RECOGNITION OF ACHIRAL AND CHIRAL AMMONIUM SALTS BY NEUTRAL DITOPIC RECEPTORS BASED ON CHIRAL SALEN-UO_2 MACROCYCLES

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Supporting Information

Determination of Stoichiometry. Complexes stoichiometry was determined by the Job plot method[6] using spectrophotometric measurements. The samples were prepared by mixing appropriate host and guest equimolar stock solutions (2 x 10^{-4} M) to cover the whole range of molar fractions keeping constant the total concentration. The UV absorbance was recorded at 341 nm and the changes in absorbance, compared to uncomplexed host species (ΔA), were calculated and reported versus the host mole fraction. These plots show invariably a maximum at 0.5 mol fraction of host indicating the formation of 1:1 complexes with guests.

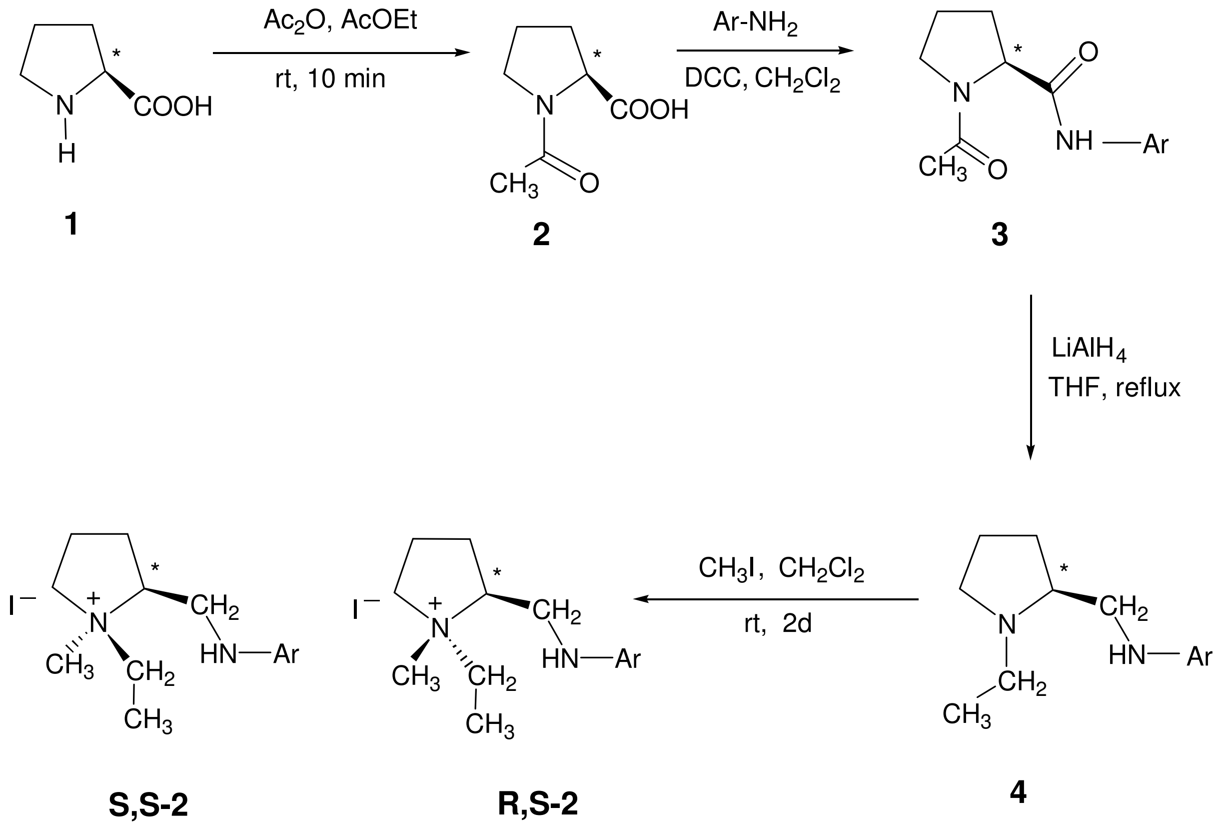
^{1}H NMR Complexation Experiments. Typically, solutions with host/guest molar ratios in the 0.2/1- 10/1 range were prepared (the final concentration of the guest solution was 1.00 x 10^{-3}M). The following stock solutions were used: [M40] = [M20] = 20 mM in $CDCl_3$; [guest] = 2 mM in $CDCl_3$. However, in the case of **S,S-2** and **R,R-2** guests, because their poor solubility in $CDCl_3$, stock solutions were prepared in water. Then, the pertinent aliquots containing the appropriate amounts of the **S,S-2** and **R,R-2** guest were frozen dry. The subsequent treatment of the white solid obtained with appropriate volume of host stock solution in $CDCl_3$ gave complete solubilization due to host/guest complexation.

Titration data points were fitted by eq. 1, which is a standard binding isotherm for the case of 1:1 association.

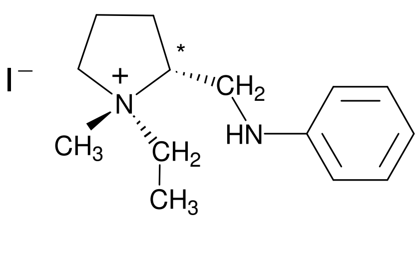
$$\Delta\delta = \frac{\Delta\delta_{\infty} \cdot K \cdot [H]}{1 + K \cdot [H]} \qquad \text{(eq. 1)}$$

The upfield shift of the guest fully saturated by the host ($-\Delta\delta_{\infty}$) and the binding constants values (K) were obtained as best fit parameters in a nonlinear least square fitting procedure.[7]

SCHEME S1. Synthesis of *S*-2-Anilinomethyl-*S*-1-ethylmethylpyrrolidinium iodide and *S*-2-Anilinomethyl-*R*-1-ethylmethylpyrrolidinium iodide

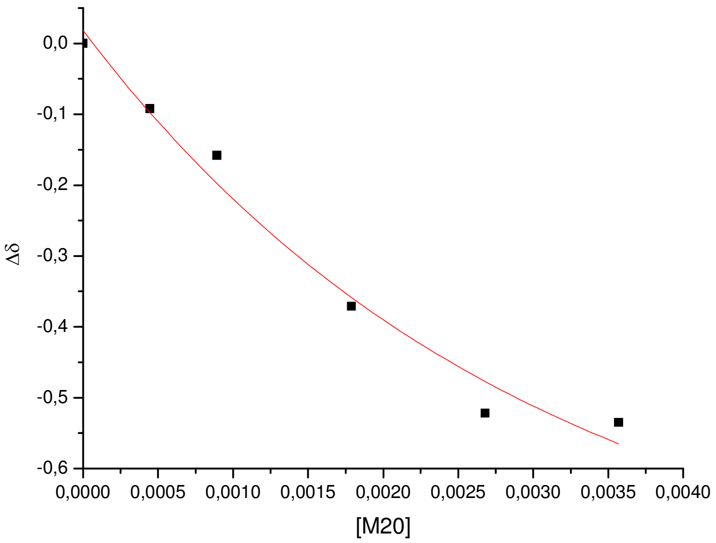


The same experimental procedure reported above was followed to synthesize the *R*-2-Anilinomethyl-*R*-1-ethylmethylpyrrolidinium iodide and *R*-2-Anilinomethyl-*S*-1-ethylmethylpyrrolidinium iodide. Only the R,R stereoisomer (**R,R-2**) was obtained as pure compound.



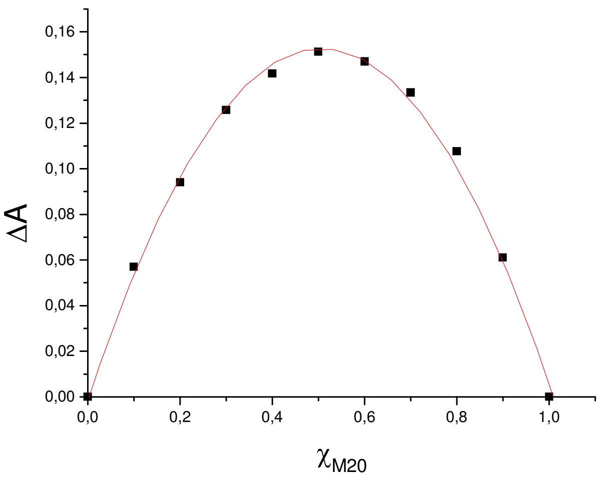
R,R-2

M20/TBACl



(a)

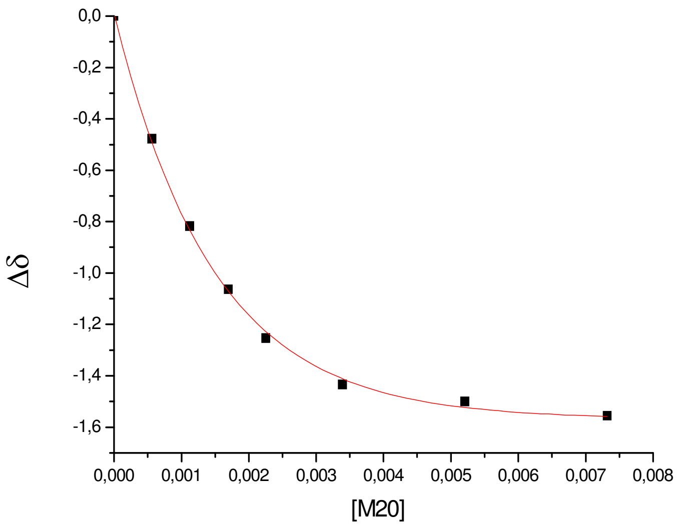
K = 169±15
$\Delta\delta_\infty$ = -0.505
R^2 = 0.98



(b)

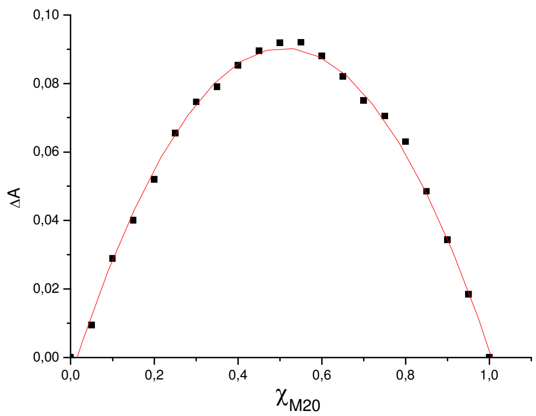
Figure S1. (a) ^{1}H NMR titration curve of 1 mM **TBACl** with receptor **M20** (Host concentrations in the titration experiments are in the range 0.2-3.5 mM) in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **TBACl** monitoring N-CH_3 protons; (b) Job plot of **M20** and **TBACl** in $CHCl_3$ at 27 °C ([**M20**] + [**TBACl**])= 0.1mM

M20/ TMACl



(a)

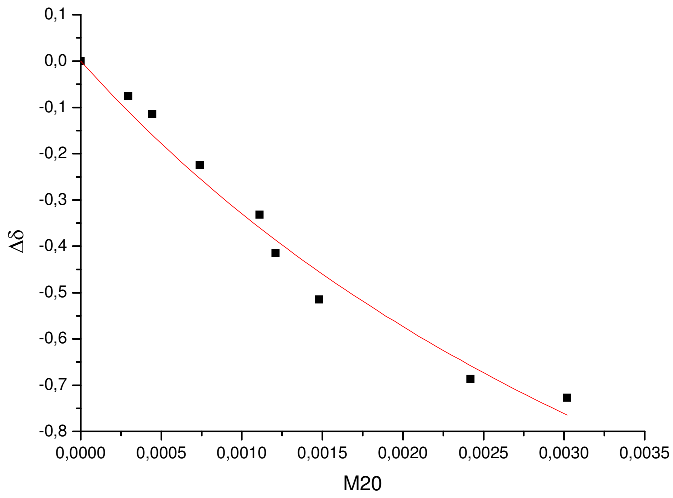
K = 476±42
$\Delta\delta_{\infty}$ = -1.93
R^2 = 0.991



