Selective blue emission from an HPBO–Li^+ complex in alkaline media

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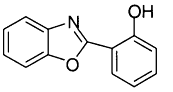
Received (in New Haven, CT, USA) 19th April 2001, Accepted 13th August 2001
First published as an Advance Article on the web

2-(2-Hydroxyphenyl)benzoxazole (HPBO) exhibits enhanced fluorescence and specificity for Li^+ compared to Na^+ and K^+, in an alkaline medium. The selectivity was observed in several organic solvents in the presence of bases such as pyridine, triethylamine and trimethylamine. HPBO–Li^+ complex formation results in an intense blue emission readily observed by the naked eye under UV light. Spectroscopic titrations suggest that the structure of the complex is one in which two HPBO anionic ligands coordinate to one Li^+, with a second Li^+ as a counterion.

Li^+ sensors are currently in demand for biomedical applications[1–8] as well as for monitoring Li^+ transport in Li^+ batteries.[9–11] Fluorescent receptors specific for metal ions are desirable since they allow both direct and real-time detection.[12–27] Hiratani's group has demonstrated the selectivity of 2,9-disubstituted 1,10-phenanthroline derivatives that upon excitation at 298 nm exhibit fluorescence enhancement, in the ultraviolet, upon Li^+ complexation.[28–31] We previously reported a 3,6-disubstituted dipyrido[3,2-*a*:2′3′-*c*]phenazine derivative that exhibits a color change upon Li^+ complexation, depending on the local environment.[32]



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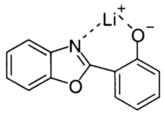

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Kim *et al.* reported the synthesis of a "unidentate organometallic complex", composed of lithium as the central metal and 2-(2-hydroxyphenyl)benzoxazole (**1**; HPBO) as the coordinating ligand.[33] The complex emitted at 430 nm in an organic electroluminescent device.[33] Kim *et al.* suggested **2** as the HPBO–Li^+ complex structure, based on elemental analysis that indicated a 1 : 1 HPBO : Li^+ stoichiometry.[33] Since Li^+ prefers tetrahedral coordination, we have conducted optical and NMR spectroscopic studies to determine the remaining coordination sites for Li^+. Herein, we report that HPBO is selective for Li^+ amongst other alkali metal ions, and can therefore be used successfully as a Li^+ sensor. Li^+ concentrations down to 10^{-7} M are detectable.

Experimental

Materials and instrumentation

All compounds were purchased from Aldrich Chemicals and used as received. Solvents were of HPLC grade and were used as received. Acetonitrile-d_3 (99.6%; Aldrich) and deuterium oxide (D_2O; 99.9%; Cambridge Isotope Laboratories, Inc.) were used as received.

Fluorescence studies were performed on a Model 8100 SLM-AMINCO spectrofluorometer with excitation at 295 nm using 4 nm slits. UV-visible absorption spectra were acquired on a Lambda 14 Perkin Elmer UV-Vis spectrophotometer. ^1H NMR spectra were recorded on a 300 MHz Bruker spectrometer and ^7Li NMR spectra were recorded on a 500 MHz Bruker spectrometer. For both types of NMR experiments, the solvent was CD_3CN and the base was triethylamine.

Determination of stoichiometry and equilibrium binding constants

Solutions of HBPO in acetonitrile (millimolar concentrations; with one equivalent of base) were titrated with solutions of lithium perchlorate in acetonitrile and complex formation was monitored by both absorption spectroscopy and fluorescence spectroscopy. In the absorption spectrum, a new band at 370 nm was associated with the formation of a Li^+–HPBO–base complex. In the fluorescence spectra, a new peak at 421 nm was associated with the formation of a Li^+–HPBO–base complex (see Results for more details). Both absorption and fluorescence data were treated with the method of continuous variation, to yield the ratio of ligand-to-metal ion in a complex.[34] The ratio of ligand-to-metal ion thus calculated suggested a 2 : 1 stoichiometry. The integrated areas (= intensities) of the fluorescence spectra were evaluated as a function of lithium ion concentration, at constant HPBO concentration, to calculate binding constants as described below.

