

A Novel Reaction-based, Chromogenic and “Turn-on” Fluorescent Chemodosimeter For Fluoride Detection

Clément Padié, Kirsten Zeitler*

*Institut für Organische Chemie, Universität Regensburg,
Universitätsstrasse 31, D-93053 Regensburg, Germany*
kirsten.zeitler@chemie.uni-regensburg.de

Supporting Information

Table of Contents

General Considerations	S2
Synthetic Procedures	S2
Fluoride induced Polymerisation of <i>N</i> -Methylmaleimide (NMM)	S2
Synthesis of the Fluorochrome-Substituted Maleimide	S4
Fluorogenic maleimide 1 as fluoride sensor	S5
¹ H and ¹³ C NMR Spectra	S9–S12

General Considerations

NMR spectra were recorded on a Bruker Avance 300 (300.13 MHz) spectrometer using the solvent peak as internal reference (CDCl_3 : δ H 7.26; δ C: 77.0). Multiplicities are indicated, s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet); coupling constants (J) are in Hertz (Hz).

Mass spectra (MS ESI) were recorded with a Finnigan MAT 95 or Varian MAT 311A. All reactions were monitored by thin-layer chromatography (TLC) using Merck silica gel plates 60 F₂₅₄; visualization was accomplished with UV light and/or staining with appropriate stains (anisaldehyde, vaniline). Standard chromatography procedures were followed (particle size 63 – 200 μm).

Infrared Spectra were obtained using neat samples on a Biorad Excalibur FTS 3000 FT IR spectrometer equipped with a universal ATR sampling accessory (Specac Golden Gate Diamond Single Reflection ATR system); wave numbers $\tilde{\nu}$ are reported in cm^{-1} .

Fluorescence spectra were recorded on a Varian Cary Eclipse fluorescence spectrometer at 25 °C.

All chemicals were obtained from commercial sources and were used as received. Solvents were distilled prior to use.

Synthetic Procedures

Fluoride Induced Polymerisation of *N*-Methylmaleimide (NMM)

To a solution of *N*-methylmaleimide (1.1 g, 10 mmol) in 5 mL of THF 1 mL of a 1M tetrabutylammonium fluoride (TBAF) solution in THF (1.0 mmol, 10 mol%) is added at 0 °C (alternatively: addition of 152mg of cesium fluoride (1.0 mmol, 10 mol%)). Upon this addition the solution turns red-pink immediately and a precipitate appears. TLC control after 1 hour using NMM as a reference shows the complete disappearance of the starting material.

For further analysis a half of the suspension is kept and 1 mL of a 1 M hydrochloric acid is added to the other half. The red colour immediately vanishes (see Fig. S3)

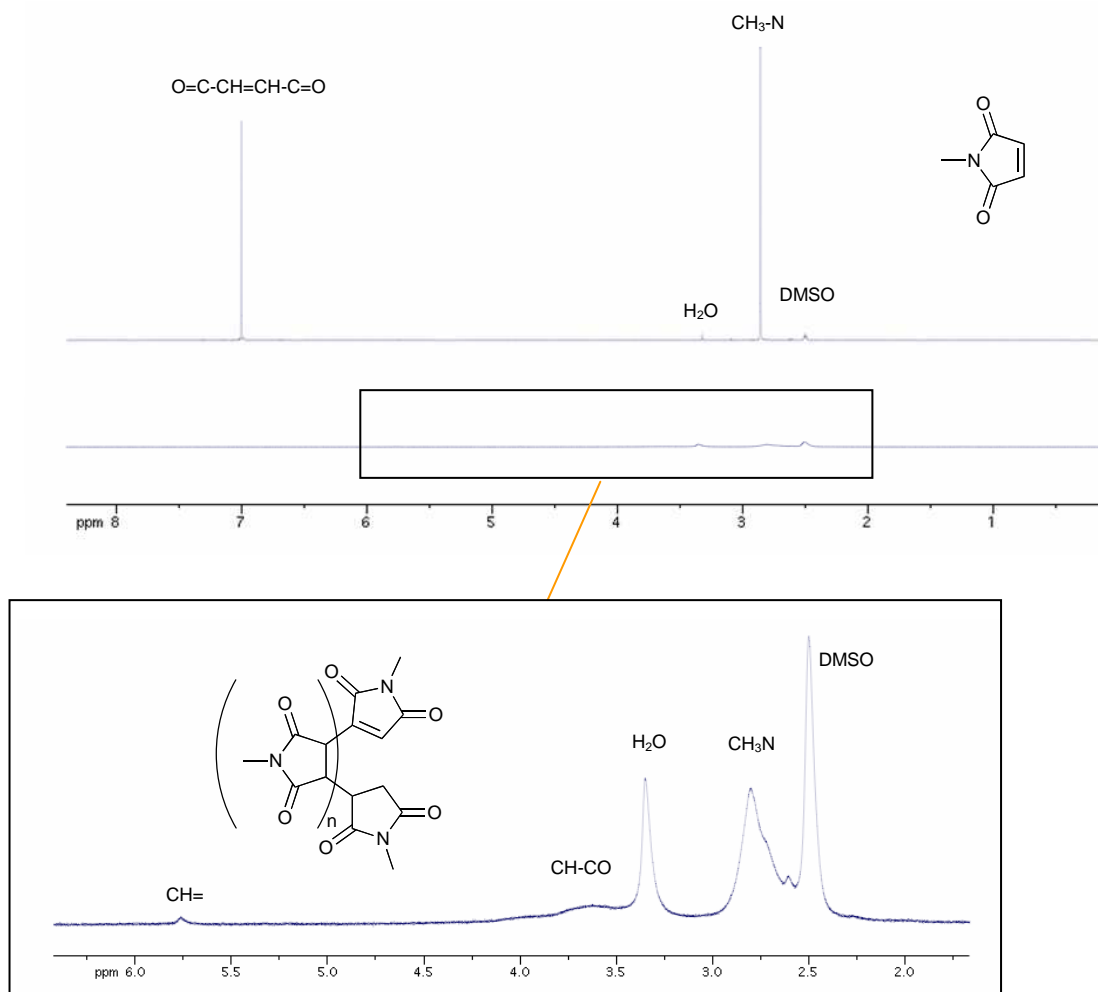
The precipitate is isolated by centrifugation and elimination of the supernatant, washed twice with 5 mL of THF and dried under reduced pressure to give a grey powder.

