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# Cancellation of contact quenching: A simple concept for selective chemosensing of basic fluoride and acetate anions

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A weakly fluorescent acid-base pair formed by reacting fluorescent acridine orange with the quencher picric acid is reported for the detection of basic fluoride and acetate anions. Deprotonation by these anions causes disengagement of the fluorescent acridine orange from the quencher, picric acid. This phenomenon cancels the quenching existing in the native probe, thereby allowing for the optical signalling of fluoride and acetate anions by colour modulation as well as fluorescence switch-on response. Anions such as $Br^-$, $I^-$, $Cl^-$, $NO_3^-$, $SCN^-$, $HSO_4^-$, and $H_2PO_4^-$ offer no detectable interference even when in excess concentration.

**Keywords**: Chemosensor, Cancellation of contact quenching, Detection of fluoride and acetate

Development of inexpensive and selective molecular probes for the detection of anions is of crucial importance in the areas of biology, medicine and environment[1]. Anions such as $AcO^-$, $Cl^-$, $NO_3^-$ and $H_2PO_4^-$ are involved in a range of physiological and enzymatic functions[2-6]. On the other hand, $F^-$ and $CN^-$, notwithstanding their clinical and industrial importance[7-12] are detrimental to human and livestock[13-17]. Among various available analytical techniques, the optical sensing has proven highly useful for the selective and sensitive detection of analytes of biological and environmental interest[18]. Typically, chromogenic hosts for anions are assembled by covalently attaching suitable anion receptors to chromo- or fluorophore units[1c,19].

Over the past decades, design strategies used for anion recognitions include H-bonding or deprotonation, Lewis acid/metal ion interaction and chemodosimeter approaches, which offer signal transductions in the form of photophysical perturbations and or NMR chemical shifts changes[20].

Molecular complexes formed between the fluorophore and another non-fluorescent molecule are known to exhibit fluorescent 'switched off' state *via* static quenching of the excited state[21]. Such fluorophore-quencher pairs have been exploited to design inexpensive methods for labelling nucleic acids, enabling the development of fluorescence 'switch on' signalling of nucleic acid hybridization probes for clinical diagnostic applications[22]. In continuation of our interest in anion chemosensors[23], we now wish to report a novel application of the above concept to design an easily accessible fluorophore-quencher probe, **ACR-1** which allows for the optical signalling of basic fluoride and acetate anions.

## Experimental Details

Compounds and solvents used were purchased from S. D. Fine Chemicals or Sigma-Aldrich, India. UV-visible spectra were recorded using Shimadzu UV-Vis recording spectrophotometer, model no. UV-2401PC. Fluorescence studies were carried out using Perkin-Elmer Fluorescence spectrophotometer, model no. LS-55. IR was recorded using Perkin-Elmer FT-IR spectrometer and pellets were made by using KBr. $^1H$ NMR spectra were recorded on Bruker make, model Advance II 300 (300 MHz).

## Synthesis of ACR-I

The picric acid was dissolved in absolute alcohol. To this solution acridine orange was added and refluxed for 1 h. Reddish colored solid was precipitated. Reaction was allowed to stand to settle down the solid. Alcohol layer was decanted out and again refluxed for 10 min and then allowed to settle down and then the alcohol layer decanted out. The washing process is repeated twice to remove unreacted picric acid. The product designated as **ACR-I** was obtained in 67% yield. IR (KBr): 3106,

2980, 1592, 1557, 1503, 1639, 1503, 1432, 1382, 1268, 1160, 1075, 970, 910 $cm^{-1}$ (Spectrum 2.1, see SI); $^1$H NMR (300 MHz, DMSO-$d_6$): δ 13.59 (s, 1H); 8.85 (s, 1H); 8.55 (s, 2H); 7.92 (d, 2H, *J* = 9.3Hz); 7.23 (d, 2H, *J* = 9.3Hz); 6.63 (s, 2H); 3.20 (s, 12H) (Spectrum 2.2, see SI); $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 160.7, 154.4, 142.5, 141.7, 141.6, 131.2, 125.1, 124.1, 116.2, 114.9, 92.3 (Spectrum 2.3, see SI). Anal. Calcd for $C_{24}H_{22}N_6O_7$: C, 56.89; H, 4.38; N, 16.59. Found: C, 56.71; H, 4.48; N, 16.47%.

