

Electronic Supplementary Information (ESI)

Isatin pentafluorophenylhydrazones: interesting conformational change during anion sensing

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EXPERIMENTAL SECTION – Supporting information

Synthesis

GENERAL PROCEDURE:

A solid pentafluorophenylhydrazine (3.4 mmol, 1eq.) was added to a solution of isatin or 1-methylisatin (3.4 mmol, 1eq.) in absolute ethanol (80ml). The reaction mixture was refluxed for 24 hours under vigorous stirring. The mixture was then cooled to room temperature and the precipitated residue was filtered off, washed with absolute ethanol (50ml) and air dried.⁴⁹

CHARACTERISATION OF PREPARED ISATIN PENTAFLUOROPHENYLHYDRAZONES:

Isatin *N*²-pentafluorophenylhydrazone **1**:

Obtained from pentafluorophenylhydrazine (0.50 g) and isatin (0.67 g) in 99% yield (1.11 g),

¹H NMR (600 MHz, DMSO-*d*₆, 25°C) δ = 12.47 (s, 1H, NH), 11.15 (s, 1H, =N-NH), 7.35 (d, H4, *J* = 7.4Hz), 7.23 (td, H5, *J* = 1.1Hz, 7.7Hz), 6.97 (td, H6, *J* = 0.5Hz, 7.5Hz), 6.85 (d, H7, *J* = 7.8Hz).

¹³C NMR (75 MHz, DMSO-*d*₆, 25°C) δ = 163.56, 141.25, 138.65 (dd, C_{orto}, *J*_{C-F} = 247.70, 13.99Hz), 138.09 (ddd, C_{meta}, *J*_{C-F} = 260.67, 231.84, 15.12Hz), 135.48 (t, C_{para}, *J*_{C-F} = 12.24Hz), 132.90, 130.46, 122.76, 120.51, 119.76, 119.49, 111.35.

¹⁹F NMR (600 MHz, DMSO-*d*₆, 25°C) δ = 155.27 (d, 2F_{orto}, *J* = 22.4Hz), 163.45 (m, 2F_{meta}), 165.14 (t, 1F, *J*_{para} = 23.1Hz).

IR (ATR) ν /cm⁻¹: 3177, 3063, 1683, 1617, 830, 789.

Anal. Calcd. for C₁₄H₆F₅N₃O (327.21): C, 51.39; H, 1.85; N, 12.84; F, 29.03. Found: C, 51.37; H, 1.84; N, 12.84; F, 28.99.

M.p.: 238-239°C.

1-Methylisatin *N*²-pentafluorophenylhydrazone **2**:

Obtained from pentafluorophenylhydrazine (0.70 g) and 1-methylisatin (0.57 g) in 99% yield (1.2 g),

¹H NMR (600 MHz, DMSO-*d*₆, 25°C) δ = 12.47ppm (s, 1H, NH), 7.47 (d, H4, *J* = 7.4Hz), 7.39 (td, H5, *J* = 7.9Hz, 1Hz), 7.13 (m, H6, H7), 3.24 (s, CH₃).

¹³C NMR (75 MHz, DMSO-*d*₆, 25°C) δ = 161.66, 142.57, 138.86 (dd, C_{orto}, *J*_{C-F} = 248.57, 11.08Hz), 138.15 (ddd, C_{meta}, *J*_{C-F} = 275.31, 247.17, 14.56Hz), 135.69 (t, C_{para}, *J*_{C-F} = 11.22Hz), 132.17, 130.43, 123.31, 119.78, 119.47, 110.18, 26.02 (d, CH₃, *J* = 2.44Hz).

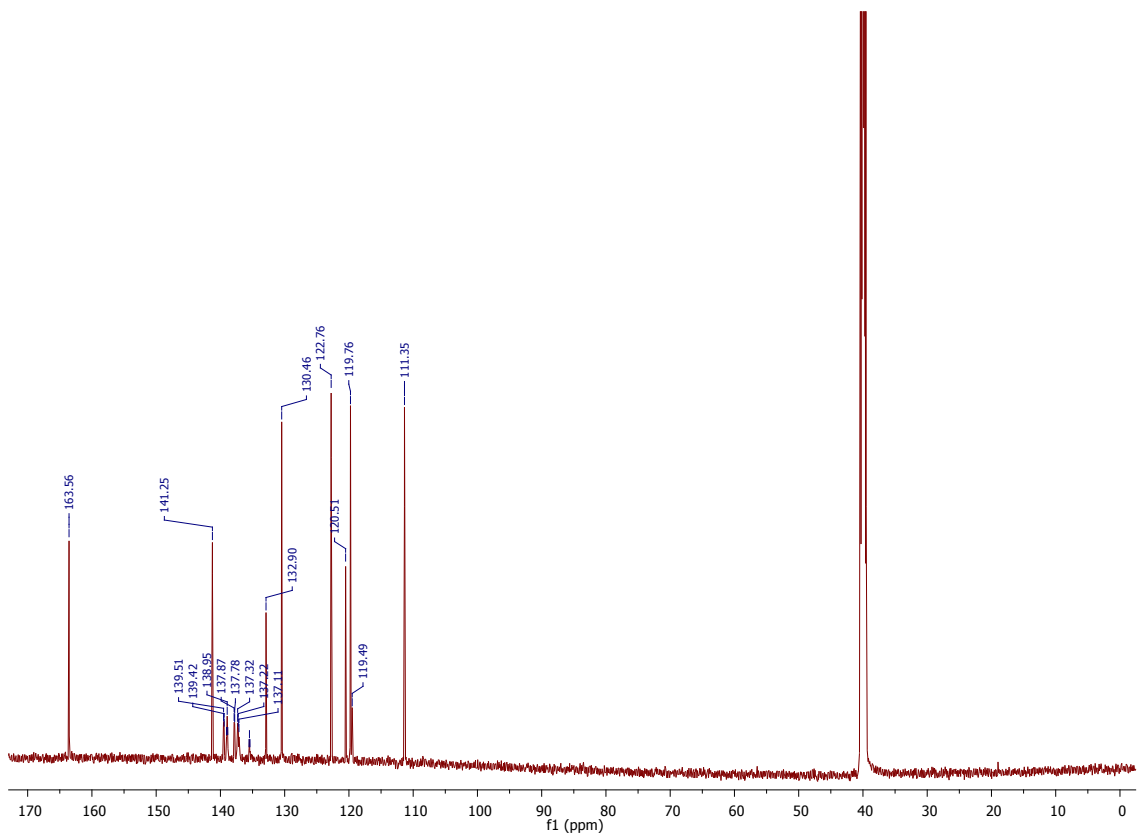
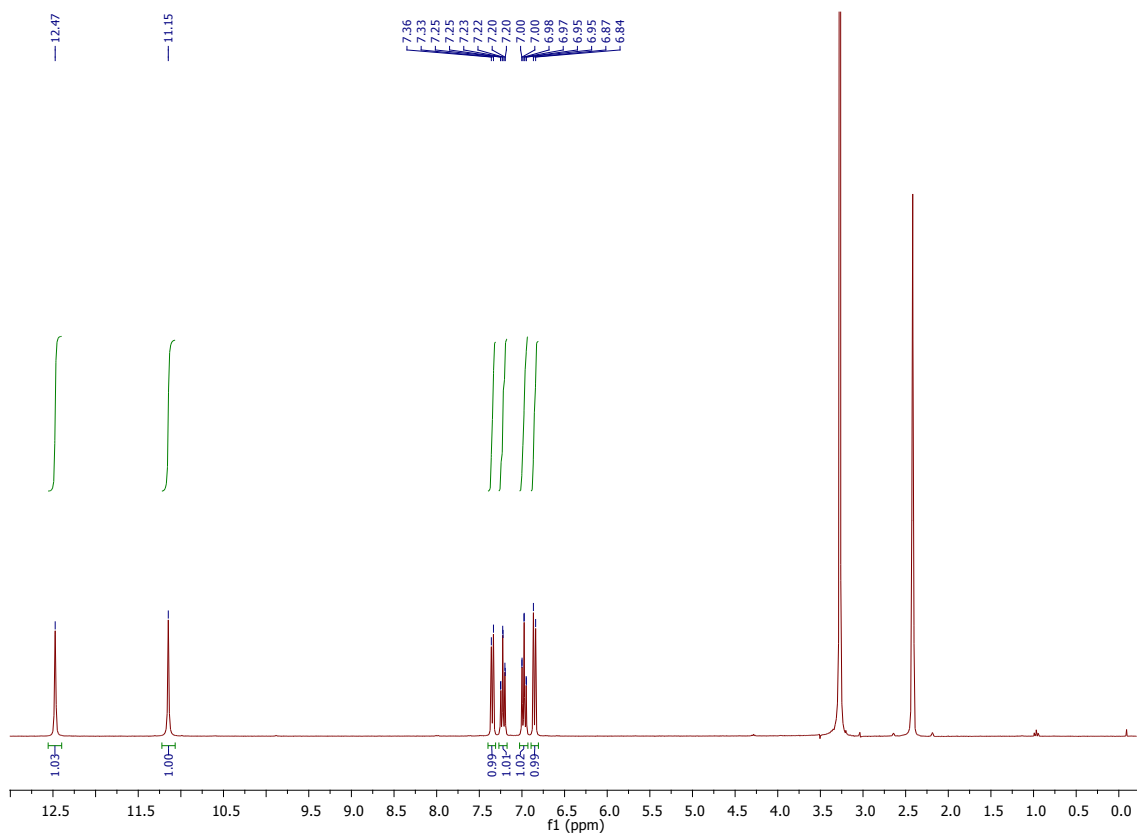
¹⁹F NMR (600 MHz, DMSO-*d*₆, 25°C) δ = -154.994 (m, F_{orto}), -163.38 (qd, F_{meta}, *J* = 5.6, 1.3Hz), -164.45 (m, F_{para}).

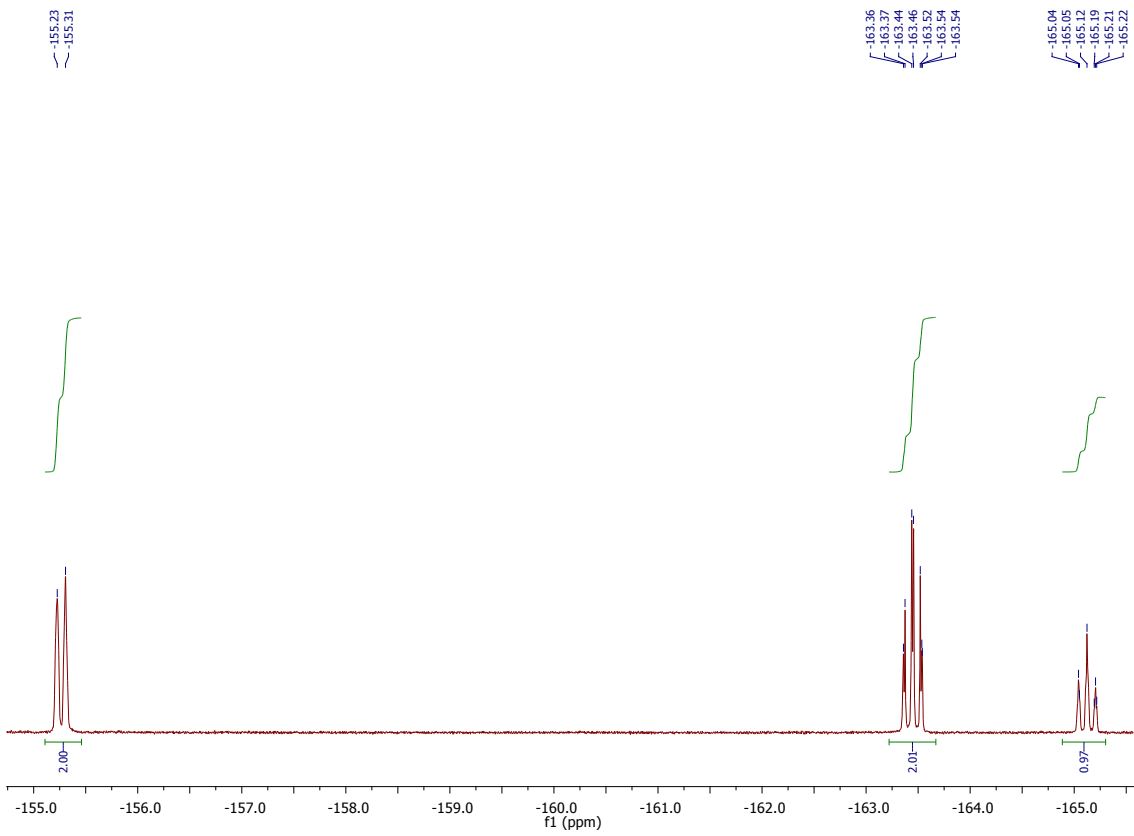
IR (ATR) ν /cm⁻¹: 3058, 1677, 1609, 889, 787, 750.

