Electronic Supplementary Information

A bio-inspired enantioselective small-molecule artificial receptor for β adrenergic agonists and antagonists and its application for enantioselective extraction

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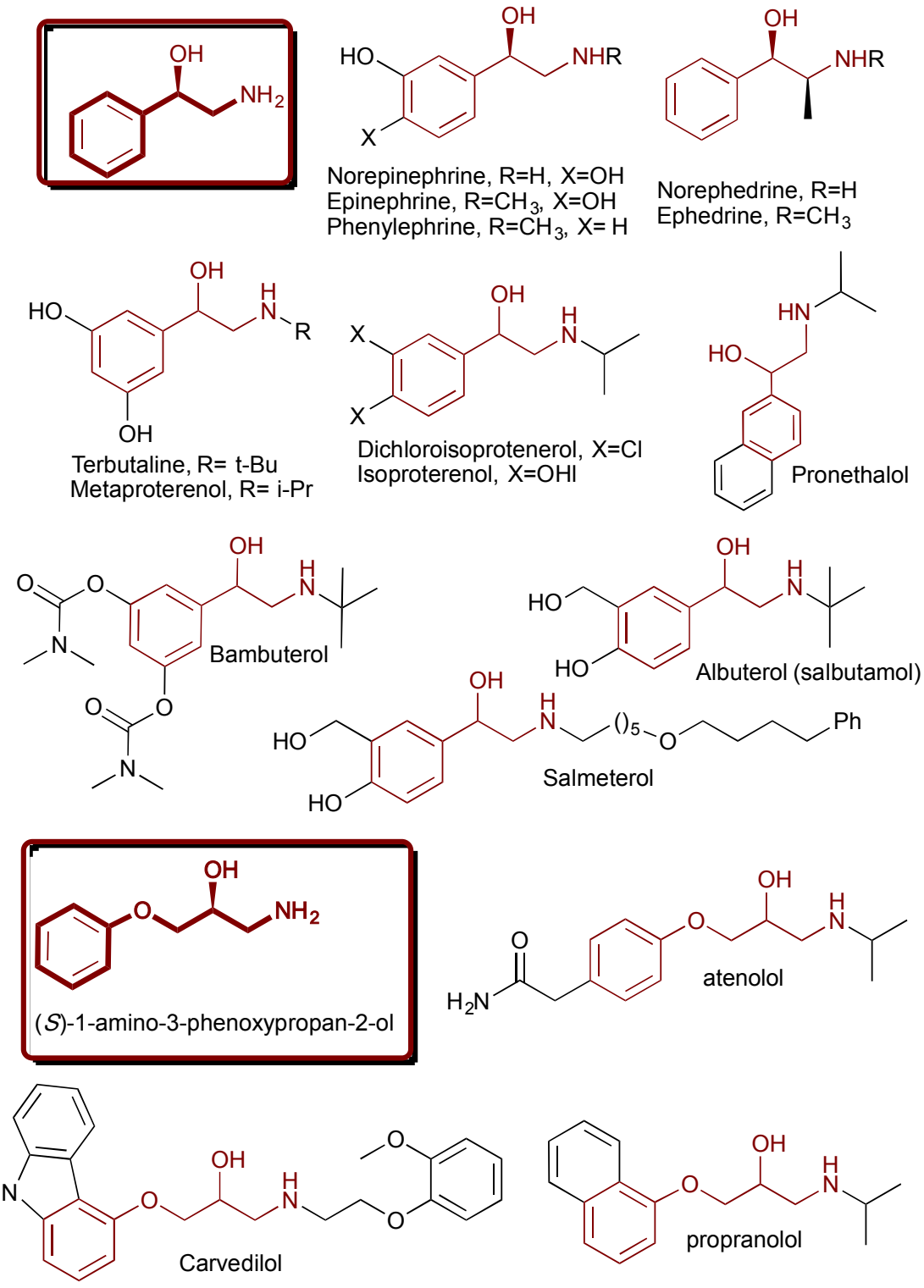
1. Figure S-1



Structure of several phenylethanolamine adrenergic agonists. Compounds commercialized as racemic mixtures do not show the stereochemistry on the chiral carbon atom.

2. General information

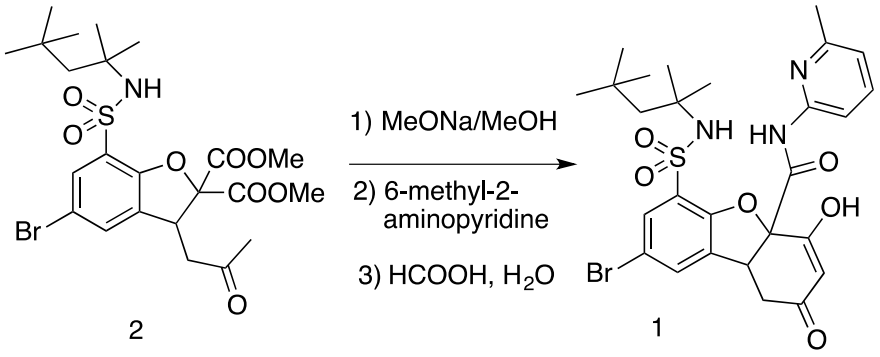
Solvents were purified by standard procedures and distilled before use. Reagents and starting materials obtained from commercial suppliers were used without further purification. IR spectra were recorded as neat film or in nujol and frequencies are given in cm^{-1}. Melting points are given in °C. NMR spectra were recorded on 200 MHz and 400 MHz spectrometers. ^{1}H NMR chemical shifts are reported in ppm with tetramethylsilane (TMS) as the internal standard. Data for ^{1}H are reported as follows: chemical shift (in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br s = broad singlet), coupling constant (in Hz), number of hydrogen atoms. Splitting patterns that could not be clearly distinguished are designated as multiplets (m). Data for ^{13}C NMR are reported in ppm and carbon multiplicity is included. High-resolution mass spectrometry analyses (HRMS) were measured using ESI ionization and a quadrupole TOF mass analyzer. Flash chromatography was performed on 70-200 mesh silica gel. Enantiomeric excesses (*ee*) of the products were determined by chiral HPLC in an Agilent 1100 equipment using a Daicel IA-3 or a Chirex-3022 column. Hexane/isopropanol 8:2 was used as eluent. Detection was done by UV at 210 nm.

3. Synthesis and properties of small-molecule artificial receptor (SMAR) 1

Preparation of SMAR 1

SMAR **1** can be prepared from the hydrolysis of the methyl-enol ether by KOH in tetrahydrofuran[1]. However, it is also readily available from ketodiester intermediate **2**, by the same sequence of reactions that leads to the methyl-enol ether with the only difference that the last acidulation step is performed in water instead of methanol.

8-Bromo-4-hydroxy-*N*-(6-methylpyridin-2-yl)-2-oxo-6-(*N*-(2,4,4-trimethylpentan-2-yl)sulfamoyl)-1,2,4a,9b-tetrahydrodibenzo[*b*,*d*]furan-4a-carboxamide (1)



In 75 mL of MeOH (previously dried using 3.0 mL of methyl orthoformate and two drops of methanesulfonic acid), a solution of Na (6.0 g, 0.26 mol) was prepared. When sodium was completely dissolved, the mixture was cooled with an ice-salt bath and compound **2** (25.0 g, 0.044 mol, prepared according to literature[1]) was added. The temperature was raised to 10 °C. Initially compound **2** slowly dissolved in the reaction medium but then, the appearance of a

precipitate was observed. To check the progress of the reaction, an aliquot was added over water acidulated with $MeSO_3H$, appearing a white precipitate whose ^1H NMR spectrum indicated that its structure corresponded to the cyclization product. At this time, 2-amino-6-methylpyridine (15.8 g, 0.15 mol) was added to the reaction flask. The new reaction mixture was refluxed for two hours until all solid had been dissolved. Then the reaction mixture was cooled and added to excess of formic acid in water and ice, and the obtained solid was filtered. The mother liquor was extracted with EtOAc, the layers were separated, and after evaporation of the organic solvent, the product obtained could be coupled with the above solid to afford 25.0 g of crude compound **1** (94 % yield).

This product could be purified according to the following procedure: the obtained solid (10.0 g, 0.016 mol) was dissolved in 20 mL of THF and 100 mL of ether. Then NH_3 was bubbled, appearing a precipitate. The solution was stirred a few more minutes until no more precipitate appeared and was filtered, obtaining 7.5 g of pure compound as a white solid corresponding to the ammonium salt of SMAR **1** with a yield of 75 %.

mp: 228-230 °C.

^{1}H NMR (DMSO-d_6) δ (ppm): 0.94 (s, 9H), 1.09 (s, 3 H), 1.19 (s, 3H), 1.42 (d, *J* = 14.6 Hz, 1H), 1.63 (d, *J* = 14.6 Hz, 1H), 2.41 (s, 3H), 3.00 (br s, 2H), 4.44 (t, *J* = 5.1 Hz, 1H), 5.47 (s, 1H), 7.06 (d, *J* = 7.3 Hz, 1H), 7.63 (d, *J* = 2.6 Hz, 1H), 7.72 (dd, *J* = 7.3, 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.83 (s, 1H), 9.99 (s, NH).

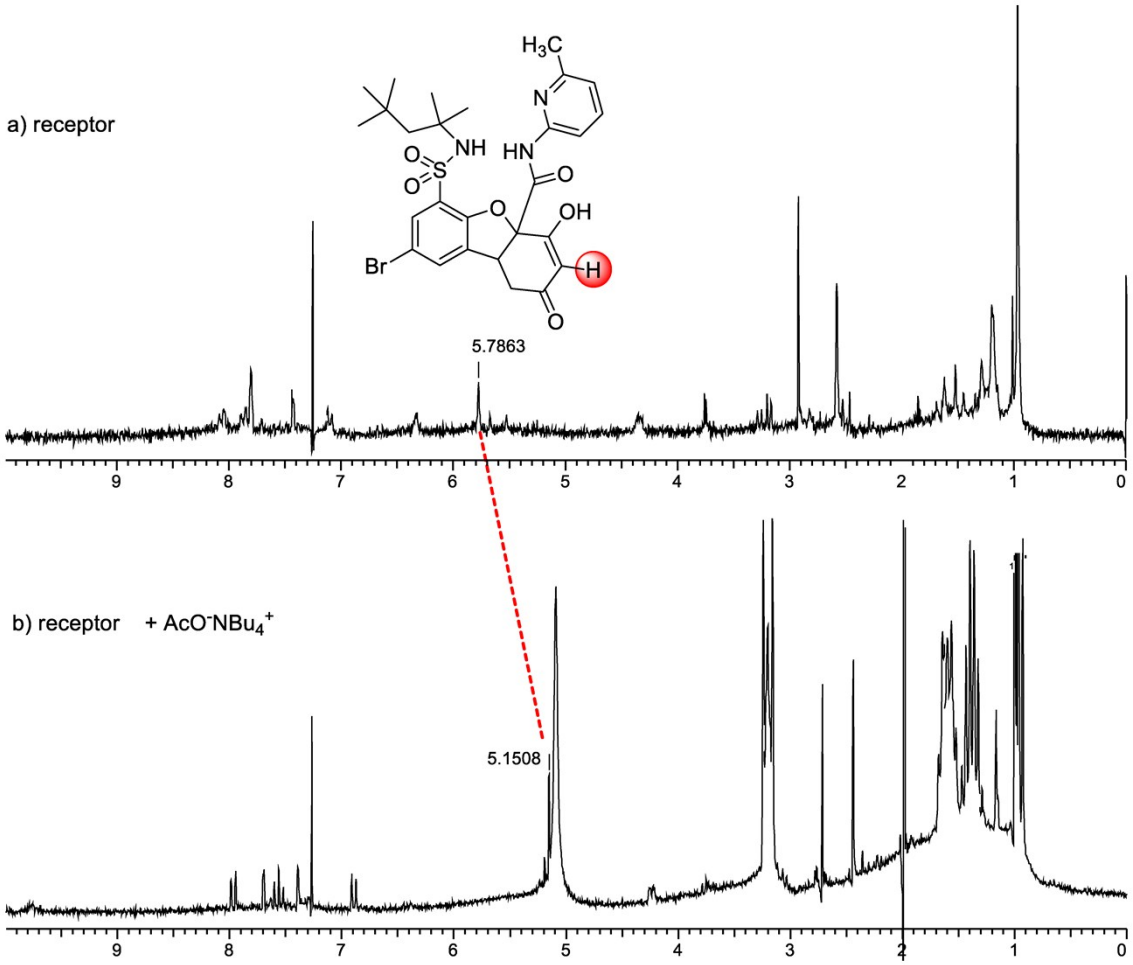
^{13}C NMR (DMSO-d_6) δ (ppm): 23.5 (CH_3), 28,7 (CH_3), 29,1 (CH_3), 31.0 (CH_2), 31.2 (C), 31.4 ($3CH_3$), 41.8 (CH), 53.6 (CH_2), 57.5 (C), 109.1 (C), 111.6 (CH), 112.9 (C), 120.0 (CH), 121.6 (C), 128.7 (CH), 129.1 (C), 130.3 (CH), 134.5 (CH), 138.6 (CH), 149.4 (C), 151.8 (C), 156.9 (C), 166.9 (C), 175.7 (C), 196.9 (C).

IR (nujol, cm^{-1}): 3390, 3306, 2916, 2839, 1710, 1606, 1521, 1456, 1366, 1249, 1203, 1152.

HRMS (ESI): 606.1284 $(M + H)^+$, calcd for $C_{27}H_{33}BrN_3O_6S$ 606.1268.

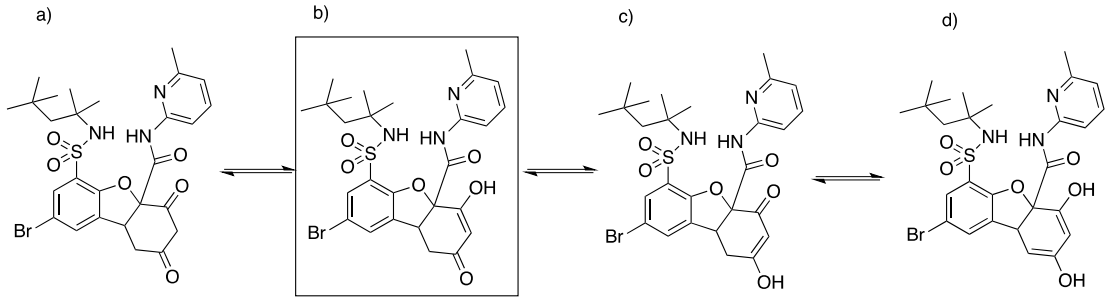
Acidity of the enol of SMAR 1

As we expected, the enol group in this receptor can be easily deprotonated due to the stability of the 1,3 dicarbonyl compound enolate. However, its acidity exceeded our expectations. Acetic acid is not strong enough to protonate its sodium salt, and indeed attempts to workup the previous reaction with acetic acid failed, yielding only small amounts of the receptor whereas most of it remained in the aqueous solution as its sodium salt. The high acidity of SMAR **1** can also be confirmed in a simple NMR experiment. The addition of the tetrabuthylammonium salt of acetic acid to a SMAR **1** solution in deuterochloroform, results in a strong shifting of the enol CH proton from 5.786 to 5.151 ppm (see figure below). This large shift can be explained due to proton transfer from SMAR **1** to the acetate group.



On the contrary, formic acid is strong enough to protonate SMAR **1** sodium salt yielding the pyridine group in its neutral form, offering a simple method for the reaction workup, since the neutral receptor crystallizes from the aqueous solution. These experiments confirm that pK_a of SMAR **1** is between the pK_a values of acetic (4.76) and formic (3.77) acids and SMAR **1** easily undergoes proton transfer with amines. Indeed, it is extracted from a chloroform solution using an ammonia solution.

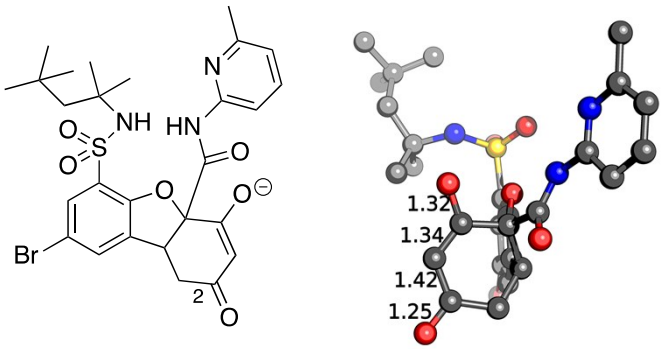
Diketone, dienol and the two possible keto-enol tautomers are possible for SMAR **1**:



In order to characterize which of these tautomers is present in solution we analysed its NMR spectra. The identification of only a methylene group in ^{13}C NMR spectrum allows to discard both diketone and dienol structures as abundant in solution. We also conducted a

long-range carbon-proton HMBC-CIGAR correlation with *J* = 10 and 20 Hz. With these constants, 1-bond C-H correlations are eliminated. This experiment shows a 2-bond correlation between the furan β CH and ketone carbon, as well as a 2-bond correlation between furan α quaternary carbon and the alkene CH carbon. This is consistent with the tautomer "b" as the most populated in solution.

This tautomer is also the most stable one in solid state. X-ray diffraction experiments on crystals obtained from SMAR **1** in THF show C-C and C-O bond distances consistent with this structure: the bond distance of the ketone carbonyl of 2 is the shortest of all, with only 1.25 Å; the carbon-oxygen distance in the enol is 1.32 Å, in agreement with a lower bond order. The same conclusion can be reached from the carbon-carbon bonds distances: while the double bond shows 1.35 Å, the formally single carbon-carbon bond elongates to 1.42 Å, as shown below:



Chiral resolution of SMAR 1

SMAR **1** (6.4 g, 10.5 mmol) and cinchonine (3.1 g, 10.5 mmol) were dissolved in 56 mL of a $CHCl_3$-MeOH (8:1) solution. This solution was transferred into a container with magnetic stirring which at the same time was introduced within a receptacle with ether (figure 1). The outer vessel was closed and allowed to stir overnight. After 13 hours, the solid obtained was filtered, yielding the crystals of the salt of one of the receptor enantiomers with cinchonine whereas the other enantiomer remains in the filtrate.

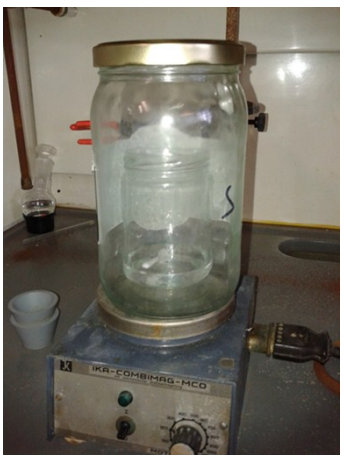


Figure 1

Then the complex with cinchonine was dissolved in methanol and was added to an aqueous solution of formic acid, crystallising the enantiomerically pure receptor. Direct filtration of the solution led to a receptor which typically has small amounts of cinchonine, but the extraction with ethyl acetate and subsequent concentration allowed isolation of the free receptor with a high purity and a yield of 70 %.

$[\alpha]^{20}_{D}$ = +212.3 (*c* = 0.99, $CHCl_3$).

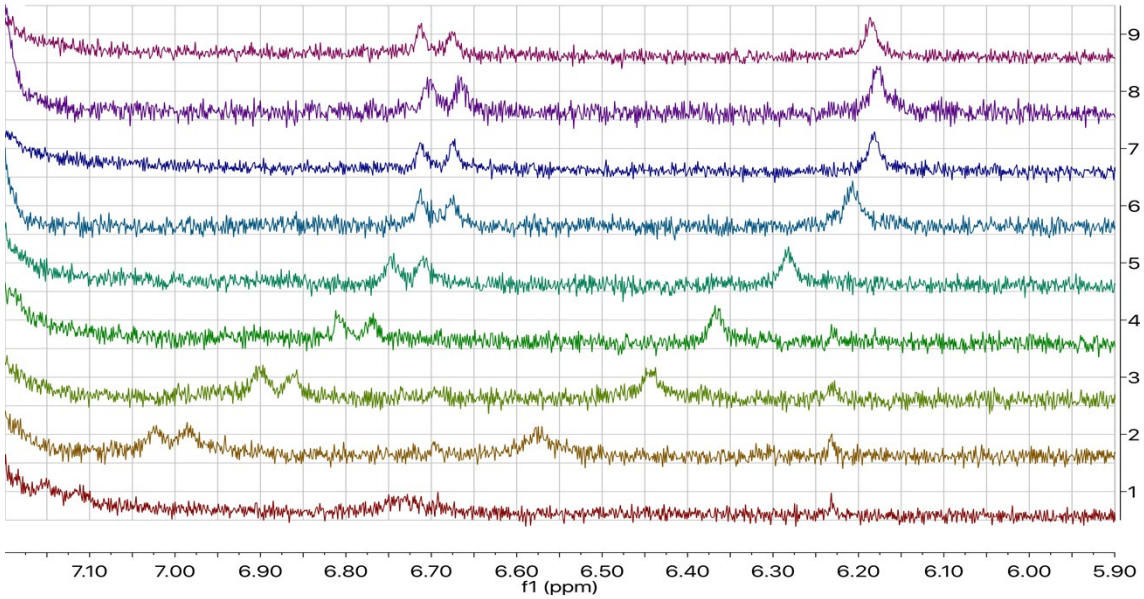
From the mother liquor, it was possible to obtain the other enantiomer of SMAR **1**, continuing fractional crystallization and after the subsequent breakdown of the salt with an aqueous solution of formic acid and extraction with ethyl acetate (72 % yield).

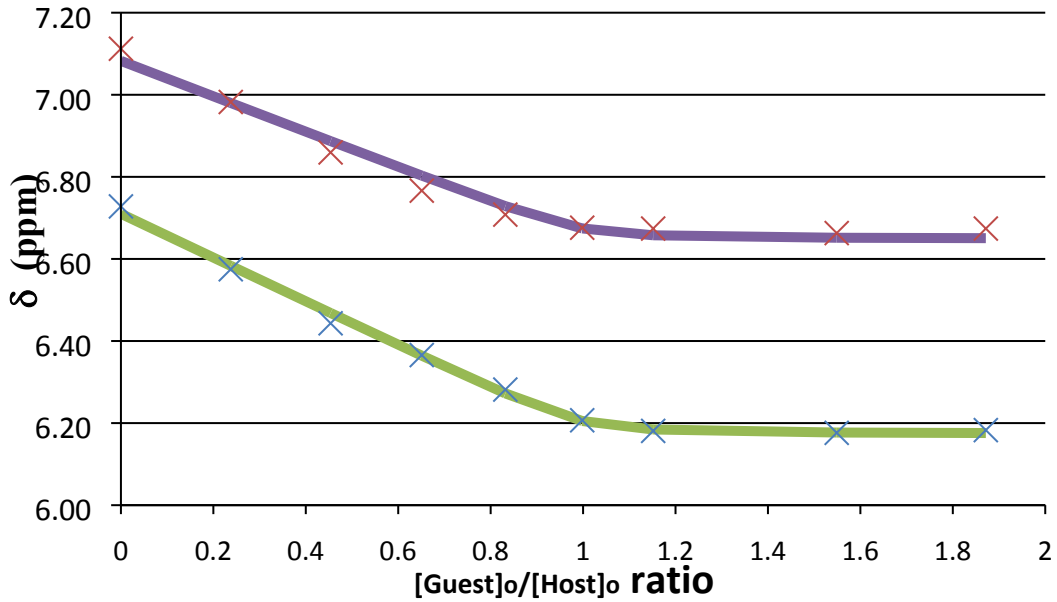
$[\alpha]^{\mathbf{20}}_{\mathbf{D}}$ = -203.9 (*c* = 1.09, $CHCl_3$).