## Results and Discussion

The probe, **ACR-1** constitutes an acid-base pair derived from acridine orange and picric acid. **ACR-1** is readily obtained as an orange solid simply by mixing an equimolar amount of acridine orange and picric acid in alcohol solvent. Being a fluorescence quencher, picrate ion in **ACR-1** quenches the fluorescence of the associated acridinium ring by energy transfer process, thereby giving rise to a 'switched off' state. As illustrated in Scheme 1, we anticipated that in the presence of basic anions, the protonated acridinium ring in **ACR-1** would undergo base induced deprotonation. As a consequence, the fluorescent acridine orange would be disengaged from the quencher, picric acid. This phenomenon is expected to revive the fluorescence due to the native acridine orange, allowing for a new spectroscopic signature for the detection of basic anions.

Optical sensitivity of **ACR-1** towards anions such as $F^-$, $OAC^-$, $Cl^-$, $Br^-$, $I^-$, $HSO_4^-$, $H_2PO_4^-$, $NO_3^-$, and $SCN^-$ was evaluated by UV-Vis and fluorescence spectral studies. As shown in Fig. 1, the absorption profile of **ACR-1** ($5\times10^{-5}$ M) in the presence of 100-fold of $Cl^-$, $Br^-$, $I^-$, $HSO_4^-$, $H_2PO_4^-$, $NO_3^-$, and $SCN^-$remained virtually unchanged, implying the absence of ground state interaction between these anions and **ACR-1**. In contrast, addition of $F^-$ or $AcO^-$ ($1.5\times10^{-4}$ M) caused the absorption maxima to blue shift from 497 to 426 nm. This 71 nm blue shift leads to change in color from orange to yellow, offering ready naked eye detection of $F^-$ and $AcO^-$.

Absorption spectra of **ACR-1** ($5\times10^{-5}$ M), was monitored with respect to incremental addition of TBAF. As shown in Fig. 2, we observed steady decrease in the probe's absorbance at 497 nm with concomitant appearance of a new blue shifted band at 426 nm. The absorption changes reached a plateau at a limiting concentration of $1.27\times10^{-4}$ M with a single well defined isosbestic point being observed at 450 nm. Job's plot analysis suggested a well-defined

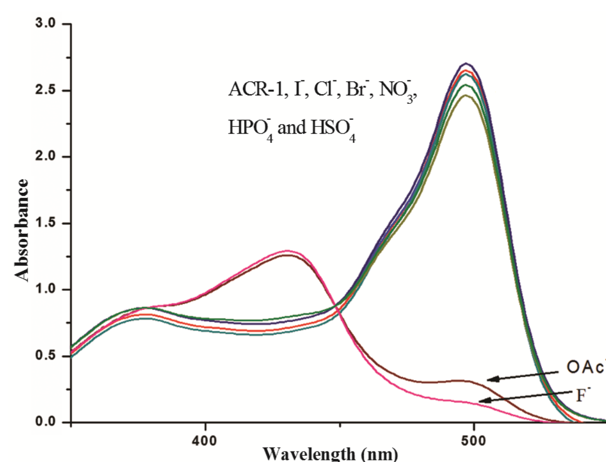
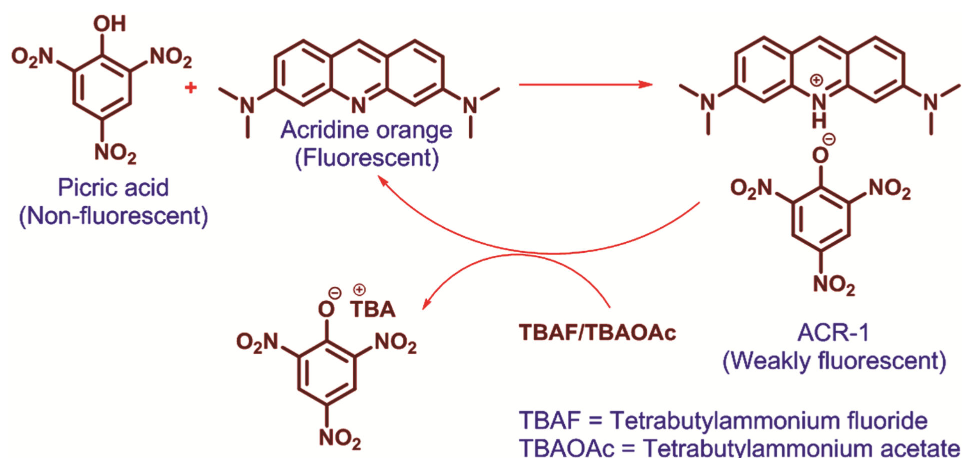