Anal. Calcd. for C₁₅H₈F₅N₃O (341.24): C, 52.80; H, 2.36; N, 12.31; F, 4.69. Found: C, 52.77; H, 2.35; N, 12.31; F, 27.83.

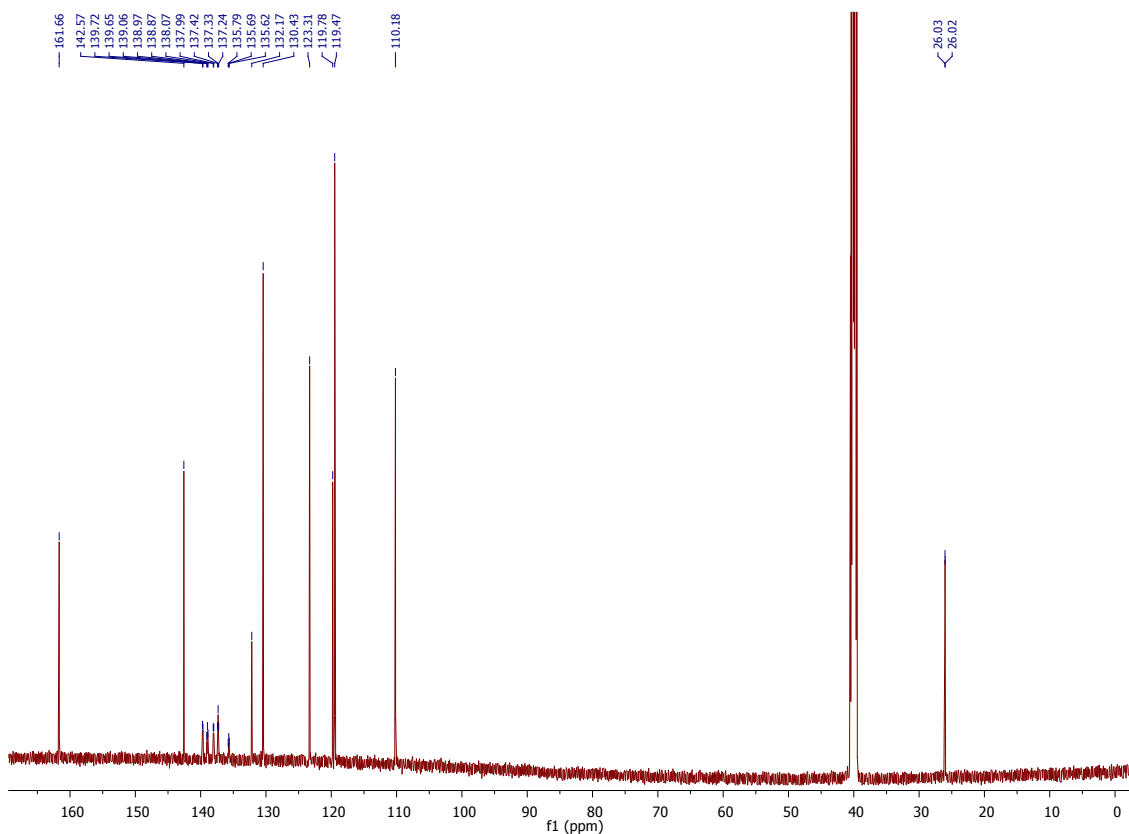
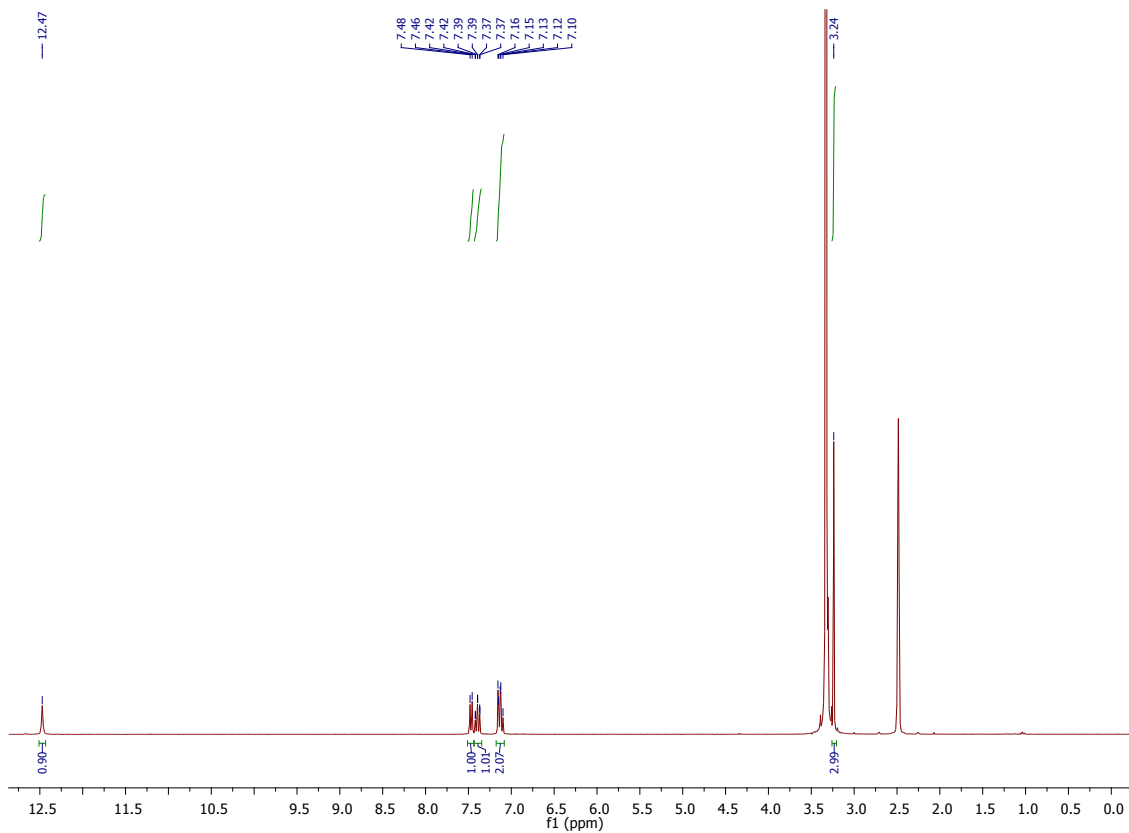
M.p.: 176-177°C.

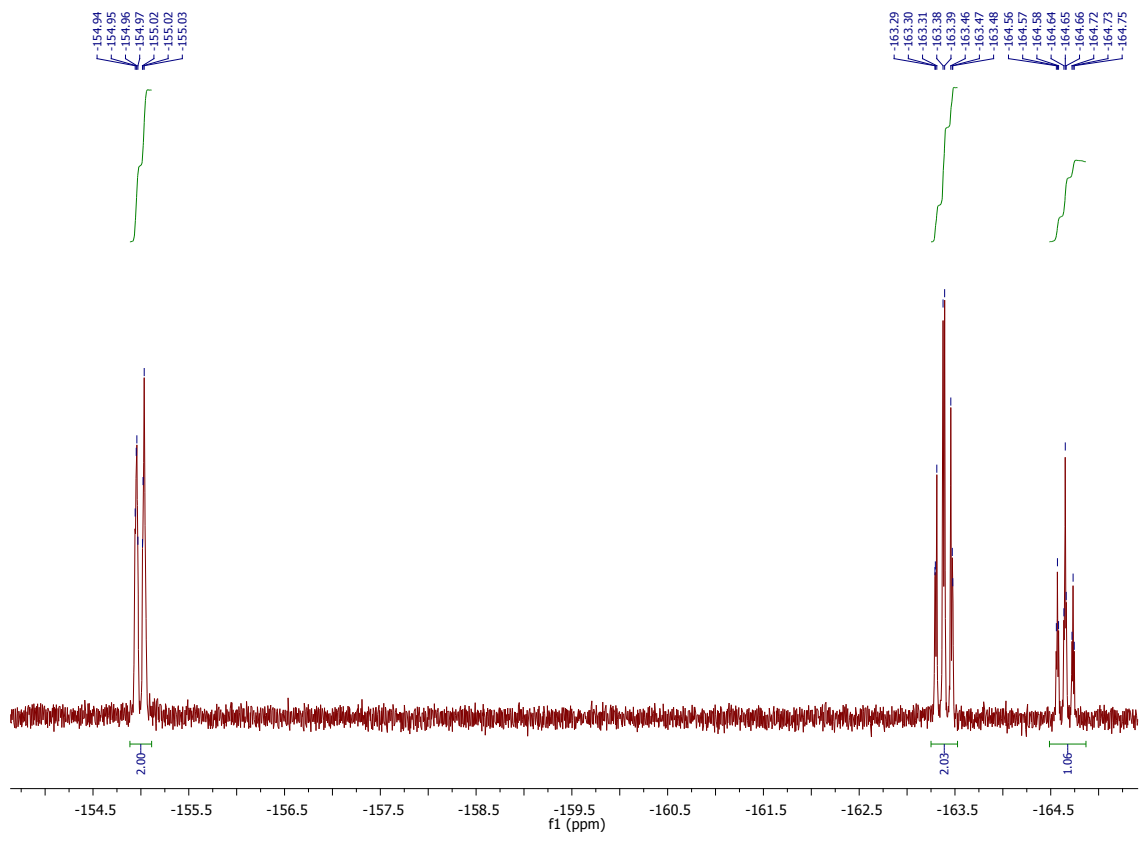
Isatin *N*²-pentafluorophenylhydrazone **1**: ¹H NMR, ¹³C NMR, ¹⁹F NMR, respectively.





1-Methylisatin *N*²-pentafluorophenylhydrazone **2**: ¹H NMR, ¹³C NMR, ¹⁹F NMR, respectively.





Association constant determinations

Association constants K_{ass} for apparent isatin pentafluorophenylhydrazone:anion 1:1 complex formation were determined by the acknowledged formula describing complex anion concentration:⁵⁰

$$A = A_0 + \frac{A_{\text{lim}} - A_0}{2c_0} \left[c_0 + c_{A^-} + 1/K_{\text{ass}} - \left[(c_0 + c_{A^-} + 1/K_{\text{ass}})^2 - 4c_0c_{A^-} \right]^{1/2} \right], \quad (\text{S1})$$

where: A_0 is the absorbance of free isatin pentafluorophenylhydrazone, A is the isatin pentafluorophenylhydrazone absorbance measured after anion addition, A_{lim} is the isatin pentafluorophenylhydrazone absorbance measured with excess of the particular anion, c_0 is the overall concentration of isatin pentafluorophenylhydrazone and c_{A^-} is the overall concentration of the added anion A^- .

Equation (S1) was rewritten to the following form for nonlinear fit in OriginPro 8.1 software:

$$A = A_0 + c_1 * (P1 - A_0) * (c_0 + x + 1/P2 - \sqrt{(c_0 + x + 1/P2)^2 - 4 * c_0 * x}), \quad (\text{S2})$$

where: $c_0 = 1 \times 10^{-4}$, $c_1 = 1/2c_0 = 5 \times 10^3$, parameter $P1 = A_{\text{lim}}$, parameter $P2 = K_{\text{ass}}$ and $x = c_{F^-}$. The A_0 value was fixed to the absorbance A value for $x = 0$.

pK_a constant determinations

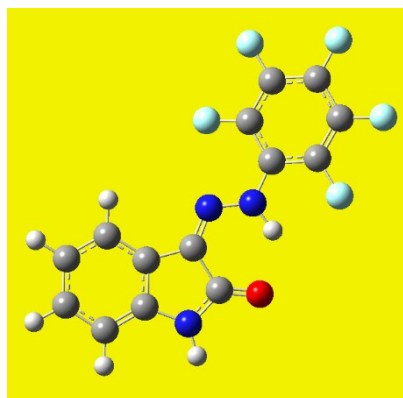
Experimental pK_a values were obtained through pH-spectrophotometric titrations in a DMF:buffer solution mixture (9/1 v/v).

