Dyes and Pigments 119 (2015) 108–115

Contents lists available at ScienceDirect

Dyes and Pigments

journal homepage: www.elsevier.com/locate/dyepig

Sulfonamide and urea-based anions chemosensors

Fang Hu, Meijiao Cao, Juanyun Huang, Zhao Chen, Di Wu, Zhiqiang Xu, Sheng Hua Liu*, Jun Yin*

Key Laboratory of Pesticide and Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, Wuhan 430079, PR China

ARTICLE INFO

Article history:
Received 23 February 2015
Received in revised form
18 March 2015
Accepted 19 March 2015
Available online 7 April 2015

Keywords:
Sulfonamide
Urea
Hydrogen-bonding donor
Cyanide
Gel
Chemosensors

ABSTRACT

The detection of anions has attracted considerable interest because of their importance in various physiological processes. In this study, two sulfonamide and urea-based compounds (**1a** and **1b**) were successfully developed and their spectroscopic and anion recognition properties were fully investigated. These results showed that: (1) compounds showed high selectivity towards cyanide and fluoride ions in CH_3CN; (2) compounds only exhibited a large change in fluorescence in the presence of cyanide ions in $CH_3CN–H_2O$ (95:5, v/v); and (3) compound **1b** could act as a gel in dimethyl sulfoxide that transforms into a homogeneous solution upon exposure to cyanide ions. This research suggests that sulfonamide and urea can act as hydrogen-bond donors and provides an alternative approach to the design of novel anion chemosensors.

1. Introduction

Biologically and environmentally important anions have played a fundamental role in a wide range of organic and inorganic systems, and their application in sensing and anion transport has gained considerable interest [1–21]. In addition to the development of anion chemosensors, the binding between the chemosensor and the anion involves three main types of interaction, which include: 1) electrostatic interactions, 2) reaction-based sensors, 3) hydrogen bonding and 4) metal–ligand interactions [22–24]. Recently, hydrogen bonding has become one of the most frequently used interactions due to their relatively high energy, the significant availability of H-bond donors and their strong and selective binding with anions [25–27]. Among the various anion chemosensors, amides, hydrazides, pyrroles, ureas and thioureas are often used as hydrogen bond donors with both high affinity and selectivity [28–30]. Sulfonamides, which are similar to amides, have always served as a cation and thiol amino acid chemosensor [31–34]. Currently, a research towards anion chemosensors combining sulfonamides has been reported. Therefore, a sulfonamide can also act as a hydrogen-bond donor and form intramolecular or intermolecular hydrogen bonds. It is therefore important to design anion chemosensors with novel topological structures.

In this work, two anion chemosensors (**1a** and **1b**), based on both sulfonamide and urea were successfully developed and their spectroscopic and anion recognition properties fully investigated. Both of them show highly selective chemical signaling behavior towards cyanide and fluoride ions in CH_3CN. In particular, both compounds only exhibited a large change in fluorescence in the presence of cyanide ions in $CH_3CN–H_2O$ (95:5, v/v). The signaling process was confirmed using fluorescence spectroscopy and the limit of detection for compounds **1a** and **1b** was 12 nM and 4 nM, respectively. Significantly, compound **1b** could act as a gel in dimethyl sulfoxide that transforms into a homogeneous solution upon exposure to cyanide ions. Density functional theory (DFT) calculations and NMR titration studies suggest that both compounds act as cyanide ion fluorescence chemosensors via hydrogen bonding. Herein, we provide an alternative approach to the design of novel anion chemosensors with high sensitivity and selectivity.

2. Materials and methods

2.1. Experimental

All manipulations were carried out under an argon atmosphere using standard Schlenk techniques, unless otherwise stated. Tetrahydrofuran was dried with Na then distilled under vacuum. All

* Corresponding authors. Tel./fax: +86 027 6786 7725.
E-mail addresses: chshliu@mail.ccnu.edu.cn (S.H. Liu), yinj@mail.ccnu.edu.cn (J. Yin).

http://dx.doi.org/10.1016/j.dyepig.2015.03.036
0143-7208/

reagents and starting materials were obtained from commercial suppliers and were used without further purification. All anions for binding experiments used tetrabutylammonium salts as sources. Anions in CH_3CN were obtained by dissolution of the anions in CH_3CN. Time course for the signaling of cyanide and fluoride ions by compounds **1a** and **1b** was followed by monitoring the changes in fluorescence intensity of the solutions at 531 nm. The concentrations of the probe **1a** or **1b** and cyanide or fluoride ion were 10 μM and 10 mM, respectively, in DMSO or a mixture of DMSO and water solution (95:5, v/v). Column chromatography was used on silica gel (200–300 mesh). NMR spectra were analysed using an American Varian Mercury Plus 400 spectrometer (400 MHz) and their chemical shifts are relative to TMS. Elemental analyses (C, H, N) were performed by the Microanalytical Services, College of Chemistry, CCNU. Electrospray (EI) mass spectra were carried on Firmigan Trace. UV–Vis spectra were analysed using a U-3310 UV Spectrophotometer. Fluorescence spectra were analysed using a Fluoromax-P luminescence spectrometer (HORIBA JOBIN YVON INC.).

