Electronic Supplementary Material (ESI) for RSC Advances.

Facile synthesis and anion binding studies of fluorescein/benzo-12-crown-4 ether based *bis*-dipyrromethane (DPM) receptors

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Experimental section

General information: Chemicals used for the synthesis of functionalized dipyrromethanes **DPM3** & **DPM4** were purchased from the Merck, GLR, CDH, LOBA Chemie, Spectrochem, and SRL chemical companies. For pyrrole related reactions, pyrrole was distilled prior to its usage at atmospheric pressure. In most of the cases solvents were dried through proper procedure and were used freshly under inert (N_2) atmosphere. All the synthesized compounds were isolated by column chromatography by using silica gel of mesh size 100-200. The isolated compounds were characterized and confirmed by means of ^{1}H-NMR, ^{13}C-NMR (Bruker 400 MHz andJeol 500 MHz spectrometers) utilizing $CDCl_3$/DMSO solvent. The ^{1}H-NMR data of known compounds were matched with the reported ones in the literature. The chemical shifts are expressed in δ (ppm) units with respect to tetramethylsilane (TMS). The progress of the reactions was monitored by thin-layer chromatography (TLC), performed on aluminium plates coated with silica gel utilizing various appropriate mixture of ethyl acetate: hexane, and the spots were developed under UV chamber or in iodine chamber. The UV-vis titration measurements were performed in HPLC grade acetonitrile with standard concentration of receptor and guest molecules at 32°C ±2°C, utilizing Perkin Elmer UV-vis spectrophotometer instrument, and the spectra were recorded between 700 and 200 nm. The data was calculated by utilizing Nelder-Mead fit method from online supramolecular Bindfit v0.5 program[1,2].

Synthesis of 4-(1,1-di(1H-pyrrol-2-yl)ethyl)phenol (DPM1): A mixture of *N,N'*-dimethyl urea (DMU) and tartaric acid (TA) in 7:3 molar ratio by total weight 3g was heated to 70°C with moderate stirring until a clear solution is formed. To this clear and hot solution, *p*-hydoxyacetophenone (2 g, 14.65 mmol) and pyrrole (12.16 ml, 188.84 mmol) was added slowly. After complete addition of both the substrates, the reaction was further stirred moderately at same temperature for 16 h. The completion of the reaction was monitored by TLC using 20% ethyl acetate and hexane solution. After completion, the reaction mixture was quenched by addition of water and was cooled to room temperature. The desired compound was separated by simple workup in which aqueous layer was extracted with ethyl acetate (40 ml×3), dried by anhydrous Na_2SO_4. The solvent and the excess pyrrole were removed by concentrated under reduced pressure. The crude products were purified by column chromatography by using 20% ethyl acetate and hexane solution. The desired white product was dried under reduced pressure

characterized by ^{1}H-NMR spectroscopy (2.22 g yield 60%), ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 2H), 7.26 (s, 2H), 6.98 (d, *J* = 7.5 Hz, 2H), 6.73 (d, *J* = 7.5 Hz, 2H), 6.67 (s, 2H), 6.17 (s, 2H), 5.96 (s, 2H), 4.73 (s, 1H), 2.02 (s, 3H). The spectral data are in agreement with the literature.[3]

Synthesis of2-(4-(1,1-di(1*H*-pyrrol-2-yl)ethyl)phenoxy)ethan-1-ol (DPM2): To a stirred solution of **DPM** (0.9 g, 3.5 mmol) in acetonitrile, K_2CO_3 (2.95 g, 6 21 mmol) was added, and the temperature of solution was raised up to 80 ^{o}C, after 30 minutes, 1,2-dibromoethane (4.32 ml, 49.82 mmol) was added slowly and the resulting mixture was refluxed under nitrogen atmosphere for 14 hours. The completion of the reaction was monitored by TLC, and allowed to cool down to room temperature, after that acetonitrile was removed under reduced pressure. To the resulting brownish oily residue, ethyl acetate (50 ml) and water (100 ml) was added, and the organic layer was separated out and washed twice with 50 ml of water. The organic layer was then dried over anhydrous Na_2SO_4, and the solvent was evaporated under vacuum to give a brownish solid, which was purified by column chromatography over silica gel 15% ethyl acetate hexane solution furnished desired white solid compound (0.88 g, 69% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ* 7.77 (s, 2H), 7.07-7.01 (m, 2H), 6.84-6.79 (m, 2H), 6.65 (t, *J* = 2.6, Hz, 2H), 6.16 (d, *J* = 2.7 Hz, 2H), 5.95 (dd, *J* =1.6 Hz, 2H), 4.26 (t, *J* = 6.3 Hz, 2H), 3.62 (t, *J* = 6.3 Hz, 2H), 2.01 (s, 3H).[4]

Synthesis of the DPM3: Fluorescein **16** (0.35g, 1.05 mmol**)**, **DPM2** (0.95g, 2.65 mmol), and K_2CO_3 (0.87 g, 6.26 mmol) were mixed in acetonitrile (50 ml) and the resulting mixture was refluxed under nitrogen atmosphere for overnight. The completion of the reaction was monitored by TLC and allowed the reaction mixture to cool down to room temperature, after that acetonitrile was removed under reduced pressure. The resulting brownish oily residue was extracted with ethyl acetate (50 ml) and water (100 ml) in which the organic layer was separated off and washed twice with 50 ml of water. The organic layer was then dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuum to give a dark red solid, which was purified by column chromatography over silica gel in 25% ethyl acetate hexane solution furnished first eluent as desired orange solid compound **DPM3** (0.43 g, 48%).^{1}H-NMR (400 MHz, DMSO-d_6) *δ* 10.37 (s, 4H), 8.19 (d, *J* = 7.6 Hz, 2H), 7.82 (d, *J* = 31.9 Hz, 4H), 7.47 (s, 2H), 6.83 (d, *J* = 9.7 Hz, 5H), 6.64 (d, *J* = 9.7 Hz, 5H), 5.89 (s, 4H), 5.58 (s, 4H), 4.24 (s, 4H), 3.81 (s, 4H), 1.92 (s, 6H).^{13}C-NMR (101 MHz, $CDCl_3$) *δ* 171.68, 169.23, 152.88, 152.04, 151.55, 136.61, 135.34,

130.09, 128.93, 126.15, 125.25, 124.13, 117.75, 117.60, 116.34, 110.41, 108.50, 107.99, 105.15, 81.77, 38.71, 35.38, 30.04, 26.32. HRMS (ESI) calculated for $C_{56}H_{48}N_4O_7H^+$: 889.3596, found: 889.3625.

Synthesis of the compound 19: To a stirred solution of 4-toluenesulfonyl chloride (7 g, 36.72 mmol) and triethylene glycol (2 ml, 18.36 mmol) in dichloromethane, was added KOH (8.2 g, 146 mmol) in portion wise at 0 ^oC. The resulting mixture was stirred at room temperature for about 12 hours. The progress of the reaction was monitored by TLC, after completion of reaction, water was added to the reaction mixture and the organic layer was separated out and further washed with brine solution twice. the crude mixture was purified by column chromatography to deliver the desired white solid product **19** (5.6 g) in 70% yields.[5]

Synthesis of the benzo-12-crown-4 (21): To a stirred solution of catechol (0.5 g, 4.54 mmol) and Bu_4NI (25 mole%) in toluene (50 ml), was added 50% aq. NaOH (50 ml) at 60 °C. After 30 minutes, the solid ditosylate (**19**) (2.0 g, 4.54 mmol) was added and the resulting mixture was kept for stirring at the same temperature for 24 hours. Completion of the reaction was monitored by using TLC (30% ethyl acetate &hexane solution). After reaction completion, the reaction mixture was cooled to room temperature and the solvent was concentrated under reduced pressure. The brown residue was purified through column chromatography by utilizing 30% ethyl acetate and hexane solution, and the first eluent was concentrated to give the desired product **21** in (0.11 g) 11% yield.[6]^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.06–6.85 (m, 4H), 4.22–4.17 (m, 4H), 3.92–3.86 (m, 4H), 3.82 (s, 4H).

Synthesis of the 4,5-dibromomethyl benzo-12-crown-4 (22): To the stirred solution of benzo-12-crown-4 (0.5 g,2.22 mmol), and paraformaldehyde (0.26 g, 8.91 mmol) in 20 ml dichloromethane, 2 ml HBr/AcOH (30%) was added carefully at room temperature, and the resulting mixture was stirred at refluxing temperature under nitrogen atmosphere for about 12 hours. The completion of the reaction was monitored by TLC tracking, after completion; the reaction mixture was poured into ice-water and neutralized by the addition of saturated solution of K_2CO_3. The neutralized solution was extracted with dichloromethane and the organic layer was separated out. The solution was dried by addition of Na_2SO_4 and the solvent was concentrated under reduced pressure. The brownish residue was further purified by column

chromatography to afford the desired product in (0.5 g) 55% yield.[7] ^{1}H-NMR (500 MHz, $CDCl_3$) δ6.95 (s, 2H), 4.58 (s, 4H), 4.18 (t, *J*=54H), 3.85–3.77 (m, 8H).

Synthesis of the benzo-12-crown-4 based *bis*-dipyrromethane (DPM4): To a stirred solution of **DPM** (0.1 g, 0.24 mmol) in acetonitrile, K_2CO_3 (0.169g, 1.22 mmol) was added, and the temperature of solution was raised up to 80 ^{o}C, after 30 minutes, 4,5-dibromomethyl benzo-12-crown-4 **22** (0.136 g, 0.53 mmol) was added slowly and the resulting mixture was refluxed under nitrogen atmosphere for 12 hours. The completion of the reaction was monitored by TLC, and allowed to cool down to room temperature, after that acetonitrile was removed under reduced pressure. To the resulting brownish oily residue, ethyl acetate (50 ml) and water (100 ml) was added, and the organic layer was separated out, washed twice with 50 ml of water. The organic layer was then dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuum to give a brownish solid, which was purified by column chromatography over silica gel using 15% ethyl acetate/hexane to furnish the desired creamy colored solid **DPM4** in (0.11 g), 60% yield.^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 4H), 7.10 (s, 2H), 7.04–6.97 (m, 4H), 6.88–6.81 (m, 4H), 6.65 (td, *J* = 2.7, 1.5 Hz, 4H), 6.15 (q, *J* = 2.9 Hz, 4H), 5.95 (td, *J* = 3.1, 1.6 Hz, 4H), 5.02 (s, 4H), 4.22–4.15 (m, 4H), 3.87–3.81 (m, 4H), 3.78 (s, 4H), 1.3–1.23 (m, 6H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 157.19, 150.34, 140.02, 137.70, 129.64, 128.59, 119.20, 116.92, 114.37, 108.23, 106.18, 71.87, 71.15, 69.89, 67.60, 44.14, 28.98. HRMS (ESI) calculated for $C_{46}H_{48}N_4O_6H^+$: 753.3647, found: 753.3690.

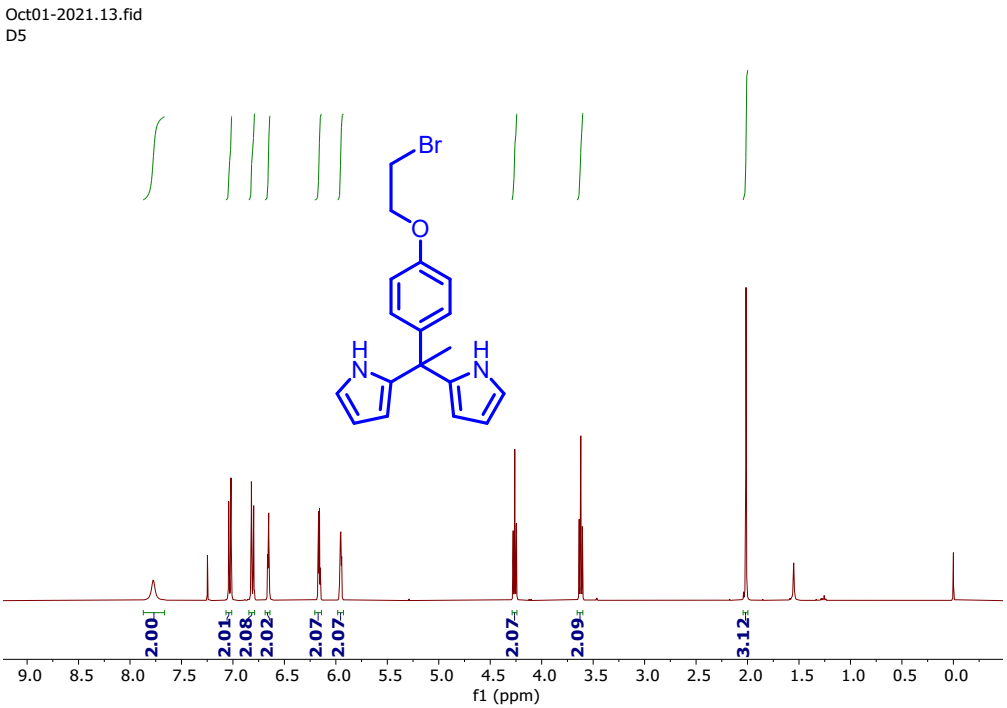


Figure S1. [1]H-NMR of 2-(4-(1,1-di(1*H*-pyrrol-2-yl)ethyl)phenoxy)ethan-1-ol (**DPM2**) recorded in $CDCl_3$

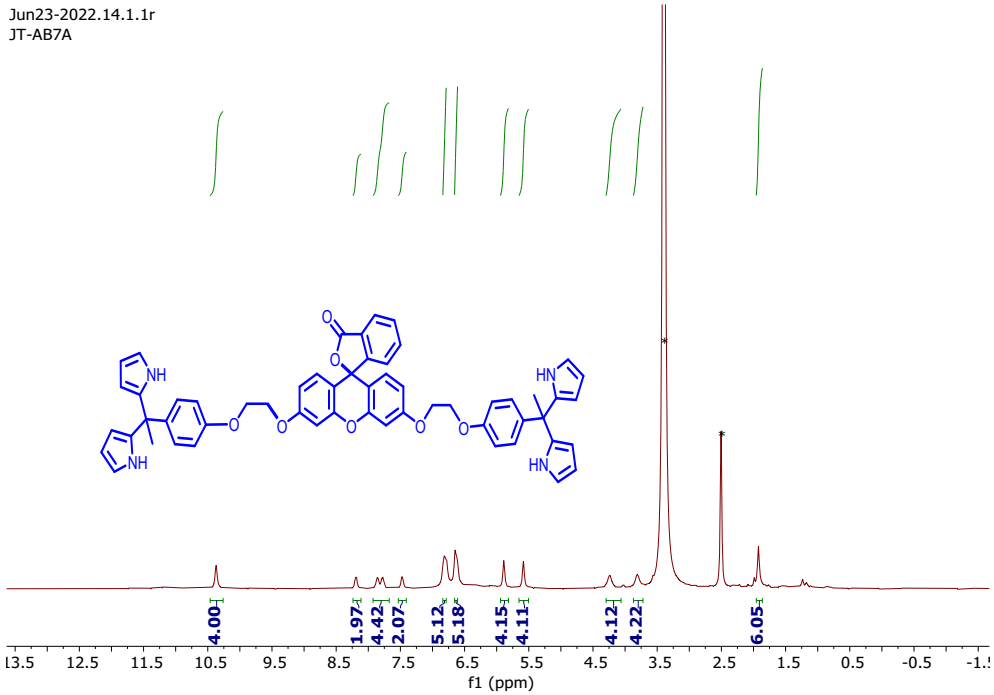


Figure S2. [1]H-NMR of fluorescein based *bis*-dipyrromethane derivative (**DPM3**) recorded in DMSO-d_6