(b)

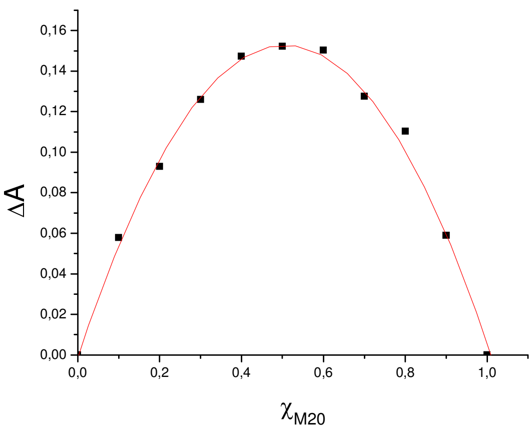
Figure S2. (a) ^{1}H NMR titration curve of 1 mM **TMACl** with receptor **M20** (Host concentrations in the titration experiments are in the range 0.4-7.5 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **TMACl** monitoring N-CH_3 protons; (b) Job plot of **M20** and **TMACl** in $CHCl_3$ at 27 °C ([**M20**] + [**TMACl**])= 0.1 mM)

M20/TEACl



(a)

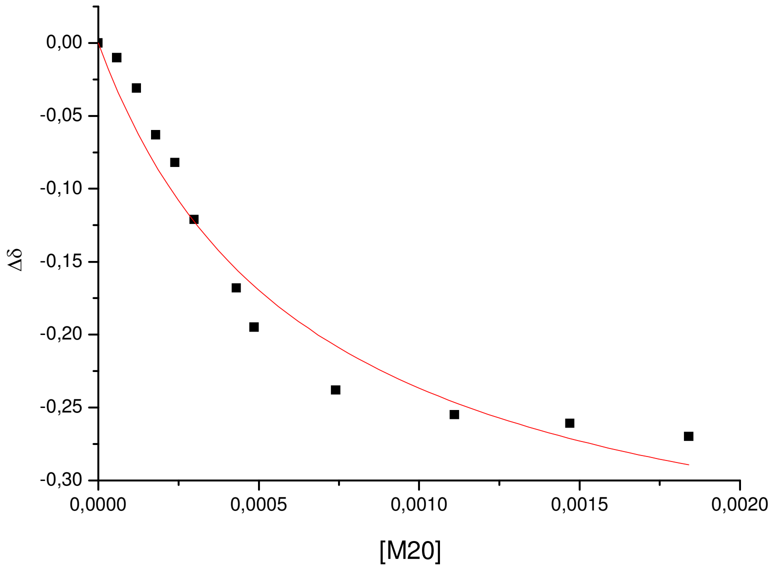
K = 175±68
$\Delta\delta_{\infty}$ = -2.2±0.63
R^2 = 0.98



(b)

Figure S3. (a) ^{1}H NMR titration curve of 1 mM **TEACl** with receptor (Host concentrations in the titration experiments are in the range 0.2-3.0 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **TEACl** monitoring N-CH_2 protons; (b) Job plot of **M20** and **TEACl** in $CHCl_3$ at 27 °C ([**M20**] + [**TEACl**])=0.1 mM).

M20/TMeACl



K = 1512±351
$\Delta\delta_{\infty}$ = -0.39±0.07
R^2 = 0.96

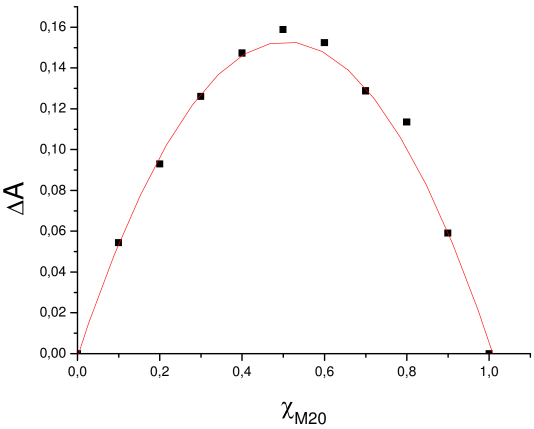
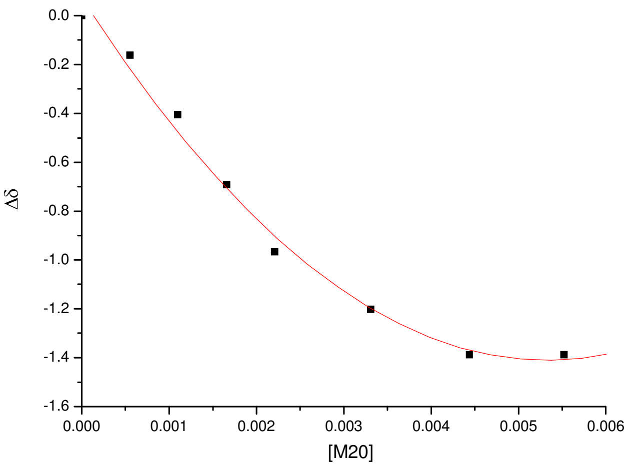


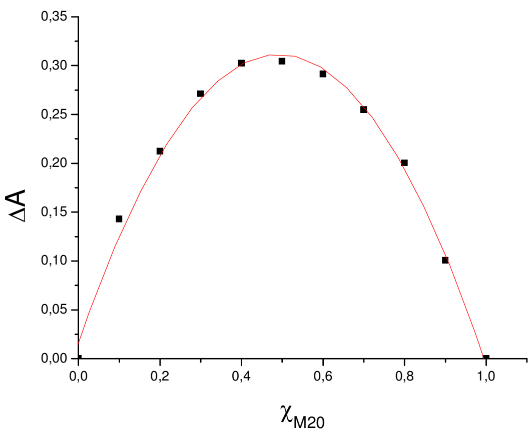
Figure S4. (a) ^{1}H NMR titration curve of 1 mM **TMeACl** with receptor **M20** (Host concentrations in the titration experiments are in the range 0.1-2.0 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **TMeACl** monitoring N-CH_3 protons; (b) Job plot of **M20** and **TMeACl** in $CHCl_3$ at 27 °C ([**M20**] + [**TMeACl**])=1 mM).

M20/AChCl



(a)

K = 112±3
$\Delta\delta_{\infty}$ = -1.39±0.08
R^2 = 0.96

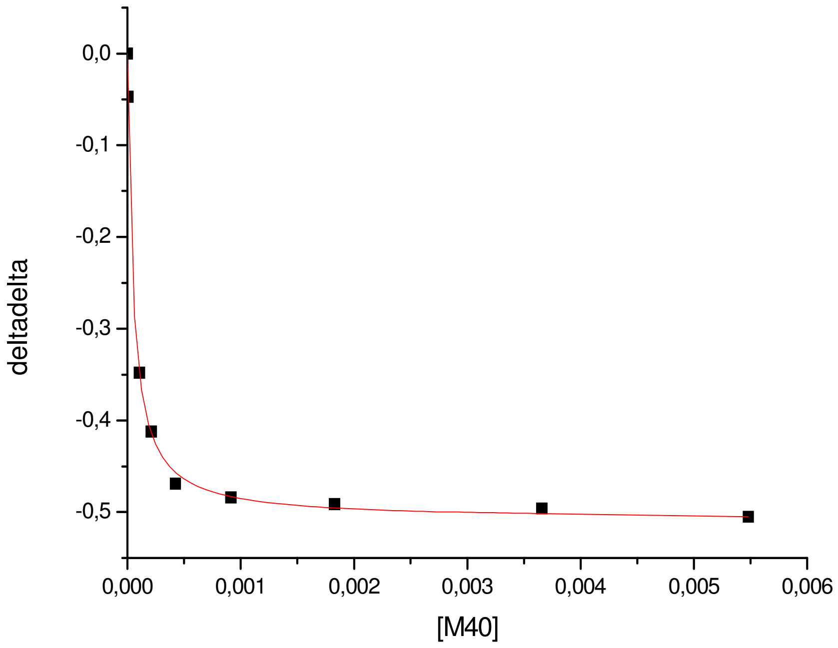


(b)

Figure S5. (a) ^{1}H NMR titration curve of 1 mM **AChCl** with receptor **M20** (Host concentrations in the titration experiments are in the range 0.4-7.5 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **AChCl** monitoring N-CH_3 protons; (b) Job plot of **M20** and **AChCl** in $CHCl_3$ at 27 °C ([**M20**] + [**AChCl**])=0.1 mM)

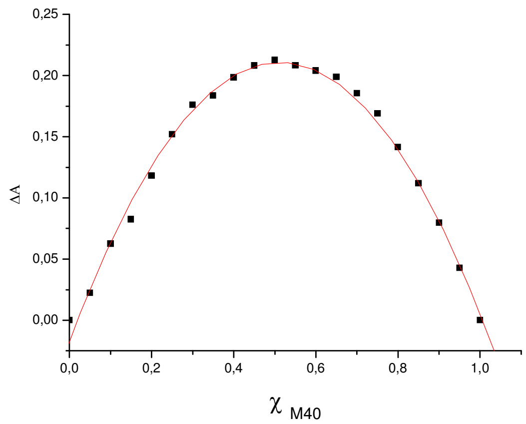
.

M40/TBACl



(a)

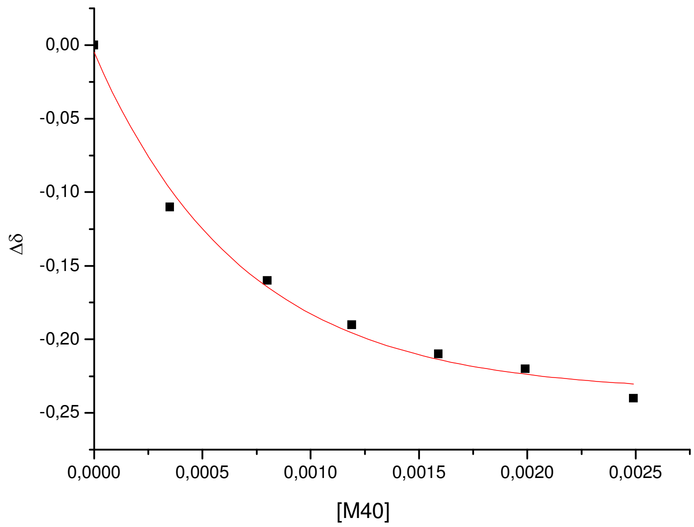
K = 20826±1011
$\Delta\delta_{\infty}$ = -0.506±0.003
R^2 = 0.99



(b)

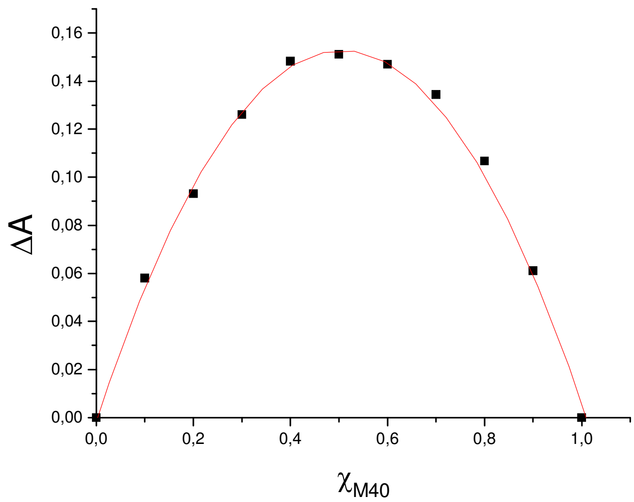
Figure S6. (a) ^{1}H NMR titration curve of 1 mM **TBACl** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.1-5.5 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **TBACl** monitoring N-*CH_3* protons ; (b) Job plot of **M40** and **TBACl** in $CHCl_3$ at 27 °C ([**M40**] + [**TBACl**])=0.1 mM).