GENERAL PROCEDURE:

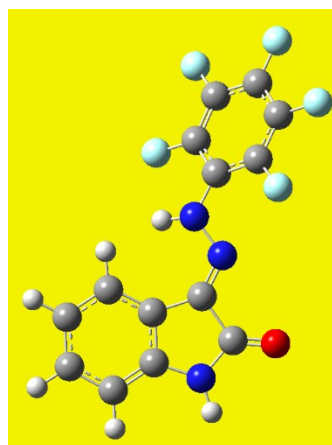
Isatin hydrazone derivatives were dissolved in DMF (to obtain 1×10^{-4} mol dm^{-3} overall hydrazone concentrations) at 298.15 K. A buffer solution (Britton-Robinson, universal buffer solution I, 0.3 mL) with adjusted pH was then added to 2.7 mL of hydrazone solution. The pH of buffer solutions was measured with Laboratory pH Meter WTW inoLab 720.

Britton-Robinson buffer solution consists of a mixture of 0.04 M H_3BO_3 , 0.04 M H_3PO_4 and 0.04 M AcOH ($M = \text{mol dm}^{-3} = \text{mol L}^{-1}$). Desired pH was adjusted by titration with 0.2 M NaOH.

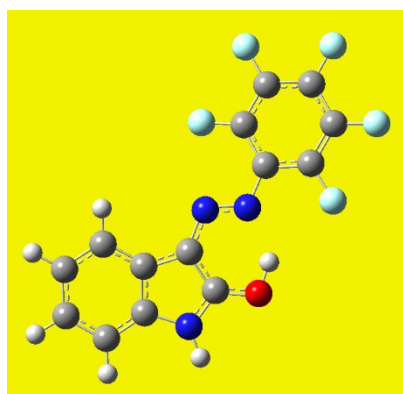
SUPPORTING SCHEMES, TABLES AND FIGURES



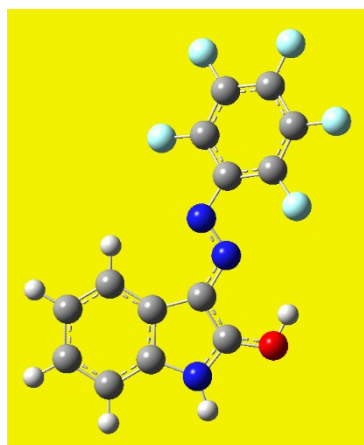
Z-hydrazo



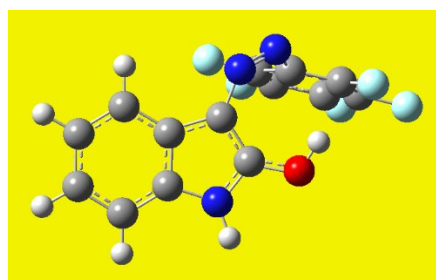
E-hydrazo



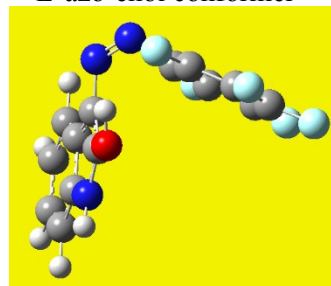
E-azo-enol



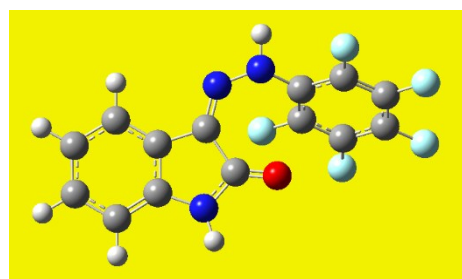
E-azo-enol conformer



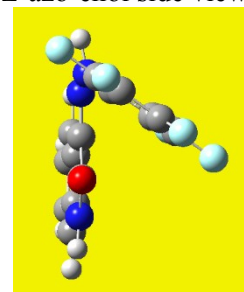
Z-azo-enol side view



Z-azo-enol side view

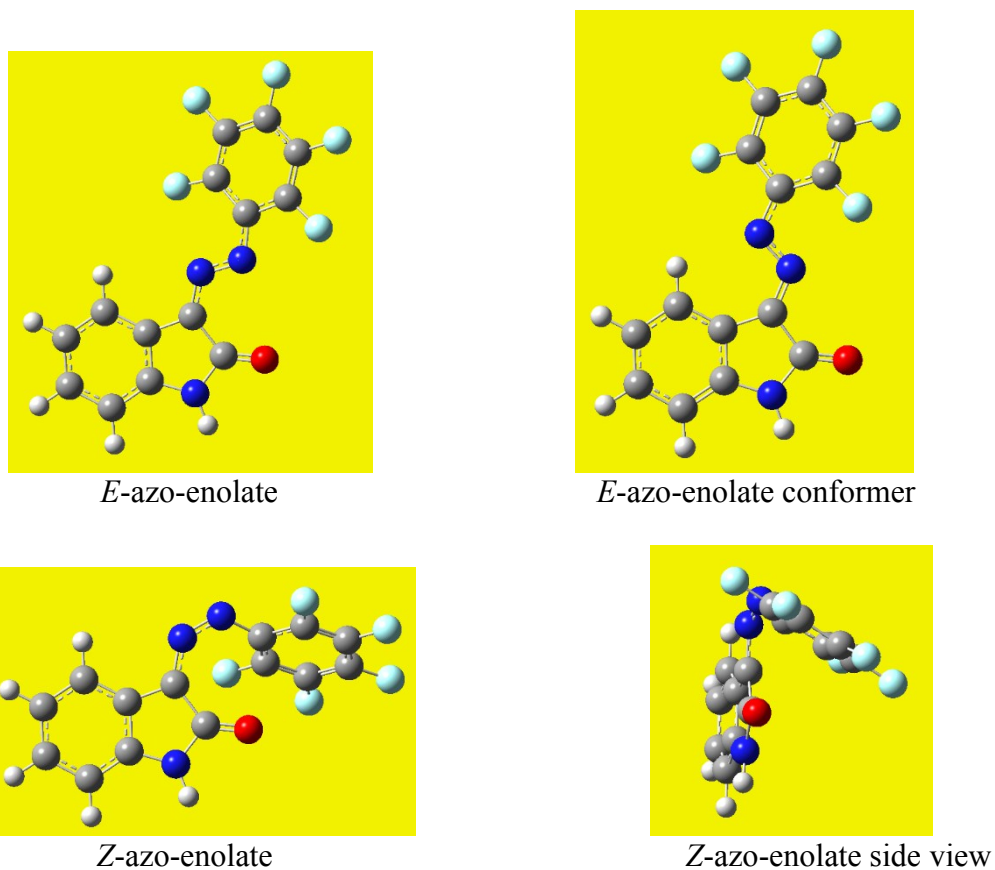


Z- π -hydrazo



Z- π -hydrazo side view

Scheme S1. Calculated geometries of possible isatin pentafluorophenylhydrazone **1** isomers (including important conformational isomer) and their anionic (enolate) forms in vacuum at the at the M062x 6-31+g(dp) level ($T = 298.15$ K).



Scheme S1. Calculated geometries of possible isatin pentafluorophenylhydrazone **1** isomers (including important conformational isomer) and their anionic (enolate) forms in vacuum at the at the M062x 6-31+g(dp) level ($T = 298.15$ K).

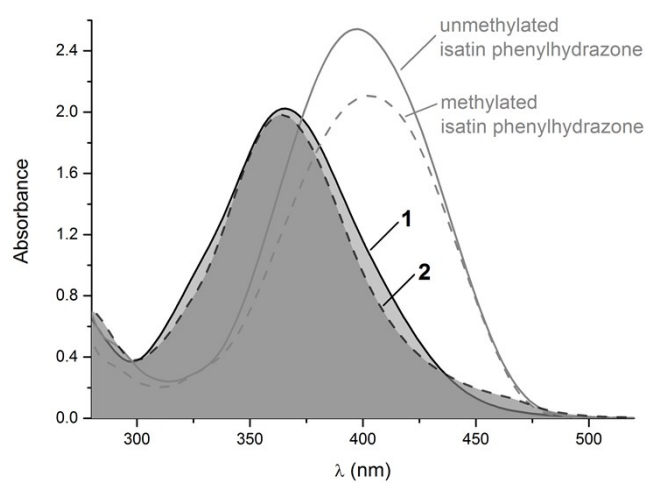


Fig. S1. UV-Vis spectra of isatin pentafluorophenylhydrazones **1** and **2** and corresponding basic isatin phenylhydrazones in DMF ($c = 1 \times 10^{-4}$ mol dm⁻³).

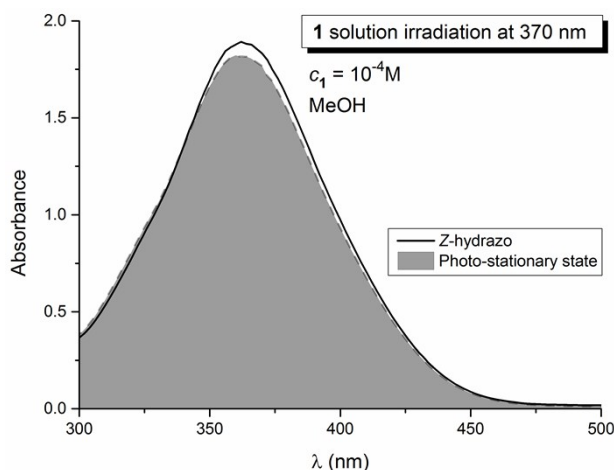


Fig. S2. UV-Vis spectral changes during isatin pentafluorophenylhydrazone **1** solution irradiation at 370 nm in MeOH (light source: four 370 nm LED diodes Thorlabs; initial Z-hydrazo isomer concentration: $c_1 = 10^{-4}$ M; 1 cm cuvette; $T = 298.15$ K).

Table S1. Determined pK_a values for studied isatin pentafluorophenylhydrazones **1** and **2**, and corresponding basic isatin phenylhydrazones **Z1** and **Z2** isomers in DMF:buffer solution mixture (9/1 v/v) at 298.16 K (determined from absorption spectra).

Compd	1	2
pK_a^*	8.23 ± 0.04 ($R^2 = 0.9983$)	8.06 ± 0.05 ($R^2 = 0.9979$)
Compd	Z1	Z2
pK_a^*	9.00 ± 0.07 ($R^2 = 0.9951$)	8.95 ± 0.04 ($R^2 = 0.9985$)

* – determined from nonlinear sigmoidal (Boltzmann) fit of experimentally determined absorbance values at various pH of added buffer solution; R^2 – coefficient of determination (average value)

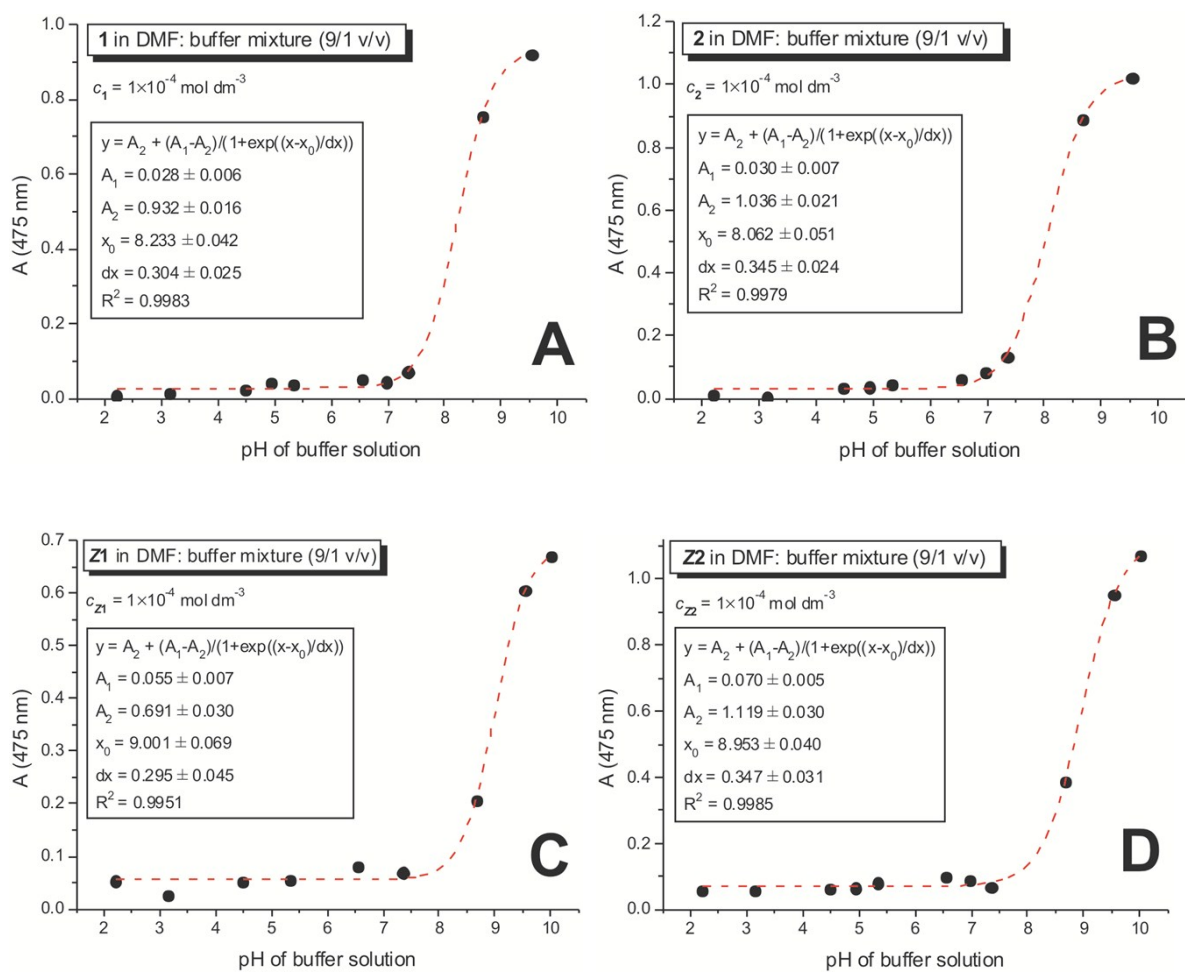


Fig. S3. Evolution of absorbance at 475 nm for isatin pentafluorophenylhydrazones **1** and **2** and corresponding basic isatin phenylhydrazones **Z1** and **Z2** isomers in DMF:buffer solution mixture (9/1 v/v; $c_{\text{SENSOR}} = 1 \times 10^{-4} \text{ mol dm}^{-3}$; $T = 298.15 \text{ K}$).

