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Interaction of aryl tetrazolones with anions: Proton transfer vs hydrogen bonding

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Abstract

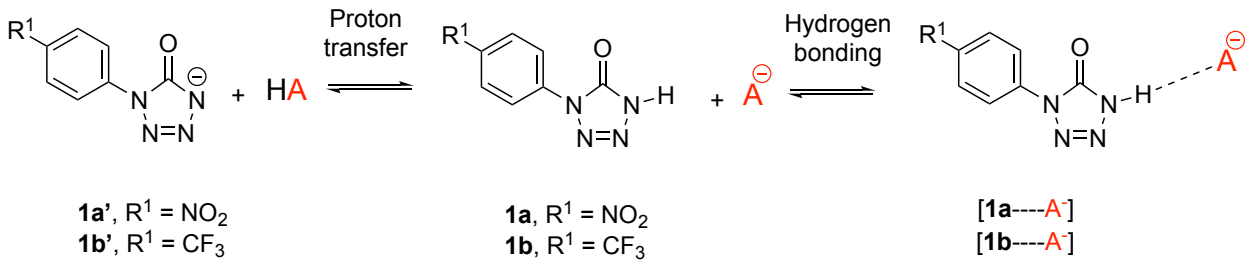
In this study, the interaction two monosubstituted aryl tetrazolones, namely 1-(4-nitrophenyl)-1,4-dihydro-tetrazol-5-one **1a** and 1-(4-trifluoromethylphenyl)-1,4-dihydro-tetrazol-5-one **1b**, with anions of varying basicity *e.g.* hydrogen sulfate (HSO_4^-), bromide (Br^-), nitrate (NO_3^-), thiocyanate (NCS^-), chloride (Cl^-) and acetate (AcO^-) was investigated in acetonitrile and DMSO. UV and NMR titrations indicated that tetrazolones interact through hydrogen bonding or weak electrostatic interactions with HSO_4^-, Br^-, NO_3^-, NCS^-, and Cl^-. The association constants (K_a) were found to be in the order $Cl^- > Br^- > NO_3^- > NCS^- > HSO_4^-$. Tetrazolones **1a**,**b** exhibited almost 9 times higher selectivity towards Cl^- compared to Br^- which may be attributed to the higher basicity of the former. The affinity of **1a** towards most anions was higher than **1b**, except for HSO_4^-. This was attributed to higher electron withdrawing ability of $–NO_2$ group compared to $–CF_3$ that renders the N-H proton more acidic for interaction with anions resulting in higher K_a values. Significant UV changes were observed upon addition of the AcO^- anion to the solution of **1a**,**b** in acetonitrile as new bands formed and isosbestic points were observed indicating the formation of a new species. NMR titrations in DMSO-d_6 further confirmed that **1a**,**b** underwent deprotonation with AcO^- owing to its higher basicity.

Introduction

Over the past three decades, there has been a sudden growth in the field of selective recognition of anions by synthetic receptors[1] which is attributed to the fundamental role anions play in various biological,[2-5] and industrial processes,[6, 7] as well as to their behavior as environmental pollutants.[8, 9] Artificial anion-binding receptors can be positively charged or neutral. The charged receptors include protonated polyamines and azamacrocycles,[10-12] guanidiniums,[13, 14] as well as transition metal or lanthanide-based complexes,[15, 16] where the attractive force between the receptor and the anion is predominantly electrostatic. On the other hand, the neutral anion receptors are based on amides and thioamides,[17, 18] carbamides,[19] ureas and thioureas,[20] as well as pyrroles,[21, 22] indoles,[23, 24] amidoureas,[25] and calixpyrroles.[26] These functional groups contain –N-H fragments at the binding site where the anion is held by hydrogen bonds (H-bonds). Several studies in the literature have revealed that the stability of the receptor-anion complex (measured by its association constant, K_a) is dependent on the acidity of the receptor (H-bond donor) and basicity of the anion (H-bond acceptor). As a result, the strongest complexes are formed with anions of most electronegative atoms, *i.e.* F and O, and the stability of a complex typically decreases with the decreasing basicity of the anion.[27] Similarly, substituents attached to the receptor moiety can influence the acidity of the receptor.[28, 29] For example, diarylureas form stable complexes with anions compared to alkyl substituted ureas, due to the higher acidity of the -N-H groups in the former.[20] This effect is even more pronounced for thioureas[30] where the N-H group is significantly more acidic (pK_a of thiourea is 21.1 and that of urea is $pK_a = 26.7$).[31]

Hof and coworkers evaluated the scope of tetrazoles as anion-binding motifs.[22, 32-34] The N-H moiety in these frameworks have same order of acidity as carboxylic acids (-COOH), and studies

have revealed that these heterocycles are excellent anion-binding units displaying K_a values of 590 M^{-1} and 11000000 M^{-1} for the interaction of 5-benzyl-1*H*-tetrazole and tris-tetrazole with a chloride anion, respectively.[33] Tetrazolones which are derivatives of tetrazoles, are widely distributed in pharmaceutical agents,[35] high energy materials,[36] agricultural[37] and industrial products.[38, 39] Analogous to the parent tetrazoles, these feature an acidic N-H moiety capable of interacting with anions, but the scope of these ring structures as anion-binding motifs has not been previously evaluated. Owing to the widespread utility of these frameworks in aforementioned fields, investigations to better understand their interaction with anions is a worthwhile effort. Thus, in this work, the interaction of 1-(4-nitrophenyl)-1,4-dihydro-tetrazol-5-one **1a**, and 1-(4-trifluoromethylphenyl)-1,4-dihydro-tetrazol-5-one **1b** (Scheme 1) with anions of varying basicity such as hydrogen sulfate (HSO_4^-), bromide (Br^-), nitrate (NO_3^-), thiocyanate (NCS^-), chloride (Cl^-) and acetate (AcO^-), was explored using UV and NMR spectroscopy. The most common type of interaction that is expected between tetrazolones **1a**,**b** and an anion A^- is H-bonding resulting in the formation of host-guest complex [**1a**,**b**----A^-] (Scheme 1, right). However, `the presence of electron withdrawing groups on **1a**,**b** is expected to increase the acidity of the proton involved in the H-bond, and subsequently, increasing the possibility of proton transfer,[27] especially with anions of higher basicity, resulting in the formation tetrazolonide anion **1a**,**b'** and conjugate acid (HA) of the anion (Scheme 1, left).



Scheme 1. General scheme showing hydrogen bonding (right) and proton transfer (left) between the tetrazolones **1a**,**b** and an anion A^-.

