Supplementary Information of

Directed Molecular Recognition: Design and Synthesis of Neutral Receptors for Biotin to bind both its functional groups

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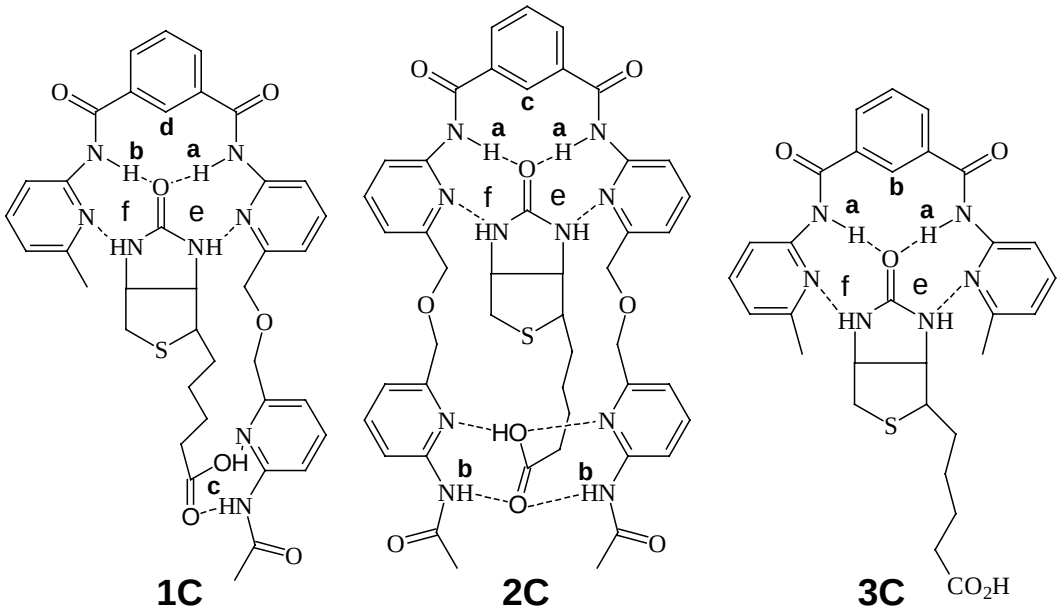
General Experimental Methods:

^{1}H NMR spectra were recorded either on 300 MHz and 500 MHz spectrometers. ^{13}C NMR spectra were recorded on 125 MHz spectrometer. Chemical shifts (δ in ppm) are given from internal solvent $CDCl_3$ (7.26 for 1H and 77.0 for 13C). Unless otherwise mentioned TMS is used as internal standard. UV-VIS spectra were recorded using spectroscopic grade $CHCl_3$.