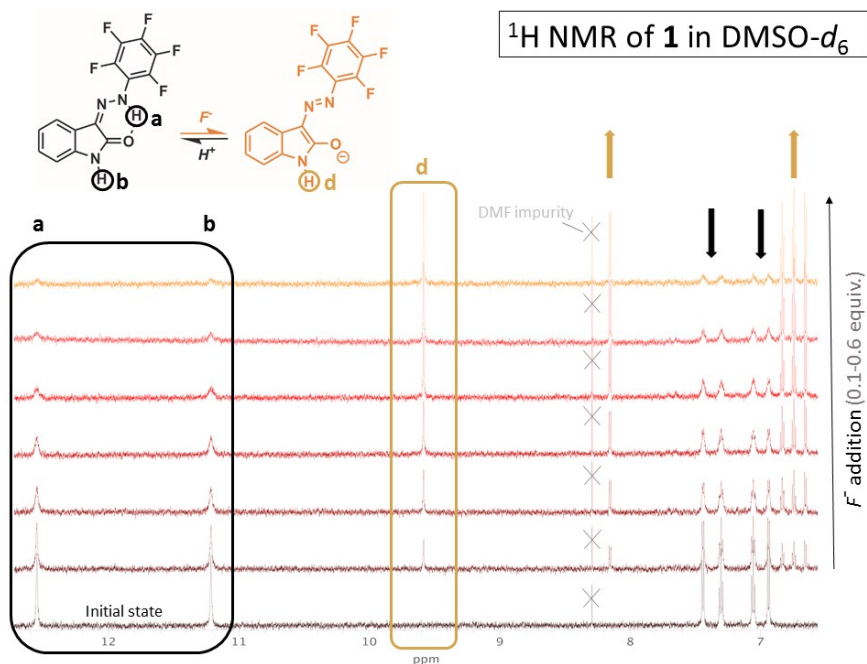


Fig. S4. Evolution of the ¹H NMR spectrum of isatin pentafluorophenylhydrazone **1** in DMSO-*d*₆ during **1** solution titration with TBA⁺F⁻ (*T* = 298.15 K).

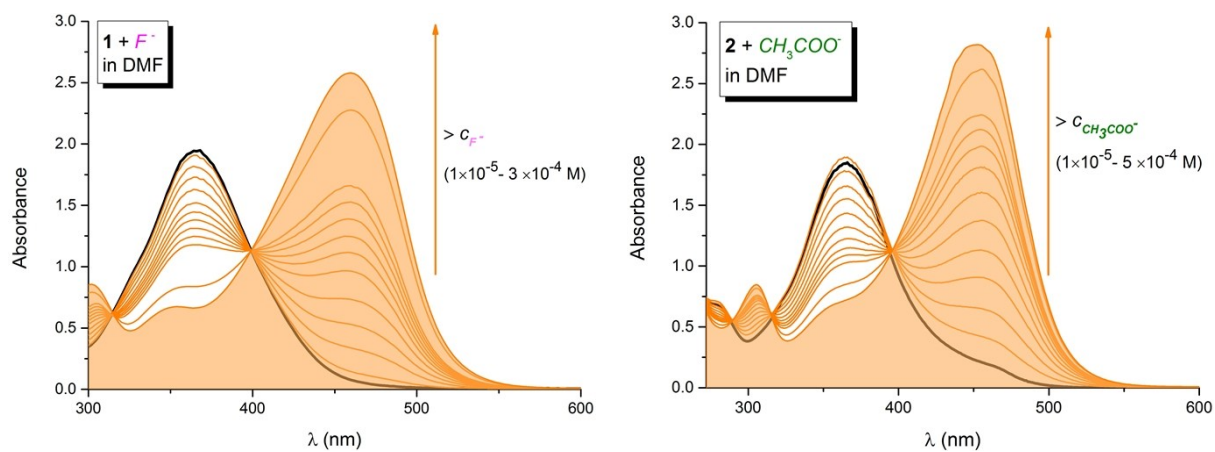


Fig. S5. UV-Vis spectrum of isatin pentafluorophenylhydrazones **1** a **2** after F⁻ and CH₃COO⁻ addition in DMF (*c*_{SENSOR} = 1 × 10⁻⁴ M).

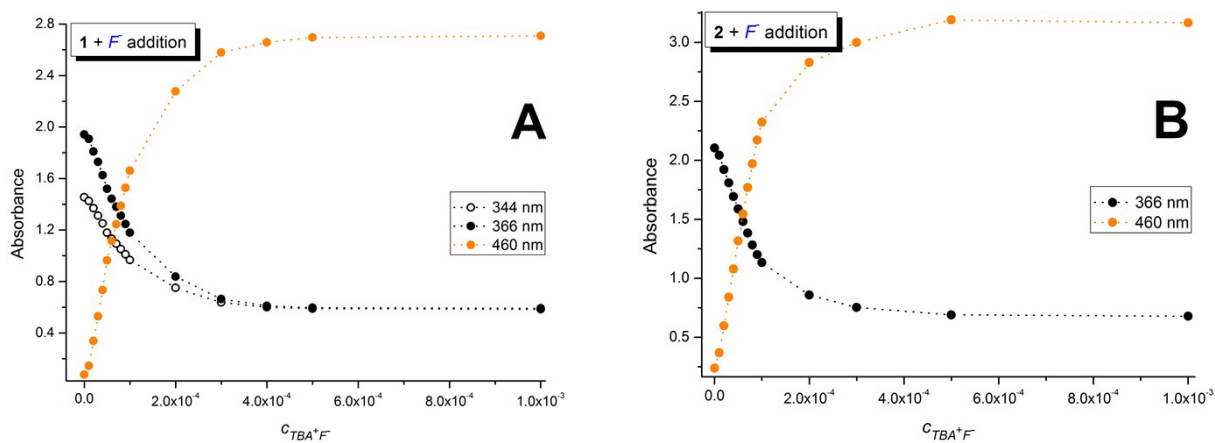


Fig. S6. Evolution of absorbance at 344, 366 and 460 nm for isatin pentafluorophenylhydrazone sensors **1** & **2** in DMF during **1** and **2** solution titration with TBA^+F^- ($c_{\text{SENSOR}} = 1 \times 10^{-4}$ mol dm^{-3}).

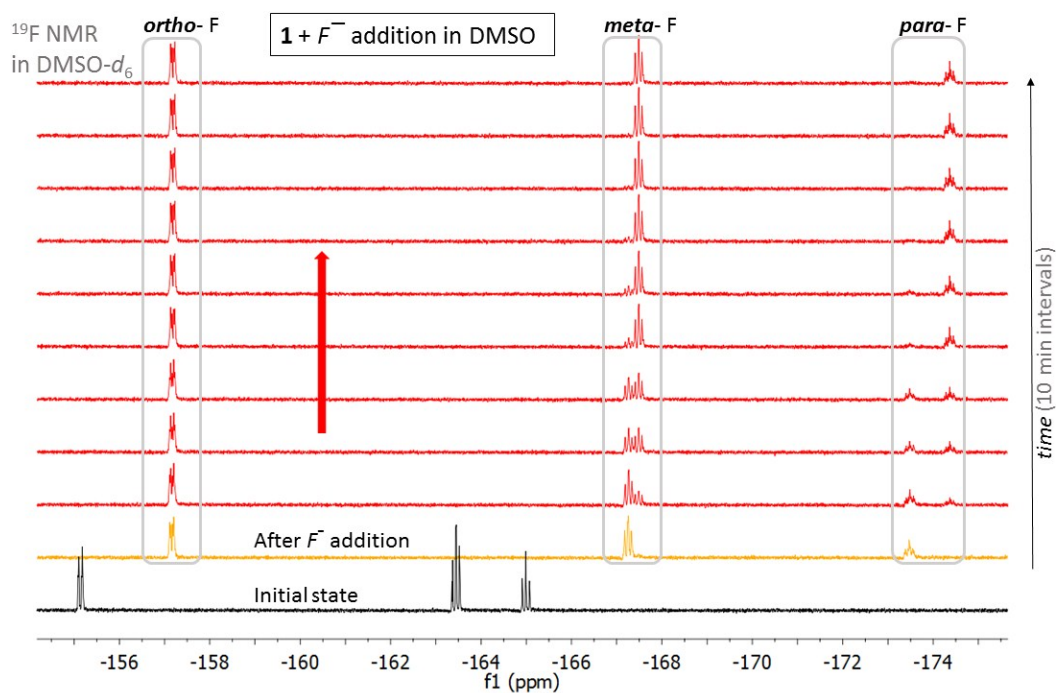


Fig. S7. Evolution of the ^{19}F NMR spectrum of isatin pentafluorophenylhydrazone **1** in $DMSO-d_6$ after TBA^+F^- addition ($T = 298.15$ K).

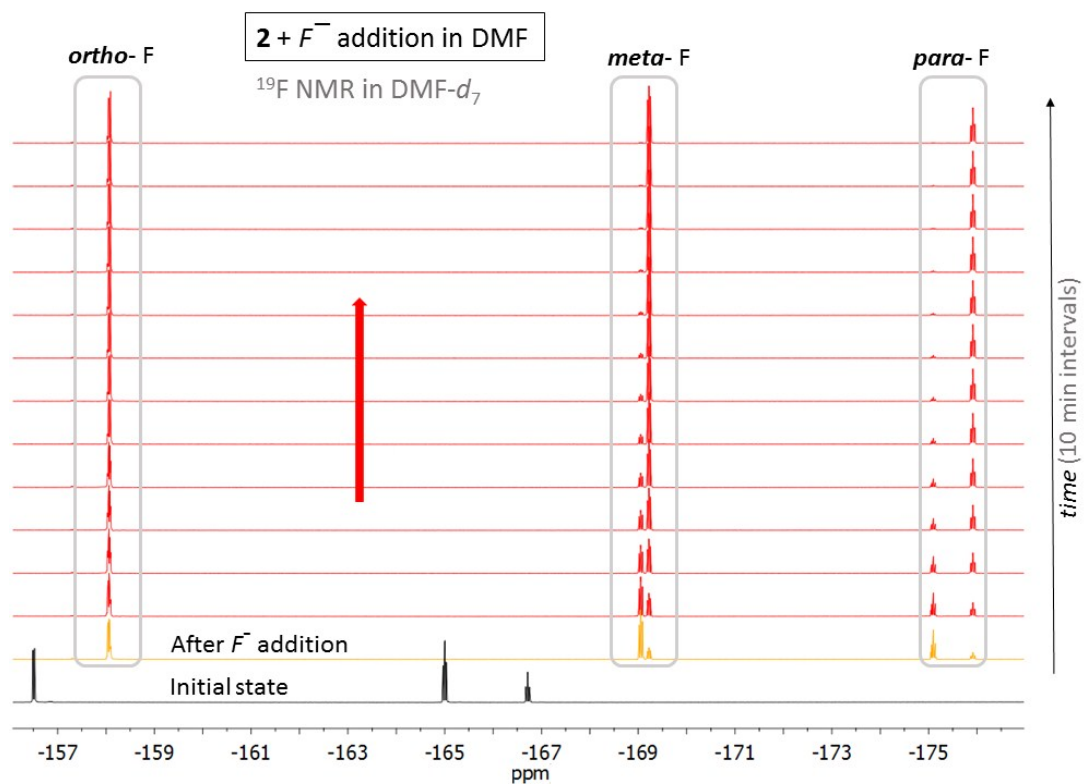


Fig. S8. Evolution of the ^{19}F NMR spectrum of isatin pentafluorophenylhydrazone **2** in $\text{DMF-}d_7$ after TBA^+F^- addition ($T = 298.15$ K).

