride was added to a solution of the xanthone amino derivative in dry THF (1 g in 10 ml). The reaction was heated to 50ºC for 2 hours. Then, water (2 ml) was added drop-wise with magnetic stirring. The desired compound crystallized. Yield: 87%.

Physical data for receptor 7: m.p. 194-196 ºC; $^{1}H$ NMR (200 MHz, $CDCl_3$), δ=10.44 (s 1H), 10.11 (s 1H), 9.25 (d, $^{3}J$(H,H) = 2.1 Hz, 1H) 8.82 (d, $^{3}J$(H,H) = 2.1, 1H) 8.14 (d, $^{3}J$(H,H) = 8.4 Hz, 1H) 7.97 (d, $^{3}J$(H,H) = 8.4 Hz, 1H) 4.47 (q, $^{3}J$(H,H) = 7.1 Hz, 2H), 2.61 (t, $^{3}J$(H,H) = 7.3 Hz, 2H) 2.08 (m, 2H) 1.86 (m, 4H) 1.46 (t, $^{3}J$(H,H) = 7.1 Hz, 3H) 1.40 (m, 10H) 1.21 (m, 8H) 0.89 (d, $^{3}J$(H,H) = 6.6 Hz, 3H) 0.79 (t, $^{3}J$(H,H) = 6.4 Hz, 3H); $^{13}C$ RMN (50 MHz, $CDCl_3$): δ= 196.5 (C), 178.5 (C), 175.2 (C), 172.9 (C), 165.5 (C), 149.4 (C), 143.7 (C), 130.9 (CH), 130.5 (C), 128.6 (C), 126.5 (C), 124.5 (CH), 123.3 (C), 122.6 (C), 122.3 (CH), 122.0 (C), 62.9 ($CH_2$), 62.4 (C), 41.4 ($CH_2$), 37.6 ($CH_2$), 32.4 ($CH_2$), 30.2 ($CH_2$), 28.2 ($CH_2$), 26.0 ($CH_2$), 23.6 ($CH_2$), 23.2 ($CH_2$), 14.9 ($CH_3$), 14.5 ($CH_3$), 14.3 ($CH_3$), 14.0 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 632 ($M+H^+$), 655 ($M+Na^+$), 681 ($M+K^+$); I.R. $\lambda^{-1}$ (nujol): 3403, 3248, 2926, 2855, 1713, 1682, 1651, 1609, 1584, 1537, 1464, 1377, 1285, 1246, 1213, 1099, 1022, 916, 762; Elemental analysis calculated for $C_{37}H_{48}N_2O_7$ (632.79): C 70.23, H 7.65, N 4.43; found: C 70.44, H 7.72, N 4.34.

**Preparation of receptor 3:**



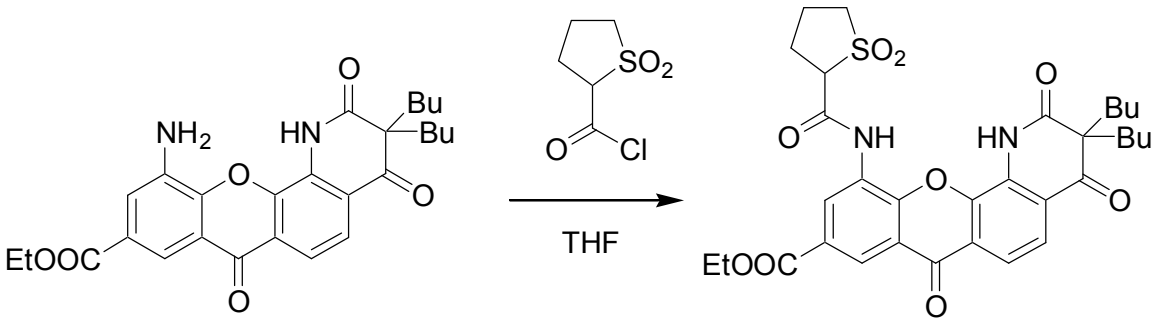

To obtain the intermediate compound, xanthone amine was dissolved in THF (0.5 g in 5 ml) and phenylthioacetic acid chloride (0.5 g) was added. After 20 minutes, water (0.5 ml) was added and the reaction mixture was heated to 50ºC during 5 minutes. The solvent was evaporated off under a vacuum and the residue was dissolved in ethyl acetate. This solution was washed with $Na_2CO_3$ ac. 4%. From the organic layer, the intermediate compound was recovered. Yield: 93%. 0.3 g of the intermediate compound was dissolved in $CH_2Cl_2$ and an excess (4 equivalents) of *m*-chloroperbenzoic acid was added. TLC chromatography was used to follow the reaction progress. When it had finished, the solvent was evaporated off and residue was dissolved in ethyl acetate. This solution was washed first with $Na_2SO_3$ ac. 4% and then with $Na_2CO_3$ ac. 4%. The organic layer was then dried with anhydrous $Na_2SO_4$, and receptor 3 was recovered after evaporation of the solvent. Yield: 94%.

Physical data for the intermediate compound: m.p. 175-177 ºC; $^1$H NMR (200 MHz, $CDCl_3$): δ= 10.00 (s, 1H), 9.28 (d, $^3J$(H,H) = 2.0 Hz, 1H), 8.77 (d, $^3J$(H,H) = 2.0 Hz, 1H), 8.73 (s, 1H), 8.04 (d, $^3J$(H,H) = 8.4 Hz, 1H), 7.96 (d, $^3J$(H,H) = 8.4 Hz, 1H), 7.44 (d, $^3J$(H,H) = 7.2 Hz, 2H), 7.24 (m, 3H), 4.46 (q, $^3J$(H,H) = 7.1 Hz, 2H), 3.98 (s, 2H), 2.06 (m, 4H), 1.45 (t, $^3J$(H,H) = 7.1 Hz, 3H), 1.18 (m, 8H), 0.76 (t, $^3J$(H,H) = 6.8 Hz, 6H); $^{13}$C RMN (50 MHz, $CDCl_3$): δ= 196.8 (C), 174.8 (C), 174.5 (C), 167.6 (C), 164.7 (C), 148.3 (C), 142.6 (C), 134.1 (C), 131.2 (C), 129.1 (CH), 128.9 (CH), 127.4 (CH), 127.1 (C), 126.9 (CH), 125.3 (C), 123.6 (CH), 122.3 (C), 121.9 (CH), 121.3 (C), 119.7 (CH), 62.5 (C), 61.6 ($CH_2$), 39.5 ($CH_2$), 38.6 ($CH_2$), 27.0 ($CH_2$), 22.6 ($CH_2$), 14.0 ($CH_3$), 13.3 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 651 (M+$Na^+$); I.R. $\lambda^{-1}$ (nujol): 3320, 2926, 2855, 1724, 1701, 1665, 1603, 1545, 1458, 1375, 1279, 1209, 1155, 1123, 1121, 1043, 790, 754; Elemental analysis calculated for $C_{34}H_{34}N_2O_7S$ (614.71): C 66.43, H 5.57, N 4.56; found: C 66.71, H 5.38, N 4.62.

Physical data for receptor 3: m.p. 105-107 ºC; $^1$H NMR (200 MHz, $CDCl_3$): δ= 10.12 (s, 1H), 9.63 (s, 1H), 9.23 (d, $^3J$(H,H) = 2.0 Hz, 1H), 8.83 (d, $^3J$(H,H) = 2.0 Hz, 1H), 8.12 (d, $^3J$(H,H) = 7.0 Hz, 2H),8.07 (d, $^3J$(H,H) = 8.9 Hz, 1H), 8.00 (d, $^3J$(H,H) = 8.4 Hz, 1H), 7.71 (m, 3H), 4.45 (q, $^3J$(H,H) = 7.2 Hz, 2H),

4.35 (s, 3H), 2.03 (m, 4H), 1.44 (t, $^3J$(H,H) = 7.1 Hz, 3H), 1.21 (m, 8H), 0.76 (t, $^3J$(H,H) = 6.8 Hz, 6H). $^{13}$C RMN (50 MHz, $CDCl_3$): δ= 196.4 (C), 174.9 (C), 174.4 (C), 164.6 (C), 160.0 (C), 147.6 (C), 142.3 (C), 134.2 (C), 131.0 (C), 129.3 (CH), 128.8 (C), 128.4 (CH), 127.2 (CH), 126.6 (C), 122.2 (C), 122.0 (CH), 121.0 (C), 119.6 (CH), 63.1 (C), 62.2 (C), 61.6 ($CH_2$), 39.7 ($CH_2$), 26.8 ($CH_2$), 22.8 ($CH_2$), 14.3 ($CH_3$), 13.6 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 683 ($M+Na^+$); I.R. $\lambda^{-1}$ (nujol): 3322, 2926, 2855, 1713, 1678, 1604, 1559, 1377, 1306, 1289, 1246, 1208, 1159, 1118, 1121, 1084, 1028, 918, 851, 754, 723, 665; Elemental analysis calculated for $C_{34}H_{34}N_2O_9S$ (646.71): C 63.15, H 5.30, N 4.33; found: C 63.31, H 5.21, N 5.42.

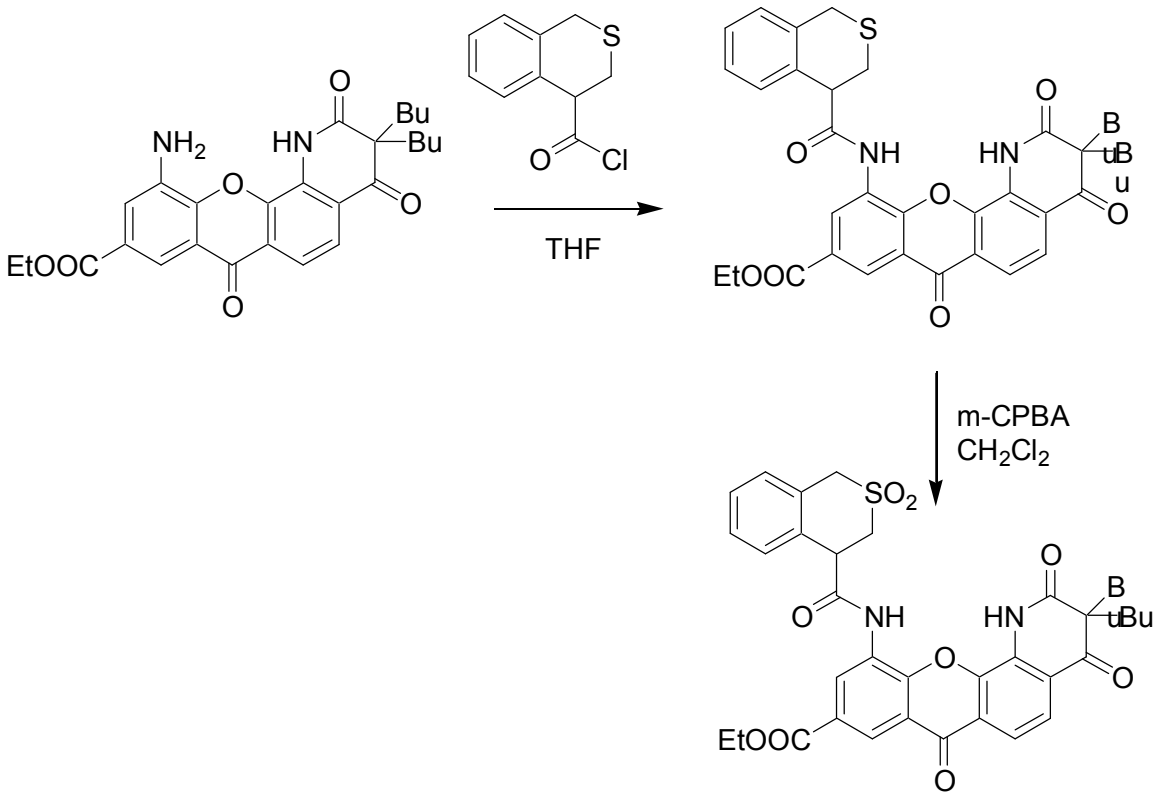
**Preparation of receptor 4:**




This receptor was prepared using same reaction conditions as for receptor 2, starting with the chloride of the sulfolane derivative.