1. Figure 1: Complex structure of receptors 1, 2 and 3.



2. Figure 2: Energy minimized complex structure; (a) receptor 1 with biotin; (b) receptor 2 (c) receptor 3 with biotin.

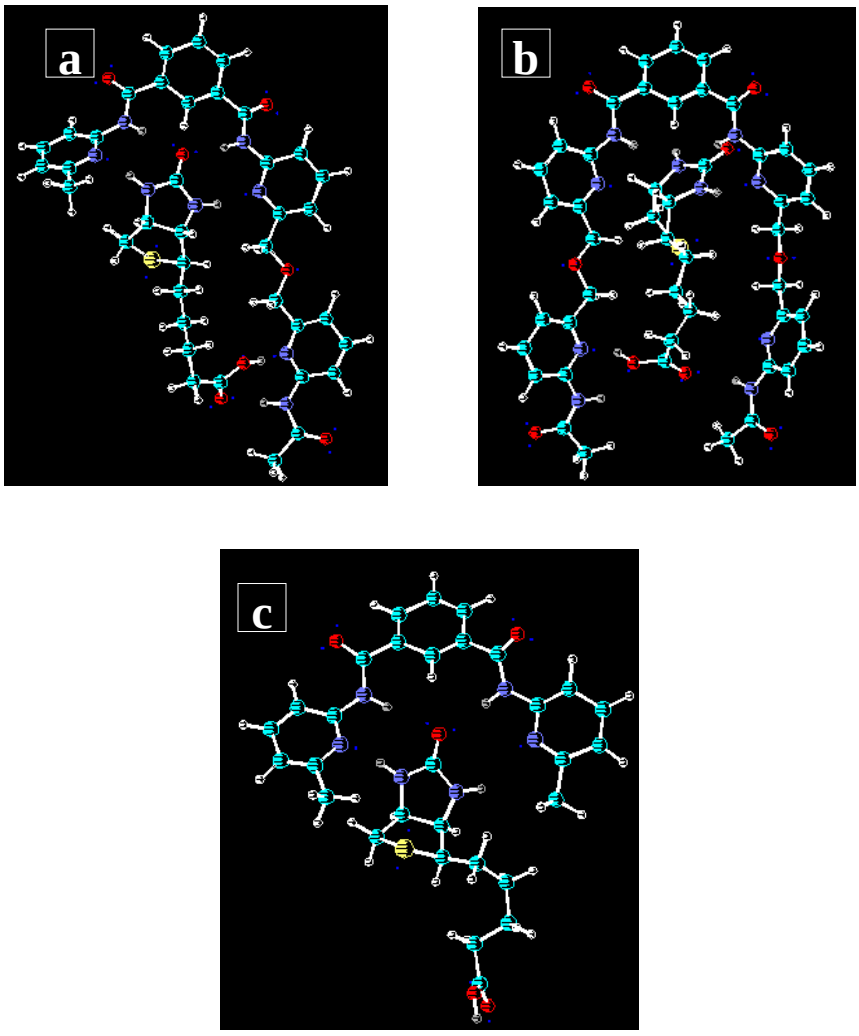


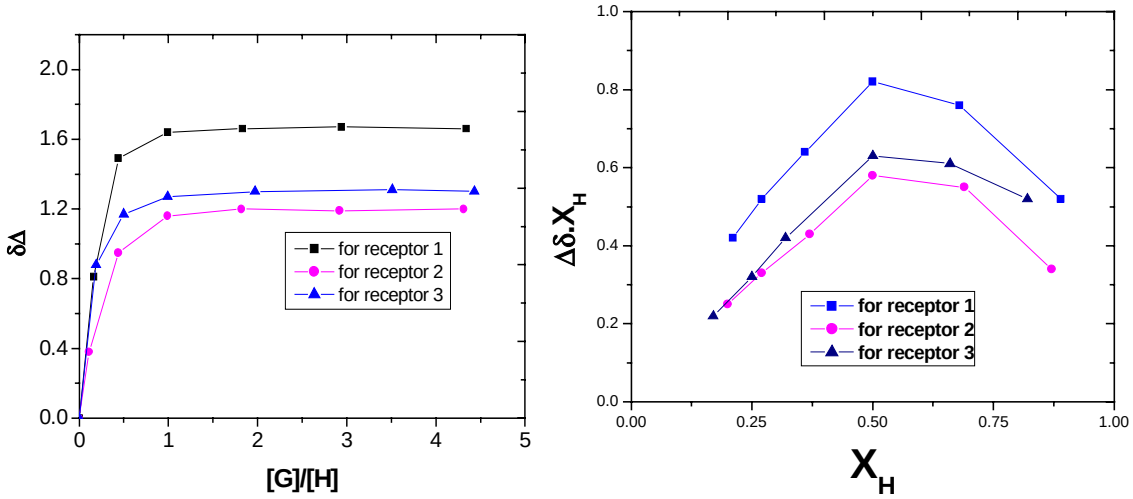
Table 1: Energy values (kJ/mol) of docking complexes of receptors 1, 2 and 3 with biotin.