The corresponding analytical data of this powder are provided below in comparison with NMM used as starting material.

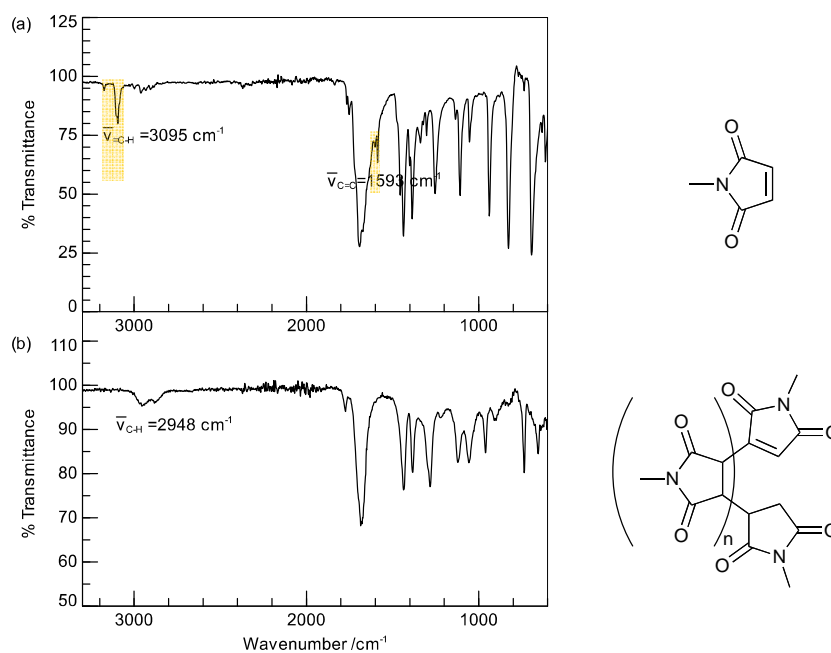
ESI MS m/z 332 [“trimer” 3M]⁺, 226 [“dimer” 2M].

For NMR investigation 110 mg NMM are dissolved in 1.8 mL d^6 -DMSO. ¹H NMR of two tubes with 0.7 mL solution each were compared after 20 min while to one 75 mg CsF were added.

NMR:

**Figure S1** Comparison of ^1H NMR spectra before (a) and after (b) fluoride addition.

IR:

**Figure S2** Comparison of IR spectra before (a) and after (b) fluoride addition.

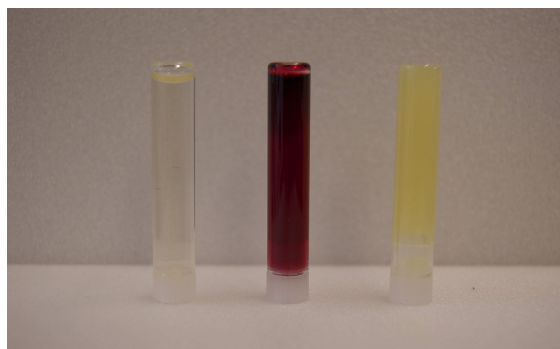
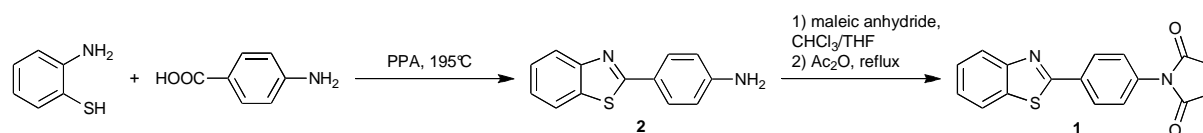