Physical data for receptor 4: m.p. 147-149 ºC; $^1$H NMR (200 MHz, $CDCl_3$): δ= 9.94 (s, 1H), 9.71 (s, 1H), 9.03 (d, $^3J$(H,H) = 1.7 Hz, 1H), 8.83 (d, $^3J$(H,H) = 1.7 Hz, 1H), 8.05 (d, $^3J$(H,H) = 8.4 Hz, 1H), 7.96 (d, $^3J$(H,H) = 8.3 Hz, 1H), 4.45 (q, $^3J$(H,H) = 7.1 Hz, 2H), 4.22 (t, $^3J$(H,H) = 7.6 Hz, 1H), 3.43 (m, 2H), 2.68 (m, 2H), 2.36 (m, 2H), 1.97 (m, 4H), 1.45 (t, $^3J$(H,H) = 7.1 Hz, 3H), 1.13 (m, 8H), 0.70 (m, 6H); $^{13}$C RMN (50 MHz, $CDCl_3$): δ= 196.6 (C), 175.0 (C), 174.6 (C), 164.4 (C), 163.2 (C), 149.3 (C), 142.8 (C), 131.4 (C), 129.2 (CH), 127.3 (C), 126.4 (C), 125.4 (C), 125.0 (CH), 122.4 (C), 121.9 (CH), 121.6 (C), 119.8 (CH), 64.7 (CH), 62.3 (C) 61.6 ($CH_2$), 50.8 ($CH_2$), 39.8 ($CH_2$), 39.3 ($CH_2$), 27.2 ($CH_2$), 25.6 ($CH_2$), 22.7 ($CH_2$), 20.0 ($CH_2$), 14.2 ($CH_3$), 13.4 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 625 ($M+H^+$), 647 ($M+Na^+$); I.R. $\lambda^{-1}$ (nujol): 3337, 3252, 3208, 3055, 2926, 2855, 1724, 1703, 1669, 1603, 1582, 1553, 1464, 1418, 1377, 1344, 1312, 1287, 1248, 1215, 1152, 1128, 1101, 1018, 972, 907, 868, 843, 810, 762, 718; ; Elemental analysis calculated for $C_{34}H_{34}N_2O_9S$ (624.70): C 61.52, H 6.01, N 4.36; found: C 61.38, H 5.88, N 4.45.

**Preparation of receptor 5:**



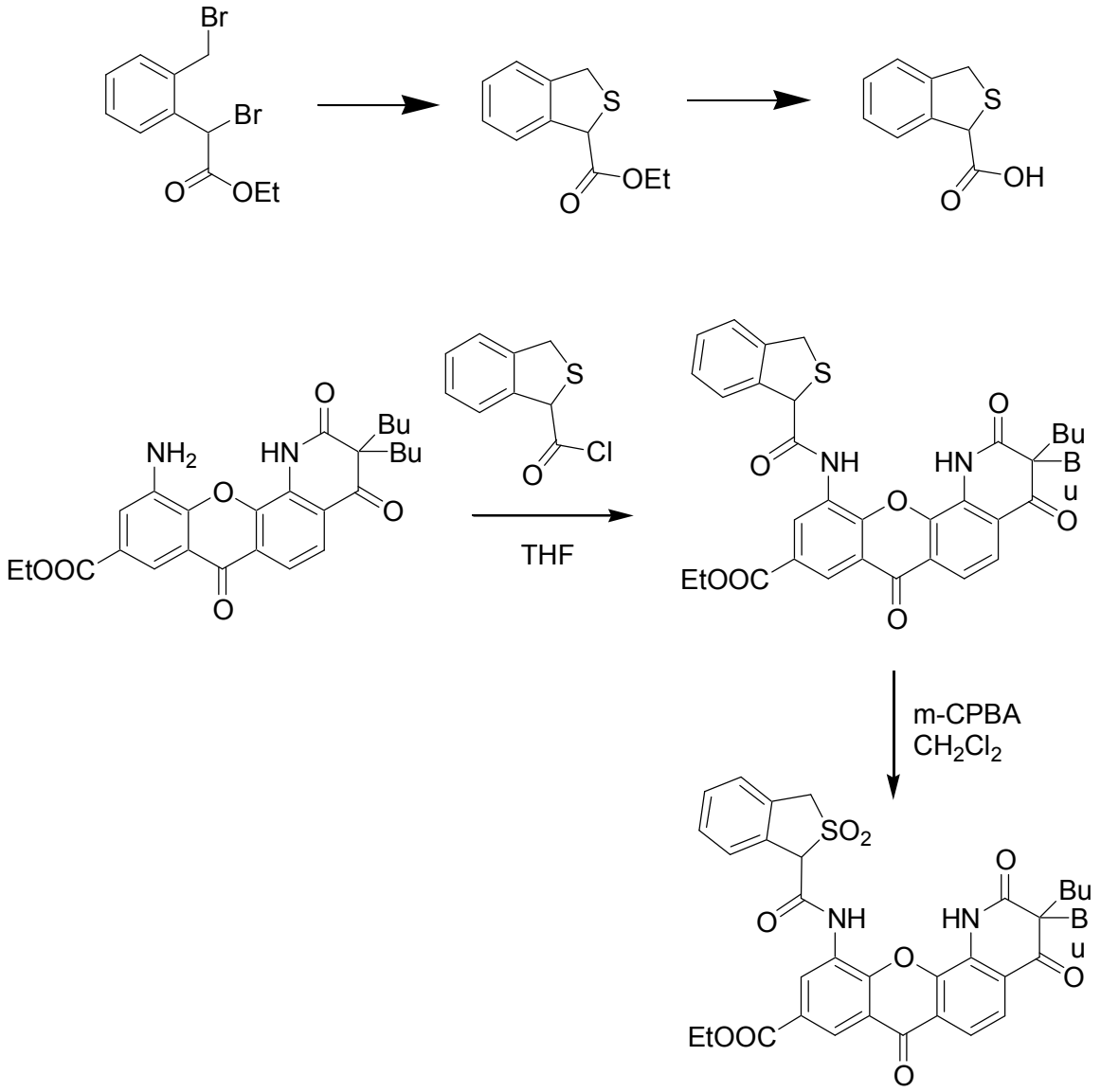

The reaction of isothiocroman-4-carbonyl chloride with xanthone amine was performed in similar conditions to those used in the previous reactions. Yield : 92%. Receptor 5 was obtained by oxidation of the intermediate compound with m-chloroperbenzoic acid, following the same procedure as that used toobtain receptor 3. Yield: 89%.

Physical data the intermediate compound: m.p. 136-138 ºC; $^{1}$H NMR (200 MHz, $CDCl_3$): δ= 9.40 (d, $^{3}J$(H,H) = 1.7 Hz, 1H), 9.18 (s, 1H), 8.87 (s, 1H), 8.72 (d, $^{3}J$(H,H) = 1.7 Hz, 1H), 8.00 (d, $^{3}J$(H,H) = 8.4 Hz, 1H), 7.93 (d, $^{3}J$(H,H) = 8.4 Hz, 1H), 7.52 (d, $^{3}J$(H,H) = 7.3 Hz, 1H), 7.30 (d, $^{3}J$(H,H) = 7.8 Hz, 1H), 7.23 (m, 2H), 4.44 (q, $^{3}J$(H,H) = 7.1 Hz, 2H), 4.38 (d, $^{3}J$(H,H) = 16.4 Hz, 1H), 4.24 (m, 1H), 4.17 (d, $^{3}J$(H,H) = 16.4 Hz, 1H), 3.43 (m, 2H), 2.06 (m, 4H), 1.44 (t, $^{3}J$(H,H) = 7.1 Hz, 3H), 1.25 (m, 8H), 0.82 (m, 6H); $^{13}$C RMN (50 MHz, $CDCl_3$): δ= 197.1 (C), 174.9 (C), 173.5 (C), 171.8 (C), 164.8 (C), 147.6 (C), 142.5 (C), 133.7 (C), 131.6 (C), 131.3 (C), 130.6 (CH), 129.4 (CH), 127.9 (CH), 127.7 (CH), 127.6 (C), 127.5 (C), 126.5 (CH), 125.3 (C), 123.4 (CH), 122.1 (CH), 122.0 (C), 121.4 (C), 119.5 (CH), 62.7 (C), 61.7 ($CH_2$), 46.2 (CH), 39.6 ($CH_2$), 39.5 ($CH_2$), 30.3 ($CH_2$), 29.3 ($CH_2$), 27.2 ($CH_2$), 22.9 ($CH_2$), 22.8 ($CH_2$), 14.3 ($CH_3$), 13.6 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 677 ($M+Na^+$), 693 ($M+K^+$); I.R. $\lambda^{-1}$ (nujol): 3314, 2926, 2855, 1709, 1672, 1603, 1532, 1462, 1377, 1285, 1244, 1209, 1163, 1101, 1024, 959, 916, 856, 843, 758, 723; Elemental analysis calculated for $C_{37}H_{38}N_2O_7S$ (654.77): C 67.87, H 5.85, N 4.28; found: C 67.56, H 5.64, N 4.39.

Physical data for receptor 5: m.p. decomposition around 140 ºC; $^{1}$H NMR (200 MHz, $CDCl_3$): δ= 9.55 (s, 1H), 9.52 (s, 1H), 9.29 (d, $^{3}J$(H,H) = 2.0 Hz, 1H), 8.77 (d, $^{3}J$(H,H) = 2.0 Hz, 1H), 8.00 (d, $^{3}J$(H,H) = 8.4 Hz, 1H), 7.94 (d, $^{3}J$(H,H) = 8.4 Hz, 1H), 7.58 (d, $^{3}J$(H,H) = 7.0 Hz, 1H), 7.35 (m, 3H), 5.49 (d, $^{3}J$(H,H) = 16.1 Hz, 1H), 4.88 (m, 1H), 4.53 (d, $^{3}J$(H,H) = 16.1 Hz, 1H), 4.49 (q, $^{3}J$(H,H) = 7.1 Hz, 2H), 3.94 (m, 2H), 2.08 (m, 4H), 1.49 (t, $^{3}J$(H,H) = 7.1 Hz, 3H), 1.29 (m, 8H), 0.86 (m, 6H); $^{13}$C RMN (50 MHz, $CDCl_3$): δ= 197.7 (C), 175.3 (C), 174.4 (C), 169.7 (C), 165.1 (C), 148.4 (C), 143.1 (C), 132.1 (C), 131.8 (CH), 130.1 (CH), 129.9 (CH), 129.1 (CH), 128.8 (C), 128.5 (C), 127.5 (C), 127.0 (CH), 125.6 (C), 124.0 (CH), 122.5 (C), 122.1 (CH), 121.7 (C), 119.6 (CH), 62.6 (C), 62.0 ($CH_2$), 52.2 (CH), 50.3 ($CH_2$), 49.2 ($CH_2$), 40.5 ($CH_2$), 39.3 ($CH_2$), 27.4 ($CH_2$), 27.2 ($CH_2$), 23.2 ($CH_2$), 23.1 ($CH_2$), 14.5 ($CH_3$),

14.0 ($CH_3$), 13.9 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 709 ($M+Na^+$); I.R. $\lambda^{-1}$ (nujol): 3310, 2927, 2853, 1705, 1670, 1603, 1541, 1458, 1377, 1287, 1244, 1209, 1171, 1117, 1024, 916, 899, 866, 756, 723; Elemental analysis calculated for $C_{37}H_{38}N_2O_9S$ (686.77): C 64.71, H 5.58, N 4.43; found: C 64.71, H 5.65, N 4.23.

**Preparation of receptor 6:**




Preparation of 1,3-dihydro-benzo[c]thiophene-1-carbonyl chloride: Bromo-(2-bromomethyl-phenyl)-acetic acid ethyl ester was dissolved in THF (8 g in 360 ml) and an aqueous solution of $Na_2S$ (3 equivalents in 40 ml) was added very slowly with magnetic stirring. The reaction mixture was cooled externally with an ice bath and addition was stopped when the $^1$H-NMR spectrum revealed that the starting material had reacted completely. Then, 2.0 M HCl was added up to neutral pH. THF was evaporated under a vacuum without heating the reaction mixture, and the 1,3-dihydro-benzothiophene ester derivative was extracted with ethyl acetate and purified by chromatography over silica gel. Yield: 43%. Hydrolysis was accomplished by dissolving this compound in a saturated KOH solution in methanol/water 9/1. Most of the solvent was evaporated off under a vacuum, water was added, and the solution was acidulated with a 2.0M HCl solution such that the dihydrobenzothiophene acid derivative precipitated. Yield: 87%. This acid was dissolved in $CH_2Cl_2$ (1 g in 10 ml) and 0.9 equivalents of $PCl_5$

were added. When green crystals of $PCl_5$ had completely dissolved, the solvent was evaporated off under a vacuum without heating the solution.

