Synthesis, Evaluation and Immobilisation of Anion Sensors Based on the 4-amino-1,8-naphthalimide Fluorophore

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Doctor of Philosophy

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Declaration

"I certify this thesis does not incorporate, without acknowledgement, any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another, except where due reference is made in the text".

Andrew J. Blok

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Summary

Molecules based on the 4-amino-1,8-naphthalimide fluorophore combined with powerful urea and thiourea recognition units have been shown to be excellent sensors for anions including dihydrogen phosphate, acetate and fluoride. The majority of the literature with regards to these particular sensors however reports solution phase sensing. This thesis details the synthesis of a series of sensors based on the combination of the 4-amino-1,8-naphthalimide fluorophore and a urea recognition unit, incorporating a terminal double bond at the imide position. This terminal double bond can then be used to immobilise the sensors onto a silica surface, broadening the potential applications of this sensing technology.

The synthesis of eight different sensors each containing the 4-amino-1,8-naphthalimide fluorophore and a urea or thiourea recognition group is described. The fluorophore and the recognition group are connected covalently *via* a spacer molecule, with the use of three different spacer molecules investigated; 2-aminobenzylamine, 4-aminobenzylamine and 3-aminobenzylamine. Previous literature reports had indicated that small changes in the sensor molecule influenced the properties of the sensors towards different anions. Several changes to the recognition group were also investigated (urea *vs*. thiourea, addition of a chloro group on the phenyl ring attached to the recognition group, introduction of triethoxysilyl groups to enable a different method of immobilisation).

The use of microwave irradiation as an alternative to conventional heating methods was also trialled for the synthesis of three of the sensors. Reaction time was decreased, whilst in some cases purity and yield were also improved. In one step the reaction time was reduced from fourty-eight hours to sixty minutes, whilst in another a product was able to be purified using recrystallisation, whereas column chromatography was usually required when using conventional heating techniques.

After successful synthesis of the sensors, their ability to sense anions (dihydrogen phosphate, acetate, fluoride and bromide) was monitored in the solution phase using

both fluorescence spectrophotometry and ^{1}H NMR spectroscopy. Strong interactions were observed upon addition of both dihydrogen phosphate and acetate to a solution of sensor in DMSO, with quenching of the fluorescent emission signal observed and also significant downfield shifts for the resonances assigned to the urea protons of each sensor in the ^{1}H NMR spectrum. Significant shifts were also observed for the 4-amino NH proton resonance dependant on the sensor being evaluated. Little quenching or changes in the ^{1}H NMR spectrum were observed upon addition of bromide to a solution of sensor. The most interesting results were obtained upon the addition of fluoride, with a colour change from yellow to red as greater amounts of fluoride were added due to deprotonation of the 4-amino NH proton. Again significant changes were noted in the ^{1}H NMR spectrum of each sensor.

Finally after establishing the sensors were suitable for the detection of anions, immobilisation onto a silica surface was investigated. Initially the terminal double bond included in the sensor design was used to covalently attach the sensor to a hydride modified silica gel using hydrosilation chemistry. Definitive spectroscopic characterisation of the surface was hard to obtain, however deprotonation of the 4-amino NH proton by addition of fluoride to the surface was observed, suggesting successful attachment. Alternative immobilisation methods including building the sensor onto a 3-aminopropyl functionalised silica surface and by condensing triethoxysilyl groups (introduced in three of the sensors as part of the recognition unit) onto mesoporous silica were also investigated, proving that immobilisation of the sensors onto a silica surface is viable and may be an alternative to solution phase sensing.