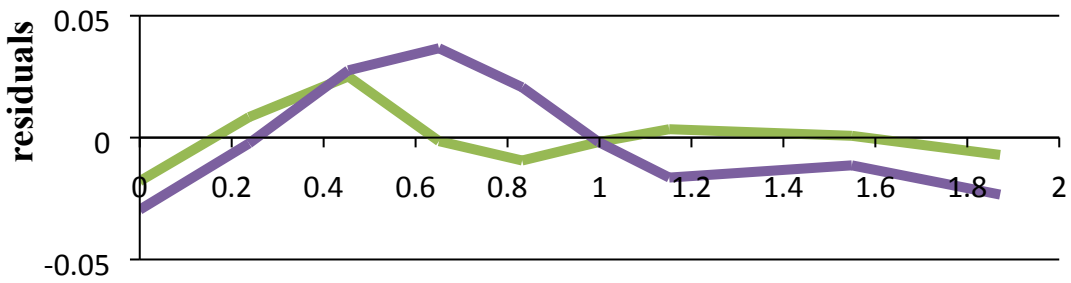
Alternatively, the enantioselective extraction of the receptor can be employed to the preparation of SMAR **1** enantiomerically pure. A suspension of SMAR **1** (2 equivs.), LiOH (1 equiv.) and ephedrine (1 equiv.) in chloroform is washed with the same volume of water. After the equilibrium is reached, the two phases are separated and a second extraction of the receptor mixture already enriched after a first extraction with 1 eq LiOH aq offers a compound with a reasonable enantiomeric purity, which, after washing with aq formic acid and further crystallization provides the optically pure receptor.

Determination of the association constant for SMAR 1 and ephedrine

The titration was performed on a 2.5 mM solution of SMAR **1** by adding increasing amounts of the guest. Data fit was made using BindFit v0.5 (http://app.supramolecular.org/bindfit/) using a NMR 1:1 model and Neldel-Mear method. K= 112068.49 M^{-1} ; K error (%): 179.94

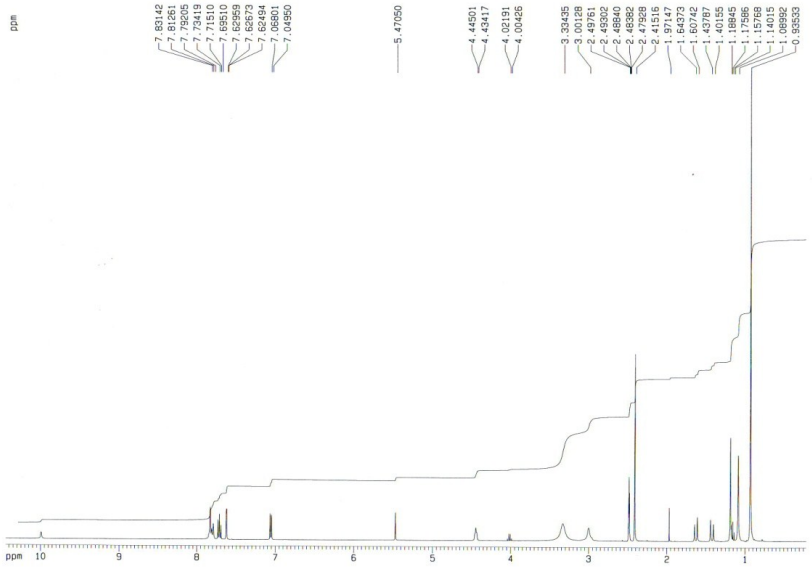




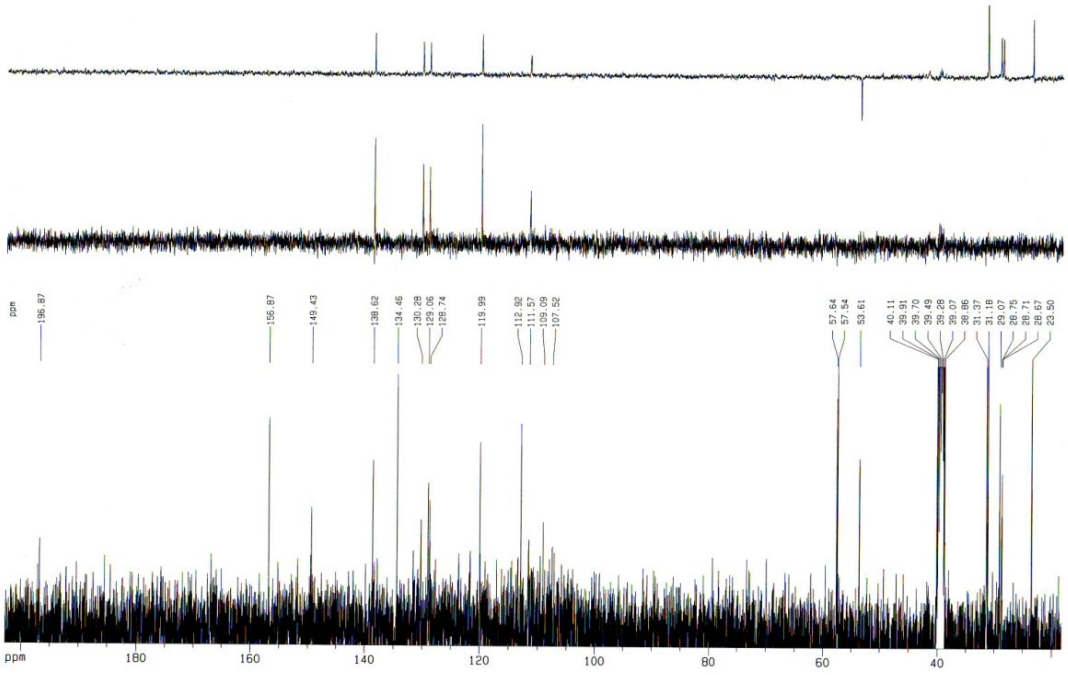


^{1}H and ^{13}C NMR, IR and HRMS of SMAR 1

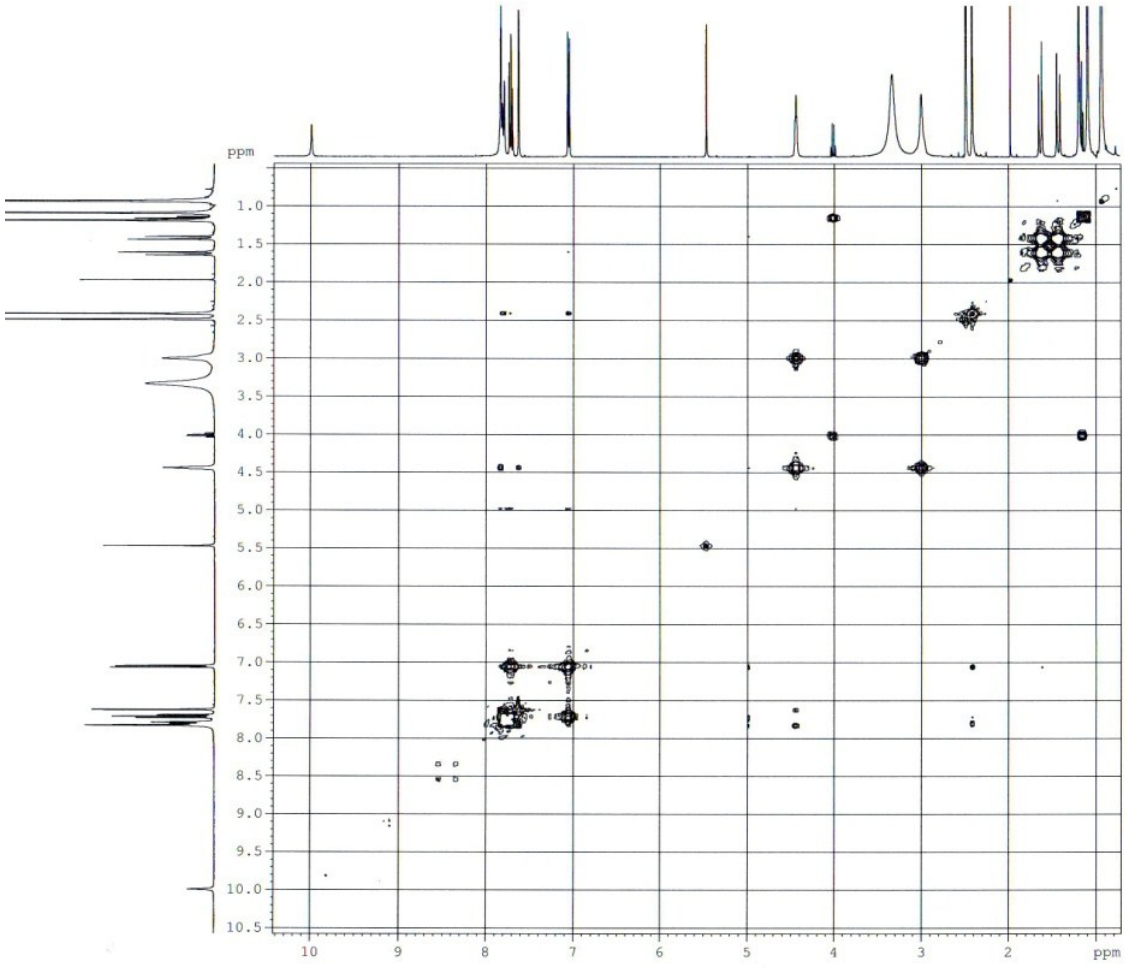
RMN ^{1}H (DMSO-d_6, 400 MHz)



RMN ^{13}C (DMSO-d_6, 100 MHz)



COSY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8.0
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7
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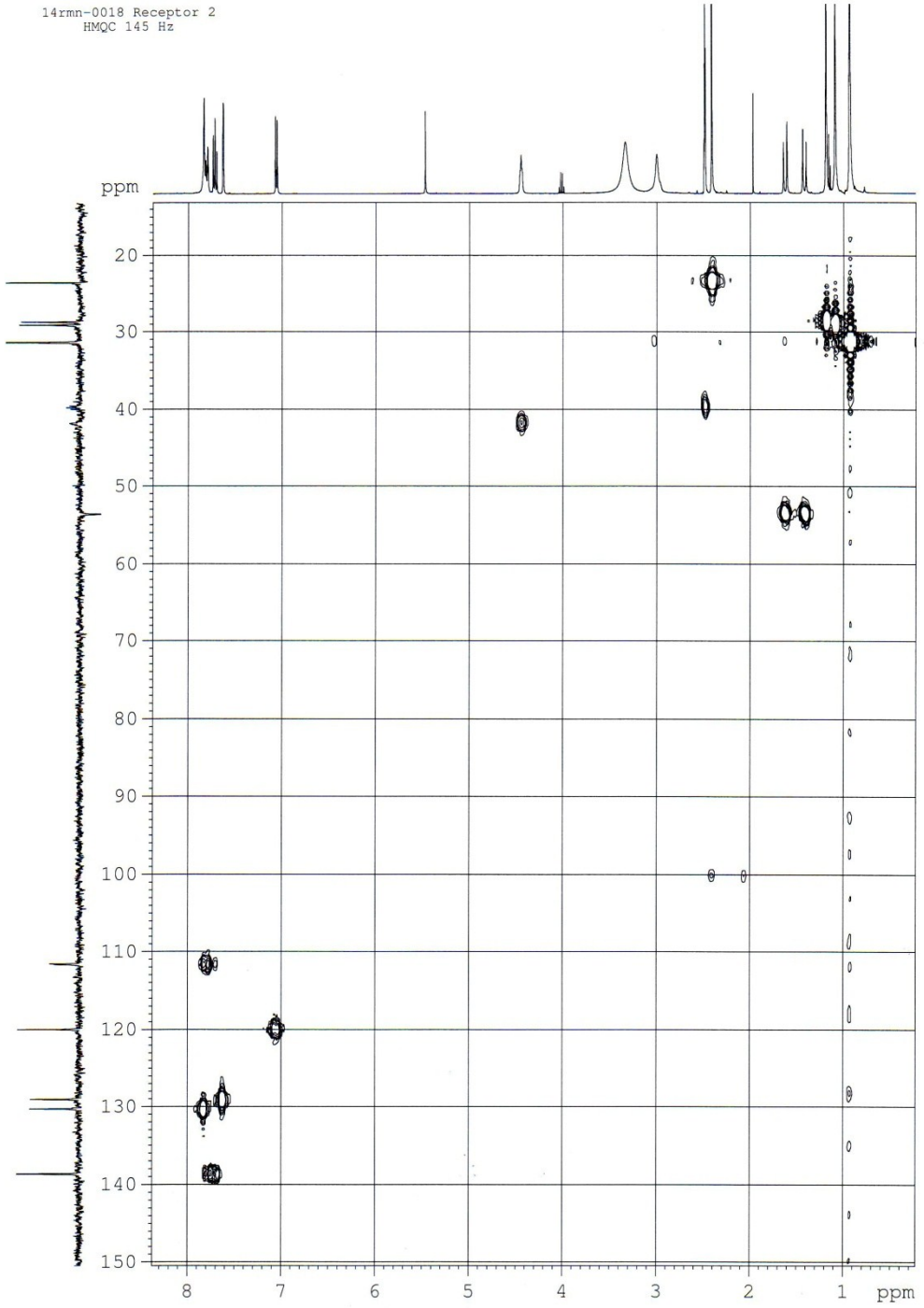
3
2
ppm

HMQC


14rmn-0018 Receptor 2
HMQC 145 Hz
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60
70
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90
100
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120
130
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150
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6
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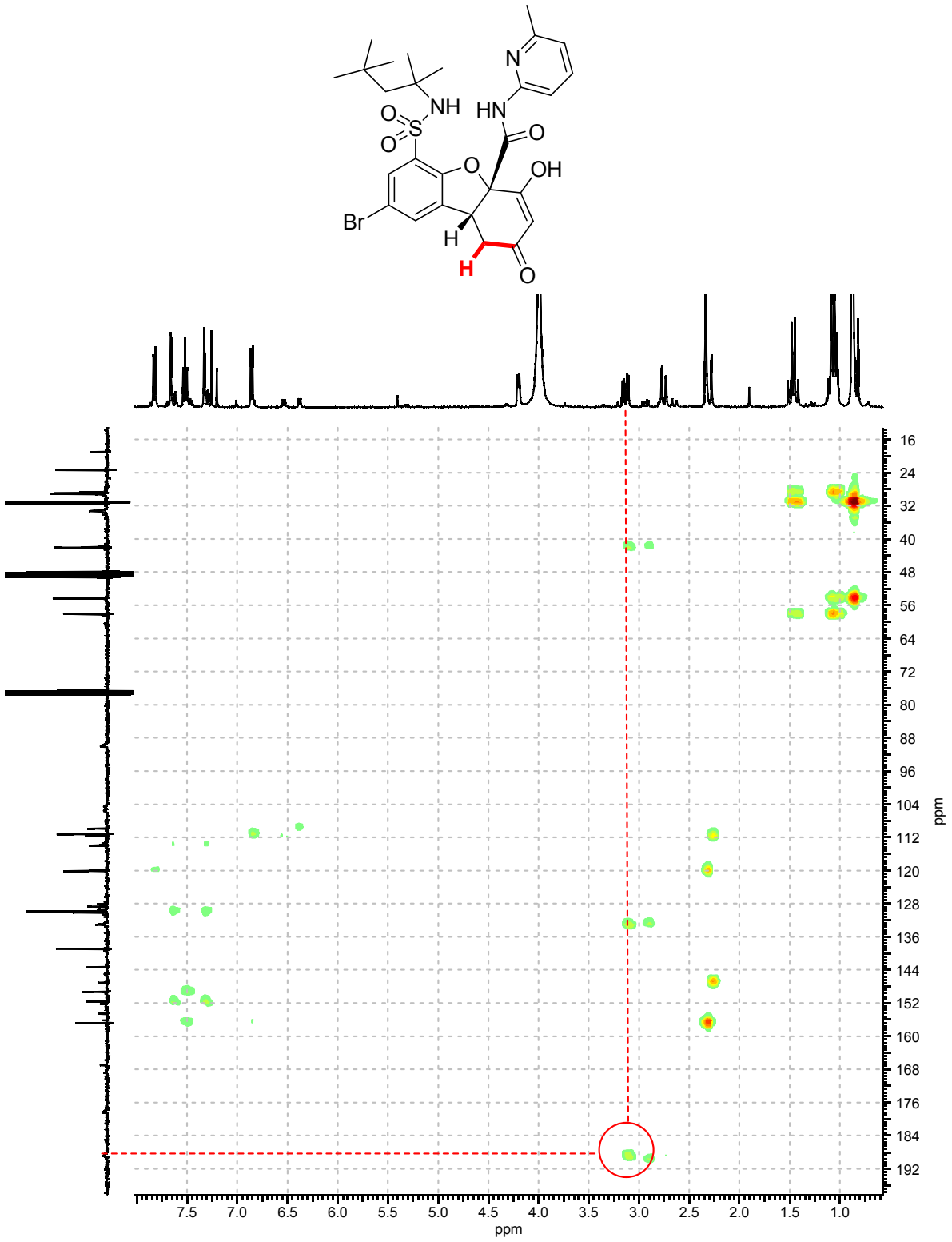
3
2
1
ppm

HMBC-CIGAR[2]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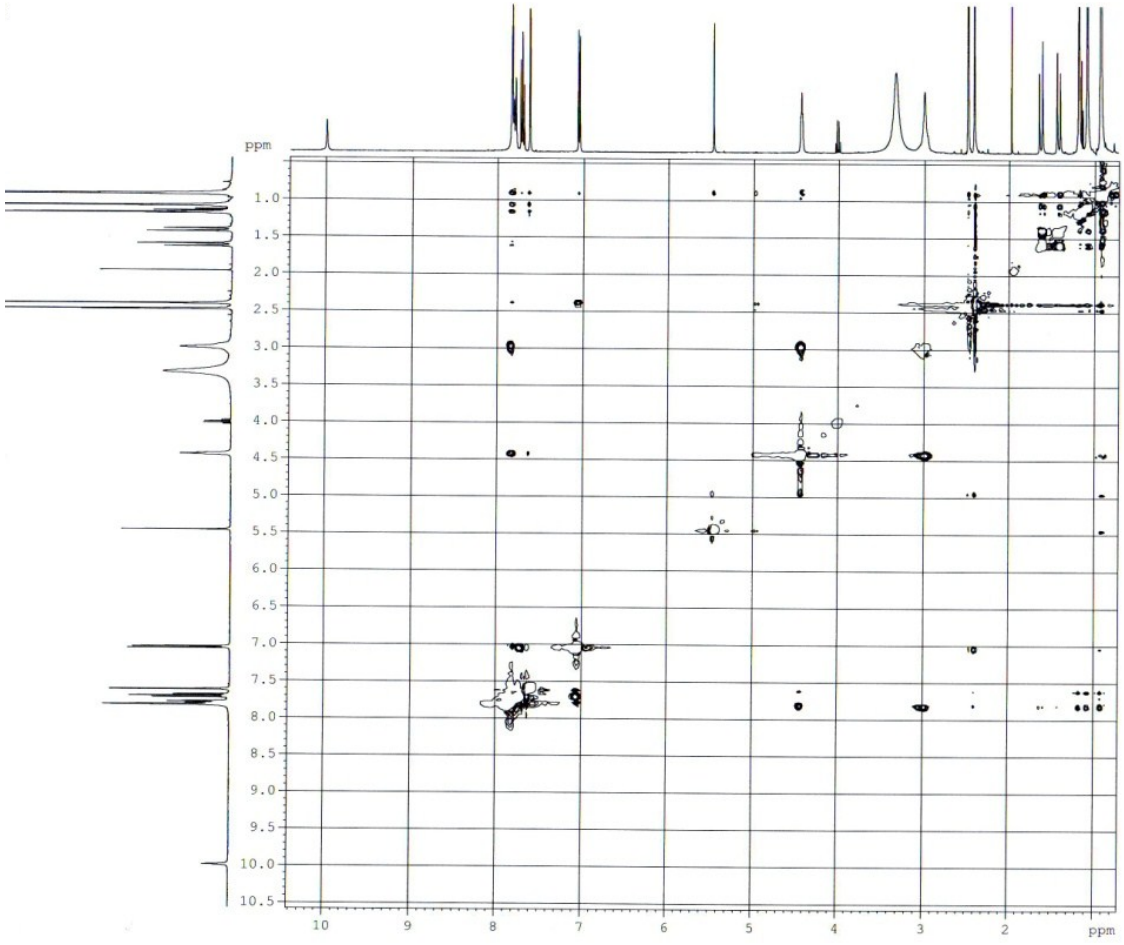
ROESY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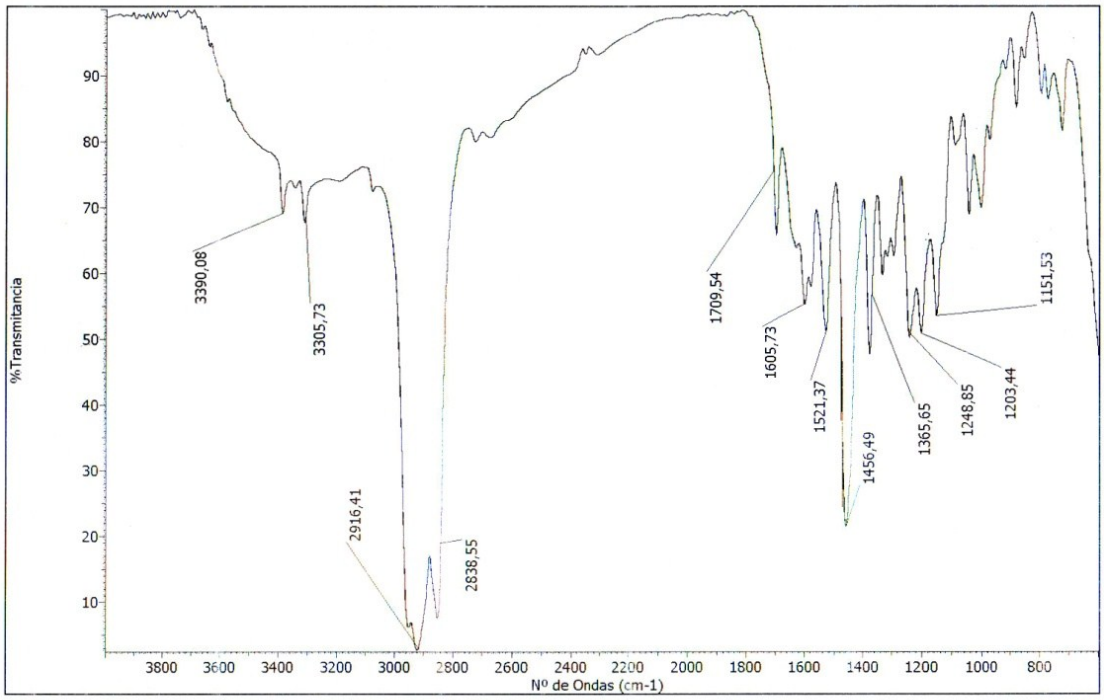
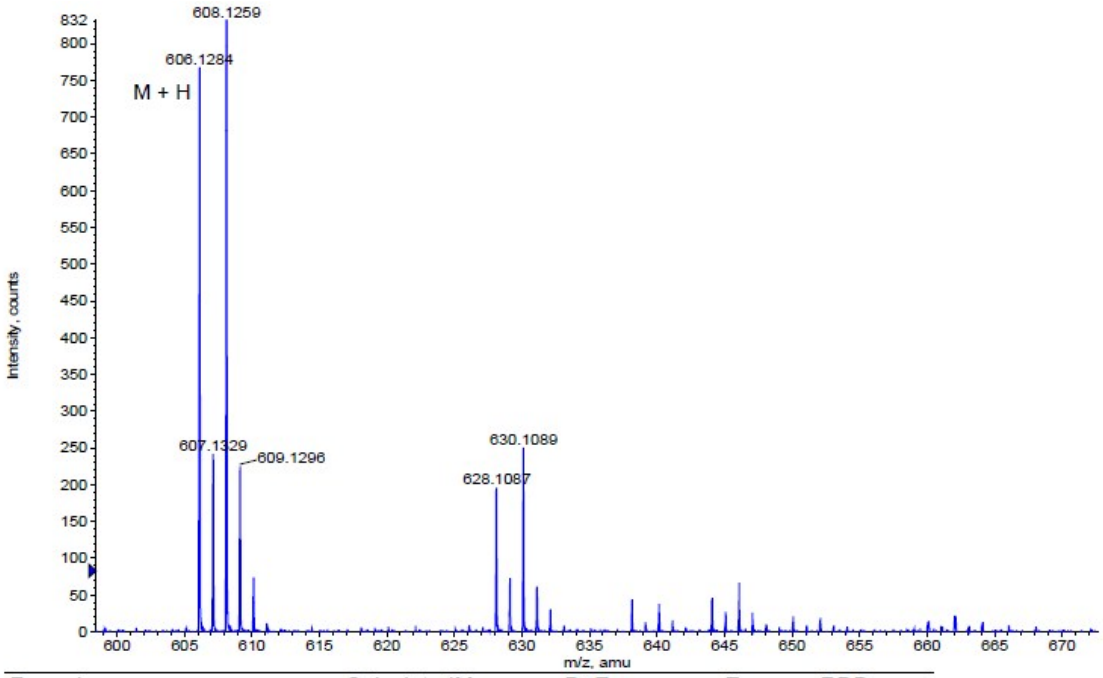
IR