Figure S3 Photo of “naked eye” detection: **(left)** NMM in DMSO (175 mM), **(middle)** NMM in DMSO (175 mM) 20 minutes after addition of TBAF (45 mM, 0.25 eq), **(right)** NMM in DMSO (175 mM)+ TBAF (45 mM) incubated for 20 min followed by addition of HCl.

Synthesis of the Fluorochrome Substituted Maleimide



Synthesis of 2-(4-Aminophenyl)-benzothiazole (2):

A well stirred mixture of *o*-aminothiophenol (1.4 mL, 13 mmol), *p*-aminobenzoic acid (2.0 g, 13 mmol) and 20 g of polyphosphoric acid is heated to 195 °C overnight. The mixture is then poured into 150 mL of ice-cold water and stirred at room temperature for 20 minutes. The solid is recovered by filtration and washed twice with 20 mL of water. The solid is then poured into 100 mL of a saturated solution of NaHCO₃ and the mixture is stirred at room temperature during 10 minutes. The solid is collected by filtration, washed twice with 30 mL of water and pressed as dry as possible. The resulting greenish yellow solid is further dried under reduced pressure over phosphorus pentoxide (2.55 g, yield 86%).

¹H NMR (d⁶ DMSO): δ = 5.91 (s, 2H), 6.67 (d, *J* = 8.5 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 2H), 7.90 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 8.1 Hz, 1H).

¹³C NMR (d⁶ DMSO): δ = 113.8, 120.0, 121.4, 121.8, 124.5, 126.4, 128.7, 133.3, 151.8, 153.3, 168.6.

HRMS (EI) calcd for C₁₃H₁₀N₂S [M⁺]: 226.0565 Found 226.0564.

Synthesis of 2-(4-Maleimidophenyl)-benzothiazole (1):

To a solution of **2** (2.0 g, 8.85 mmol) in 75 mL of THF is added at 0 °C a solution of maleic anhydride (1.0 g, 10.2 mmol) in 100 mL of chloroform. The mixture is allowed to stir at room temperature overnight. The solid is collected by filtration and washed twice with 50 mL of THF. The isolated solid is dried under reduced pressure and then poured into 50 mL of acetic anhydride and the mixture is refluxed for 4 hours. Subsequently, the mixture is poured into 150 mL of water. The solid is collected by filtration and then dissolved in ethyl acetate. The organic layer is washed twice with 100 mL of a

This journal is (c) The Royal Society of Chemistry and The Centre National de la Recherche Scientifique, 2011

saturated solution of NaHCO_3 and once with 100 mL of brine, dried over Na_2SO_4 , filtered and evaporated under reduced pressure to give a greenish solid that is purified by column chromatography (SiO_2 , eluent: dichloromethane 100%). Subsequent evaporation of the pure fractions ($R_f = 0.75$) yields the title compound as a bright yellow solid (2.0 g, yield 74%).

^1H NMR (CDCl_3): $\delta = 6.90$ (s, 2H), 7.40 (t, $J = 7.6$ Hz, 1H), 7.53 (m, 3H), 7.92 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 8.1$ Hz, 1H), 8.20 (d, $J = 9.0$ Hz, 2H).

^{13}C NMR (CDCl_3): $\delta = 121.7, 123.4, 125.5, 126.0, 126.5, 128.2, 132.8, 133.6, 134.4, 135.2, 154.2, 166.8, 169.1$.

HRMS (EI) calcd for $\text{C}_{17}\text{H}_{10}\text{N}_2\text{O}_2\text{S}$ [M^+]: 306.0463 Found 306.0468.

Use of the Fluorogenic Maleimide **1** as Fluoride Sensor

Reactivity Study

50 mg of cesium fluoride (0.33 mmol; 1 equiv) are added to 100 mg of **1** (0.33 mmol) in 5 mL of THF. The mixture turns red immediately and a precipitate appears. The mixture is stirred at room temperature overnight. The solid is recovered by centrifugation and washed twice with 5 mL of water and 5 mL of THF and dried under reduce pressure to give a pale brown solid.