The UV titrations between the hosts **1a**,**b** and the guests, A^- were conducted in acetonitrile and association constants K_a were obtained. The NMR titrations were performed in DMSO-d_6 that showed N-H proton at 14.95 ppm permitting the study of hydrogen bonding vs. proton transfer. Note that N-H proton is not observed in MeCN-d_3.

Results and discussion

Computational studies

The interaction of **1a**,**b** with anions HSO_4^-, Br^-, NO_3^-, NCS^-, Cl^- and AcO^- was investigated by density functional theory with the hybrid meta exchange-correlation functional M06-2X using the 6-311+G* basis set in the presence of polarized continuum model (PCM) to approximate the acetonitrile environment. In order to study proton transfer (Scheme 1, left), the structures of **1a**,**b** and the anions A^- as well as the tetrazolonide anions **1a**,**b'** and their conjugate acids HA were fully optimized.

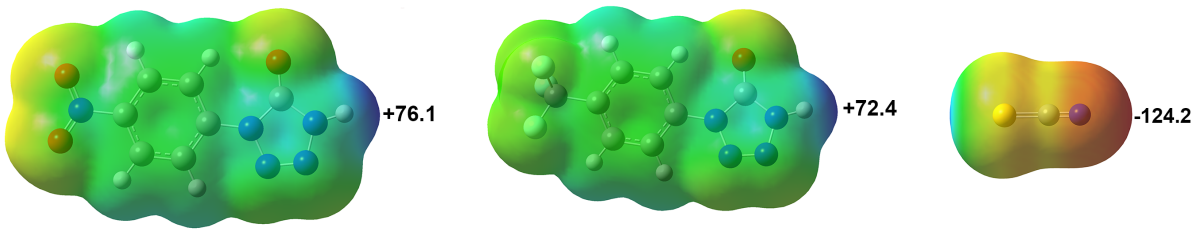


Figure 1. Molecular electrostatic surface potential (MESP) maps on 0.001 a.u. iso-surface of electron density for **1a** (left), **1b** (center) and NCS^- anion (right) calculated at M06-2X/6-311+G*/PCM=MeCN. The MESP values of the surface maxima (Vs, max) and minima (Vs, min) at selected points are in kcal mol^{-1}.

Analyses of molecular electrostatic surface potential (MESP) maps for **1a** and **1b** revealed that strong electrostatic positive potential is exhibited by the N-H moiety, indicating a likely site for interaction with an anion (Figure 1, left & center). Proton transfer from tetrazolones **1a**,**b** to the anions A^- (HSO_4^-, Br^-, NO_3^-, NCS^-, and Cl^-) leading to the formation of the tetrazolonide anions **1a**,**b'** and the respective conjugate acids HA (H_2SO_4, HBr, HNO_3, HSCN (HNCS) and HCl) was found to be extremely endothermic (Table 1, entries 1 – 7). In case of thiocyanate ion (NCS^-), the MESP map indicated the most negative potential to be localized on the nitrogen atom (Figure 1, right). Accordingly, proton transfer to N-atom of NCS^- to form **1a**,**b'** and isothiocyanic acid (HNCS) was predicted to be 9.0 kcal/mole less endothermic than transfer to the S-atom of NCS^- to form thiocyanic acid (HSCN) (entries 4 & 5). On the contrary, proton transfer from tetrazolones **1a,b** to AcO^- to form **1a**,**b'** and acetic acid was found to be exothermic (-6.4 and -5.1 kcal/mole).

Similarly, the van der Waals complexes [**1a**,**b**----A^-] were fully optimized at M06-2X/6-311+G*/PCM=MeCN, and are shown in Figures 2 and S2. The formation of van der Waals complexes [**1a**,**b**----A^-] between **1a**,**b** and HSO_4^-, Br^-, NO_3^-, NCS^-, and Cl^- was found to be favorable as the binding enthalpies were found to be exothermic by -5.1 to -8.5 kcal/mole, for the

interaction of the two tetrazolones with anions studied (entries 8 – 13). Again, in case of thiocyanate ion (NCS^-), the N---H hydrogen bond was found to be ~3 kcal/mole more stabilizing than S---H interaction (Figure 2d, entries 11 and 12), owing to the greater electronegativity of the nitrogen atom. Attempts to optimize a van der Waals complex between **1a**,**b** and AcO^- resulted in proton transfer to the anion (Figures 2f & S2f) and the process was found to be significantly exothermic (-16.0 and -14.9 kcal/mole). Overall, DFT calculations predicted that **1a,b** will form H-bond or weak electrostatic interactions with HSO_4^-, Br^-, NO_3^-, NCS^-, and Cl^-, and undergo proton transfer with more basic AcO^- anion.

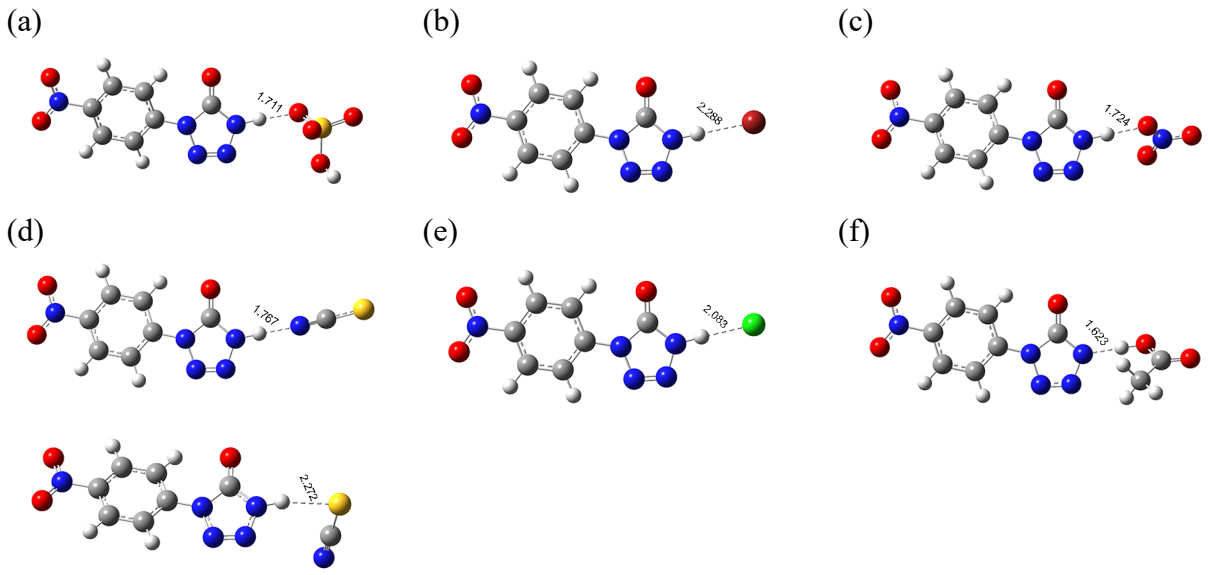


Figure 2. Complexes of **1a** with (a) HSO_4^-, (b) Br^-, (c) NO_3^-, (a) NCS^-, and (e) Cl^- optimized at M06-2X/6-311+G*/PCM=MeCN, and (f) proton transfer during the optimization of **1a** with AcO^-. Distances are in Å.