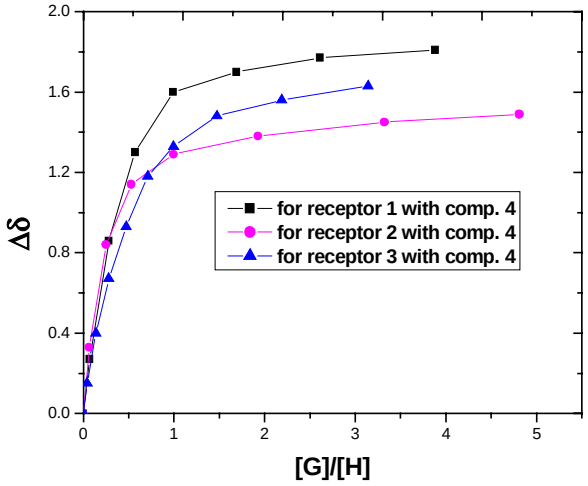
Receptors	**Stabilization Energy of complexes (Receptor with biotin; kJ/mol)**
Receptors **1**	-3.03
Receptors **2**	17.04
Receptors **3**	14.16

4. Table 2. Chemical shifts of different amide and peri protons of receptors 1, 2, 3 and their changes on complexation with biotin and ethyl ester of biotin.

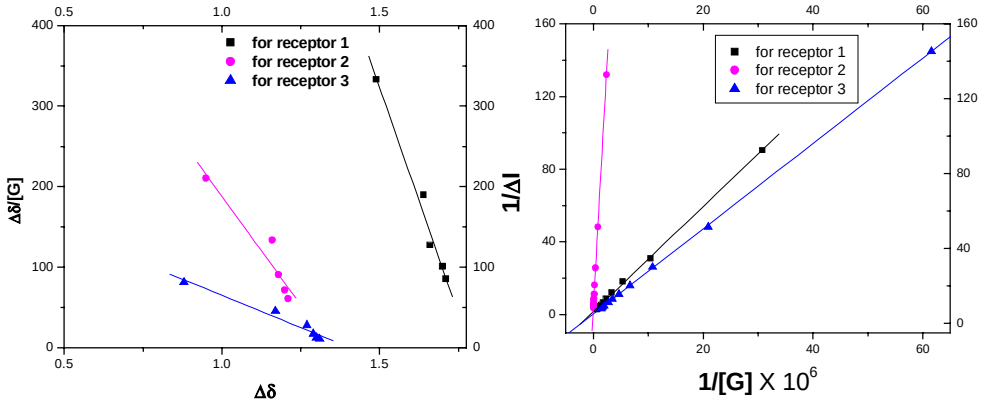
	Complex 1C				Complex 2C			Complex 3C	
	a	**b**	**c**	**Peri(d)**	**a**	**b**	**Peri(c)**	**a**	**Peri(b)**
Receptor Itself	**8.94**	**8.94**	**8.11**	**8.56**	**9.16**	**8.33**	**8.61**	**8.81**	**8.56**
With Biotin	**10.24**	**10.45**	**9.20**	**8.70**	**10.24**	**9.30**	**8.66**	**10.08**	**8.67**
With Biotin Ethyl Ester	**10.12**	**10.18**	**8.33**	**8.68**	**9.94**	**8.37**	**8.67**	**9.99**	**8.66**

4. Figure 3. (a) NMR titration curve; (b) Job's plot of receptors 1, 2 and 3 with biotin from NMR titration in 2% d_6-DMSO in $CDCl_3$. (c) NMR titration curve of receptors 1, 2 and 3 with biotin ethyl ester in $CDCl_3$.





5. Figure 4: Association constant (K_a) calculation curve of receptor 1, 2 and 3 with biotin (a) in 2% d_6-DMSO-$CDCl_3$ by NMR; (b) in $CHCl_3$ by UV-vis. (c) receptors 1, 2 and 3 with biotin ethyl ester in $CDCl_3$.