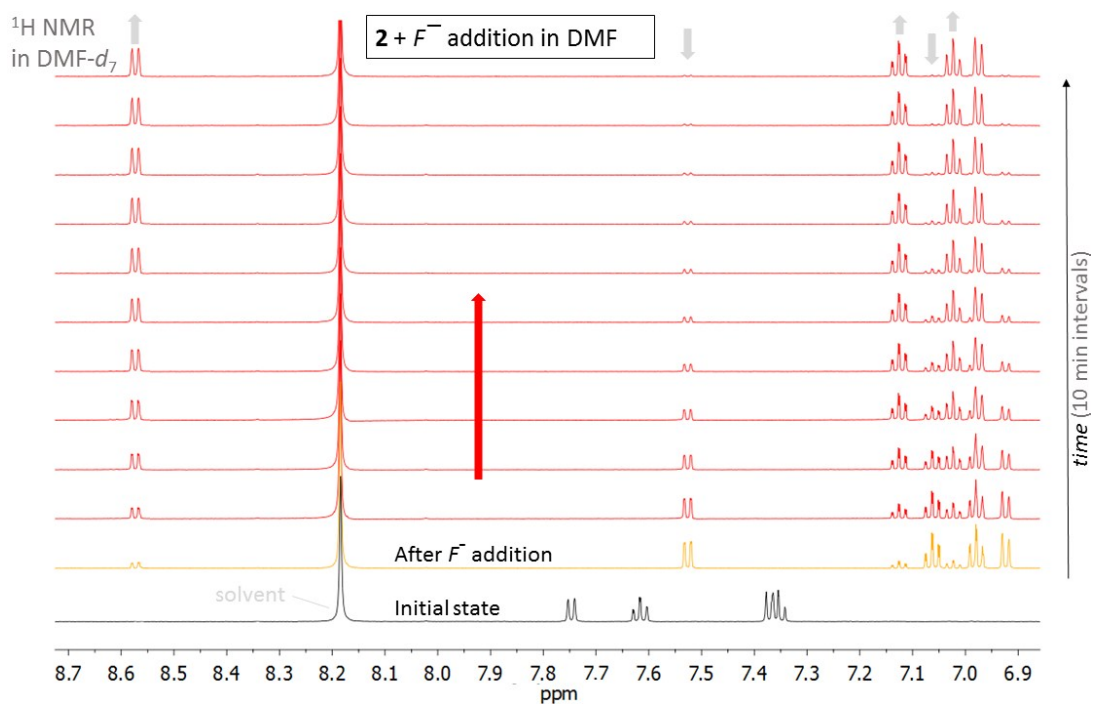


Fig. S9. Evolution of the ^1H NMR spectrum of isatin pentafluorophenylhydrazone **2** in $\text{DMF-}d_7$ after TBA^+F^- addition ($T = 298.15$ K).

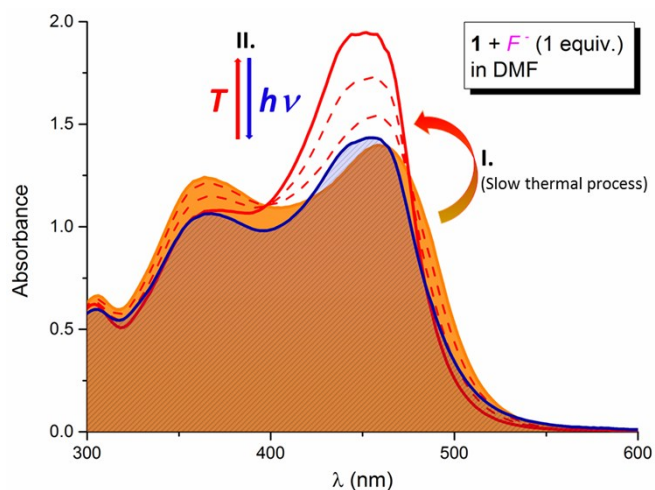


Fig. S10. Evolution of the UV-Vis spectrum of isatin pentafluorophenylhydrazone **1** after F^- anion addition in DMF ($c_{\text{SENSOR}} = 5 \times 10^{-5} \text{ M}$; $c_{F^-} = 1 \times 10^{-2} \text{ M}$; $\lambda_{\text{irr}} = 405 \text{ nm}$; $T = 303.15 \text{ K}$; $M = \text{mol dm}^{-3}$).

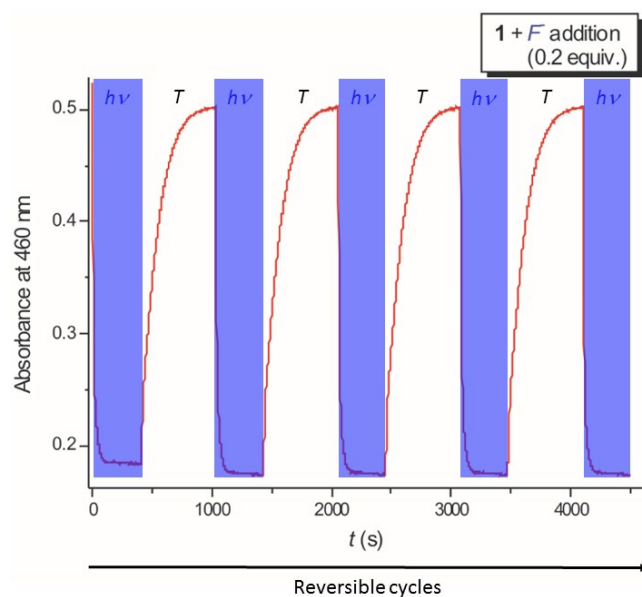
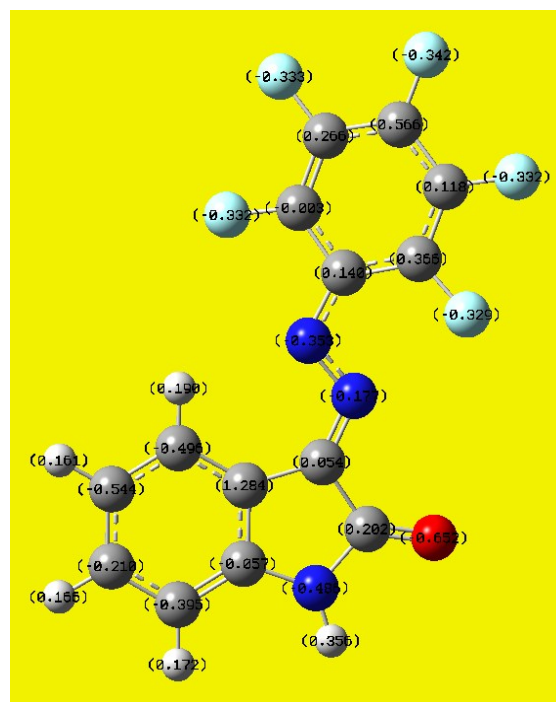
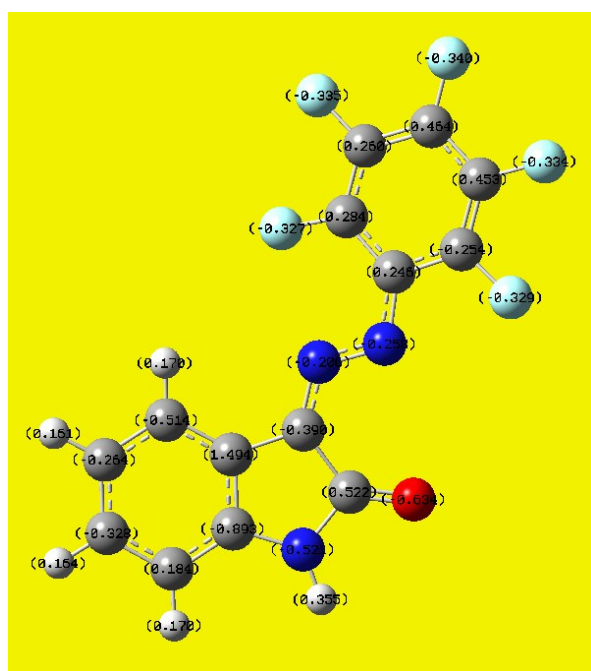
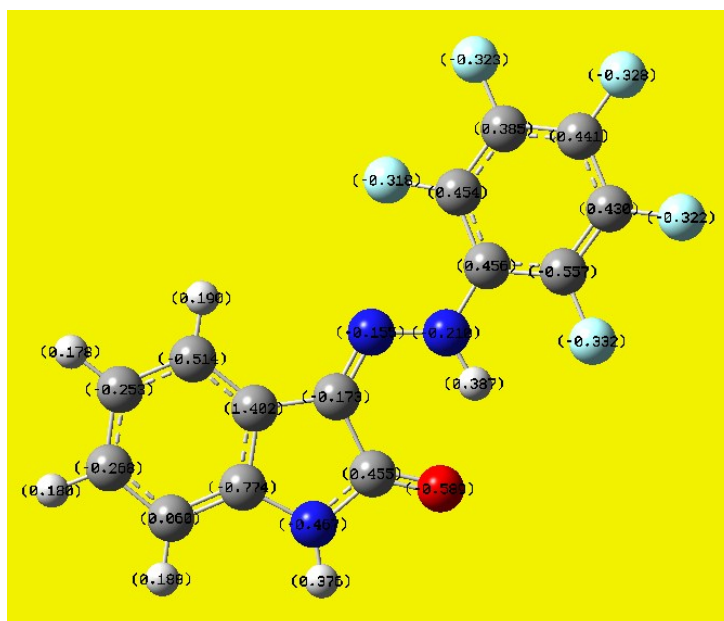


Fig. S11. Evolution of absorbance at 460 nm for isatin pentafluorophenylhydrazone **1** in DMF after $10^{-5} \text{ M } F^-$ anion addition after slow thermal process followed by back photochemical reaction ($c_{\text{SENSOR}} = 5 \times 10^{-5} \text{ M}$; $\lambda_{\text{irr}} = 405 \text{ nm}$; $M = \text{mol dm}^{-3}$).



Scheme S2. Charge distribution in the initial *Z*-hydrazo form of **1** and in two deprotonated *E*-azo enolate conformers after F^- anion addition to *Z*-hydrazo form in vacuum at the M062x 6-31+g(dp) level ($T = 298.15$ K).

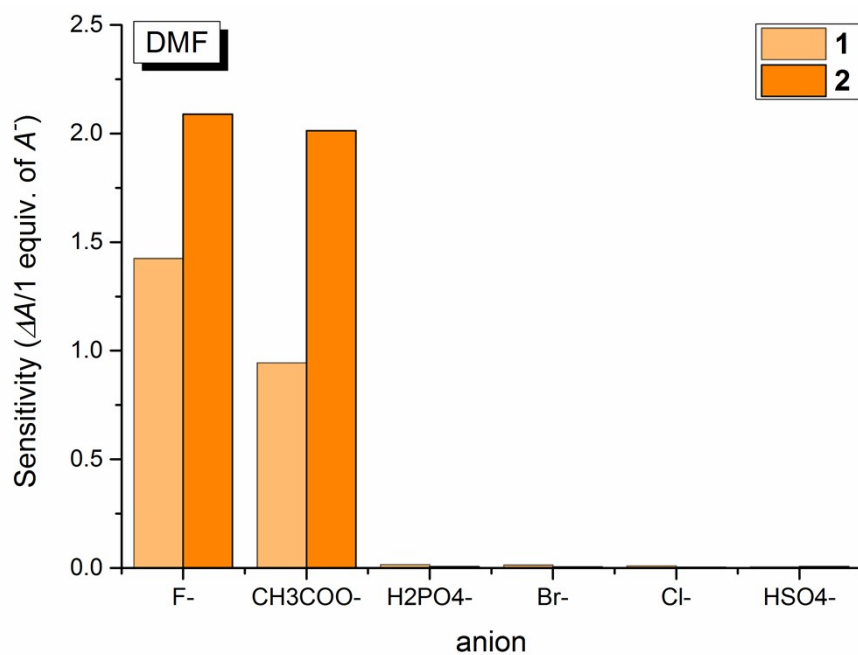


Fig. S12. The sensitivity of the studied isatin pentafluorophenylhydrazones **1** and **2** at 460 nm for various anions in DMF at 298.16 K ($c_1 = c_2 = 1 \times 10^{-4} \text{ mol}^{-1} \text{ dm}^3$).