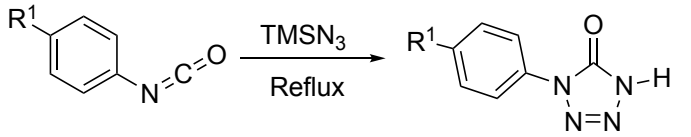
Table 1. Reaction energies for proton transfer and complexation between **1a**,**b** and anions at M06-2X/6-311+G*/PCM=MeCN.

Entry	Reaction	ΔE (kcal/mole)	
	Proton Transfer	**1a**	**1b**
1	**1a**,**b** + HSO_4^- ⟶ **1a**,**b'** + H_2SO_4	24.1	25.4
2	**1a**,**b** + Br^- ⟶ **1a**,**b'** + HBr	28.5	29.8
3	**1a**,**b** + NO_3^- ⟶ **1a**,**b'** + HNO_3	17.1	18.4
4	**1a**,**b** + NCS^- **1a**,**b'** + HSCN	23.1	24.4
5	**1a**,**b** + NCS^- ⟶ **1a**,**b'** + HNCS	14.4	15.7
6	**1a**,**b** + Cl^- ⟶ **1a**,**b'** + HCl	23.1	24.4
7	**1a**,**b** + AcO^- ⟶ **1a**,**b'** + AcOH	-6.4	-5.1
	Van der Waals Complexes[a]		
8	**1a**,**b** + HSO_4^- ⟶ [**1a**,**b**----HSO_4^-]	-7.2	-7.0
9	**1a**,**b** + Br^- ⟶ [**1a**,**b**----Br^-]	-6.2	-5.9
10	**1a**,**b** + NO_3^- ⟶ [**1a**,**b**----NO_3^-]	-8.5	-8.1
11	**1a**,**b** + NCS^- [**1a**,**b**----$^-$NCS]	-8.0	-7.7
12	**1a**,**b** + NCS^- ⟶ [**1a**,**b**----$^-$SCN]	-5.4	-5.1
13	**1a**,**b** + Cl^- ⟶ [**1a**,**b**----Cl^-]	-7.1	-6.8
14	**1a**,**b** + AcO^- ⟶ [**1a**,**b'**----HOAc]	-16.0	-14.9

[a]Energies were corrected for the basis set superposition error by counterpoise method.[40]

Synthesis of aryl tetrazolones

Tetrazolones **1a**,**b** were synthesized from the corresponding aryl isocyanates in a 1,3-dipolar cycloaddition reaction with trimethysilyl azide (Scheme 2). The reaction mixture was refluxed at 100 °C for 24 hours. Proton NMR spectra after purification confirmed the formation of the desired tetrazolones **1a**,**b** by comparison to the literature data.[41, 42]



1a, $R^1 = NO_2$ (72%)
1b, $R^1 = CF_3$ (43%)

Scheme 2. Synthesis of aryl tetrazolones **1a**,**b**.

Interaction with hydrogen sulfate, bromide, nitrate, and thiocyanate

The UV spectra of tetrazolones **1a**,**b** were collected in acetonitrile. **1a** showed three bands at 193, 220, 297 nm, while **1b** exhibited two bands at 196 and 252 nm (Figure S3, Table S1).

The interaction of tetrazolones **1a**,**b** with HSO_4^-, Br^-, NO_3^-, and NCS^- in acetonitrile was first investigated using UV spectroscopy. Figure 3a depicts the UV absorption spectra obtained by titrating **1a** with HSO_4^-. As the concentration of HSO_4^- increased, the absorption at 321 nm also increased. This observation was more evident in the difference spectrum which is a plot of the host-guest (HG) complex absorbance vs. wavelength (Figure 3b). The absorption at 321 nm in the difference spectrum was fitted to a 1:1 binding isotherm (Figure 4a) in order to determine the association constant, K_a of 23.4 ±0.8 M^{-1}. UV spectral changes observed upon addition of the anions Br^-, NO_3^- and NCS^- to a solution of **1a** in MeCN were identical to that of HSO_4^- (Figures S4 – S6). The corresponding binding isotherms are shown in Figure 4b – c, and the association constants K_a were found to be 76.0 ± 9.0 M^{-1}, 64.4 ± 7.2 M^{-1}, and 36.1 ± 4.4 M^{-1} for Br^-, NO_3^-, and NCS^-, respectively (average of three separate binding fits. Figure S7).

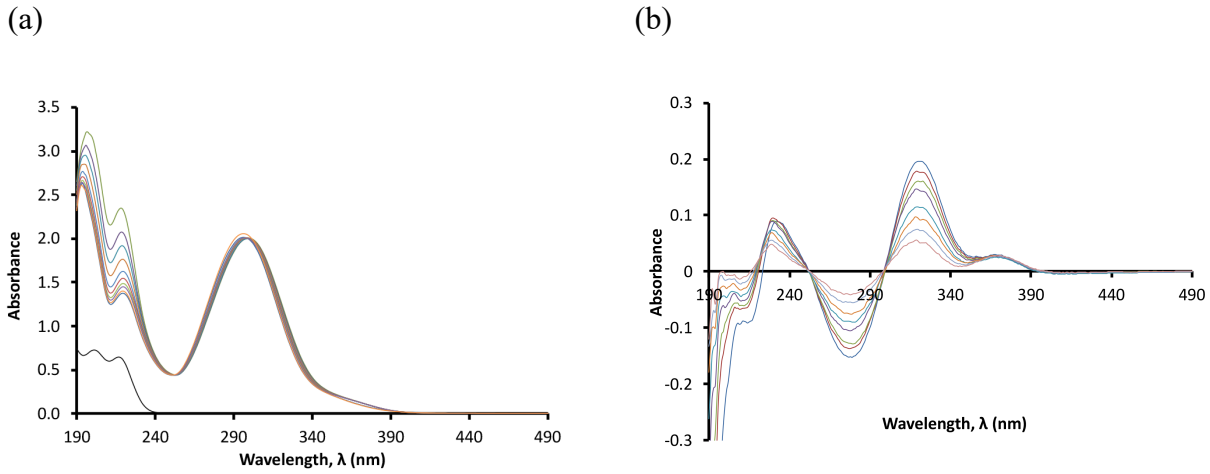


Figure 3. UV titration of 1.5 mM solution of **1a** (a) with increasing amounts of HSO_4^- in acetonitrile (the spectrum of the anion is also shown in black) and (b) the corresponding

difference spectrum displaying the increased absorption at 321nm. The concentration of HSO_4^- ranged between 11 – 175 mM.