Kinetic Study

A kinetic measurement was performed by recording the fluorescence at 420 nm ($\lambda_{\text{excitation}} 365$ nm). The kinetic measurement is initiated with the addition of 100 μL of a solution of **1** in DMSO ($c = 0.47$ mmolL $^{-1}$) to 1.0 mL of DMSO. After 5 minutes, 100 μL of a solution of TBAF in DMSO ($c = 1.8$ mmolL $^{-1}$) are added

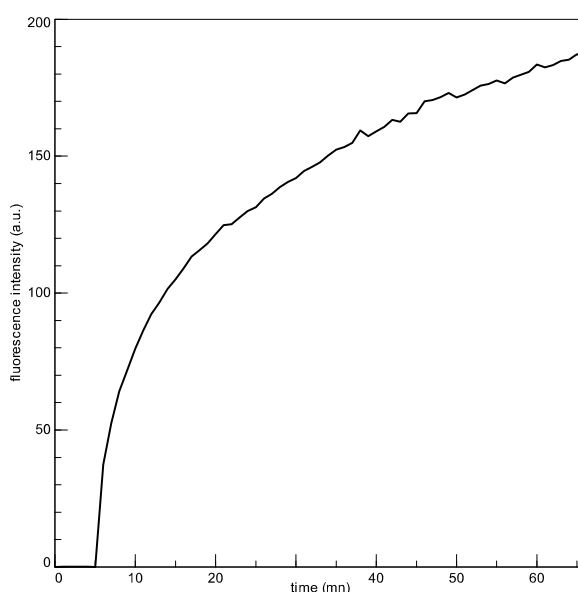


Figure S4 Kinetics of the reaction of the fluorogenic maleimide **1** (0.039 mmolL $^{-1}$) with TBAF (0.15 mmolL $^{-1}$) in DMSO followed by fluorescence emission at 420 nm ($\lambda_{\text{excitation}} 365$ nm).

Titration Study

To a solution of TBAF in DMSO (0.5×10^{-4} , 1.0×10^{-4} , 2.0×10^{-4} , 3.0×10^{-4} , 4.0×10^{-4} , 5.0×10^{-4} , 6.0×10^{-4} , 7.0×10^{-4} , 8.0×10^{-4} , 9.0×10^{-4} , 1.0×10^{-3} , 1.1×10^{-3} , 1.2×10^{-3} or $1.3 \times 10^{-3} \text{ molL}^{-1}$) are added 250 μL of a solution of **1** in DMSO ($c = 4.7 \times 10^{-4} \text{ molL}^{-1}$). The mixture is left at room temperature for 2 hours before recording the fluorescence emission ($\lambda_{\text{excitation}} 365\text{nm}$).

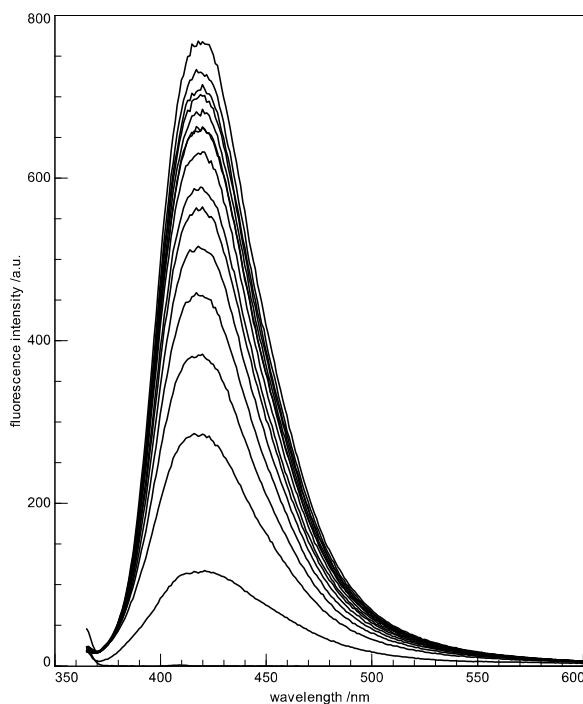


Figure S5 Titration of **1** ($c = 3.9 \times 10^{-5} \text{ molL}^{-1}$) with TBAF ($0 < c < 13.0 \times 10^{-4} \text{ molL}^{-1}$) in DMSO followed by fluorescence ($\lambda_{\text{excitation}} 365\text{nm}$).

