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SUPPORTING INFORMATION

pH-Dependent complex formation with TAR RNA and DNA: Application towards logic gates

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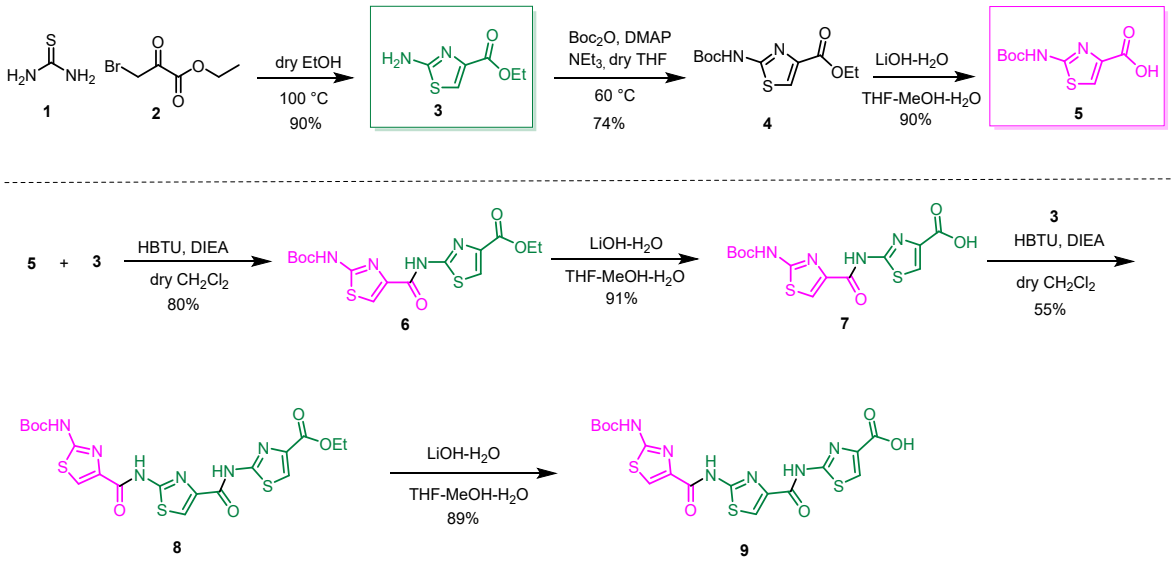
1.0 General Information

All experiments were carried out under an inert argon atmosphere in flame-dried flasks. Solvents were dried using standard procedures. All starting materials were obtained from commercial suppliers and used as received. Products were purified by flash chromatography on silica gel (100-200 mesh, Merck). Unless otherwise stated, yields refer to analytically pure samples. Melting points were measured with BÜCHI Melting point B-545 and are uncorrected. NMR spectra were recorded in $CDCl_3$ unless otherwise stated. **^{1}H NMR** spectra were recorded at 500 MHz using Brüker ADVANCE 500 MHz and JEOL 400 MHz instruments at 298 K. Signals are quoted as δ values in ppm using residual protonated solvent signals as internal standard ($CDCl_3$: δ 7.26 ppm). Data is reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet), and coupling constants (Hz). **^{13}C NMR** spectra were recorded on either a JEOL-400 (100 MHz) or a Brüker ADVANCE 500 MHz (125 MHz) with complete proton decoupling. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.16 ppm). **HRMS** analyses were performed with Q-TOF YA263 high-resolution (Water Corporation) instruments by +ve mode electrospray ionisation. The general chemicals required for biophysical analysis were purchased from Sigma-Aldrich. For best results, all oligomers of the highest purity were purchased from Sigma-Aldrich and Eurofins.

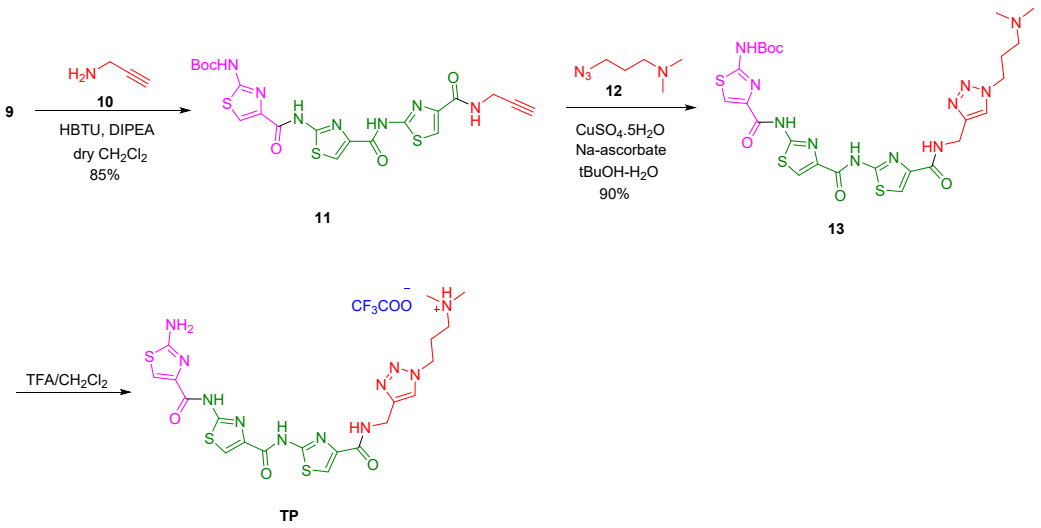
2.0 Synthesis of thiazole peptide (TP)

The thiazole peptides were synthesised by step-wise amide coupling of thiazole amino acid building blocks **3** and **5**. The Boc protection followed by the ester hydrolysis of the resulting ester **4** yielded the acid building block **5** (Scheme S1). The amide coupling of thiazole amino acid building blocks **3** and **5** was carried out using HBTU in the presence of DIEA in anhydrous CH_2Cl_2 to afford the dipeptide **6** in 80% yield. Subsequent ester hydrolysis of **6** followed by an amide coupling of the resulting acid **7** with the building block **3** afforded the tripeptide **8** in 55% yield. Ester hydrolysis of tripeptide **8** using LiOH yielded the trimeric acid **9**. The tertiary amine side chain was incorporated into the tripeptide **9** using azide-alkyne cycloaddition.



Scheme S1. Synthesis of thiazole dipeptide **7** and tripeptide **9**.

Tripeptide **9** was coupled with propargyl amine **10** to generate the alkyne-terminated thiazole peptide **11** in 85 % yield. The Cu(I) catalysed cycloaddition of alkyne **11** with azide **12** provided the product **13** in 90% yield. Subsequent Boc deprotection of compound **13** using trifluoroacetic acid provided the triazole-linked thiazole peptide **TP** in high yield. Peptides **TP** was obtained as its TFA salt.