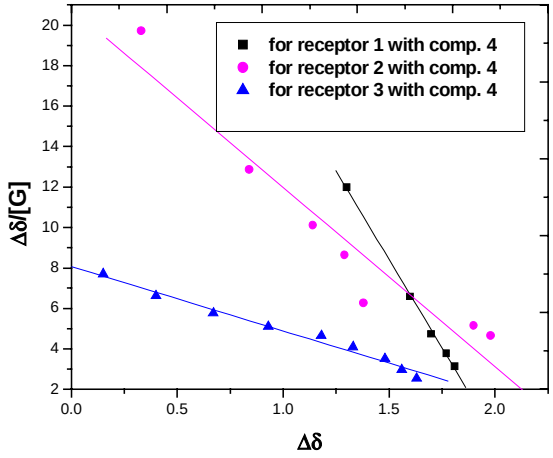
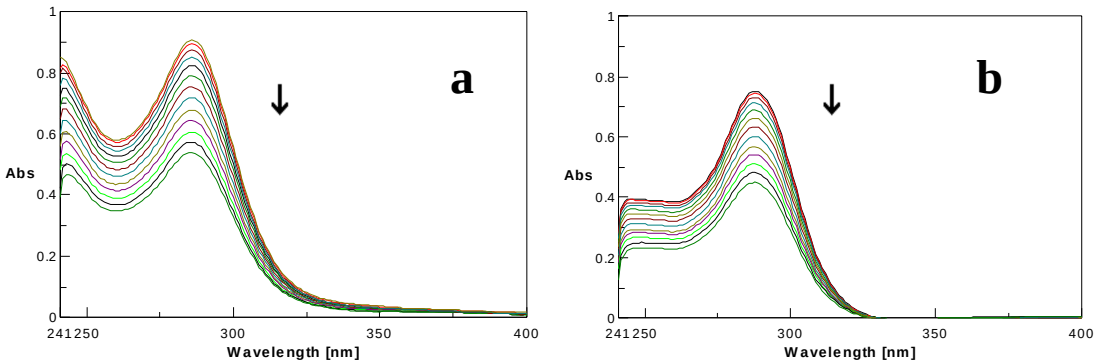
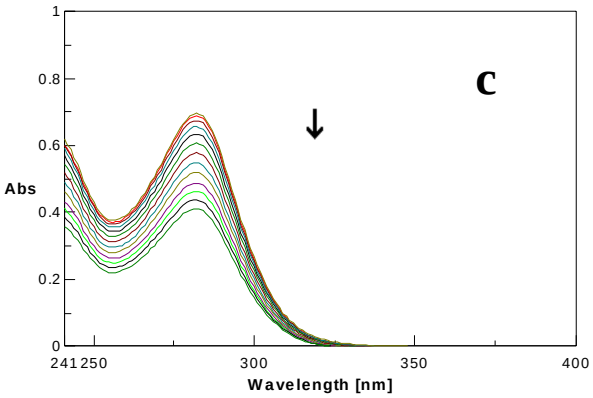


TABLE 2: Association constants (K_a) of receptors **1**, **2**, and **3** respectively with biotin and biotin ethyl ester (compound **4**).