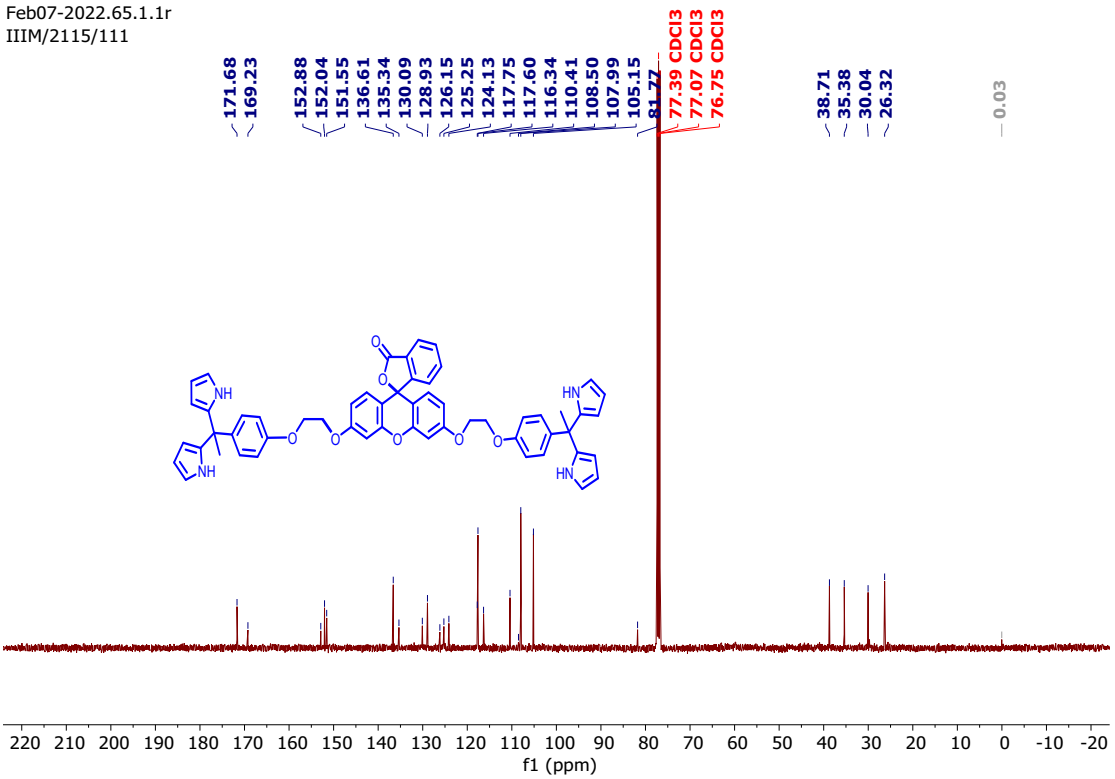


Figure S3. ^{13}C-NMR of fluorescein based *bis*-dipyrromethane (**DPM3**) recorded in $CDCl_3$.

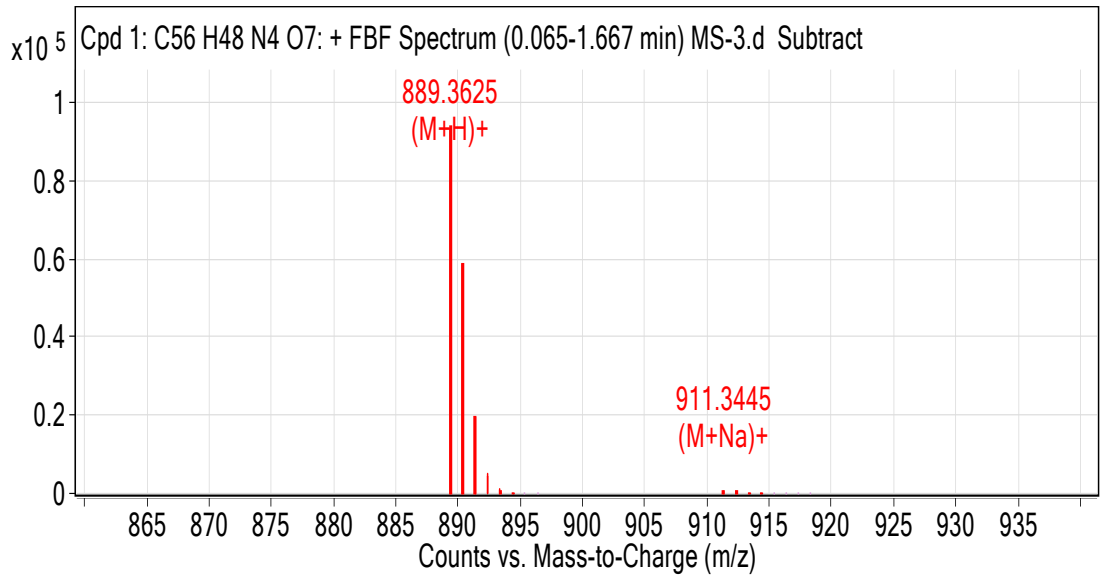


Figure S4. HRMS of fluorcein based *bis*-dipyrromethane derivative (**DPM3**).

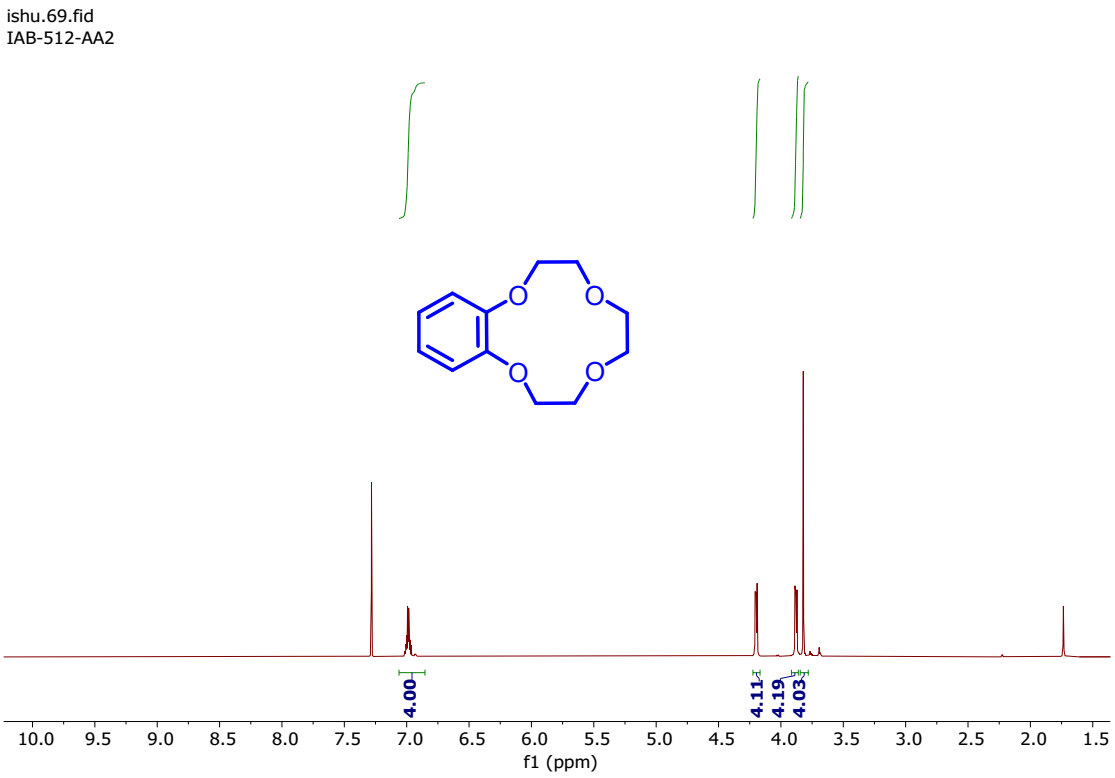


Figure S5. ^{1}H-NMR of benzo-12-crown-4 (**21**) recorded in $CDCl_3$

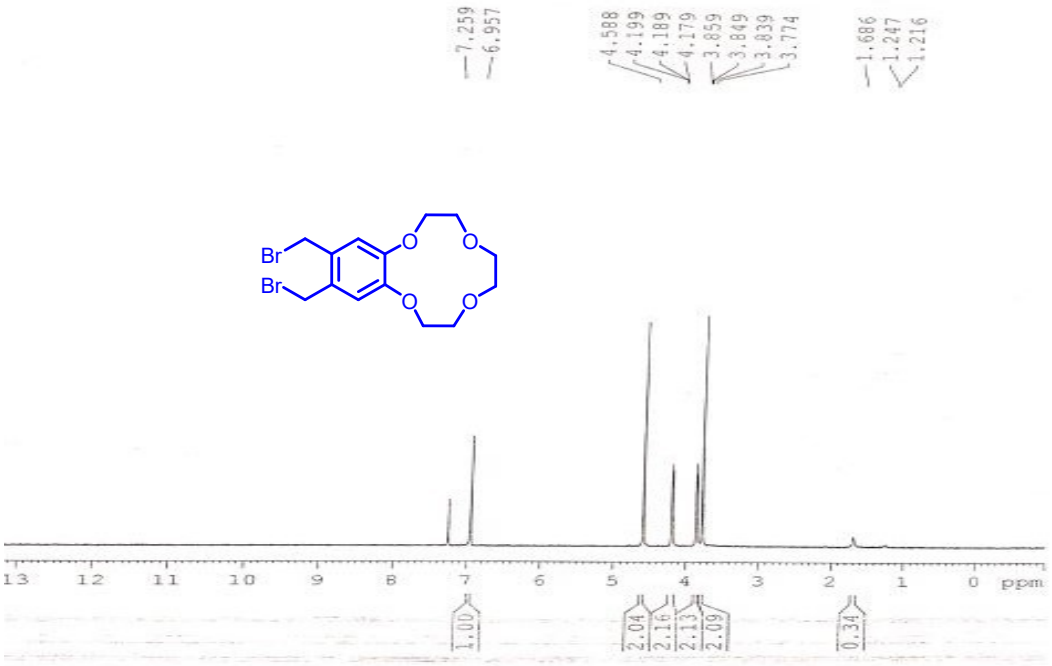


Figure S6. ^{1}H-NMR of 4,5-dibromomethyl benzo-12-crown-4 (**22**) recorded in $CDCl_3$.

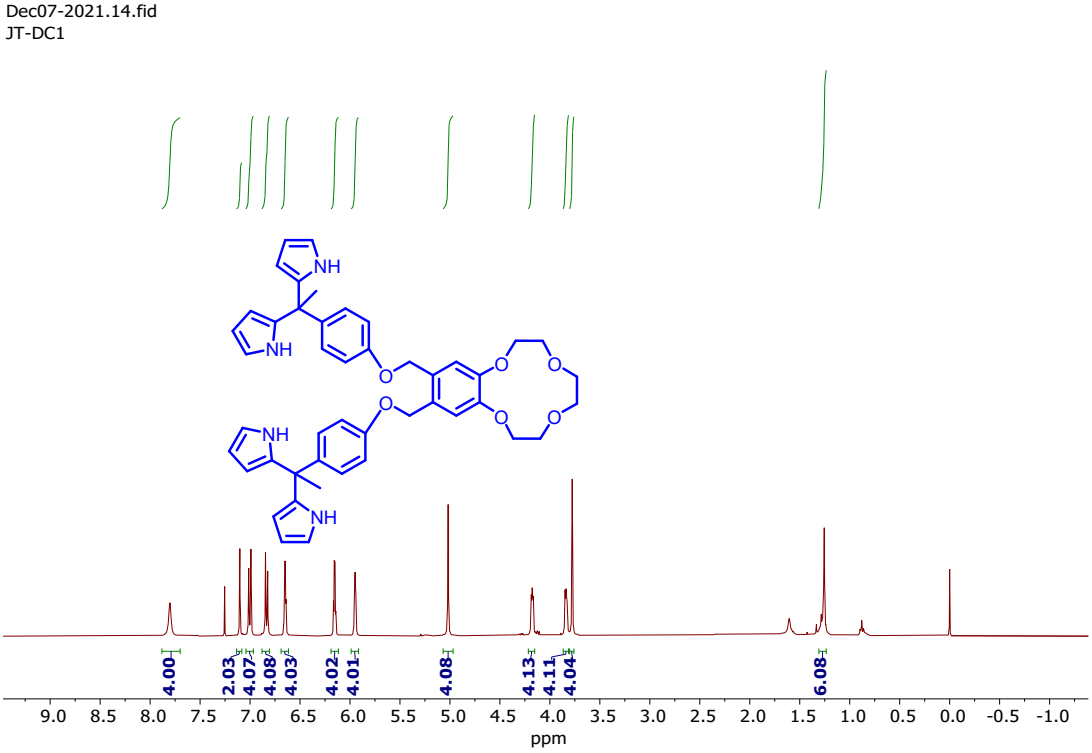


Figure S7. ^{1}H-NMR of benzo-12-crown-4 based *bis*-dipyrromethane (**DPM4**) recorded in $CDCl_3$

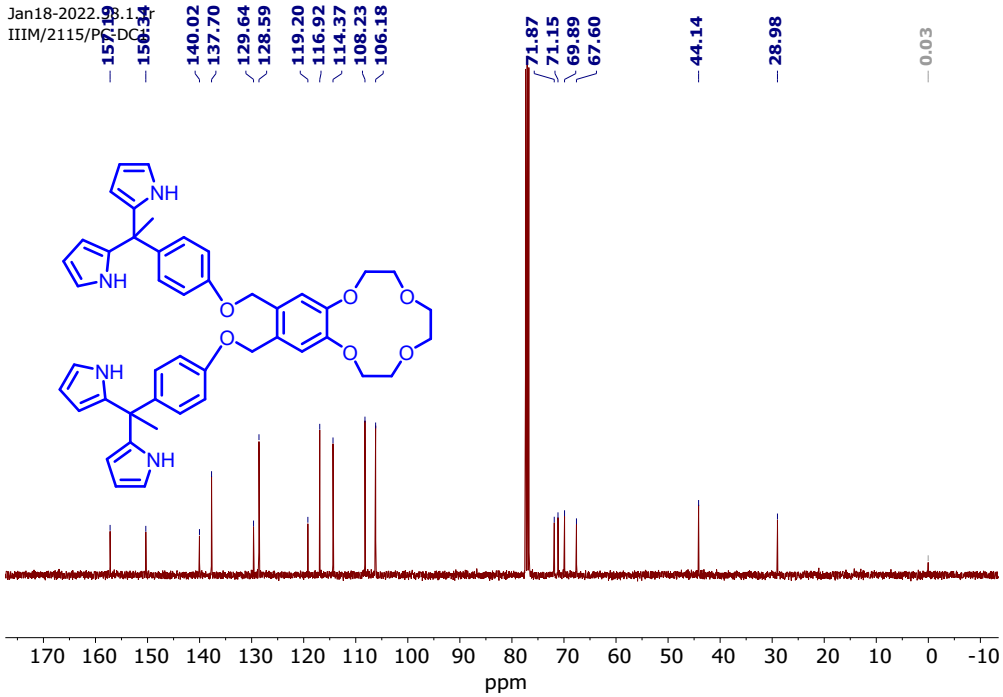


Figure S8. ^{13}C-NMR of benzo-12-crown-4 based *bis*-dipyrromethane (**DPM4**) recorded in $CDCl_3$.