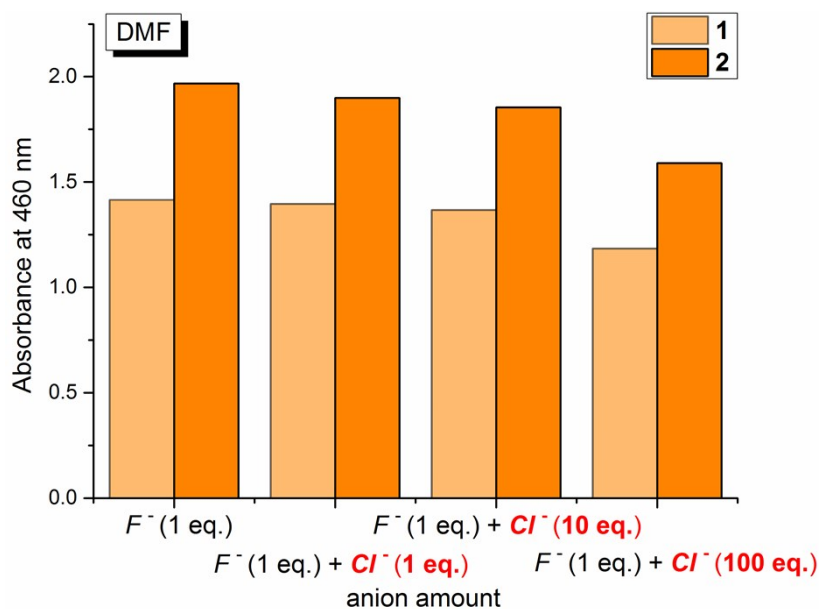
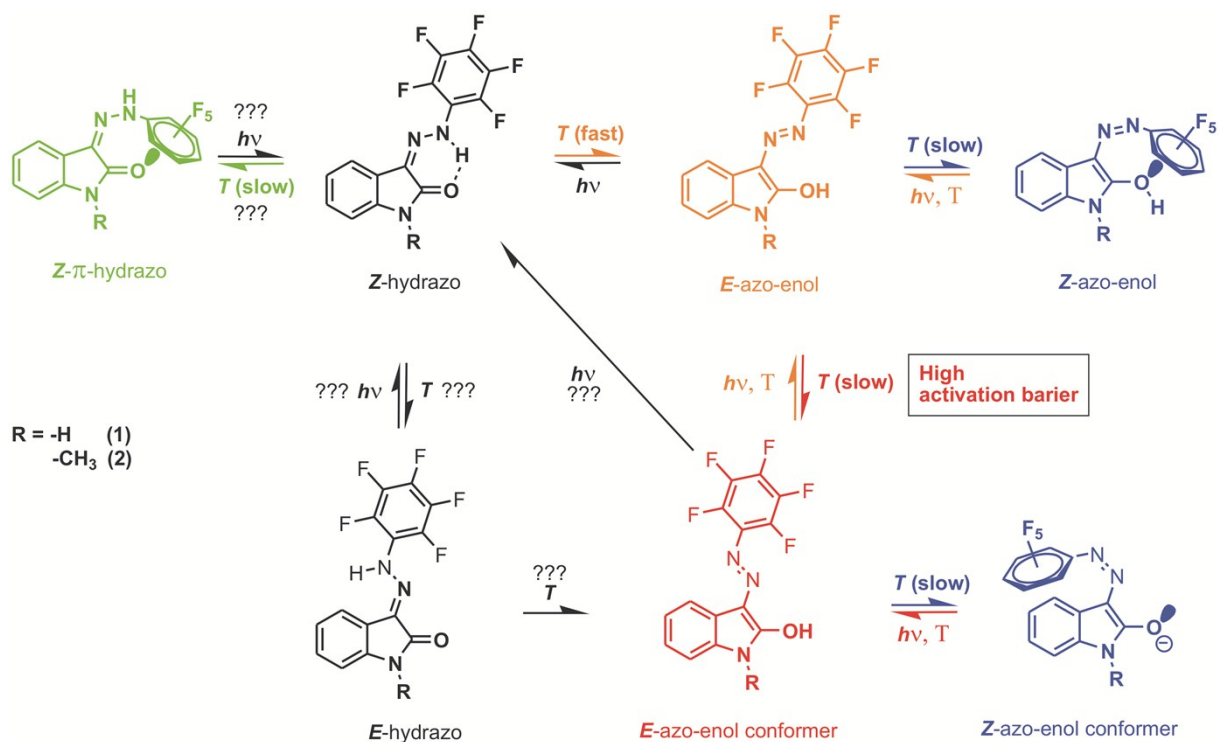


Fig. S13. The selectivity of the studied isatin pentafluorophenylhydrazones **1** and **2** at 460 nm for F⁻ anion in the presence of various amount of TBA⁺Cl⁻ in DMF at 298.16 K ($c_1 = c_2 = 1 \times 10^{-4} \text{ mol}^{-1} \text{ dm}^3$).



Scheme S3. Proposed temperature and light influence on hydrazo/azo (keto/enol) tautomeric equilibrium of **1** and **2**.

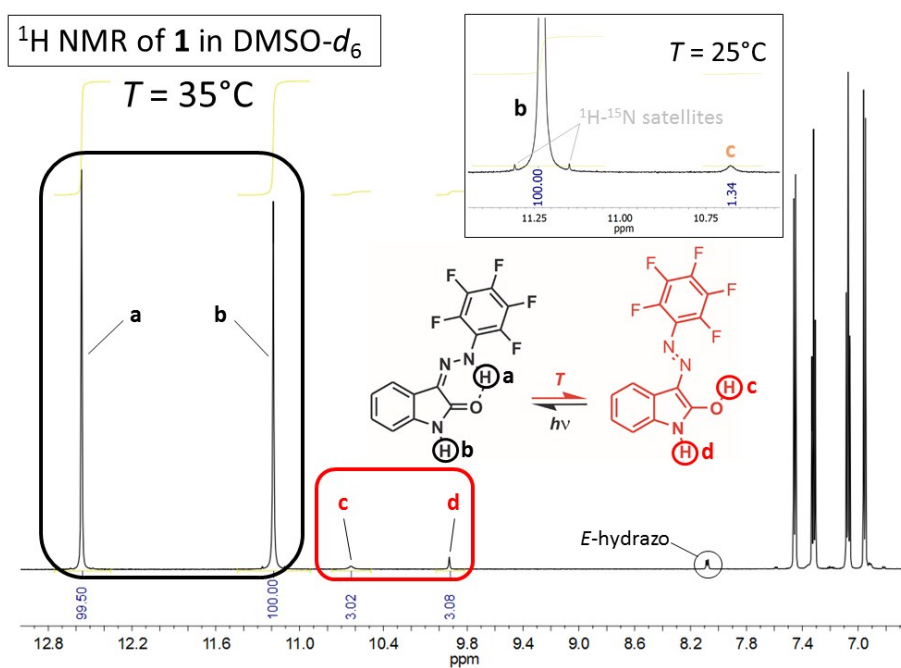


Fig. S14. 1H NMR spectrum of isatin pentafluorophenylhydrazone **1** in $DMSO-d_6$.

Table S2. Apparent association constants K_{ass} ($\text{mol}^{-1} \text{dm}^3$) for studied isatin pentafluorophenylhydrazones **1** and **2**, and corresponding basic isatin phenylhydrazones **Z1** and **Z2** isomers, with strongly basic F^- anion in DMF at 298.16 K (determined from absorption spectra).

Compd	1	2
$K_{\text{ass}} (\times 10^3)^*$	29.2 ± 2.6 ($R^2 = 0.9965$)	85.0 ± 13.7 ($R^2 = 0.9940$)
Compd	Z1	Z2
$K_{\text{ass}} (\times 10^3)^*$	3.9 ± 0.2 ($R^2 = 0.9680$)	8.9 ± 0.3 ($R^2 = 0.9630$)

* – apparent association constant: addition of strongly basic anion leads to the NH group deprotonation and not to the anion:hydrazone 1:1 complex formation; R^2 – coefficient of determination (average value)

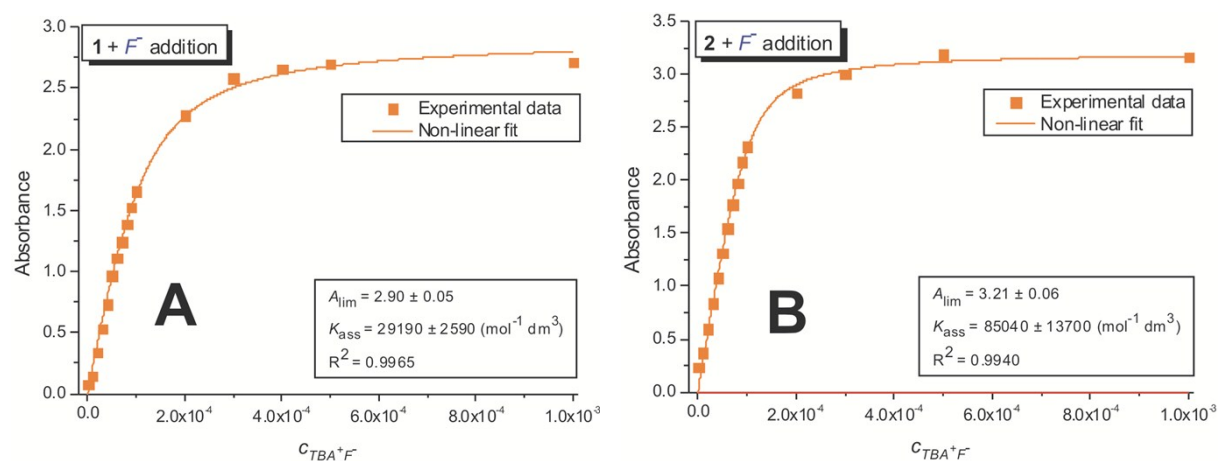


Fig. S15. Evolution of absorbance at 460 nm for isatin pentafluorophenylhydrazone sensors **1** and **2** in DMF during **1** and **2** solution titration with TBA^+F^- and non-linear fitting of experimental data using 1:1 sensor: anion binding model ($c_{\text{SENSOR}} = 1 \times 10^{-4} \text{mol dm}^{-3}$).

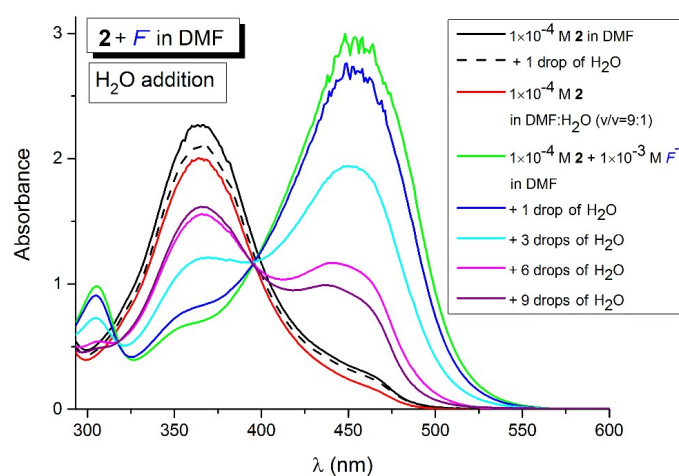


Fig. S16. Evolution of the UV-Vis spectrum of isatin pentafluorophenylhydrazone **2** after F^- anion addition in DMF and DMF:H₂O (v/v = 9:1) solvent mixture and effect of the H₂O addition ($c_{\text{SENSOR}} = 1 \times 10^{-4} \text{M}$; $T = 293.15 \text{K}$).