M40/TBABr



(a)

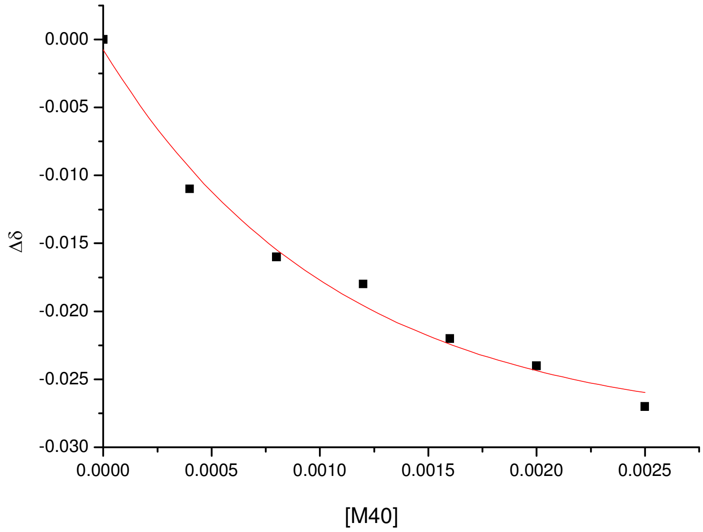
K = 1574±130
$\Delta\delta_\infty$ = -0.294±0.008
R^2 = 0.99



(b)

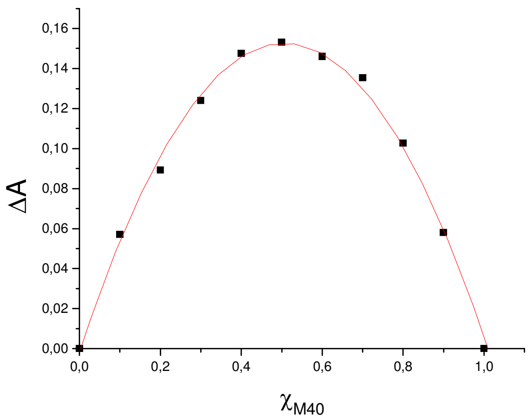
Figure S7. (a) ^{1}H NMR titration curve of 1 mM **TBABr** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.2-2.5 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **TBABr** monitoring N-*CH_3* protons; (b) Job plot of **M40** and **TBABr** in $CHCl_3$ at 27 °C ([**M40**] + [**TBABr**])= 0.1 mM)

M40/TBAI



(a)

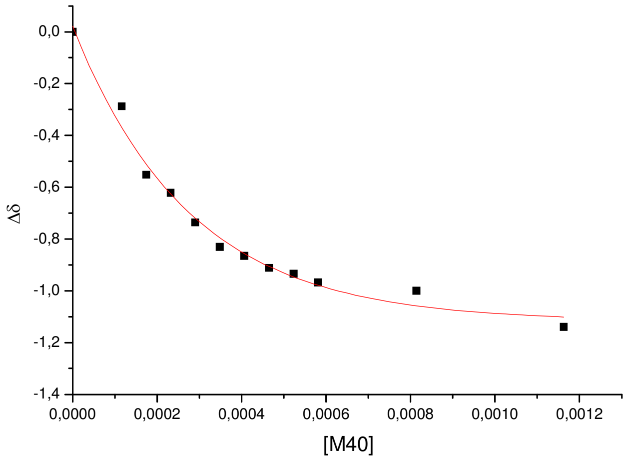
K = 808±126
$\Delta\delta_\infty$ = -0.0383±0.0026
R^2 = 0.993



(b)

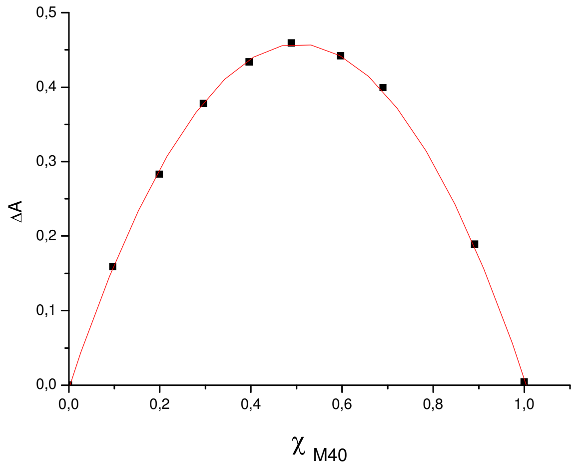
Figure S8. (a) ^{1}H NMR titration curve of 1 mM **TBAI** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.2-2.5 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **TBAI** monitoring N-*CH₃* protons; (b) Job plot of **TBAI** and **M40** in $CHCl_3$ at 27 °C ([**M40**] + [**TBAI**])=0.1 mM)

M40/TMACl



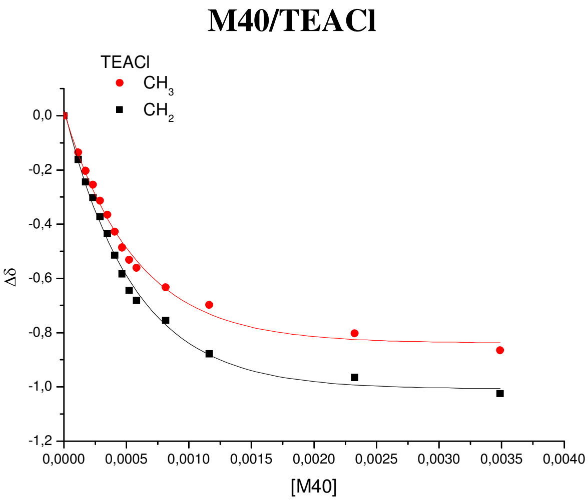
(a)

K = 3354±465
$\Delta\delta_\infty$ = -1.44±0.07
R^2 = 0.980



(b)

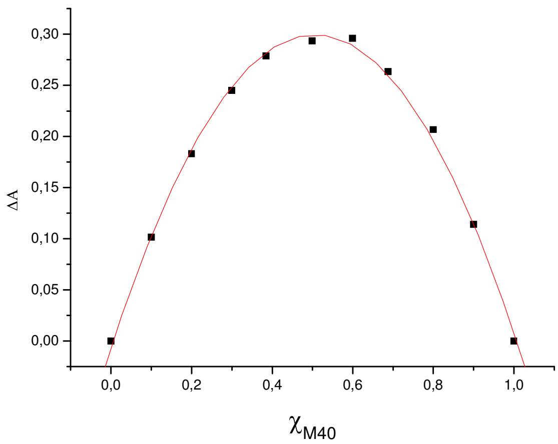
Figure S9. (a) ^{1}H NMR titration curve of 1 mM **TMACl** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.1-1.0 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **TMACl** monitoring N-CH_3 protons; (b) Job plot of **M40** and **TMACl** in $CHCl_3$ at 27 °C ([**M40**] + [**TMACl**])=0.1 mM)



(a)

CH_2 Signal
K = 1745±170
$\Delta\delta_\infty$ = -1.23±0.05
R^2 = 0.982

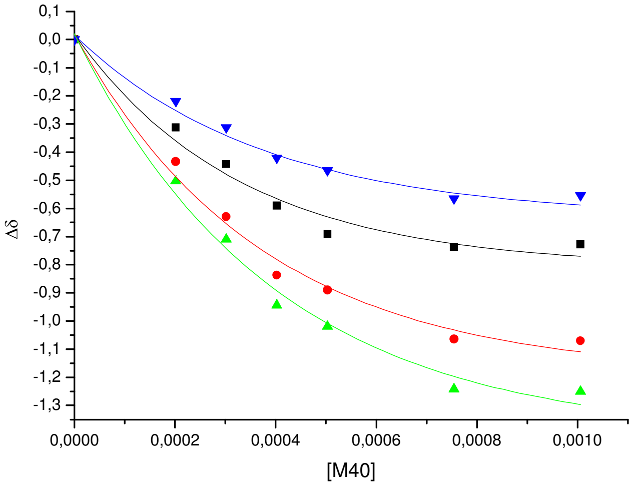
CH_3 Signal
K = 1731±150
$\Delta\delta_\infty$ = -1.03±0.04
R^2 = 0.985

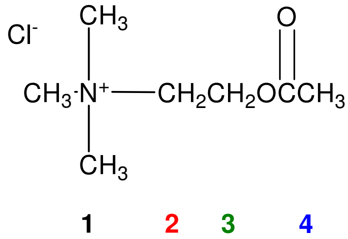


(b)

Figure S10. (a) ^{1}H NMR titration of 1 mM **TEACl** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.1-1.0 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **TEACl** monitoring N-CH_2 and CH_2-CH_3 protons; (b) Job plot of **M40** and **TEACl** in $CHCl_3$ at 27 °C ([**M40**] + [**TEACl**])=0.1 mM)

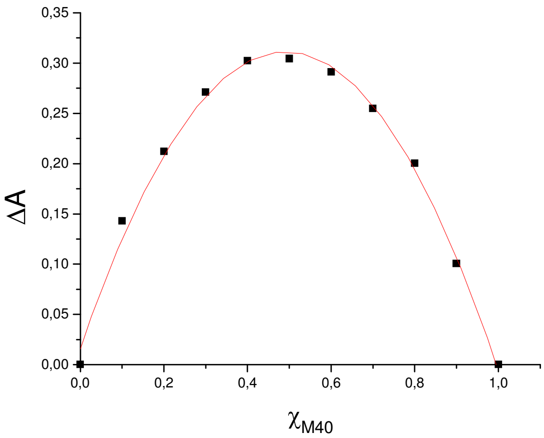
M40/ AChCl





(a)

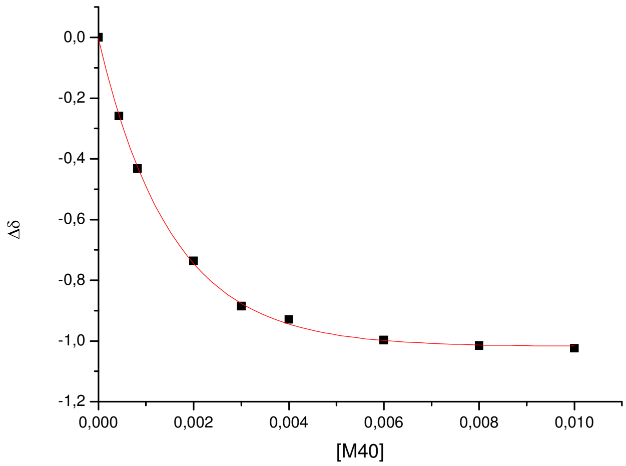
N-CH_3	N-CH_2	NCH_2-CH_2-	-CO-CH_3
K = 2568±534	K =2204±513	K =2020±432	K =1967±514
$\Delta\delta_\infty$ = -1.08	$\Delta\delta_\infty$ = -1.63	$\Delta\delta_\infty$ = -1.96	$\Delta\delta_\infty$ = -0.89
R^2 = 0.98	R^2 = 0.98	R^2 = 0.98	R^2 = 0.98



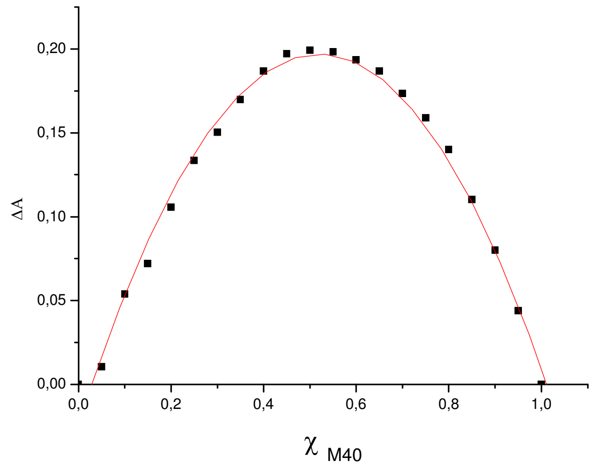
(b)

Figure S11. (a) ^{1}H NMR titration of 1 mM **AChCl** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.2-1.0 mM), in $CDCl_3$ at 27 °C, $\Delta\delta$ is the chemical shift difference in ppm of **TEACl** monitoring N-CH_3, N-CH_2, NCH_2-CH_2, CH_2-O-CO-CH_3 protons; (b) Job plot of **M40** and **AChCl** in $CHCl_3$ at 27 °C ([**M40**] + [**AChCl**])=0.1 mM).