HRMS



Formula	CalculatedMass	mDaError	ppmError	RDB
C30 H34 N O4 Na S Br	606.128413	-0.012948	-0.021362	13.5
C31 H30 N5 Na S Br	606.12975	-1.35026	-2.227678	18.5
C27 H33 N3 O6 S Br	606.126796	1.604496	2.64712	12.5
C32 H33 N O4 S Br	606.130818	-2.418208	-3.989593	16.5
C33 H29 N5 S Br	606.132156	-3.75552	-6.195909	21.5
C25 H34 N3 O6 Na S Br	606.12439	4.009756	6.615351	9.5
C22 H33 N5 O8 S Br	606.122773	5.6272	9.283833	8.5
C23 H38 N O9 Na S Br	606.134286	-5.886308	-9.711313	4.5

4. Chiral discrimination studies

The methodology described for the evaluation of the chiral discrimination of SMAR **1** was adopted due to the impossibility of employing conventional ^{1}H-NMR titrations, considering first the difficulty in assigning the broad signals observed for the free receptor spectra and secondly, its small solubility in $CDCl_3$. To illustrate the difficulty in the assignment and interpretation of free receptor ^{1}H-NMR spectra, the following figure shows the spectra of a chloroform solution of SMAR **1** (above) and after the addition of ephedrine (below).

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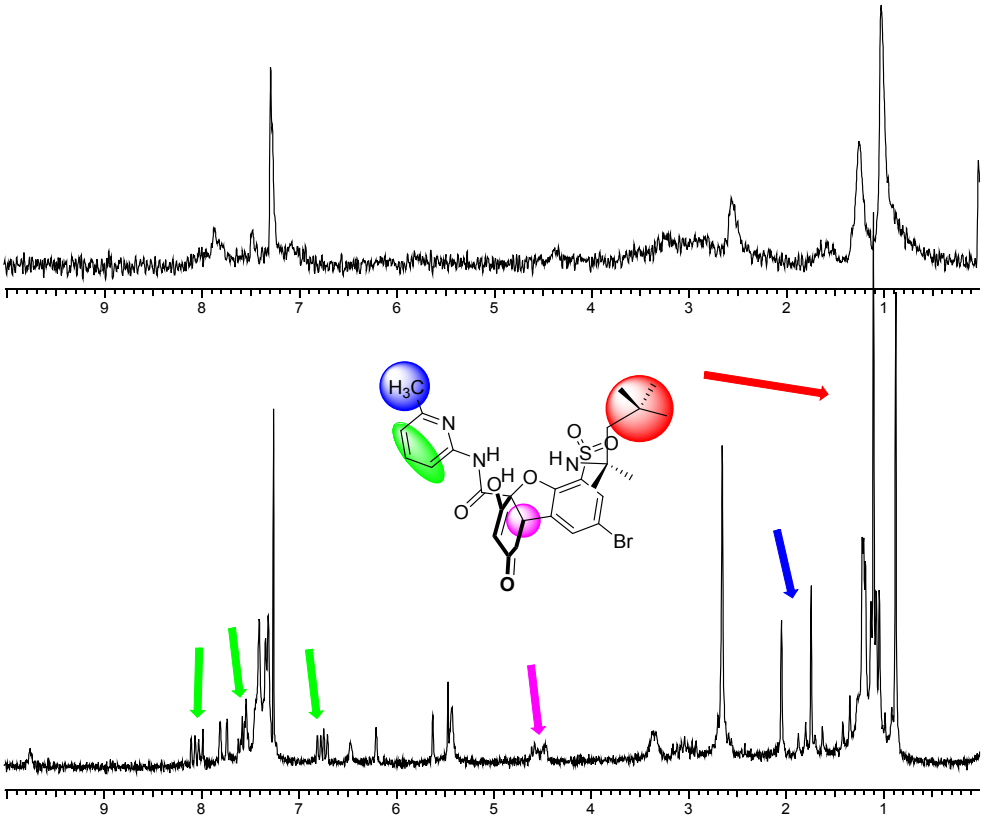


Extraction of the commercial racemic amino alcohols

Commercial amino alcohols (atenolol, propranolol, carvedilol, albuterol, tertbutaline and bambuterol) were grinded in a mortar and the fine solid obtained was dissolved in aqueous HCl 2 M. Impurities were extracted with EtOAc and the aqueous phase was then basified with KOH. Pure amino alcohol was obtained after extraction with EtOAc, drying with Na_2SO_4 and evaporation under reduced pressure.

Liquid-liquid extraction experiments with hydroxyl-amine guests (Table 1)

The experiments in which the racemic receptor mixture was extracted with enantiopure chiral guests (table 1, entries 1-10) were performed as follows: in an NMR tube, racemic receptor **1** (10 mg, 0.016 mmol) was suspended in 0.5 mL of $CDCl_3$. 0.5 mL of an aqueous

solution of LiOH (0.016 M) were added as well as 0.008 mmol of the corresponding chiral amine. The NMR tube was stirred and then centrifuged to promote phase separation. In this manner the ^{1}H NMR spectrum could be directly registered. If the separation is enantioselective the split signals will have different sizes. The integration of the split signals gives the preference of the chiral amine for the receptor enantiomers.

The experiments in which the enantio-pure (*4aS,9bR*) SMAR **1** was used and the guest was employed as a racemic mixture (table 1, entries 11-16) were performed as follows: 1mL of a 10^{-2} M solution of the receptor in deuterochloroform was placed on an NMR tube. To this solution, 10 equivalents of the guest hydrochloride, 1 equivalent of LiOH and 1 mL of distilled water were added. The tube was agitated and centrifuged to allow the two phases to separate. In the case of terbutaline, sulphate salt was used instead of hydrochloride. For atenolol, carvedilol and propranolol (entries 11-13), metanosulfonate salt was used instead of hydrochloride, also, no LiOH was added but 1 eq of free aminoalcohol. The amount of acid was tuned to favour a better extraction.

The procedure was modified for albuterol (entry 14) and terbutaline (entry 15) due to the high solubility of these compounds in water even in their neutral form. Only 3 equivalents of guest were used and no LiOH was needed to extract to the aqueous layer the fraction of the guest that was not making a complex with the receptor. In the case of bambuterol (entry 16), due to the high solubility of the hydrochloride in chloroform, the volume of the aqueous layer was increased to 4 ml to prevent the unselective extraction of this salt.

Calculation of the relative association constants from extraction experiments

The relative association constant is expressed as the ratio between the association constant of both guest enantiomers with enantiopure host:

$$K_{rel} = \frac{K_{ass}^{(R)}}{K_{ass}^{(S)}}$$

These association constants are:

$$K_{ass}^{(R)} = \frac{[complex]_{(R)}^{CDCl_3}}{[host]^{CDCl_3}[guest]_{(R)}^{CDCl_3}};\ K_{ass}^{(S)} = \frac{[complex]_{(S)}^{CDCl_3}}{[host]^{CDCl_3}[guest]_{(S)}^{CDCl_3}};$$

where $[guest]^{CDCl3}$ are the chloroform solution concentrations of only the guest that is not associated to the host (free guest).

Therefore:

$$K_{rel} = \frac{[complex]_{(R)}^{CDCl_3} \cdot [guest]_{(S)}^{CDCl_3}}{[guest]_{(R)}^{CDCl_3} \cdot [complex]_{(S)}^{CDCl_3}}$$

The ratio between the complex concentrations in $CDCl_3$ can be identified, without committing a big error, as the ratio between the *R* and *S* enantiomers of the guest in the organic layers,

since the solubility of the (salts) of the guest in chloroform is small. However, the ratio between the guest concentrations not associated to the receptors cannot be directly measured in the organic layer.

The partition ratio is identical for both guest enantiomers:

$$K_{part} = \frac{[guest]^{water}_{(R,S)}}{[guest]^{CDCl_3}_{(R,S)}}.$$

Substituting in previous equation:

$$K_{rel} = \frac{[complex]^{CDCl_3}_{(R)}}{[complex]^{CDCl_3}_{(S)}} \cdot \frac{[guest]^{water}_{(S)}}{[guest]^{water}_{(R)}}$$

where the ratio between free concentrations in water of the guest can be measured by analysing the aqueous layer.

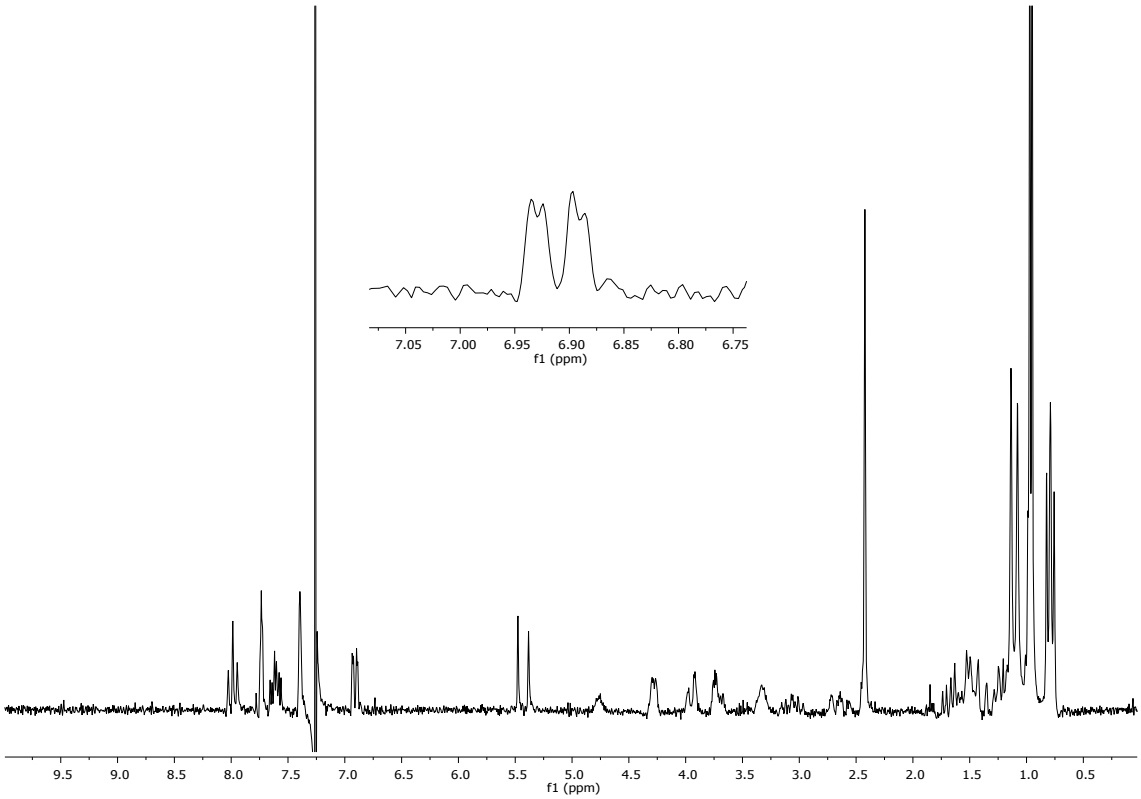
A similar reasoning could apply for those cases in which the racemic host was extracted using enantiopure guest.

In those experiments in which 10 equivalents of guest were used, the ratio $\frac{[guest]^{water}_{(S)}}{[guest]^{water}_{(R)}} \approx 1$ and therefore, the relative association constant was identified as the ratio between guest enantiomers in the organic layers.

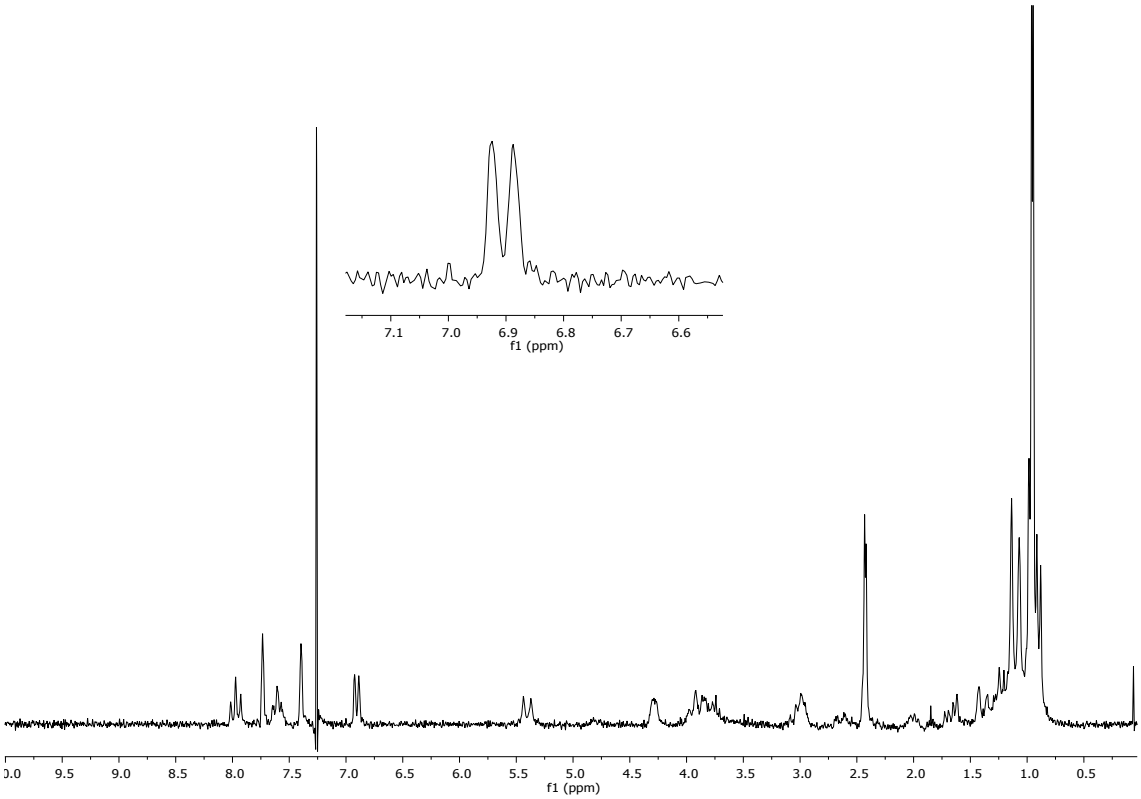
In experiments in which 2 equivalents of racemic host were extracted with 1 equivalent of enantiopure guest, conservation of mass requires that the inverse ratio observed in the organic layer is also present in the aqueous layer. This was empirically corroborated for ephedrine, in which the ratio in the aqueous layer was inverted with respect to the organic layer:

$$\frac{[complex]^{CDCl_3}_{(R)}}{[complex]^{CDCl_3}_{(S)}} = \left(\frac{[guest]^{water}_{(R)}}{[guest]^{water}_{(S)}}\right)^{-1} \quad ; \quad \text{Therefore,} \quad K_{rel} = \left(\frac{[complex]^{CDCl_3}_{(R)}}{[complex]^{CDCl_3}_{(S)}}\right)^{2}$$