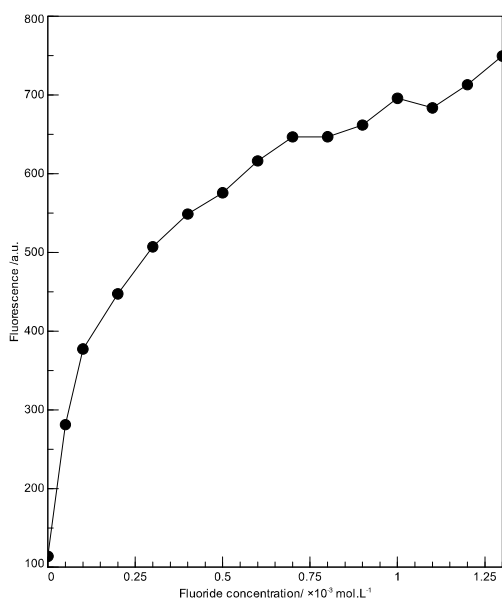


Figure S6 Titration of **1** ($c = 3.9 \times 10^{-5} \text{ molL}^{-1}$) with TBAF in DMSO.

Influence of Counterions

250 μL of a solution of fluorogenic maleimide **1** in DMSO (0.47 mmol L^{-1}) are added to 2.75 mL of a solution of sodium, tetrabutylammonium, potassium, cesium or ammonium fluoride respectively in DMSO ($[\text{F}^-] = 0.43 \text{ mmol L}^{-1}$).

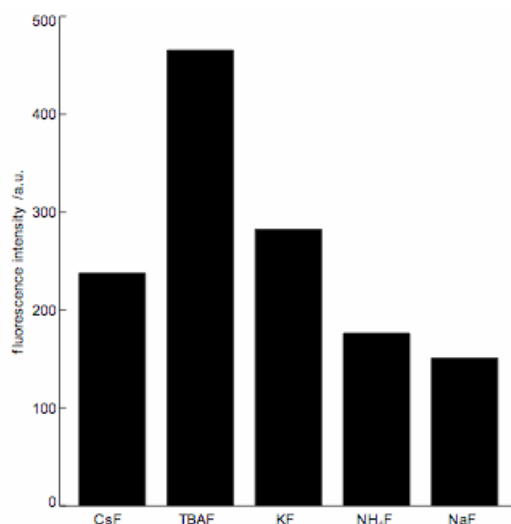


Figure S7 Influence of different counterions.

Selectivity towards Fluoride

250 μL of a solution of fluorogenic maleimide **1** in DMSO (0.47 mmol L^{-1}) are added to 2.75 mL of a solution of tetrabutylammonium fluoride, tetrabutylammonium chloride, tetrabutylammonium bromide, tetrabutylammonium iodide, tetrabutylammonium toluenesulfonate, tetrabutylammonium hexafluorophosphate, tetrabutylammonium tetrafluoroborate, tetrabutylammonium hydrogensulfate, sodium acetate, potassium cyanide or tetrabutylammonium hydroxide ($c = 0.43 \text{ mmol L}^{-1}$).

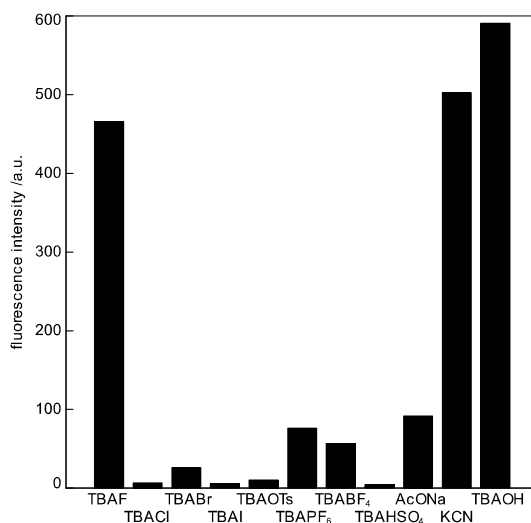


Figure S8 Fluorescence response for different anions.

This journal is (c) The Royal Society of Chemistry and The Centre National de la Recherche Scientifique, 2011

Perturbation of the Fluoride Induced Answer in the Presence of other Anions

250 μL of a solution of fluorogenic maleimide **1** in DMSO (0.47 mmolL^{-1}) are added to 2.75 mL of a solution of tetrabutylammonium fluoride ($c = 0.4 \text{ mmolL}^{-1}$) and acetic acid (50 μL) or tetrabutylammonium chloride or tetrabutylammonium bromide or tetrabutylammonium iodide or tetrabutylammonium toluenesulfonate or tetrabutylammonium hexafluorophosphate or tetrabutylammonium tetrafluoroborate or tetrabutylammonium hydrogenosulfate ($c = 0.4 \text{ mmolL}^{-1}$).