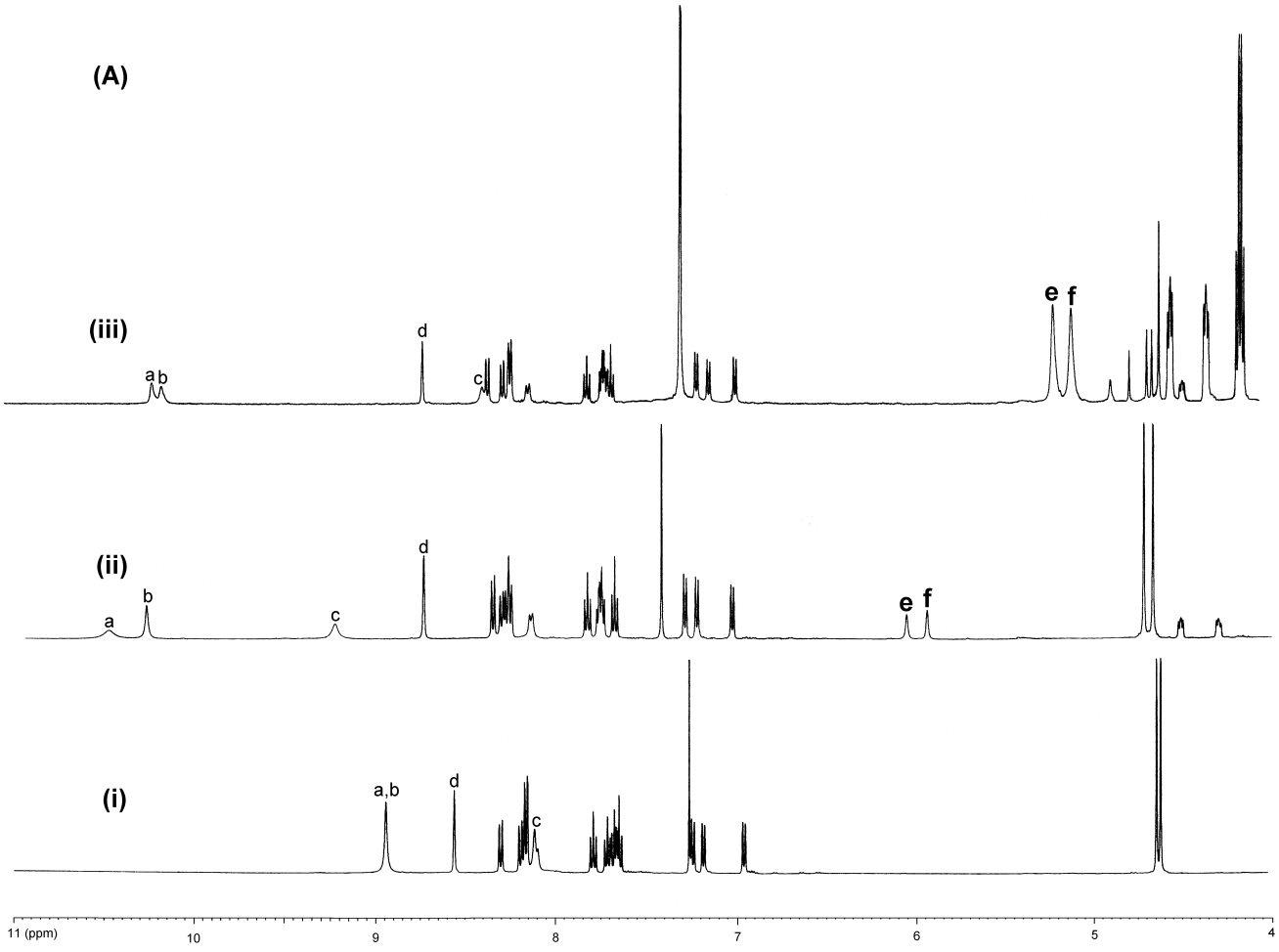
Receptors	UV-VIS method K_a (M^{-1}) ($CHCl_3$)		NMR-method K_a(M^{-1}) (2% d_6 DMSO-$CDCl_3$)		Free energy change ΔG (Kcal mol^{-1})	
	with biotin	with biotin ethyl ester	with biotin	with biotin ethyl ester	with biotin	with biotin ethyl ester
Receptor **1**	4.51 (±0.01) X 10^4	3.33 (±0.01) X 10^4	1.3 (± 0.01) X 10^4	1.74 (± 0.01) X 10^3	-5.60	-4.41
Receptor **2**	2.23 (±0.01) X 10^4	2.24 (±0.01) X 10^3	9.0 (±0.1) X 10^3	8.84 (±0.1) X 10^2	-5.39	-4.01
Receptor **3**	5.23 (±0.01) X 10^3	1.95 (±0.01) X 10^3	2.4 (±0.2) X 10^3	3.18 (±0.2) X 10^2	-4.60	-3.41