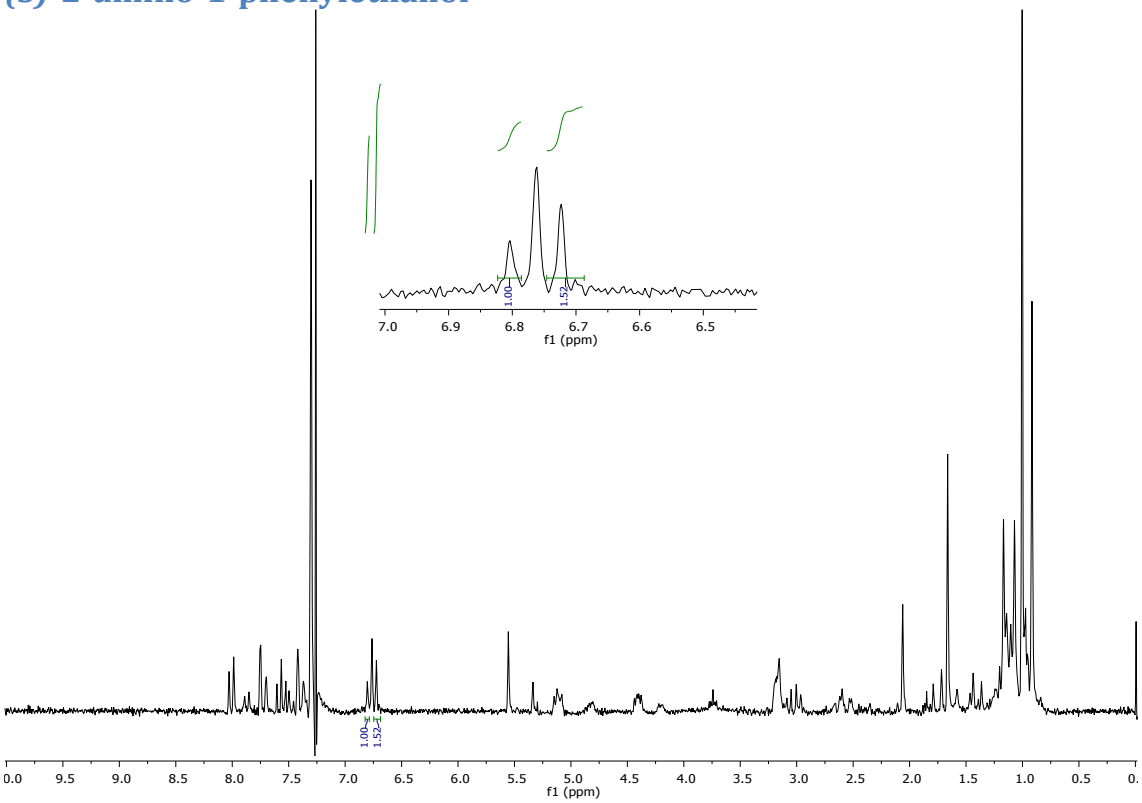
L-leucinol



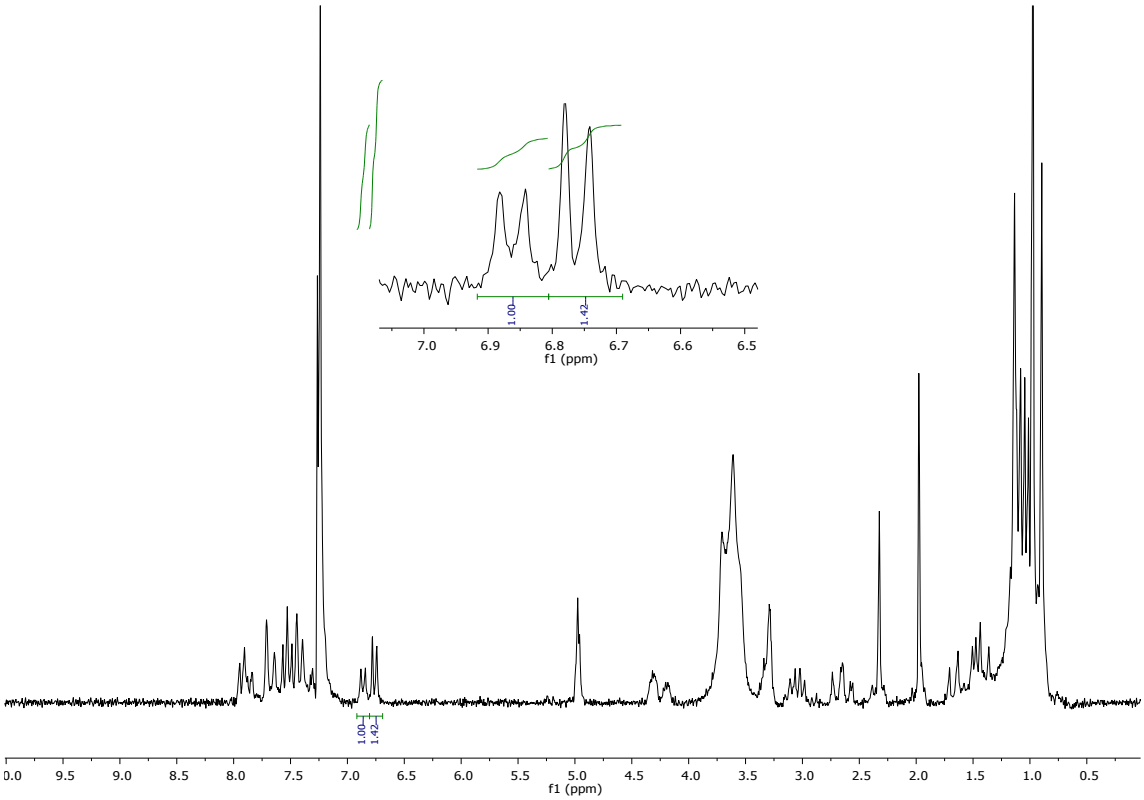
L-valinol



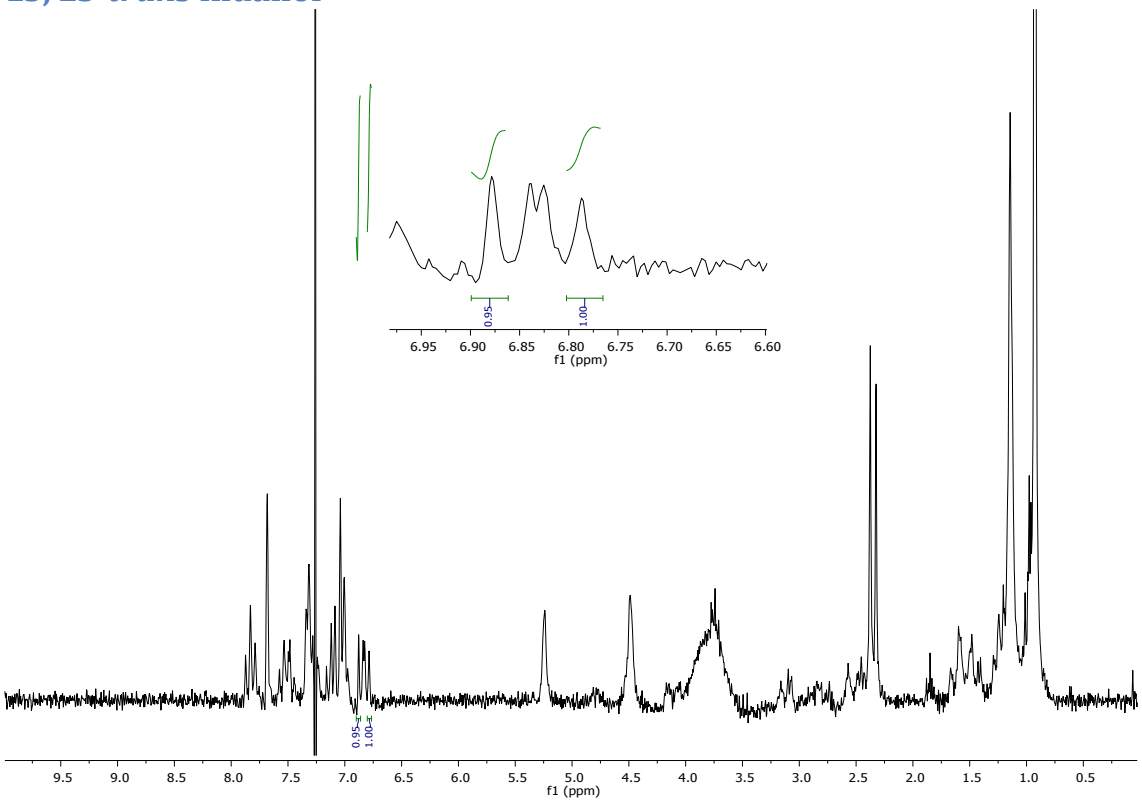
(S)-2-amino-1-phenylethanol



Norephedrine



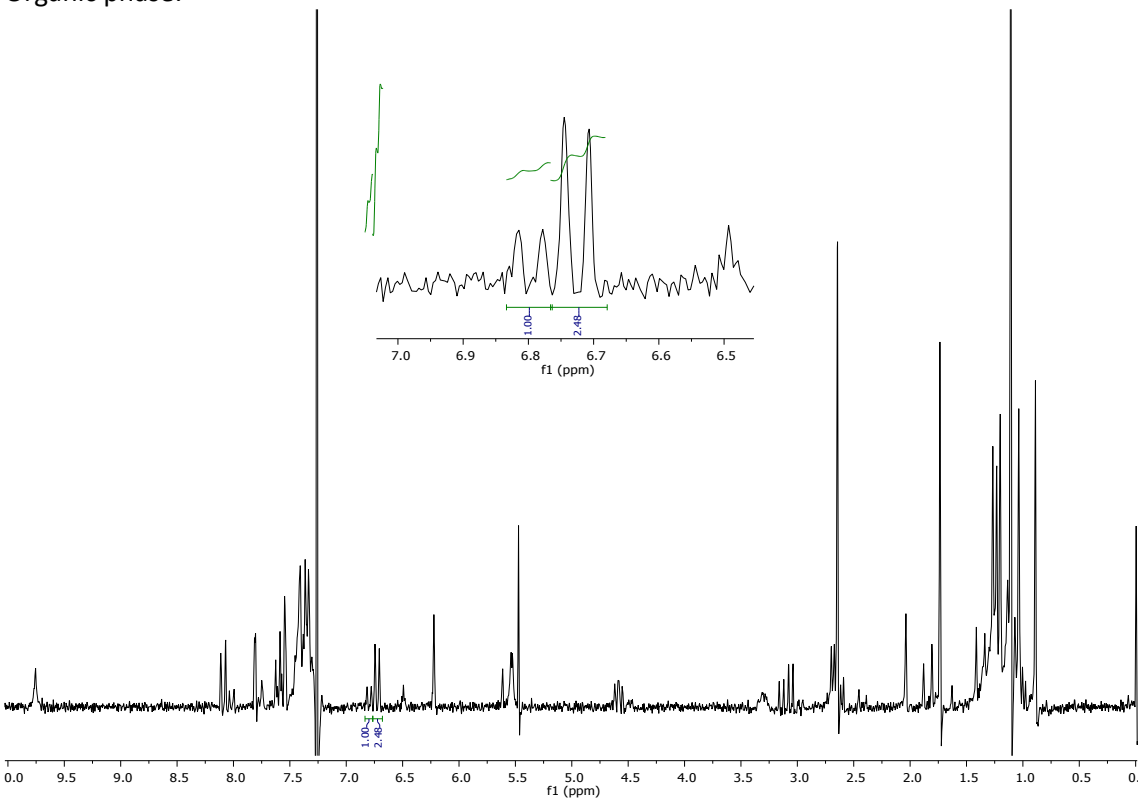
1*S*, 2*S*-*trans* indanol



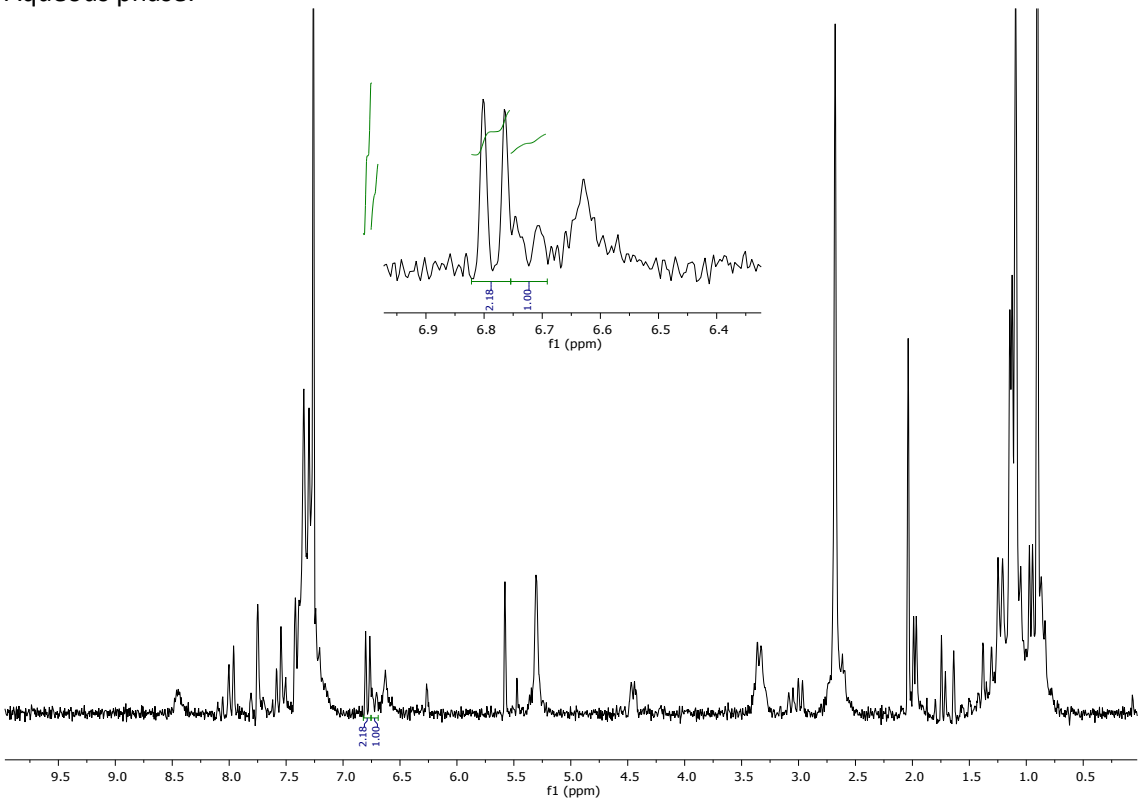
Ephedrine

(the experiment was scaled-up to 100 mg receptor)

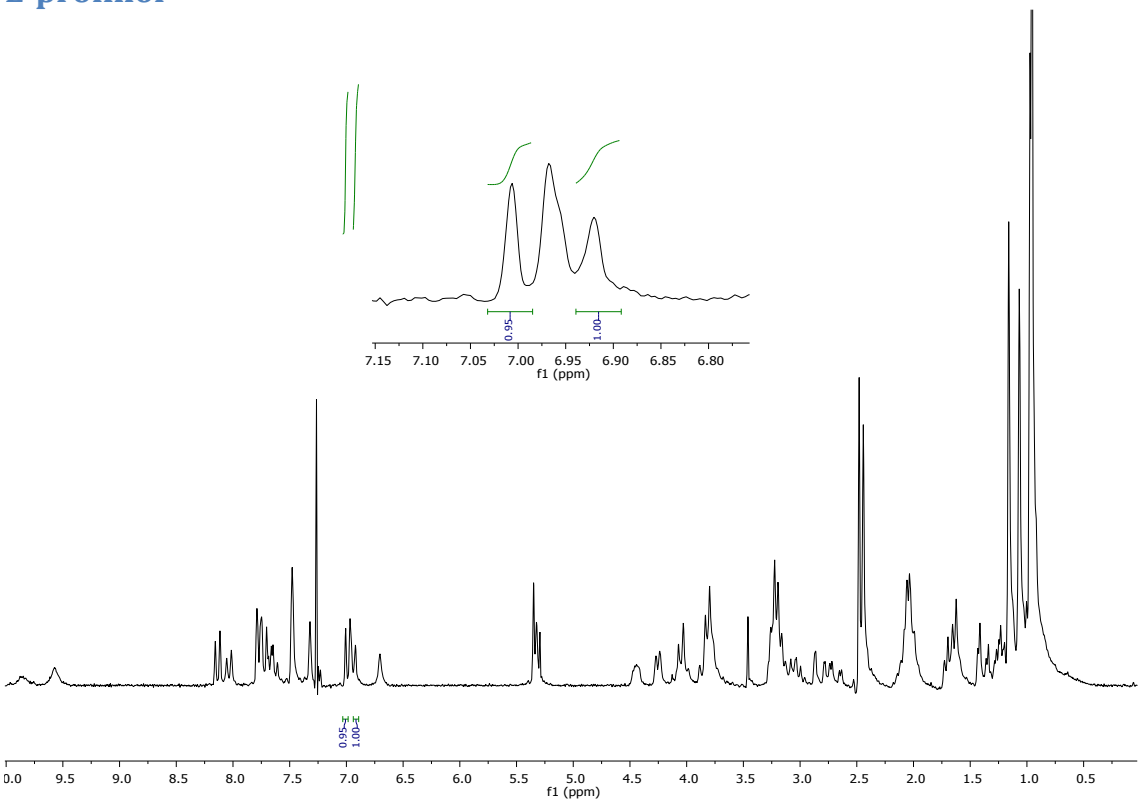
Organic phase:



Aqueous phase:

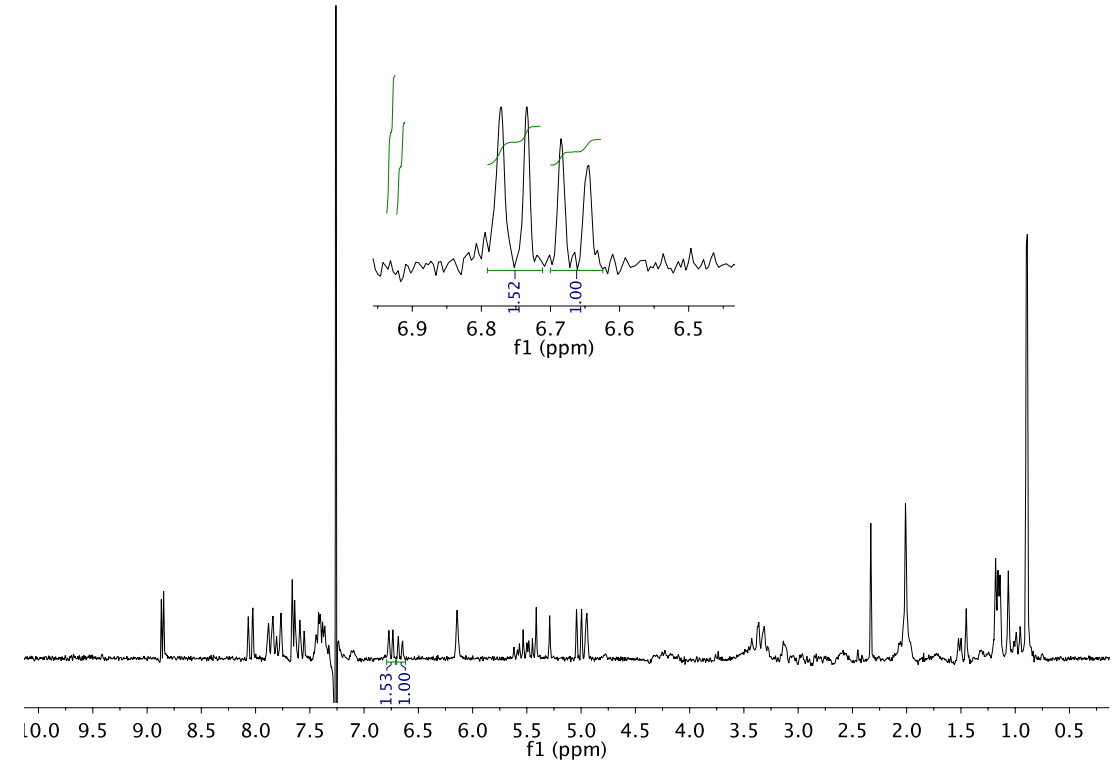


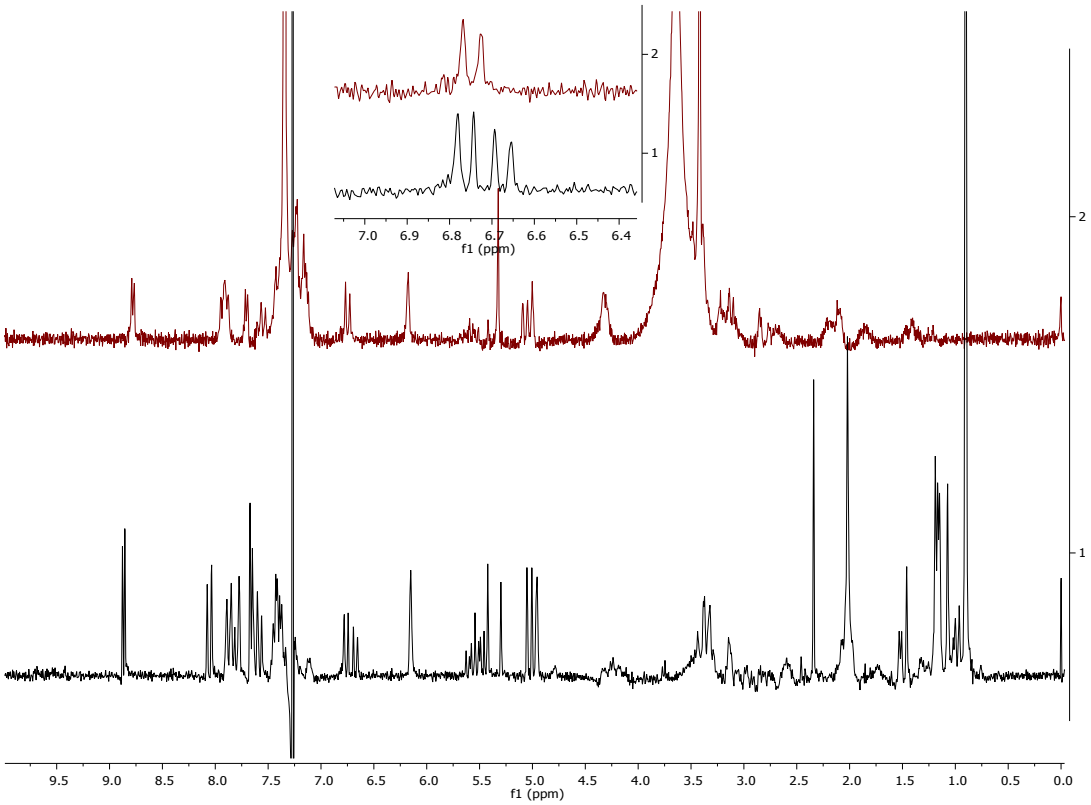
L-prolinol


0.95
1.00
7.15 7.10 7.05 7.00 6.95 6.90 6.85 6.80
f1 (ppm)
0.95
1.00
0.0 9.5 9.0 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
f1 (ppm)

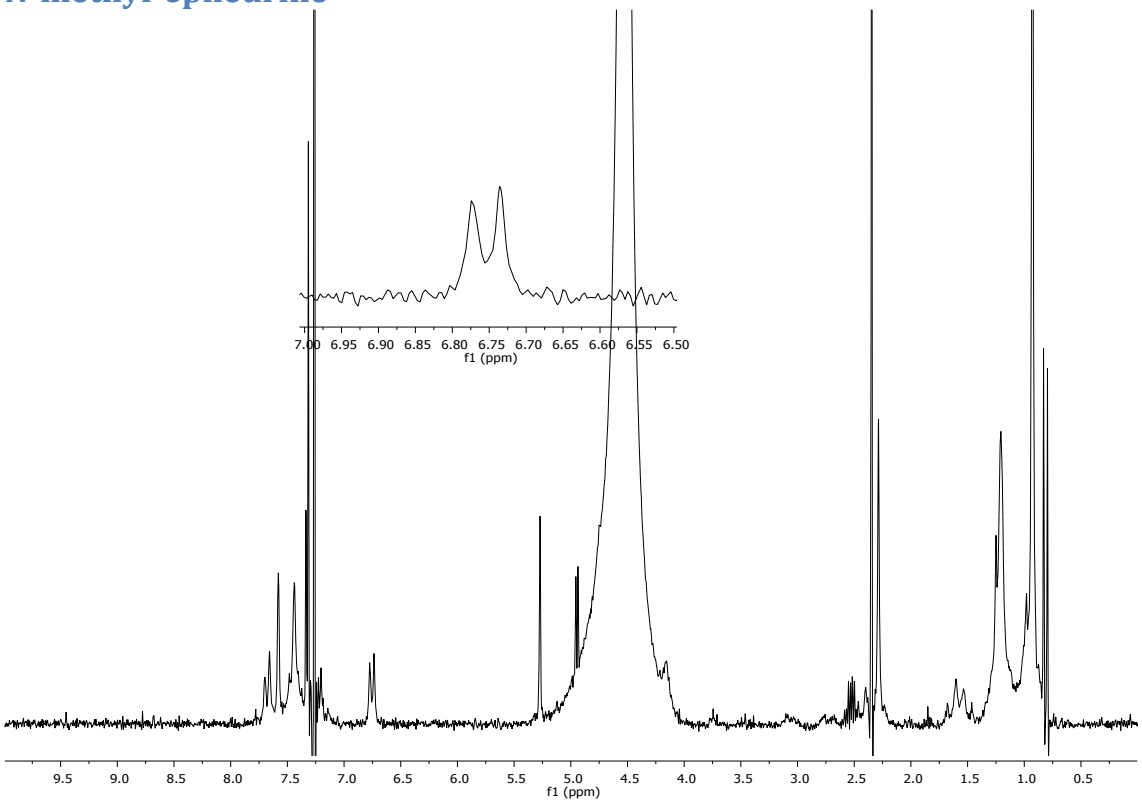
Cinchonine

^{1}H-NMR spectrum, compared with the spectrum from the most insoluble salt obtained from the racemic SMAR 1 and cinchonine, reveals that the stronger complex correspond to the (*4aS,9bR*) absolute configuration.