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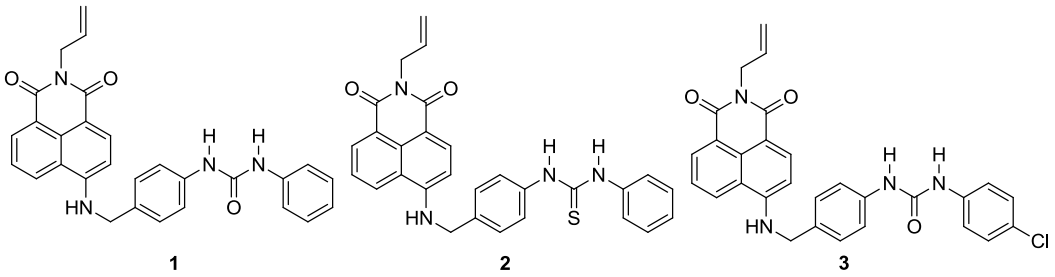
Abbreviations and Symbols

Abbreviation, Symbol or Unit	Explanation
°C	Degrees Celsius
^{13}C	Carbon-13
^{19}F	Fluorine-19
^{1}H	Proton (Hydrogen-1)
^{29}Si	Silicon-29
Å	Angstrom
AcO^-	Acetate
ADP	Adenosine diphosphate
AMP	Adenosine monophosphate
API	Atmospheric Pressure Ionization
AR	Analytical Reagent
ATP	Adenosine 5'-triphosphate
ATR	Attenuated total reflectance
Br^-	Bromide
bs	Broad singlet
cf.	Compared with
CE	Capillary Electrophoresis
CH_3COO^-	Acetate
Cl^-	Chloride
cm	Centimetre
cm^{-1}	Wavenumbers
cm^3	Cubic centimetres
CO_3^{2-}	Carbonate
COSY	Correlation Spectroscopy
CP-MAS	Cross Polarisation – Magic Angle Spinning
CPTS	3-chloropropyltrimethoxysilane
C-TAB	Cetyl Trimethyl Ammonium Bromide
d	Doublet
dATP	Deoxyadenosine triphosphate
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
DMSO-d_6	Deuterated dimethyl sulfoxide
dq	Doublet of quartets
dt	Doublet of triplets
EPA	Environmental Protection Authority
ESI	Electrospray Ionisation
EtOH	Ethanol
F^-	Fluoride
FDA	Food and Drug Administration
FTIR	Fourier Transform Infrared Spectroscopy
g	Grams
G	Guest

GR	**Guaranteed Reagent**
h	Hours
H	Host
Hz	Hertz
H_2O	Water
$H_2PO_4^-$	Dihydrogen Phosphate
HCO_3^-	Bicarbonate
HDMS	High Definition Mass Spectrometry
HF_2^-	Bifluoride
HG	Host-Guest complex
HMBC	Heteronuclear Multiple-Bond Correlation
HMQC	Heteronuclear Multiple-Quantum Correlation
HOMO	Highest Occupied Molecular Orbital
HPLC	High Performance Liquid Chromatography
HPMA	2-hydroxypropyl methacrylate
HPO_4^{2-}	Monohydrogen Phosphate
HSO_4^-	Hydrogen Sulfate
I	Intensity
i.e.	*id est* (that is)
I_0	Initial Intensity
IC	Ion Chromatography
ICT	Internal Charge Transfer
K	Binding constant
K^+	Potassium Ion
KBr	Potassium Bromide
kHz	Kilohertz
$kJ.mol^{-1}$	Kilojoule/mol
lb	Line broadening
Lit.	Literature
λmax	Maximum wavelength
Log	Logarithmic
m	Multiplet
m.p.	Melting point
m/z	Mass to charge ratio
MAS	Magic Angle Spinning
Me	Methyl
MeCN	Acetonitrile
mg/mL	Milligram
μg/mL	Micrograms per millilitre
mg/mL	Milligrams per millilitre
MHz	Megahertz
min	Minutes
mL	Millilitres
μL	Microlitres
mM	Millimolar
μm	Micrometre
mm	Millimetre
$mol.L^{-1}$	Moles per litre

ms	Milliseconds
μs	Microseconds
MW	Microwave
N	Newtons
N/A	Not available
nm	Nanometre
NMR	Nuclear Magnetic Resonance
NO_2	Nitrogen Dioxide
NO_3^-	Nitrate
ODTMA	Octadecyltrimethyl ammonium bromide
PET	Photoinduced Electron Transfer
Ph	Phenyl
ppm	Parts Per Million
PTFE	Polytetrafluoroethylene
q	Quartet
quin	Quintet
rt	Room temperature
s	Singlet
Sec	Seconds
t	Triplet
TEA	Triethylamine
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TSPM	3-(trimethoxysilyl)propyl methacrylate
USA	United States of America
UV-Visible	Ultraviolet-Visible
v/v%	Volume/Volume
W	Watts
ZnSe	Zinc Selenide
ZrO_2	Zirconium Dioxide