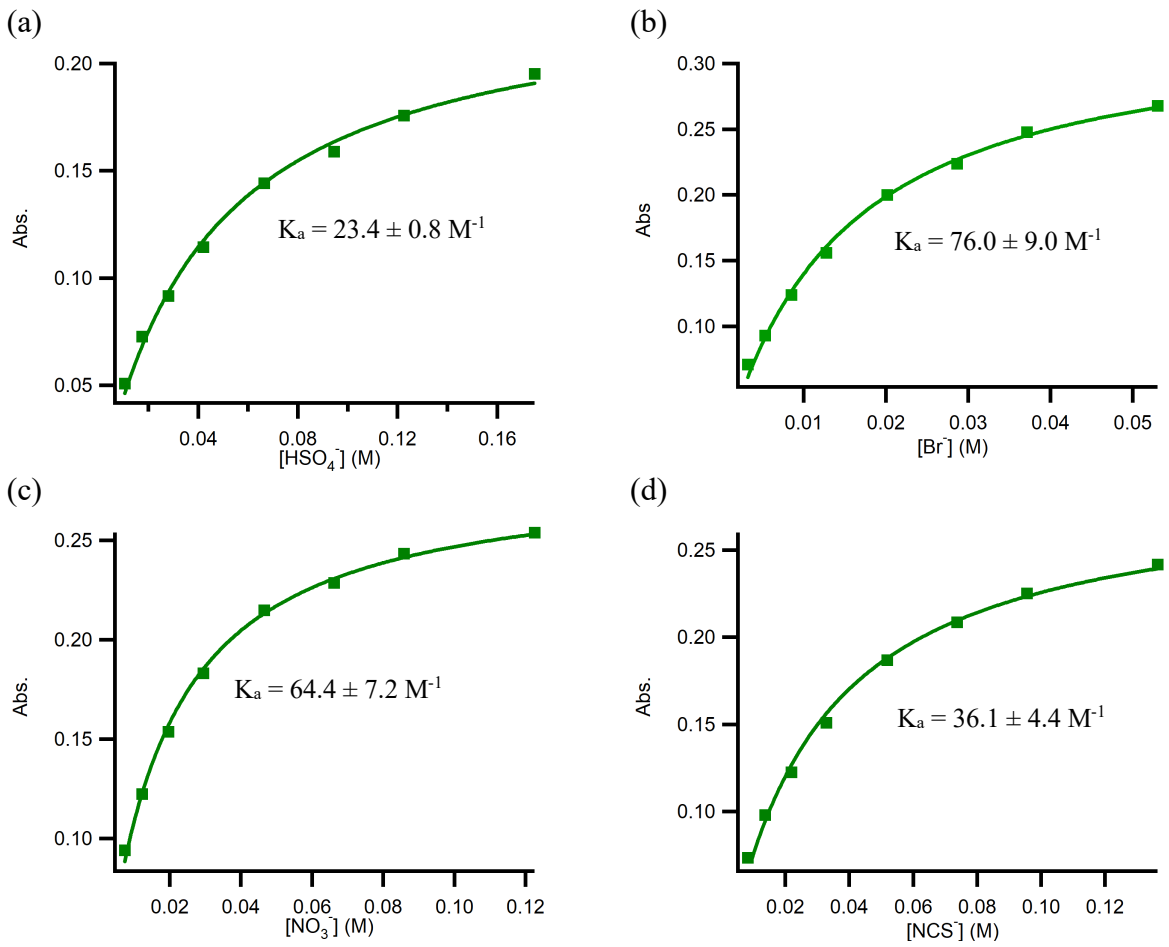


Figure 4. Binding isotherm of **1a** with (a) HSO_4^-; (b) Br^-; (c) NO_3^-; (d) NCS^- in acetonitrile. The K_a values are average from three separate binding fits.

Similarly, the UV titrations of **1b** with HSO_4^-, Br^-, and NO_3^- exhibited an increase in the absorption at 263 nm as the concentration of anion increased (See Figures S8 – S10). The corresponding binding isotherms are shown in Figure 5a – c, and the association constants K_a were found to be HSO_4^-, 31.7 ± 5.3 M^{-1}, Br^-, 67.0 ± 5.5 M^{-1}, and NO_3^-, 50.5 ± 4.4 M^{-1} (average of three

separate binding fits, Figure S11). The low association constants of **1a** and **1b** with these anions suggested that the interaction between two species was relatively weak.

NMR titrations of **1a**,**b** with varying amounts HSO_4^-, Br^-, and NO_3^- in DMSO-d_6 broadened the N-H peak with the increasing concentration of the anion, and no changes in the chemical shift values of the N-H or aromatic protons of the tetrazolones were observed. This supported weak interactions of **1a**,**b** with HSO_4^-, Br^-, and NO_3^-, which was in agreement with association constants measured using UV spectroscopy.