Fig. 1 — Absorption spectra of **ACR-1** ($5\times10^{-5}$M) in presence and absence of, tetrabutylammonium salts of $Cl^-$, $Br^-$, $I^-$, $HSO_4^-$, $HPO_4^-$, $NO_3^-$, and $SCN^-$($5\times10^{-3}$ M), and $F^-$($1.27\times10^{-4}$ M) and $AcO^-$ ($1.5\times10^{-4}$ M) in DMSO solution




Scheme 1 — Synthesis of **ACR-1** and the design concept for $F^-$ and $AcO^-$

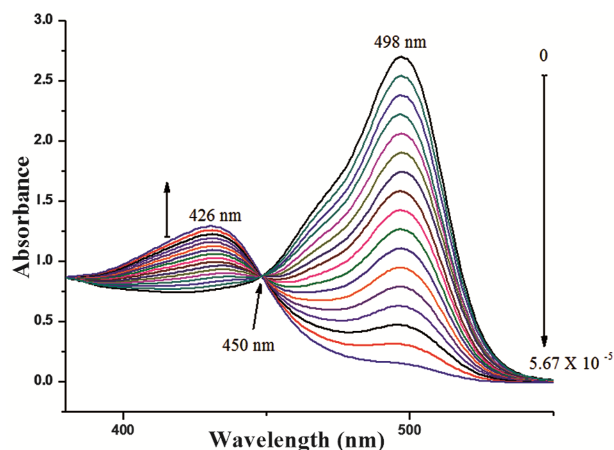



Fig. 2 — Spectrophotometric titration of ACR-1 ($5\times10^{-5}$ M) with TBAF ($0\text{-}1.27\times10^{-4}$ M)

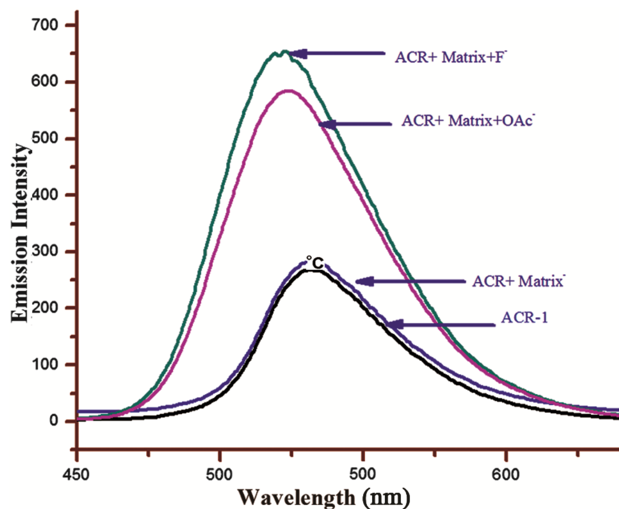



Fig. 3 — Fluorescence spectra of (i) **ACR-1** ($5\times10^{-6}$ M), (ii) **ACR-1** + a matrix consisting of 500 equivalents each of $Br^-$, $I^-$, $Cl^-$, $NO_3^-$, $SCN^-$, $HSO_4^-$, and $H_2PO_4^-$, (iii) **ACR-1**+ matrix + TBAF ($1.2\times10^{-5}$ M), (iv) **ACR-1**+ matrix + TBAOAc ($1.5\times10^{-5}$ M) recorded in DMSO solution, $\lambda_{ex}$ = 426 nm

equilibrium state with 1:1 stoichiometric interaction between **ACR-1** and fluoride anion (see SI). Similar behavior was noticeable in the titration of **ACR-1** with acetate anion, though a slightly higher concentration ($1.5\times10^{-4}$ M) of this anion was required to achieve saturation (see SI).