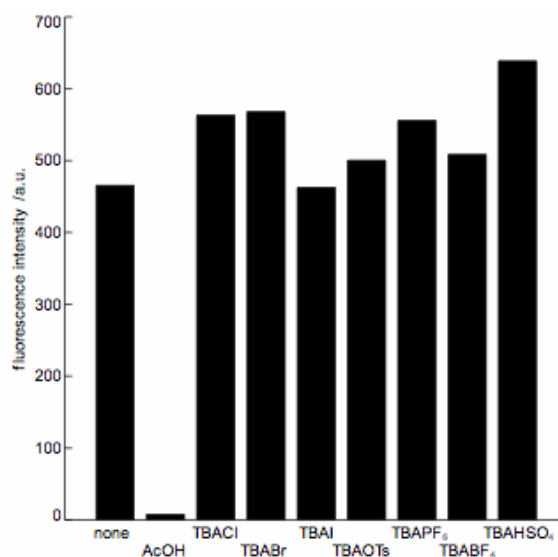


Figure S9 Fluorescence response for different anions.

Influence of the Water Content

250 μL of a solution of fluorogenic maleimide **1** in DMSO (0.47 mmol/L) are added to 2.75 mL of a solution of tetrabutylammonium fluoride ($c = 0.43 \text{ mmolL}^{-1}$) into DMSO containing 0, 2.5, 5.0 or 10% water.