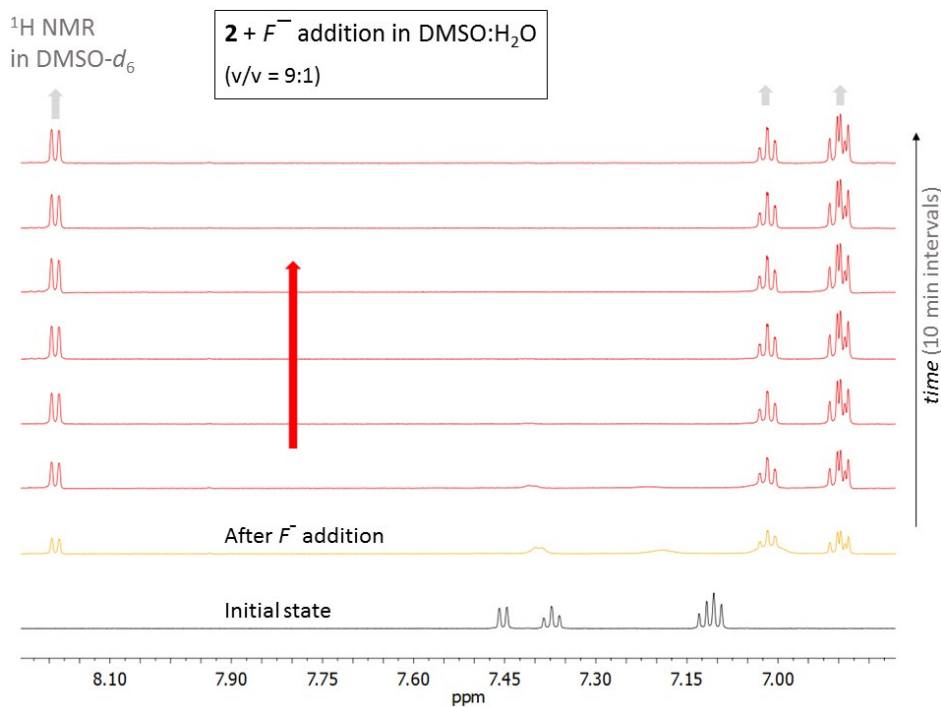


Fig. S17. Evolution of the ¹H NMR spectrum of isatin pentafluorophenylhydrazone **2** in DMSO-*d*₆/distilled H₂O solvent mixture (v/v = 9:1) after TBA⁺F⁻ addition (*T* = 298.15 K).

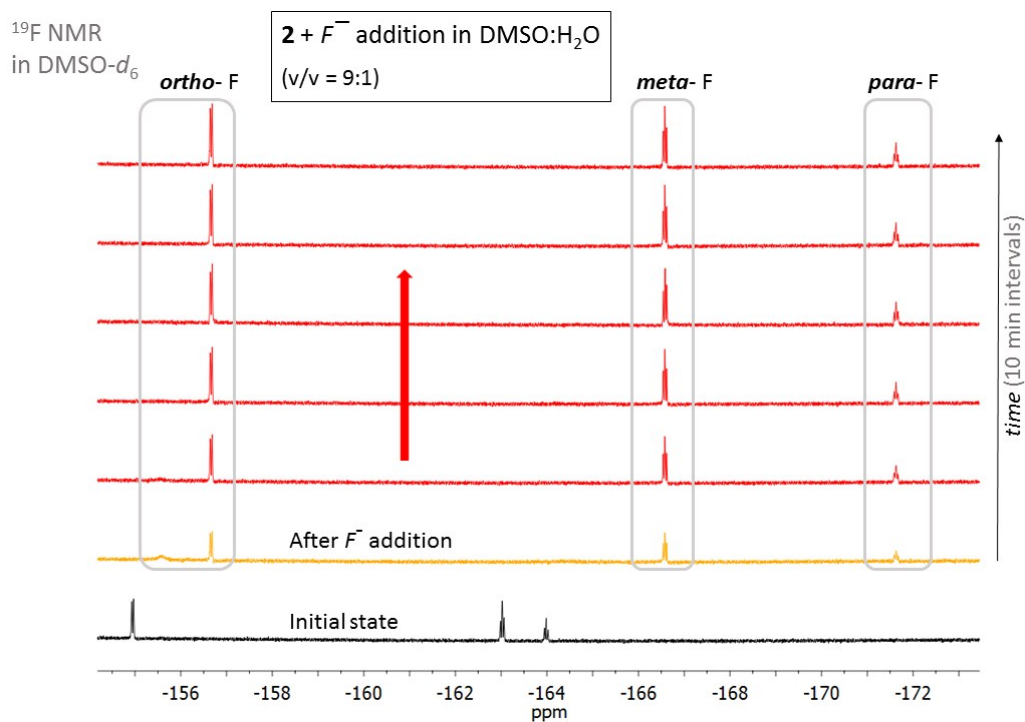


Fig. S18. Evolution of the ¹⁹F NMR spectrum of isatin pentafluorophenylhydrazone **2** in DMSO-*d*₆/distilled H₂O solvent mixture (v/v = 9:1) after TBA⁺F⁻ addition (*T* = 298.15 K).

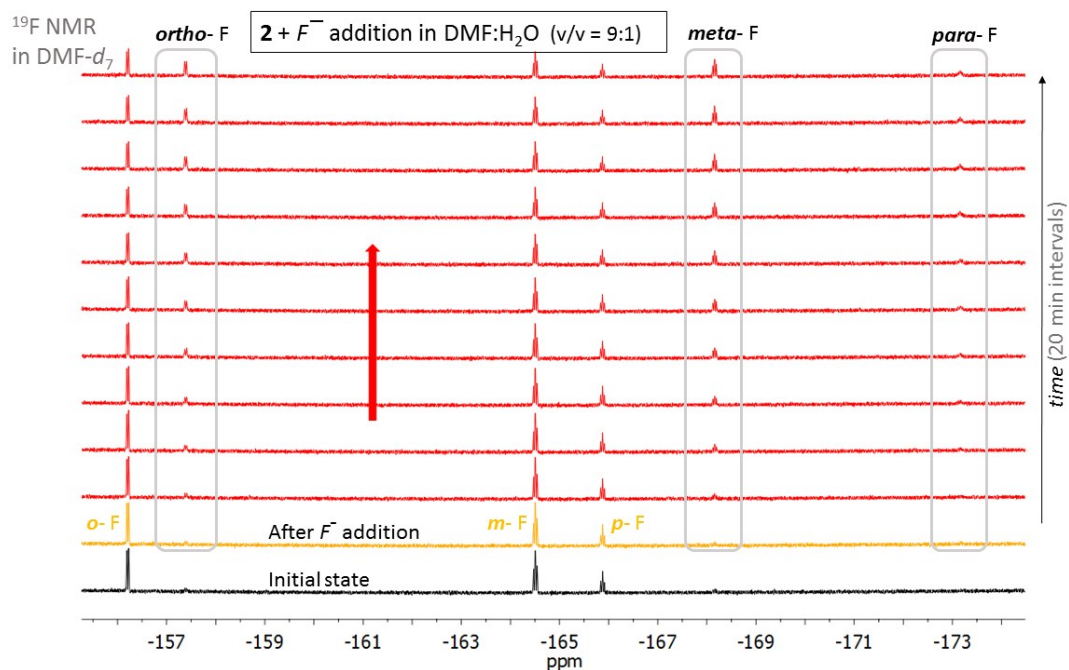


Fig. S19. Evolution of the ¹⁹F NMR spectrum of isatin pentafluorophenylhydrazone **2** in DMF-*d*₇/distilled H₂O solvent mixture (v/v = 9:1) after TBA⁺F⁻ addition (*T* = 298.15 K).

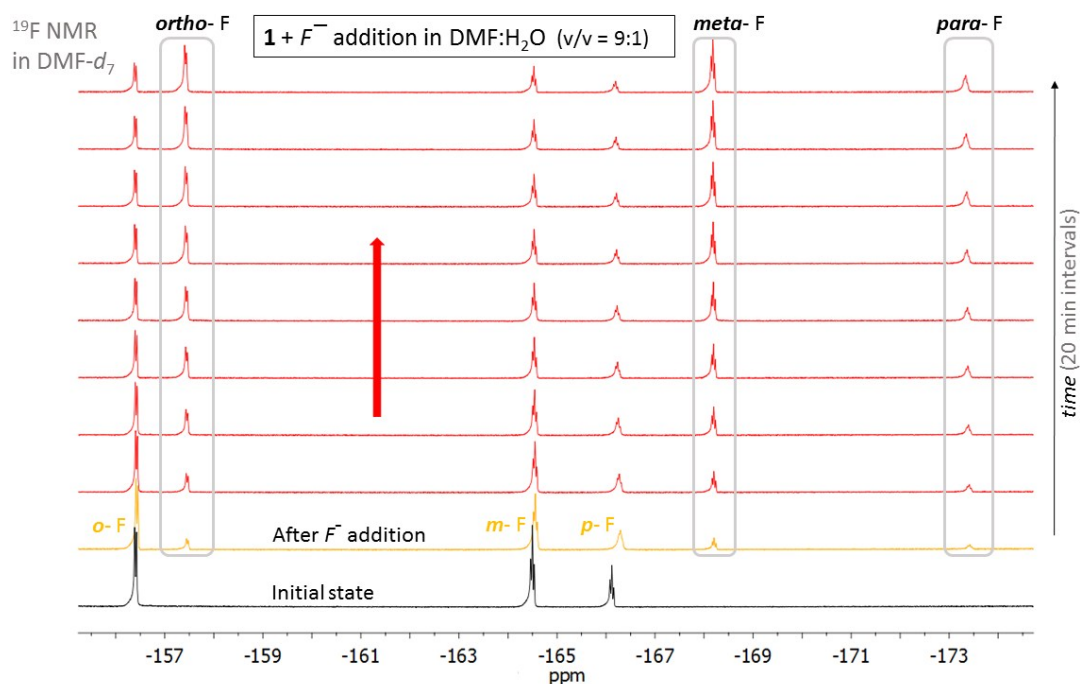


Fig. S20. Evolution of the ¹⁹F NMR spectrum of isatin pentafluorophenylhydrazone **2** in DMF-*d*₇/distilled H₂O solvent mixture (v/v = 9:1) after TBA⁺F⁻ addition (*T* = 298.15 K).

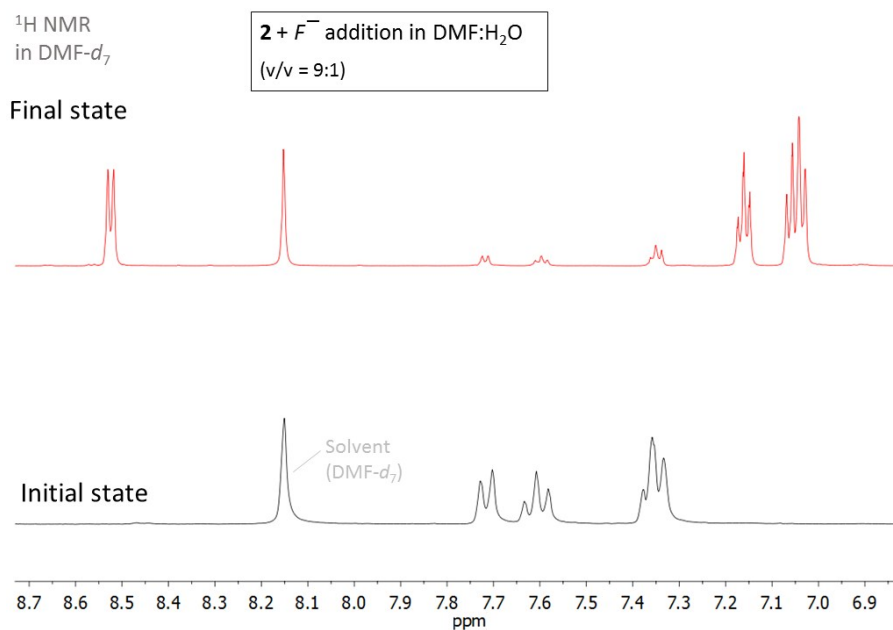


Fig. S21. Initial and final ¹H NMR spectrum of isatin pentafluorophenylhydrazone **2** in DMF-*d*₇/distilled H₂O solvent mixture (v/v = 9:1) after TBA⁺F⁻ addition (*T* = 298.15 K).

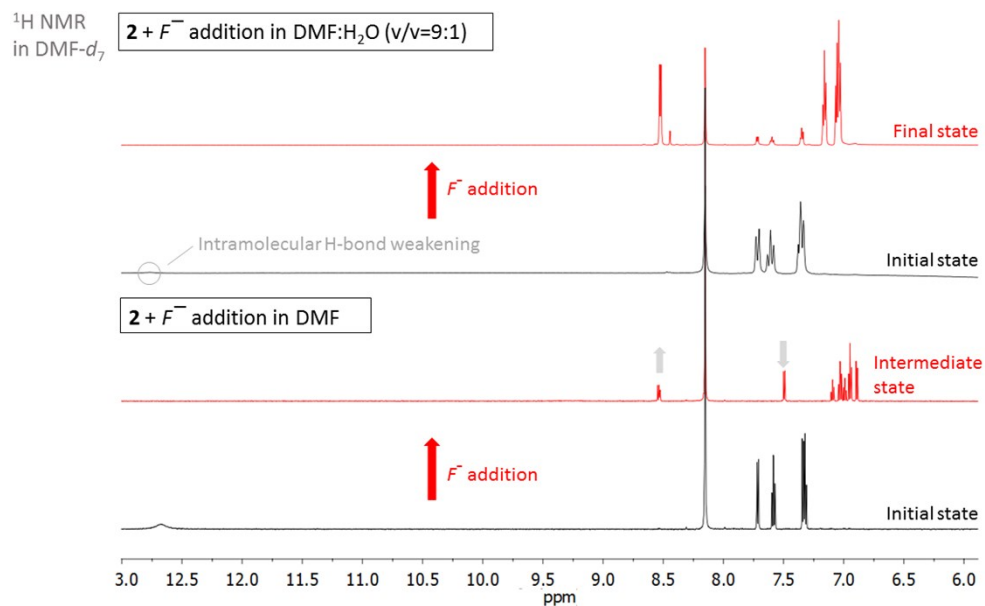


Fig. S22. Comparison of the ¹H NMR spectra of isatin pentafluorophenylhydrazone **2** in pure DMF-*d*₇ and DMF-*d*₇/distilled H₂O solvent mixture (v/v = 9:1) after TBA⁺F⁻ addition (*T* = 298.15 K).