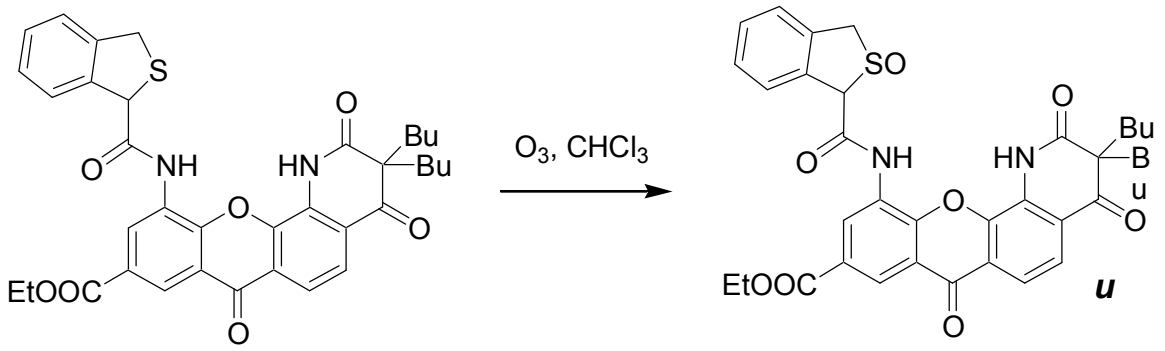
Preparation of receptor 6: The intermediate receptor was prepared by reacting the xanthone amine derivative with 1,3-dihydro-benzo[c]thiophene-1-carbonyl chloride under conditions similar to those used for the preparation of the intermediate compounds of receptors 5 and 3. Oxidation of the intermediate compound was carried out with m-chloroperbenzoic acid using the same conditions as for the preparation of receptors 5 and 3.

Physical data for 1,3-Dihydro-benzo[c]thiophene-1-carboxylic acid: m.p. 66-68 ºC; $^1$H NMR (200 MHz, $CDCl_3$): δ= 7.15 (m, 4H), 5.02 (s, 1H), 4.36 (dt, $^3J$(H,H) = 13.8 Hz, $^3J$(H,H) = 1.8 Hz, 1H), 4.07 (d, $^3J$(H,H) = 13.8 Hz, 1H); $^{13}$C RMN (50 MHz, $CDCl_3$): δ= 174.0 (C), 140.6 (C), 127.2 (CH), 126.3 (CH), 124.4 (CH), 124.0 (CH), 54.0 (CH), 37.1 ($CH_2$); M.S. (positive electrospray, 3.5 KV): 695 ($M+Na^+$); I.R. $\lambda^{-1}$ (nujol): 3455, 2926, 2855, 2621, 2077, 1738, 1715, 1454, 1377, 1325, 1281, 1248, 1202, 1086, 968, 916, 816, 746, 719; Elemental analysis calculated for $C_9H_8O_2S$ (180.22): C 59.98, H 5.58; found: C 60.09, H 5.41.

Physical data for the intermediate compound: m.p. 266-268 ºC; $^1$H NMR (200 MHz, $CDCl_3$): δ= 11.11 (s, 1H), 10.70 (s, 1H), 9.00 (d, $^3J$(H,H) = 2.1 Hz, 1H), 8.52 (d, $^3J$(H,H) = 2.1 Hz, 1H), 7.87 (d, $^3J$(H,H) = 8.4 Hz, 1H), 7.83 (d, $^3J$(H,H) = 8.4 Hz, 1H), 7.36 (d, $^3J$(H,H) = 7.5 Hz, 1H), 7.32 (d, $^3J$(H,H) = 7.5 Hz, 1H), 7.24 (dt, $^3J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.4 Hz, 1H), 7.18 (dt, $^3J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.4 Hz, 1H), 5.62 (d, $^3J$(H,H) = 2.1 Hz, 1H), 4.55 (dd, $^3J$(H,H) = 2.1 Hz, $^3J$(H,H) = 14.1 Hz, 1H), 4.32 (q, $^3J$(H,H) = 7.1 Hz, 2H), 4.26 (d, $^3J$(H,H) = 14.1 Hz, 1H), 1.95 (m, 4H), 1.34 (t, $^3J$(H,H) = 7.3 Hz, 3H), 1.18 (m, 8H), 0.76 (t, $^3J$(H,H) = 6.9 Hz, 6H); $^{13}$C RMN (50 MHz, $CDCl_3$): δ= 197.0 (C), 174.8 (C), 173.6 (C), 170.7 (C), 164.3 (C), 148.8 (C), 141.3 (C), 138.8 (C), 132.5 (C), 128.8 (CH), 128.3 (CH), 127.8 (C), 127.4 (CH), 126.0 (C), 125.6 (CH), 125.2 (CH), 124.5 (C), 123.9 (CH), 122.6 (C), 122.1 (CH), 121.2 (C), 119.4 (CH), 61.6 ($CH_2$), 62.8 (C), 61.6 ($CH_2$), 56.3 (CH), 38.1 ($CH_2$), 26.4 ($CH_2$), 23.3, 14.0 ($CH_3$), 13.2 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 641 ($M+H^+$) 663 ($M+Na^+$); I.R. $\lambda^{-1}$ (nujol): 3248, 3077, 2926, 2854, 1723, 1705, 1674, 1651, 1605, 1549, 1464, 1377, 1341, 1287, 1244, 1215, 1167, 1101, 1026, 978, 920, 872, 851, 764, 729; Elemental analysis calculated for $C_{36}H_{36}N_2O_7S$ (640.75): C 67.48, H 5.66, N 4.37; found: C 67.66, H 5.55, N 4.19.

Physical data for receptor 6: m.p. 266-268 ºC; $^1$H NMR (200 MHz, $CDCl_3$): δ= 10.67 (s, 1H), 10.19 (s, 1H), 9.15 (d, $^3J$(H,H) = 2.0 Hz, 1H), 8.90 (d, $^3J$(H,H) = 2.1 Hz, 1H), 8.13 (d, $^3J$(H,H) = 8.4 Hz, 1H), 8.01 (d, $^3J$(H,H) = 8.4 Hz, 1H), 7.43 (m, 4H), 5.63 (s, 1H), 4.69 (d, $^3J$(H,H) = 15.8 Hz, 1H), 4.50 (q, $^3J$(H,H) = 7.1 Hz, 2H), 4.26 (d, $^3J$(H,H) = 15.7 Hz, 1H), 2.00 (m, 4H), 1.49 (t, $^3J$(H,H) = 7.1 Hz, 3H), 1.09 (m, 8H), 0.59 (m, 6H); $^{13}$C RMN (50 MHz, $CDCl_3$): δ= 197.0 (C), 176.2 (C), 175.0 (C), 164.9 (C), 162.4 (C), 149.4 (C), 143.2 (C), 131.9 (C), 131.7 (C), 131.4 (C), 130.0 (CH), 129.6 (CH), 129.2 (CH), 127.7 (C), 127.1 (CH), 126.7 (C), 126.3 (CH), 125.8 (C), 125.3 (CH), 122.8 (C), 122.3 (CH), 121.7 (C), 120.6 (CH), 71.2 (CH), 62.6 (C), 62.1 ($CH_2$), 56.5 ($CH_2$), 41.2 ($CH_2$), 39.9 ($CH_2$), 27.9 ($CH_2$), 27.3 ($CH_2$), 23.3 ($CH_2$), 23.1 ($CH_2$), 14.6 ($CH_3$), 13.9 ($CH_3$), 13.8 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 673 ($M+H^+$); I.R. $\lambda^{-1}$ (nujol): 3347, 3244, 2926, 2857, 1709, 1669, 1607, 1578, 1557, 1534, 1462, 1377, 1329, 1285, 1252, 1213, 1144, 1096, 1022, 918, 862, 764, 748, 723; Elemental analysis calculated for $C_{36}H_{36}N_2O_9S$ (672.75): C 64.27, H 5.39, N 4.16; found: C 64.39, H 5.50, N 4.06.

**Preparation of receptor 7*u*:**




The Intermediate compound was dissolved in chloroform (0.3 g in 5 ml) and ozone was bubbled through until analysis of the reaction mixture by 1H-NMR revealed that starting material had reacted completely. The solvent was then evaporated off under a vacuum. Yield: 99%.

Physical data for receptor 7*u*: m.p. 151-153 ºC; $^{1}$H NMR (200 MHz, $CDCl_3$): δ= 10.38 (s, 1H), 10.01 (s, 1H), 9.16 (d, $^{3}J$(H,H) = 2.1 Hz, 1H), 8.81 (d, $^{3}J$(H,H) = 2.1 Hz, 1H), 8.07 (d, $^{3}J$(H,H) = 8.4 Hz, 1H), 7.99 (d, $^{3}J$(H,H) = 8.4 Hz, 1H), 7.60 (s, 1H), 7.34 (m, 3H), 5.79 (s, 1H), 4.79 (d, $^{3}J$(H,H) = 14.9 Hz, 1H), 4.43 (q, $^{3}J$(H,H) = 7.1 Hz, 2H), 4.32 (d, $^{3}J$(H,H) = 15.0 Hz, 1H), 2.03 (m, 4H), 1.42 (t, $^{3}J$(H,H) = 6.9 Hz, 3H), 1.17 (m, 8H), 0.76 (m, 6H); $^{13}$C-RMN ($CDCl_3$): δ= 197.9 (C), 175.5 (C), 173.8 (C), 165.8 (C), 165.0 (C), 143.4 (C), 136.8 (C), 135.1 (C), 132.3 (C), 129.8 (CH), 128.8 (CH), 128.6 (CH), 127.6 (C), 127.2 (CH), 126.9 (C), 126.8 (CH), 125.6 (C), 124.8 (C), 124.7 (CH), 123.9 (CH), 122.6 (C), 122.3 (CH), 121.8 (C), 119.6 (CH), 72.1 (CH), 62.6 ($CH_3$), 62.0 (C), 59.7 ($CH_2$), 39.9 ($CH_2$), 39.8 ($CH_2$), 27.3 ($CH_2$), 23.0 ($CH_2$), 14.3 ($CH_3$), 13.7 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 657 ($M+H^+$), 679 ($M+Na^+$); I.R. $\lambda^{-1}$ (nujol): 3206, 2926, 2855, 1707, 1670, 1599, 1541, 1458, 1377, 1287, 1208, 1032, 918, 729; Elemental analysis calculated for $C_{36}H_{36}N_2O_8S$ (656.75): C 65.84, H 5.53, N 4.27; found: C 65.65, H 5.44, N 4.13.

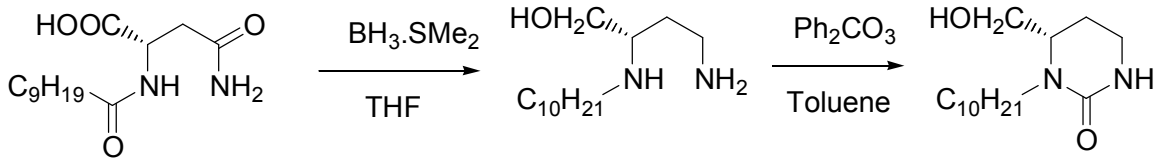
**Preparation of receptor 7*l*:**

Receptor 7*u* was dissolved in ethyl acetate (1 g in 30 ml). This solution was stirred with a water solution of $Na_2CO_3$ 4% over 30 minutes. The organic layer was dried over anhydrous $Na_2CO_3$ and, after evaporation of the solvent, receptor 7*l* was recovered quantitatively.

Physical data for receptor 7*l*: m.p. 140-142 ºC; $^{1}$H NMR (200 MHz, $CDCl_3$): δ= 10.75 (s, 1H), 10.43 (s, 1H) 9.34 (d, $^{3}J$(H,H) = 2.1 Hz, 1H), 8.75 (d, $^{3}J$(H,H) = 2.1 Hz, 1H), 7.98 (d, $^{3}J$(H,H) = 8.3 Hz, 1H), 7.92 (d, $^{3}J$(H,H) = 8.3 Hz, 1H), 7.65 (m, 1H), 7.46 (m, 3H), 5.06 (s, 1H), 4.75 (d, $^{3}J$(H,H) = 6.7 Hz, 1H), 4.58 (d, $^{3}J$(H,H) = 6.7 Hz, 1H), 4.48 (t, $^{3}J$(H,H) = 7.1 Hz, 2H), 2.02 (m, 4H), 1.46 (t, $^{3}J$(H,H) = 7.1 Hz, 3H), 1.22 (m, 8H), 0.80 (m, 6H); $^{13}$C-RMN ($CDCl_3$): δ= 197.5 (C), 175.1 (C), 174.8 (C), 174.0 (C), 164.8 (C), 163.5 (C), 148.1 (C), 143.0 (C), 134.8 (C), 134.4 (C), 132.6 (C), 129.8 (CH), 129.4 (CH), 127.5 (C), 126.9 (CH), 126.7 (CH), 126.0 (CH), 125.5 (C), 123.6 (CH), 122.5 (C), 122.1 (CH), 121.4 (C), 119.0 (CH), 67.9 (CH), 62.5 (C), 61.7 ($CH_2$), 58.2 ($CH_2$), 39.5 ($CH_2$), 39.3 ($CH_2$), 27.2 ($CH_2$), 23.0 ($CH_2$), 14.3 ($CH_3$), 13.6 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 657 ($M+H^+$), 679 ($M+Na^+$); I.R. $\lambda^{-1}$ (nujol): 3175, 2926, 2855, 1705, 1669, 1601, 1576, 1539, 1464, 1377, 1341, 1285, 1244, 1206, 1159, 1020, 916,

866, 843, 723; Elemental analysis calculated for $C_{36}H_{36}N_2O_8S$ (656.75): C 65.84, H 5.53, N 4.27; found: C 66.05, H 5.58, N 4.36.