Summary of Host Molecules

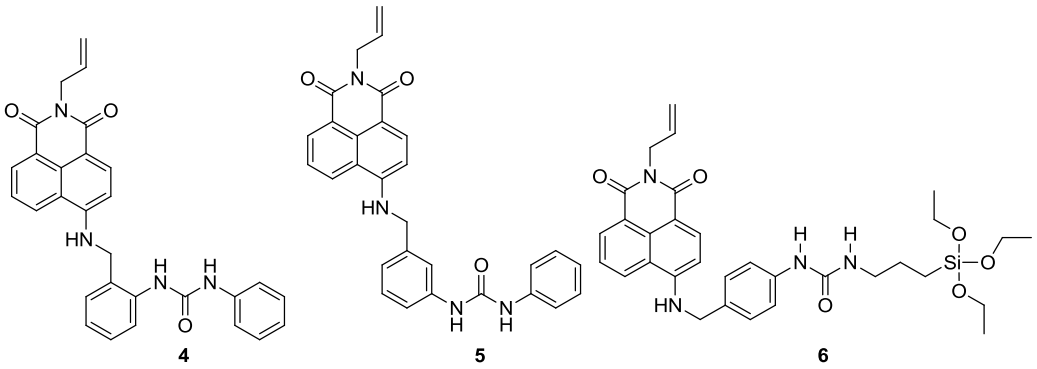


1 **2** **3**

***N*-Allyl-4-(4-(*N*-phenylureido)benzylamino)-1,8-naphthalimide (1)**

***N*-Allyl-4-(4-(*N*-phenylthioureido)benzylamino)-1,8-naphthalimide (2)**

***N*-Allyl-4-(4-(*N*-chlorophenylureido)benzylamino)-1,8-naphthalimide (3)**

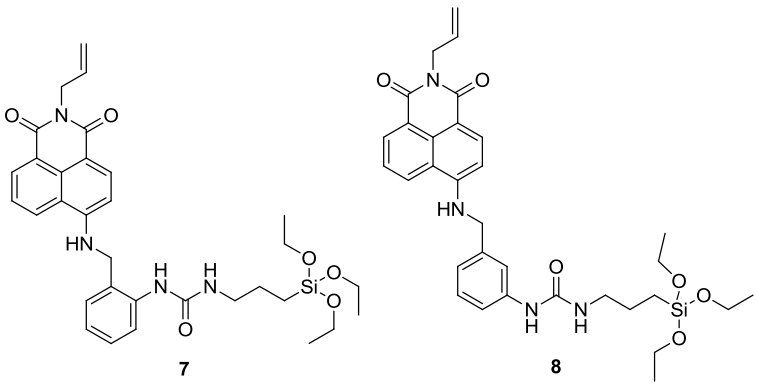


4 **5** **6**

***N*-Allyl-4-(2-(*N*-phenylureido)benzylamino)-1,8-naphthalimide (4)**

***N*-Allyl-4-(3-(*N*-phenylureido)benzylamino)-1,8-naphthalimide (5)**

***N*-Allyl-4-(4-(*N*-3-(triethoxysilyl)propylureido)benzylamino)-1,8-naphthalimide (6)**



7 **8**

***N*-Allyl-4-(2-(*N*-3-(triethoxysilyl)propylureido)benzylamino)-1,8-naphthalimide (7)**

***N*-Allyl-4-(3-(*N*-3-(triethoxysilyl)propylureido)benzylamino)-1,8-naphthalimide (8)**