Synthesis and evaluation of heterocyclic pyrrolidene imines as optical chemosensors

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Abstract: Imine derivatives are an important class of compounds due their biological and optical properties making them suitable for several applications such as chemosensors, photochromic compounds, among others. In recent years the search for new colorimetric chemosensors for anions has been of great interest because of the role that ions play in chemical and biological processes. In this context and as part of an on-going research to develop efficient heterocyclic systems for photochromic and chemosensory applications, we report the synthesis, the photophysical characterization and the chemosensory ability of pyrrolidene heterocyclic imines functionalized with aryl or naphthyl moieties.

Keywords: Imines, Pyrrole, Chemosensors, Colorimetric sensors, UV-Vis.

1. Introduction

Organic compounds with an imine bridge are very versatile and have been the subject of great interest as photosensitive materials in a diversity of applications in medicine, supramolecular chemistry and materials sciences due to their biological properties and their ability as chemosensors, photochromic compounds, two-photon absorbers and nonlinear optical compounds. Imines can also be used as ligands, as they are capable of complexing with different metals exhibiting an excellent catalytic activity.[1]

In recent years, there has been a growing interest in the research on chemical sensors that show optical response (colorimetric and fluorescence) with selective binding to transition metal ions due to their important role in biological processes in medicinal chemistry, environmental chemistry and catalysis.[2] This growing interest is also due to their comparative low cost, simple structure, high sensitivity, selectivity and real-time monitoring ability. In the class of optical sensors, those that have attracted most interest are the colorimetric sensors because they provide an opportunity to detect analytes by naked eye.[3]

The demand for chemosensors for cyanide and fluoride anions is a current thrust in research due to their biological and environmental importance. The F^- ion is important in dental care and the treatment of osteoporosis.[4] The CN^- ion is well known for its toxicity to the human being, affecting various functions such as the vascular system, and central nervous system.[5]

Therefore, as part of an on-going research to develop efficient heterocyclic systems for photochromic and chemosensory applications[6] we now report the synthesis, the photophysical characterization and the chemosensory ability of pyrrole-based heterocyclic imines functionalized with aryl or naphthyl moieties.

2. Experimental

2.1. Instruments

NMR spectra were obtained on a Varian Unity Plus Spectrometer at an operating frequency of 300 MHz for ^{1}H NMR and 75.4 MHz for ^{13}C NMR or a Brucker Avance III 400 at an operating frequency of 400 MHz for ^{1}H NMR and 100.6 MHz for ^{13}C NMR using the solvent peak as internal reference at 25 ^{o}C (δ relative to TMS). All chemical shifts are given in Hz. Assignments were made by comparison of chemical shift, peak multiplicities and *J* values and were supported by spin decoupling-double resonance and bidimensional heteronuclear HMBC and HMQC correlation techniques. IR spectra were determined on a BOMEM MB 104 spectrophotometer. UV-Visible absorption spectra (200-800 nm) were obtained using a

Shimadzu UV/2501PC spectrophotometer. All melting points were measured on a Gallenkamp melting point apparatus and are uncorrected.

2.2. Synthesis

General procedure for the synthesis of imines **2**, **4** and **5**: a solution of the aldehyde **1a**-**b** (2 mmol), amine derivatives (2 mmol), and acetic acid (2 drops) in ethanol (15 mL) was heated at reflux for 5-24 h. After cooling and solvent evaporation, the crude product was recrystallized from light petroleum/dichloromethane or ethanol to afford the pure imines **2**, **4** and **5**.

***N*-((*1H*-Pyrrol-2-yl)methylene)-4-methoxybenzenamine (2)**[1a] (reaction time 15 h). Brown solid (72%). Mp 95-96 °C. ^{1}H NMR (DMSO-d_6) δ 3.75 (s, 3H, OCH_3), 6.17 (t, 1H, *J* = 2.8 Hz, 4'-H), 6.64-6.65 (m, 1H, 3'-H), 6.92 (d, 2H, *J* = 8.8 Hz, 3-H and 5-H), 6.97-7.02 (m, 1H, 5'-H), 7.16 (d, 2H, *J* = 8.8 Hz, 2-H and 6-H), 8.29 (s, 1H, C*H*=N), 11.63 (br s, 1H, N*H*) ppm. ^{13}C NMR (DMSO-d_6) δ 55.2, 109.5, 114.4, 115.6, 121.8, 123.3, 130.7, 145.0, 148.8, 157.1 ppm. IR (Nujol): υ 3460, 2729, 2680, 2052, 1878, 1866, 1691, 1619, 1578, 1551, 1503, 1241, 1203, 1179, 1133 cm^{-1}. MS (EI) m/z (%) = 200 ([M]$^+$, 100), 199 (94), 185 (52), 184 (15), 157 (10), 156 (28), 134 (10). HMRS: m/z (EI) for $C_{12}H_{12}N_2O$; calcd 200.0950; found: 200.0945.