**Preparation of urea guest 8:**




N-decanoyl asparagine (5.25 g) was dissolved in 50 ml of a solution in THF of 2.0 M borane-dimethyl sulfide adduct. After 12 hours at room temperature, the reaction mixture was heated to 50 ºC for 6 hours, after which 100 ml of dioxane was added and 35 ml of 35% HCl. The dioxane was then evaporated off under steam distillation, and half of the volume of water was evaporated off under reduced pressure. NaOH was added until basic pH and the intermediate compound was extracted several times using mixtures of ether and toluene. The organic layers were washed with a small amount of water to avoid the presence of salts. Yield: 80%.

The intermediate compound was solved in toluene (6.5 g in 150 ml) and 0.95 equivalents (5.4 g) of diphenyl carbonate were added. The solution was refluxed over 1 hour. The solvent was evaporated off and a saturated solution of KOH in methanol was added to hydrolize the unreacted diphenyl carbonate. After heating the reaction to 50 ºC for 5 minutes, the methanol was evaporated off and the residue was dissolved in ether and washed with water. Urea 8 was purified by silica gel chromatography. Yield: 60%.

Physical data for the intermediate compound: m.p. 84-86 ºC; $^1$H NMR (200 MHz, $CDCl_3$): δ= 3.60 (dd, $^3J$(H,H) = 4.9 Hz, $^3J$(H,H) = 11.1 Hz, 1H), 3.44 (dd, $^3J$(H,H) = 4.2 Hz, $^3J$(H,H) = 11.1 Hz, 1H), 2.82 (m, 2H), 2.72 (m, 1H), 2.62 (t, $^3J$(H,H) = 7.2 Hz, 2H), 1.63 (m, 2H), 1.47 (m, 2H), 1.26 (m, 14H), 0.88 (t, $^3J$(H,H) = 6.7 Hz, 3H); $^{13}$C-RMN ($CDCl_3$): δ= 63.4 ($CH_2$), 58.1 (CH), 47.2 ($CH_2$), 38.4 ($CH_2$), 35.9 ($CH_2$), 31.8 ($CH_2$), 30.3 ($CH_2$), 29.5 ($CH_2$), 29.5 ($CH_2$), 29.2 ($CH_2$), 27.3 ($CH_2$), 22.6 ($CH_2$), 14.0 ($CH_2$); M.S. (positive electrospray, 3.5 KV): 245 ($M+H^+$); I.R. $\lambda^{-1}$ (nujol): 3385, 3279, 2928, 2860, 1649, 1613, 1553, 1462, 1377, 1333, 1188, 1161, 1125, 1059, 968, 934, 897, 845, 818, 774, 723; Elemental analysis calculated for $C_{14}H_{32}N_2O$ (244.42): C 68.80, H 13.20, N 11.46; found: C 68.34, H 13.41, N 11.26.

Physical data for urea 8: m.p. 84-86 ºC; $[\alpha]_D^{20}$= -3.30 (c= 0.85, $CHCl_3$); $^1$H NMR (200 MHz, $CDCl_3$): δ= 4.78 (s, 1H), 3.77 (dd, $^3J$(H,H) = 7.7 Hz, $^3J$(H,H) = 14.4 Hz, 1H), 3.67 (dd, $^3J$(H,H) = 14.4 Hz, $^3J$(H,H) = 11 Hz, 1H), 3.46 (d, $^3J$(H,H) = ? Hz, 1H), 3.39 (dd, $^3J$(H,H) = 4.5 Hz, $^3J$(H,H) = 11.9 Hz, 1H), 3.24 (d, $^3J$(H,H) = ?, 1H), 2.91 (q, $^3J$(H,H) = 7.1 Hz, 1H), 2.88 (q, $^3J$(H,H) = 7.2 Hz, 1H), 2.07 (m, 1H), 1.90 (m, 1H), 1.53 (m, 2H), 1.25 (m, 14H), 0.87 (t, $^3J$(H,H) = 6.4 Hz, 3H); $^{13}$C-RMN ($CDCl_3$): δ= 156.0 (C), 60.9 ($CH_2$), 54.9 (CH), 46.0 ($CH_2$), 36.0 ($CH_2$), 31.2 ($CH_2$), 28.9 ($CH_2$), 27.8 ($CH_2$), 26.3 ($CH_2$), 21.9 ($CH_2$), 13.4 ($CH_3$); M.S. (positive electrospray, 3.5 KV): 271 ($M+H^+$), 293 ($M+Na^+$); I.R. $\lambda^{-1}$ (película): 3337, 3069, 2926, 2857, 2240, 1717, 1647, 1522, 1466, 1370, 1306, 1248, 1188, 1125, 1109, 1055, 976, 910, 727; Elemental analysis calculated for $C_{15}H_{30}N_2O_2$ (270.41): C 66.62, H 11.18, N 10.36; found: C 66.43, H 11.30, N 10.44.

**Experimental procedure for the chiral resolution of the racemic mixture of compound 7*u*:**

0.6 g of receptor 7*u* was dissolved in benzene (6 ml). Then, urea 8 (1.0 equivalents) and a catalytic amount of imidazol (10 mg) were added. After 30 minutes, the reaction mixture was chromatographed over 100 g of silica gel. The silica gel used in this chromatography was previously treated with tartaric acid to avoid the presence of basic groups which could have isomerized the sulfoxide: 100 g of silica was stirred in a solution of 10% tartaric acid in water; the silica was filtered and dried under a vacuum. Elution with $CH_2Cl_2$/ether 9/1 allowed the recovery of enantiomerically enriched isomer 7*l* (200 mg). Then, enantiomerically enriched receptor 7*u* was eluted with ether, yielding 230 mg. The remaining fractions contained similar amounts of each enantiomer.

The 1H-NMR signals of receptor 7*u* split in presence of the chiral urea 8 when dissolved in deuterated chloroform. This method was used to establish the enantiomeric excess of the receptor 7*u* fraction in 70% e.e. and the receptor 7*l* fraction in 66% e.e.

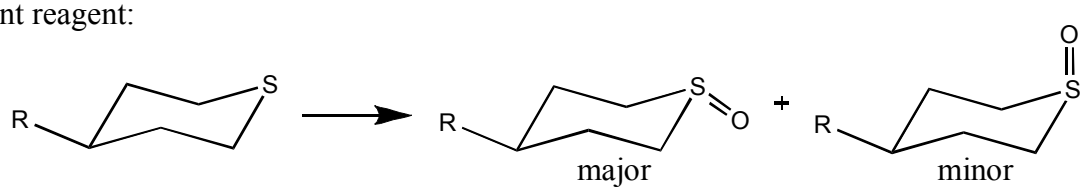
The isomerization procedure in the presence of the chiral guest was repeated with the receptor 7*u* fraction. After a new chromatography 190 mg of receptor 7*u* with e.e>95% were obtained; m.p.: 138-140 ºC, $[\alpha]_D^{20}$= -4.95 (c=0.46, $CHCl_3$).

The fraction containing the enantiomerically enriched receptor 7*l* was isomerized in the presence of the mirror antipode of urea 8, yielding 120 mg of receptor 7*u*; e.e.: 90%, m.p. 140-142 ºC, $[\alpha]_D^{20}$= +4.50 (c=0.37, $CHCl_3$).

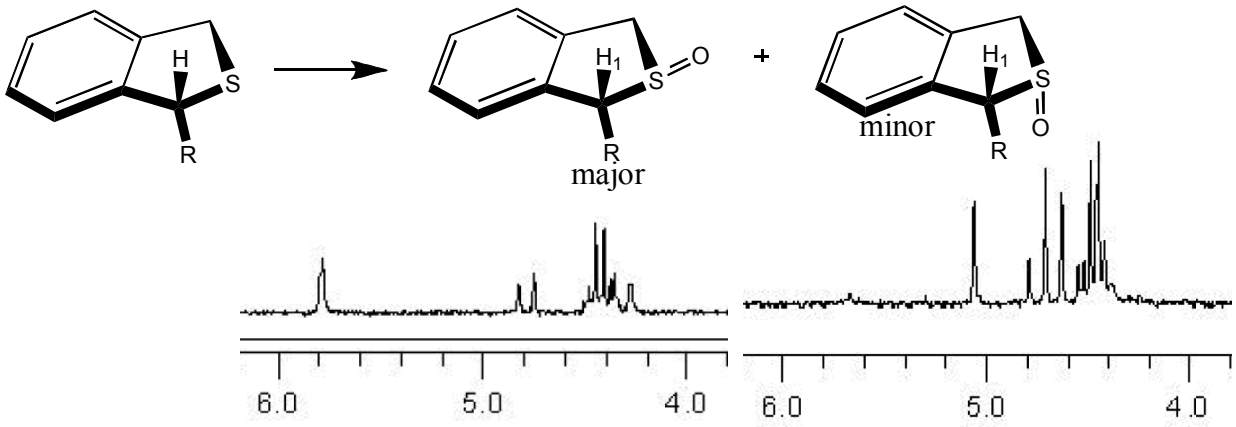
# Determination of the relative stereochemistry of receptors 7u and 7l

So far, we have not been able to obtain crystals suitable for X-ray crystallographic analysis from these receptors. The search in the literature of similar compounds, that could offer spectroscopic data useful in assigning the relative stereochemistry of receptors *7u* and *7l*, was unsuccessful as well. Nevertheless, Johnson and McCants (Johnson, C. R.; McCants, D. Jr *J. Am. Chem. Soc.*, *87*, 1109-1114, **1965**) studied the oxidation to sulfoxides of several 4 substituted thianes with ozone and other oxidants.

In this work, under kinetic conditions, it was observed that the major product has *trans* relative stereochemistry, which corresponds to a sterically favoured equatorial approach of the sulfur to the oxidant reagent:




In our case, we considered that the xanthone substituent of the dihydro-benzo[c]thiophene is placed in a pseudoequatorial position. The same preference observed in thiane oxidation would lead to oxidation in the pseudoequatorial position of the sulfur atom (the *trans* product); this approach corresponds to the less hindered face of the ring. Therefore, the product obtained after oxidation of the thioeter with ozone corresponds to a trans relative stereochemistry, equivalent to the "u" sulfoxide:




$^1$H NMR espectra reveal that proton Ha is de-shielded 0.7 ppm in the isomer obtained directly by the oxidation with respect to the isomer generated after the base catalyzed isomerization. This is coherent with a structure in which this proton and the sulfoxide oxygen are in the same face of the ring, since the proximity between both atoms probably deshield this proton.

Additionally, CPK models and calculations show that receptor with the *cis* relative stereochemistry can establish an intramolecular H-bond that might reduce the polarity of this compound. The less polar of the two isomers is the one obtained after the base catalyzed isomerization, in agreement with previous observations. The higher stability of one of the isomers, that disappears when a substrate that can compete with H-bonds is added to the solution, can also be related with the presence of this intramolecular H-bond in this isomer. Finally, the less polar isomer also has a smaller association constant with urea 8, which is consistent with the necessity of breaking the intramolecular H-bonds to form the complex.

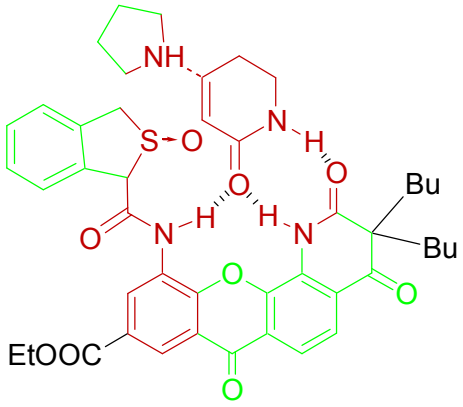
All these results suggest that the more polar sulfoxide, obtained by oxidation of the thioeter with ozone, is indeed the trans 7u sulfoxide, and that the less polar sulfoxide, that is prepared by isomerization, is the cis 7l isomer.

# Complete list of authors in ref. 69

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

# Details of computational studies and cartesian atomic coordinates for optimized structures and TS

Calculations were performed using Gaussian98 program. Due to the large size of the system and to reduce the computational cost of the calculations, the ONIOM method, combining DFT and semiempirical methods was used. The distribution of atoms between high (red) and low level layers (green) is shown below; groups that are not important for catalysis or for the structure of the catalyst were not included (in black). Calcualtions were performed at the B3LYP/3-21G** level of theory for the atoms in the high level layer and semiempirical PM3MM for those in the low level layer.