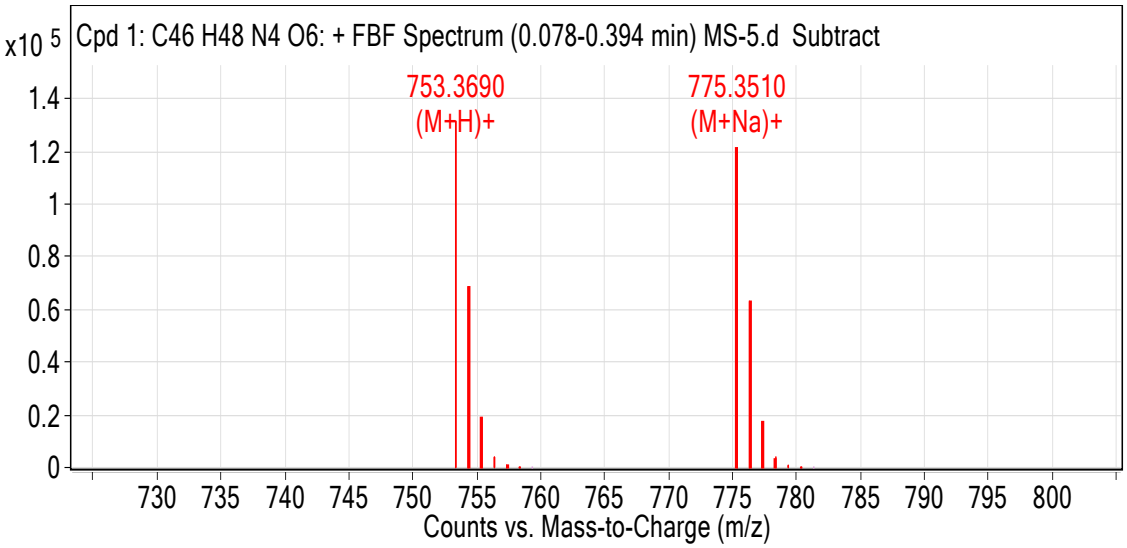


Figure S9. HRMS of benzo-12-crown-4 based *bis*-dipyrromethane (**DPM4**).

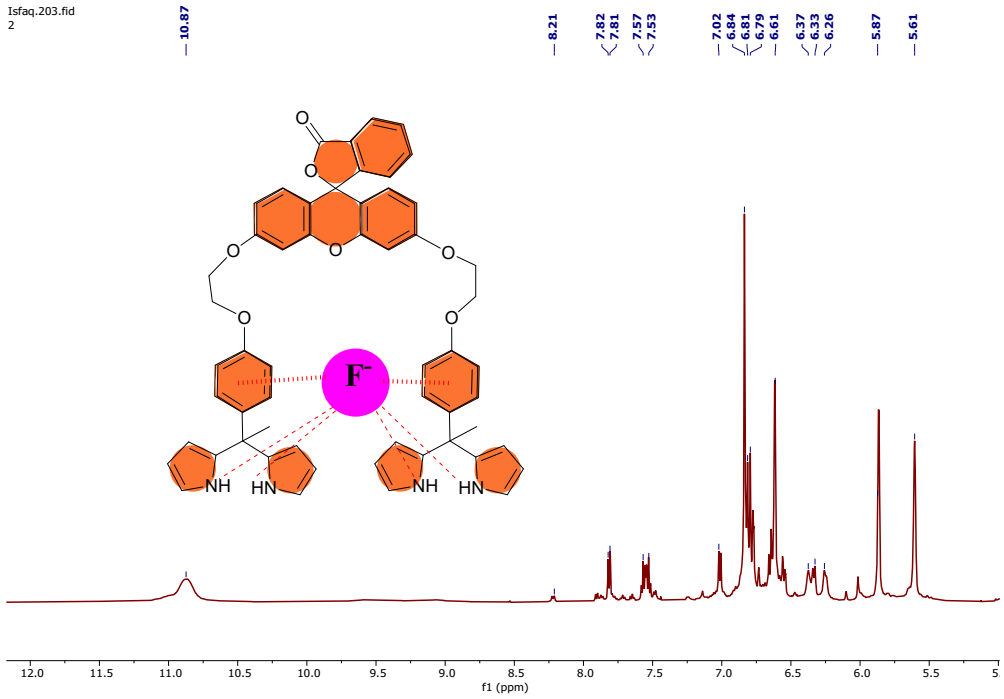


Figure S10. ^{1}H-NMR of complex *bis*-dipyrromethane with fluoride (**DPM3@F^{-}**) recorded in DMSO-d^{6}

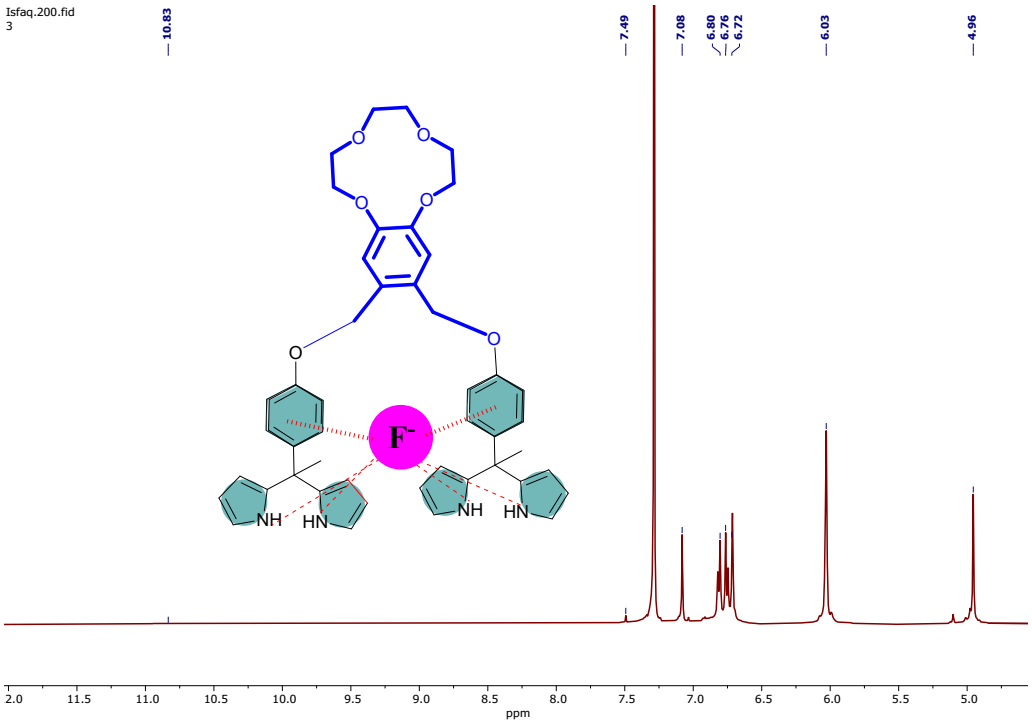


Figure S11. ^{1}H-NMR of complex *bis*-dipyrromethane with fluoride (**DPM4@F^{-}**) recorded in $CDCl_3$

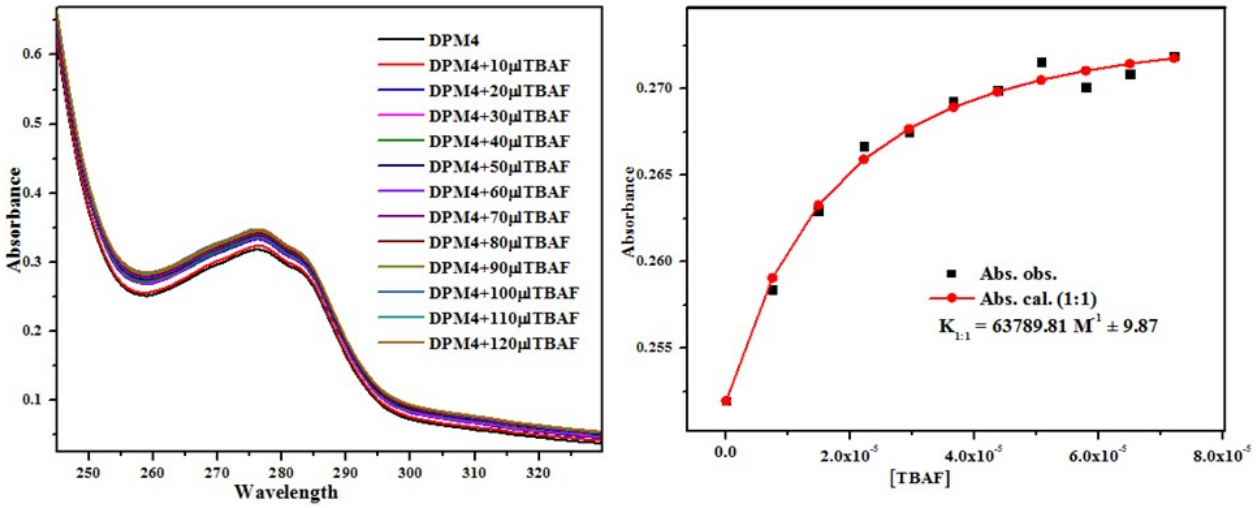


Figure S12. UV-vis titration of receptor **DPM3** with **TBAF** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program

Figure S13. Snapshot capture of Bindfit plots for **DPM3** and **TBAF** titration, displaying 1:1 stoichiometry with satisfied value of $K_{11}$with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

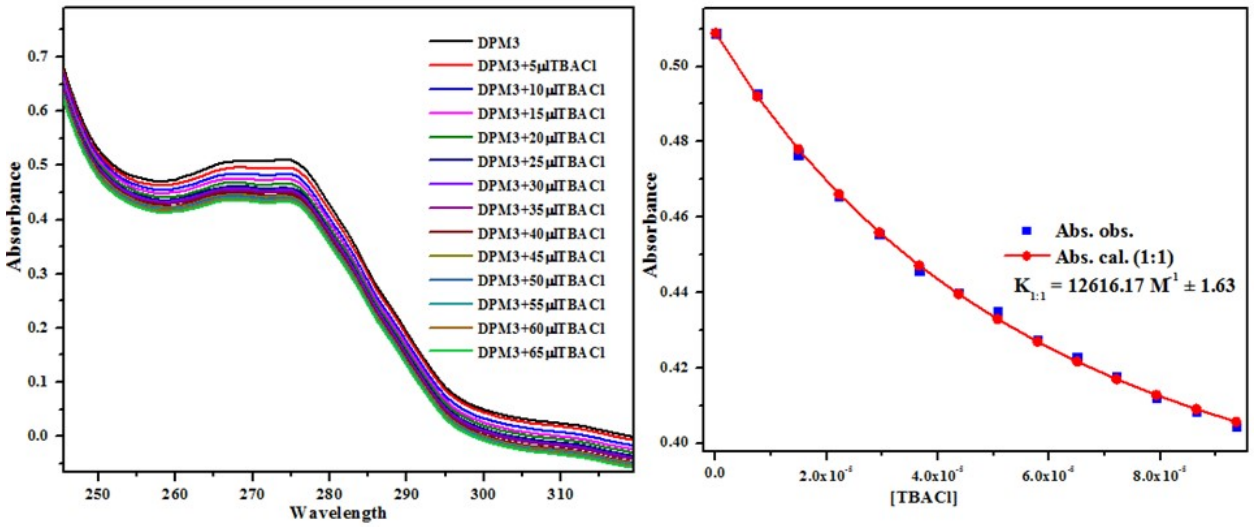
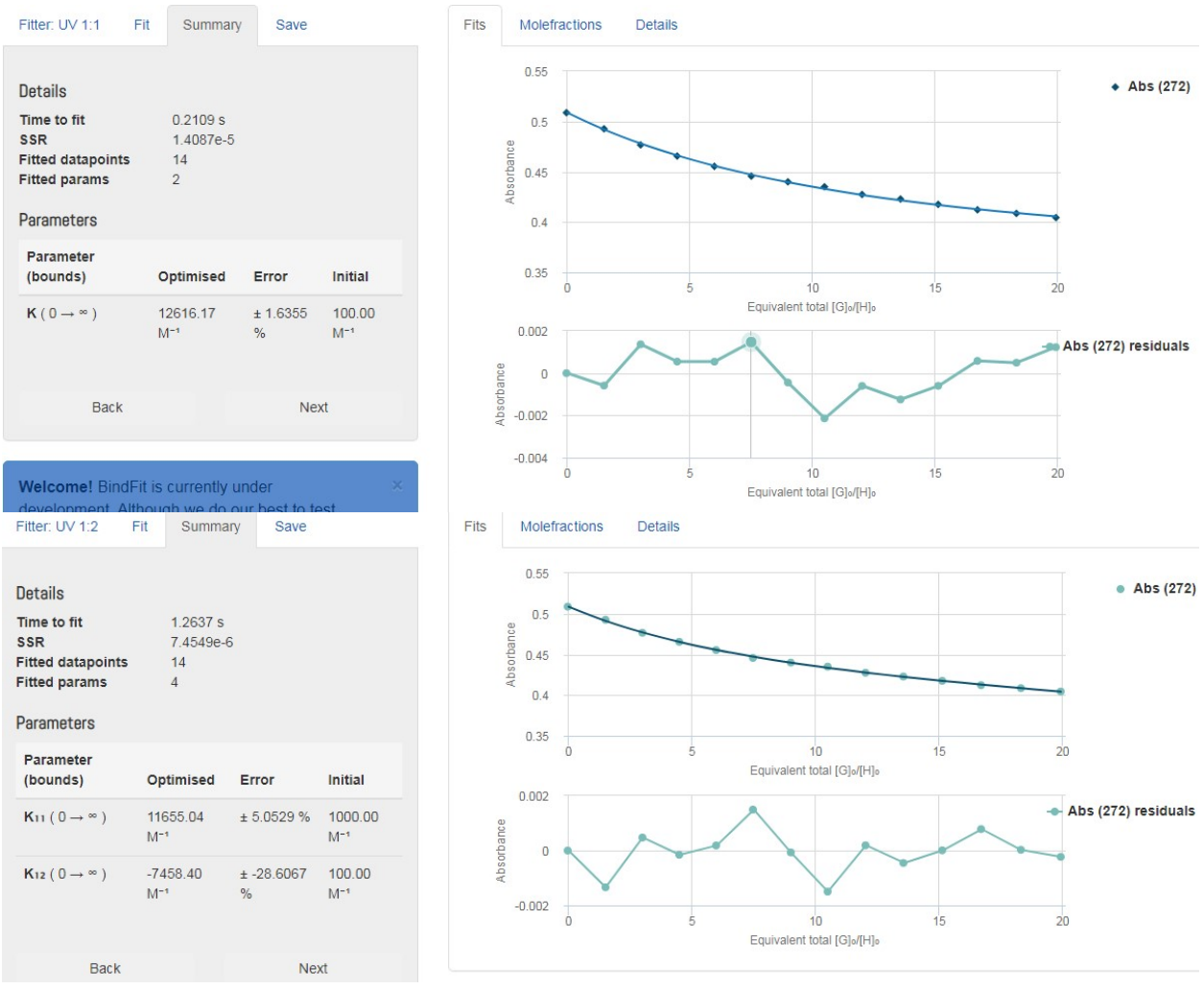