M40/ BnTriMACl



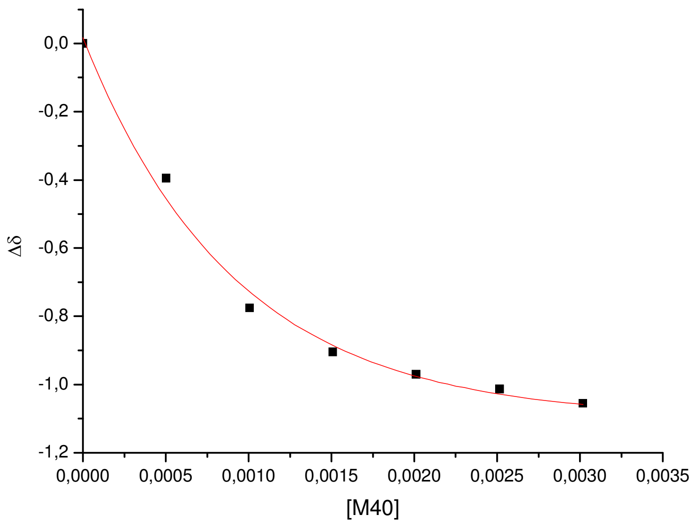
K $= 621 \pm 81$
$\Delta\delta_{\infty} = -1.318$
$R^2 = 0.98$



(b)

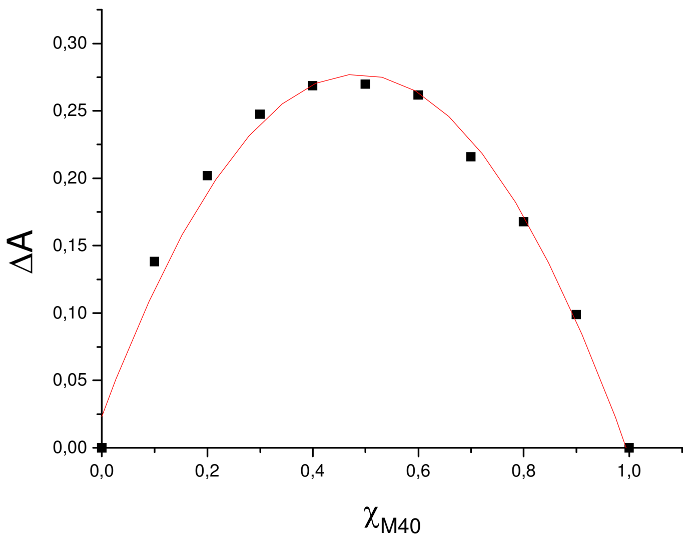
Figure S12. (a) ^{1}H NMR titration curve of 1 mM **BnTriMACl** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.5-10 mM), in $CDCl_3$ at 27 °C, $\Delta\delta$ is the chemical shift difference in ppm of **BnTriMACl** monitoring N-CH_3 protons ; (b) Job plot of **M40** and **BTMACl** in $CHCl_3$ at 27 °C ([**M40**] + [**BnTriMACl**])=0.1 mM)

M40/R-1



(a)

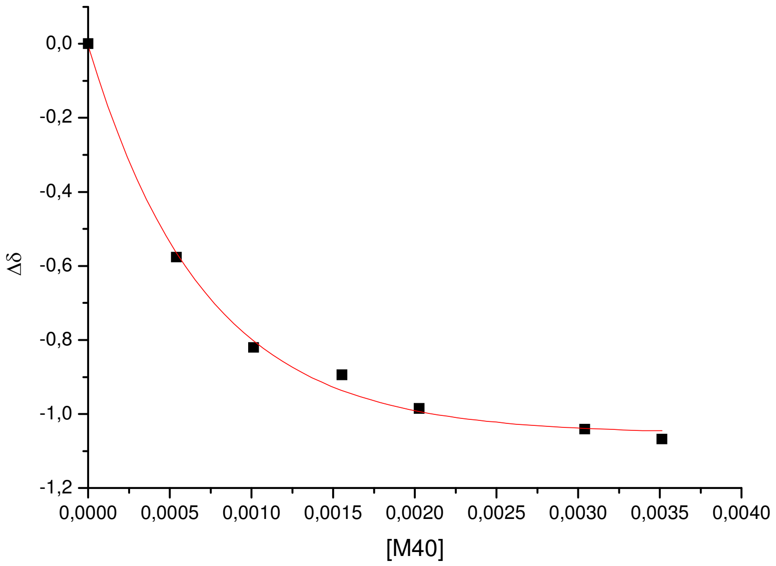
K = 968±115
$\Delta\delta_{\infty}$ = -1.454±0.115
R^2 = 0.98



(b)

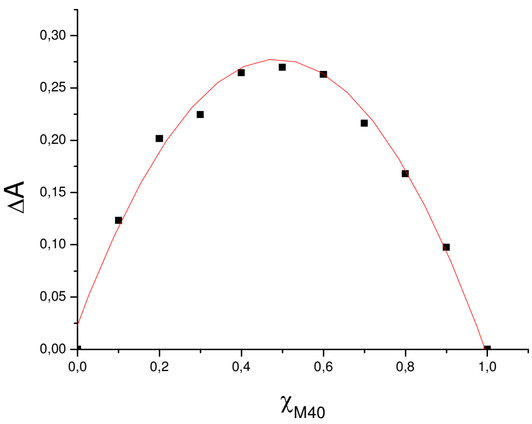
Figure S13. (a) ^{1}H NMR titration of 1 mM of **R-1** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.5-3.5 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **R-1** monitoring N-CH_3 protons; (b) Job plot of **M40** and **R-1** in $CHCl_3$ at 27 °C ([**M40**] + [**R-1**])=0.1 mM)

M40/S-1



(a)

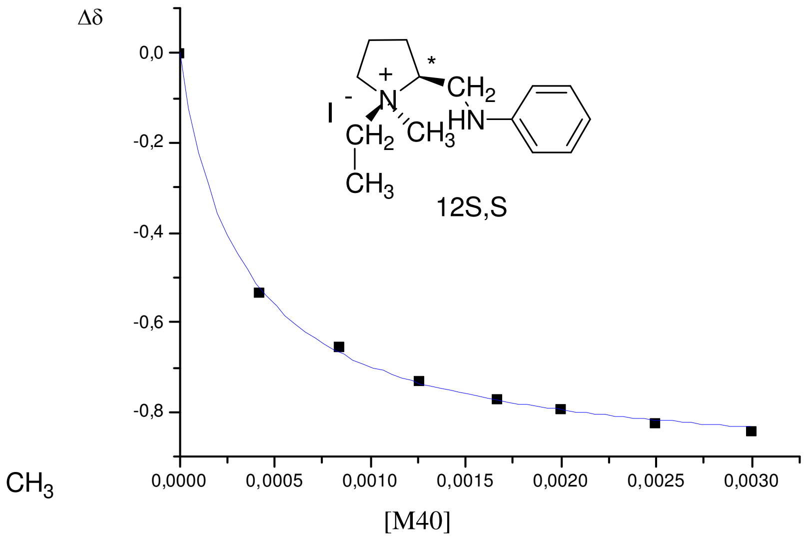
K = 1668±135
$\Delta\delta_\infty$ = -1.250±0.115
R^2 = 0.98



(b)

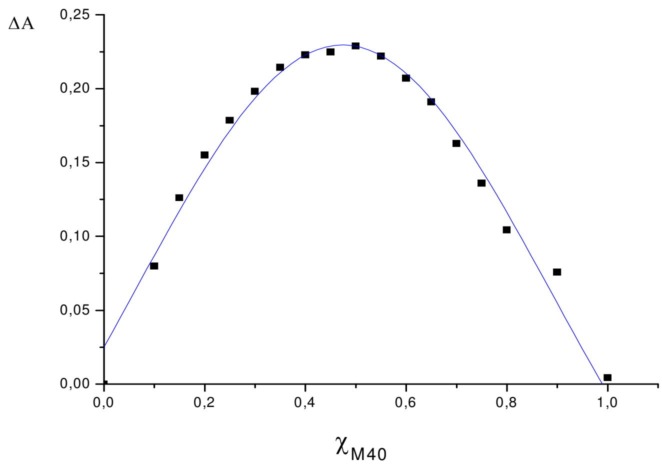
Figure S14. (a) ^{1}H NMR titration of 1 mM of **S-1** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.5-4.0 mM), in $CDCl_3$ at 27 °C, , Δδ is the chemical shift difference in ppm of **S-1** monitoring N-*CH₃* protons ; (b) Job plot of **M40** and **S-1** in $CHCl_3$ at 27 °C ([**M40**] + [**S-1**])=0.1 mM)

M40/S,S-2



(a)

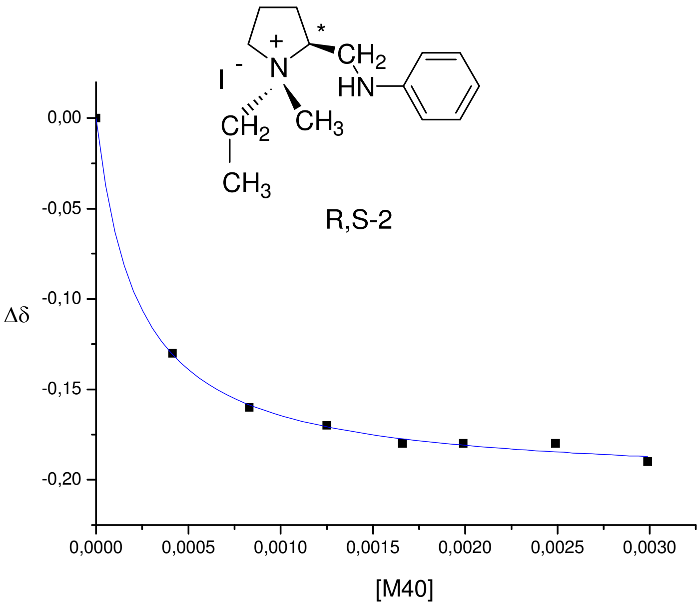
K = 3092 ± 462
$\Delta\delta_\infty$ = -0.83
R^2 = 0.99



(b)

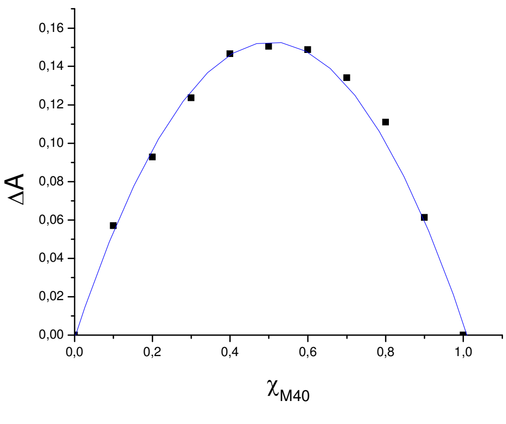
Figure S15. (a) ^{1}H NMR titration of 1 mM of **S,S-2** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.2-3.0 mM), in $CDCl_3$ at 27 °C, , Δδ is the chemical shift difference in ppm of **S,S-2** monitoring N-CH_3 protons ; (b) Job plot of **M40** and **S,S-2** in $CHCl_3$ at 27 °C ([**M40**] + [**S,S-2**])=0.1 mM)