Scheme S2. Synthesis of thiazole peptide **TP**.

General procedure for the deprotection of the ethyl ester (GP-1): To a solution of the respective ethyl ester protected peptide (1 eq) in THF/MeOH/H_2O = 3: 3: 1, LiOH-H_2O (3 eq) was added at 0 ˚C. The reaction mixture was stirred for about 3-4 h at room temperature until starting material was entirely consumed. After completion of the reaction, the solvent was dried in a rotary evaporator. The crude reaction mixture was diluted with little water followed by drop wise addition of saturated $KHSO_4$ solution under cold conditions to get precipitated under acidic conditions. The resulting solid precipitate was filtered and dried to afford the respective title hydrolysed compound as a white solid in quantitative yield.

General procedure for the peptide coupling (GP-2): All amide coupling reactions were carried out using O-(benzotriazol-1-yl)-*N*, *N*, *N'*, *N'*-tetramethyluronium hexafluorophosphate (HBTU) as a peptide coupling reagent as this coupling reagent provided the desired coupled products in high yield. To a stirred solution of carboxylic acid component (1.1 eq) in dry CH_2C_{l2}, HBTU (1.5 eq) was added followed by the addition of *N*, ***N'***-diisopropylethylamine (DIEA) (3 eq) at 0 ºC. After 10 minutes, the amine component (1 eq) was added at same temperature. The reactions were typically allowed to stir for 16-24 h at room temperature. After completion of the reaction, the reaction mixture was concentrated and the resulting residue was dissolved in ethylacetate and the organic layer was successively washed thrice with 1(N) HCl solution, saturated $NaHCO_3$ solution and brine. After drying with Na_2SO_4 and the solvents were removed under reduced pressure and the desired coupling products were purified by column

chromatography. Yields for the individual coupling steps were good to excellent ranging from 55% to 85%.

Synthesis of ethyl 2-amino-4-thiazolecarboxylate (**3**)**:** Ethyl bromopyruvate **2** (5.31 g, 26.3 mmol) was added to a cold solution of thiourea **1** (2 g, 26.3 mmol) in dry ethanol (5 mL) in a sealed tube. The resulting mixture was heated for 4 h at 100 °C. Upon cooling to room temperature, the reaction mixture was poured into ice water and brought to pH ~ 8 with aqueous sodium carbonate solution. The resulting solid precipitate was filtered, washed several times with water and air dried to obtain pure yellowish solid compound **3** (4.07 g) in 90% yield. ^{1}H NMR (400 MHz, DMSO-d_6): 7.45 (1H, s), 7.22 (2H, s_{br}), 4.19 (2H, q, *J* = 7.3 Hz), 1.25 (3H, t, *J* = 6.7 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): 168.2, 161.0, 142.2, 116.9, 60.1, 14.1; HRMS (ESI) calcd for $C_6H_9N_2O_2S$ $[M+H]^+$: 173.0379; Found: 173.0391.

Synthesis of Boc-protected thiazole amino ester 4: To a stirred solution of aminothiazole ester **3** (2 g, 11.6 mmol) in tetrahydrofuran (40 mL) at 25 °C was added triethylamine (2.12 mL, 15.2 mmol), 4-(dimethylamino)pyridine (140 mg, 1.16 mmol), and di-*tert*-butyl-dicarbonate (3 mL, 12.7 mmol) sequentially, and the reaction mixture was heated to 60 °C. After 1 h, the reaction mixture was cooled to 25 °C, and quenched with saturated aqueous ammonium chloride solution (50 mL). The two phases were separated, and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The obtained residue was purified by column chromatography to afford pure thiazolyl carbamate **4** (2.34 g, 74%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6): 11.77 (1H, s_{br}), 7.99 (1H, s), 4.25 (2H, q, *J* = 6.7 Hz), 1.47 (9H, s), 1.27 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): 160.9, 159.8, 153.0, 141.3, 122.2, 60.4, 27.8, 14.1; HRMS (ESI) calcd for $C_{11}H_{16}N_2O_4SNa$ $[M+Na]^+$: 295.0728; Found: 295.0728.

Synthesis of Boc-protected thiazole amino acid 5: Using the general procedure **GP-1,** LiOH-H_2O (5.7 g, 136 mmol) and Boc-protected thiazole ester **4 (**12.64 g, 45.3 mmol) were stirred in THF/MeOH/H_2O (60 mL) for 4 h to provide the corresponding thiazole acid **5** (10.2 g, 90%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6): 7.87 (1H, s), 1.45

(9H, s); ^{13}C NMR (100 MHz, DMSO-d_6): 162.7, 159.8, 153.3, 142.8, 121.9, 81.9, 28.1; HRMS (ESI) calcd for $C_9H_{12}N_2O_4SNa$ $[M+Na]^+$: 267.0415; Found: 267.0403.

Synthesis of Boc-protected thiazole dipeptide 6: Using the general procedure **GP-2,** Boc protected thiazole amino acid **5** (6.24 g, 25.5 mmol), HBTU (13.19 g, 34.8 mmol), DIEA (12.12 mL, 69.6 mmol) and thiazole amine **3** (4 g, 23.2 mol) in dry CH_2Cl_2 (60 mL) **were**with stirred for 16 h to provid the desired dipeptide **6** (7.4 g, 80%) as an off-white solid; ^{1}H NMR (500 MHz, $CDCl_3$): 10.68 (1H, s_{br}), 9.01 (1H, s_{br}), 7.85 (1H, s), 7.82 (1H, s), 4.27 (2H, q, *J* = 7.3 Hz), 1.47 (9H, s), 1.33 (3H, t, *J* = 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): 161.5, 160.2, 159.2, 157.8, 152.3, 142.5, 142.0, 122.5, 120.5, 83.3, 61.4, 28.2, 14.3; HRMS (ESI) calcd for $C_{15}H_{19}N_4O_5S_2$ $[M+H]^+$: 399.0791; Found: 399.0778.

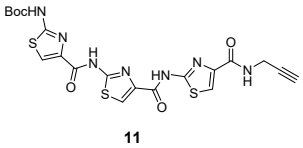
Synthesis of Boc-protected thiazole dimeric acid 7: Using the general procedure **GP-1,** LiOH-H_2O (2.34 g, 55.7 mmol) and dipeptide **6 (**7.4 g, 18.6 mmol) in THF/MeOH/H_2O (40 mL) were stirred for 4 h to give the corresponding thiazole acid **7** (6.26 g, 91%) as a white solid; ^{1}H NMR (500 MHz, DMSO-d_6): 12.29 (1H, s_{br}), 11.82 (1H, s_{br}), 8.20 (1H, s), 8.03 (1H, s), 1.49 (9H, s); ^{13}C NMR (100 MHz, DMSO-d_6): 162.4, 160.1, 159.4, 157.7, 142.4, 142.3, 122.9, 120.5, 81.9, 27.9; HRMS (ESI) calcd for $C_{13}H_{14}N_4O_5S_2Na$ $[M+Na]^+$: 393.0303; Found: 393.0289.