2-((*1H*-Pyrrol-2-yl)methyleneamino)phenol (4a)[1a] (reaction time 5 h). Brown solid (78%). Mp 133-136 °◦C. ^{1}H NMR ($CDCl_3$) δ 6.35-6.37 (m, 1H, 4'-H), 6.83 (dd, 1H, *J* = 3.6 and *J* = 1.2 Hz, 3'-H), 6.90 (dt, 1H, *J* = 7.2 and *J* = 1.2 Hz, 4-H), 7.01 (dd, 1H, *J* = 7.8 and *J* = 1.4 Hz, 3-H), 7.12-7.17 (m, 2H, 5'- and 5-H), 7.25 (dd, 1H, *J* = 7.8 and *J* = 1.4 Hz, 6-H), 8.44 (s, 1H, C*H*=N), 9.53 (s, 1H, O*H*), 10.13 (br s, 1H, N*H*) ppm. ^{13}C NMR ($CDCl_3$) δ 111.7, 115.6, 116.6, 119.6, 120.4, 125.7, 128.1, 129.6, 146.9, 151.2, 179.3 ppm. IR (Nujol): υ 3337, 3274, 3116, 1928, 1692, 1623, 1596, 1586, 1533, 1300, 1282, 1247, 1215, 1173, 1247, 1173, 1118, 1090, 1028 cm^{-1}. MS (EI) m/z (%) = 186 ([M]$^+$, 38), 185 (34), 184 (100), 170 (21), 169 (72), 157 (14), 156 (13), 155 (15), 144 (39), 92 (12), 91 (15), 64 (17), 63 (23). HMRS: m/z (EI) for $C_{11}H_{10}N_2O$; calcd 186.0793; found: 186.0797.

2-((1-Methyl-*1H*-pyrrol-2-yl)methyleneamino)-5-methylphenol (4b)[1a] (reaction time 5 h). Brown solid (59%). Mp 123-124 ◦C. ^{1}H NMR (DMSO-d_6) δ 2.27 (s, 3H, CH_3), 3.96 (s, 3H, NCH_3) 6.13-6.15 (m, 1H, 4'-H), 6.59-6.63 (m, 1H, 4-H), 6.67 (br d, 1H, *J* = 1.2 Hz, 6-H), 6.73 (dd, 1H, *J* = 4.0 Hz and *J* = 1.2 Hz, 3'-H), 6.98 (d, 1H, *J* = 8.0 Hz, 3'-H), 7.02 (t, 1H, *J* = 2.4 Hz, 5'-H), 8.44 (s,

1H, C*H*=N), 9.51 (s, 1H, O*H*) ppm. ^{13}C NMR (DMSO-d_6) δ 20.7, 36.1, 108.4, 116.1, 117.4, 118.1, 120.1, 129.1, 130.3, 135.6, 136.5, 149.2, 179.5 ppm. IR (Nujol): υ 3111, 2727, 1864, 1741, 1694, 1603, 1570, 1528, 1341, 1315, 1296, 1268, 1245, 1194, 1158, 1114, 1093, 1057 1012 cm^{-1}. MS (EI) m/z (%) = 213 ([M-H]$^+$, 12), (12), 212 (62), 211 (100). HMRS: m/z (EI) for $C_{13}H_{13}N_2O$; calcd 213.1028; found: 213.1026.

1-((1H-Pyrrol-2-yl)methyleneamino)naphthalen-2-ol (5)[1a] (reaction time 24 h). Green solid (102 mg, 59%). Mp 230-232 ^{o}C. ^{1}H NMR (DMSO-d_6) δ 6.56 (t, 1H, *J* = 2.0 Hz, 4'-H), 6.96 (br d, 1H, *J* = 8.8 Hz, naphthyl-H), 7.06 (br d, 1H, *J* = 8.8 Hz, 1H, naphthyl- *H*),7.22-7.25 (m, 1H, 3'-H), 7.40 (br t, 1H, *J* = 7.6 Hz, naphthyl-H), 7.51-7.60 (m, 2H, 5'-H and naphthyl-H), 7.66 (br s, 1H, naphthyl-H), 7.95 (br d, 1H, *J* = 8.4 Hz, naphthyl-H), 8.13 (s, 1H, C*H*=N), 13.5 (br s, 2H, N*H* and O*H*) ppm. IR (Nujol): υ 2726, 1656, 1631, 1513, 1603, 1322, 1285, 1268, 1254, 1211, 1114, 1089, 1077, 1045, 1000 cm^{-1}. MS (EI) m/z (%) = 236 ([M]$^+$, 16), 235 (16), 234 (100), 219 (22), 206 (16), 205 (28), 194 (30), 178 (12), 114 (18), 113 (11). HMRS: m/z (ESI) for $C_{15}H_{12}N_2O$; calcd 236.0950; found: 236.0948.