M40/R,S-2



(a)

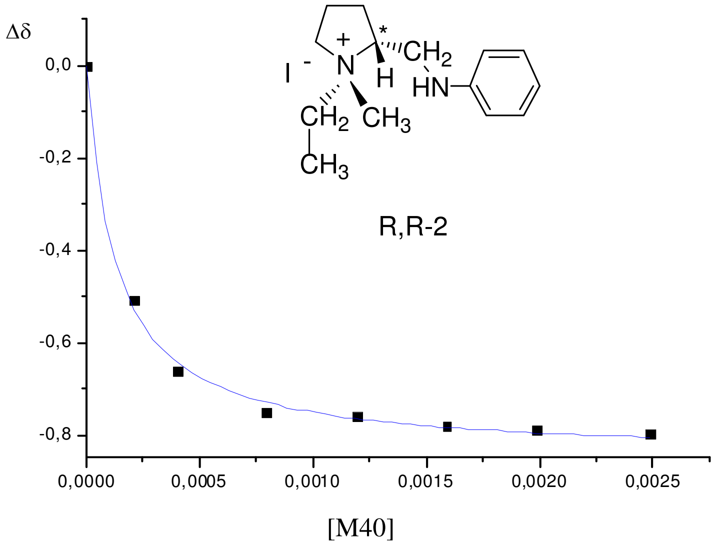
K = 3923 ± 388
$\Delta\delta_{\infty}$ = -0.17
R^2 = 0.995



(b)

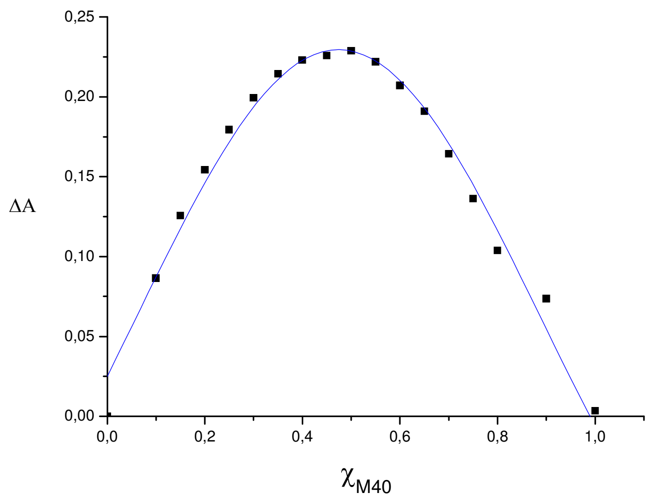
Figure S16. (a) ^{1}H NMR titration of 1 mM of **R,S-2** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.3-3.0 mM), in $CDCl_3$ at 27 °C, , Δδ is the chemical shift difference in ppm of **R,S-2** monitoring N-CH_3 protons ; (b) Job plot of **M40** and **R,S-2** in $CHCl_3$ at 27 °C ([**M40**] + [**R,S-2**])=0.1 mM).

M40/R,R-2



(a)

K $= 7847 \pm 687$
$\Delta\delta_\infty = -0.8$
$R^2 = 0.99$



(b)

Figure S17. (a) [1]H NMR titration of 1 mM of **R,R-2** with receptor **M40** (Host concentrations in the titration experiments are in the range 0.2-2.5 mM), in $CDCl_3$ at 27 °C, Δδ is the chemical shift difference in ppm of **R,R-2** monitoring N-*CH_3* protons; (b) Job plot of **M40** and **R,R-2** in $CHCl_3$ at 27 °C ([**M40**] + [**R,R-2**])=0.1 mM).

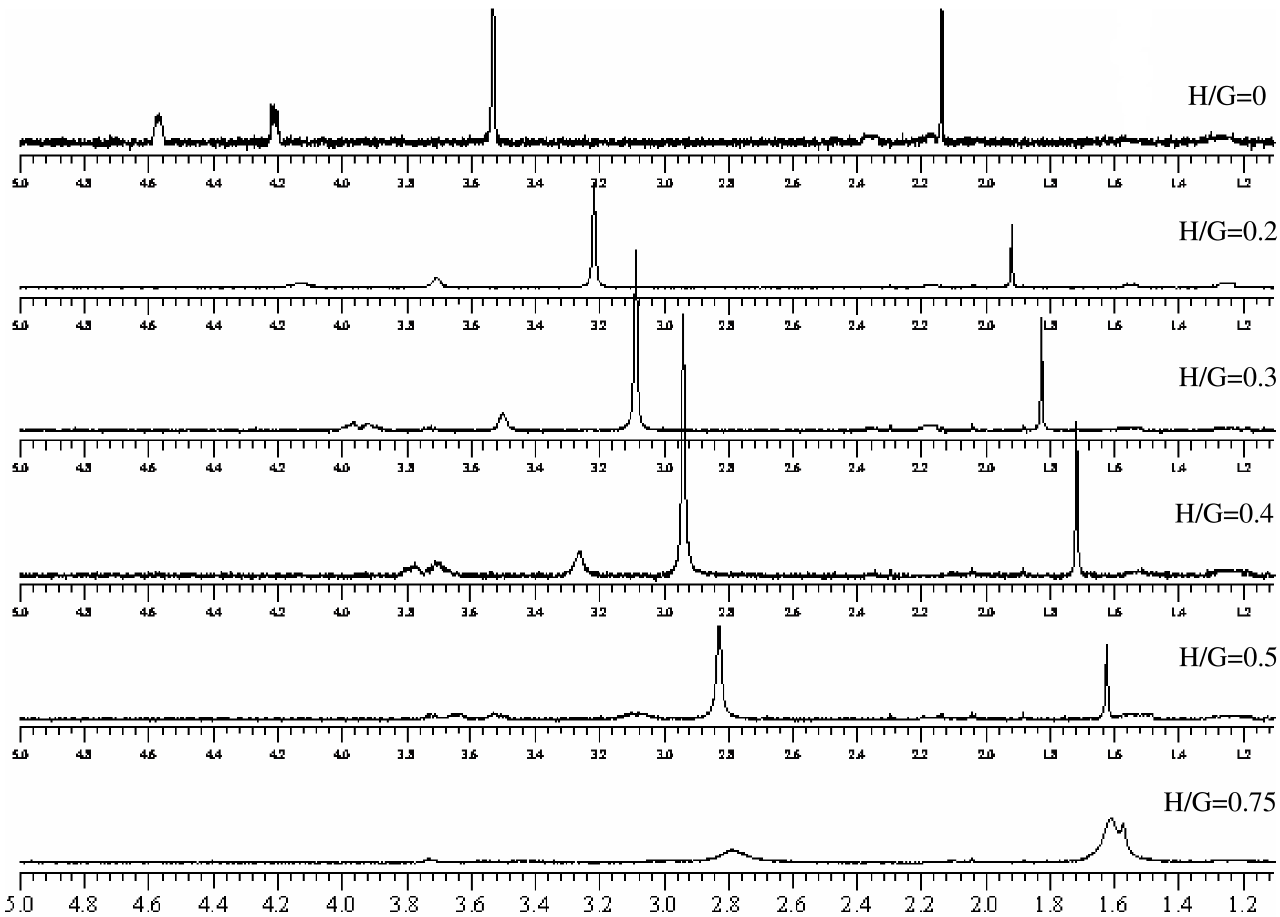


Figure S18. Portion of [1]H NMR titration spectra of **M40/AChCl** (500 MHz; $CDCl_3$ at 27 °C)