**Cartesian atomic coordinates of the structure found for the intermolecular H-bonds of receptor 7*l*:**

| | | | |
|---|---|---|---|
| C | -3.29710 | 0.19490 | -0.26599 |
| C | -4.03499 | -0.97228 | 0.03630 |
| C | -3.38939 | -2.19735 | 0.22383 |
| C | -1.98764 | -2.29561 | 0.12772 |
| C | -1.26932 | -1.13031 | -0.16420 |
| C | -1.91384 | 0.12280 | -0.37435 |
| C | -1.23888 | -3.58884 | 0.34237 |
| C | 0.26782 | -3.44764 | 0.27387 |
| C | 0.83790 | -2.21968 | -0.01541 |
| O | 0.12479 | -1.05350 | -0.27389 |
| C | 1.10661 | -4.54493 | 0.52015 |
| C | 2.47190 | -4.39939 | 0.48797 |
| C | 3.05136 | -3.15461 | 0.20904 |
| C | 2.24319 | -2.06011 | -0.05748 |
| C | -5.54820 | -0.93090 | 0.16170 |
| O | -6.05305 | 0.35225 | -0.04945 |
| O | -6.25860 | -1.88811 | 0.41572 |
| C | -7.48401 | 0.39539 | 0.06651 |
| C | 4.55148 | -2.96224 | 0.19117 |
| C | 5.01631 | -1.50363 | 0.41274 |
| C | 4.09439 | -0.43559 | -0.21914 |
| N | 2.77491 | -0.80215 | -0.37542 |
| H | 2.17406 | -0.09349 | -0.83012 |
| O | 5.34094 | -3.88415 | 0.05610 |
| O | 4.51555 | 0.69864 | -0.52368 |
| N | -1.04183 | 1.17910 | -0.66992 |
| H | -0.08725 | 0.88427 | -0.90676 |

| | | | |
|---|---|---|---|
| C | -1.34069 | 2.49652 | -0.84232 |
| O | -2.47202 | 3.00223 | -0.80391 |
| C | -0.05855 | 3.37705 | -0.99282 |
| O | -1.79403 | -4.65828 | 0.56435 |
| S | 1.36340 | 2.61310 | -2.00808 |
| C | 2.64662 | 3.25705 | -0.84637 |
| C | 1.93996 | 3.69124 | 0.43330 |
| C | 0.55737 | 3.75703 | 0.35915 |
| C | 2.59595 | 4.02316 | 1.61173 |
| C | 1.85661 | 4.42152 | 2.71333 |
| C | 0.47043 | 4.49095 | 2.63870 |
| C | -0.18369 | 4.15989 | 1.46352 |
| O | 1.32787 | 1.07563 | -1.83600 |
| H | -7.78343 | 1.42908 | -0.11373 |
| H | -7.82000 | 0.09480 | 1.06287 |
| H | -7.97077 | -0.25086 | -0.66928 |
| H | 2.36096 | 4.67870 | 3.63636 |
| H | 3.14789 | 4.08603 | -1.35899 |
| H | 3.36519 | 2.42970 | -0.73023 |
| H | 3.67598 | 3.96812 | 1.66696 |
| H | -0.10176 | 4.80324 | 3.50324 |
| H | -1.26391 | 4.21246 | 1.40336 |
| H | -0.36445 | 4.25559 | -1.56876 |
| H | 6.02793 | -1.37060 | 0.03771 |
| H | 5.04199 | -1.32144 | 1.48877 |
| H | 3.12390 | -5.24217 | 0.68241 |
| H | -3.77655 | 1.15022 | -0.41524 |
| H | 0.65100 | -5.50138 | 0.74282 |
| H | -3.96796 | -3.08444 | 0.45135 |

**Cartesian atomic coordinates of the transition state structure found after the addition of pyrrolidine to lactam 1 catalyzed by receptor 7u, leading to the R enantiomer of the product:**

| | | | |
|---|---|---|---|
| C | 1.00168 | -3.55662 | -2.04574 |
| C | 2.08252 | -4.09633 | -2.75344 |
| C | 3.35614 | -3.54019 | -2.67270 |
| C | 3.57612 | -2.41544 | -1.85197 |
| C | 2.48735 | -1.87150 | -1.13426 |
| C | 1.17289 | -2.42765 | -1.23104 |
| C | 4.91260 | -1.81487 | -1.71578 |
| C | 4.96748 | -0.60109 | -0.85893 |
| C | 3.80945 | -0.15728 | -0.21505 |
| O | 2.60550 | -0.82034 | -0.27329 |
| C | 6.15997 | 0.11195 | -0.68339 |
| C | 6.19343 | 1.23285 | 0.12760 |
| C | 5.03461 | 1.68666 | 0.76780 |
| C | 3.81924 | 1.01663 | 0.58458 |
| C | 5.07306 | 2.87569 | 1.65546 |
| C | 3.93362 | 2.97194 | 2.64397 |
| C | 2.59656 | 2.56693 | 2.05902 |
| N | 2.60465 | 1.51319 | 1.16726 |
| O | 5.90477 | -2.27133 | -2.26012 |
| N | 0.11736 | -1.83695 | -0.49683 |
| C | -1.10761 | -2.39332 | -0.27535 |
| O | 1.55706 | 3.19503 | 2.38036 |
| O | 5.96343 | 3.70304 | 1.62172 |
| H | 1.91615 | -4.96597 | -3.37445 |
| O | -1.56084 | -3.44071 | -0.79031 |
| C | -1.97654 | -1.50950 | 0.66127 |
| S | -3.57132 | -1.27542 | -0.31176 |
| C | -4.25827 | -2.83099 | 0.46172 |
| C | -3.61699 | -2.91716 | 1.78982 |

| | | | |
|---|---|---|---|
| C | -2.38472 | -2.23786 | 1.88146 |
| C | -4.11869 | -3.61005 | 2.88028 |
| C | -3.38559 | -3.62868 | 4.06763 |
| C | -2.17075 | -2.96169 | 4.15845 |
| C | -1.66250 | -2.25805 | 3.06545 |
| O | -4.38377 | -0.07612 | 0.22615 |
| H | 0.01906 | -3.99627 | -2.09207 |
| H | 4.18188 | -3.96965 | -3.22647 |
| H | 7.07093 | -0.23125 | -1.19002 |
| H | 7.13376 | 1.77985 | 0.27088 |
| H | 3.86892 | 3.99399 | 3.07371 |
| H | 4.16209 | 2.30868 | 3.50490 |
| H | 1.64649 | 1.16239 | 0.85783 |
| H | 0.23528 | -0.85572 | -0.14401 |
| H | -1.44814 | 0.51315 | -1.68575 |
| H | -3.86725 | -3.62984 | -0.18410 |
| H | -5.35423 | -2.78539 | 0.45686 |
| H | -5.07678 | -4.13492 | 2.80825 |
| H | -3.77502 | -4.17411 | 4.93368 |
| H | -1.60517 | -2.98269 | 5.09602 |
| H | -0.70956 | -1.72232 | 3.13994 |
| O | 0.15509 | 0.70733 | 0.38702 |
| C | -0.66203 | 1.64659 | -0.06934 |
| C | -1.53245 | 1.44100 | -1.14305 |
| C | -2.39751 | 2.49924 | -1.64501 |
| C | -1.97216 | 3.90488 | -1.18281 |
| C | -1.58539 | 3.91013 | 0.31278 |
| N | -0.61238 | 2.85375 | 0.58226 |
| H | -2.53546 | 2.48418 | -2.72602 |
| H | -2.73365 | 4.65898 | -1.38894 |
| H | -1.08687 | 4.15838 | -1.77013 |
| H | -2.48792 | 3.78196 | 0.92807 |
| H | -1.14603 | 4.87263 | 0.57908 |
| H | 0.07444 | 2.97098 | 1.32751 |
| N | -4.00718 | 2.18615 | -1.16272 |
| C | -4.84746 | 1.61141 | -2.31710 |
| C | -4.90383 | 3.30197 | -0.60139 |
| H | -3.93639 | 1.40068 | -0.47181 |
| H | -5.61623 | 2.81493 | 0.08196 |
| C | -5.60211 | 3.88712 | -1.81189 |
| H | -4.30956 | 4.01515 | -0.02248 |
| H | -4.18940 | 1.08573 | -3.02062 |
| C | -5.57894 | 2.80211 | -2.90217 |
| H | -5.52061 | 0.87554 | -1.85548 |
| H | -5.09716 | 4.80838 | -2.16210 |
| H | -6.63523 | 4.19326 | -1.56482 |
| H | -6.60040 | 2.52413 | -3.22050 |
| H | -5.07624 | 3.17408 | -3.81536 |
| H | -1.48677 | -0.54337 | 0.84105 |

**Cartesian atomic coordinates of the transition state structure found after the addition of pyrrolidine to lactam 1 catalyzed by receptor 7u, leading to the S enantiomer of the product:**

| | | | |
|---|---|---|---|
| C | -1.32572 | 4.15788 | -0.50645 |
| C | -2.46612 | 4.91108 | -0.80480 |
| C | -3.69859 | 4.30733 | -1.03878 |
| C | -3.80522 | 2.90715 | -0.95567 |
| C | -2.65407 | 2.14364 | -0.64898 |
| C | -1.37917 | 2.75423 | -0.43882 |
| C | -5.09468 | 2.22174 | -1.15044 |
| C | -5.12211 | 0.82904 | -0.63011 |

| | | | |
|---|---|---|---|
| C | -3.91274 | 0.20088 | -0.31941 |
| O | -2.68351 | 0.78131 | -0.55302 |
| C | -6.32406 | 0.14665 | -0.41378 |
| C | -6.31478 | -1.12853 | 0.12711 |
| C | -5.10885 | -1.74824 | 0.47110 |
| C | -3.88948 | -1.10044 | 0.24071 |
| C | -5.09079 | -3.08965 | 1.10380 |
| C | -3.86211 | -3.38361 | 1.93273 |
| C | -2.56875 | -2.86705 | 1.33591 |
| N | -2.64039 | -1.73099 | 0.55988 |
| O | -6.06132 | 2.74677 | -1.67545 |
| N | -0.23509 | 1.95402 | -0.18700 |
| C | 0.96865 | 2.44360 | 0.25787 |
| O | -1.49337 | -3.47658 | 1.56688 |
| O | -6.00139 | -3.88858 | 0.99946 |
| H | -2.37842 | 5.98811 | -0.85087 |
| O | 1.21636 | 3.63004 | 0.53640 |
| C | 2.05160 | 1.33197 | 0.34179 |
| S | 1.72019 | 0.05057 | 1.69210 |
| C | 2.76990 | 1.03943 | 2.89103 |
| C | 3.74952 | 1.75556 | 2.04801 |
| C | 3.36962 | 1.90461 | 0.69869 |
| C | 4.95884 | 2.26489 | 2.49760 |
| C | 5.79536 | 2.92654 | 1.59888 |
| C | 5.42474 | 3.07255 | 0.26807 |
| C | 4.21035 | 2.56126 | -0.19006 |
| O | 2.55748 | -1.18833 | 1.33138 |
| H | -0.38481 | 4.63596 | -0.29567 |
| H | -4.57291 | 4.90136 | -1.27351 |
| H | -7.27256 | 0.63212 | -0.67492 |
| H | -7.25841 | -1.66287 | 0.29345 |
| H | -3.77451 | -4.47301 | 2.13129 |
| H | -4.00008 | -2.91759 | 2.93142 |
| H | -1.71528 | -1.33493 | 0.20562 |
| H | -0.28911 | 0.92307 | -0.35168 |
| H | 1.44205 | -0.37631 | -2.35274 |
| H | 3.20215 | 0.33373 | 3.61287 |
| H | 2.10155 | 1.74179 | 3.41217 |
| H | 5.24861 | 2.15049 | 3.54740 |
| H | 6.74834 | 3.33727 | 1.94889 |
| H | 6.08478 | 3.60122 | -0.42783 |
| H | 3.91111 | 2.69095 | -1.23597 |
| O | -0.28216 | -0.75714 | -0.35280 |
| C | 0.59898 | -1.62116 | -0.82463 |
| C | 1.55519 | -1.29110 | -1.79472 |
| C | 2.66092 | -2.20447 | -2.05310 |
| C | 2.28412 | -3.68200 | -1.83672 |
| C | 1.62159 | -3.86377 | -0.45796 |
| N | 0.54988 | -2.88179 | -0.28271 |
| H | 3.16264 | -2.05507 | -3.00912 |
| H | 3.13149 | -4.35956 | -1.94947 |
| H | 1.56082 | -3.92289 | -2.61759 |
| H | 2.37177 | -3.74972 | 0.33568 |
| H | 1.20467 | -4.86913 | -0.37609 |
| H | -0.11245 | -3.04743 | 0.47632 |
| N | 3.88928 | -1.81339 | -0.95621 |
| C | 4.64067 | -0.58538 | -1.48148 |
| C | 5.00607 | -2.82775 | -0.66035 |
| H | 3.36776 | -1.55680 | -0.07866 |
| H | 5.39833 | -2.59376 | 0.34100 |
| C | 6.04104 | -2.58510 | -1.73966 |
| H | 4.59687 | -3.84217 | -0.63676 |
| H | 3.94683 | 0.02139 | -2.07711 |
| C | 5.81784 | -1.15152 | -2.25162 |

| | | | |
|---|---|---|---|
| H | 4.96258 | 0.01960 | -0.61809 |
| H | 5.94086 | -3.31659 | -2.56441 |
| H | 7.06564 | -2.72187 | -1.34778 |
| H | 6.71954 | -0.52702 | -2.11358 |
| H | 5.62269 | -1.15062 | -3.34132 |
| H | 2.03560 | 0.71475 | -0.57156 |