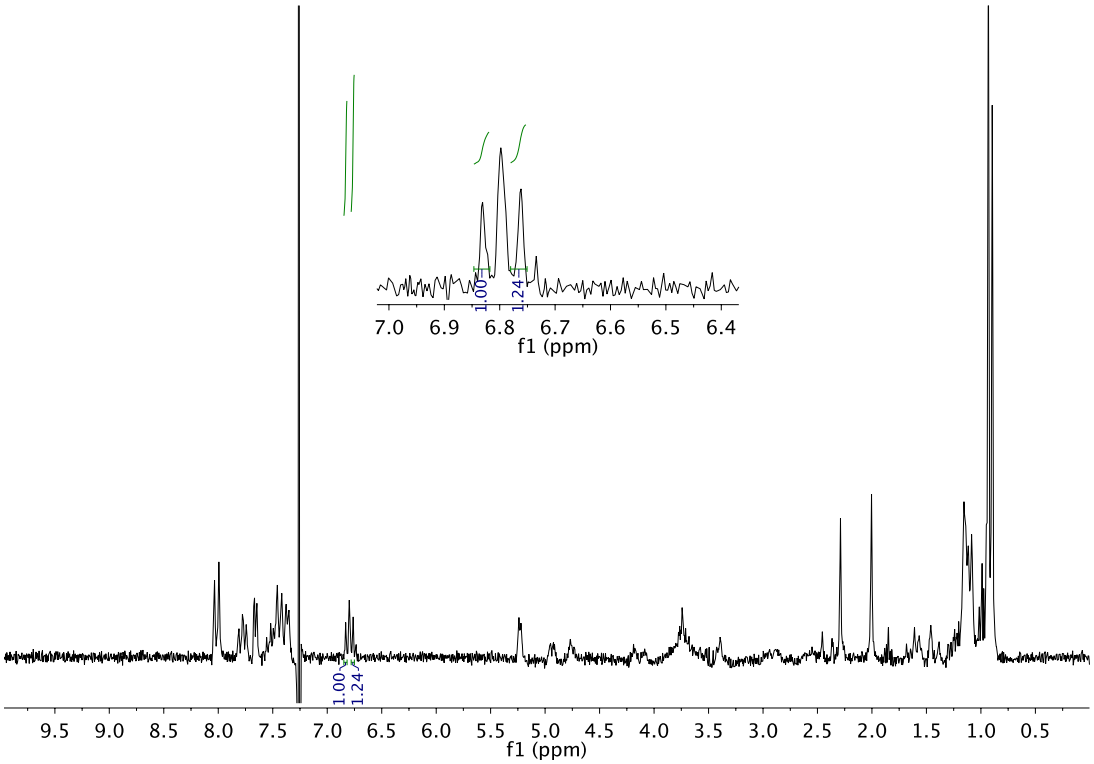




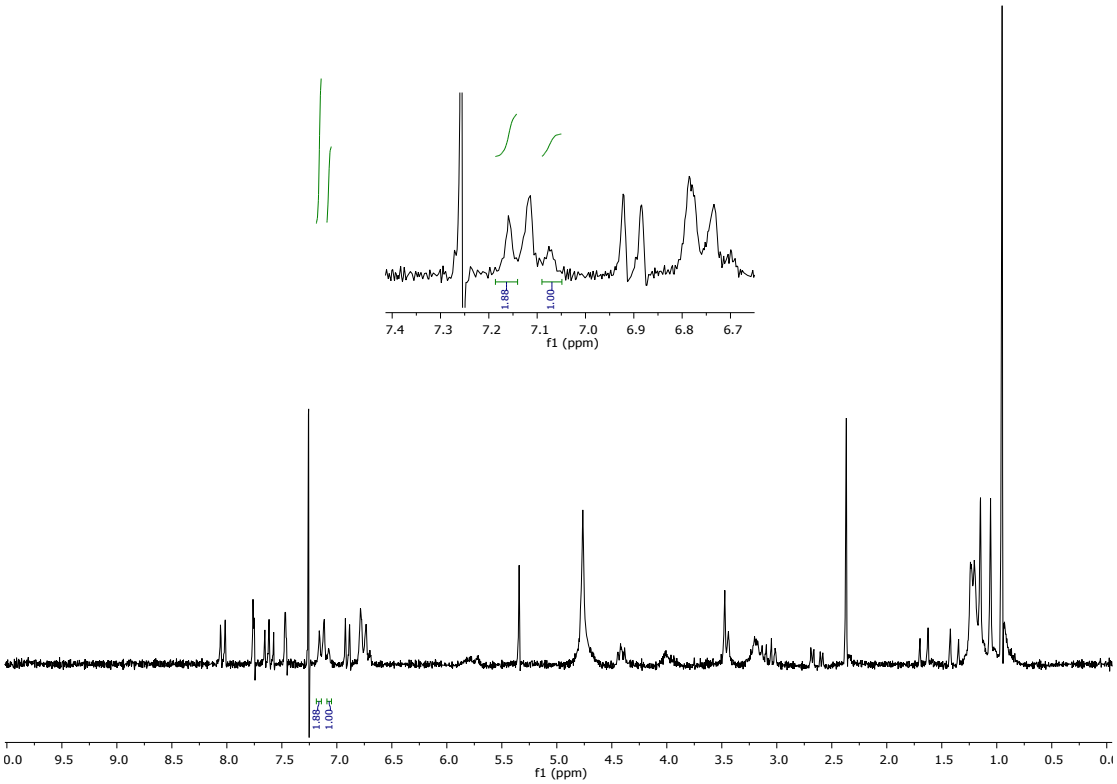
N-methyl-ephedrine



Cloramphenicol



Atenolol



Propanolol

Samples were analysed with a Daicel IB-3 HPLC column, using a 10% ethanol: 90% ammonium formate 10mM: formic acid water solution with pH=3.5

Servicio General de Espectrometría de Masas
Plaza de los Caídos 1-5. 37008 Salamanca

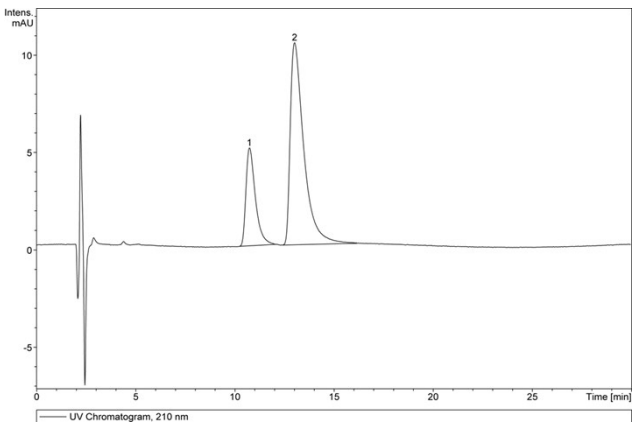
1 of 1

Emitido por César Raposo (Responsable SGEM)

Analysis Name: QUINO227.D
Method: QUIRIB3.M
Sample Na sumial quiral

Instrument LC-MSD-Trap-XCT
Operator: Administrator

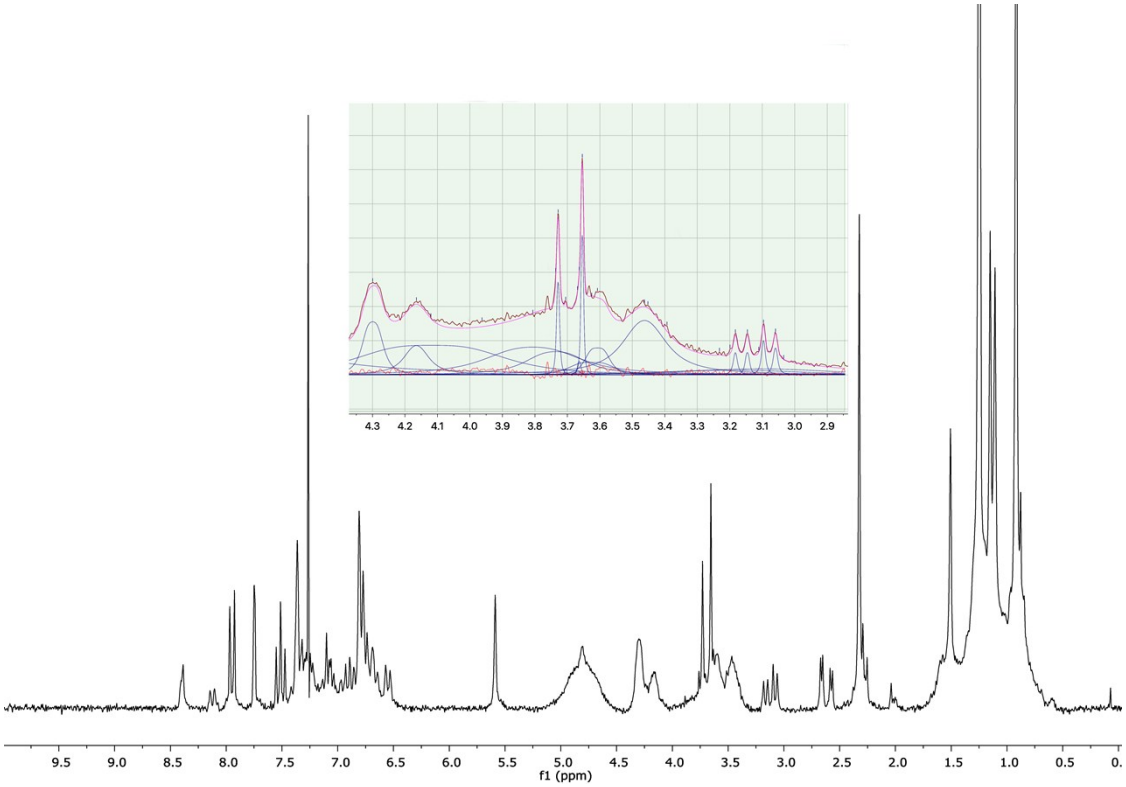
Print Date: 12/01/2014 01:43:13 PM
Acq. Date: 12/01/2014 01:11:06 PM



Compound List:

#	RT [min]	Range [min]	Height	Area	Area Frac %
1	10.7	10.2 - 12.1	34	1130	25.2
2	13.0	12.4 - 16.2	71	3359	74.8

Carvedilol



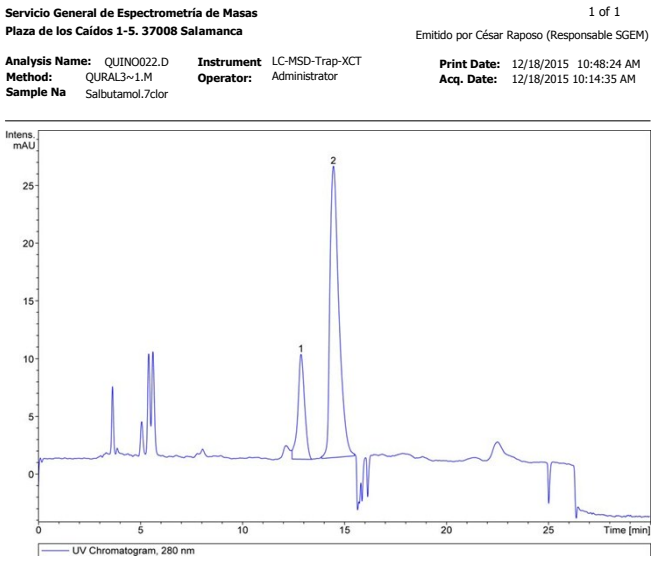
Direct integration of ^{1}H-NMR spectra was not possible due to overlapping of signals. Analysis was performed by deconvolution of the signals using MestReNova v10.0 software. The areas of the gaussians corresponding to both enantiomers' signals yield a 1.3 ratio.

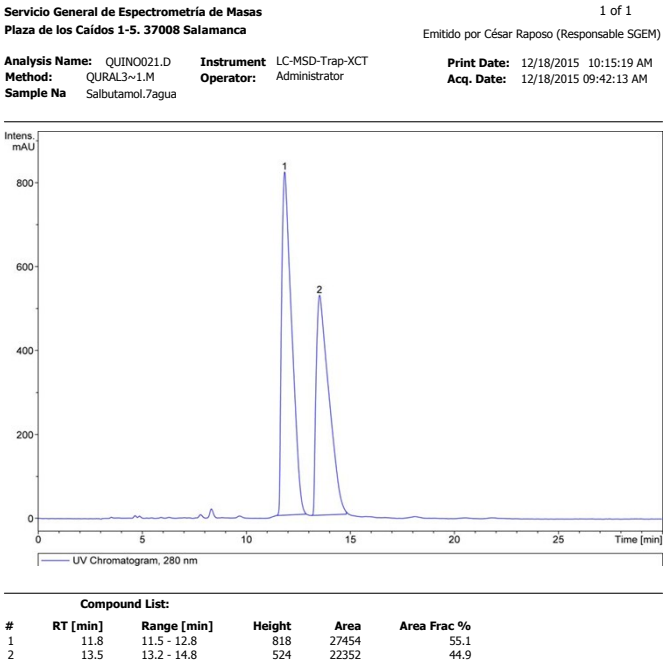
Albuterol (salbutamol)

Samples were analysed with a Chirex-3022 HPLC-column, using a 10% ethanol : 90% ammonium formate 10mM: formic acid water solution with pH=3.5.

Organic layer: comparison with literature data[3] reveals that the organic layer is enriched in the (*R*) enantiomer.

Aqueous layer: comparison with literature data[3] reveals that the aqueous layer is enriched in the (*S*) enantiomer.





$$Krel = {}^{78.7}/_{21.3} \times {}^{55.1}/_{44.9} = 4.5$$

Terbutaline

Samples were analysed with a Chirex-3022 HPLC-column, using a 10% ethanol: 90% ammonium formate 10mM: formic acid water solution with pH=3.5.

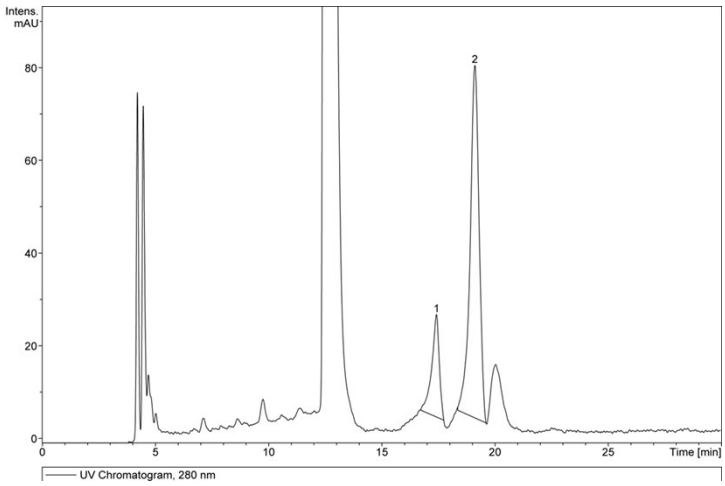
Organic layer:

Servicio General de Espectrometría de Masas
Plaza de los Caídos 1-5. 37008 Salamanca

Emitido por César Raposo (Responsable SGEM)

Analysis Name: QUINO025.D **Instrument** LC-MSD-Trap-XCT
Method: QURAL3~1.M **Operator:** Administrator
Sample Na Terbutalina sale

Print Date: 01/14/2016 09:16:06 AM
Acq. Date: 01/13/2016 06:49:11 PM



Compound List:

#	RT [min]	Range [min]	Height	Area	Area Frac %
1	17.4	16.7 - 17.7	22	511	19.6
2	19.1	18.3 - 19.6	76	2101	80.4

Aqueous layer:

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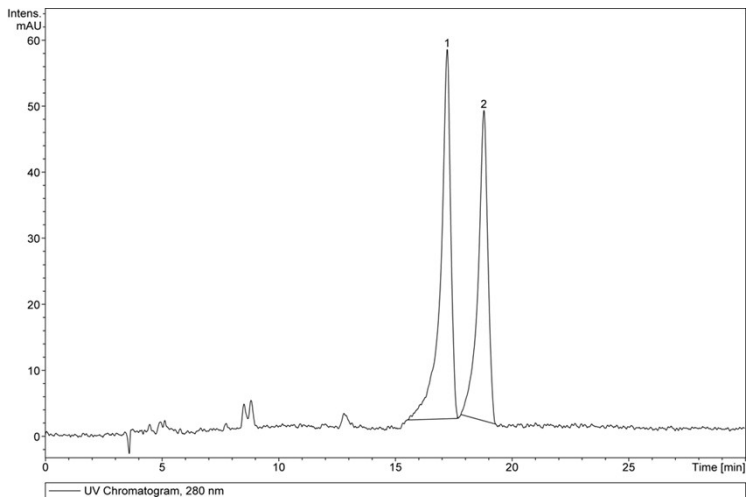
Plaza de los Caídos 1-5. 37008 Salamanca

Emitido por César Raposo (Responsable SGEM)

Analysis Name: QUINO024.D **Instrument** LC-MSD-Trap-XCT
Method: QURAL3~1.M **Operator:** Administrator
Sample Na Terbutalina agua

Print Date: 01/14/2016 09:09:46 AM
Acq. Date: 01/13/2016 06:16:51 PM



Compound List:

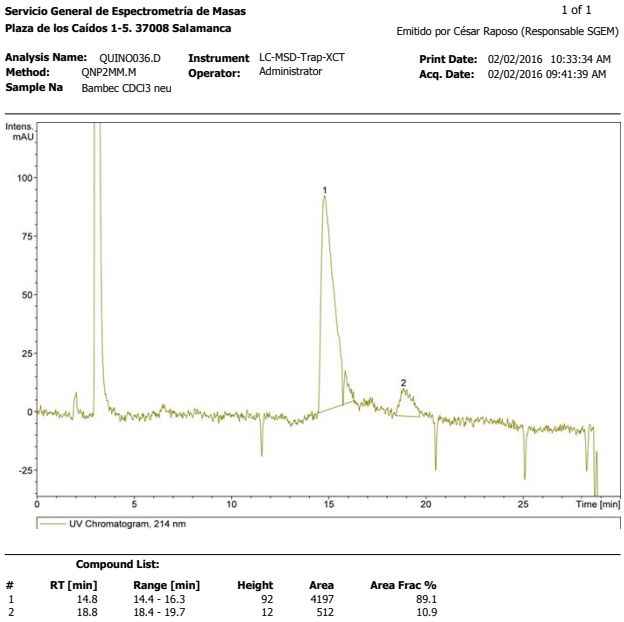
#	RT [min]	Range [min]	Height	Area	Area Frac %
1	17.2	15.5 - 17.7	56	1685	55.0
2	18.8	17.8 - 19.3	47	1380	45.0

$$Krel = {}^{80.4.}/_{19.6} \times {}^{55.0}/_{45.0} = 5.0$$

Bambuterol

Samples were analysed with a Daicel IA-3 HPLC column, using a 10% ethanol: 90% ammonium formate 10mM: formic acid water solution with pH=3.5.

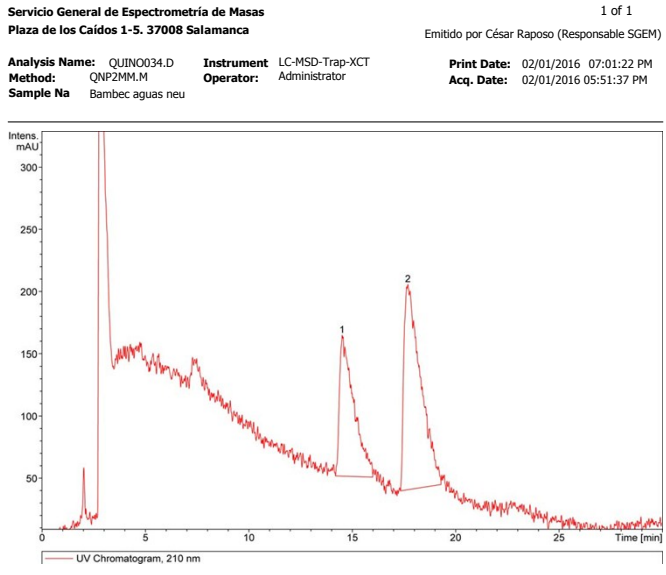
Organic layer:



Compound List:

#	RT [min]	Range [min]	Height	Area	Area Frac %
1	14.8	14.4 - 16.3	92	4197	89.1
2	18.8	18.4 - 19.7	12	512	10.9

Aqueous layer:



Compound List:

#	RT [min]	Range [min]	Height	Area	Area Frac %
1	14.5	14.2 - 16.0	113	5435	37.1
2	17.7	17.3 - 19.3	165	9210	62.9

$$Krel = {}^{89.1}/_{10.9} \times {}^{62.9}/_{37.1} = 13.9$$

5. Computational Details

Calculations were performed with the *Gaussian09*[4] program using the dispersion corrected ωB97XD[5] functional combined with 6-31G(d,p)[6] basis set. Solvent effects (chloroform) were introduced by means of an IEFPCM[7] calculation using the SMD intrinsic solvation model[8]. Bromine atom of SMAR **1** was substituted by an H atom in the interest of computational tractability, since we do not expect that this atom has any relevant effect in the enantioselectivity. The Boltzman average populations, obtained at 298.15 K from the ΔG energies, were used to calculate the relative association constants.

For the calculations on the relative stability of *anti* and *gauche* conformations of the guests, ωB97XD[5] functional and 6-31G(d,p)[6] basis set were used for optimizing the geometries, and the single-point energy of the optimized structures was used for comparison. The calculations were performed in the gas phase to prevent contribution from cavitation energy, since implicit solvation models would employ very different cavities for each conformation.

Comparison of the relative energy of host geometries was done using the single point ωB97XD/6-31G(d,p) energy in the gas phase after deleting, from the optimized complex structure, the atoms corresponding to the guest.