Excitation of **ACR-1** ($5\times10^{-6}$ M) produced a structure-less emission band centered at 531 nm. As shown in Fig. 3, both $F^-$ and $AcO^-$ induced marked changes in the emission wavelength and intensity. However, addition of a matrix consisting of 500 equivalents each of $Br^-$, $I^-$, $Cl^-$, $NO_3^-$, $SCN^-$, $HSO_4^-$, and $H_2PO_4^-$ caused no significant changes in the emission spectral profile of the probe. As depicted in Fig. 4, with increasing concentration of fluoride, the emission band progressively blue shifted to its new position at 521 nm, while its emission intensity at saturating $5.67\times10^{-5}$ M of $F^-$ increased by 250% with respect to that of **ACR-1**. Acetate anion also induced similar emission spectral change, though it's limiting concentration was marginally higher at $7.5\times10^{-5}$ M (see SI).

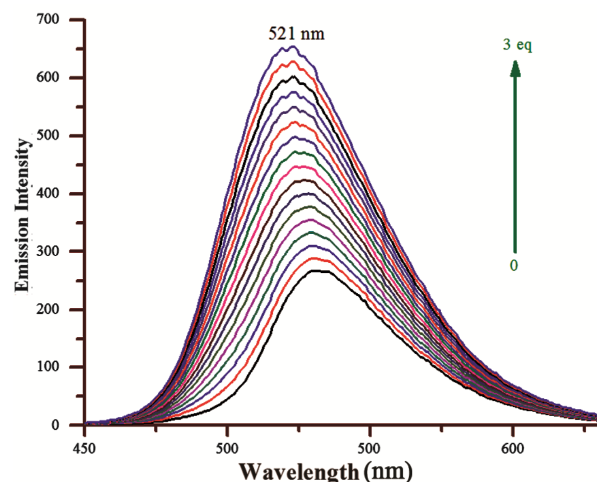



Fig. 4 — Fluorescence spectra of **ACR-1** ($5\times10^{-6}$ M) on titration with TBAF ($0\text{–}1.2\times10^{-5}$ M) in DMSO solution, $\lambda_{ex}$ = 450 nm

The detection limits for $F^-$ and $AcO^-$ calculated fluorometrically were found to be $5.1\times10^{-6}$ M and $6.3\times10^{-6}$ M, respectively[24] (See SI). Since, no significant photophysical perturbations were induced by $Br^-$, $I^-$, $Cl^-$, $NO_3^-$, $SCN^-$, $HSO_4^-$, and $H_2PO_4^-$ even in abundant concentrations, it is fair to conclude that no measurable interaction exists between these anions with **ACR-1**. To validate the deprotonation mechanism, we recorded $^1$H NMR of **ACR-1** without and with added TBAF in DMSO-$d_6$. As shown in Fig. 5, addition of just 1.5 equivalent of TBAF resulted in the disappearance of the NH signal at δ 13.6 of **ACR-1**, and the rest of $^1$H NMR peak assignments fully matched with that of the native acridine orange itself. Clearly, the observed colorimetric response and revival of fluorescence in the presence of basic $F^-$ or $AcO^-$ are consistent with Scheme 1. As additional evidence of deprotonation, we measured UV-Vis and fluorescence profiles of the probe **ACR-1** in the presence of added $1.2\times10^{-5}$ M of tetrabutylammonium hydroxide. As expected, we observed modulations of the optical spectra similar to those induced by basic $F^-$ or $AcO^-$.