Synthesis of Boc-protected thiazole tripeptide 8: Using the general procedure **GP-2,** Boc protected thiazole dimeric acid **7** (4.73 g, 12.8 mmol), HBTU (6.6 g, 17.4 mmol), DIEA (6.1 mL, 34.8 mmol) and thiazole amine **3** (2 g, 11.6 mmol) in dry CH_2Cl_2 (50 mL), were stirred for 24 h to afford the desired tripeptide **8** (3.34 g, 55%) as an off-white solid**;** ^{1}H NMR (500 MHz, DMSO-d_6): 8.28 (1H, s), 8.13 (1H, s), 8.08 (1H, s), 4.27 (2H, q, *J* = 6.9 Hz), 1.49 (9H, s), 1.29 (3H, t, *J* = 6.9 Hz). ^{13}C NMR (125 MHz, DMSO-d_6): 161.0, 160.0, 159.4, 158.2, 158.0, 156.8, 152.9, 142.4, 142.2, 141.2, 123.3, 121.6, 120.6, 81.9, 60.7, 27.9, 14.2; HRMS (ESI) calcd for $C_{19}H_{20}N_6O_6S_3Na$ $[M+Na]^+$: 547.0504; Found: 547.0469.

Synthesis of Boc-protected thiazole trimeric acid 9: Using the general procedure **GP-1,** LiOH-H_2O (0.6 g, 14.2 mmol) and Boc-protected thiazole tripeptide **8** (2.5 g, 4.7 mmol) in THF/MeOH/H_2O (20 mL) were stirred for 4 h **to**provide the

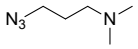
corresponding thiazole acid **9** (2.1 g, 89%) as a white solid; ^{1}H NMR (500 MHz, DMSO-d_6): 12.65 (1H, s_{br}), 12.37 (1H, s_{br}), 11.77 (1H, s_{br}), 8.32 (1H, s), 8.19 (1H, s), 8.05 (1H, s), 1.51 (9H, s); ^{13}C NMR (100 MHz, DMSO-d_6): 162.3, 160.1, 159.4, 159.3, 158.0, 157.7, 153.0, 142.9, 142.3, 142.2, 122.9, 121.5, 120.7, 81.9, 27.8; HRMS (ESI) calcd for $C_{17}H_{16}N_6O_6S_3Na$ $[M+Na]^+$: 519.0191; Found: 519.0191.

Synthesis of alkyne containing thiazole peptide 11: To a stirred solution of thiazole trimeric acid **9** (300 mg, 0.6 mmol) in dry CH_2Cl_2, HBTU (341 mg, 0.9 mmol) was added at once, followed by the addition of DIEA (0.316 mL, 1.8 mmol) at 0 °C. After 10 minutes at 0 °C, propargyl amine **10** (0.046 mL, 0.72 mmol) was added. The reaction was stirred for 24 hours at room temperature. After completion of the reaction, the reaction mixture was concentrated and the residue was taken up in ethylacetate and the organic layer was successively washed with saturated $NaHCO_3$ solution (3×) and brine. After drying with Na_2SO_4 and filtration, the solvents were removed under vacuum and purifiedby column chromatography to provid the desired compound **11** (274 mg, 85 %) as a white solid; ^{1}H NMR (500 MHz, DMSO-d_6): 12.32 (1H, s_{br}), 12.08 (1H, s_{br}), 11.78 (1H, s_{br}), 8.39 (1H, t, *J* = 5.7 Hz), 8.30 (1H, s), 8.22 (1H, s), 7.91 (1H, s), 4.07 (2H, dd, *J* = 2.5, 3.15 Hz), 3.13 (1H, s), 1.51 (9H, s); ^{13}C NMR (100 MHz, DMSO-d_6): 160.3, 160.1, 159.3, 159.1, 157.9, 157.4, 152.9, 144.2, 142.2, 142.1, 121.5, 120.7, 118.4, 81.8, 81.0, 72.9, 28.2, 27.8; HRMS (ESI) calcd for $C_{20}H_{20}N_7O_5S_3$ $[M+H]^+$: 534.0683; Found: 534.0686.



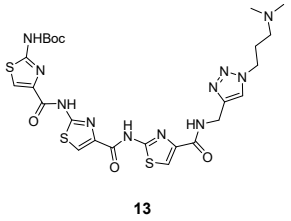
11

Synthesis of water soluble azide 12: Sodium azide (2.47 g, 0.038 mol) was added to a solution of *N, N´*-dimethyl (3-chloropropyl) amine hydrochloride (3 g, 0.0189 mol) in 40 mL water. Then the reaction mixture was heated at 70 °C for 5 h. After cooling to ambient temperature, KOH was added to the reaction mixture and extracted 3 times with diethyl ether. Removal of the diethyl ether at 0 °C under reduced pressure gave crude **12** as a colourless liquid (1.14 g, 47%), which was directly used for copper (I) catalysed cycloaddition without any purification.



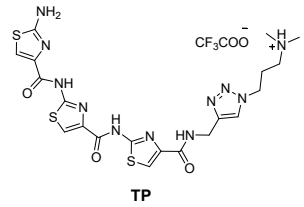
Synthesis of triazole containing thiazole peptide 13:

Terminal alkyne containing thiazole peptide **11** (100 mg, 0.187 mmol) was dissolved in a 3:1 mixture of *t*-BuOH/H_2O (2 mL). Copper (II) sulphate pentahydrate (7 mg, 0.0187 mol) and sodium ascorbate (10 mg, 0.0374 mol) were added, and the solution was stirred for 10 min. An azide **12** (240 mg, 0.187 mol) was added, and the resulting mixture was stirred for 24 h at room temperature. After the completion, the reaction mixture was concentrated and purified by column chromatography to provide the desired compound **13** (112 mg, 90 %) as a white solid; ^{1}H NMR (500 MHz, DMSO-d_6): 8.44 (1H, t, *J* = 5.85 Hz), 8.26 (1H, s), 8.18 (1H, s), 7.98 (1H, s), 7.89 (1H, s), 4.53 (2H, d, *J* = 5.85 Hz), 4.34 (2H, t, *J* = 7.5 Hz), 2.22 (2H, t, *J* = 6.7 Hz), 2.14 (6H, s), 1.96-1.90 (2H, m), 1.51 (9H, s); ^{13}C NMR (100 MHz, DMSO-d_6):160.5, 160.0, 159.6, 159.3, 158.4, 157.6, 152.9, 144.4, 144.3, 142.6, 142.2, 122.9, 121.3, 120.5, 118.1, 81.9, 55.5, 47.4, 44.9, 34.4, 27.9, 27.6; HRMS (ESI) calcd for $C_{25}H_{32}N_{11}O_5S_3$ $[M+H]^+$: 662.1745; Found: 662.1743.