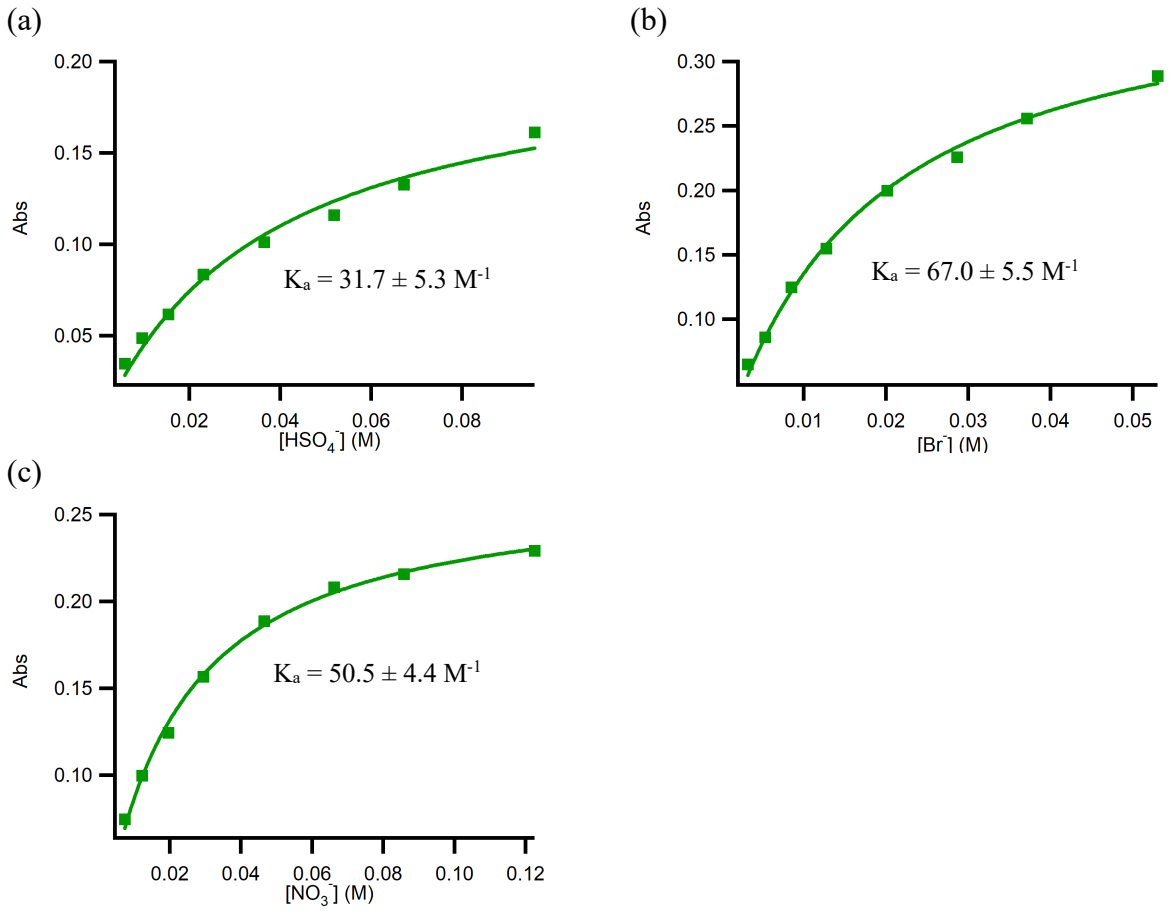


Figure 5. Binding isotherm of **1b** with (a) HSO_4^-; (b) Br^-; (c) NO_3^- in acetonitrile. The K_a values are average from three separate binding fits.

Interaction of tetrazolones 1a,b with chloride

UV titrations of tetrazolones **1a**,**b** with Cl^- in acetonitrile showed changes similar to that observed with HSO_4^-, Br^-, NO_3^-, and NCS^- discussed above. As the concentration of Cl^- increased, the difference spectra showed an increase in absorbance at 321 nm and 263 nm for **1a** and **1b** respectively (Figures S12 & S13). The UV absorbance values from the difference spectra were fitted to the 1:1 binding isotherms (Figure 6) to determine the association constants, K_a which were found to be 661.4 ± 26.5 M^{-1} and 553.2 ± 30.0 M^{-1} for **1a** and **1b** respectively (average of three and two separate binding fits, see Figure S14). Tetrazolones **1a** and **1b** displayed highest affinity for chloride among all the anions investigated, and approximately, 9 times greater than bromide. This can be attributed to the higher basicity of the chloride ion compared to the bromide.

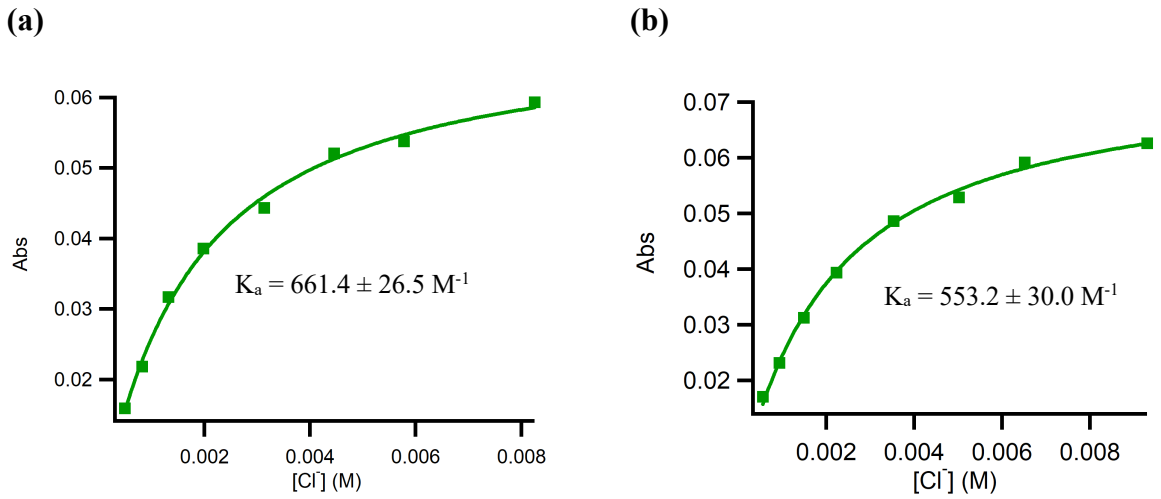


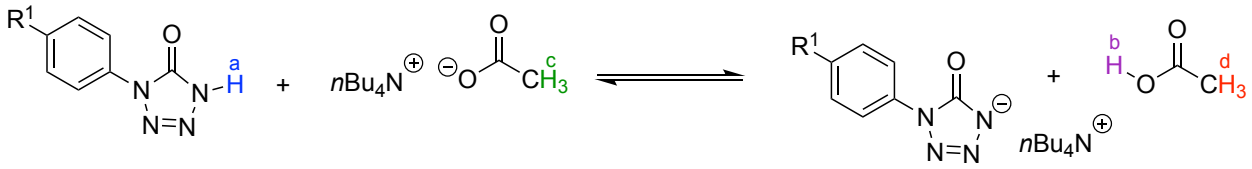
Figure 6. Binding isotherm for the interaction of (a) **1a** and (b) **1b** with Cl^- in acetonitrile. The K_a values are average from three and two separate binding fits, respectively.

The NMR titrations of tetrazolones **1a** and **1b** were conducted in DMSO-d_6 in varying equivalents of Cl^- (1, 2, 3, 4, 5 equivalents), which displayed a gradual downfield shift of the N-H proton from 14.95 to 15.21 ppm for **1a** (Figure S16) and from 14.88 to 15.12 ppm for **1b** (Figure

S18). A downfield shift of the N-H proton is indicative of a H-bonding interaction between the hosts **1a**,**b** and the guest, Cl^- anion.[22, 43] No change in the chemical shift value of the aromatic protons was noted, due to the fact that the N-H proton interacting with Cl^- is not in direct conjugation with the aromatic protons, therefore, the effect on chemical shift is negligible (Figures S15 & S17). The large K_a values and downfield shift of the N-H proton peak was supportive of a stronger hydrogen bonded interaction between **1a**,**b** and the chloride anion, compared to the HSO_4^-, Br^-, NO_3^-, and NCS^- discussed earlier.