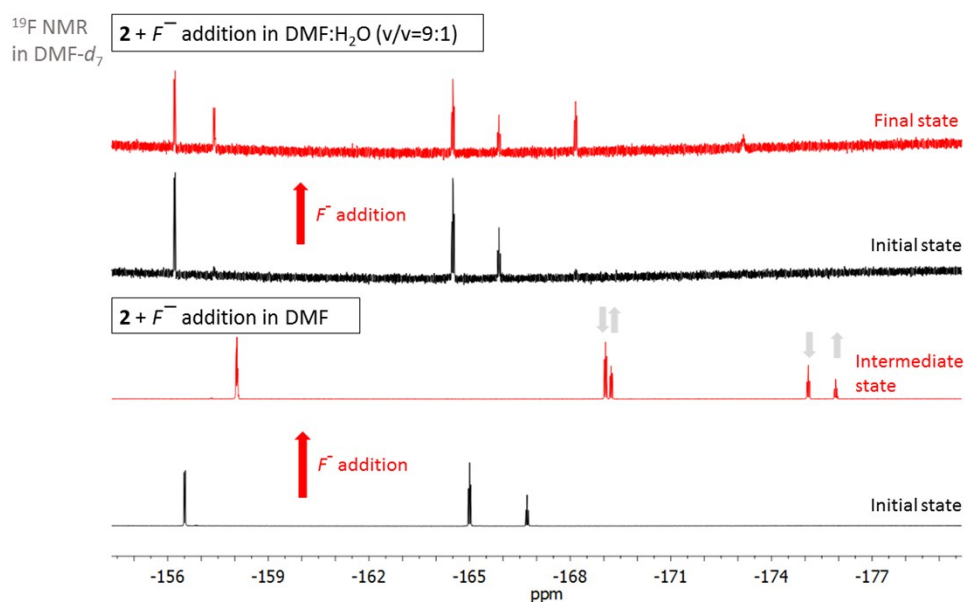


Fig. S23. Comparison of the ¹⁹F NMR spectra of isatin pentafluorophenylhydrazone **2** in pure DMF-*d*₇ and DMF-*d*₇/distilled H₂O solvent mixture (v/v = 9:1) after TBA⁺F⁻ addition (*T* = 298.15 K).

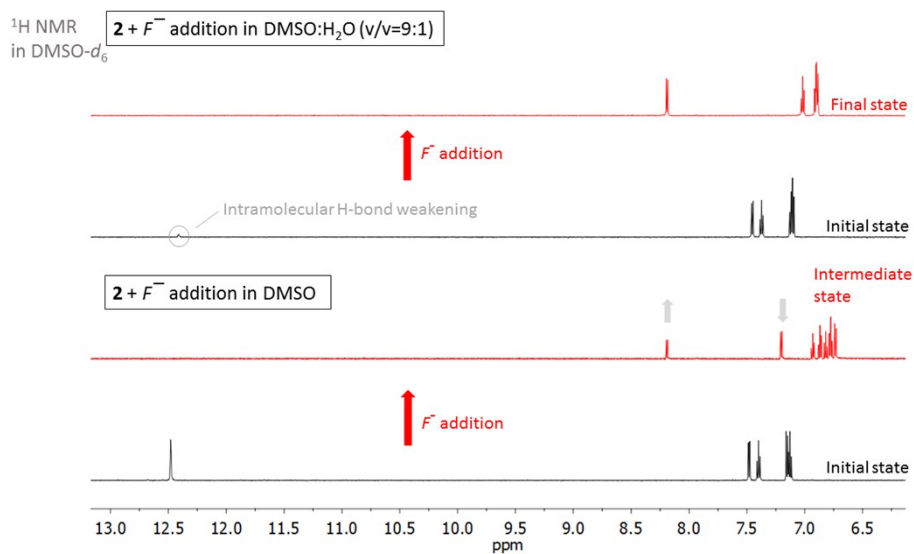


Fig. S24. Comparison of the ¹H NMR spectra of isatin pentafluorophenylhydrazone **2** in pure DMSO-*d*₆ and DMSO-*d*₆/distilled H₂O solvent mixture (v/v = 9:1) after TBA⁺F⁻ addition (*T* = 298.15 K).

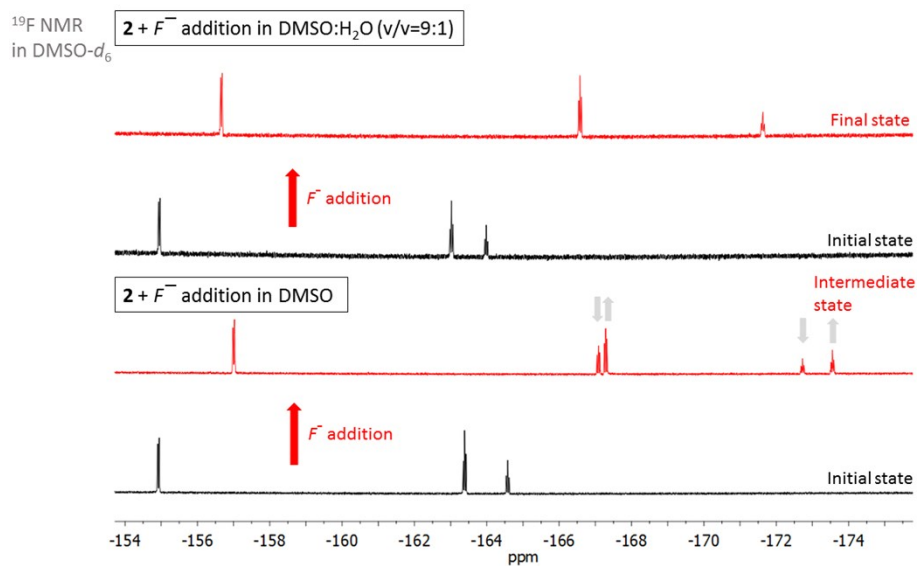


Fig. S25. Comparison of the ¹⁹F NMR spectra of isatin pentafluorophenylhydrazone **2** in pure DMSO-*d*₆ and DMSO-*d*₆ /destilled H₂O solvent mixture (v/v = 9:1) after TBA⁺F⁻ addition (*T* = 298.15 K).

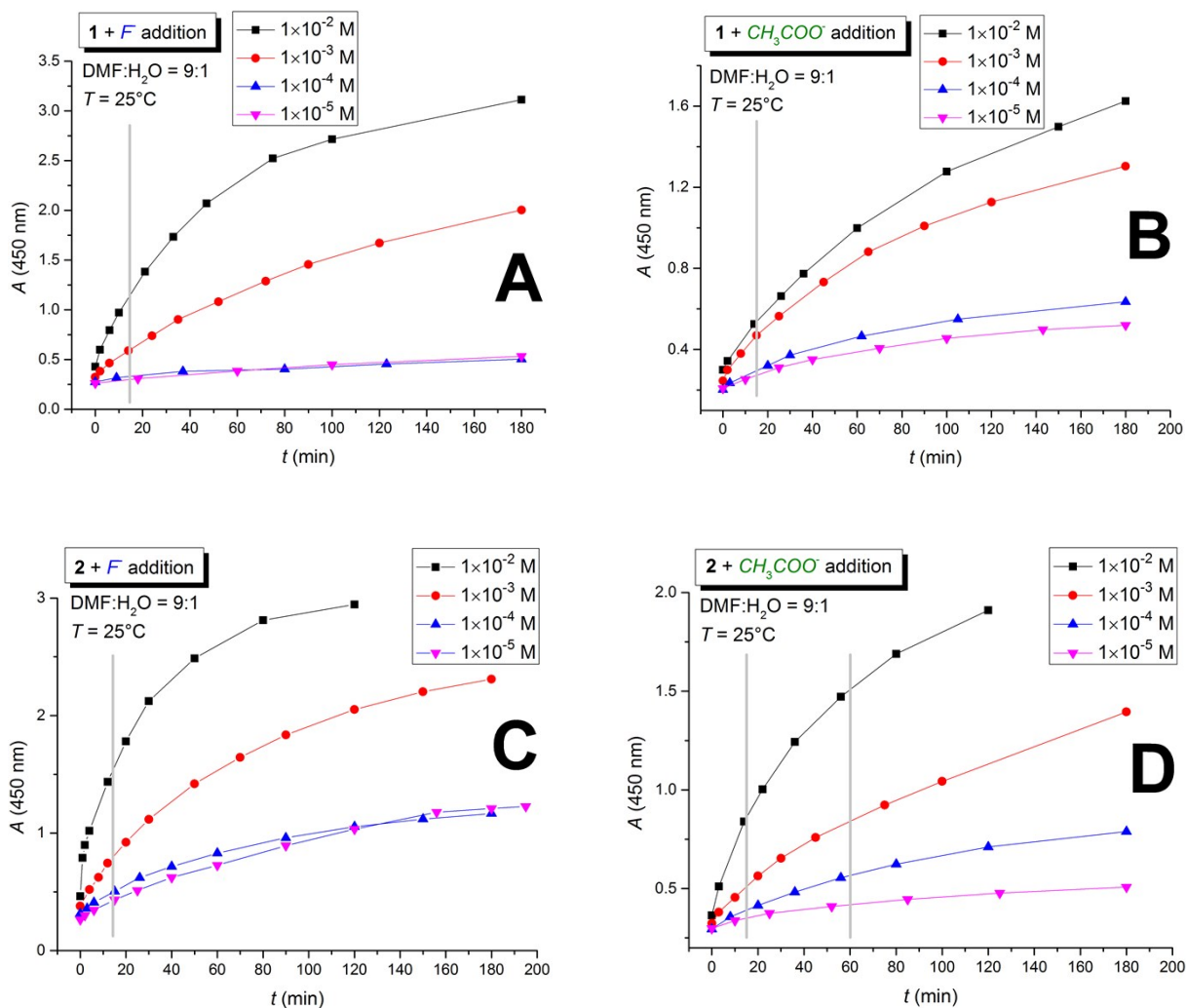


Fig. S26. Evolution of absorbance at 450 nm for isatin pentaffluorophenylhydrazone sensors **1** and **2** in DMF:H₂O solvent mixture (v/v = 9:1) during **1** and **2** solution titration with TBA^+F^- and $TBA^+CH_3COO^-$ ($c_{\text{SENSOR}} = 1 \times 10^{-4} \text{ mol dm}^{-3}$).

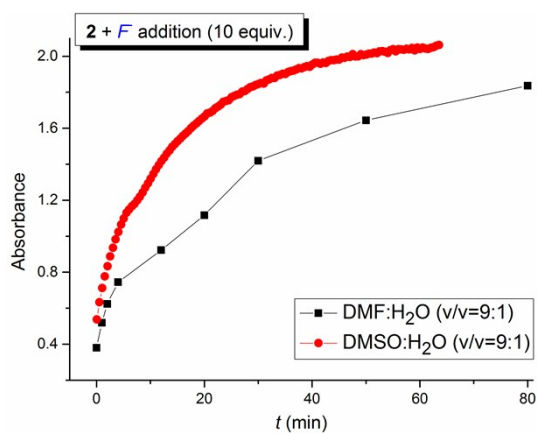


Fig. S27. Evolution of the absorbance at 450 nm of isatin pentaffluorophenylhydrazone **2** after F^- anion addition in DMF:H₂O (v/v = 9:1) and DMSO:H₂O (v/v = 9:1) solvent mixture ($c_{\text{SENSOR}} = 1 \times 10^{-4} \text{ M}$; $c_{F^-} = 1 \times 10^{-3} \text{ M}$; $T = 293.15 \text{ K}$).

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