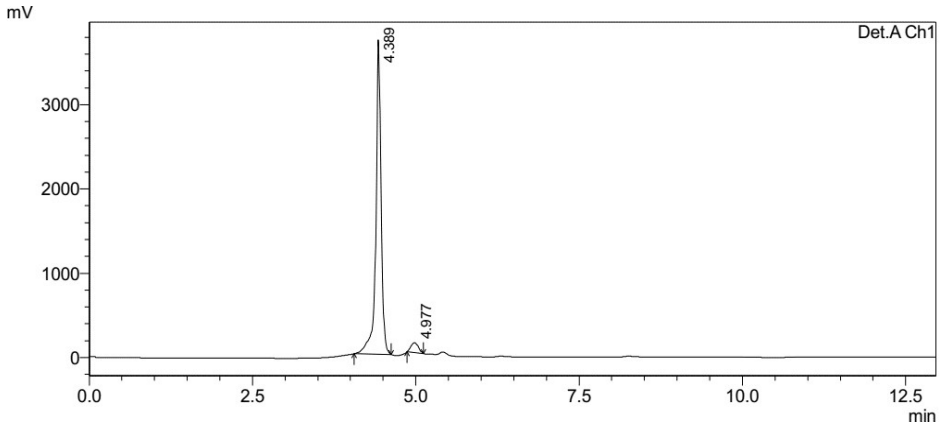


13

Synthesis of triazole containing thiazole peptide TP: Boc-protected thiazole peptide **13** (100 mg, 0.15 mmol) was dissolved in CH_2Cl_2 (1 mL) and cooled to 0 °C. 1 mL trifluoroacetic acid (an equal amount as the solvent) was added and the solution was warmed to room temperature. The reaction mixture was stirred for about 3-4 hours at room temperature until the starting material was entirely consumed. After completion of the reaction, the solvent was removed in vacuo and the residue was washed with ether. The solid residue was dried under vacuum to provide the corresponding thiazole peptide **TP** (89 mg, 89%) as a white solid; ^{1}H NMR (500 MHz, D_2O/DMSO-d_6= 4:1): 7.86 (1H, s), 7.71 (1H, s), 7.56 (1H, s), 7.45 (1H, s), 4.38-4.35 (4H, merged), 3.01 (2H, t, *J* = 6.7 Hz), 2.71 (6H, s), 2.21-2.15 (2H, m); ^{13}C NMR (125 MHz, D_2O/DMSO-d_6= 4:1): 170.7, 163.5, 162.7 (q, *J* = 33.7 Hz), 160.7, 158.9, 158.8, 146.0, 144.6, 142.8, 136.1, 125.3, 123.9, 120.7, 117.7 (q, *J* = 290.7 Hz), 116.9, 114.2, 55.7, 48.3, 44.0, 35.4, 26.0; peaks for trifluoroacetate salt were observed at 162.7 (q, *J* = 33.7 Hz), 117.7 (q, *J* = 290.7 Hz) in ^{13}C NMR; HRMS (ESI) calcd for $C_{20}H_{24}N_{11}O_3S_3$ $[M+H]^+$: 562.1220; Found: 562.1225. HPLC purity: 95%. The HPLC chromatogram of thiazole peptide **TP** is given below.