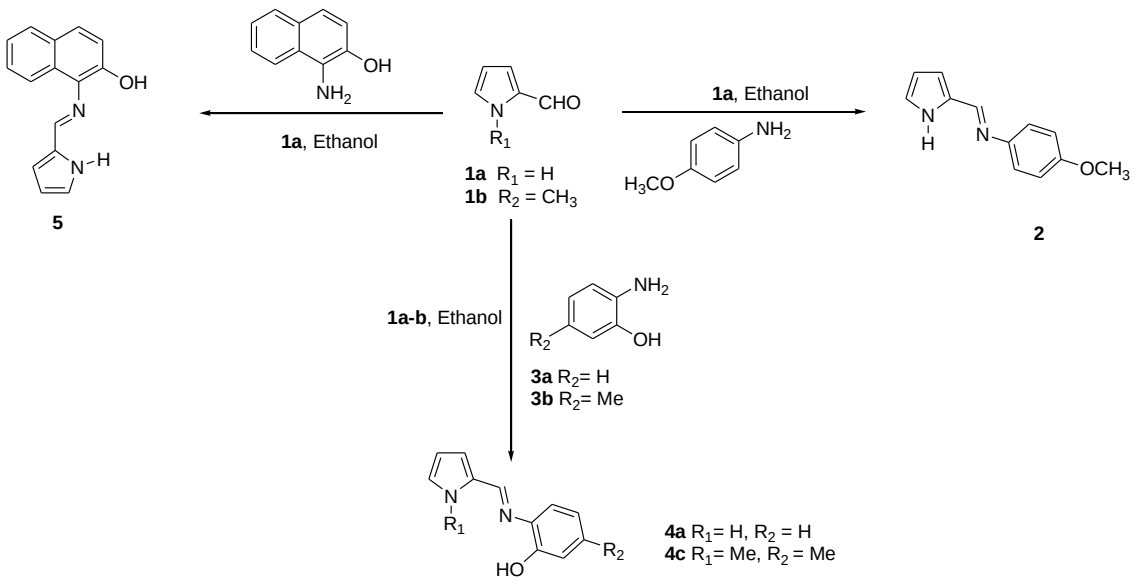
2.3. Spectrophotometric titrations of imines 2, 4 and 5

Solutions of imines **2**, **4** and **5** (*ca*. 1.0 × 10^{-5} M) and of the ions under study (ca. 1.0 × 10^{-2}) were prepared in ACN in the presence of relevant ions ($H_2SO_4^-$, CN^-, AcO^-, F^-, BzO^-, Br^-, Cl^-, HSO_4^-, NO_3^-, Fe^{3+}, Fe^{2+}, Cr^{3+}, Hg^{2+}, Zn^{2+}, Ni^{2+}, Cd^{2+}, Pd^{2+} and Cu^{2+}).
Titration of the compounds was performed by the sequential addition of the ion to the imine solution, in a 10 mm path length quartz cuvette and absorption spectra were measured.

3. Results and discussion

3.1. Synthesis

Imines **2**, **4** and **5** were synthesized through condensation of commercially available pyrrole-2-carboxaldehyde and *N*-methylpyrrole-2-carboxaldehyde with amino-aryl and amino-naphthalene precursors, in ethanol at room temperature (Scheme 1). Purification of the crude products by recrystallization in ethanol gave the pure compounds in good yields (59-78%) (Table 1). All compounds were characterized by ^{1}H and ^{13}C NMR, UV-Vis and IR, the data obtained are in full agreement with the proposed formulation.[1a]



Scheme 1. Synthesis of heterocyclic imines **2**, **4** and **5**.

Table 1. Yields and UV-visible data for imines **2, 4** and **5** in acetone.