**Cartesian atomic coordinates of the structure derived from the transition state structure found after the addition of pyrrolidine to lactam 1 catalyzed by receptor 7u, leading to the R enantiomer of the product, after removing lactam and pyrrolidine:**

| | | | |
|---|---|---|---|
| N | -2.25020 | -1.98729 | -0.40516 |
| H | -1.33389 | -1.73411 | -0.73126 |
| N | 1.10204 | 1.00281 | -0.43817 |
| H | 0.68085 | 0.13862 | -0.72673 |
| C | 0.75866 | 3.44369 | -0.18788 |
| C | -0.11176 | 4.52123 | 0.01614 |
| C | -1.48012 | 4.32970 | 0.18593 |
| C | -2.00997 | 3.02358 | 0.16679 |
| C | -1.13267 | 1.93461 | -0.03546 |
| C | 0.27102 | 2.12916 | -0.23108 |
| C | -3.44590 | 2.77526 | 0.37135 |
| C | -3.85441 | 1.34962 | 0.26575 |
| C | -2.88460 | 0.36765 | 0.04714 |
| O | -1.53606 | 0.63188 | -0.01722 |
| C | -5.19689 | 0.96739 | 0.37938 |
| C | -5.55590 | -0.36615 | 0.28983 |
| C | -4.58968 | -1.35270 | 0.06225 |
| C | -3.24375 | -0.99964 | -0.09099 |
| C | -4.96977 | -2.78560 | -0.01218 |
| C | -3.84001 | -3.75963 | 0.23210 |
| C | -2.53523 | -3.33799 | -0.41108 |
| O | -4.24662 | 3.66461 | 0.61006 |
| C | 2.46407 | 0.99560 | -0.37523 |
| O | -1.78527 | -4.20237 | -0.92950 |
| O | -6.10620 | -3.16270 | -0.22360 |
| H | 0.29623 | 5.52247 | 0.04192 |
| O | 3.21608 | 1.99082 | -0.26732 |
| C | 3.03731 | -0.43769 | -0.54988 |
| S | 4.28340 | -0.24427 | -1.94801 |
| C | 5.60676 | 0.16977 | -0.69610 |
| C | 5.22069 | -0.55991 | 0.52906 |
| C | 3.84422 | -0.85290 | 0.61737 |
| C | 6.08316 | -0.92878 | 1.54935 |
| C | 5.56943 | -1.59026 | 2.66564 |
| C | 4.21351 | -1.87755 | 2.75469 |
| C | 3.34061 | -1.51312 | 1.72838 |
| O | 4.63355 | -1.61103 | -2.57818 |
| H | 1.82044 | 3.58781 | -0.30108 |
| H | -2.14016 | 5.17389 | 0.34284 |
| H | -5.96208 | 1.73581 | 0.54767 |
| H | -6.60804 | -0.66028 | 0.39215 |
| H | -4.11932 | -4.78067 | -0.10393 |
| H | -3.68568 | -3.84660 | 1.32843 |
| H | 5.47463 | 1.24889 | -0.53428 |
| H | 6.59103 | -0.07503 | -1.11387 |
| H | 7.15201 | -0.70273 | 1.47814 |
| H | 6.24428 | -1.88483 | 3.47620 |
| H | 3.82244 | -2.39812 | 3.63527 |
| H | 2.27261 | -1.74944 | 1.79294 |
| H | 2.24087 | -1.13785 | -0.83457 |

**Cartesian atomic coordinates of the structure derived from the transition state structure found after the addition of pyrrolidine to lactam 1 catalyzed by receptor 7u, leading to the S enantiomer of the product, after removing lactam and pyrrolidine:**

| | | | |
|---|---|---|---|
| N | -2.21672 | -1.91886 | -0.42298 |
| H | -1.31867 | -1.66748 | -0.79855 |
| N | 1.10360 | 1.06399 | -0.39615 |
| H | 0.72896 | 0.25851 | -0.86631 |
| C | 0.71860 | 3.40936 | 0.31059 |
| C | -0.15977 | 4.47054 | 0.55394 |
| C | -1.53724 | 4.32398 | 0.41490 |
| C | -2.06122 | 3.07406 | 0.03819 |
| C | -1.17491 | 1.99787 | -0.20351 |
| C | 0.24186 | 2.14957 | -0.09351 |
| C | -3.51305 | 2.85342 | -0.07993 |
| C | -3.90778 | 1.41981 | -0.07317 |
| C | -2.92419 | 0.44815 | -0.27835 |
| O | -1.61282 | 0.75786 | -0.57313 |
| C | -5.22703 | 1.01975 | 0.16493 |
| C | -5.54831 | -0.32644 | 0.22212 |
| C | -4.56136 | -1.30281 | 0.05097 |
| C | -3.23807 | -0.93216 | -0.21568 |
| C | -4.88389 | -2.74587 | 0.16739 |
| C | -3.71676 | -3.62837 | 0.54444 |
| C | -2.40804 | -3.24867 | -0.11805 |
| O | -4.32518 | 3.75876 | -0.16055 |
| C | 2.44382 | 1.03355 | -0.09705 |
| O | -1.55460 | -4.14018 | -0.35919 |
| O | -6.00263 | -3.19427 | 0.00704 |
| H | 0.25078 | 5.42363 | 0.85870 |
| O | 3.07793 | 1.91801 | 0.50478 |
| C | 3.13146 | -0.24801 | -0.64504 |
| S | 2.58352 | -1.83430 | 0.22595 |
| C | 4.02300 | -1.67947 | 1.41804 |
| C | 5.06810 | -0.95034 | 0.67016 |
| C | 4.59469 | -0.19789 | -0.42387 |
| C | 6.42025 | -0.96644 | 0.97903 |
| C | 7.30685 | -0.22930 | 0.19429 |
| C | 6.84347 | 0.51098 | -0.88600 |
| C | 5.48490 | 0.52990 | -1.20217 |
| O | 2.94692 | -2.99540 | -0.71525 |
| H | 1.77936 | 3.52389 | 0.45191 |
| H | -2.20626 | 5.15462 | 0.60164 |
| H | -6.00277 | 1.78226 | 0.30747 |
| H | -6.58400 | -0.63792 | 0.40633 |
| H | -3.94754 | -4.69452 | 0.33476 |
| H | -3.58343 | -3.57229 | 1.64566 |
| H | 4.29858 | -2.69312 | 1.73814 |
| H | 3.67209 | -1.09838 | 2.28452 |
| H | 6.78359 | -1.54908 | 1.83206 |
| H | 8.37478 | -0.23200 | 0.43697 |
| H | 7.54663 | 1.09329 | -1.49088 |
| H | 5.11783 | 1.12688 | -2.04430 |
| H | 2.81628 | -0.43455 | -1.68489 |

**Cartesian atomic coordinates of the structure derived from the transition state structure found after the addition of pyrrolidine to lactam 1 catalyzed by receptor 7u, leading to the R enantiomer of the product, after removing the xanthone skeleton:**

| | | | |
|---|---|---|---|
| C | 1.89383 | 0.54049 | -0.98627 |

| | | | |
|---|---|---|---|
| S | 1.03602 | -1.13545 | -0.96894 |
| C | 2.69942 | -1.97264 | -0.81988 |
| C | 3.55297 | -1.00869 | -0.09548 |
| C | 3.13762 | 0.33360 | -0.21416 |
| C | 4.68842 | -1.32986 | 0.63150 |
| C | 5.41579 | -0.30629 | 1.24047 |
| C | 5.00883 | 1.01637 | 1.12256 |
| C | 3.86357 | 1.34581 | 0.39597 |
| O | 0.26963 | -1.35781 | 0.35429 |
| H | -1.03600 | 0.88652 | -2.07034 |
| H | 3.03972 | -2.04889 | -1.86225 |
| H | 2.57083 | -2.95401 | -0.34701 |
| H | 5.00820 | -2.37276 | 0.72473 |
| H | 6.31425 | -0.55177 | 1.81641 |
| H | 5.58734 | 1.81073 | 1.60595 |
| H | 3.53570 | 2.38798 | 0.31194 |
| O | 0.07130 | 3.03238 | -1.03418 |
| C | -1.02612 | 2.42482 | -0.60441 |
| C | -1.51563 | 1.24654 | -1.17430 |
| C | -2.74089 | 0.61613 | -0.70368 |
| C | -3.62105 | 1.55217 | 0.14456 |
| C | -2.77181 | 2.36350 | 1.14803 |
| N | -1.66729 | 3.02087 | 0.45290 |
| H | -3.33398 | 0.15474 | -1.49311 |
| H | -4.42246 | 1.01805 | 0.65786 |
| H | -4.08371 | 2.24772 | -0.55907 |
| H | -2.39934 | 1.69736 | 1.93991 |
| H | -3.39020 | 3.12325 | 1.62838 |
| H | -1.29972 | 3.90622 | 0.80207 |
| N | -2.34463 | -0.78542 | 0.19092 |
| C | -2.56920 | -2.06849 | -0.62902 |
| C | -3.03550 | -1.10116 | 1.52776 |
| H | -1.30599 | -0.73743 | 0.32604 |
| H | -2.31200 | -1.67844 | 2.12355 |
| C | -4.24376 | -1.93558 | 1.15473 |
| H | -3.26226 | -0.17751 | 2.06847 |
| H | -2.46628 | -1.84106 | -1.69766 |
| C | -3.93955 | -2.56487 | -0.21565 |
| H | -1.75764 | -2.75064 | -0.33960 |
| H | -5.16167 | -1.31773 | 1.10949 |
| H | -4.44534 | -2.70689 | 1.92060 |
| H | -3.96557 | -3.66906 | -0.17046 |
| H | -4.71064 | -2.28165 | -0.95740 |
| H | 1.22888 | 1.32039 | -0.59233 |
| H | 2.06592 | 0.74619 | -2.04703 |

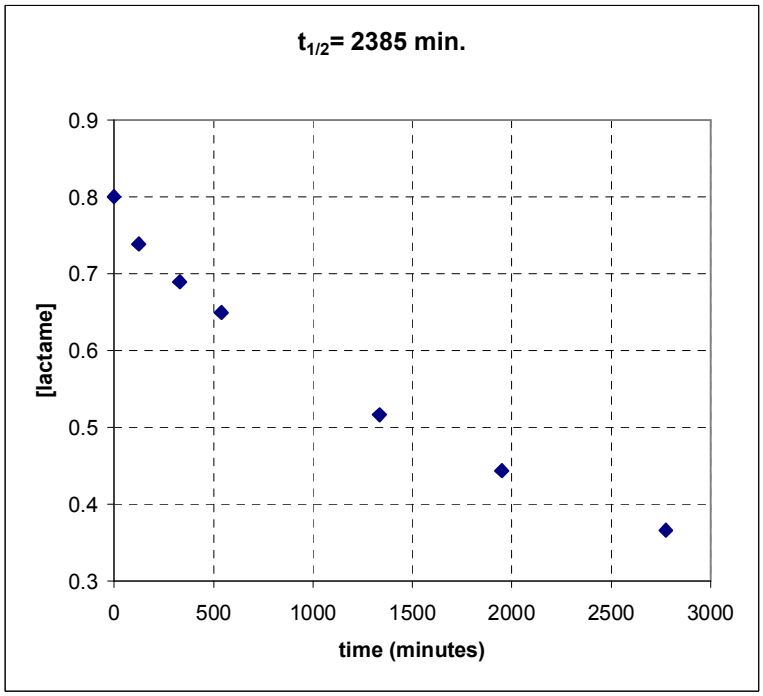
**Cartesian atomic coordinates of the structure derived from transition state structure found after addition of pyrrolidine to lactam 1 catalyzed by receptor 7u, leading to the S enantiomer of the product, after removing the xanthone skeleton:**

| | | | |
|---|---|---|---|
| C | 1.29279 | -1.36270 | 1.09340 |
| S | 0.70442 | -2.12353 | -0.53453 |
| C | 2.41437 | -1.88443 | -1.26670 |
| C | 2.98196 | -0.72199 | -0.55273 |
| C | 2.38361 | -0.44486 | 0.69321 |
| C | 4.02281 | 0.06527 | -1.02266 |
| C | 4.47095 | 1.13500 | -0.24801 |
| C | 3.88141 | 1.41202 | 0.97896 |
| C | 2.83342 | 0.62453 | 1.45607 |
| O | -0.18791 | -1.06863 | -1.21055 |