TP



PeakTable

Detector A Ch1 280nm

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2	4.977	916593	117755	4.233	3.061
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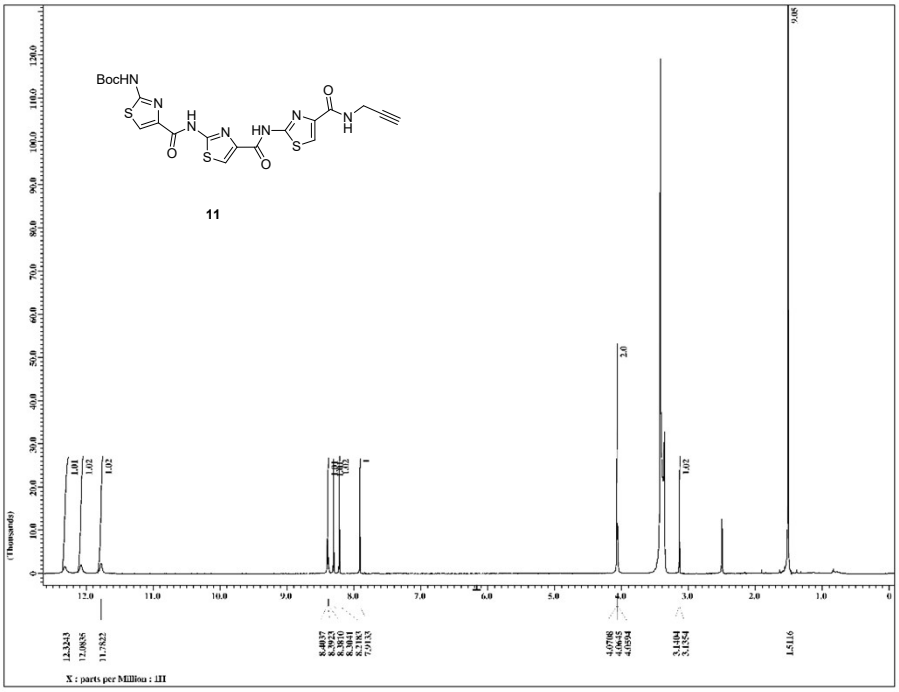
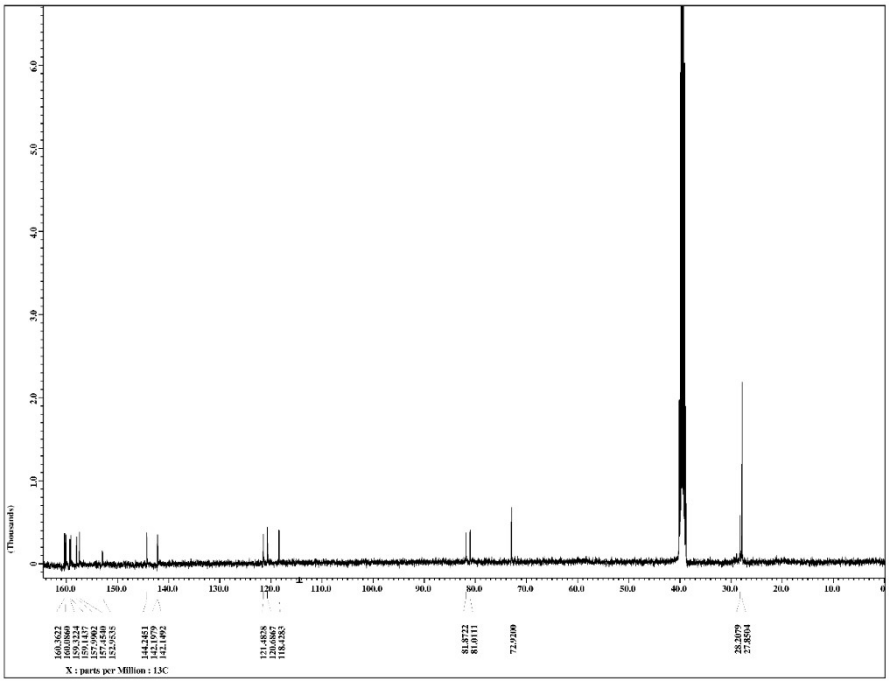
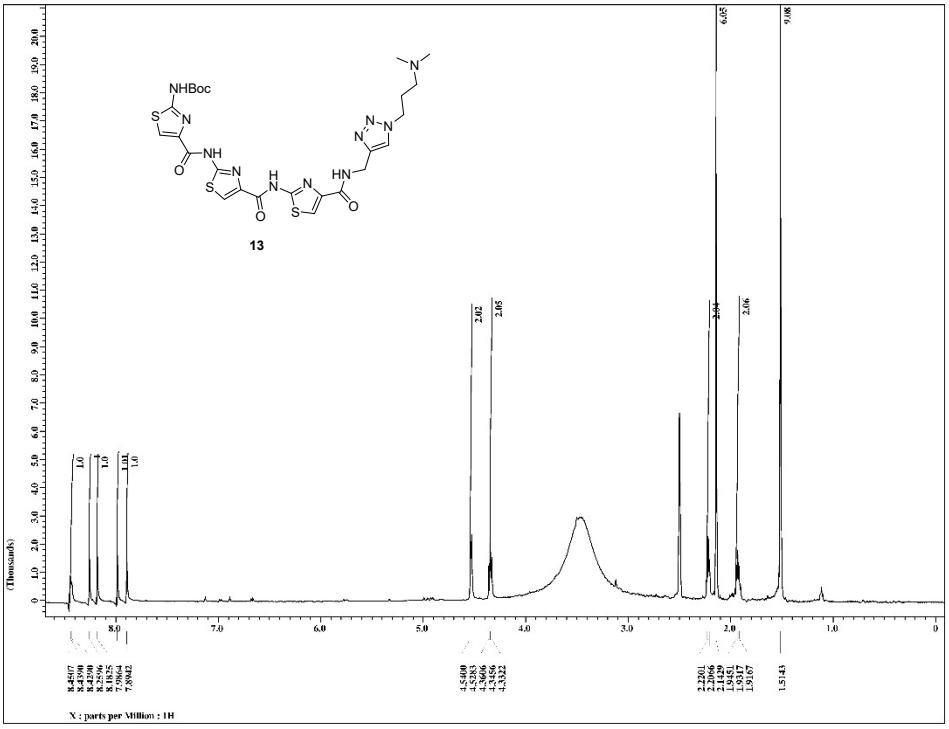
3.0 NMR spectra of synthesized compounds

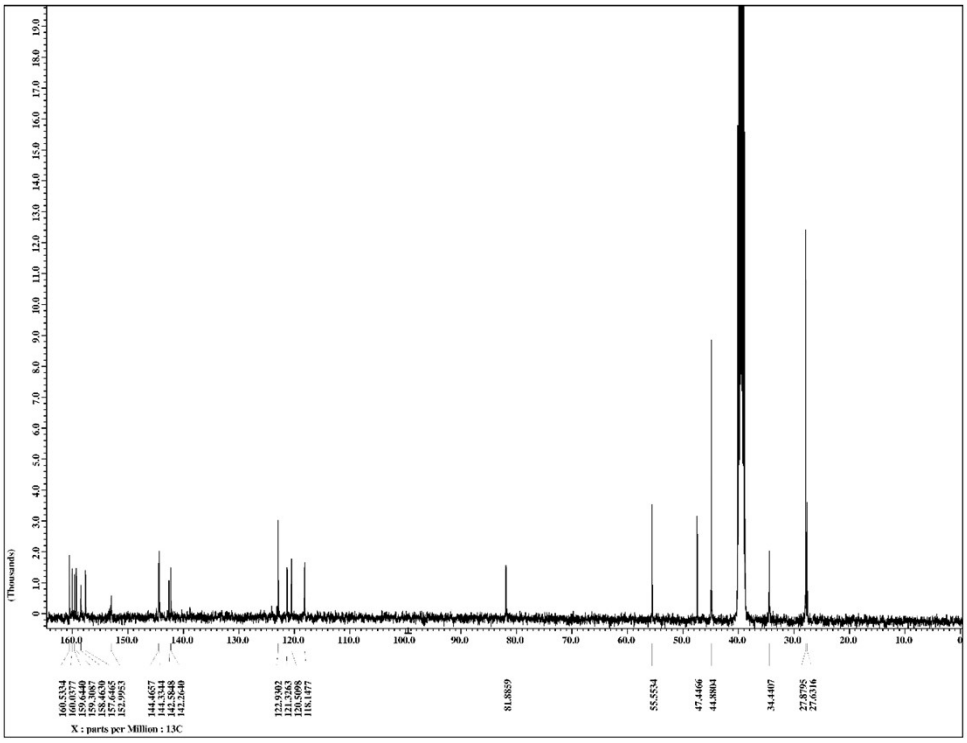
^{1}H and ^{13}C NMR of compound 11:



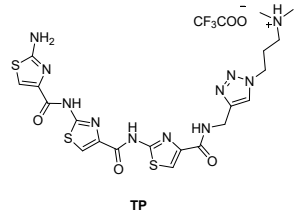


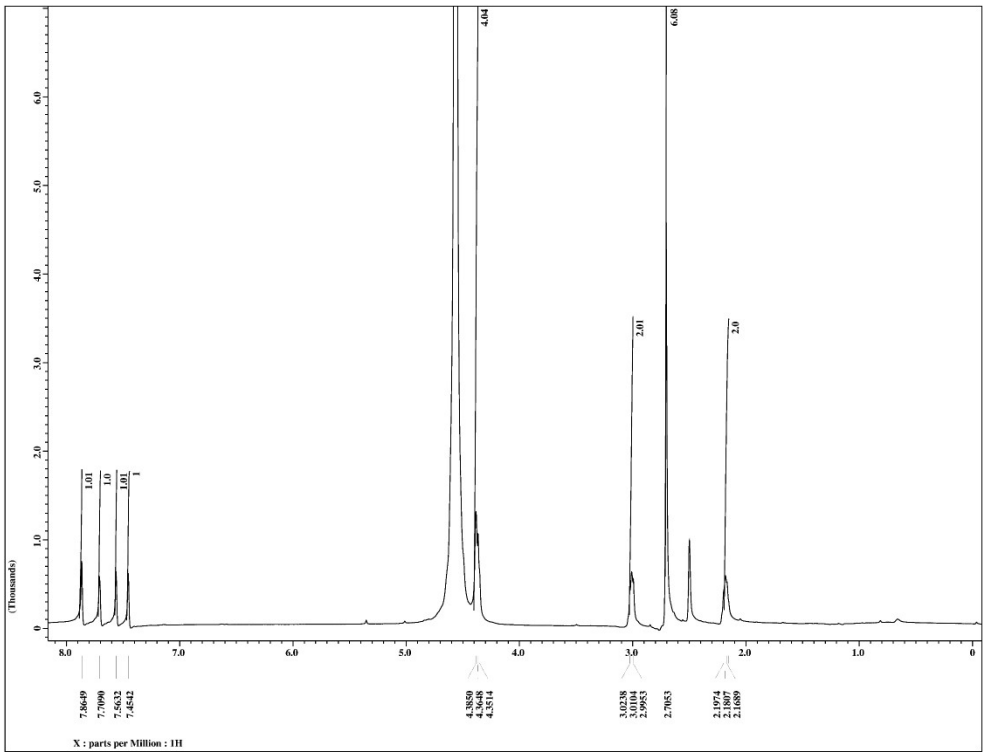
^{1}H and ^{13}C NMR of compound 13:

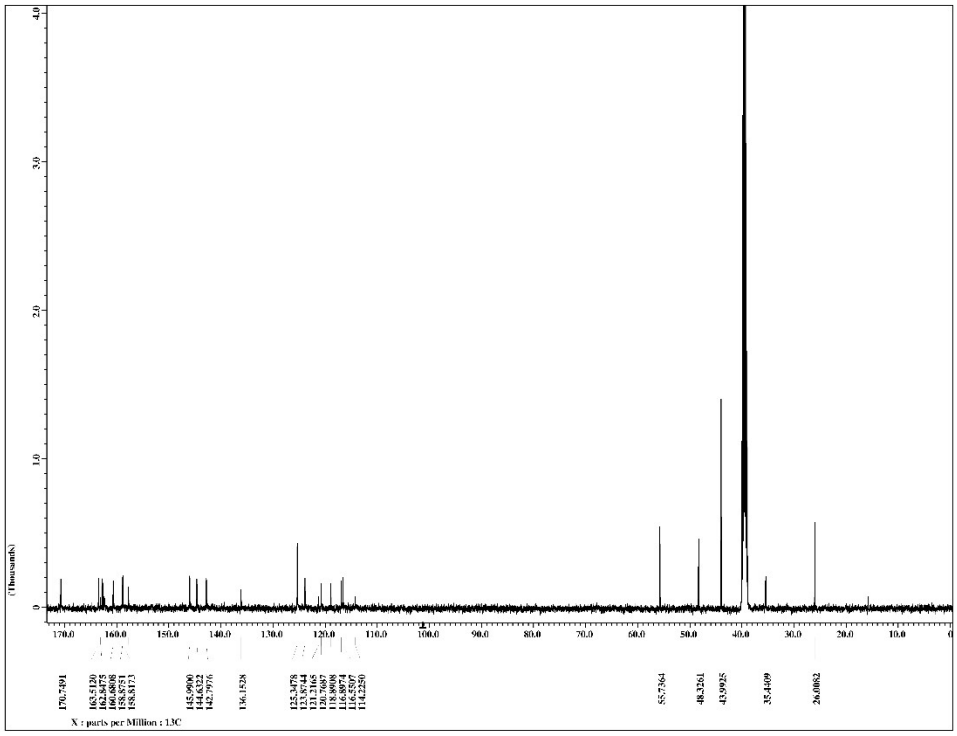




^{1}H and ^{13}C NMR of compound TP:







4.0 Fluorescence titration study

Fluorescence spectra were measured in a Horiba JobinYvon FluoroLog-3 spectrofluorimeter at 25 °C in thermostated cell holder using 1 mm path length micro quartz cuvette with filtered buffer (20mM Na cacodylate, 180 mM NaCl and 10 mM $MgCl_2$ buffer pH 7.4). TAR RNA or DNA was pre-annealed in 20 mM sodium cacodylate, 180 mM NaCl, 10 mM $MgCl_2$ buffer, pH 7.4. Annealing was performed by heating at 85 °C for 5 min followed by rapid cooling at 4 °C to get the kinetically favoured folded structure. Fluorescence titrations were performed with successive addition of pre-annealed RNA or DNA solution into the 2 μM ligand solution. Fluorescence spectral data were recorded by excitation at 280 nm giving emission maxima at 435 nm for TAR RNA and at 435 nm and 502 nm for TAR DNA. Final analysis of the data was carried out using Originpro 8.0 (OriginLab Corp.) and the dissociation constant value (K_d) was calculated using the Hill-1 formula:

$$F = F_0 + \{(F_{max} - F_0)[\text{DNA}]\}/K_d + [\text{DNA}] \quad \ldots\ldots\ldots\ldots\ldots (1)$$

F is the fluorescence intensity, F_{max} is the maximum fluorescence intensity, F_0 is the fluorescence intensity in the absence of DNA and K_d is the dissociation constant.

TAR RNA, TAR DNA and Tat peptide sequences used in the fluorescence studies are as follows:

TAR RNA: 5′ -GGCAGAUCUGAGCCUGGGAGCUCUCUGCC- 3′

TAR DNA: 5′ -GGCAGATCTGAGCCTGGGAGCTCTCTGCC- 3′

Tat peptide: H_2N-YGRKKRRQRRRP-COOH

For solvatochromatic studies fluorescence spectra of ligand **TP** (2 μM) where recorded in presence of various solvents (Hexane, ethyl acetate, ethanol, DMSO, water). Spectral data were recorded in Horiba JobinYvon FluoroLog-3 spectrofluorimeter at 25 °C in thermostated cell holder using 1 mm path length micro quartz cuvette. Fluorescence spectral data of ligand **TP** were recorded with excitation at 280 nm. Final analysis of the data was carried out using Originpro 8.0 (OriginLab Corp.).