2.2. Synthesis

2.2.1. Synthesis of all new compounds

*2.2.1.1. Synthesis of **3**, **4a**, **4b**, **5a** and **5b**.* Compounds **3**, **4a**, **4b**, **5a** and **5b** were prepared by literature methods [35].

*2.2.1.2. Synthesis of **6a**, **6b**, **7a** and **7b**.* Compounds **6a**, **6b**, **7a** and **7b** were prepared by literature methods [36].

*2.2.1.3. Synthesis of **8a**.* A solution of benzene-1, 2-diamine (1.4 mmol) in acetone (50 mL) was cooled in an ice bath under an argon atmosphere and **7a** (0.53 mmol) in acetone (20 mL) was added dropwisely to the above solution. This solution was stirred for 2 h at room temperature. The formed precipitate was collected and the crude product was washed with ice acetone, the dried solid was recrystallized from methylene chloride to give a white solid **8a**. Yield: 42 mg, 25%. ^{1}H NMR (400 MHz, DMSO-d_6): δ ppm = 3.60 (s, 3H, CH_3), 3.74 (s, 6H, CH_3), 4.77 (s, 2H, NH_2), 6.57 (d, J = 8 Hz, 1H, Ar–H), 6.74 (d, J = 8 Hz, 1H, Ar–H), 6.80 (s, 2H, Ar–H), 6.83 (d, J = 4 Hz, 1H, Ar–H), 7.32 (d, J = 4 Hz, 1H, Ar–H), 7.69 (s, 1H, urea N–H), 8.73 (s, 1H, urea N–H). ^{13}C NMR (100 MHz, DMSO): δ ppm = 55.69, 60.21, 95.75, 115.96, 116.89, 124.01, 124.58, 124.69, 132.23, 136.34, 141.03, 152.91, 153.28. Anal. calcd for $C_{16}H_{19}N_3O_4$: C, 60.56; H, 6.03; N, 13.24. Found: C, 60.41; H, 5.99; N, 13.20. EI MS m/z = 317.26 [M]; calculated exact mass = 317.14.

*2.2.1.4. Synthesis of **8b**.* A solution of benzene-1, 2-diamine (1.4 mmol) in acetone (50 mL) was cooled in an ice bath under an argon atmosphere and **7b** (0.53 mmol) in acetone (20 mL) was added dropwisely to the above solution. This solution was stirred for 2 h at room temperature. The formed precipitate was collected and the crude product was washed with ice acetone, the dried solid was recrystallized from methylene chloride to give a white solid **8b**. Yield: 65 mg, 20%. ^{1}H NMR (400 MHz, DMSO-d_6): δ ppm = 0.84 (d, J = 8 Hz, 9H, CH_3), 1.25 (s, 24H, CH_2), 1.41 (d, J = 4 Hz, 6H, CH_2), 1.60 (t, J = 4 Hz, 2H, CH_2), 1.69 (t, J = 4 Hz, 4H, CH_2), 3.76 (t, J = 8 Hz, 2H, CH_2), 3.87 (t, J = 8 Hz, 4H, CH_2), 4.73 (s, 2H, NH_2), 6.56 (t, J = 8 Hz, 1H, Ar–H), 6.72 (d, J = 4 Hz, 3H, Ar–H), 6.83 (d, J = 8 Hz, 1H, Ar–H), 7.30 (d, J = 8 Hz, 1H, Ar–H), 7.62 (s, 1H, urea N–H), 8.60 (s 1H, urea N–H). ^{13}C NMR (100 MHz, DMSO): δ ppm = 13.87, 22.16, 25.68, 28.83, 29.85, 31.30, 31.38, 55.69, 68.10, 72.40, 96.80, 115.89, 116.79, 123.78, 124.36, 124.73, 131.98, 135.87, 140.85, 152.43, 153.14. Anal. calcd for $C_{37}H_{61}N_3O_4$: C, 72.63; H, 10.05; N, 6.87. Found: C, 72.42; H, 9.99; N, 6.85. EI MS m/z = 611.71 [M]; calculated exact mass = 611.47.