Figure S14. UV-vis titration of receptor **DPM3** with **TBACl** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program



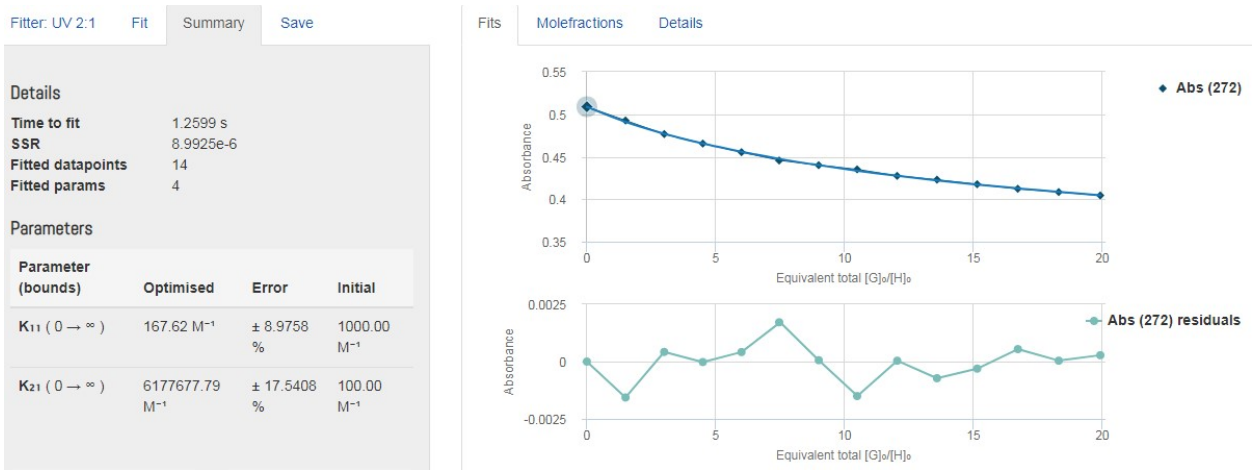


Figure S15. Snapshot capture of Bindfit plots for **DPM3** and **TBACl** titration, displaying 1:1 stoichiometry with satisfied value of $K_{11}$with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

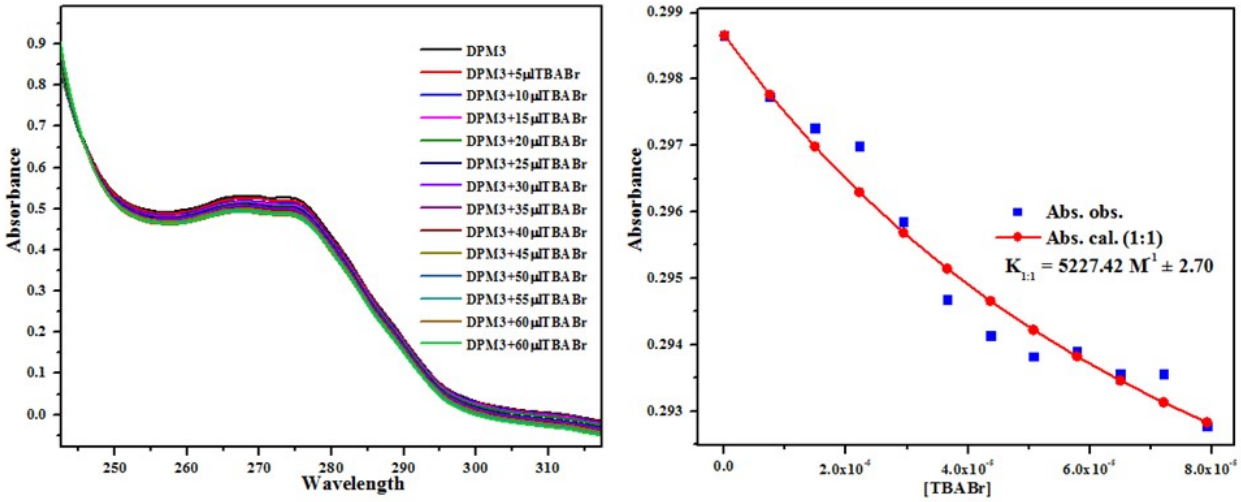


Figure S16. UV-vis titration of receptor **DPM3** with **TBABr** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program

Figure S17. Snapshot capture of Bindfit plots for **DPM3** and **TBABr** titration, displaying 1:1 stoichiometry with satisfied value of $K_{11}$with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

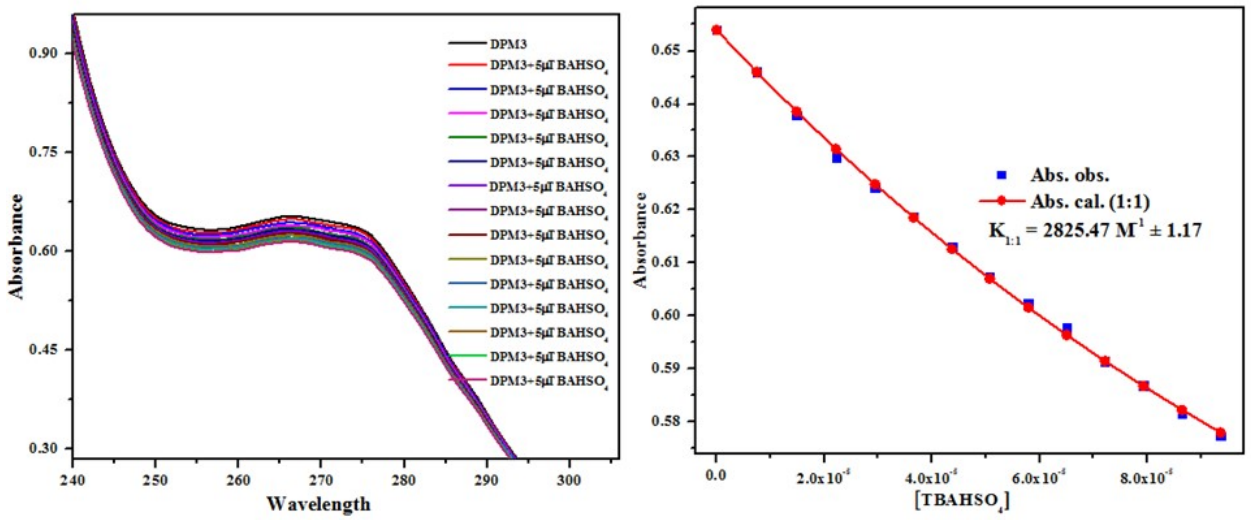


Figure S18. UV-vis titration of receptor **DPM3** with **$TBAHSO_4$** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program

Fitter: UV 1:1 Fit Summary Save

Details

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Fitted params	2

Parameters

Parameter (bounds)	Optimised	Error	Initial
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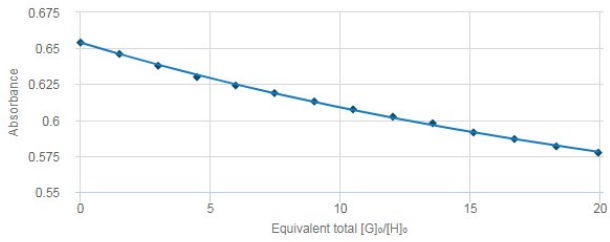
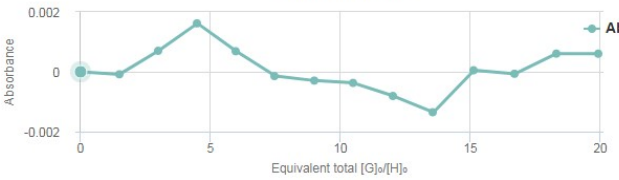
Back Next

Fits Molefractions Details





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Parameters

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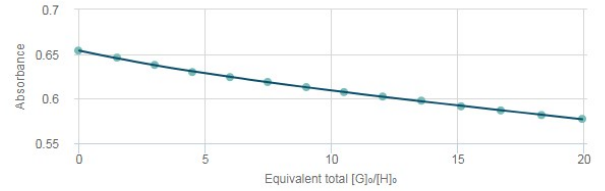
Fits Molefractions Details



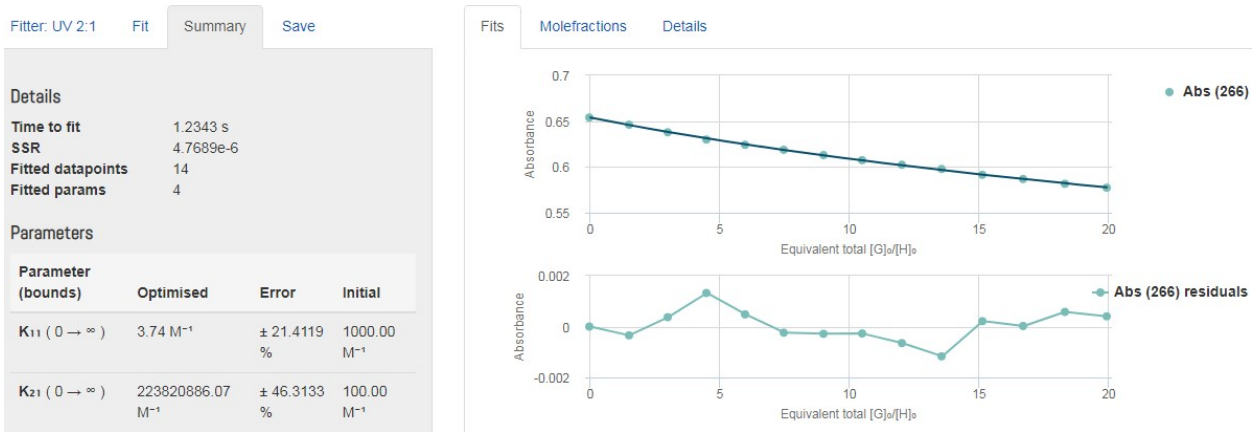


Figure S19. Snapshot capture of Bindfit plots for **DPM3** and **$TBAHSO_4$** titration, displaying 1:1 stoichiometry with satisfied value of K_{11} with error < 10 andnegative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

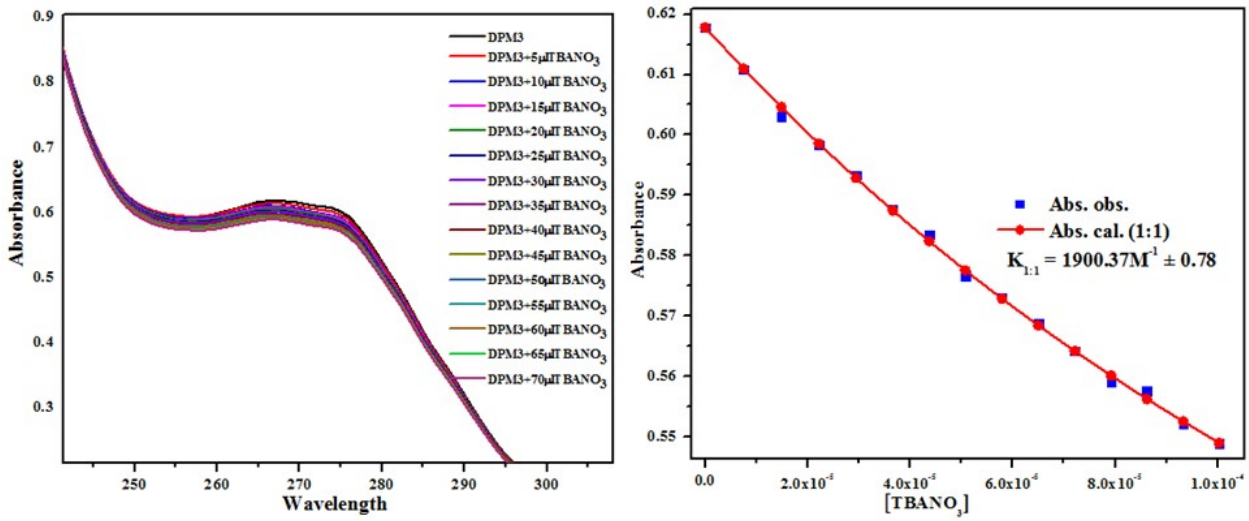


Figure S20. UV-vis titration of receptor **DPM3** with **$TBANO_3$** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program

Figure S21. Snapshot capture of Bindfit plots for **DPM3** and **$TBANO_3$** titration, displaying 1:1 stoichiometry with satisfied value of K_{11} with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