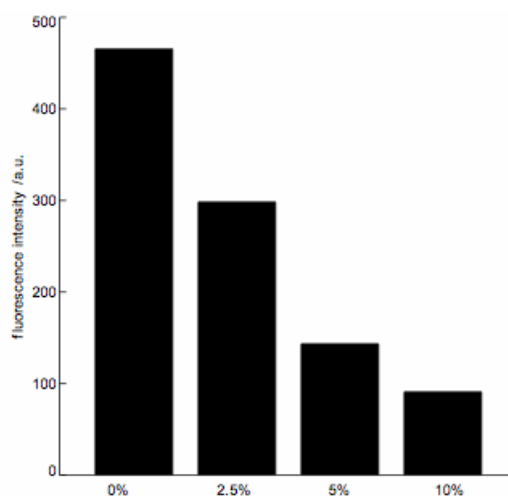
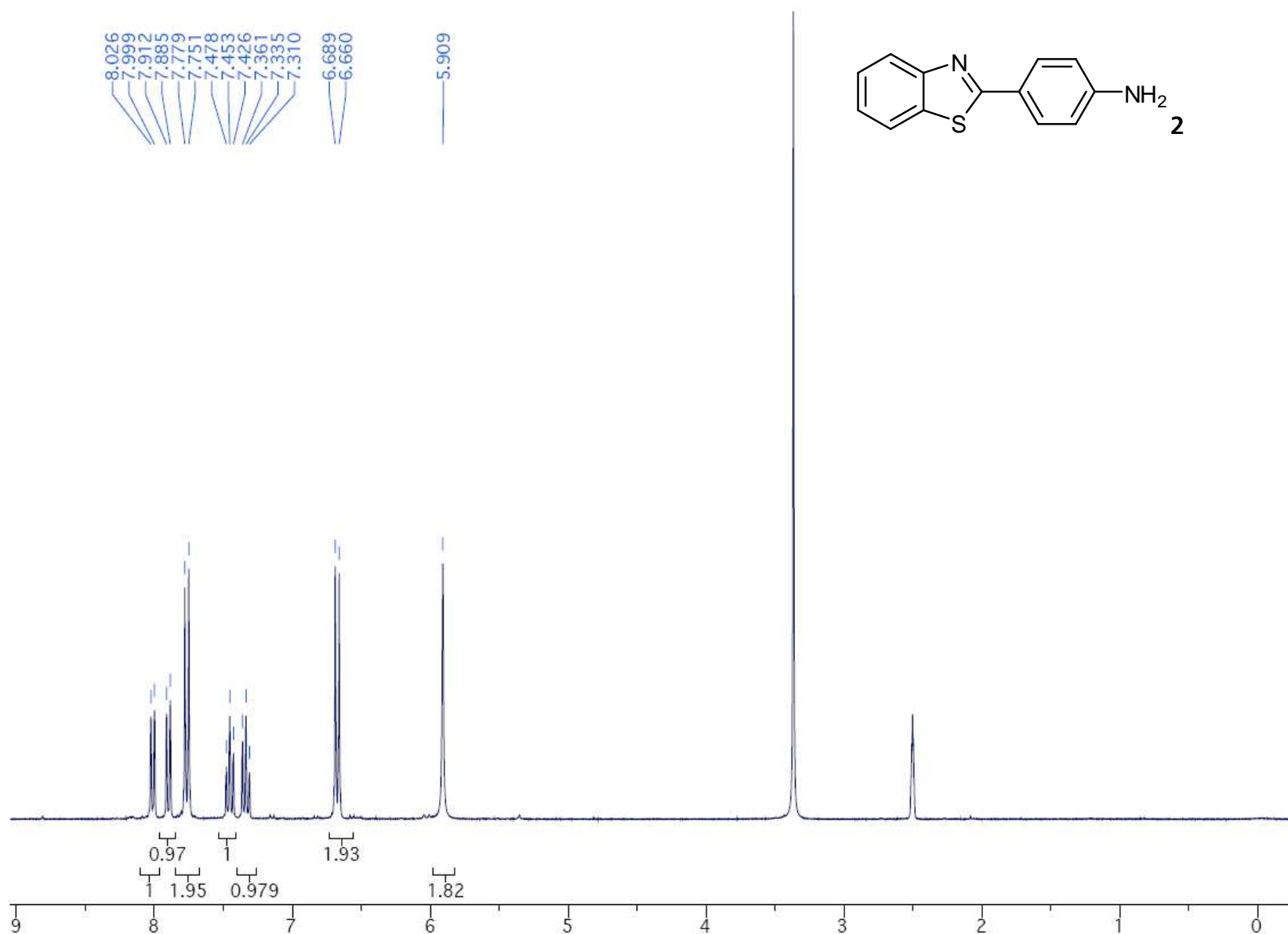
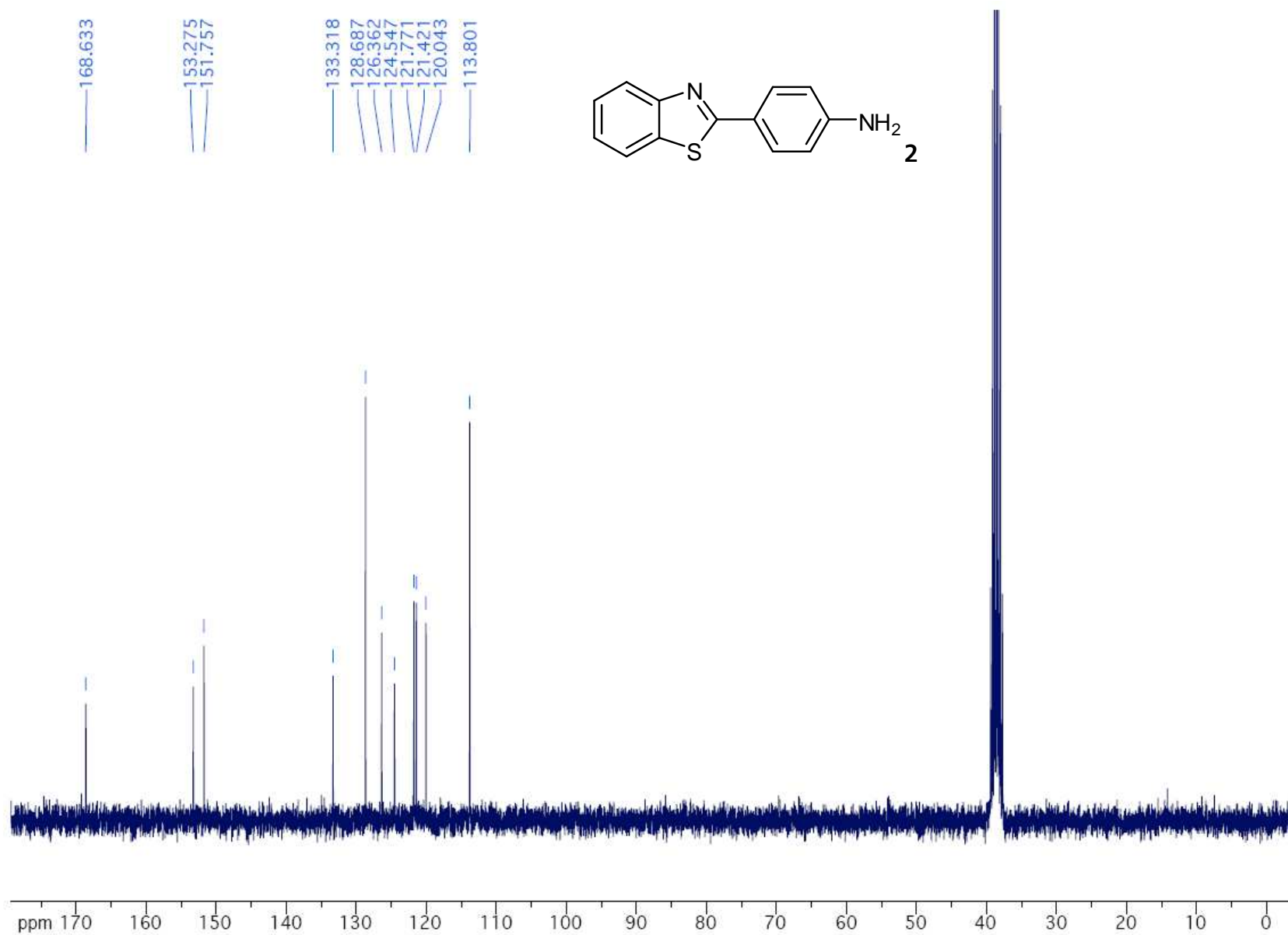