6. Figure 4: UV-vis titration spectra; (a) receptors 1, (b) receptor 2; (c) receptor 3 with biotin in $CHCl_3$.

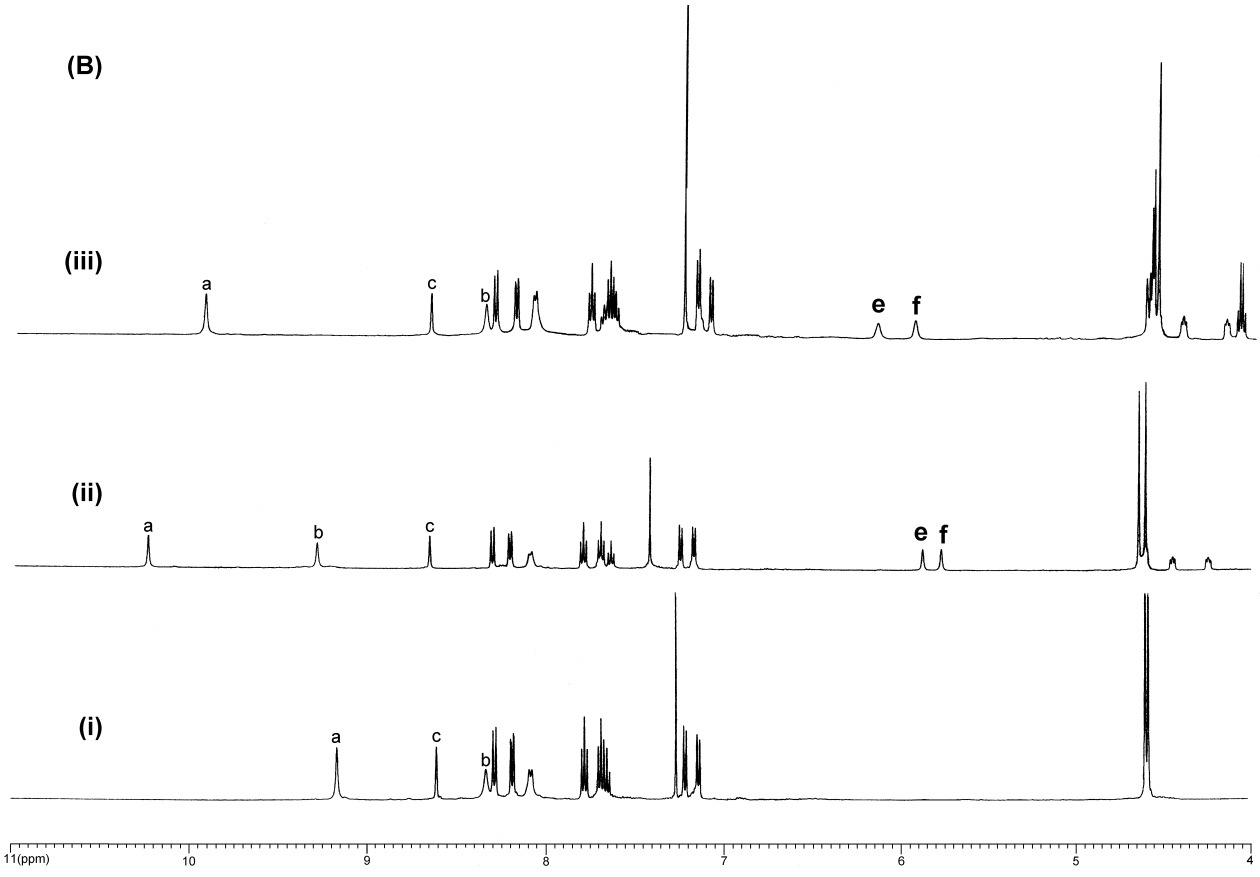




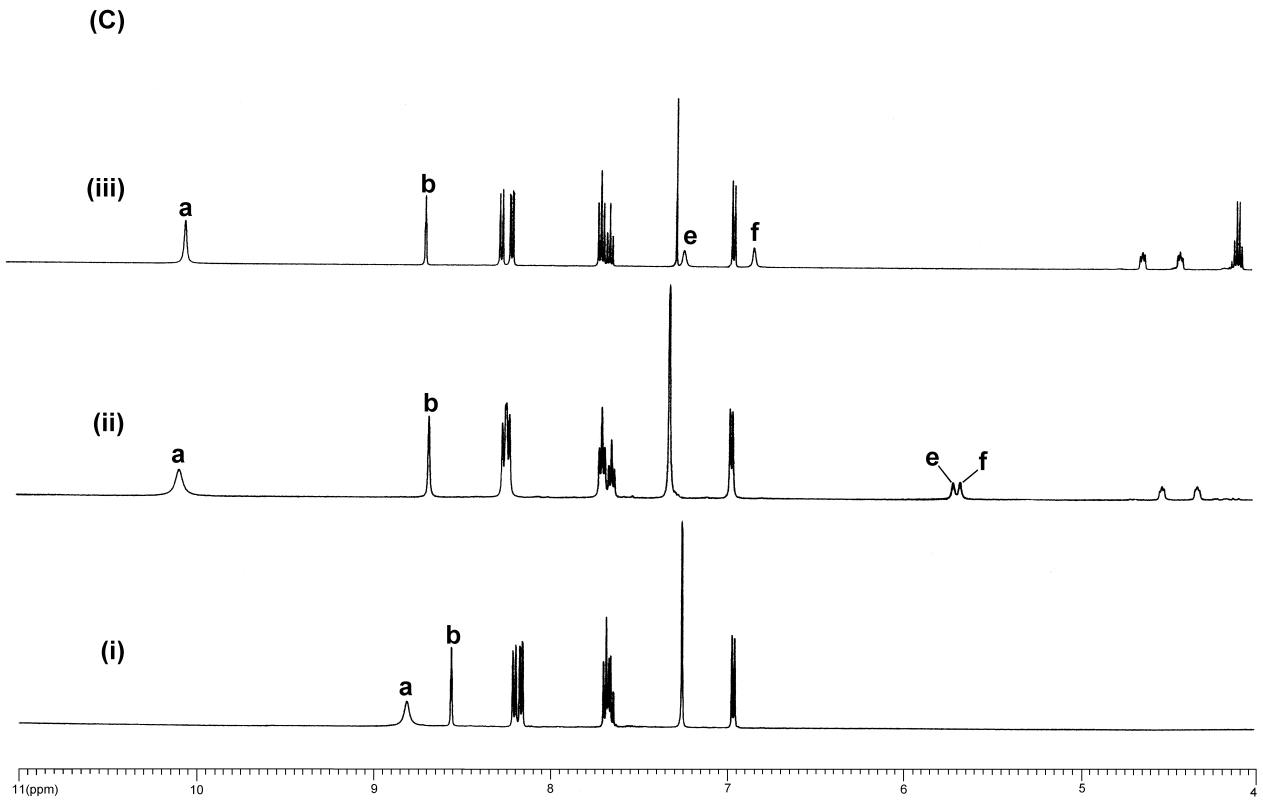
7. (A) NMR spectra of (i) receptor 1, (ii) (1:1) complex between biotin and receptor 1 in 2% d_6-DMSO- $CDCl_3$ (iii) (1:1) complex between ethyl ester of biotin and receptor 1 in $CDCl_3$:



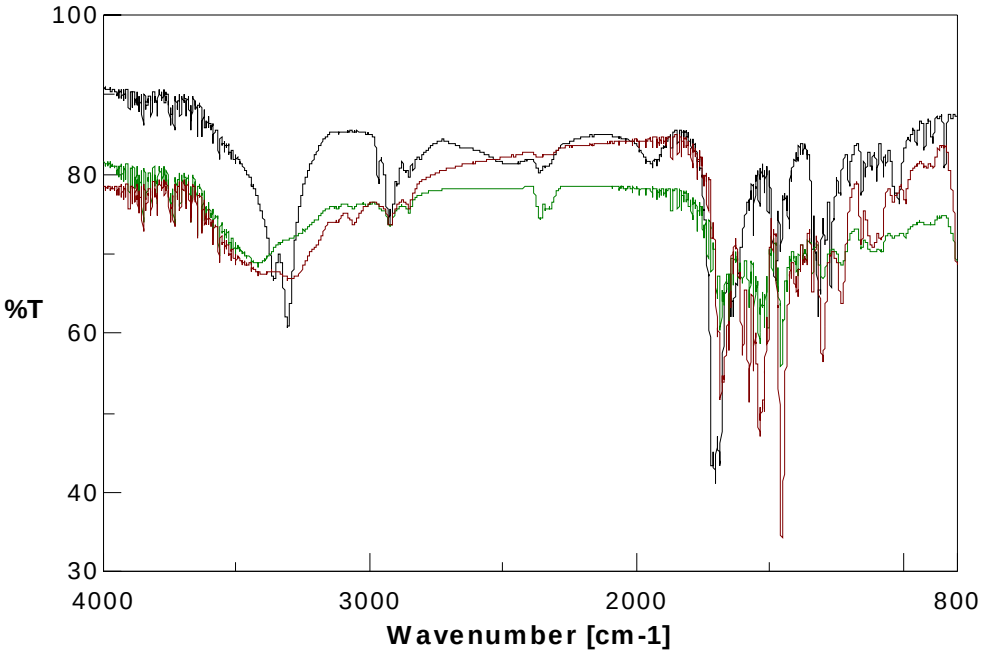
8. (B) NMR spectra of (i) receptor 2, (ii) (1:1) complex between biotin and receptor 2 in 2% d_6-DMSO- $CDCl_3$. (iii) (1:1) complex between ethyl ester of biotin and receptor 2 in $CDCl_3$:



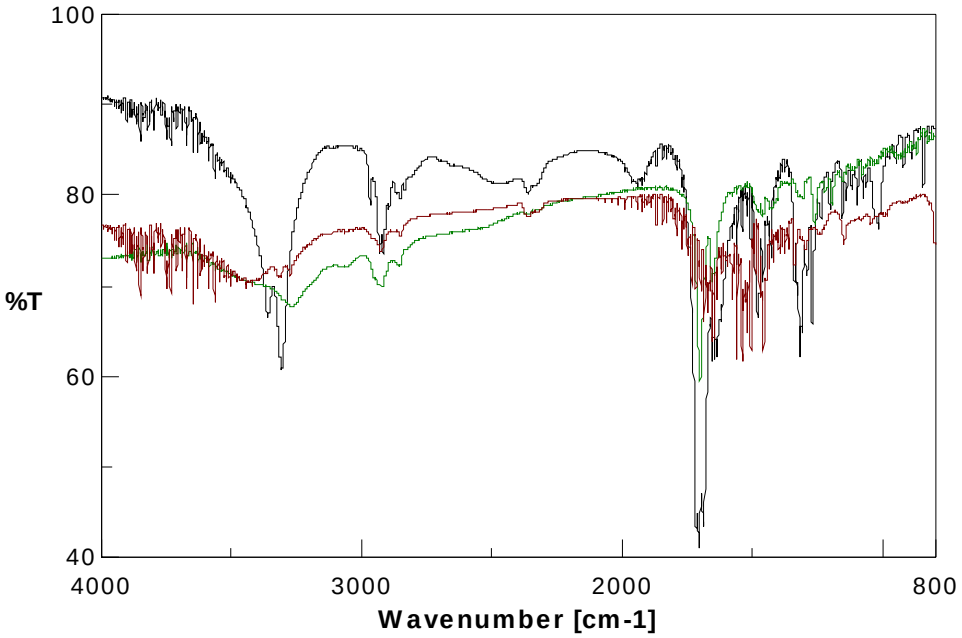
9. (C) NMR spectra of (i) receptor 3, (ii) 1:1 complex between biotin and receptor 3 in 2% d_6-DMSO- $CDCl_3$ (iii) 1:1 complex between ethyl ester of biotin and receptor 3 in $CDCl_3$.



10. FTIR-spectra of biotin (black), receptor 1(gray) and complex of receptor 1 with biotin (green).



11. FTIR-spectra of biotin (black), receptor 2(gray) and complex of receptor 2 with biotin (green).



12. FTIR-spectra of biotin (gray), receptor 3(black) and complex of receptor 3 with biotin (green).