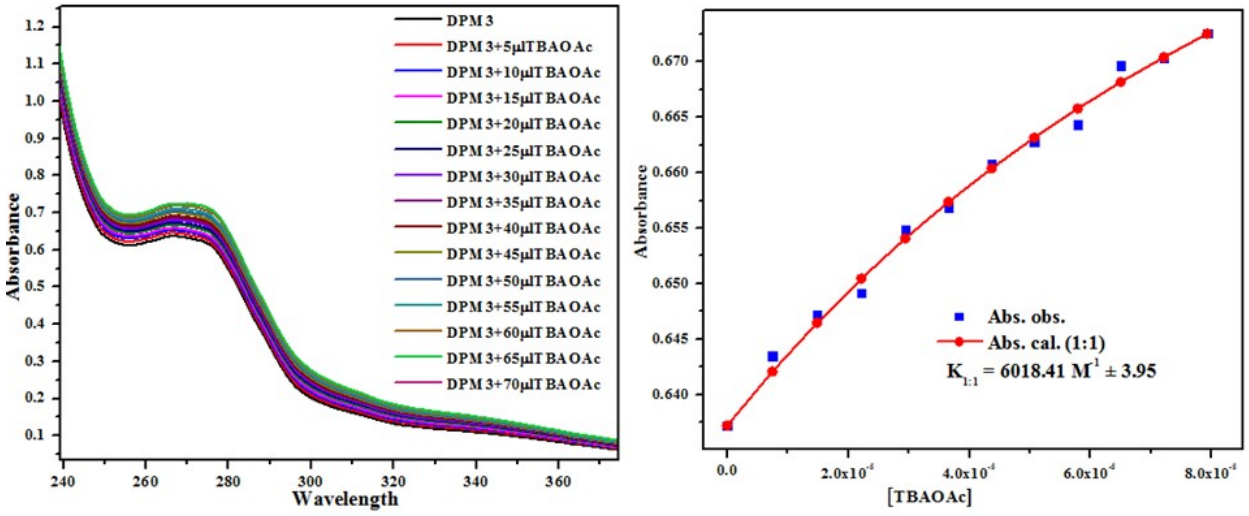
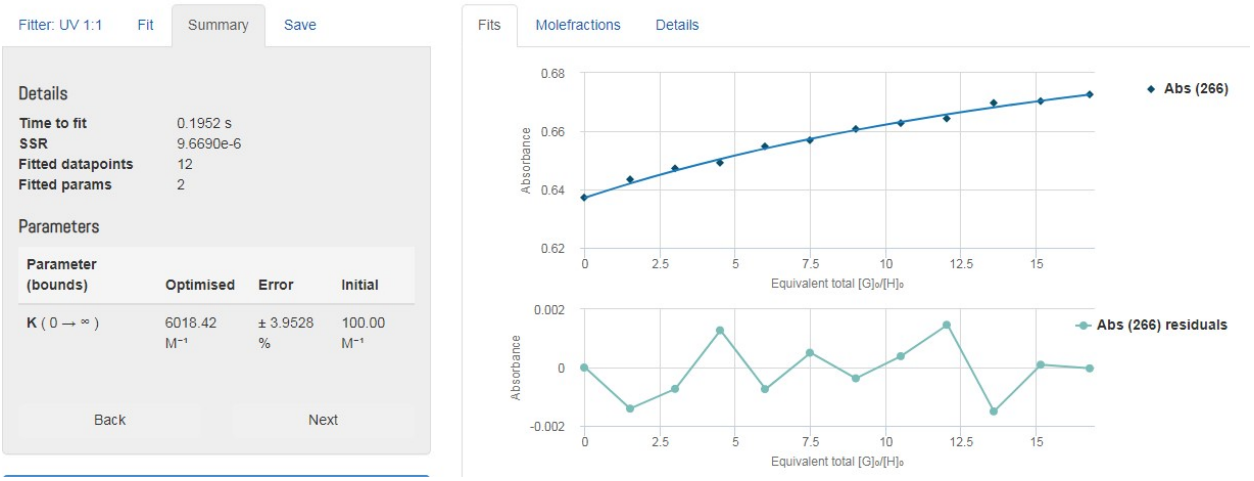


Figure S22. UV-vis titration of receptor **DPM3** with **TBAOAc** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program



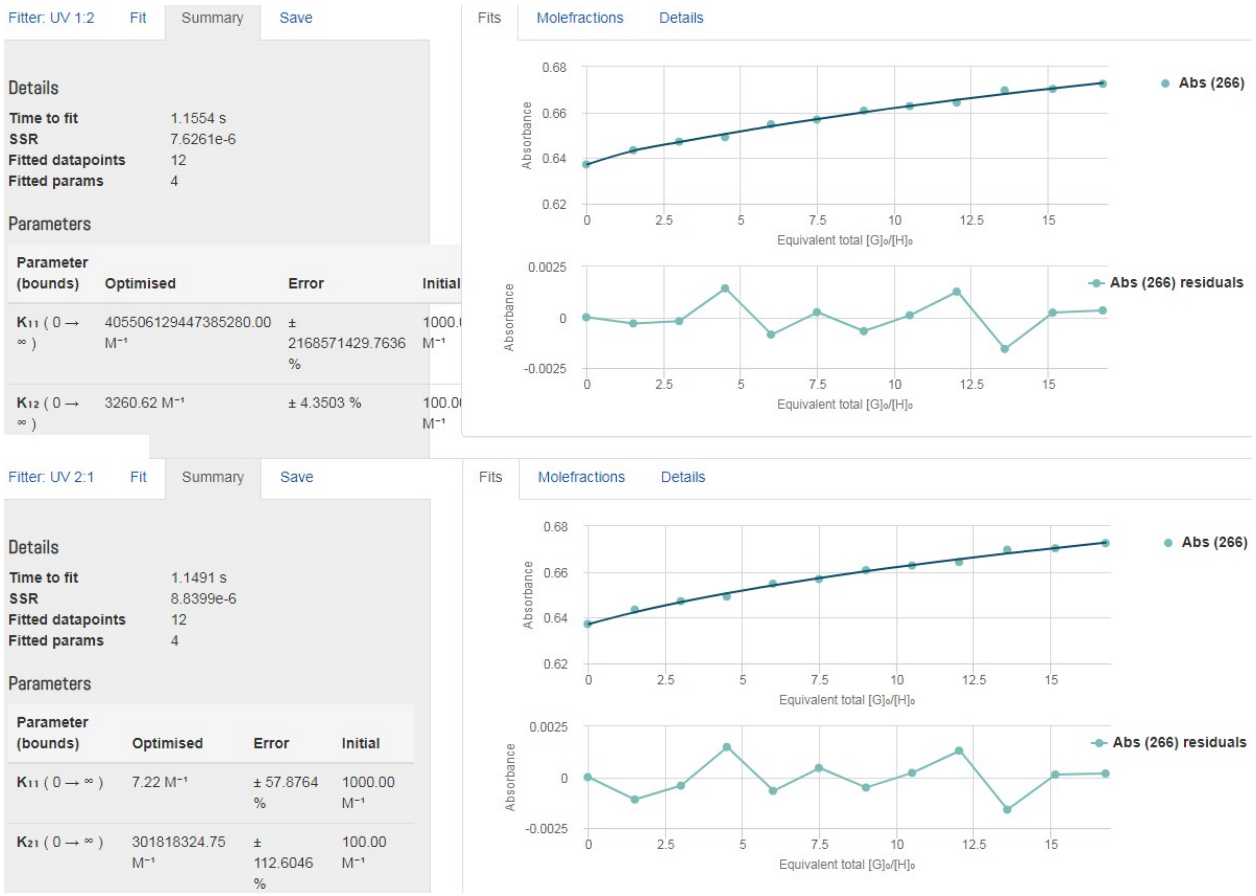


Figure S23. Snapshot capture of Bindfit plots for **DPM3** and **TBAOAc** titration, displaying 1:1 stoichiometry with satisfied value of $K_{11}$with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

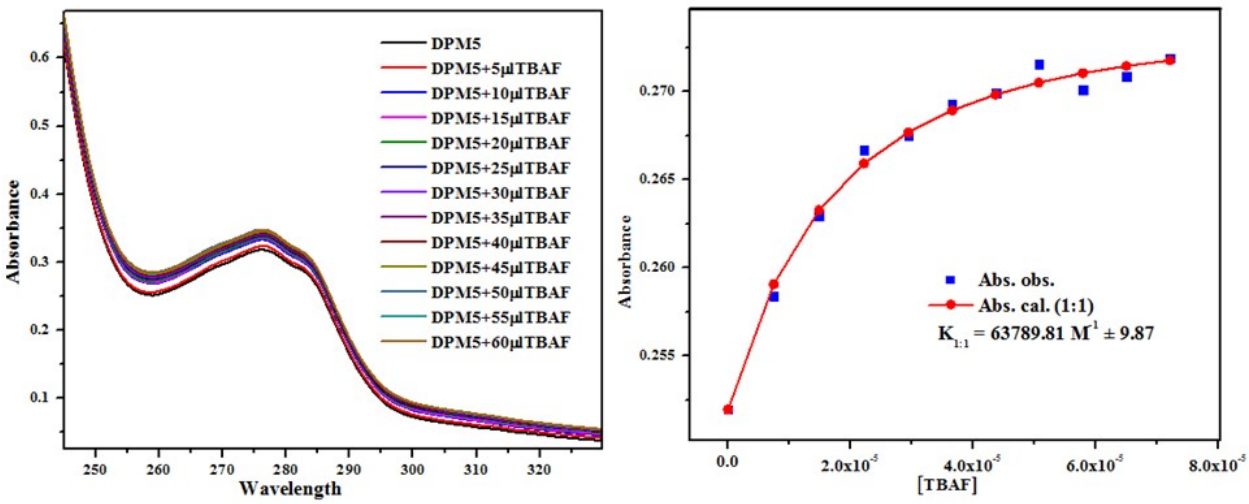
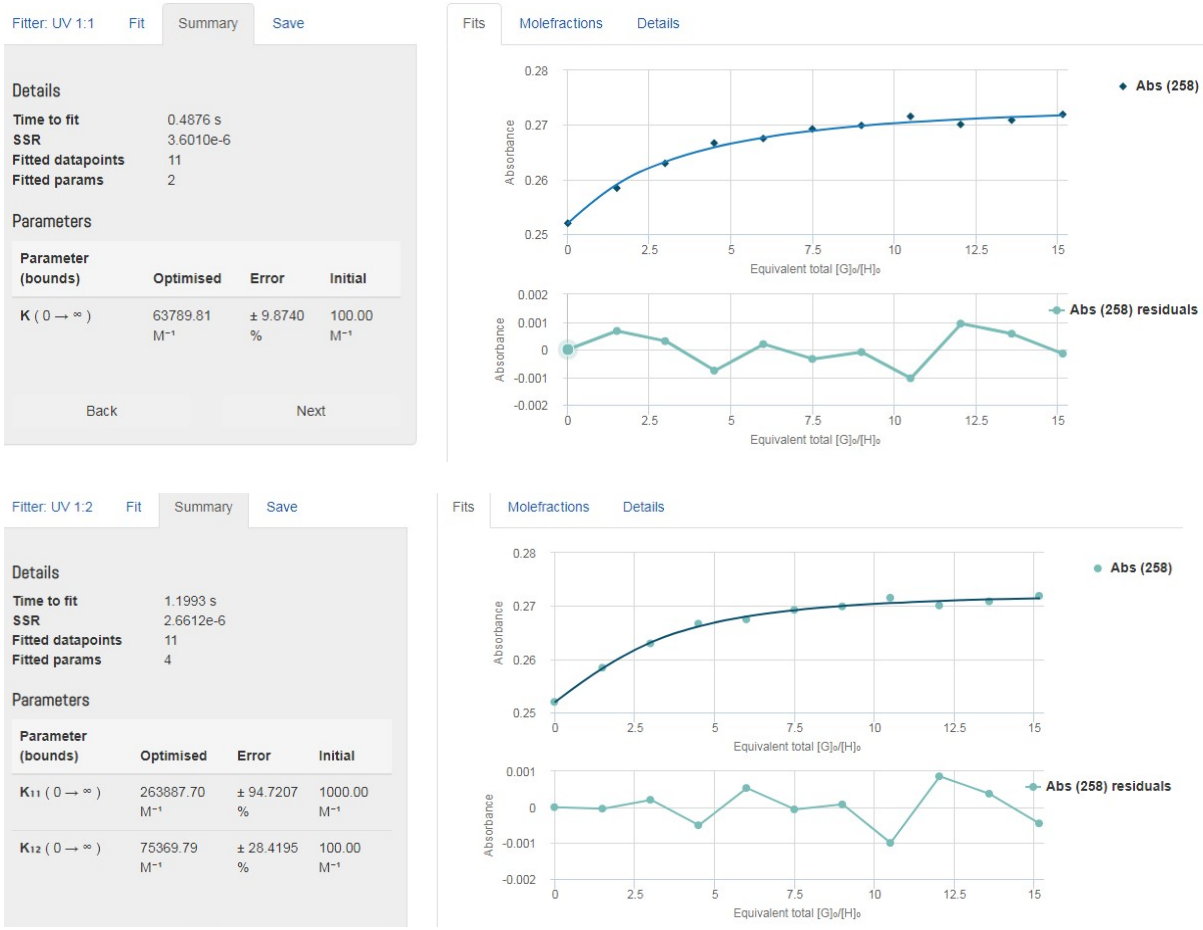


Figure S24. UV-vis titration of receptor **DPM4** with **TBAF** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program



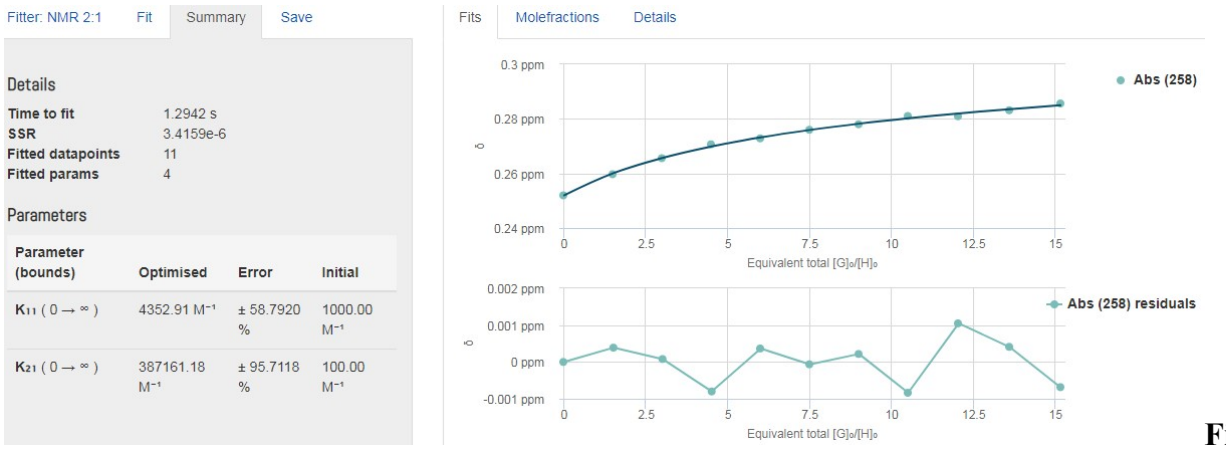


Figure S25. Snapshot capture of Bindfit plots for **DPM4** and **TBAF** titration, displaying 1:1 stoichiometry with satisfied value of K_{11} with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