Figure S10 Influence of the water content on the reaction of fluoride ($c = 0.394 \text{ mmolL}^{-1}$) with fluorogenic maleimide **1** ($c = 0.0391 \text{ molL}^{-1}$)

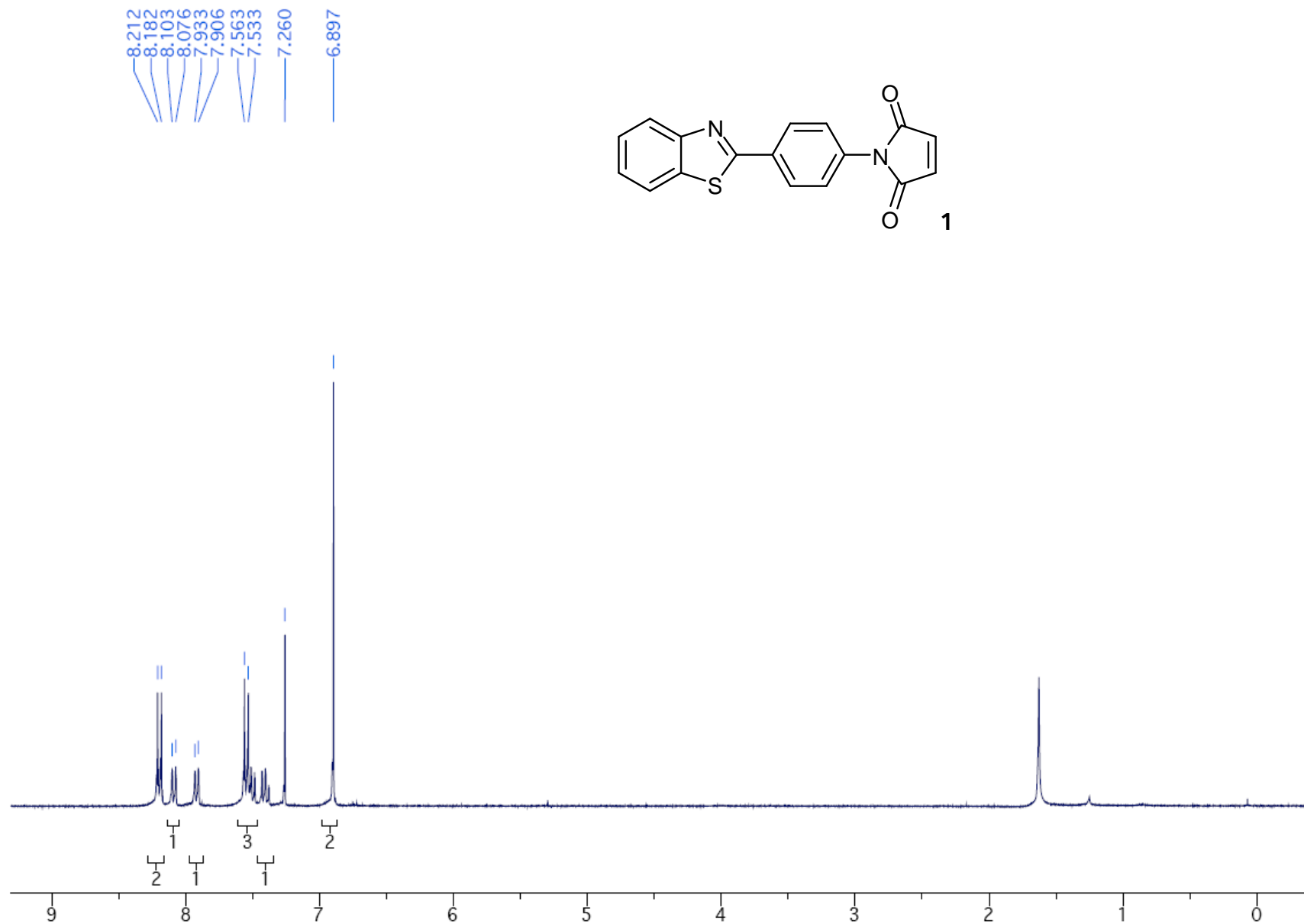
This journal is (c) The Royal Society of Chemistry and The Centre National de la Recherche Scientifique, 2011

 ^1H and ^{13}C NMR Spectra of Products

This journal is (c) The Royal Society of Chemistry and The Centre National de la Recherche Scientifique, 2011



This journal is (c) The Royal Society of Chemistry and The Centre National de la Recherche Scientifique, 2011



This journal is (c) The Royal Society of Chemistry and The Centre National de la Recherche Scientifique, 2011