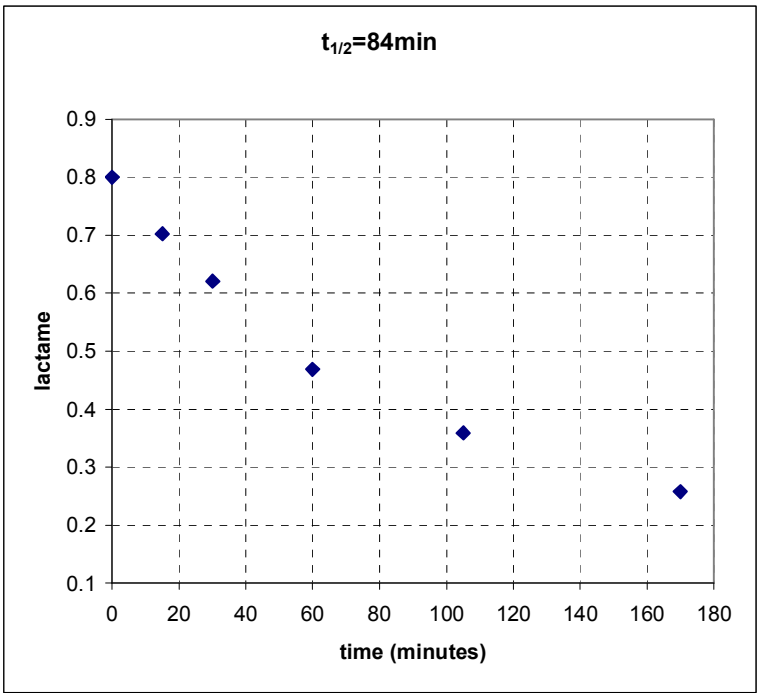
| | | | |
|---|---|---|---|
| H | -1.51310 | -0.43058 | 2.43815 |
| H | 2.29546 | -1.75460 | -2.35063 |
| H | 2.99092 | -2.79964 | -1.06283 |
| H | 4.48763 | -0.15562 | -1.98926 |
| H | 5.29707 | 1.75623 | -0.60994 |
| H | 4.24624 | 2.24909 | 1.58361 |
| H | 2.37969 | 0.83342 | 2.43115 |
| O | -1.55743 | -2.82575 | 1.26390 |
| C | -2.17217 | -1.72705 | 0.86326 |
| C | -1.98832 | -0.47820 | 1.47228 |
| C | -2.47234 | 0.72398 | 0.80584 |
| C | -3.73439 | 0.47578 | -0.04123 |
| C | -3.51427 | -0.72443 | -0.98146 |
| N | -2.99779 | -1.86656 | -0.22493 |
| H | -2.59082 | 1.59039 | 1.45647 |
| H | -4.04951 | 1.35458 | -0.60535 |
| H | -4.52767 | 0.23548 | 0.66863 |
| H | -2.81118 | -0.45083 | -1.77924 |
| H | -4.45760 | -1.00354 | -1.45422 |
| H | -3.03489 | -2.77995 | -0.67946 |
| N | -1.24018 | 1.24107 | -0.23309 |
| C | -0.18912 | 1.99223 | 0.59125 |
| C | -1.56202 | 2.20730 | -1.38483 |
| H | -0.82629 | 0.34365 | -0.59536 |
| H | -0.79375 | 2.05570 | -2.15819 |
| C | -1.47084 | 3.58685 | -0.76557 |
| H | -2.53562 | 1.96322 | -1.82024 |
| H | -0.18845 | 1.58663 | 1.61098 |
| C | -0.58382 | 3.45242 | 0.48431 |
| H | 0.80192 | 1.79736 | 0.14972 |
| H | -2.47247 | 3.97367 | -0.49641 |
| H | -1.05535 | 4.31903 | -1.48205 |
| H | 0.30906 | 4.10099 | 0.41912 |
| H | -1.12711 | 3.78883 | 1.38829 |
| H | 0.37659 | -0.87500 | 1.46510 |
| H | 1.59292 | -2.17901 | 1.75140 |

# Kinetic experiments with receptors:

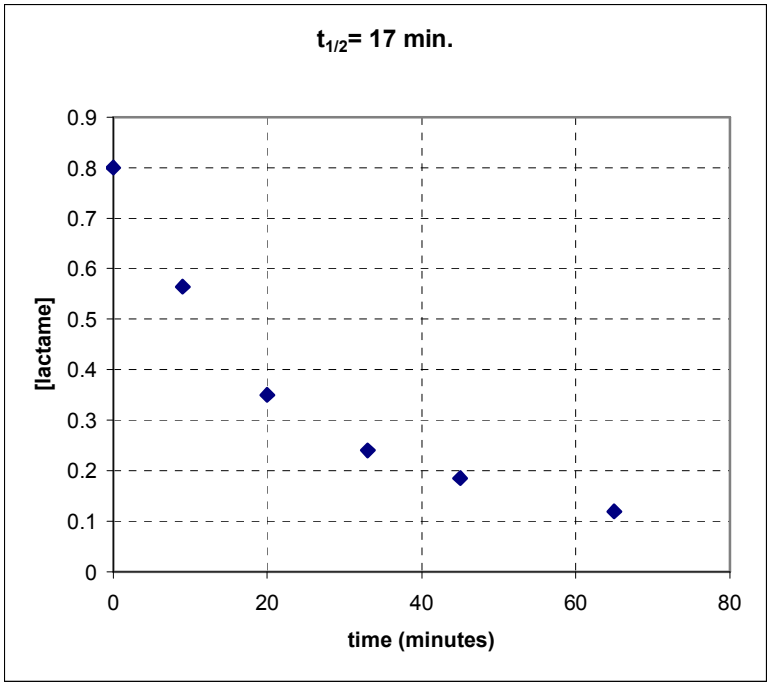
Reaction without receptor:



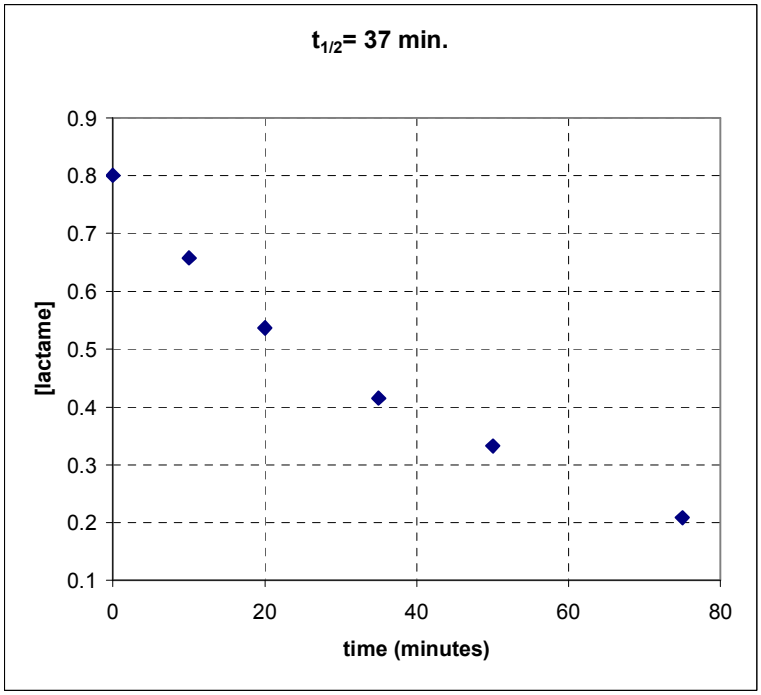

Receptor 2:



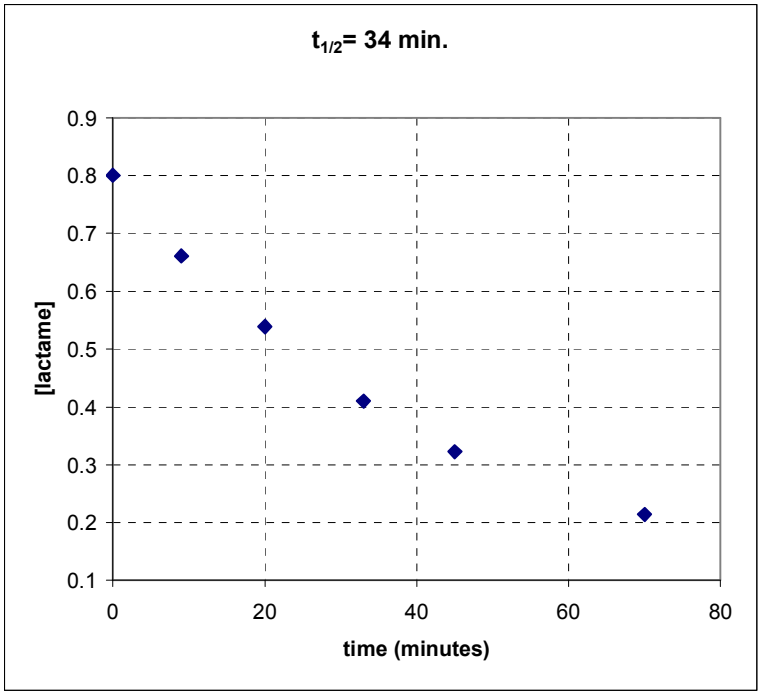
Receptor 3:



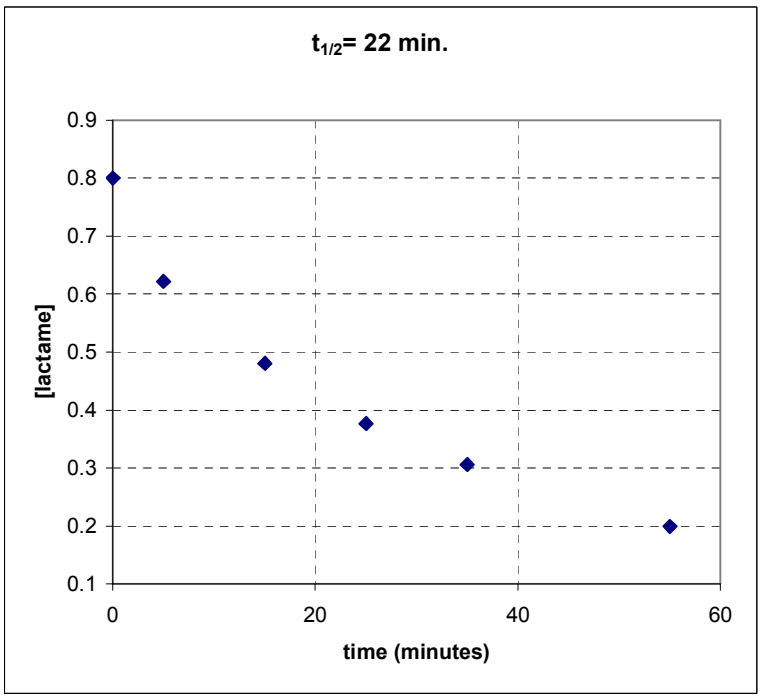

Receptor 4:



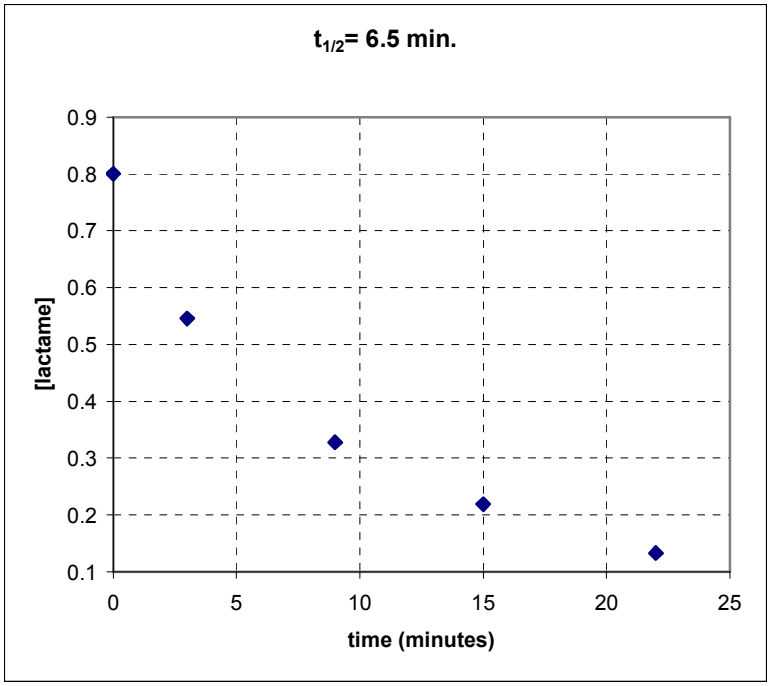
Receptor 5:



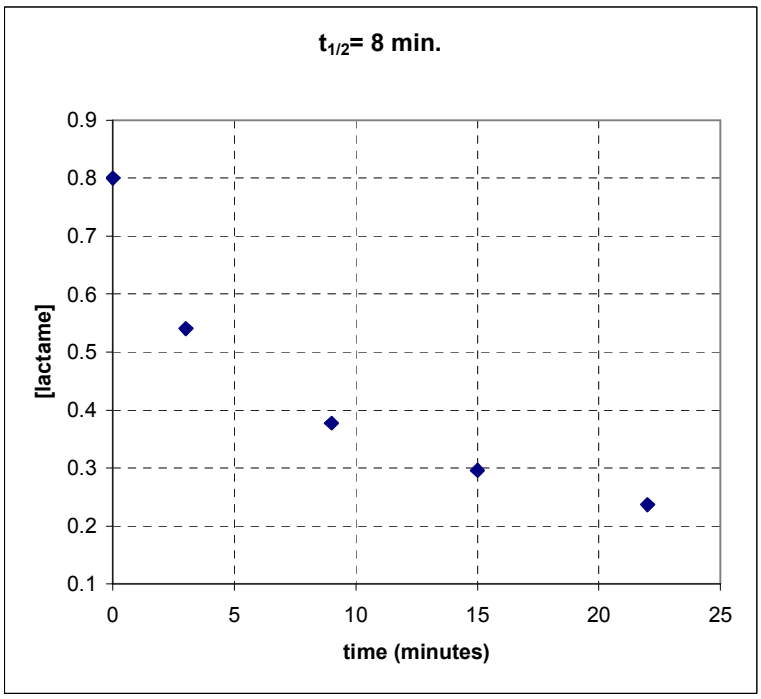

Receptor 6:



Receptor 7*u*:



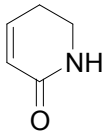

Receptor 7*l*:

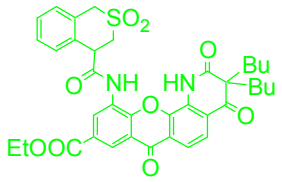


# Competitive titration experiments

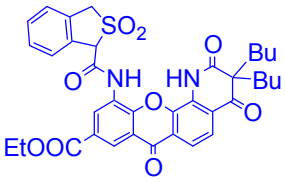
## Competitive titration with:

solvent: benzene-$D_6$

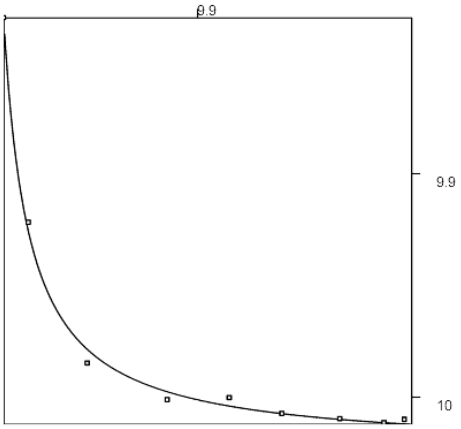


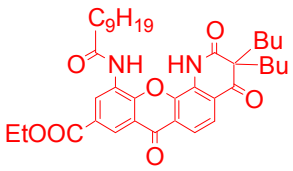




$K_{rel}$=0.058
$\delta_{max}$=9.8439

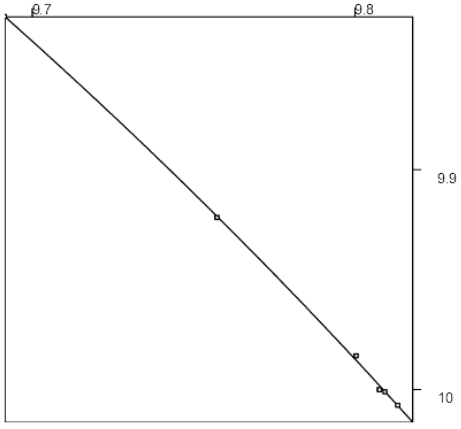


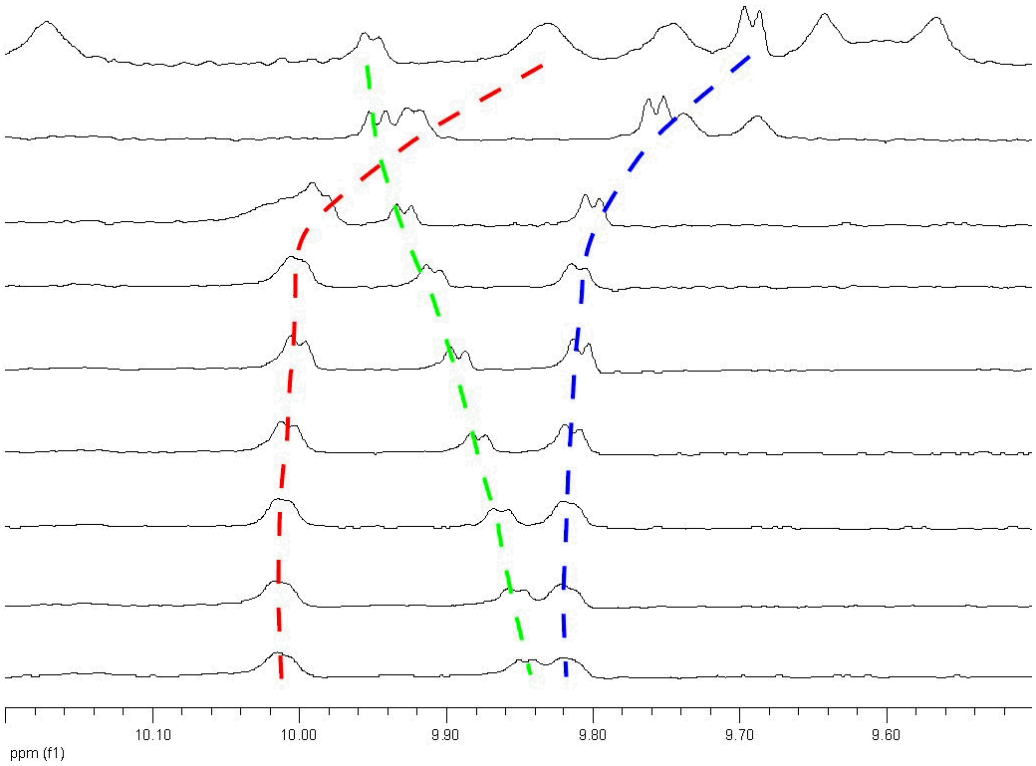

$K_{rel}$=1.1
$\delta_{max}$=9.818



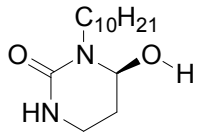

$K_{rel}$=1.00
$\delta_{max}$=10.015

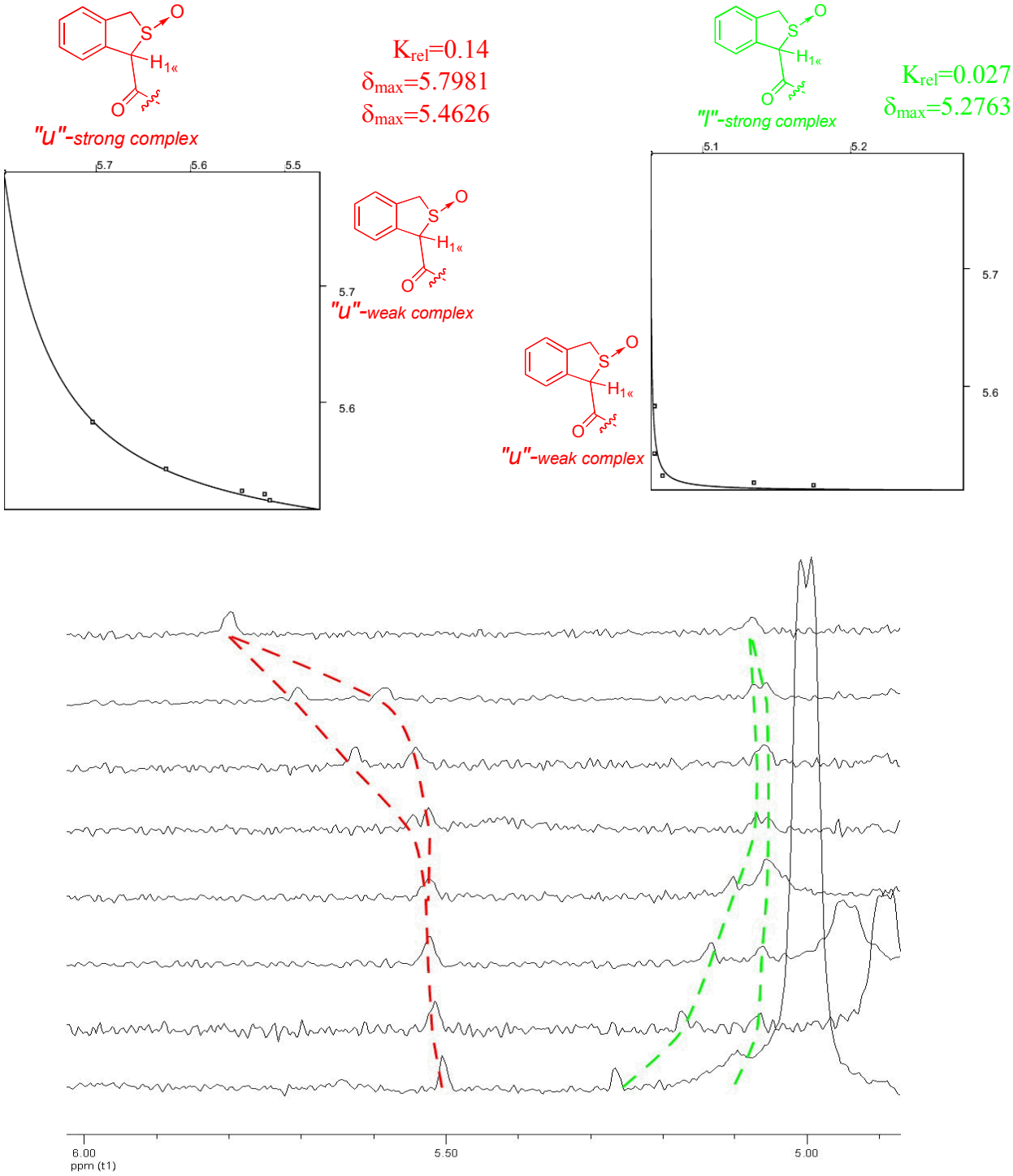


# Competitive titration with:

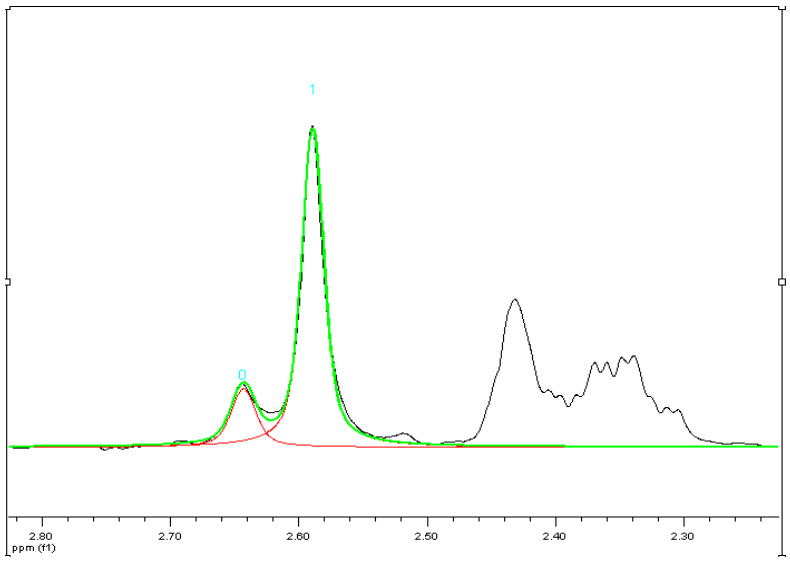
solvent: $CDCl_3$



# Determination of enantiomer ratio induced by receptor (-)7*u* and absolute configuration

Enantiomer ratio induced by enantiomerically pure receptor (-)7*u* in the reaction of pyrrolidine with lactam 1. Integration was performed by Gaussian deconvolution of the signals. Chiral shift receptor 8 was used.




Circular dichroism of the enriched reaction product of pyrrolidine with lactam 1 obtained with receptor (-)7*u*; λ= 225 nm, Δε= +1.37, solvent: tert-butyl methyl ether; extrapolated from the enantiomeric excess obtained in the product.