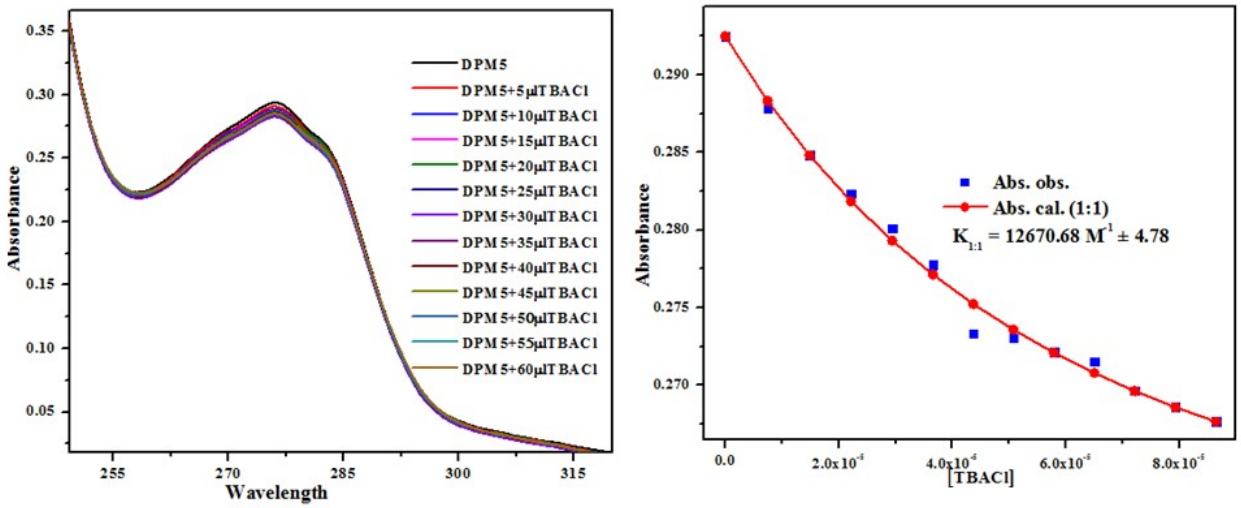
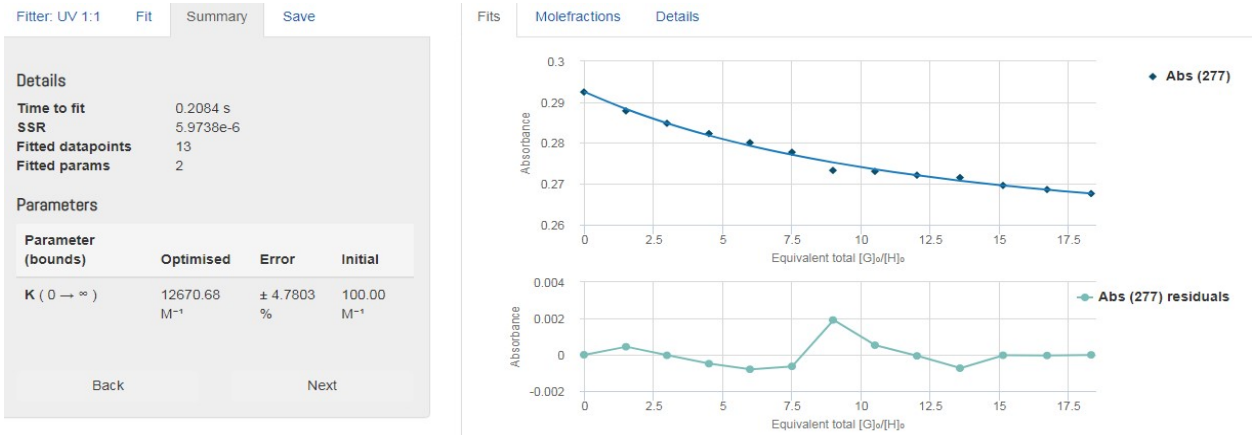


Figure S26. UV-vis titration of receptor **DPM4** with **TBACl** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program



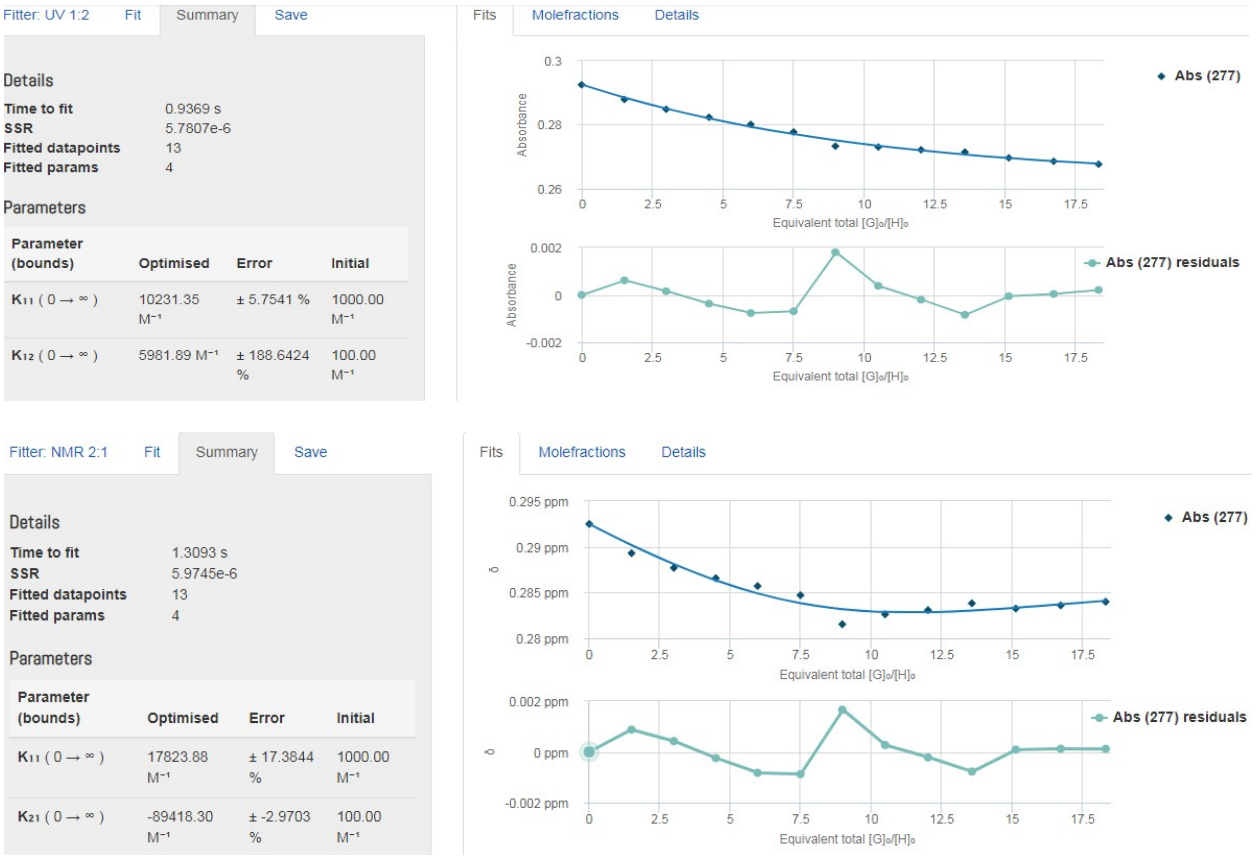


Figure S27. Snapshot capture of Bindfit plots for **DPM4** and **TBACl** titration, displaying 1:1 stoichiometry with satisfied value of $K_{11}$with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

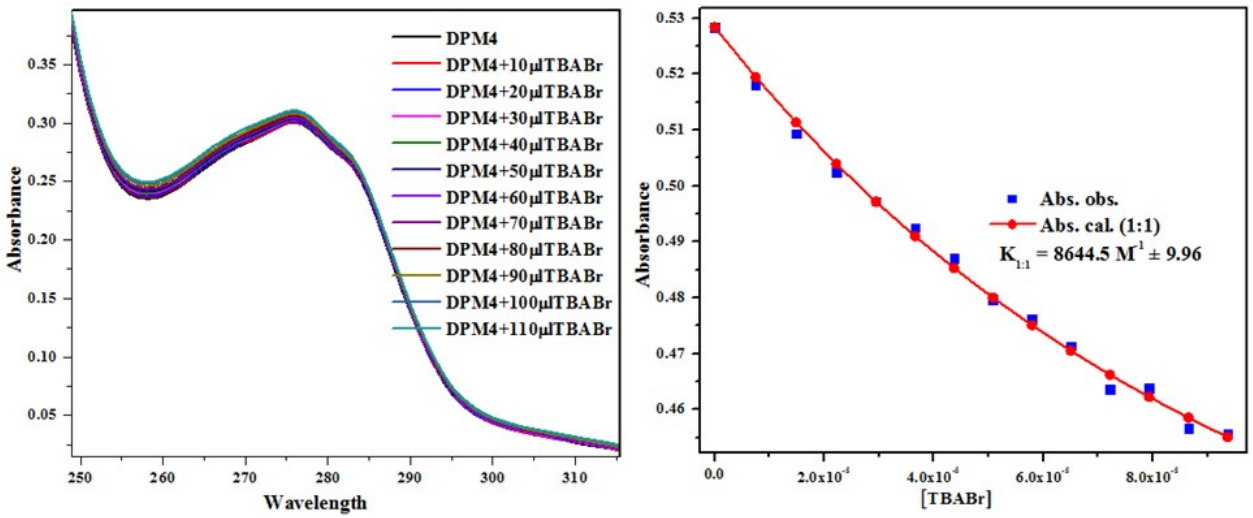


Figure S28. UV-vis titration of receptor **DPM4** with **TBABr** inCH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program

Figure S29. Snapshot capture of Bindfit plots for **DPM4** and **TBABr** titration, displaying 1:1 stoichiometry with satisfied value of K_{11} with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

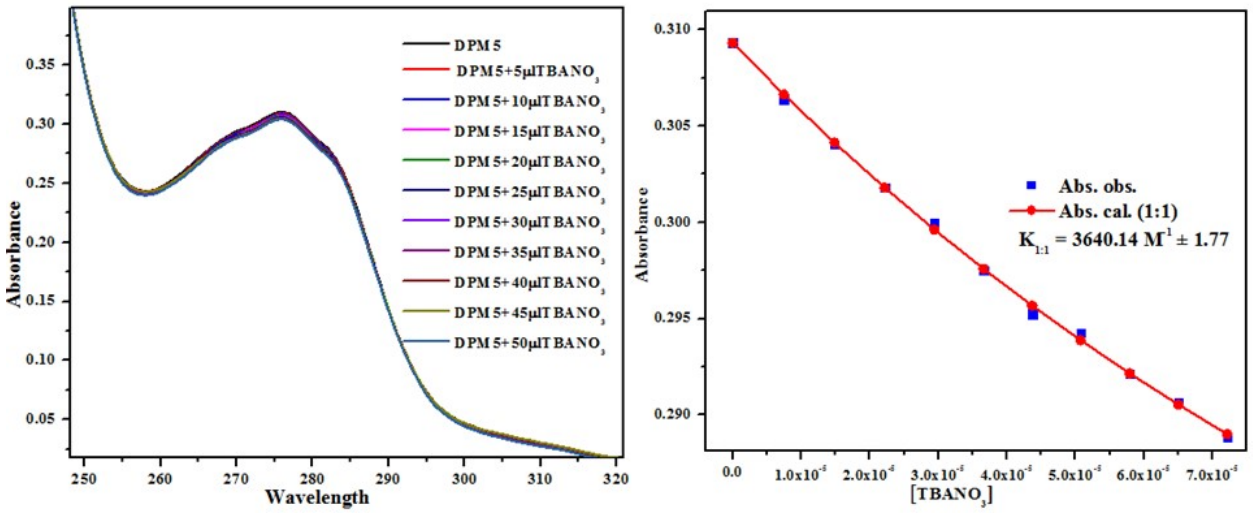
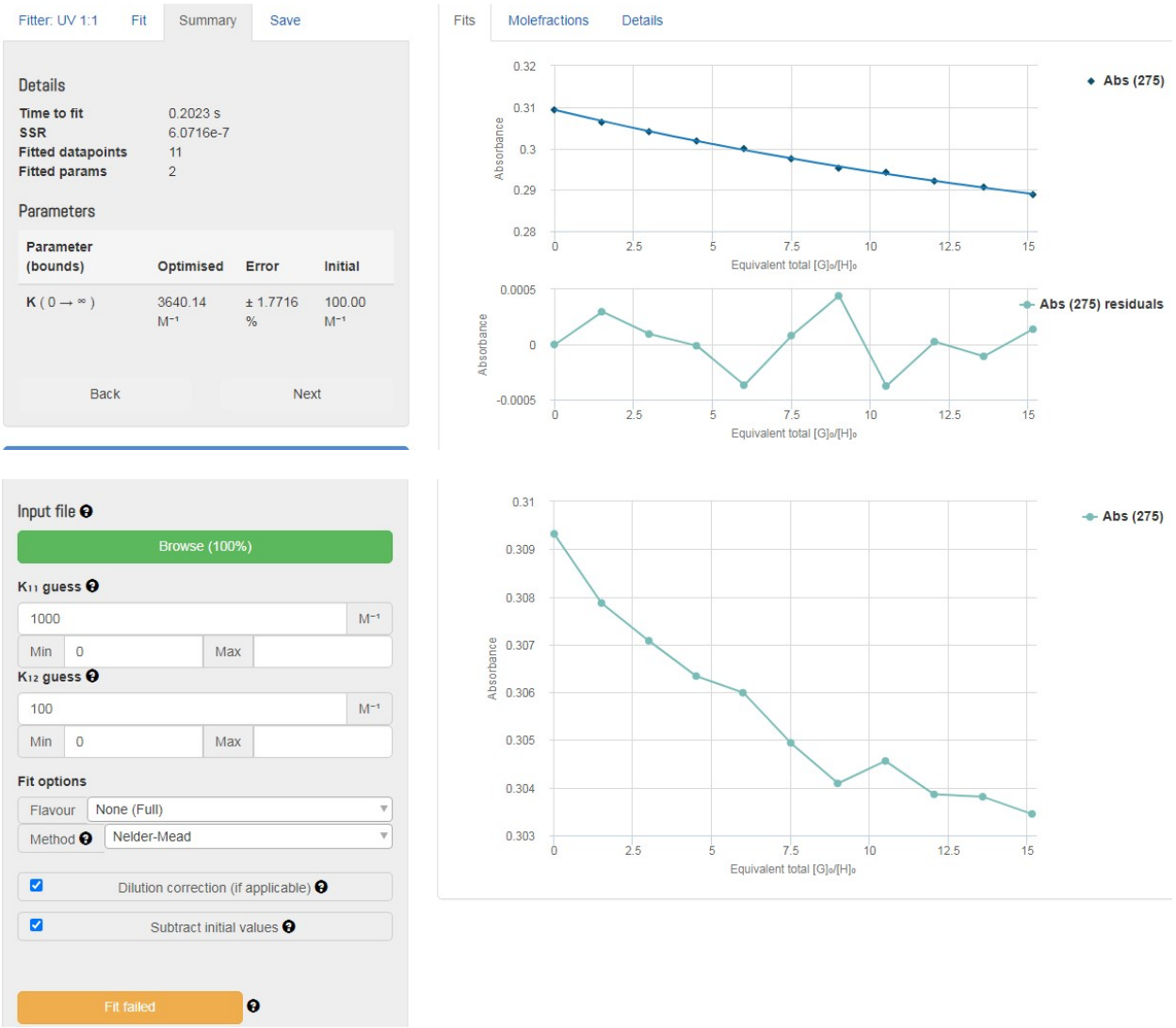