Cartesian coordinates for complex structures found

Ephedrine complexes

(4a*S*,9b*R*)-*anti*

O	-1.53912	-0.76643	0.03292
O	-0.80429	-1.21279	3.50680
N	0.37623	-0.31155	1.75490
C	-4.10288	1.15012	-1.77875
H	-4.25323	1.67729	-2.71389
C	-5.11688	1.07603	-0.83310
C	-4.90856	0.40131	0.37344
H	-5.69242	0.35794	1.12322
C	-3.68669	-0.20387	0.60717
C	-3.15462	-0.90140	1.83116
H	-3.00414	-0.15183	2.61467
C	-4.04775	-2.00294	2.40081
H	-5.08518	-1.66199	2.44588
C	-3.99604	-3.32298	1.64708
C	-2.71961	-3.72178	1.12196
H	-2.61121	-4.74917	0.78483
C	-1.61043	-2.90577	1.07333
C	-1.76643	-1.39445	1.34114
C	-2.68165	-0.14335	-0.34818
C	-2.86498	0.53994	-1.54676
C	-0.67447	-0.96276	2.31914
H	0.33802	-0.20289	0.74687
H	-3.72862	-2.21374	3.42767
C	1.45314	0.31371	2.38659
C	1.60357	0.39686	3.77163
C	3.34412	1.59454	1.99366
C	2.67762	1.13443	4.24747

H	0.89629	-0.08752	4.42834
C	3.55390	1.75103	3.36085
H	2.82495	1.23579	5.31785
H	4.39116	2.34007	3.71714
C	4.26608	2.19444	0.97338
H	4.96065	1.43600	0.59688
H	3.69909	2.57895	0.12131
H	4.85317	3.00779	1.40507
N	2.30718	0.88333	1.52664
O	-0.43379	-3.26285	0.74318
O	-5.00345	-4.03256	1.59969
H	-6.07019	1.55268	-1.03144
H	2.09156	0.31668	-0.15597
O	1.79913	-0.23003	-0.92926
C	2.34933	-1.52374	-0.74708
H	1.99147	-1.94383	0.20488
C	1.82443	-2.43722	-1.86600
H	2.27413	-3.42305	-1.71610
H	0.12243	-2.76166	-0.64050
C	2.11956	-1.92390	-3.26784
H	3.19761	-1.81780	-3.40304
H	1.76008	-2.62111	-4.02768
H	1.65049	-0.95120	-3.43600
C	3.86566	-1.50500	-0.71469
C	4.55097	-2.48985	-0.00125
C	4.59061	-0.53008	-1.40110
C	5.94234	-2.50538	0.02154
H	3.98990	-3.24371	0.54546
C	5.98343	-0.54332	-1.37721
H	4.06024	0.24331	-1.94719
C	6.66200	-1.53064	-0.66680
H	6.46464	-3.27392	0.58281
H	6.53811	0.22059	-1.91350
H	7.74738	-1.53885	-0.64592
N	0.35515	-2.61503	-1.66888
S	-1.59403	0.64997	-2.78198
O	-1.12399	-0.71760	-3.04831
O	-2.15718	1.40290	-3.89086
N	-0.28340	1.41562	-2.18132
H	0.37240	0.74302	-1.77300
C	-0.21361	2.78301	-1.57726
H	-0.13729	-1.76146	-1.97155
C	1.21626	3.24100	-1.89410
H	1.94685	2.53077	-1.49195
H	1.36203	3.30441	-2.97611
H	1.41883	4.22040	-1.45797
C	-0.42785	2.61590	-0.04718
H	-1.24318	1.90061	0.09160
H	0.47807	2.12172	0.32265
C	-1.20708	3.71776	-2.26277
H	-1.02489	4.73994	-1.92521
H	-1.07228	3.68900	-3.34598

H	-2.24602	3.46570	-2.03719
C	-0.72938	3.78847	0.92270
C	-0.58999	3.19775	2.33814
H	0.44481	2.90280	2.54172
H	-0.88280	3.93281	3.09568
H	-1.22633	2.31392	2.46415
C	-2.16853	4.30581	0.77148
H	-2.88959	3.48132	0.81796
H	-2.40573	5.00262	1.58339
H	-2.32753	4.83784	-0.16855
C	0.25858	4.95480	0.79767
H	0.08123	5.68551	1.59512
H	1.29444	4.60817	0.88939
H	0.15505	5.48255	-0.15531
C	-0.25377	-3.75579	-2.38659
H	-1.31372	-3.78385	-2.13411
H	-0.13991	-3.63302	-3.46269
H	0.22673	-4.67706	-2.05673

(4a*S*,9b*R*)-*gauche*

O	-0.82324	-1.38052	0.38212
O	1.17329	-3.32780	-1.84411
N	1.65144	-2.04958	0.00782
C	-3.70864	-1.73621	2.60671
H	-4.20485	-1.23143	3.42817
C	-4.22561	-2.91257	2.07752
C	-3.60478	-3.54135	0.99062
H	-4.02525	-4.44946	0.56975
C	-2.45561	-2.98629	0.45685
C	-1.54158	-3.42162	-0.66420
H	-0.92780	-4.25533	-0.30485
C	-2.23160	-3.85324	-1.95422
H	-3.01863	-4.58029	-1.73859
C	-2.82840	-2.70792	-2.75824
C	-2.10314	-1.46924	-2.76696
H	-2.41275	-0.71409	-3.48446
C	-1.00066	-1.19857	-1.98071
C	-0.63577	-2.16654	-0.82824
C	-1.93881	-1.82158	1.00502
C	-2.55295	-1.16866	2.06218
C	0.83135	-2.57422	-0.94749
H	1.22039	-1.36646	0.61890
H	-1.49427	-4.34850	-2.59601
C	3.03895	-2.17630	0.12366
C	3.77979	-3.13448	-0.57205
C	4.92665	-1.28115	1.11205
C	5.15474	-3.12694	-0.39448
H	3.28638	-3.83519	-1.22931
C	5.74360	-2.19439	0.45318
H	5.76758	-3.85065	-0.92216
H	6.81707	-2.16966	0.60201
C	5.48526	-0.24347	2.04267

H	5.16168	0.75709	1.73660
H	5.12818	-0.41366	3.06333
H	6.57667	-0.26504	2.05263
N	3.59484	-1.27555	0.94221
O	-0.27409	-0.15967	-2.07371
O	-3.84601	-2.90525	-3.42741
H	-5.12635	-3.33911	2.50468
H	0.36765	0.57952	-0.86377
O	0.66609	0.92712	0.03498
C	1.46423	2.08177	0.02575
H	0.87272	2.96953	-0.24371
C	1.84568	2.29263	1.52011
H	0.95174	2.68278	2.01705
H	1.13028	0.48027	2.11163
C	2.62204	2.00664	-0.95745
C	3.03868	0.79293	-1.49924
C	3.26325	3.17981	-1.36997
C	4.10721	0.73964	-2.39149
H	2.49882	-0.10981	-1.25076
C	4.33310	3.13091	-2.25658
H	2.91563	4.14140	-1.00280
C	4.76767	1.90637	-2.76207
H	4.41467	-0.21810	-2.80023
H	4.82067	4.05119	-2.56319
H	5.59882	1.86764	-3.45934
N	2.04934	0.94439	2.15167
S	-1.93470	0.40014	2.61965
O	-2.89773	0.92046	3.58096
O	-0.54629	0.17931	3.05440
N	-1.81142	1.40261	1.34332
H	-0.95856	1.17196	0.81434
H	2.69258	0.33193	1.60520
C	3.01311	3.22473	1.77625
H	3.95055	2.81988	1.38546
H	2.82295	4.18104	1.28465
H	3.12886	3.42769	2.84280
C	2.46536	0.94689	3.57106
H	1.76392	1.55147	4.14604
H	2.43944	-0.08289	3.92655
H	3.47446	1.34313	3.66495
C	-2.92485	1.99478	0.52808
C	-3.98284	0.94161	0.18252
C	-2.14724	2.47320	-0.72675
C	-3.55584	3.13069	1.33234
H	-3.55234	0.11625	-0.39323
H	-4.44285	0.53623	1.08797
H	-4.78469	1.38666	-0.40622
H	-1.25133	2.98479	-0.35299
H	-1.79309	1.56339	-1.22679
C	-2.72948	3.40431	-1.82130
H	-4.38948	3.57044	0.77896
H	-3.94345	2.75235	2.28127

H	-2.82053	3.91161	1.54706
C	-1.70888	3.35048	-2.97437
C	-2.82923	4.86466	-1.35345
C	-4.09001	2.95027	-2.36240
H	-1.61896	2.33750	-3.38079
H	-2.00816	4.01987	-3.78848
H	-0.71269	3.65985	-2.63541
H	-1.87268	5.21687	-0.94986
H	-3.09207	5.51262	-2.19763
H	-3.59184	5.00789	-0.58475
H	-4.35674	3.54068	-3.24657
H	-4.07322	1.89587	-2.65802
H	-4.88818	3.09015	-1.62689

(4a*R*,9b*S*)-*anti*

O	-0.48867	-1.43434	-0.43486
O	1.21927	-3.69033	1.70496
N	1.92595	-2.06857	0.23276
C	-3.28116	-1.43317	-2.80149
H	-3.65839	-0.88723	-3.65897
C	-3.98573	-2.50891	-2.27539
C	-3.48411	-3.22846	-1.18216
H	-4.02836	-4.08235	-0.79100
C	-2.28520	-2.84071	-0.61361
C	-1.41655	-3.44760	0.46535
H	-0.84752	-4.26296	0.00305
C	-2.11299	-4.00328	1.70181
H	-2.97130	-4.61554	1.41245
C	-2.57630	-2.96337	2.70881
C	-1.81564	-1.75205	2.81078
H	-2.07416	-1.06788	3.61423
C	-0.81565	-1.36691	1.94268
C	-0.44233	-2.27647	0.74822
C	-1.61010	-1.73789	-1.12165
C	-2.07017	-1.03457	-2.22467
C	0.99230	-2.76264	0.94541
H	1.56977	-1.29970	-0.32549
H	-1.41100	-4.65891	2.22856
C	3.30915	-2.25484	0.20841
C	3.95294	-3.31075	0.86110
C	5.30842	-1.40227	-0.58903
C	5.33254	-3.38027	0.75615
H	3.37960	-4.03017	1.42620
C	6.02742	-2.41896	0.02901
H	5.86632	-4.18697	1.24811
H	7.10713	-2.45309	-0.06010
C	5.98610	-0.32735	-1.39035
H	5.66319	0.66360	-1.05478
H	5.73394	-0.42312	-2.45154
H	7.07157	-0.38788	-1.29161
N	3.96926	-1.33155	-0.50176

O	-0.15219	-0.28690	2.03132
O	-3.53597	-3.22316	3.44022
H	-4.92699	-2.80134	-2.72709
H	0.57313	0.40004	0.86707
O	0.96019	0.91948	0.08916
C	2.17687	1.54266	0.40544
H	2.89059	0.78829	0.77203
C	2.73716	2.08339	-0.92728
H	3.78995	2.34399	-0.78897
H	1.73721	0.63149	-2.02699
C	2.05858	2.62082	1.47123
C	3.17622	3.37788	1.83713
C	0.84603	2.85038	2.11931
C	3.07291	4.36165	2.81534
H	4.13607	3.19920	1.35918
C	0.74302	3.83276	3.10203
H	-0.01807	2.24398	1.87353
C	1.85347	4.59529	3.44943
H	3.94805	4.94447	3.08645
H	-0.20947	3.99318	3.59835
H	1.77493	5.36153	4.21429
N	2.71847	0.92728	-1.88166
S	-1.17127	0.36479	-2.84179
O	-1.85620	0.80608	-4.04758
O	0.24011	-0.03675	-2.95075
N	-1.16305	1.55593	-1.72078
H	-0.42050	1.36055	-1.03386
C	-2.34736	2.23062	-1.09878
H	3.19136	0.11228	-1.42165
C	-2.90650	1.28033	-0.00370
H	-3.42970	0.47898	-0.53768
H	-2.04449	0.80657	0.48347
C	-3.38474	2.55869	-2.17464
H	-4.13720	3.23300	-1.76397
H	-3.89663	1.66446	-2.53936
H	-2.91149	3.05426	-3.02572
C	-1.75773	3.53690	-0.55750
H	-1.32641	4.11317	-1.38137
H	-0.97126	3.34789	0.17752
H	-2.53074	4.14570	-0.08483
C	-3.84249	1.75331	1.14223
C	-4.49900	0.47760	1.69952
H	-5.08832	0.70103	2.59612
H	-3.74609	-0.26946	1.96914
H	-5.16981	0.02626	0.95907
C	-3.03628	2.40535	2.27833
H	-2.55279	3.33503	1.96718
H	-2.25906	1.72093	2.63807
H	-3.69186	2.64304	3.12408
C	-4.96457	2.69582	0.68874
H	-5.53386	2.26427	-0.14149
H	-4.59013	3.67458	0.37424

H	-5.66390	2.86720	1.51515
C	1.97262	3.26300	-1.50886
H	2.49069	3.68166	-2.37473
H	1.89497	4.05243	-0.75886
H	0.96325	2.97363	-1.81294
C	3.32471	1.16712	-3.20954
H	2.68399	1.82905	-3.79012
H	3.41112	0.20808	-3.72000
H	4.31135	1.61316	-3.08232

(4a*R*,9b*S*)-*gauche*

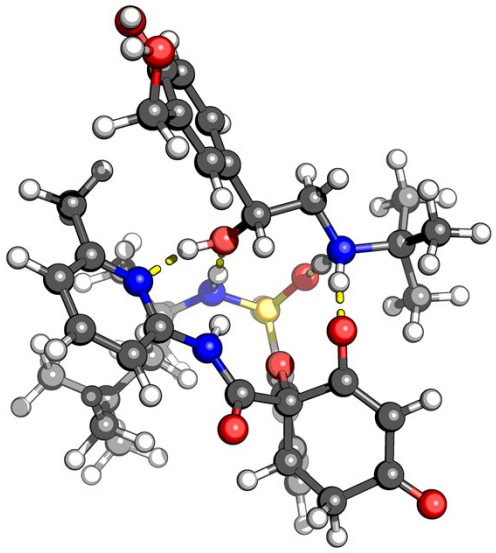
O	1.27863	-0.93672	0.07676
O	-0.23771	-1.33598	3.29343
N	-0.79183	-0.12529	1.42100
C	4.47238	0.56218	-0.96236
H	4.91301	1.11773	-1.78218
C	5.23116	0.21021	0.14619
C	4.65080	-0.50010	1.20092
H	5.23710	-0.76304	2.07605
C	3.31723	-0.86062	1.12077
C	2.42547	-1.54594	2.12347
H	2.27426	-0.87148	2.97178
C	2.96069	-2.87175	2.66714
H	4.02126	-2.77601	2.91289
C	2.77441	-4.06478	1.74237
C	1.54707	-4.11963	0.99896
H	1.28453	-5.06421	0.52990
C	0.64841	-3.07783	0.90277
C	1.08861	-1.66270	1.34146
C	2.56775	-0.52290	0.00271
C	3.12253	0.20331	-1.04778
C	-0.05586	-1.02007	2.12835
H	-0.52984	-0.01543	0.44747
H	2.42978	-3.10865	3.59607
C	-1.91197	0.60294	1.82024
C	-2.45992	0.55967	3.10266
C	-3.49702	2.11858	1.07403
C	-3.58017	1.34370	3.33729
H	-2.02200	-0.07004	3.86307
C	-4.11072	2.13496	2.32282
H	-4.04308	1.33454	4.31881
H	-4.98716	2.75008	2.49102
C	-3.98270	2.94614	-0.07940
H	-4.04823	2.33529	-0.98484
H	-3.27929	3.76167	-0.27983
H	-4.96308	3.38120	0.12456
N	-2.41713	1.36031	0.83920
O	-0.51234	-3.14408	0.38822
O	3.61284	-4.96924	1.74247
H	6.27662	0.49356	0.19241
H	-1.91813	0.81590	-0.79804

O	-1.47308	0.28194	-1.50326
C	-2.43987	-0.51113	-2.18001
H	-2.88972	0.07814	-2.98963
C	-1.69520	-1.65950	-2.90182
H	-1.21317	-1.22386	-3.78245
H	-0.79441	-2.46722	-1.10028
C	-2.62884	-2.77860	-3.33107
H	-2.14174	-3.45591	-4.03551
H	-3.50043	-2.34794	-3.83112
H	-2.98147	-3.35226	-2.46966
C	-3.57069	-0.92216	-1.25245
C	-4.87201	-0.52009	-1.55903
C	-3.34460	-1.64001	-0.07397
C	-5.93161	-0.81970	-0.70488
H	-5.05900	0.03892	-2.47251
C	-4.40098	-1.93663	0.78052
H	-2.34309	-1.95500	0.20399
C	-5.69606	-1.52449	0.47121
H	-6.93676	-0.49518	-0.95579
H	-4.20758	-2.48437	1.69769
H	-6.51608	-1.75346	1.14478
N	-0.55590	-2.16356	-2.07744
S	2.18278	0.68142	-2.47949
O	1.47286	-0.51223	-2.95873
O	3.12005	1.33236	-3.38204
N	0.98971	1.70880	-2.05754
H	0.11091	1.19826	-1.92202
C	0.21242	-3.27919	-2.67664
H	1.13258	-3.39382	-2.10403
H	-0.36923	-4.19767	-2.61685
H	0.45001	-3.04367	-3.71409
H	0.10299	-1.38245	-1.96969
C	1.09468	2.99445	-1.30604
C	-0.09430	3.81332	-1.82651
C	0.92974	2.65204	0.20038
C	2.39604	3.71001	-1.66026
H	-1.03767	3.28816	-1.63989
H	0.00320	3.97352	-2.90401
H	-0.14598	4.78630	-1.33549
H	1.53536	1.76396	0.40088
H	-0.11483	2.33855	0.31396
C	1.23835	3.63969	1.35580
H	2.37974	4.71318	-1.22974
H	2.49723	3.80448	-2.74366
H	3.27751	3.19148	-1.27537
C	0.66602	2.98255	2.62543
C	2.74964	3.82297	1.56847
C	0.57069	5.00999	1.18801
H	-0.42339	2.88680	2.56485
H	0.90184	3.58068	3.51255
H	1.08505	1.98074	2.77680
H	3.25334	2.85324	1.65609

H	2.93410	4.37771	2.49548
H	3.22575	4.37744	0.75717
H	0.70654	5.60588	2.09762
H	-0.50651	4.90856	1.01419
H	1.00116	5.57929	0.35863

Albuterol complexes.

(4a*S*,9b*R*)-*anti*

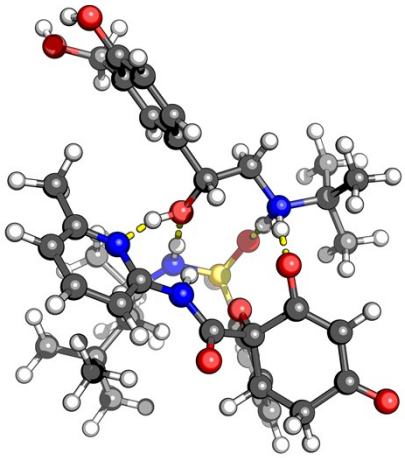


O	-1.81135	-0.51268	0.35750
O	-0.74302	0.08905	3.72007
N	0.19739	0.51394	1.66803
C	-4.73668	0.51304	-1.62353
H	-5.02006	0.75441	-2.64137
C	-5.67032	0.55846	-0.59769
C	-5.28618	0.28123	0.71779
H	-6.00616	0.34951	1.52747
C	-3.97337	-0.06695	0.97780
C	-3.24955	-0.26912	2.28363
H	-3.12200	0.71511	2.74798
C	-3.92945	-1.18165	3.30153
H	-4.99112	-0.93543	3.38325
C	-3.79103	-2.66933	3.02325
C	-2.55184	-3.11364	2.44847
H	-2.36139	-4.18345	2.43246
C	-1.57658	-2.27697	1.95033
C	-1.86311	-0.76742	1.80227
C	-3.05166	-0.15700	-0.05835
C	-3.40590	0.16009	-1.36733
C	-0.73932	-0.00379	2.50248
H	0.05965	0.32764	0.67909
H	-3.47710	-1.00319	4.28352
C	1.33174	1.26396	1.98149
C	1.69083	1.64403	3.27655

C	3.15618	2.34055	1.04012
C	2.84238	2.40519	3.41322
H	1.08607	1.34736	4.12089
C	3.58849	2.76298	2.29364
H	3.15797	2.72263	4.40204
H	4.49032	3.35724	2.38668
C	3.90019	2.66065	-0.22228
H	4.30076	1.74428	-0.66849
H	3.22727	3.11577	-0.95555
H	4.72913	3.34546	-0.03298
N	2.04306	1.60591	0.90115
O	-0.43273	-2.63720	1.52454
O	-4.68897	-3.43713	3.37640
H	-6.69742	0.82555	-0.81909
H	1.59936	0.64119	-0.56685
O	1.22940	-0.12285	-1.07247
C	1.94496	-1.26693	-0.60988
H	1.72326	-1.43075	0.45402
C	1.44935	-2.48235	-1.37875
H	2.02358	-3.35448	-1.06589
H	-0.16408	-2.62423	-0.05802
C	3.43427	-1.06324	-0.76944
C	4.26894	-1.07714	0.34598
C	3.99209	-0.78406	-2.01966
C	5.63277	-0.81457	0.24565
H	3.84378	-1.27318	1.32782
C	5.35332	-0.54879	-2.15124
H	3.35590	-0.74283	-2.89919
C	6.17944	-0.55958	-1.02400
H	5.79740	-0.34539	-3.12020
N	0.01338	-2.73081	-1.09810
S	-2.24296	0.17259	-2.71326
O	-1.58987	-1.14376	-2.76674
O	-2.98261	0.60657	-3.88786
N	-1.02249	1.20113	-2.38868
H	-0.25166	0.69409	-1.94451
C	-1.09302	2.66104	-2.07513
H	-0.54073	-1.99903	-1.56805
C	0.22997	3.21290	-2.62190
H	1.08354	2.72034	-2.14258
H	0.29468	3.03930	-3.69966
H	0.31283	4.28533	-2.43771
C	-1.16396	2.78909	-0.52902
H	-1.86940	2.03403	-0.17395
H	-0.17713	2.47975	-0.16515
C	-2.25906	3.30737	-2.81913
H	-2.19834	4.39086	-2.69969
H	-2.20734	3.07821	-3.88561
H	-3.23022	2.97776	-2.44127
C	-1.53610	4.09198	0.22496
C	-1.21732	3.81325	1.70558
H	-0.14443	3.65120	1.85523

H	-1.51888	4.65837	2.33421
H	-1.74578	2.92251	2.06584
C	-3.03725	4.40804	0.12485
H	-3.64163	3.52952	0.37935
H	-3.30084	5.20701	0.82708
H	-3.33277	4.74210	-0.87183
C	-0.71774	5.31140	-0.21612
H	-0.93223	6.16442	0.43782
H	0.35791	5.10971	-0.15729
H	-0.95422	5.61873	-1.23938
C	-0.55862	-4.07336	-1.51474
H	1.57638	-2.33631	-2.45298
C	-2.06199	-3.99387	-1.23777
H	-2.52928	-3.19959	-1.82571
H	-2.52766	-4.94384	-1.51198
H	-2.26130	-3.81151	-0.17793
C	-0.29544	-4.29501	-3.00194
H	-0.68678	-3.46492	-3.59762
H	0.77048	-4.41544	-3.21449
H	-0.80241	-5.21045	-3.31828
C	0.07795	-5.16316	-0.65391
H	1.13858	-5.30706	-0.87833
H	-0.03251	-4.92210	0.40741
H	-0.42977	-6.11136	-0.84934
O	7.49577	-0.30260	-1.19537
H	7.95408	-0.59475	-0.38382
C	6.48909	-0.70464	1.47994
H	6.65346	0.35637	1.71576
H	5.97993	-1.16284	2.33570
O	7.74494	-1.34693	1.24037
H	8.35491	-1.08227	1.93867

(4a*S*,9b*R*)-*anti; alternative 2-hydroxymethyl-phenol group orientation.*



This structure has a 0.2 kcal/mol higher energy than (4a*S*,9b*R*)-*anti, and contributes to the calculated association constant in a significant extent.*

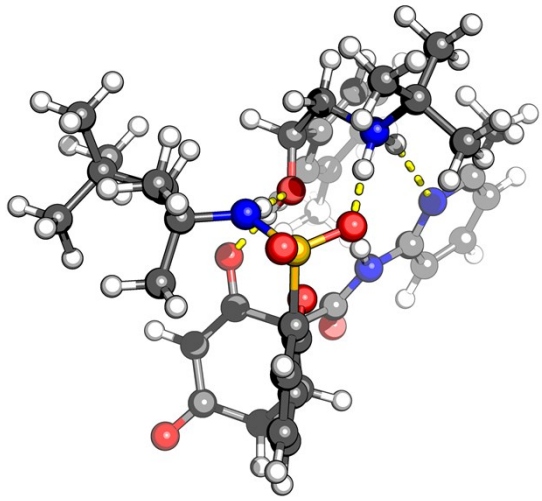
O	-1.81135	-0.51268	0.35750
O	-0.74302	0.08905	3.72007

N	0.19739	0.51394	1.66803
C	-4.73668	0.51304	-1.62353
H	-5.02006	0.75441	-2.64137
C	-5.67032	0.55846	-0.59769
C	-5.28618	0.28123	0.71779
H	-6.00616	0.34951	1.52747
C	-3.97337	-0.06695	0.97780
C	-3.24955	-0.26912	2.28363
H	-3.12200	0.71511	2.74798
C	-3.92945	-1.18165	3.30153
H	-4.99112	-0.93543	3.38325
C	-3.79103	-2.66933	3.02325
C	-2.55184	-3.11364	2.44847
H	-2.36139	-4.18345	2.43246
C	-1.57658	-2.27697	1.95033
C	-1.86311	-0.76742	1.80227
C	-3.05166	-0.15700	-0.05835
C	-3.40590	0.16009	-1.36733
C	-0.73932	-0.00379	2.50248
H	0.05965	0.32764	0.67909
H	-3.47710	-1.00319	4.28352
C	1.33174	1.26396	1.98149
C	1.69083	1.64403	3.27655
C	3.15618	2.34055	1.04012
C	2.84238	2.40519	3.41322
H	1.08607	1.34736	4.12089
C	3.58849	2.76298	2.29364
H	3.15797	2.72263	4.40204
H	4.49032	3.35724	2.38668
C	3.90019	2.66065	-0.22228
H	4.30076	1.74428	-0.66849
H	3.22727	3.11577	-0.95555
H	4.72913	3.34546	-0.03298
N	2.04306	1.60591	0.90115
O	-0.43273	-2.63720	1.52454
O	-4.68897	-3.43713	3.37640
H	-6.69742	0.82555	-0.81909
H	1.59936	0.64119	-0.56685
O	1.22940	-0.12285	-1.07247
C	1.94496	-1.26693	-0.60988
H	1.72326	-1.43075	0.45402
C	1.44935	-2.48235	-1.37875
H	2.02358	-3.35448	-1.06589
H	-0.16408	-2.62423	-0.05802
C	3.43427	-1.06324	-0.76944
C	4.26894	-1.07714	0.34598
C	3.99209	-0.78406	-2.01966
C	5.63277	-0.81457	0.24565
H	3.84378	-1.27318	1.32782
C	5.35332	-0.54879	-2.15124
H	3.35590	-0.74283	-2.89919
C	6.17944	-0.55958	-1.02400