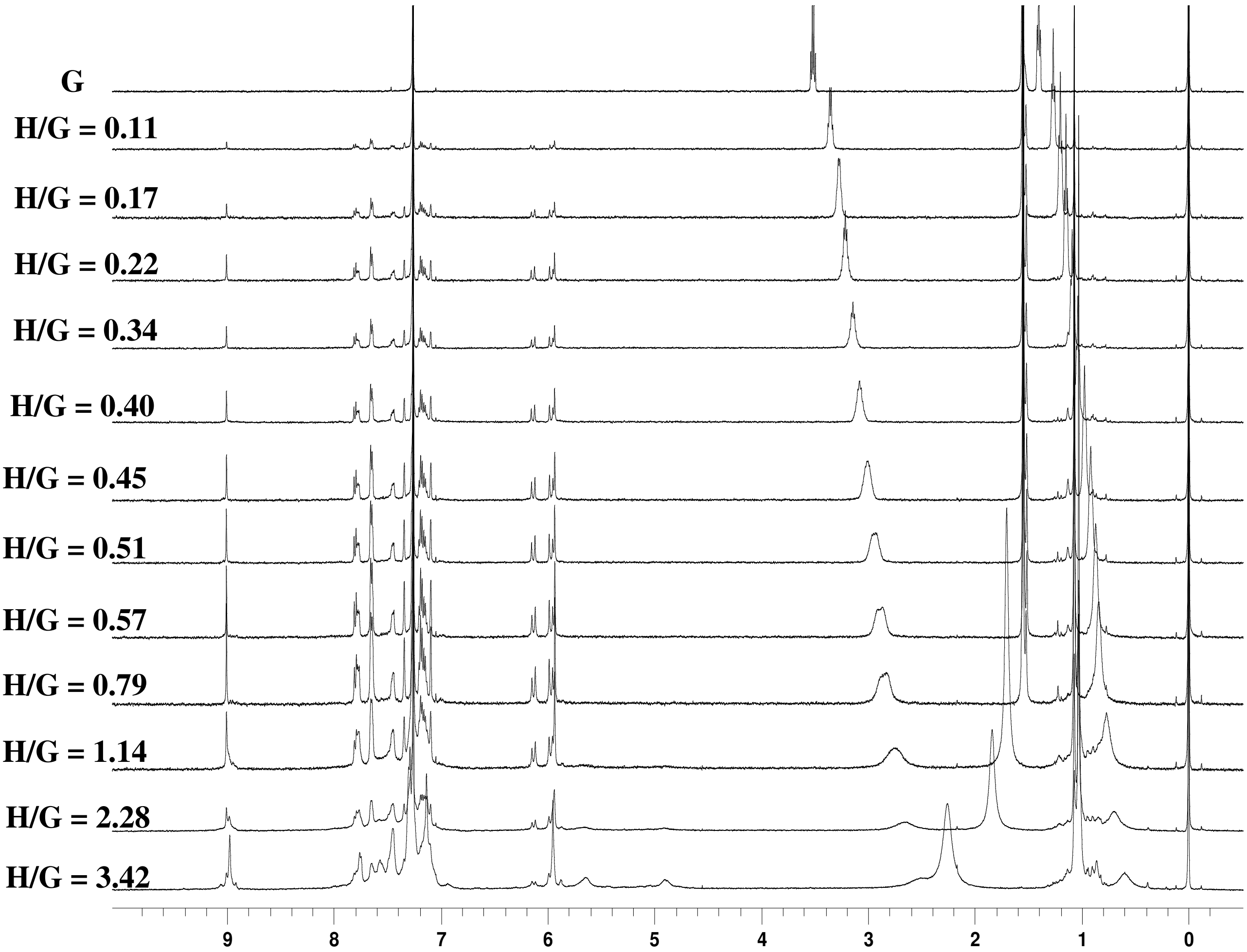
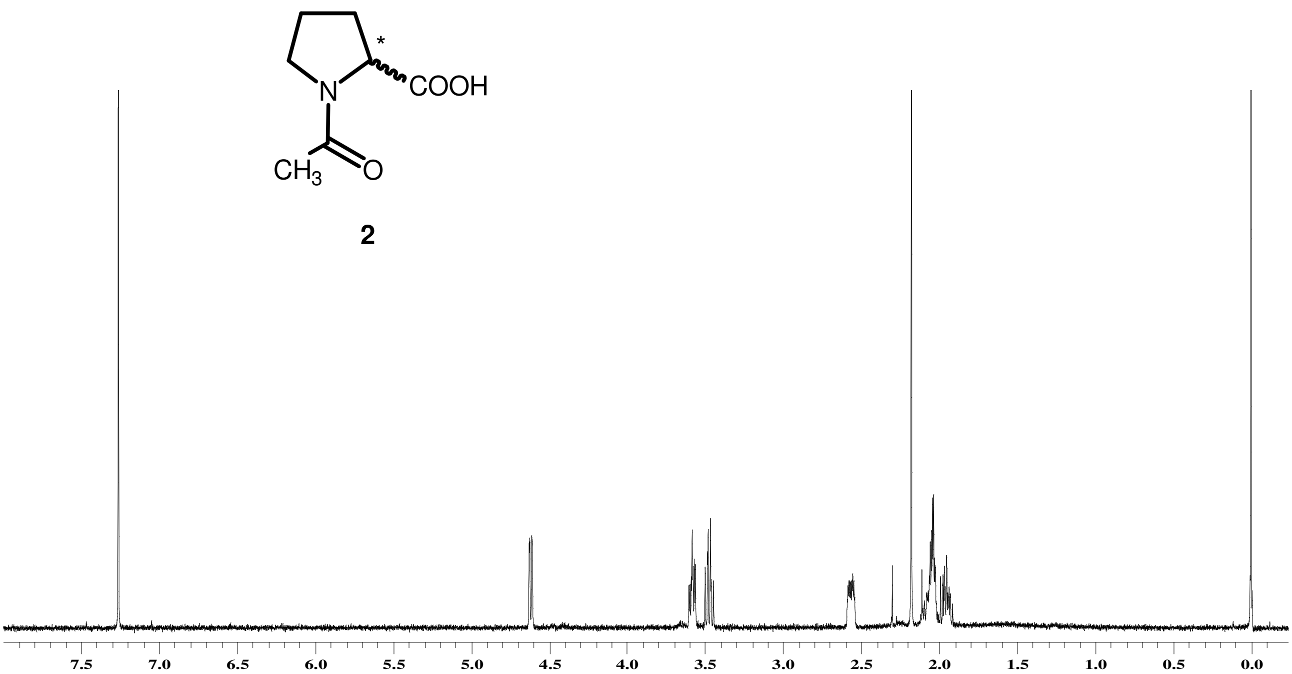
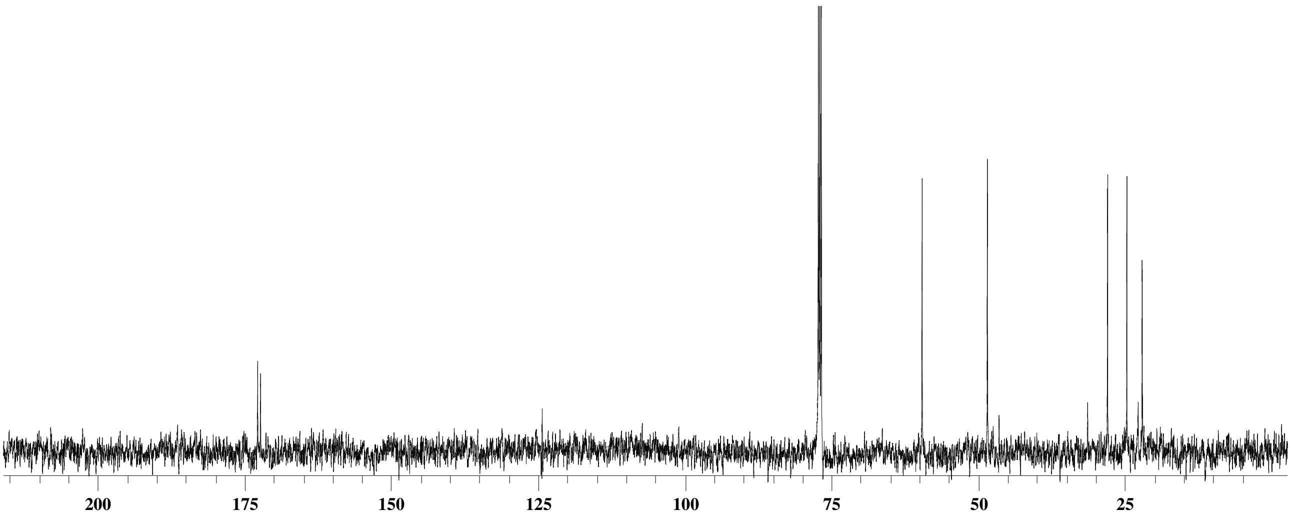


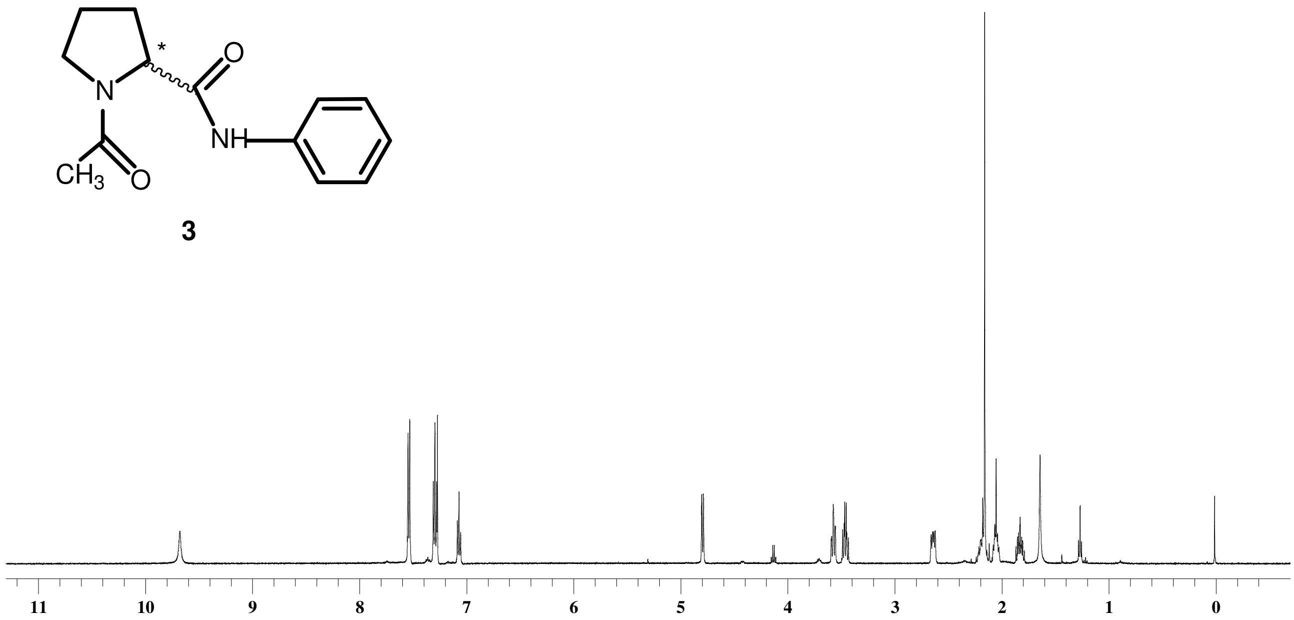
Figure S19. ^{1}H NMR titration spectra of **M40/TEACl** (500 MHz; $CDCl_3$ at 27 °C)



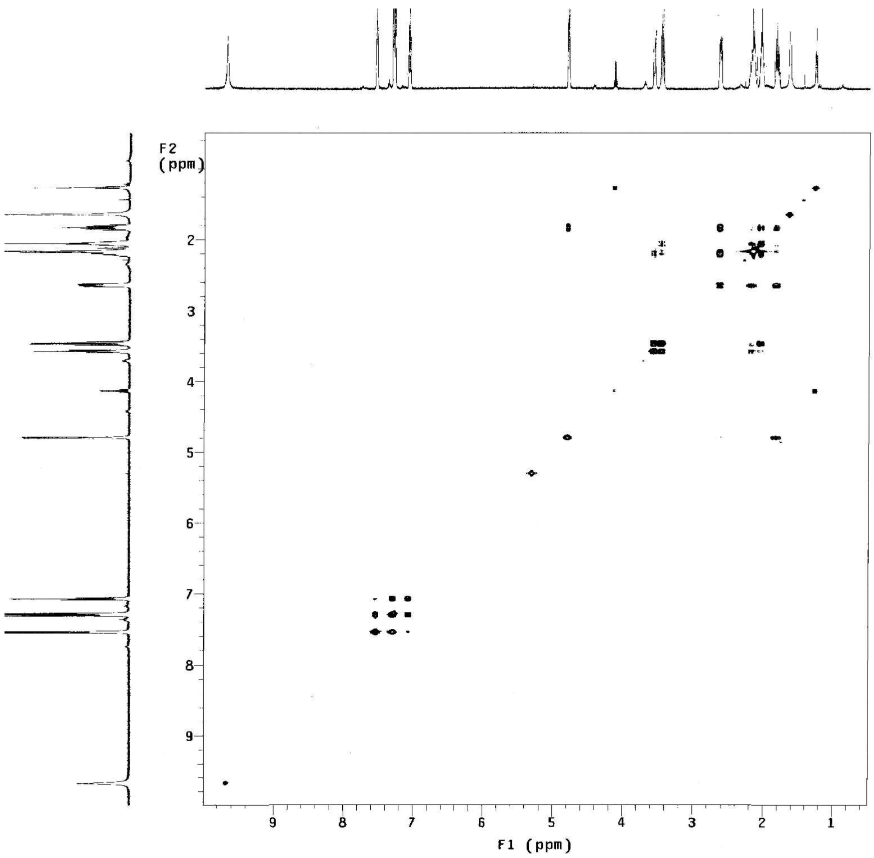
2



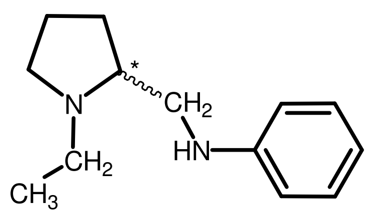
^{1}H NMR and ^{13}C NMR spectra of compound **2** (500 MHz, $CDCl_3$)