*2.2.1.5. Synthesis of **1a**.* A solution of **8a** (1 mmol) and Et_3N (1.5 mmol) in THF (50 mL) was cooled in an ice bath under an argon atmosphere and 5-(dimethylamino) naphthalene-1-sulfonyl chloride was added dropwisely to the above solution. After the mixture was stirred at room temperature, the mixture was diluted with water and extracted with EtOAc. The organic layer was washed with 2 N HCl, water, saturated $NaHCO_3$ solution and brine. Then dried over sodium sulfate, upon removed of solvent under reduced pressure and purified on a silica gel column using dichloromethane/methanol (60:1) as the eluent to obtain the target compound as a yellow solid in a yield of 60%, 307 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm = 2.85 (s, 6H, CH_3), 3.76 (s, 6H, CH_3), 3.79 (s, 3H, CH_3), 6.57–6.63 (m, 4H, Ar–H), 6.75 (t, J = 4 Hz, 1H, Ar–H), 7.03–7.14 (m, 3H, Ar–H), 7.37–7.41 (m, 2H, Ar–H), 7.48–7.56 (m, 2H, Ar–H), 8.04 (d, J = 8 Hz, 1H, urea N–H), 8.39 (d, J = 8 Hz, 1H, urea N–H), 8.51 (d, J = 8 Hz, 1H, amide N–H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm = 45.17, 55.78, 60.82, 97.24, 115.03, 118.26, 122.72, 122.88, 124.09, 126.76, 127.24, 127.72, 128.59, 129.43, 129.96, 130.86, 133.31, 133.90, 134.43, 134.63, 151.77, 152.92, 153.56. Anal. calcd for $C_{28}H_{30}N_4O_6S$: C, 61.08; H, 5.49; N, 10.18. Found: C, 61.00; H, 5.19; N, 10.28. EI MS m/z = 550.43 [M]; calculated exact mass = 550.19.

*2.2.1.6. Synthesis of **1b**.* A solution of **8b** (1 mmol) and Et_3N (1.5 mmol) in THF (50 mL) was cooled in an ice bath under an argon atmosphere and 5-(dimethylamino) naphthalene-1-sulfonyl chloride was added dropwisely to the above solution. After the mixture was stirred at room temperature, the mixture was diluted with water and extracted with EtOAc. The organic layer was washed with 2 N HCl, water, saturated $NaHCO_3$ solution and brine. Then dried over sodium sulfate, upon removed of solvent under reduced pressure and purified on a silica gel column using dichloromethane/methanol (90:1) as the eluent to obtain the target compound as a pale yellow solid in a yield of 65%, 511 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm = 0.88 (t, J = 4 Hz, 12H, CH_2CH_3), 1.44 (s, 21H, CH_2CH_3), 1.71–1.77 (m, 12H, CH_2CH_3), 2.84 (s, 6H, CH_3), 3.89 (t, J = 4 Hz, 4H, CH_2), 3.96 (t, J = 4 Hz, 2H, CH_2), 6.55 (t, J = 8 Hz, 2H, Ar–H), 6.68 (d, J = 8 Hz, 1H, Ar–H), 6.68 (t, J = 8 Hz, 1H, Ar–H), 7.03–7.09 (m, 2H, Ar–H), 7.11–7.13 (m, 1H, Ar–H), 7.21 (s, 1H, Ar–H), 7.36–7.42 (m, 2H, Ar–H), 7.48–7.55 (m, 2H, Ar–H), 8.02 (d, J = 4 Hz, 1H, urea N–H), 8.38 (d, J = 8 Hz, 1H, urea N–H), 8.48 (d, J = 8 Hz, 1H, amide N–H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm = 14.07, 22.64, 26.09, 29.36, 30.25, 31.81, 45.27, 68.91, 73.50, 98.80, 114.90, 118.47, 122.64, 122.81, 122.99,124.04, 126.82, 127.24, 127.72, 128.65, 129.55, 130.14, 130.79, 133.89, 134.06, 134.51, 151.81, 153.12, 153.50. Anal. calcd for $C_{49}H_{72}N_4O_6S$: C, 69.63; H, 8.59; N, 6.63. Found: C, 69.35; H, 8.39; N, 6.60. EI MS m/z = 844.97 [M]; calculated exact mass = 844.52.

3. Results and discussion

3.1. Synthesis

Sulfonamides, which are similar to amides, serve as a hydrogen-bond donor and can easily form intramolecular or intermolecular hydrogen bonds. A dansyl unit was chosen as the fluorophore because of its desirable spectroscopic properties as well as being the smallest available fluorophore. Therefore, the signaling process of the sulfonamide fluorescent dye could be confirmed by fluorescence spectroscopy. Hence, compounds **1a** and **1b** bearing sulfonamide and urea functionality were synthesized as shown in Scheme 1. The syntheses of compounds **1a** and **1b** are outlined in Scheme 2. 5-Isocyanato-1, 2, 3-trimethoxybenzene **7a** was prepared using a Curtius rearrangement reaction [35]. The intermediate 3, 4, 5-trimethoxybenzoyl azide was unstable and easily decomposed into its corresponding nitrene followed by rapid