Figure S30. UV-vis titration of receptor **DPM4** with **$TBANO_3$** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program



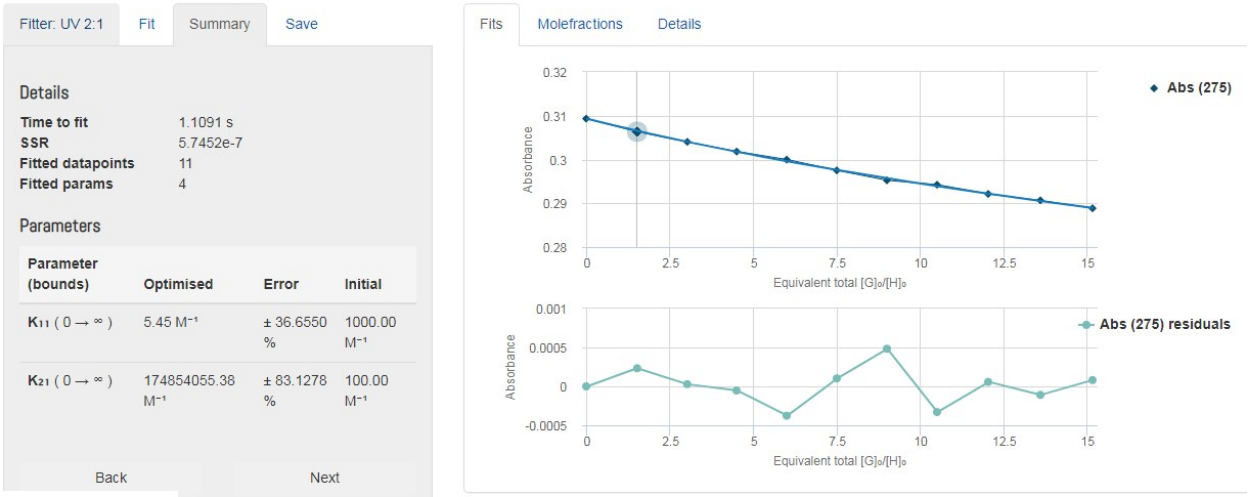


Figure S31. Snapshot capture of Bindfit plots for **DPM4** and **TBANO$_3$**titration, displaying 1:1 stoichiometry with satisfied value of $K_{11}$with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

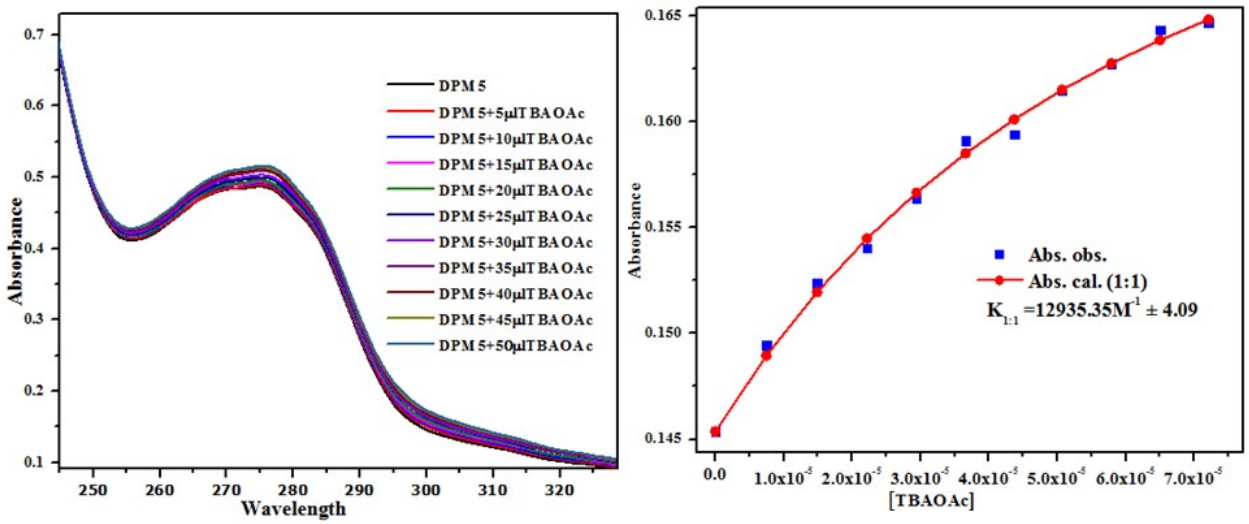


Figure S32. UV-vis titration of receptor **DPM4** with **TBAOAc** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program

Figure S33. Snapshot capture of Bindfit plots for **DPM4** and **TBAOAc** titration, displaying 1:1 stoichiometry with satisfied value of $K_{11}$with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

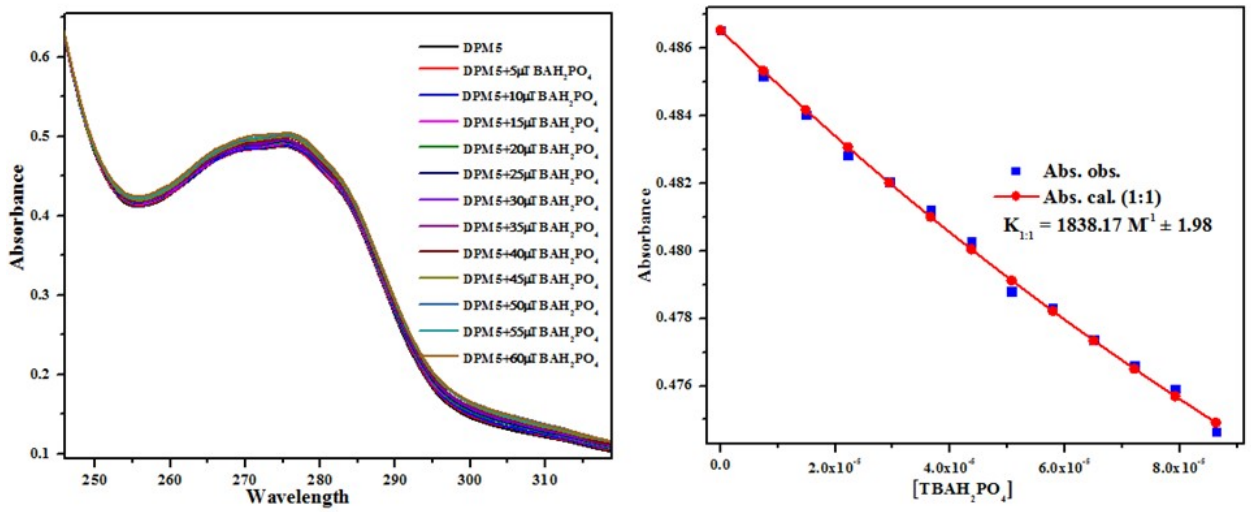
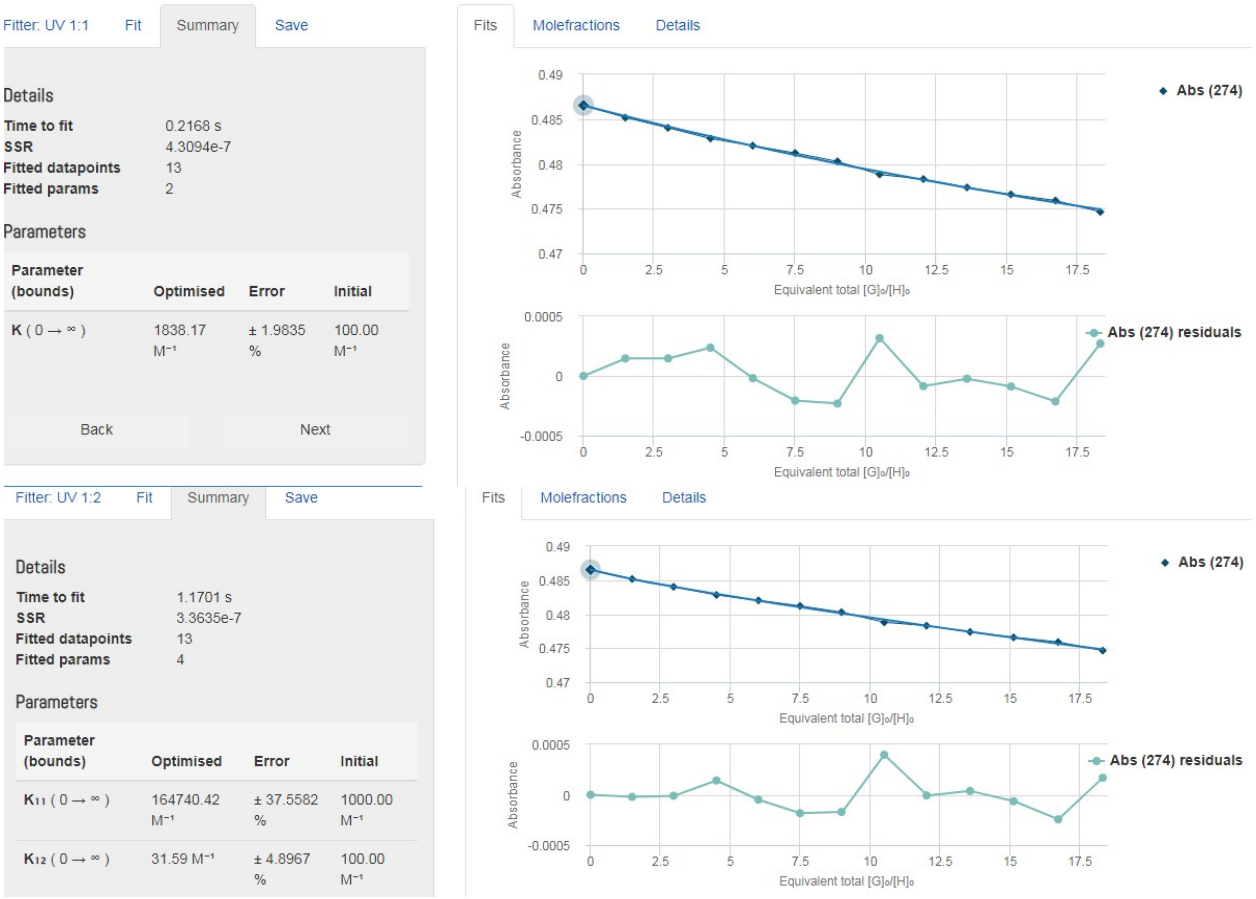


Figure S34. UV-vis titration of receptor **DPM4** with **$TBAH_2PO_4$** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program



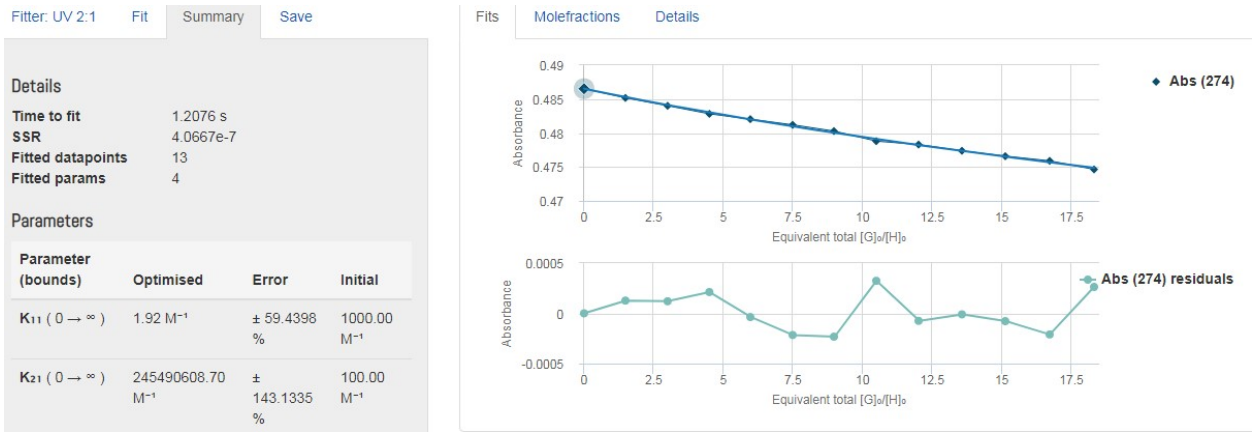


Figure S35. Snapshot capture of Bindfit plots for **DPM4** and **$TBAH_2PO_4$** titration, displaying 1:1 stoichiometry with satisfied value of $K_{11}$with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

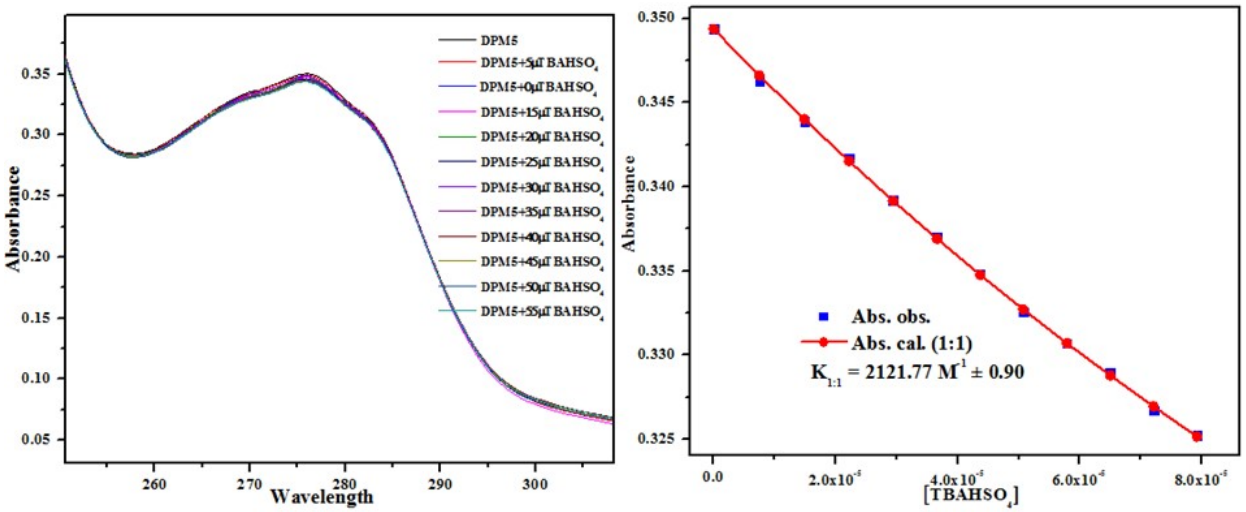
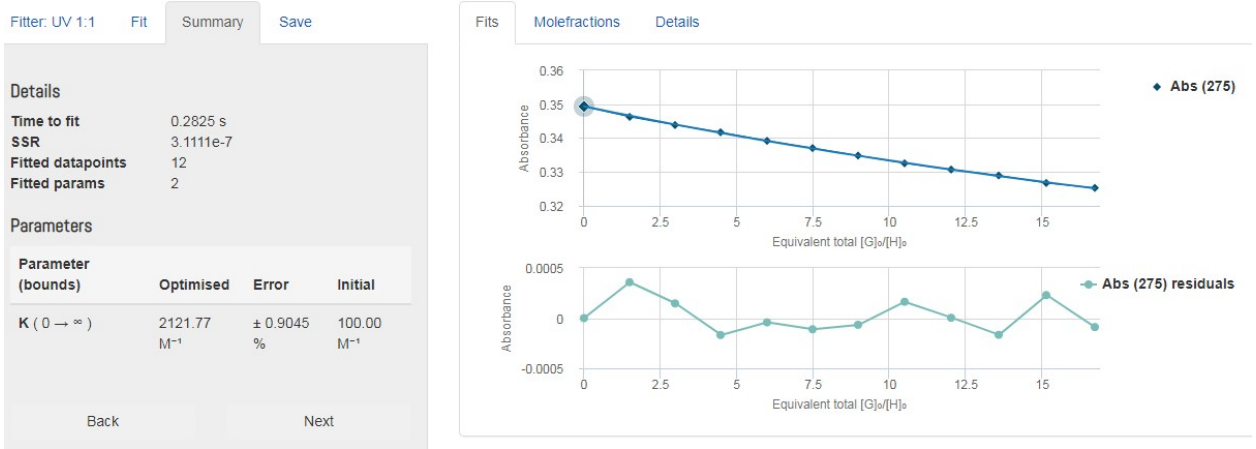