Interaction with acetate anion

Upon addition of the acetate (AcO^-) anion to a solution of tetrazolone **1a** in acetonitrile, the color of the solution changed from pale yellow to a bright yellow. Two new absorption bands appeared at 248 and 350 nm as the concentration of AcO^- was increased and two isosbestic points were also observed at 260 and 315 nm (Figures 7a – b). Similar results were exhibited for the interaction of **1b** with AcO^- as new bands formed at 230 and 290 nm and isosbestic points were noted at 240 and 266 nm (Figures 7c – d). The development of new bands and clear isosbestic points suggested the formation of a new species in the solution. It was believed that proton transfer may have occurred between tetrazolones **1a**,**b** and acetate producing tetrazolonide anions **1a**,**b'** and acetic acid as predicted by DFT studies (Scheme 3).



1a, $R^1 = NO_2$
1b, $R^1 = CF_3$

1a', $R^1 = NO_2$
1b', $R^1 = CF_3$

Scheme 3. Proton transfer between tetrazolones **1a**,**b** and the acetate anion.

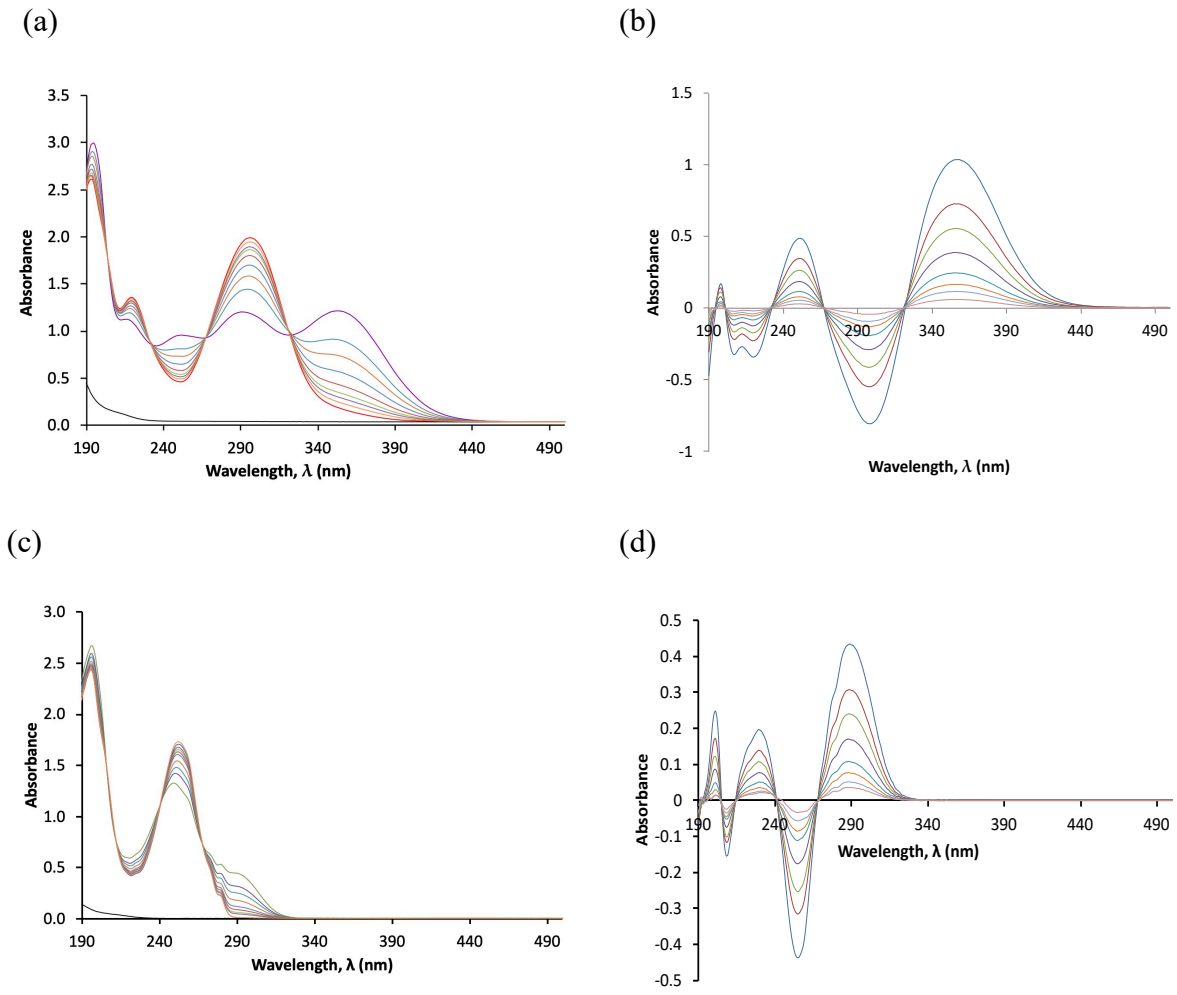


Figure 7. UV titration of (a) 1.5 mM solution of **1a** with acetate and (b) the corresponding difference spectra; (c) 1.5 mM solution of **1b** with acetate and (d) the corresponding difference spectra in acetonitrile. The concentration of acetate ranged from 0.02 – 0.4 mM. The spectrum of acetate is also shown in black.

The NMR titration of tetrazolone **1a** with AcO^- (at select equivalents of the anion) in DMSO-d_6 is shown in Figures 8 & 9 (see supporting material for full titration, Figures S19 - S21). The N-H proton peak of **1a** at 14.95 ppm (peak H_a) gradually broadened into the baseline with increasing concentration of the anion (from 0 – 1 equivalent). In addition, following observations

were made, (1) a new peak gradually appeared at 11.95 ppm which became more prominent as the concentration of anion increased (peak H_b), and (Figure 8) (2) the methyl protons (H_c) of pure TBAA (Scheme 3) which appeared at 1.48 ppm were shifted downfield to 1.86 ppm (H_d) in the presence of **1a** (Figure 9). This peak increased in intensity with increasing concentration of the AcO^- anion. Both of these observations were consistent with the formation of acetic acid in solution, where methyl protons are observed at 1.90 ppm in DMSO-d_6, further supporting proton transfer from **1a** to the AcO^- (See Figure S25 for NMR of pure acetic acid, TBAA as well as a mixture TBAA and acetic acid in DMSO-d_6).