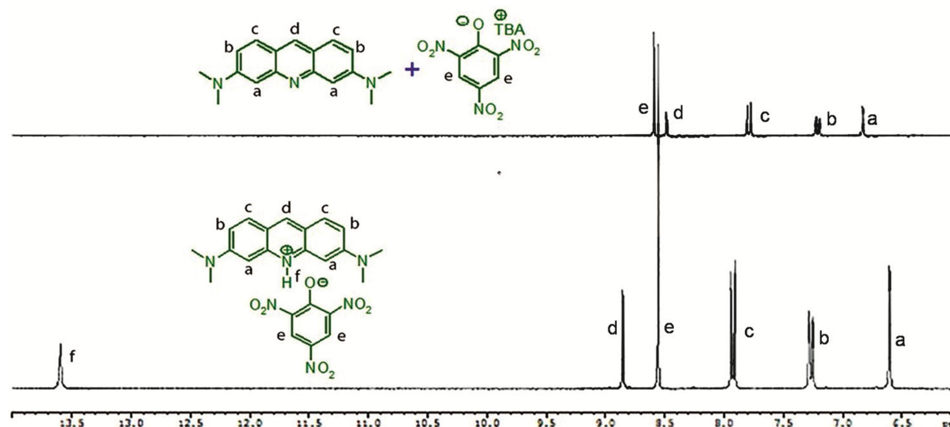


Fig. 5 — 300 MHz $^1$H NMR spectra of (a) **ACR-1** and (b) **ACR-1** + 1.5 equivalent of TBAF in DMSO-$d_6$

## Conclusion

In conclusion, we have reported an easy to make chromogenic probe **ACR-1** featuring an acid base pair of acridine orange and picric acid for the optical targeting basic anions. The deprotonation induced by $F^-$ and $AcO^-$ releases acridine orange base from its quencher, picric acid, causing cancellation of contact quenching existing in the probe. This phenomenon causes naked eye color change and fluorescence enhancement for the micromolar detection of $F^-$ and $AcO^-$. Since, $Br^-$, $I^-$, $Cl^-$, $NO_3^-$, $SCN^-$, $HSO_4^-$, and $H_2PO_4^-$ do not engage in the deprotonation pathways, they offered no interferences even in excess concentrations. Deprotonation mechanism induced by fluoride and acetate anion was confirmed by $^1$H NMR analysis. To our knowledge, the concept of cancellation of contact quenching is reported for the first time for optical targeting of $F^-$ and $AcO^-$. A limitation of the present probe is its inability to discriminate between $F^-$ or $AcO^-$ since both these anions give rise to similar optical perturbations.

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## References

1 (a) McNaughton D A, Fares M, Picci G, Gale P A & Caltagirone C, *Coord Chem Rev*, 427 (2021) 213573; (b) Gale P A & Caltagirone C, *Coord Chem Rev*, 354 (2018) 2; (c) Busschaert N, Caltagirone C, Rossom W V & Gale P A, *Chem Rev*, 115 (2015) 8038; (d) Cho D G & Sessler J L, *Chem Soc Rev*, 38 (2009) 1647; (e) Nguyen B T & Anslyn E V, *Chem Rev*, 250 (2006) 3118; (f) Suksai C & Tuntulani T, *Top Curr Chem*, 255 (2005) 163; (g) Gunnlaugsson T, Glynn M, Tocci G M, Kruger P E & Pfeffer F M, *Coord Chem Rev*, 250 (2006) 3094; (h) Anslyn E V, *J Org Chem*, 72 (2007) 687; (i) Yang Y, Zhao Q, Feng W & Li F, *Chem Rev*, 113 (2012) 192.

2 Maeda H & Ito Y, *Inorg Chem*, 45 (2006) 8205.

3 Gale P A, *Chem Rev*, 240 (2003) 191.

4 (a) *The Biochemistry of Nucleic Acids*, edited by Adams R L P, Knower J T & Leader D P (Chapman and Hall, Springer, New York) (1992); (b) Saenger W, *Principles of Nucleic Acid Structure* (Springer, New York) (1984).

5 Gunnlaugsson T, Davis A P, O'Brien J E & Glynn M, *Organic Lett*, 4 (2002) 2449.

6 Jentsch T J, Stein V, Weinreich F & Zdebik A A, *Physiol Rev*, 82 (2002) 503.

7 Kirk K L, *Biochemistry of the Halogens and Inorganic Halides* (Plenum Press, New York) (1991).

8 Briancon D, *Rev Rhum*, 64 (1997) 78.

9 Beer P D & Gale P A, *Angew Chem Int Ed*, 40 (2001) 486.

10 Kleerekoper M, *Endocrinol Metab Clin North Am*, 27 (1998) 441.

11 Lehn J M, *Science*, 227 (1985) 849.

12 Kanduti D, Sterbenk P & Artnik B, *Mater Sociomed*, 28 (2016) 133.

13 (a) Kaminsky L S, Mahoney M C, Leach J, Melius J & Miller M J, *Crit Rev Oral Biol Med*, 1 (1990) 261; (b) Waldbott G L, *Clin Toxicol*, 18 (1981) 531.