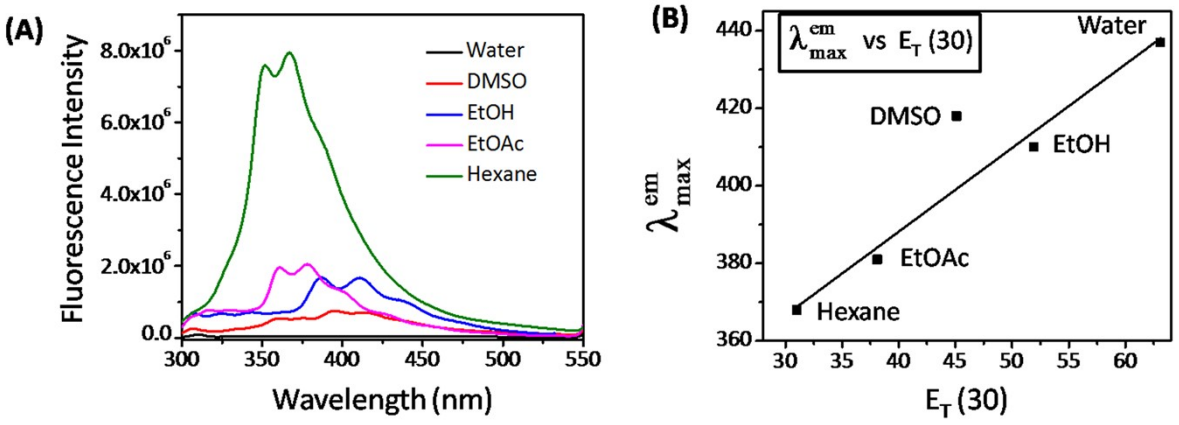


Figure S1. (A) Environment polarity effect of **TP** in various solvent environments (Hexane, ethyl acetate, ethanol, DMSO, water). (B) Plot of emission maxima (λ^{em}_{max}) of **TP** in different solvents vs. $E_T(30)$ of different solvents.

5.0 Isothermal titration calorimetric studies

Isothermal titration calorimetry experiments were performed on a Microcal PEAQ-ITC micro-calorimeter (Malvern, USA). DNA/RNA to ligand ratio was taken as 1:10 and the titration was carried out in 20mM Na cacodylate, 180 mM NaCl and 10 mM MgCl2 buffer pH 7.4 at 25 ˚C. Final analysis of the data was carried out using Microcal analysis software (Malvern, USA).

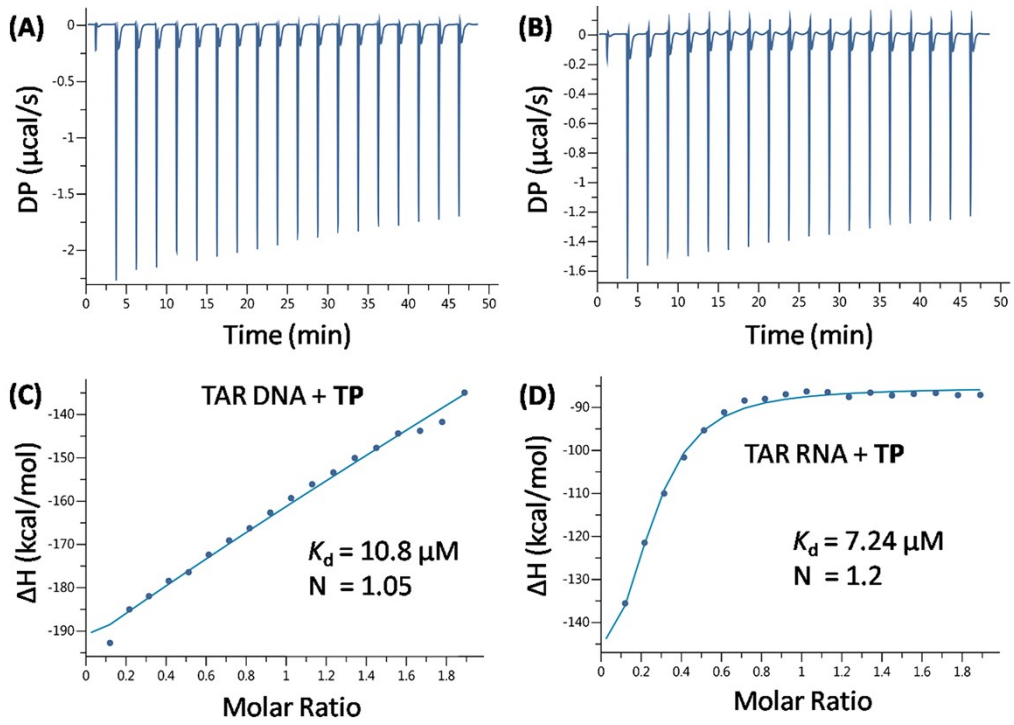


Figure S2. ITC heat bust curves and binding isotherm profile of **TP** with TAR DNA (A,C) and TAR RNA (D,B) in 20mM Na cacodylate, 180 mM NaCl and 10 mM $MgCl_2$ buffer pH 7.4.

6.0 Fluorescence study of TP in different pH

The spectra were measured in a Horiba JobinYvon FluoroLog-3 spectrofluorimeter at 25 °C in thermostated cell holder using a 1 mm path length micro quartz cuvette. Fluorescence spectral data were recorded by excitation at 280 nm giving an emission maximum of 362 nm and 435 nm. The pH of the solution was made acidic by adding 500 mM HCl, 180 mM NaCl & 10 mM $MgCl_2$ and then changed to neutral by adding 500 mM NaOH, 180 mM NaCl & 10 mM $MgCl_2$ into the solution of **TP** in buffer and recorded by excitation at 280 nm. The final data analysis was carried out using Originpro 8.0 (OriginLab Corp.).

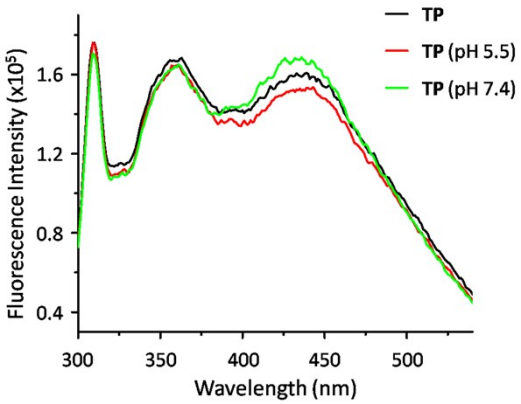


Figure S3. Fluorescence spectra of **TP** in 20mM Na cacodylate, 180 mM NaCl and 10 mM $MgCl_2$ buffer pH 7.4 in response to pH changes.