H	5.79740	-0.34539	-3.12020
N	0.01338	-2.73081	-1.09810
S	-2.24296	0.17259	-2.71326
O	-1.58987	-1.14376	-2.76674
O	-2.98261	0.60657	-3.88786
N	-1.02249	1.20113	-2.38868
H	-0.25166	0.69409	-1.94451
C	-1.09302	2.66104	-2.07513
H	-0.54073	-1.99903	-1.56805
C	0.22997	3.21290	-2.62190
H	1.08354	2.72034	-2.14258
H	0.29468	3.03930	-3.69966
H	0.31283	4.28533	-2.43771
C	-1.16396	2.78909	-0.52902
H	-1.86940	2.03403	-0.17395
H	-0.17713	2.47975	-0.16515
C	-2.25906	3.30737	-2.81913
H	-2.19834	4.39086	-2.69969
H	-2.20734	3.07821	-3.88561
H	-3.23022	2.97776	-2.44127
C	-1.53610	4.09198	0.22496
C	-1.21732	3.81325	1.70558
H	-0.14443	3.65120	1.85523
H	-1.51888	4.65837	2.33421
H	-1.74578	2.92251	2.06584
C	-3.03725	4.40804	0.12485
H	-3.64163	3.52952	0.37935
H	-3.30084	5.20701	0.82708
H	-3.33277	4.74210	-0.87183
C	-0.71774	5.31140	-0.21612
H	-0.93223	6.16442	0.43782
H	0.35791	5.10971	-0.15729
H	-0.95422	5.61873	-1.23938
C	-0.55862	-4.07336	-1.51474
H	1.57638	-2.33631	-2.45298
C	-2.06199	-3.99387	-1.23777
H	-2.52928	-3.19959	-1.82571
H	-2.52766	-4.94384	-1.51198
H	-2.26130	-3.81151	-0.17793
C	-0.29544	-4.29501	-3.00194
H	-0.68678	-3.46492	-3.59762
H	0.77048	-4.41544	-3.21449
H	-0.80241	-5.21045	-3.31828
C	0.07795	-5.16316	-0.65391
H	1.13858	-5.30706	-0.87833
H	-0.03251	-4.92210	0.40741
H	-0.42977	-6.11136	-0.84934
O	7.49577	-0.30260	-1.19537
H	7.95408	-0.59475	-0.38382
C	6.48909	-0.70464	1.47994
H	6.65346	0.35637	1.71576
H	5.97993	-1.16284	2.33570

O	7.74494	-1.34693	1.24037
H	8.35491	-1.08227	1.93867

(4a*S*,9b*R*)-*gauche*



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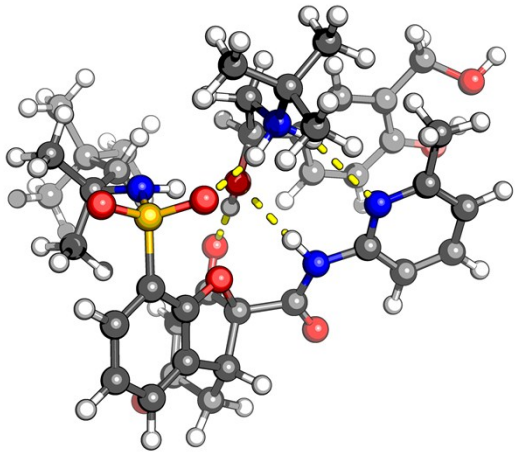
C	4.18957	0.02518	-2.97113
H	4.82821	0.87419	-3.18866
C	4.50373	-1.24396	-3.44201
C	3.69089	-2.34437	-3.13689
H	3.94929	-3.33405	-3.50063
C	2.55974	-2.15245	-2.36501
C	1.46456	-3.08525	-1.90212
H	0.78256	-3.25715	-2.74290
C	1.92170	-4.43626	-1.36382
H	2.60484	-4.91524	-2.06993
C	2.59451	-4.36890	-0.00142
C	2.09482	-3.39493	0.92861
H	2.44758	-3.45412	1.95491
C	1.15965	-2.42904	0.62372
C	0.74130	-2.19959	-0.84630
C	2.25438	-0.87980	-1.90484
C	3.05043	0.21872	-2.18382
C	-0.77574	-2.32878	-0.97850
H	-0.90919	-0.31765	-1.17739
H	1.04584	-5.08661	-1.26097
C	-2.80967	-1.01017	-1.49777
C	-3.68572	-2.09148	-1.64483
C	-4.50504	0.52404	-1.75660
C	-5.02661	-1.80950	-1.84438
H	-3.31277	-3.10301	-1.59022
C	-5.45078	-0.48778	-1.89826
H	-5.73917	-2.62073	-1.95479
H	-6.49532	-0.23897	-2.04643
C	-4.91901	1.96542	-1.78868

H	-4.74528	2.42074	-0.80896
H	-4.34401	2.52459	-2.53165
H	-5.98014	2.06847	-2.02512
N	-3.20083	0.26808	-1.55917
O	0.63509	-1.63330	1.47014
O	3.47322	-5.18725	0.28026
H	5.39522	-1.38372	-4.04319
H	0.10198	-0.24061	1.02967
O	-0.14897	0.66606	0.66735
C	-0.97902	1.41877	1.52334
H	-0.53059	1.48788	2.52556
C	-0.93502	2.82573	0.93866
H	0.06781	3.23163	1.07421
H	-0.36389	2.31059	-0.96196
C	-2.36954	0.80428	1.64500
C	-3.54995	1.54675	1.62769
C	-2.47160	-0.58266	1.78754
C	-4.79096	0.92334	1.71959
H	-3.52887	2.62879	1.53515
C	-3.69750	-1.23048	1.85819
H	-1.57051	-1.19053	1.81621
C	-4.87631	-0.46361	1.81523
H	-5.70810	1.50310	1.70006
N	-1.18239	2.77659	-0.53380
S	2.64847	1.80104	-1.48699
O	3.75559	2.69615	-1.79555
O	1.30127	2.13916	-1.97673
N	2.46466	1.66067	0.12431
H	1.54574	1.24056	0.32543
H	-1.98518	2.15859	-0.74497
C	-1.36202	4.10954	-1.24959
C	3.52997	1.37618	1.14212
C	4.44138	0.23330	0.68220
C	2.66912	0.97776	2.36954
C	4.34674	2.65006	1.35424
H	3.87508	-0.68834	0.51468
H	4.96363	0.49630	-0.24211
H	5.20742	0.03110	1.43044
H	1.86494	1.72314	2.43885
H	2.18534	0.03067	2.10241
C	3.21907	0.81807	3.81087
H	5.15283	2.46733	2.06946
H	4.79734	2.97569	0.41387
H	3.71530	3.45943	1.73245
C	2.08180	0.13324	4.59294
C	3.50620	2.16959	4.48349
C	4.46532	-0.07007	3.90575
H	1.84886	-0.84928	4.16879
H	2.35749	-0.00371	5.64439
H	1.16420	0.73350	4.56345
H	2.64230	2.84026	4.40942
H	3.71991	2.02039	5.54810

H	4.36754	2.68043	4.04702
H	4.68836	-0.28495	4.95718
H	4.31708	-1.02704	3.39409
H	5.34803	0.41745	3.48080
O	-6.10209	-1.03452	1.85766
H	-5.98165	-1.94602	2.18788
C	-3.76356	-2.73476	1.88414
H	-3.99531	-3.10773	0.87745
H	-2.79305	-3.15062	2.17777
O	-4.78529	-3.14391	2.79980
H	-4.95291	-4.08259	2.65802
C	-1.44355	3.76845	-2.73733
H	-1.65894	4.67685	-3.30490
H	-0.49869	3.35212	-3.09566
H	-2.23900	3.04373	-2.93462
C	-0.14781	4.98997	-0.96048
H	0.78289	4.47362	-1.20866
H	-0.21585	5.88856	-1.57925
H	-0.11421	5.30981	0.08431
C	-2.64640	4.77627	-0.76723
H	-3.51630	4.13848	-0.93302
H	-2.60079	5.04748	0.29071
H	-2.79145	5.69908	-1.33454
H	-1.65186	3.49593	1.40747

(4a*S*,9b*R*)-*gauche; alternative 2-hydroxymethyl-phenol group orientation.*



This structure has a 6.7 kcal/mol higher energy than (4a*S*,9b*R*)-*anti.*

O	-1.42250	1.07817	-0.88391
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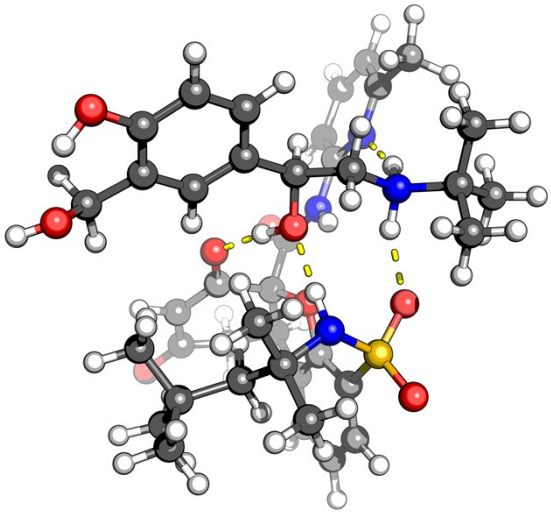
C	-4.31139	0.15189	-2.92920
H	-4.78388	-0.71860	-3.37063
C	-4.87796	1.41397	-3.05735
C	-4.28113	2.53156	-2.45778
H	-4.73810	3.51174	-2.55154

C	-3.10994	2.36708	-1.74141
C	-2.20691	3.33948	-1.01914
H	-1.60095	3.86613	-1.76508
C	-2.90574	4.37600	-0.14632
H	-3.69478	4.88023	-0.71010
C	-3.50388	3.81377	1.13377
C	-2.78866	2.74746	1.77804
H	-3.10647	2.46087	2.77710
C	-1.68865	2.10930	1.24531
C	-1.28710	2.36726	-0.22651
C	-2.54818	1.10322	-1.62808
C	-3.13083	-0.01640	-2.19921
C	0.17051	2.82294	-0.28665
H	0.70369	0.96257	-0.89604
H	-2.17274	5.13592	0.14623
C	2.43786	2.04784	-0.93048
C	3.11024	3.24818	-0.67709
C	4.38477	0.96100	-1.50159
C	4.48421	3.26131	-0.84984
H	2.56323	4.11779	-0.34622
C	5.13814	2.10773	-1.26383
H	5.04178	4.17194	-0.65518
H	6.21347	2.08684	-1.39758
C	5.04445	-0.31393	-1.93666
H	4.92196	-1.07431	-1.16040
H	4.59462	-0.69263	-2.85891
H	6.11353	-0.17122	-2.10168
N	3.05187	0.92984	-1.33546
O	-0.98327	1.24593	1.86306
O	-4.51725	4.33373	1.60723
H	-5.79922	1.53122	-3.61701
H	-0.22726	0.13163	1.10950
O	0.16192	-0.59942	0.53208
C	1.08552	-1.43546	1.19273
H	0.64560	-1.83373	2.11886
C	1.24796	-2.61990	0.24689
H	0.30991	-3.17461	0.21162
H	0.61947	-1.71385	-1.47975
C	2.37432	-0.69567	1.53536
C	2.28831	0.59656	2.06551
C	3.64290	-1.24003	1.34251
C	3.42909	1.33217	2.34471
H	1.31738	1.05491	2.23093
C	4.80537	-0.52684	1.63504
H	3.76326	-2.24301	0.94128
C	4.69292	0.78564	2.11542
H	3.35737	2.34566	2.72544
N	1.50635	-2.12473	-1.13914
S	-2.42935	-1.62049	-1.91422
O	-3.35541	-2.59748	-2.47108
O	-1.05127	-1.57265	-2.43195
N	-2.24884	-1.85883	-0.31293

H	-1.42032	-1.33993	0.01327
H	2.17989	-1.34008	-1.12200
C	1.95108	-3.14915	-2.17314
C	-3.33181	-2.02297	0.71404
C	-4.41599	-0.95269	0.54943
C	-2.52351	-1.83665	2.02530
C	-3.93934	-3.41658	0.55993
H	-3.99930	0.05496	0.64299
H	-4.90880	-1.04115	-0.42270
H	-5.18897	-1.07232	1.30814
H	-1.61609	-2.44640	1.91829
H	-2.19158	-0.79110	2.02706
C	-3.07045	-2.14220	3.44392
H	-4.74954	-3.55623	1.28010
H	-4.35480	-3.54379	-0.44237
H	-3.18503	-4.19249	0.72147
C	-2.03414	-1.53329	4.40783
C	-3.14642	-3.65007	3.73017
C	-4.43125	-1.50054	3.73870
H	-1.94519	-0.45145	4.26166
H	-2.31592	-1.71719	5.45047
H	-1.04233	-1.97372	4.24857
H	-2.19131	-4.14164	3.51176
H	-3.37166	-3.82096	4.78921
H	-3.92383	-4.14912	3.14750
H	-4.66563	-1.60317	4.80443
H	-4.43271	-0.43200	3.49844
H	-5.24023	-1.98338	3.18206
O	5.78045	1.54737	2.37852
H	6.53222	1.15080	1.90063
C	6.16210	-1.15571	1.46640
H	6.58097	-1.40924	2.45036
H	6.07794	-2.08557	0.89061
O	7.02606	-0.22852	0.80218
H	7.93011	-0.55573	0.87550
C	1.98773	-2.39649	-3.50349
H	2.36671	-3.05990	-4.28449
H	0.98730	-2.06171	-3.79051
H	2.64429	-1.52314	-3.44523
C	0.92539	-4.27960	-2.21795
H	-0.08180	-3.89009	-2.38633
H	1.17977	-4.94440	-3.04729
H	0.93195	-4.87472	-1.30085
C	3.33322	-3.67704	-1.80179
H	4.06704	-2.87104	-1.74370
H	3.32885	-4.22333	-0.85488
H	3.65865	-4.37357	-2.57870
H	2.04377	-3.29589	0.55045

(4a*R*,9b*S*)-*anti*



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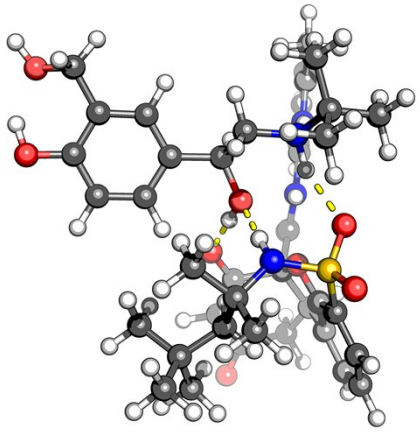
H	-3.25667	-2.68300	3.48225
C	-3.91859	-3.58039	1.63426
C	-3.64997	-3.77888	0.27264
H	-4.31123	-4.39080	-0.33308
C	-2.53003	-3.19166	-0.28682
C	-1.89368	-3.28424	-1.65536
H	-1.32493	-4.22077	-1.69191
C	-2.82908	-3.25075	-2.85821
H	-3.65849	-3.94807	-2.71356
C	-3.39557	-1.88007	-3.18940
C	-2.57238	-0.73988	-2.90602
H	-2.91647	0.22507	-3.26810
C	-1.38715	-0.77397	-2.20171
C	-0.88919	-2.10582	-1.58944
C	-1.70331	-2.40482	0.50382
C	-1.93138	-2.22644	1.85878
C	0.45663	-2.45315	-2.22177
H	1.37260	-1.56872	-0.63337
H	-2.27280	-3.58704	-3.74002
C	2.89432	-2.16454	-1.86994
C	3.31794	-2.81395	-3.03491
C	5.04964	-1.55504	-1.31424
C	4.67396	-2.80784	-3.31588
H	2.59807	-3.28530	-3.68630
C	5.55739	-2.16642	-2.45567
H	5.03935	-3.29683	-4.21322
H	6.62122	-2.13468	-2.66144
C	5.95221	-0.84462	-0.34867
H	5.54942	0.14468	-0.11162
H	6.03825	-1.41052	0.58480
H	6.95510	-0.72062	-0.76228
N	3.73831	-1.56439	-1.01961

O	-0.64425	0.23368	-1.98297
O	-4.49451	-1.79993	-3.74531
H	-4.79681	-4.03258	2.08137
H	0.35078	0.38072	-0.81061
O	0.87795	0.49876	0.04156
C	2.03565	1.28747	-0.08583
H	2.71029	0.82430	-0.82158
C	2.71089	1.22337	1.28413
H	3.69215	1.69168	1.26099
H	1.95760	-0.63646	1.77686
C	1.76870	2.72782	-0.50644
C	0.56655	3.07851	-1.12431
C	2.73595	3.72321	-0.33854
C	0.31578	4.38062	-1.54867
H	-0.19139	2.32329	-1.31031
C	2.49218	5.03609	-0.72302
H	3.70020	3.49172	0.10392
C	1.27796	5.37589	-1.31616
H	3.23714	5.80962	-0.56755
N	2.89147	-0.19740	1.69020
S	-0.81411	-1.24193	2.81784
O	-1.25280	-1.32310	4.20356
O	0.53922	-1.71642	2.48345
N	-0.82320	0.31102	2.30731
H	-0.22985	0.39225	1.46752
C	-1.99979	1.23730	2.25497
H	3.35008	-0.70044	0.90592
C	-2.90316	0.78951	1.07382
H	-3.41335	-0.11981	1.40935
H	-2.23293	0.48203	0.26118
C	-2.73114	1.21831	3.59868
H	-3.45204	2.03583	3.63780
H	-3.27110	0.28154	3.75783
H	-2.02070	1.34660	4.41956
C	-1.34760	2.60774	2.05039
H	-0.64789	2.81002	2.86720
H	-0.79754	2.65017	1.10651
H	-2.10168	3.39714	2.04524
C	-3.97907	1.69878	0.42116
C	-4.89283	0.75133	-0.37751
H	-5.61667	1.31752	-0.97439
H	-4.30952	0.12465	-1.06054
H	-5.45348	0.08862	0.29182
C	-3.33920	2.68046	-0.57321
H	-2.70667	3.42573	-0.08423
H	-2.72379	2.13362	-1.29711
H	-4.11337	3.22235	-1.12914
C	-4.85091	2.46288	1.42445
H	-5.29803	1.78550	2.16027
H	-4.29115	3.23289	1.96415
H	-5.67033	2.96610	0.89814
O	1.06705	6.66470	-1.67465

H	0.10487	6.77648	-1.79151
C	-0.93083	4.72490	-2.31610
H	-0.67298	4.92146	-3.36659
H	-1.63558	3.88826	-2.29635
O	-1.51621	5.89687	-1.73660
H	-2.21459	6.20251	-2.32720
H	2.08713	1.71559	2.03243
C	3.62846	-0.46861	2.99784
C	4.95212	0.29142	3.03076
H	4.80426	1.36862	3.14290
H	5.52015	-0.05311	3.89870
H	5.55441	0.10600	2.14020
C	3.86063	-1.97907	3.02172
H	4.34927	-2.25659	3.95867
H	2.91312	-2.52067	2.95431
H	4.50490	-2.29173	2.19329
C	2.74353	-0.03317	4.16512
H	1.80765	-0.59342	4.18693
H	3.28163	-0.22708	5.09672
H	2.51984	1.03671	4.13063

(4a*R*,9b*S*)-*anti ; alternative 2-hydroxymethyl-phenol group orientation.*



This structure has a 5.9 kcal/mol higher energy than (4a*S*,9b*R*)-*anti.*

O	-1.42250	1.07817	-0.88391
O	0.43806	3.96030	0.07376
N	1.05519	1.90692	-0.76641
C	-4.31139	0.15189	-2.92920
H	-4.78388	-0.71860	-3.37063
C	-4.87796	1.41397	-3.05735
C	-4.28113	2.53156	-2.45778
H	-4.73810	3.51174	-2.55154
C	-3.10994	2.36708	-1.74141
C	-2.20691	3.33948	-1.01914
H	-1.60095	3.86613	-1.76508
C	-2.90574	4.37600	-0.14632
H	-3.69478	4.88023	-0.71010
C	-3.50388	3.81377	1.13377

C	-2.78866	2.74746	1.77804
H	-3.10647	2.46087	2.77710
C	-1.68865	2.10930	1.24531
C	-1.28710	2.36726	-0.22651
C	-2.54818	1.10322	-1.62808
C	-3.13083	-0.01640	-2.19921
C	0.17051	2.82294	-0.28665
H	0.70369	0.96257	-0.89604
H	-2.17274	5.13592	0.14623
C	2.43786	2.04784	-0.93048
C	3.11024	3.24818	-0.67709
C	4.38477	0.96100	-1.50159
C	4.48421	3.26131	-0.84984
H	2.56323	4.11779	-0.34622
C	5.13814	2.10773	-1.26383
H	5.04178	4.17194	-0.65518
H	6.21347	2.08684	-1.39758
C	5.04445	-0.31393	-1.93666
H	4.92196	-1.07431	-1.16040
H	4.59462	-0.69263	-2.85891
H	6.11353	-0.17122	-2.10168
N	3.05187	0.92984	-1.33546
O	-0.98327	1.24593	1.86306
O	-4.51725	4.33373	1.60723
H	-5.79922	1.53122	-3.61701
H	-0.22726	0.13163	1.10950
O	0.16192	-0.59942	0.53208
C	1.08552	-1.43546	1.19273
H	0.64560	-1.83373	2.11886
C	1.24796	-2.61990	0.24689
H	0.30991	-3.17461	0.21162
H	0.61947	-1.71385	-1.47975
C	2.37432	-0.69567	1.53536
C	2.28831	0.59656	2.06551
C	3.64290	-1.24003	1.34251
C	3.42909	1.33217	2.34471
H	1.31738	1.05491	2.23093
C	4.80537	-0.52684	1.63504
H	3.76326	-2.24301	0.94128
C	4.69292	0.78564	2.11542
H	3.35737	2.34566	2.72544
N	1.50635	-2.12473	-1.13914
S	-2.42935	-1.62049	-1.91422
O	-3.35541	-2.59748	-2.47108
O	-1.05127	-1.57265	-2.43195
N	-2.24884	-1.85883	-0.31293
H	-1.42032	-1.33993	0.01327
H	2.17989	-1.34008	-1.12200
C	1.95108	-3.14915	-2.17314
C	-3.33181	-2.02297	0.71404
C	-4.41599	-0.95269	0.54943
C	-2.52351	-1.83665	2.02530