14 Matuso S, Kiyomiya K I & Kurebe M, *Arch Toxicol*, 72 (1998) 798.

15 Riggs B L, *Bone Miner Res*, 2 (1984) 366.

16 Vennesland B, Conn E E, Knowles C J, Westly J & Wissing F, *Cyanide in Biology* (Academic Press, London) (1981).

17 (a) Stock R I, Dreyer J P, Nunes G E, Bechtold I H & Machado V G, *ACS Appl Polym Mater*, 1 (2019) 1757; (b) Wang B & Anslyn E V, *Chemosensors*, *Principles*, *Strategies*, *and Applications* (Wiley, Hoboken, New Jersey) (2011); (c) You L, Zha D & Anslyn E V, *Chem Rev*, 115 (2015) 7840; (d) Keefe M H, Benkstein K D & Hupp J T, *Coord Chem Rev*, 205 (2002) 201; (e) Sun S S, Lees A J & Zavalij P Y, *Inorg Chem*, 42 (2003) 3445.

18 (a) Duke R M, Veale E B, Pfeffer F M, Kruger, P E & Gunnlaugsson T, *Chem Soc Rev*, 39 (2010) 3936.

19 (a) dos Santos C M G, Harte A J, Quinn S J & Gunnlaugsson T, *Coord Chem Rev*, 252 (2008) 2512; (b) Moragues M E, Martınez-Manez R & Sancenon F, *Chem Soc Rev*, 40 (2011) 2593; (c) Li A-F, Wang J-H, Wang F & Jiang Y-B, *Chem Soc Rev*, 39 (2010) 3729; (f) Santos-Figueroa L E, Moragues M E,

Climent E, Agostini A, Martinez-Manez R & Sancenon F, *Chem Soc Rev*, 42 (2013) 3489.

20 (a) Sharma A, Kim D, Park J-H, Rakshit S, Seong J, Jeong G H, Kwon O-H & Lah M S, *Chem Commun*, 2 (2019) 39; (b) Chatterjee S & Kumar G S, *J Photochem Photobiol B*, *Biol*, 159 (2016) 169; (b) Johansson M K, Fidder H, Dick D & Cook R M, *J Am Chem Soc*, 124 (2002) 6950.

21 (a) Sharma A, Kim D, Park J-H, Rakshit S, Seong J, Jeong G H, Kwon O-H & Lah M S, *Commun Chem*, 2 (2019) 39; (b) Chatterjee S & Kumar G S, *J Photochem Photobiol B Biol*, 159 (2016) 169; (c) Johansson M K, Fidder H, Dick D & Cook R M, *J Am Chem Soc*, 124 (2002) 6950.

22 (a) Guo J, Ju J & Turro N J, *Anal Bioanal Chem*, 402 (2012) 3115; (b) Tyagi S & Kramer F R, *Nat Biotechnol*, 14 (1996) 303; (c) Marras S A E, Kramer F R & Tyagi S, *Nucleic Acids Res*, 30 (2002) 122.

23 (a) Mashraqui S H, Betkar R, Ghorpade S, Frontera A, *J Incl Phenom Macrocycl Chem*, 76 (2013) 293; (b) Mashraqui S H, Ghorpade S S, Tripathi S & Britto S, *Tetrahedron Letters*, 53 (2012) 765; (c) Mashraqui S H, Betkar R, Chandiramani M, Estarellas C & Frontera A, *New J Chem*, 35 (2011) 57; (d) Mashraqui S H, Tripathi S, Betkar R & Chandiramani M, *Chem Lett*, 39 (2010) 650; (e) Mashraqui S H, Betkar R, Chandiramani M, Quinonero D & Frontera A, *Tetrahedron Letters*, 51 (2010) 596.

24 Shortreed M, Kopelman R, Kuhn M & Hoyland B, *Anal Chem*, 68 (1996) 1414.