Comp.	Yield (%)	Reaction time (h)	λ_{max} (nm)
2	72	15	336
4a	78	5	355
4b	50	5	355
5	59	24	373

The most characteristic signals in the ^{1}H NMR spectra of this family of imines is that corresponding to the C*H*=N proton. Imines **2**, **4** and **5** have the C*H*=N proton resonate at 8.13-8.44 ppm, where the lowest chemical shift value belongs to compound **5** as the naphthyl group as higher electron donor ability than the aryl group (Table 2). The pyrrole N*H* protons were found between 10.13-13.50 ppm and O*H* protons were found in the 9.51-9.53 ppm interval, where compound **4a** shows signals that are shifted downfield.

Table 2. Chemical shifts (in ppm) of relevant protons for imines **2**, **4** and **5**.

Comp.	C*H*=N	N*H*	O*H*
2[a]	8.29	11.63	-
4a[b]	8.44	10.13	9.53
4b[a]	8.44	-	9.51
5[a]	8.13	13.50	13.50

[a] in DMSO-d_6. [b] in $CDCl_3$

3.2. Spectrophotometric titrations and chemosensing studies of imines with different ions

Compounds **2**, **4**, **5** were evaluated as chemosensors in the presence of several ions ($H_2SO_4^-$, CN^-, AcO^-, F^-, BzO^-, Br^-, Cl^-, HSO_4^-, NO_3^-, Fe^{3+}, Fe^{2+}, Cr^{3+}, Hg^{2+}, Zn^{2+}, Ni^{2+}, Cd^{2+}, Pd^{2+} and Cu^{2+}) in acetonitrile. The ions were added to solutions of **2**, **4a**-**b** and **5** (10^{-5} M), in order to evaluate their chemosensory ability. It was found that only compound **5** behaved as colorimetric chemosensor for CN^- and F^- (Figure 1). In both cases addition of CN^- and F^- produced a marked red shift in the absorption wavelength, causing a color change from colorless to light yellow.

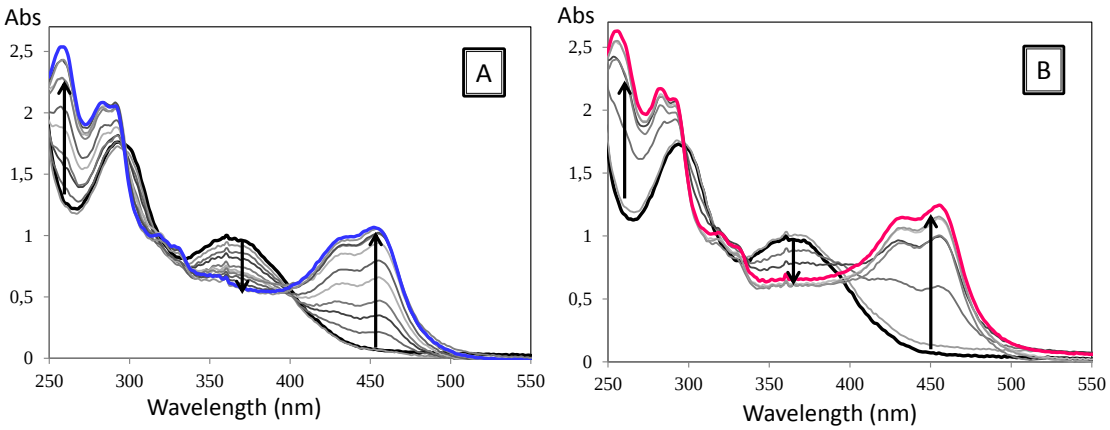


Figure 1. Spectrophotometric titration of imine **5** with addition of increasing amounts of CN^- (A) and F^- (B) in ACN. The inset represents the normalized absorption ([**5**] = 1 x 10^{-5} M, T = 298 K).

Compound **5** exhibited an absorption band at 373 nm. Upon addition of increasing amount of CN^- , this band progressively decreased while a new absorption band at 452 nm increased in intensity ($\Delta\lambda$ = 79) (Figure 2A). The same was observed for titration with F^-, a new absorption band at 455 nm was formed ($\Delta\lambda$ = 82) (Figure 2B). In both cases the addition of CN^- and F^- ions produced a color change of the solutions from colorless to light yellow.

4. Conclusions

New heterocyclic imines based on pyrrole functionalized with aryl and naphthyl acceptors groups linked to the imine-pyrrolidene moiety were synthetized in good yields using simple experimental procedures. Due to their push-pull character and marked acidity of OH protons the new heterocyclic systems could have potential application as colorimetric chemosensors.

The sensory ability was evaluated for several ions by spectrophotometric titrations in acetonitrile. These compounds showed higher sensitivity for F^- and CN^- in ACN compared to all the other ions.

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