We assume the equilibrium expression derived from the reaction $M^+ + 2L \rightarrow ML_2^+$

$$K = [ML_2^+]/[M^+][L]^2 \qquad (1)$$

where K is the equilibrium binding constant (units M^{-2}), $[ML_2^+]$ is the equilibrium concentration of the metal–ligand complex in which two ligands are bound to one metal ion, $[M^+]$ is the equilibrium concentration of free metal ion and [L] is the concentration of free ligand at equilibrium. If we assume that the total ligand concentration is $[L]_t = [L]_{bound} + [L]_{free}$, and likewise that the total metal ion concentration is

$[M^+]_t = [M^+]_{bound} + [M^+]_{free}$, the following substitutions can be made for complexes of the form ML_2^+:

$$[ML_2^+] = [M^+]_{bound} = 2[L]_{bound} \qquad (2)$$

The measured quantities are $[ML_2^+]$ (assumed to be proportional to the fluorescence signal changes, see below), the total metal ion added to the ligand solution $[M^+]_t$, and $[L]_t$. In our titrations $[L]_t$ is held constant as metal ion is added. Thus, the following equation is obtained from eqn. (1) upon substitution:

$$K = [ML_2^+]/([M^+]_t - [ML_2^+])([L]_t - 0.5[ML_2^+])^2 \qquad (3)$$

We assume that $[ML_2^+] = [(I - I_0)/(I_f - I_0)][M^+]_t$, where I is the integrated intensity of the fluorescence signal for a given $[M^+]_t$, I_0 is the initial fluorescence intensity in the absence of metal ion, and I_f is the final maximum fluorescence intensity of the solution (at maximal metal ion concentration). Least-squares fits to eqn. (3) to solve for K were performed by a home-written Maple (v. 5; Waterloo, Canada) program.

Results and discussion

Absorption and fluorescence spectroscopy

HPBO. The absorbance and emission spectra of HPBO in various organic solvents, including acidic and basic solvents, were measured and found to be similar. The absorbance spectrum showed peaks at 335, 320, 292, 282, 278, 270 and 260 nm [Fig. 1(a)]. The emission spectrum showed peaks at 360 and 380 nm, and a broad band in the region 450–500 nm [Fig. 1(b)]. The emission spectral shape of HPBO is concentration dependent; increasing the concentration of HPBO increased the intensity of the peak in the 450–500 nm region, suggesting that the peak is a result of aggregation.

HPBO with Li^+ in the presence of base. The effect of Li^+ on the emission spectrum of HPBO in different solvents was investigated. Addition of Li^+ to a HPBO solution in ethanol (EtOH) resulted in an emission enhancement of the near-UV peaks, accompanied by the appearance of a new emission peak at 421 nm. When this solution was viewed under UV light, it emitted in the blue region the emission intensity increasing with increasing Li^+ concentration (Fig. 2). In this case near-molar concentrations of Li^+ were necessary to observe the emission. Upon adding base to the HPBO solution in ethanol and repeating the titration with Li^+, the near-UV emission peaks corresponding to HPBO alone disappeared, and only the peak at 421 nm was observed.

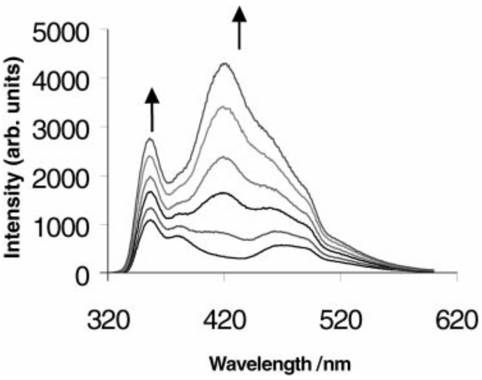


Fig. 2 Titration of HPBO (4.3×10^{-4} M) with Li^+ in ethanol. $[Li^+]$ from bottom to top = 0.00, 0.18, 0.26, 0.33, 0.46 and 0.57 M.

Fig. 3 shows the results of a fluorescence titration of HPBO solution in MeCN (8.7 mM) with Li^+ in the presence of 1 equiv. of NEt_3. The results in acetonitrile were similar to those in ethanol; the peaks characteristic of HPBO at 360 and 380 nm, and the broad band in the region 450–500 nm, remained unchanged with 1 equiv. of base alone. The peak at 421 nm appeared and increased in intensity as a function of lithium ion concentration. Similar results are were obtained in other organic solvents and with other bases such as pyridine and trimethylamine. Thus, we take the peak at 421 nm as a sign of complex formation between deprotonated HPBO and Li^+. Li^+ concentrations as low as 10^{-7} M were detectable (Fig. 3).

Titration of an HPBO solution with Li^+ in the absence of base gave no changes in the absorption spectrum, regardless of the solvent used. However, addition of 1 equiv. of base to an HPBO solution before the titration was carried out resulted in a distinct change upon Li^+ addition as shown in Fig. 4. Upon

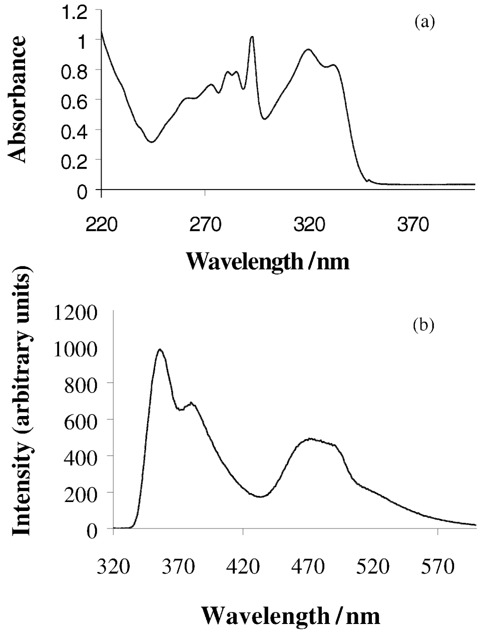


Fig. 1 (a) UV-Vis absorption spectrum and (b) emission spectrum (at 295 nm excitation) of 6.82×10^{-5} M HPBO in acetonitrile.