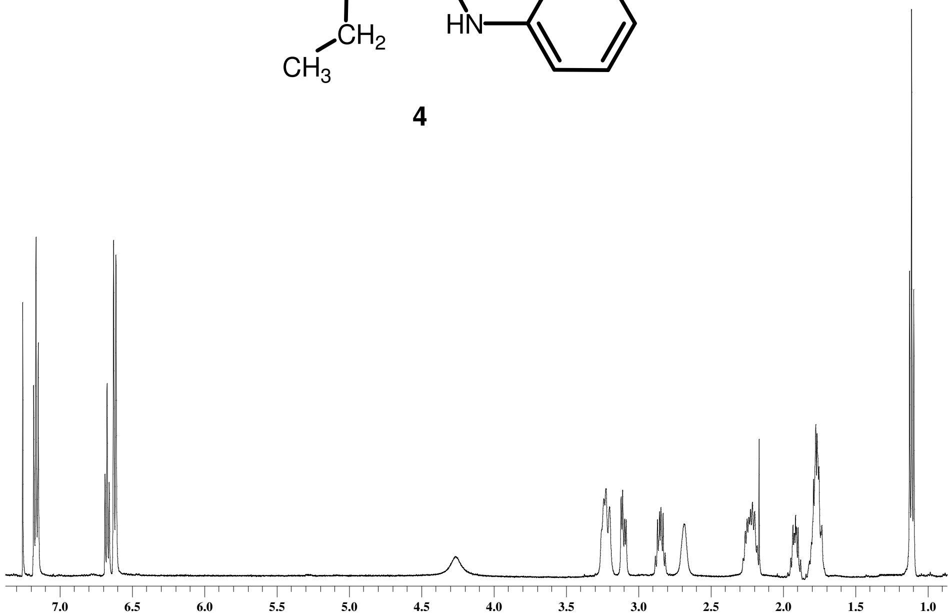
3

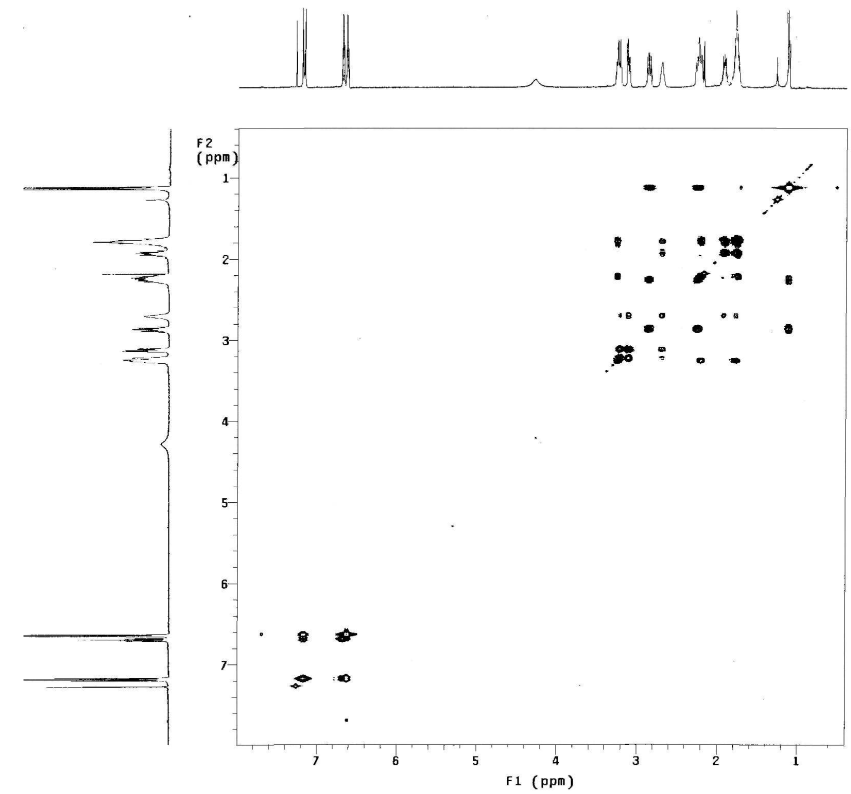


[1]H NMR and 2D NMR gCOSY spectra of compound **3** (500 MHz, $CDCl_3$)

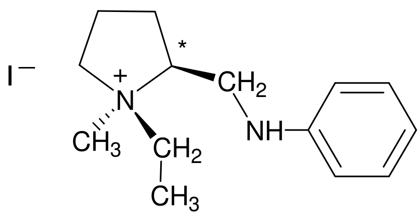


4

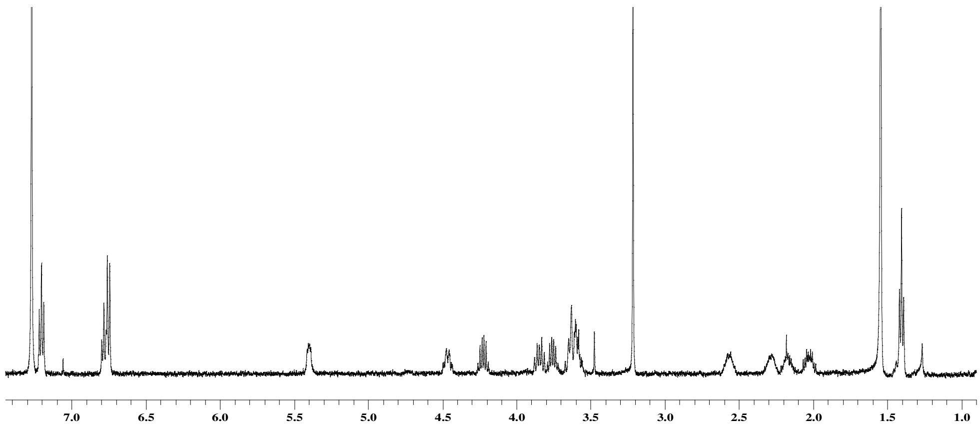


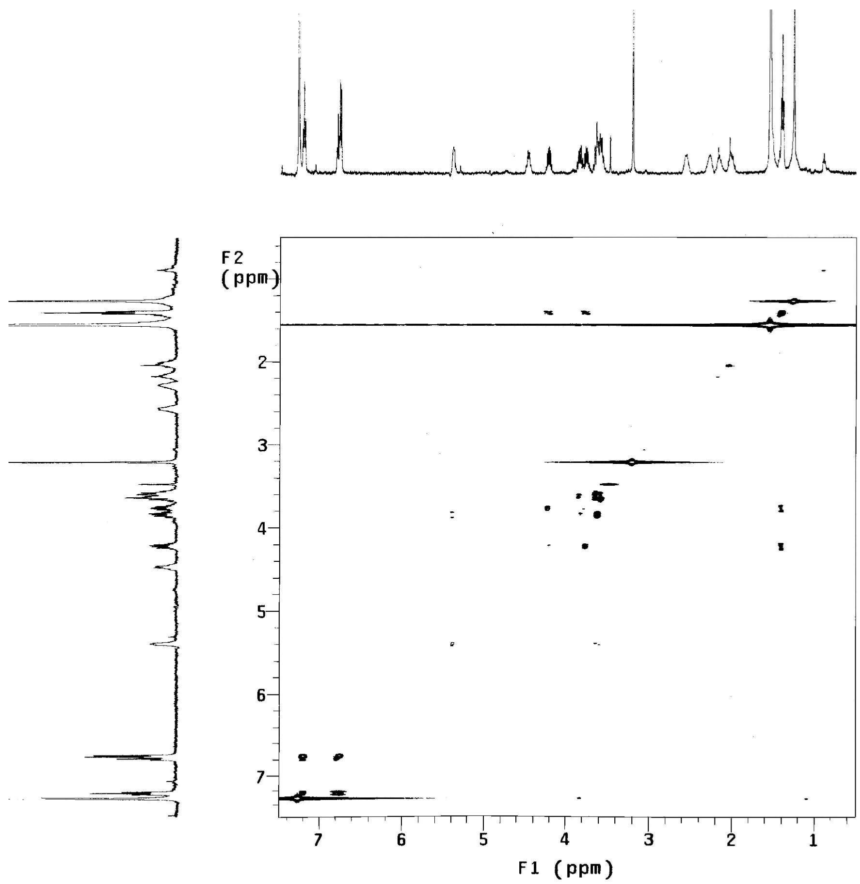


[1]H NMR and 2D NMR gCOSY spectra of compound **4** (500 MHz, $CDCl_3$)

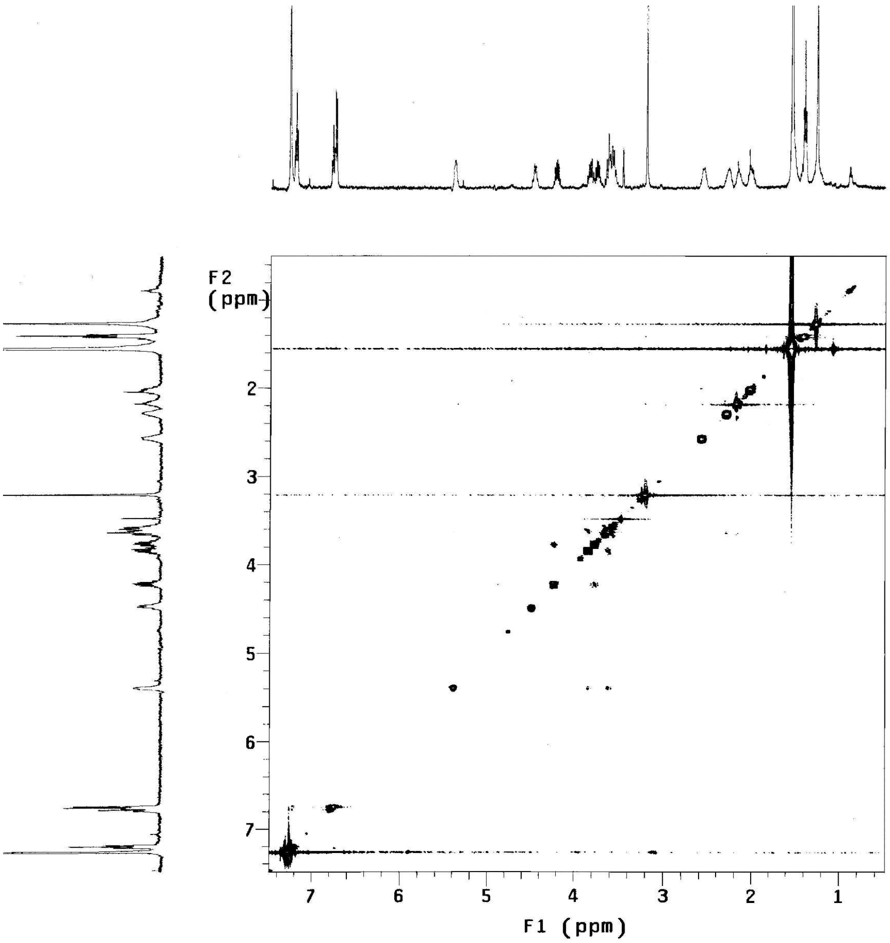


S,S-2

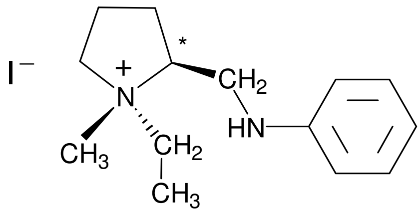




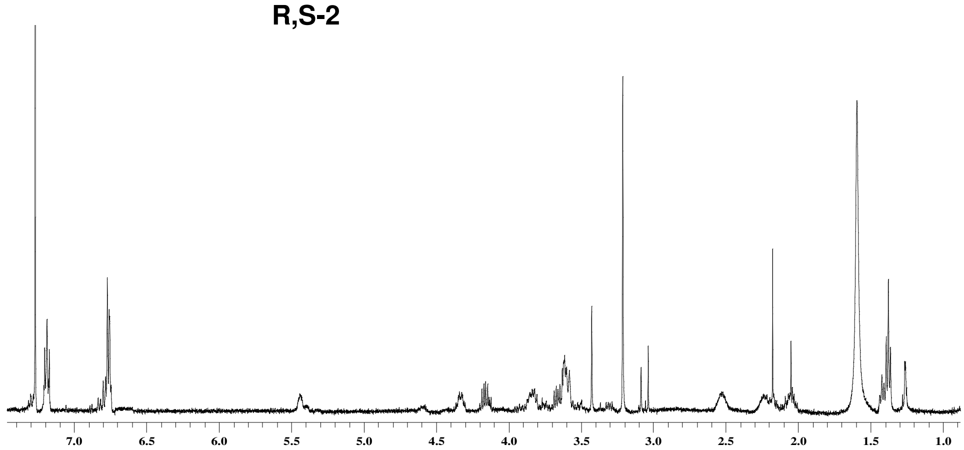
[1]H NMR and 2D NMR gCOSY spectra of compound **S,S-2**(500 MHz, $CDCl_3$)