7.0 CD spectroscopy

CD spectra were recorded on a JASCO J-815 spectrophotometer using a 1 mm path length quartz cuvette. TAR RNA/DNA was pre-annealed in 20 mM Na cacodylate, 180 mM NaCl and 10 mM $MgCl_2$ buffer pH 7.4. The CD spectrum of TAR RNA was recorded first in the range of 200 to 500 nm and the pH of the solution was changed to acidic (pH 5.5) by adding 500 mM HCl, 180 mM NaCl & 10 mM $MgCl_2$ and then to neutral (pH 7.4) by adding 500 mM NaOH, 180 mM NaCl & 10 mM $MgCl_2$ and the spectra were recorded after each addition. For titration, ligand **TP** was added into the solution of TAR RNA/DNA in increasing concentration and the spectra were recorded after each addition. The CD spectra represented an average of three scans, smoothed and zero corrected. The final data analysis was carried out by using Origin 8.0 (OriginLab Corp.).

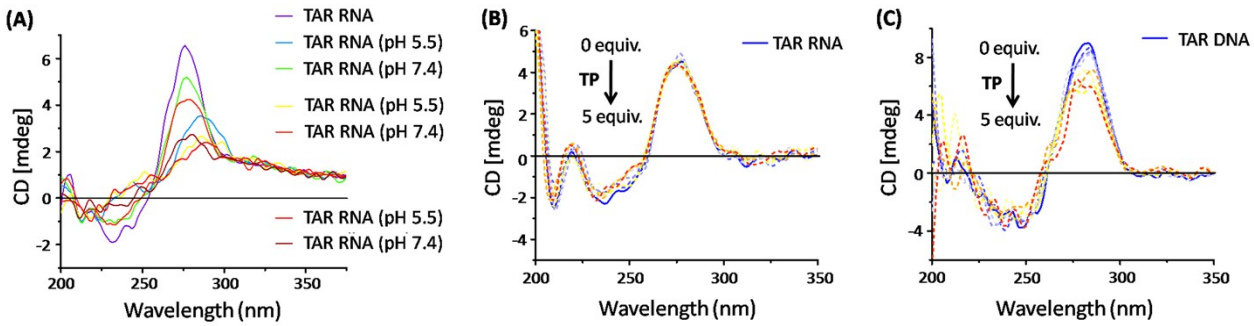


Figure S4. (A) CD spectra of TAR RNA in response to pH changes for three cycles. CD titration spectra of (B) TAR RNA and (C) TAR DNA with **TP** in 20mM Na cacodylate, 180 mM NaCl and 10 mM $MgCl_2$ buffer pH 7.4.

8.0 Fluorescence binding assay for sensor designing

TAR RNA and DNA (50 μM) were annealed in 20mM Na cacodylate, 180 mM NaCl and 10 mM $MgCl_2$ buffer pH 7.4. Ligand **TP** (2 μM) was first titrated with 0-8 equiv. of TAR RNA or DNA and the fluorescence spectra were recorded upon excitation at 280 nm after each addition. After attaining saturation due to continuous addition of TAR RNA or DNA, the pH of the solution was changed to acidic (pH 5.5) by adding 500 mM HCl, 180 mM NaCl & 10 mM $MgCl_2$ and then neutral pH was attained by adding 500 mM NaOH, 180 mM NaCl & 10 mM $MgCl_2$ into the **TP** and TAR RNA/DNA mixture and the spectra were recorded after each addition. All the measurements were performed thrice in the Horiba Jobin Yvon FluoroLog-3 instrument and the data were analyzed using Origin 8 (OriginLab Corp.).

9.0 Reusable logic device with multi-reset function

For recycling experiments, **TP** was taken in 20 mM Na cacodylate, 180 mM NaCl and 10 mM $MgCl_2$ buffer pH 7.4 at the final concentration of 2 μM. First, pre-annealed TAR RNA was added to **TP,** and the corresponding fluorescence spectra were recorded up to reaching the saturation point. Next, the pH of the solution was changed to acidic (pH 5.5) by adding 500 mM HCl, 180 mM NaCl and 10 mM $MgCl_2$ and then to neutral (pH 7.4) by adding 500 mM NaOH, 180 mM NaCl and 10 mM $MgCl_2$ into the mixture of **TP** and TAR RNA/DNA consecutively for three cycles and the spectra were recorded after each addition. The fluorescence spectra were recorded in Horiba Jobin Yvon FluoroLog-3 instrument, and the spectral data was analysed using Origin 8 (OriginLab Corp.).

10.0 Fluorescence study of TP in presence of TAR RNA and Tat peptide

The spectra were measured in a Horiba JobinYvon FluoroLog-3 spectrofluorimeter at 25 °C in thermostated cell holder using a 1 mm path length micro quartz cuvette. Fluorescence spectral data were recorded by excitation at 280 nm giving an emission maximum of 362 nm and 435 nm. TAR RNA (50 μM) were annealed in 20mM Na cacodylate, 180 mM NaCl and 10 mM $MgCl_2$ buffer pH 7.4 and then mixed with Tat peptide in 1:1 ratio and titration was carried out. The final data analysis was carried out using Originpro 8.0 (OriginLab Corp.).

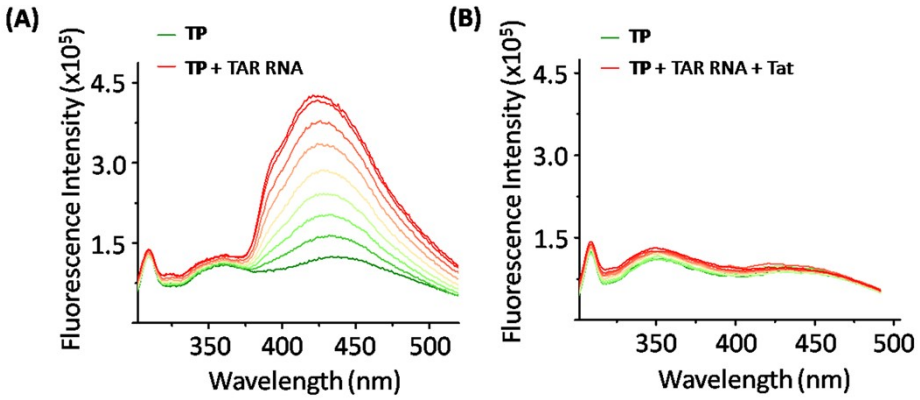


Figure S5. Fluorescence spectra of **TP** with (A) TAR RNA and (B) TAR RNA with Tat peptide mixture in 20mM Na cacodylate, 180 mM NaCl and 10 mM $MgCl_2$ buffer pH 7.4.

11.0 References

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