Figure S36. UV-vis titration of receptor **DPM4** with **$TBAHSO_4$**in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program



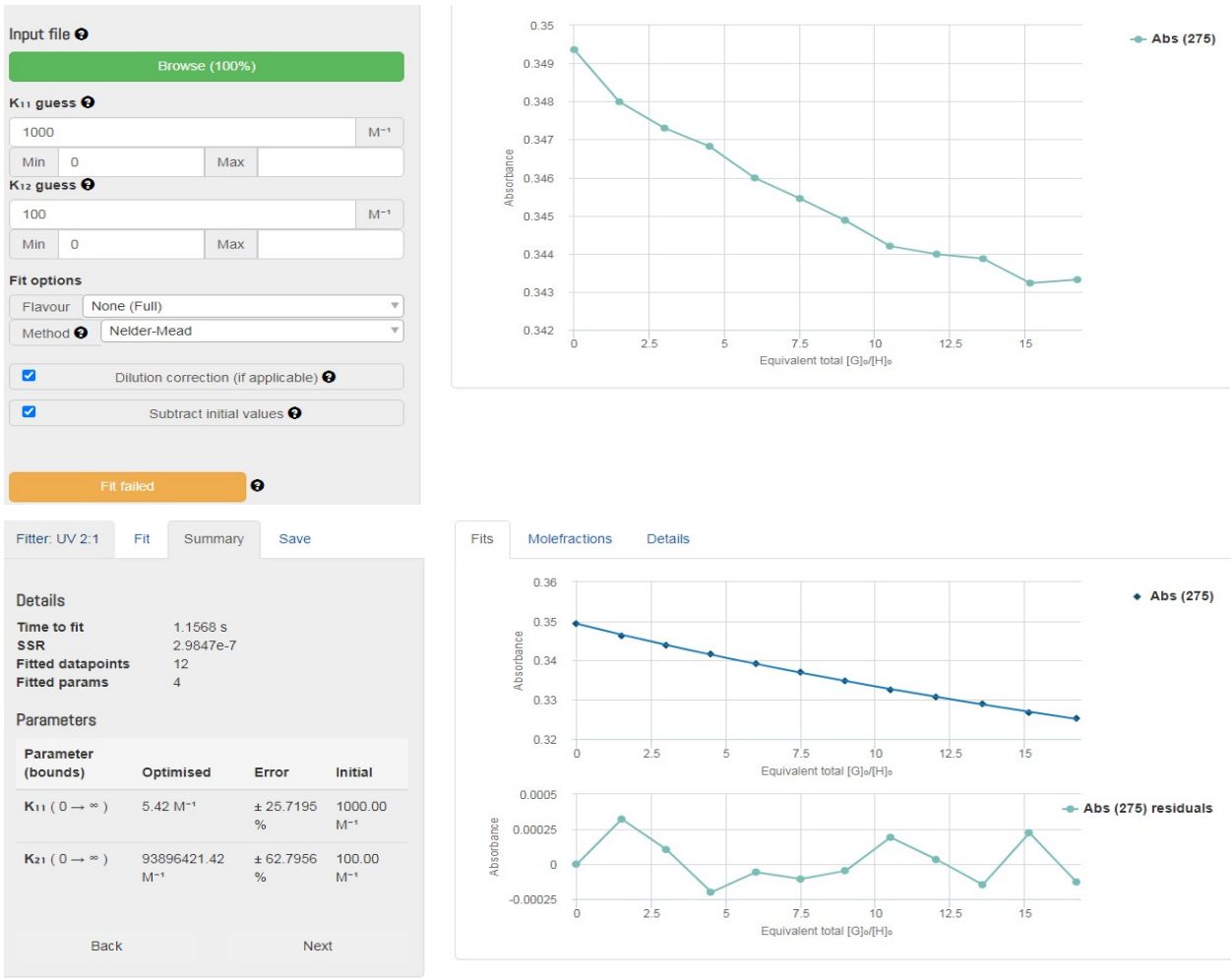


Figure S37. Snapshot capture of Bindfit plots for **DPM3** and **TBAHSO$_4$** titration, displaying 1:1 stoichiometry with satisfied value of $K_{11}$with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

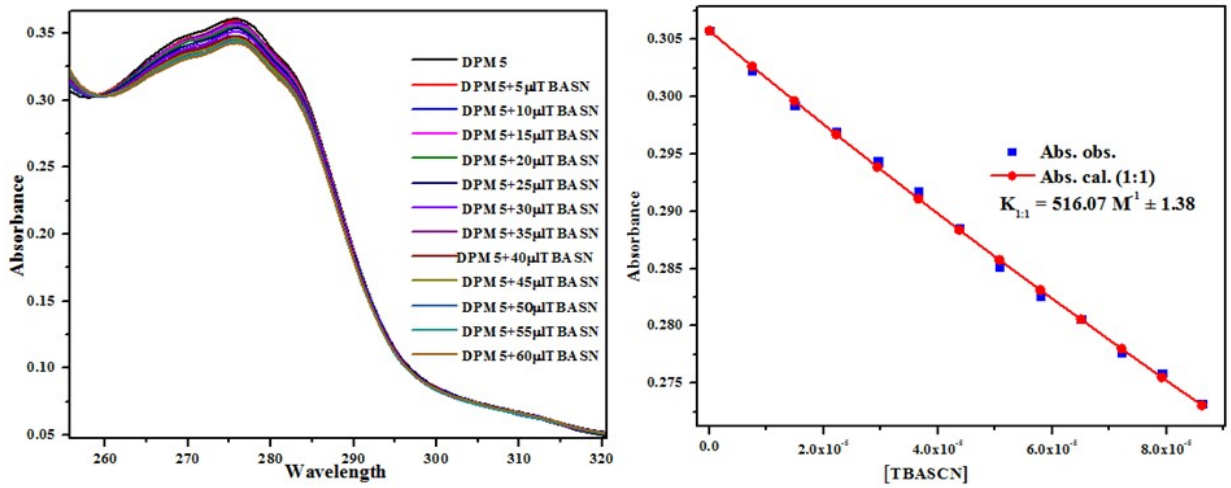


Figure S38. UV-vis titration of receptor **DPM4** with **TBASCN** in CH_3CN and binding isotherm fitting of UV-vis titration data by using Bindfit v0.5 program

Figure S39. Snapshot capture of Bindfit plots for **DPM4** and **TBASCN** titration, displaying 1:1 stoichiometry with satisfied value of K_{11} with error < 10 and negative or unsatisfied value for K_{12} and K_{12} (1:1stoichiometry) with error > 10 utilizing Nelder-Mead fit.

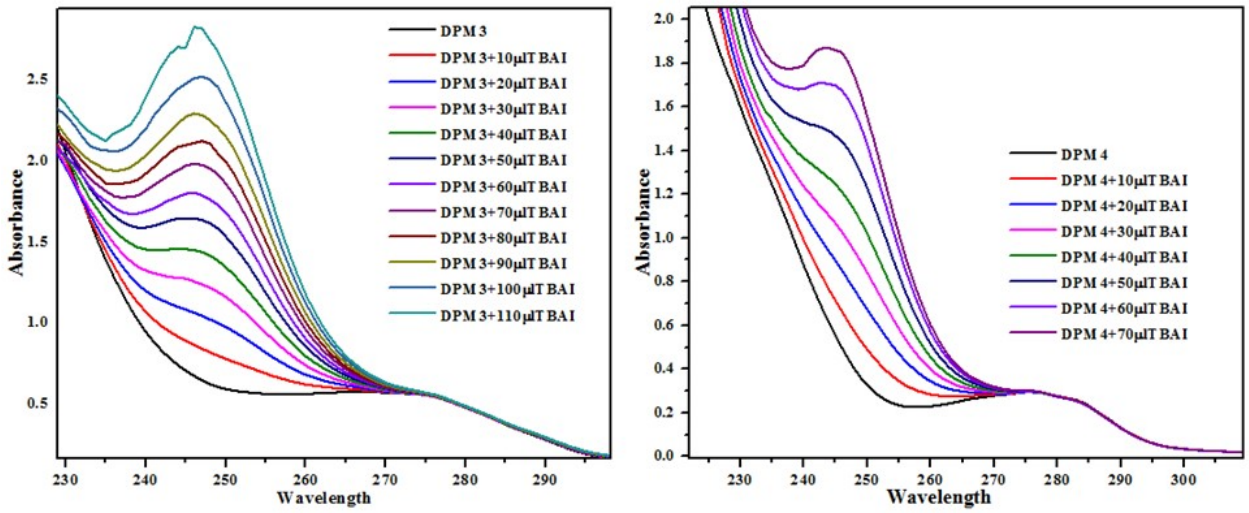


Figure S40. UV-vis titration of receptor **DPM3** and **DPM4** with TBAI in CH_3CN

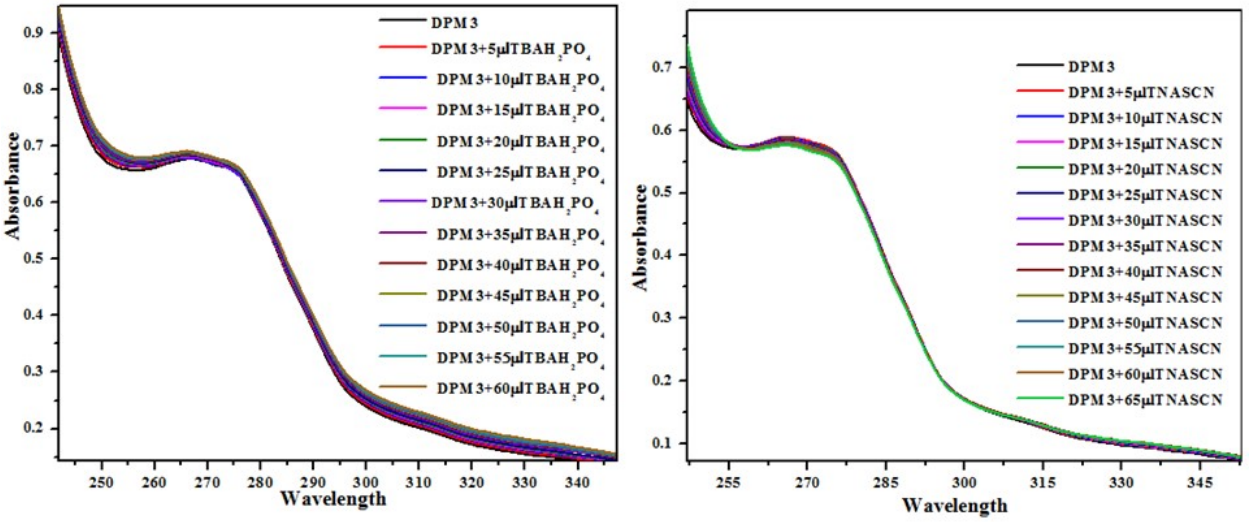


Figure S41. UV-vis titration of receptor **DPM3** with **$TBAH_2PO_4$** and **TBASCN** in CH_3CN

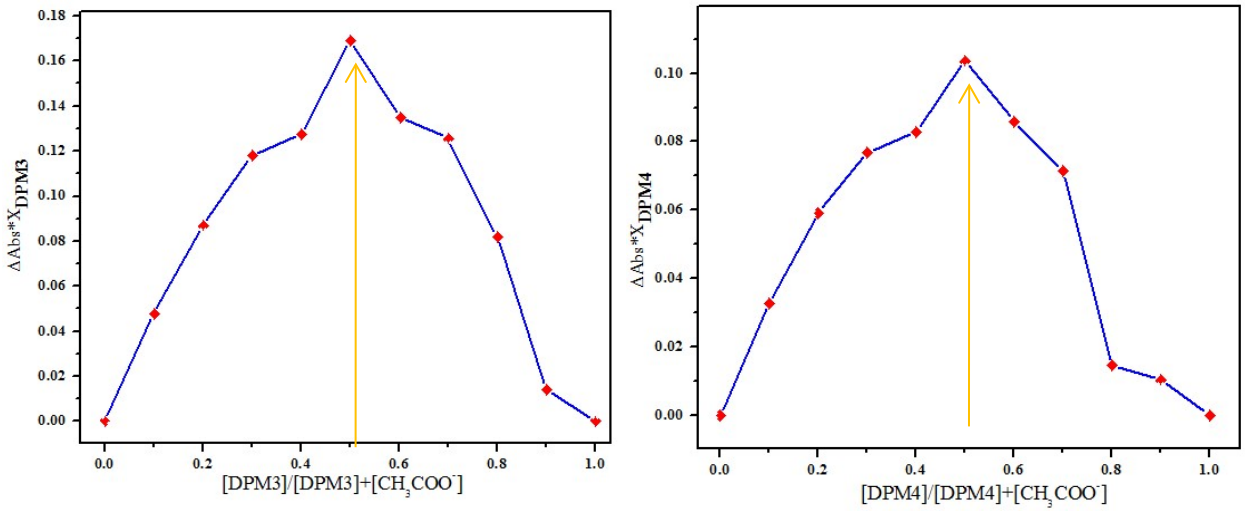


Figure 42. Job's plots of **DPM3** &**DPM4** with $TBACH_3COO^-$ in acetonitrile solution at ambient temperature.

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