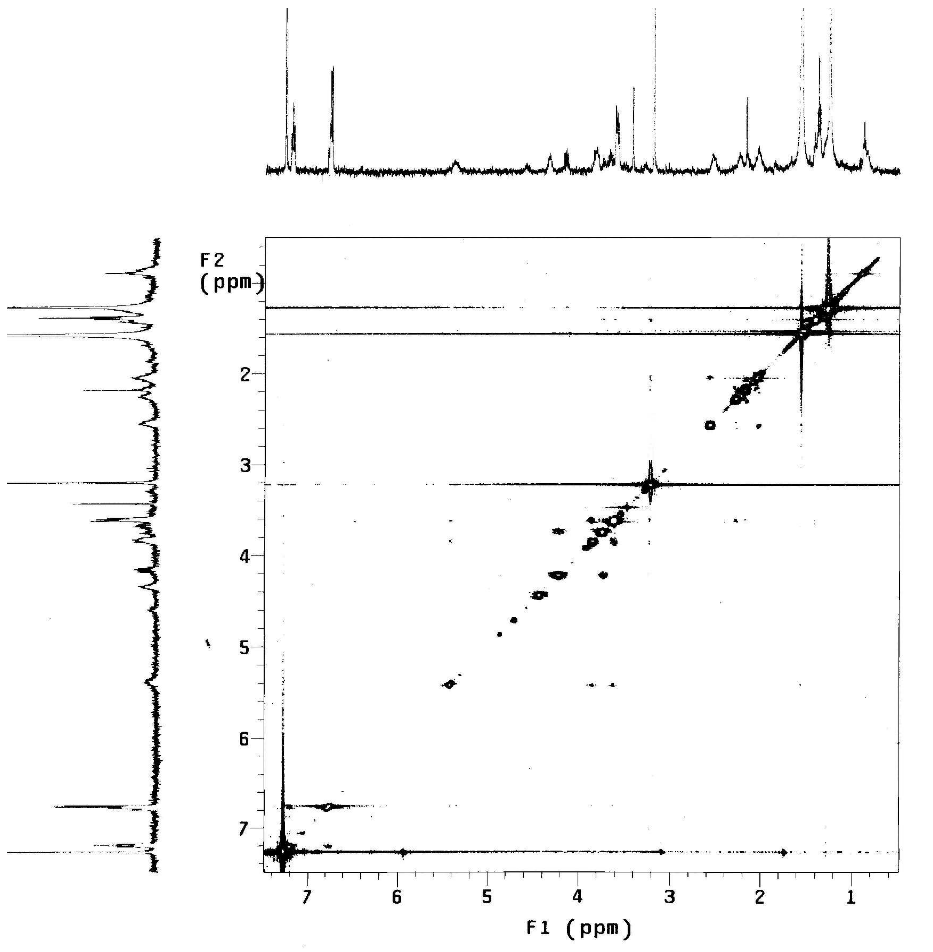


2D NMR NOESY spectrum of compound **S,S-2** (500 MHz, $CDCl_3$)

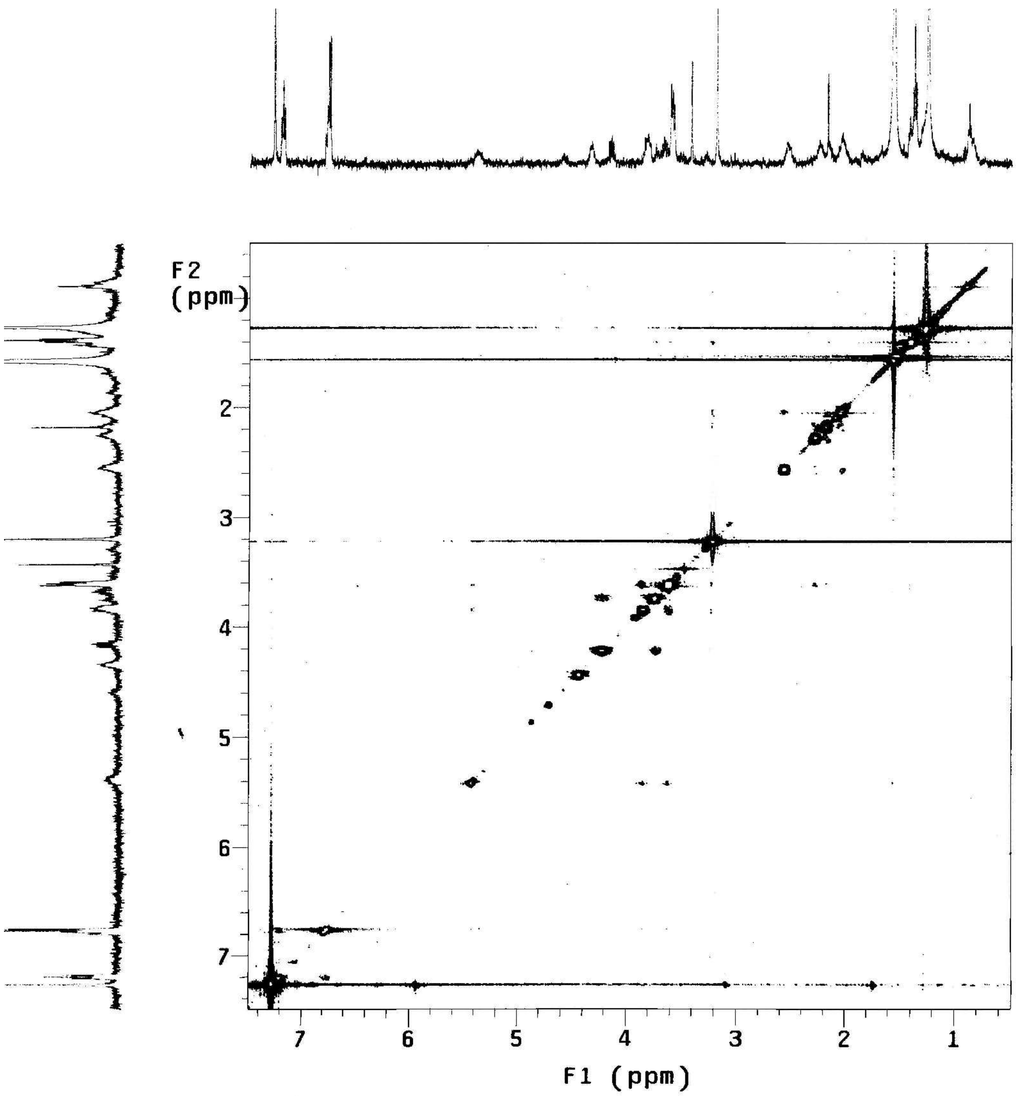


R,S-2

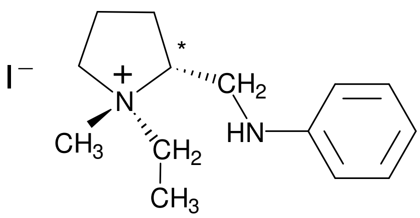




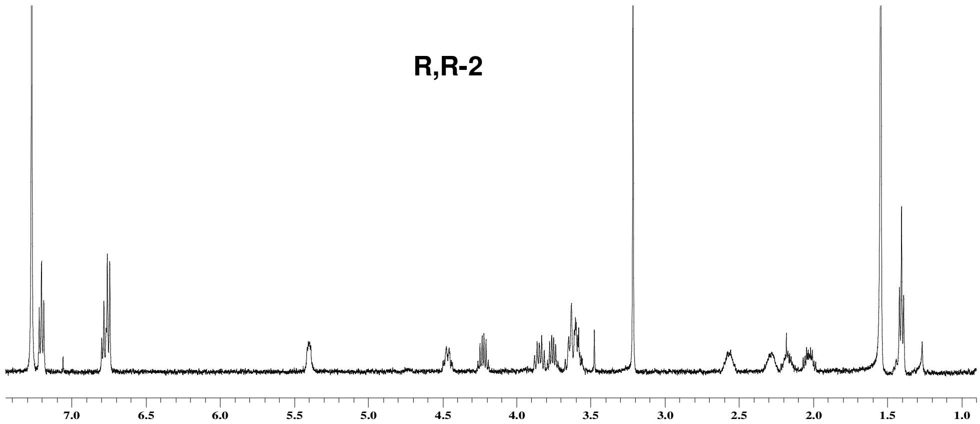
[1]H NMR and 2D NMR gCOSY spectra of compound **R,S-2** (500 MHz, $CDCl_3$)



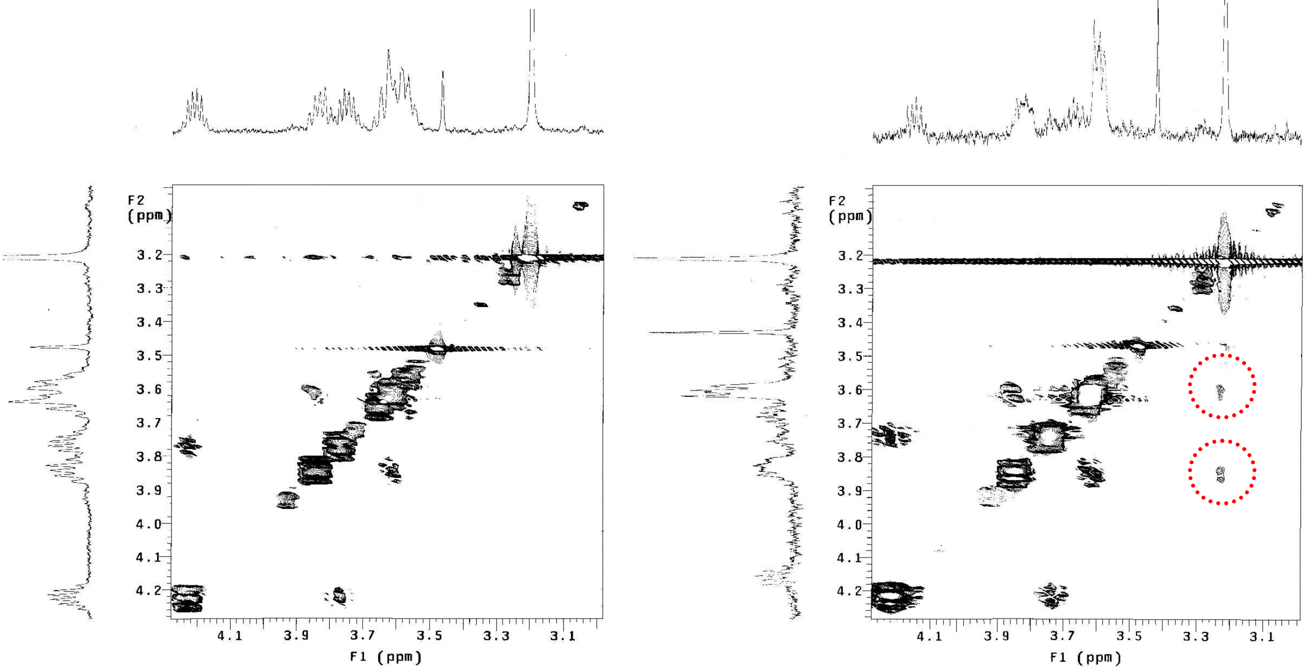
2D NMR NOESY spectrum of compound **R,S-2**(500 MHz, $CDCl_3$)

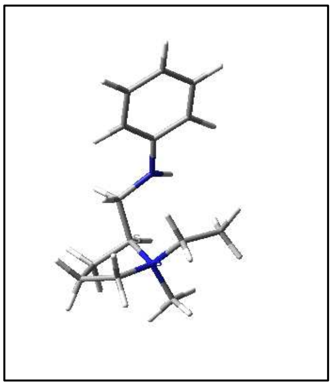


R,R-2

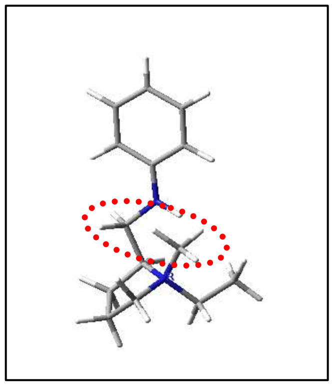


[1]H NMR spectrum of compound **R,R-2** (500 MHz, $CDCl_3$)





S,S-2



R,S-2

Selected portion of 2D-NMR NOESY spectra of compounds **S,S-2** and **R,S-2** to assign absolute configuration.