Furthermore, during the titration of **1a** with TBAA, one aromatic doublet shifted upfield while the other shifted downfield as the concentration of acetate was increased. The aromatic doublets represented a typical AB spin system showing the "roof effect". As the acetate concentration increased, the chemical shift difference and coupling constant between the doublets decreased, intensifying the so-called "roof-effect". At 0.8 equivalents (the crossing point for the peaks), the chemical shift difference and coupling constant between the doublets is zero which resulted into a singlet.[44] At 1 equivalents of acetate, aromatic doublets displayed +0.13 and -0.14 ppm displacement, respectively, with respect to the doublets in the NMR spectrum of pure **1a**.

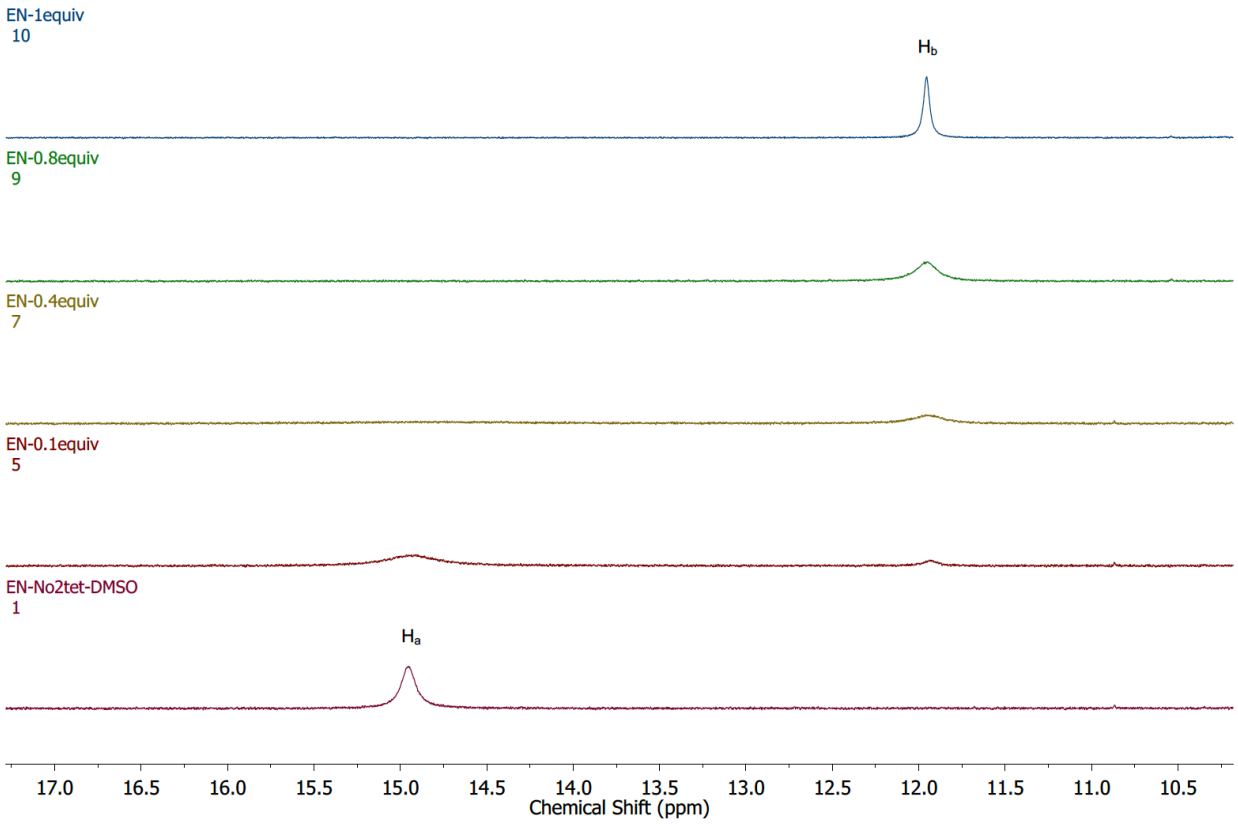


Figure 8. Partial NMR spectra during the titration of **1a** with the increasing concentration of tetra butyl ammonium acetate (TBAA) in DMSO-d_6 showing the gradual decrease in intensity of the N-H proton (H_a) and emergence of the O-H proton (H_b) indicating the formation of tetrazolonide anion (**1a'**) and acetic acid.

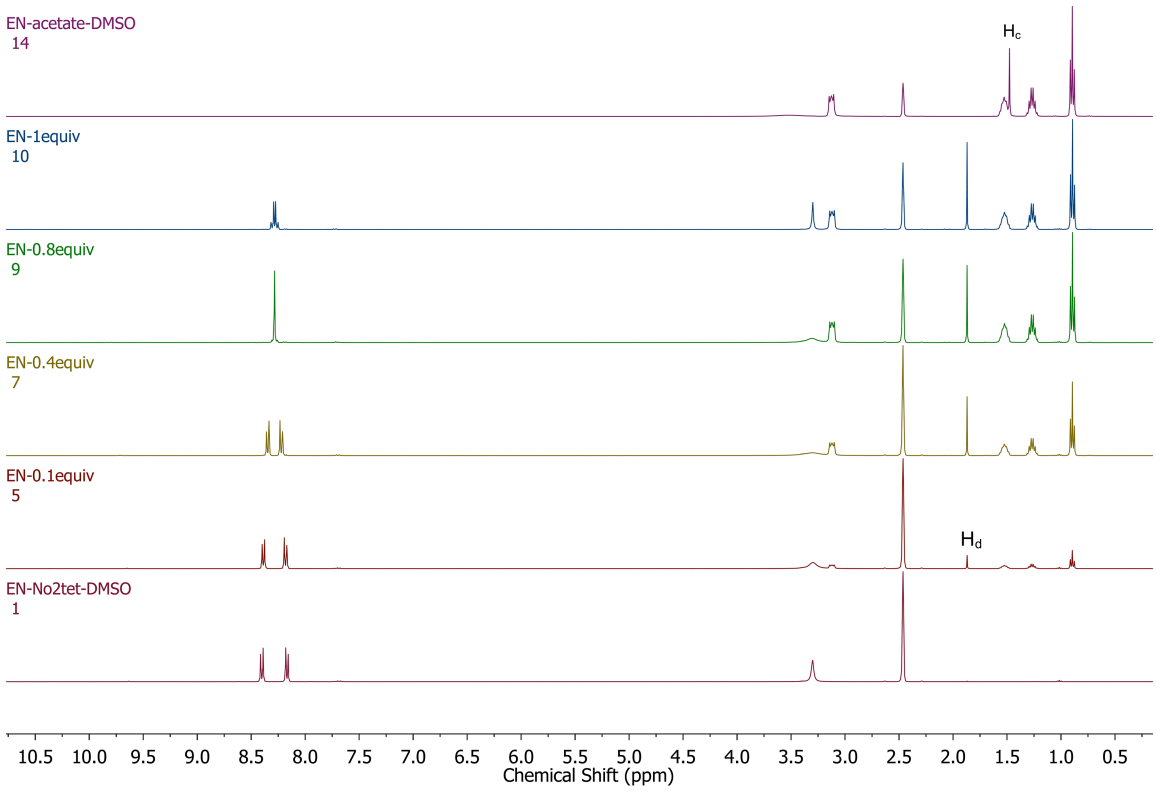


Figure 9. Partial NMR spectra during the titration of **1a** with increasing concentration of tetra butyl ammonium acetate (TBAA) in DMSO-d_6 showing aromatic peaks of **1a** as well as the acetate group peaks (H_c and H_d) from TBAA and acetic acid, respectively. The bottom spectrum is pure **1a** and the top spectrum is of pure TBAA salt in DMSO-d_6 for comparison.