C	-3.93934	-3.41658	0.55993
H	-3.99930	0.05496	0.64299
H	-4.90880	-1.04115	-0.42270
H	-5.18897	-1.07232	1.30814
H	-1.61609	-2.44640	1.91829
H	-2.19158	-0.79110	2.02706
C	-3.07045	-2.14220	3.44392
H	-4.74954	-3.55623	1.28010
H	-4.35480	-3.54379	-0.44237
H	-3.18503	-4.19249	0.72147
C	-2.03414	-1.53329	4.40783
C	-3.14642	-3.65007	3.73017
C	-4.43125	-1.50054	3.73870
H	-1.94519	-0.45145	4.26166
H	-2.31592	-1.71719	5.45047
H	-1.04233	-1.97372	4.24857
H	-2.19131	-4.14164	3.51176
H	-3.37166	-3.82096	4.78921
H	-3.92383	-4.14912	3.14750
H	-4.66563	-1.60317	4.80443
H	-4.43271	-0.43200	3.49844
H	-5.24023	-1.98338	3.18206
O	5.78045	1.54737	2.37852
H	6.53222	1.15080	1.90063
C	6.16210	-1.15571	1.46640
H	6.58097	-1.40924	2.45036
H	6.07794	-2.08557	0.89061
O	7.02606	-0.22852	0.80218
H	7.93011	-0.55573	0.87550
C	1.98773	-2.39649	-3.50349
H	2.36671	-3.05990	-4.28449
H	0.98730	-2.06171	-3.79051
H	2.64429	-1.52314	-3.44523
C	0.92539	-4.27960	-2.21795
H	-0.08180	-3.89009	-2.38633
H	1.17977	-4.94440	-3.04729
H	0.93195	-4.87472	-1.30085
C	3.33322	-3.67704	-1.80179
H	4.06704	-2.87104	-1.74370
H	3.32885	-4.22333	-0.85488
H	3.65865	-4.37357	-2.57870
H	2.04377	-3.29589	0.55045

(4a*R*,9b*S*)-*gauche*

O	1.10505	-0.88843	-0.40626
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C	4.71339	-0.16606	-0.48007
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C	4.94778	-0.44213	-1.81995

C	3.89392	-0.82508	-2.65534
H	4.06498	-1.00585	-3.71186
C	2.62534	-0.95548	-2.12124
C	1.29708	-1.19775	-2.79046
H	1.02080	-0.27066	-3.30699
C	1.23483	-2.33662	-3.80326
H	2.07846	-2.27606	-4.49548
C	1.19648	-3.72863	-3.19290
C	0.47508	-3.87935	-1.96121
H	0.27334	-4.89012	-1.61702
C	-0.02595	-2.83393	-1.21528
C	0.36067	-1.38633	-1.56602
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C	3.43020	-0.29403	0.06665
C	-0.90430	-0.55363	-1.75848
H	-0.36574	0.49992	-0.14304
H	0.31946	-2.22456	-4.39526
C	-1.95766	1.53043	-0.91395
C	-2.85150	1.78021	-1.95453
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C	-3.68601	2.87970	-1.81900
H	-2.87432	1.14789	-2.82972
C	-3.60617	3.68269	-0.68553
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H	-4.25117	4.54530	-0.56408
C	-2.51483	4.16717	1.55422
H	-2.52946	3.51326	2.43146
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H	-3.30524	4.91339	1.65608
N	-1.87447	2.29427	0.17856
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O	1.69937	-4.67194	-3.80770
H	5.94982	-0.34114	-2.22100
H	-1.08664	1.35485	1.59049
O	-0.63629	0.62741	2.07804
C	-1.63401	-0.12004	2.77947
H	-1.90329	0.42355	3.69584
C	-0.99502	-1.41682	3.28465
H	-0.38570	-1.17459	4.15548
H	-0.46316	-2.24719	1.36796
C	-2.89552	-0.24074	1.95014
C	-3.89712	0.72071	2.10080
C	-3.03013	-1.17152	0.92040
C	-4.95296	0.80997	1.20027
H	-3.82783	1.44773	2.90647
C	-4.08191	-1.11645	0.01733
H	-2.28886	-1.94362	0.75653
C	-5.01984	-0.07566	0.12519
H	-5.70452	1.58715	1.29229
N	-0.08537	-2.12194	2.33735
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O	2.43266	-0.90944	2.43329

O	4.48452	0.51412	2.29312
N	2.16707	1.44843	1.84964
H	1.20172	1.13261	1.98790
H	0.75938	-1.54019	2.22188
C	2.31710	2.78492	1.19731
C	1.55616	3.72984	2.13650
C	1.62757	2.69823	-0.19220
C	3.78968	3.18674	1.15779
H	0.51506	3.40825	2.24840
H	2.02224	3.73536	3.12581
H	1.55678	4.74946	1.74703
H	1.90552	1.73875	-0.63609
H	0.55375	2.63725	0.01953
C	1.81219	3.74666	-1.32066
H	3.86827	4.22826	0.84002
H	4.23549	3.09739	2.15080
H	4.37289	2.57639	0.46444
C	0.73771	3.41196	-2.37188
C	3.18669	3.62382	-1.99858
C	1.58783	5.19159	-0.86018
H	-0.26944	3.55838	-1.96629
H	0.84152	4.05486	-3.25275
H	0.81942	2.37053	-2.70550
H	3.39651	2.58397	-2.27583
H	3.21080	4.22409	-2.91534
H	4.00217	3.97288	-1.36170
H	1.60818	5.86933	-1.72139
H	0.61316	5.30604	-0.37272
H	2.36081	5.52899	-0.16321
H	-1.78399	-2.10164	3.59458
O	-5.99599	0.08048	-0.79822
H	-5.70138	-0.39299	-1.60120
C	-4.21170	-2.12871	-1.09461
H	-3.32543	-2.77275	-1.11954
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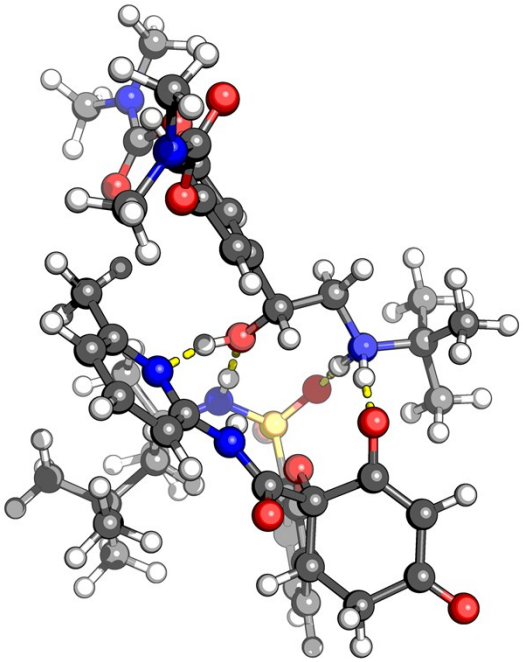
O	-4.42276	-1.50063	-2.35858
H	-3.57277	-1.09380	-2.59756
C	0.37825	-3.50659	2.79383
C	0.92561	-3.41907	4.21754
H	0.14491	-3.21593	4.95500
H	1.37661	-4.38145	4.47233
H	1.70140	-2.65152	4.29536
C	1.48768	-3.94256	1.83350
H	2.32369	-3.23934	1.84944
H	1.85766	-4.92174	2.14874
H	1.11125	-4.03073	0.81342
C	-0.80558	-4.46706	2.69923
H	-1.60571	-4.21618	3.40128
H	-1.20574	-4.47492	1.68186
H	-0.45950	-5.47511	2.94302

Bambuterol complexes.

(4a*S*,9b*R*)-*anti*



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H	5.75333	2.93459	0.46340
C	6.54312	1.09234	-0.32365
C	6.26372	-0.23330	-0.66829
H	7.02861	-0.85949	-1.11706
C	4.99496	-0.73553	-0.44409
C	4.37918	-2.05575	-0.82970
H	4.23719	-2.05170	-1.91612
C	5.18047	-3.30458	-0.46762
H	6.23363	-3.16611	-0.72495
C	5.08624	-3.73425	0.98783
C	3.82660	-3.53356	1.64873
H	3.68036	-4.02109	2.60900
C	2.78070	-2.80339	1.12911
C	2.98875	-1.96729	-0.15024
C	4.01305	0.06408	0.12787
C	4.26376	1.39689	0.44544
C	1.88002	-2.34721	-1.13115
H	1.02211	-0.57347	-0.71574
H	4.80650	-4.14296	-1.06587
C	-0.25646	-1.46508	-2.04412
C	-0.61940	-2.54846	-2.84554
C	-2.17459	-0.27851	-2.57919
C	-1.82753	-2.45343	-3.52184
H	0.02103	-3.41562	-2.91493
C	-2.61852	-1.31568	-3.39529
H	-2.15276	-3.27522	-4.15201

H	-3.56637	-1.22980	-3.91415
C	-2.95240	0.98886	-2.38835
H	-3.01032	1.25963	-1.33106
H	-2.45927	1.81647	-2.91027
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O	1.62050	-2.69342	1.64246
O	6.04219	-4.31228	1.50964
H	7.53347	1.50139	-0.48828
H	-0.63537	0.53807	-0.38479
O	-0.30668	0.65077	0.54018
C	-0.93670	-0.37527	1.30028
H	-0.59218	-1.35766	0.94883
C	-0.51729	-0.22582	2.75444
H	-1.05252	-0.96287	3.35287
H	1.21497	-1.31620	2.33410
C	-2.43821	-0.29340	1.11913
C	-3.12126	-1.35269	0.52591
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C	-5.16495	-0.05116	0.52326
N	0.94077	-0.45902	2.89801
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O	3.67758	3.77756	1.29359
N	1.78075	2.62936	0.06062
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C	1.80654	3.06882	-1.36823
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H	0.32042	4.57351	-0.88715
H	0.31889	4.08795	-2.59247
C	1.95283	1.78486	-2.23047
H	2.70610	1.15496	-1.74935
H	0.99794	1.25575	-2.12638
C	2.90439	4.10826	-1.58058
H	2.80040	4.53804	-2.57883
H	2.81169	4.91502	-0.85057
H	3.90612	3.67952	-1.49586
C	2.30628	1.78417	-3.73982
C	2.07450	0.33707	-4.21344
H	1.02003	0.05594	-4.12002
H	2.36083	0.22011	-5.26435
H	2.66691	-0.37210	-3.62308
C	3.78459	2.12339	-3.98934
H	4.43960	1.50500	-3.36450
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H	4.01551	3.17116	-3.78691

C	1.41315	2.70824	-4.57592
H	1.60558	2.55245	-5.64354
H	0.35164	2.50453	-4.39512
H	1.59984	3.76524	-4.36243
C	1.48406	-0.65776	4.30148
H	-0.75118	0.77462	3.12305
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H	3.45095	-0.90749	5.14037
H	3.29505	-1.58219	3.51145
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H	1.43260	1.47534	4.71440
H	0.01643	0.59130	5.33417
H	1.57762	0.43824	6.14379
C	0.93388	-1.96995	4.85852
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H	1.13539	-2.79074	4.16392
H	1.43087	-2.18582	5.80779
H	-6.21359	0.06213	0.27872
O	-5.05433	-2.24183	-0.48774
O	-5.18015	2.11533	1.48104
C	-4.88186	3.27136	0.80928
O	-4.08945	3.31712	-0.11441
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O	-6.69656	-2.52740	1.06239
N	-6.61984	-3.79488	-0.84664
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H	-6.27606	3.42138	3.09064
H	-6.72786	5.11544	2.84543
H	-7.55227	3.83967	1.92310
C	-5.53390	5.58720	0.62536
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H	-5.35025	6.39216	1.34308
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C	-6.02943	-4.01538	-2.15770
H	-6.44032	-3.32750	-2.90663
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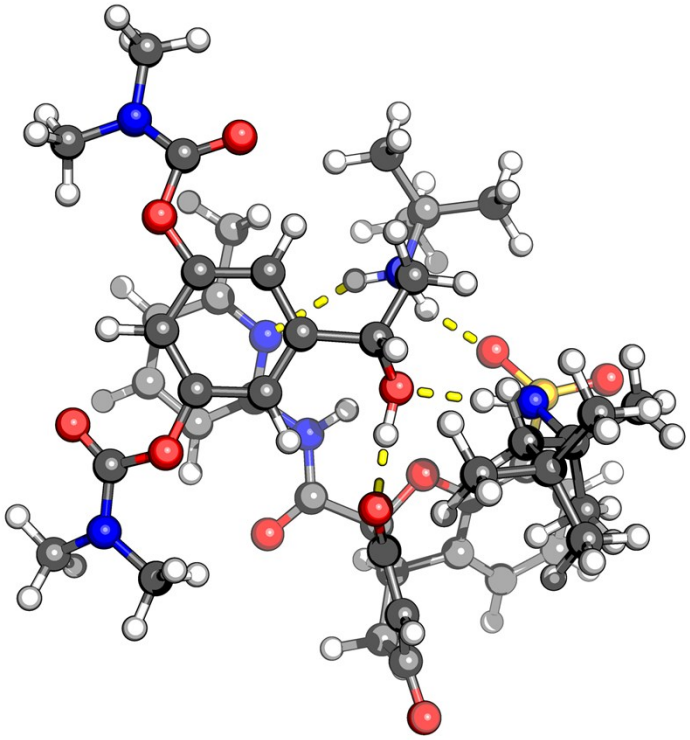
(4a*S*,9b*R*)-*gauche*



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C	-5.73172	0.38342	-3.20407
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C	-3.33575	0.41056	-1.85345
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C	3.58532	0.09413	-2.03289
C	3.75184	2.47999	-2.10650
H	1.88009	3.50505	-1.75829
C	4.36342	1.23731	-2.20106
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H	5.42680	1.14585	-2.39172
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N	2.26800	0.15294	-1.78143
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H	-0.17245	-2.36072	-1.06829
C	1.71350	-0.56337	1.43136
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C	1.06888	-3.99730	-1.39192
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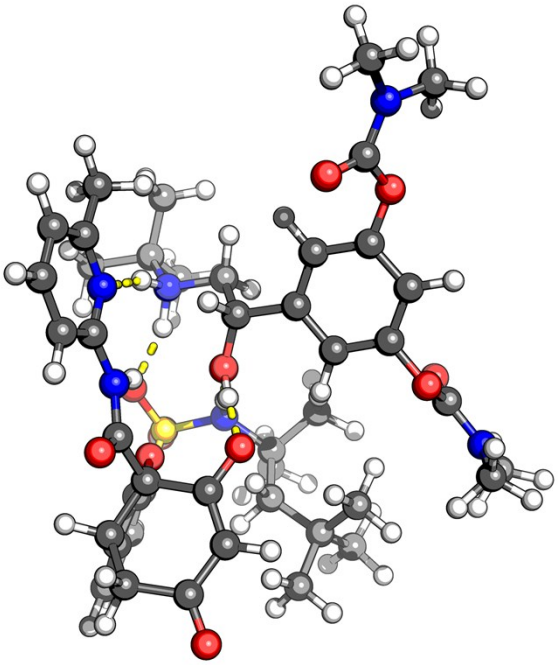
(4a*R*,9b*S*)-*anti*



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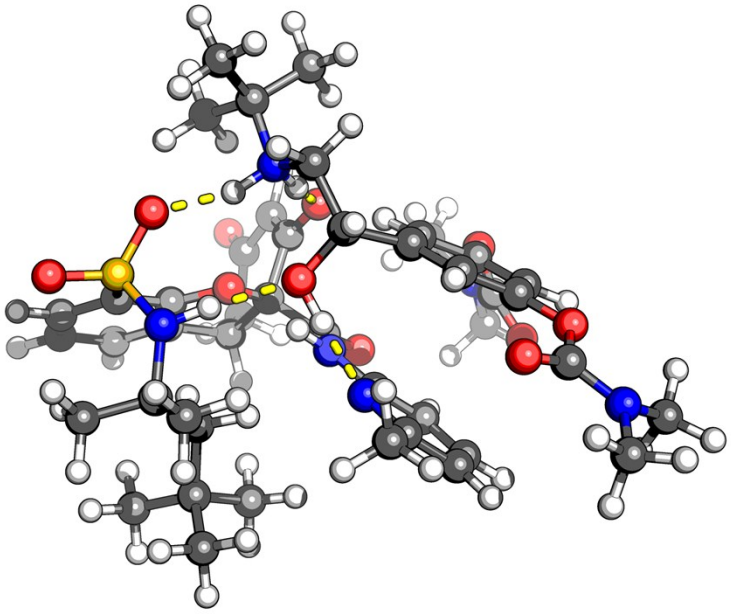
(4a*R*,9b*S*)-*gauche*



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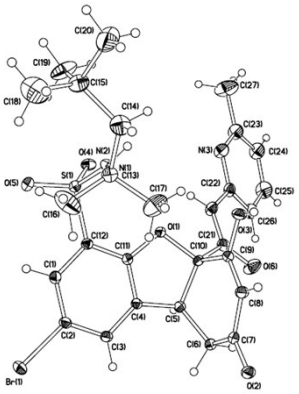
ORTEP diagrams and X-ray crystal structure data

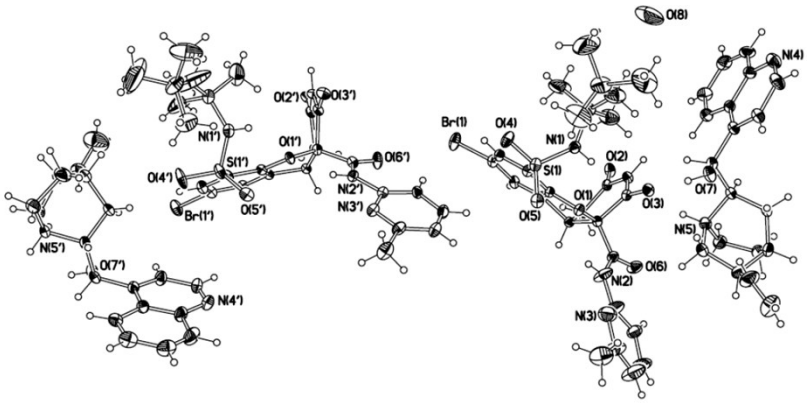
X-ray structure, crystal and refinement data of SMAR 1



CCDC 1474878

Empirical formula	$C_{27}H_{32}BrN_4O_5S$
Molecular weight	606.53
Temperature	298 (2) K
Wavelength	1.54178 Å
Crystal system, Space group	Monoclinic, $P2_1/n$
Unit cell dimensions	a = 13.4851 (5) Å α = 90.00 ° b = 8.5343 (4) Å β = 103.401(3) ° c = 25.6709 (12) Å γ = 90.00 °
Volume	2873.9(2) $Å^3$
Z; Density (calculated)	4; 1.402 mg/m^3
Absorption coefficient	3.001 mm^{-1}
F(000)	1256
Crystal size	0.18 x 0.16 x 0.10 mm
θ range	3.42 – 67.03 °
Limiting indices h, k, l	$-15 \leq h \leq 15$, $-7 \leq k \leq 10$, $-29 \leq l \leq 29$
Reflections collected/independent	20440/4819 R_{int} = 0.0491
Refinement method	Least squares method with full matrix in F^2
Data/restraints/parameters	4819/0/350
Goodness-of-fit on F^2	1.034
Final R indices [$I>2\sigma(I)$]	R_1 = 0.0572, ωR_2 = 0.1517
R índices (all data)	R_1 = 0.0718, ωR_2 = 0.1635
Largest difference peak and hole	1.063 and -0.837

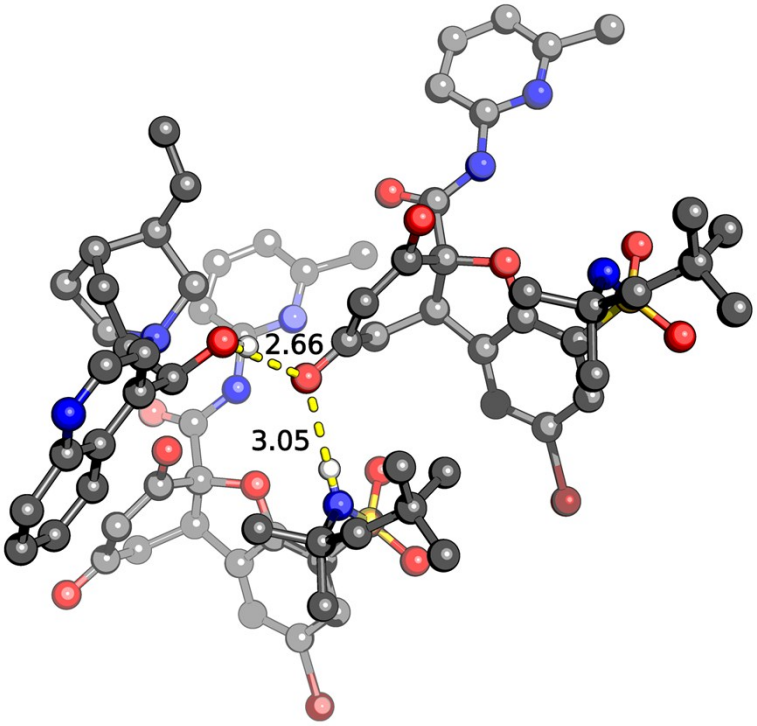
X-ray structure, crystal and refinement data of SMAR (+)-1 + cinchonine



CCDC 1474879

Empirical formula	$2(C_{27}H_{31}BrN_3O_6S)$, $2(C_{19}H_{23}N_2O)$, O
Molecular weight	908.91
Temperature	298 (2) K
Wavelength	1.54178 Å
Crystal system, Space group	Monoclinic, $P2_1$
Unit cell dimensions	a = 8.3467 (2) Å α = 90.00 ° b = 25.1787 (10) Å β = 92.223 (3) ° c = 22.2970 (8) Å γ = 90.00 °
Volume	2226.0 (5) $Å^3$
Z; Density (calculated)	4; 1.289 mg/m^3
Absorption coefficient	2.058 mm^{-1}
F(000)	1904
Crystal size	0.12 x 0.08 x 0.06
θ range	1.98 – 67.48 °
Limiting indices h, k, l	$-9 \le h \le 7$, $-27 \le k \le 29$, $-25 \le l \le 25$
Reflections collected/independent	38707/14076 R_{int} = 0.0819
Refinement method	Least squares method with full matrix in F^2
Data/restraints/parameters	14076/1/1105
Goodness-of-fit on F^2	1.029
Final R indices [I>2σ(I)]	R_1 = 0.0696, ωR_2 = 0.1723
R índices (all data)	R_1 = 0.1013, ωR_2 = 0.1966
Largest difference peak and hole	0.936 and -0.493

“Oxyanion-hole” observed in the X-ray structure of SMAR (+)-1 + cinchonine



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