NMR titrations of tetrazolones **1b** with acetate in DMSO-d_6 also suggested the formation of acetic acid supporting proton transfer. Briefly, the N-H peak disappeared upon the addition of TBAA and a new peak at 11.96 ppm emerged. In addition, the methyl protons of TBAA were shifted downfield from 1.48 ppm to 1.87 ppm. Analogous to **1a**, these observations were indicative of the formation of acetic acid and proton transfer. There was a significant shift in the aromatic doublets as observed in case of **1a**. The full NMR titration is shown in Figures S22 – S24.

Table 2. Association constants (K_a) for the interactions of tetrazolones **1a** and **1b** with anions.[a]

Anion	**1a** (M^{-1})	**1b** (M^{-1})
HSO_4^-	23.4 ± 0.8	31.7 ± 5.3
Br^-	76.0 ± 9.0	67.0 ± 5.5
NO_3^-	64.4 ± 7.2	50.5 ± 4.4
NCS^-	36.1 ± 4.4	n.d.
Cl^-	661.3 ± 26.5	553.2 ± 30.5[b]
AcO^-	Proton transfer	Proton transfer

[a]Determined by triplicate UV titrations unless specified; [b]Determined by duplicate UV titration.

Interaction with triethylamine

To gain further evidence in support of proton transfer from tetrazolones to the acetate anion, changes in the UV and NMR spectra of **1a** upon addition of excess of triethyamine (TEA) were investigated. TEA is a strong organic base, expected to spontaneously deprotonate **1a**. Upon addition of TEA to **1a** in acetonitrile, new bands emerged at 248nm and 350 nm analogous to that observed in case of TBAA (Figure S26). Furthermore, the addition of 2 equivalents of TEA to a solution of **1a** in 1:1 mixture of DMSO-d_6:MeCN-d_3 resulted in the disappearance of the N-H proton peak at 14.25 ppm in the ^{1}H NMR spectrum, and one aromatic doublet shifted upfield while the other shifted downfield. The chemical shift values of aromatic protons in the presence of TEA were similar to that observed for TBAA addition (Figure S28). These observations provided confirmation for proton transfer from **1a** to the acetate anion. Similar results can be expected for **1b**.

Conclusions

UV and NMR titrations of **1a**,**b** with anions HSO_4^-, Br^-, NO_3^-, NCS^-, Cl^-, and AcO^- suggest that tetrazolones possess the potential to be utilized as anion-binding motifs. **1a**,**b** interact through weak electrostatic interactions or H-bonding with HSO_4^-, Br^-, NO_3^-, NCS^-, and Cl^-, displaying highest affinity for Cl^-. Nitro substituted tetrazolone **1a** exhibited higher affinities for all anions (except HSO_4^-) than trifluoromethyl substituted tetrazolone **1b**. This is due to the higher electron withdrawing ability of the $–NO_2$ group compared to a $–CF_3$ group which renders the N-H group of **1a** more acidic than **1b** (Hammet constants (σ) for $–NO_2$ and $–CF_3$ are 0.81 and 0.53 respectively).[45] The association constants for both **1a**,**b** were found to be in the order $Cl^- > Br^- > NO_3^- > NCS^- > HSO_4^-$. Significant UV changes were displayed upon the addition of acetate anion to tetrazolones **1a**,**b** and clear isosbestic points were observed, consistent with the formation of a new species. NMR titrations further confirmed that **1a,b** underwent deprotonation with acetate leading to the formation of tetrazolonide anion **1a**,**b'** and acetic acid. Although, computational investigations correctly predicted the likelihood of acid-base reaction vs complex formation between the tetrazolones and various anions, no correlation was observed between the calculated binding energies and the experimental K_a values. This is attributed to the entropy contribution to the formation of complexes, which is expected to play a significant role, especially, in case of non-spherical anions *e.g.* NO_3^-, NCS^-, HSO_4^-, compared to spherically symmetrical, Cl^- and Br^- anions.

Of the various known anion-binding motifs reported in the literature, the structure of **1a**,**b** is most closely related to 5-benzyl-1*H*-tetrazole **I** that has been reported to display high affinity for Cl^- (590 M^{-1}) compared to other anions including bromide (90 M^{-1}). Tetrazolones are expected to be slightly more acidic than **I** due to the presence of carbonyl group. Accordingly, the $–NO_2$ substituted tetrazolone **1a** displayed 1.2 times higher affinity for Cl^- compared to **I** with an

association constant of 661 ± 26.5 M^{-1}. However, the association constants of $–CF_3$ substituted tetrazolone **1b** and of 5-benzyl-1*H*-tetrazole with Cl^- were comparable. Overall, **1a** and **1b** exhibited slightly better affinity for Cl^- than Br^- (76.0 ± 9.0 and 67.0 ± 5.5 M^{-1}, respectively) compared to **I**. This study contributes a new class of anion-binding motifs based on tetrazolones to the library of synthetic receptors. The incorporation of other binding motifs with tetrazolones may enable the design of more potent and selective synthetic anion receptors.

Conflicts of interest

There are no conflicts to declare.

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Electronic Supplementary Information Available

Optimized structures of tetrazolonide anions **1a,b'**; Optimized structures of complexes of **1b** with anions; Synthetic procedures, experimental details for UV and NMR titrations; UV spectra and molar absorptivities values of **1a,b**; UV titrations of **1a** with Br^-, NO_3^-, NCS^- and Cl^-; UV titrations of **1b** with HSO_4^-, Br^-, NO_3^-, and Cl^-; Binding isotherms for **1a,b** with HSO_4^-, Br^-, NO_3^-,

NCS^- , Cl^- and AcO^-; NMR titrations of **1a,b** with Cl^- and AcO^-; NMR spectra of pure TBAA, acetic acid and their mixture; UV and NMR spectra of **1a** in the presence of triethyamine.

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