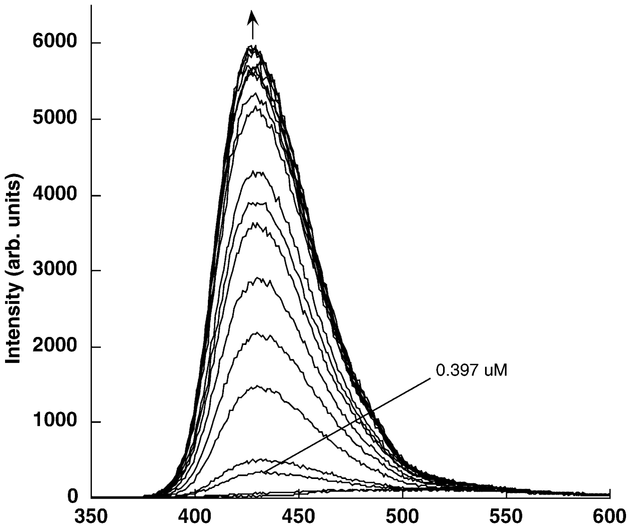


Fig. 3 Titration of HPBO (8.73×10^{-3} M) in acetonitrile with Li^+. From bottom to top: HPBO alone; HPBO + 1 equiv. NEt_3; then with Li^+ added: 0.397 (indicated with line as 0.397 μM), 0.793, 3.95, 7.88, 11.8, 15.7, 19.5, 23.3, 30.9, 38.4, 45.8, 53.0, 60.3, 67.4, 74.4, 84.7, 98.3, and 10.8×10^{-6} M.

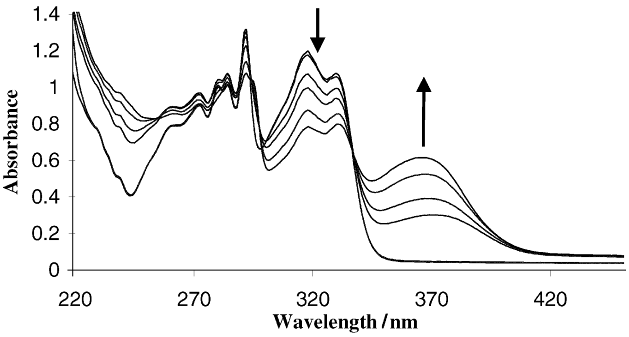


Fig. 4 Change in UV-Vis absorption spectrum of HPBO (1.0×10^{-4} M) in acetonitrile, in the presence of 1.0×10^{-4} M NEt_3, upon addition of Li^+. [Li^+] from bottom to top at 370 nm: 0.0, 7.5, 18.6, 36.6 and 54.1 mM.

adding Li^+, a new peak at 370 nm emerged, which increased in intensity with the increase in Li^+ concentration. Thus, we suggest that the 370 nm peak in the absorbance spectrum is another sign of the formation of a complex between deprotonated HPBO and lithium ions. The isosbestic point at 336 nm supports the presence of two species in solution (free HPBO and the lithium–HPBO complex). Similar experiments carried out with Na^+ and K^+ had no effect on the absorption spectrum of HPBO.

Both absorbance and fluorescence data were treated using the continuous variation method[34] to determine the stoichiometry of the HBPO–lithium ion complex, and a 2 : 1 stoichiometry was obtained. The fluorescence titration data taken at constant HPBO concentration and varying amounts of lithium ion were fit to eqn. (3) to calculate the binding constant for the $Li(HPBO)_2^-$ complex; a value of $3.6 \pm 0.5 \times 10^5$ M^{-2} was obtained. This value is similar to those found for weaker cryptand–Li^+ complexes ($K \approx 10^2$–10^8 M^{-1}).[35] However, traditional cryptands are not fluorescent in the visible region, whereas the visible spectroscopic signals for lithium ion binding to HPBO are ideal for optical sensor development. Hiratani *et al.* have reported *K*s of the order of 10^9 M^{-2} for their ligands, yet their titration concentration range (10^{-6}–10^{-4} M Li^+ for 10^{-4} M ligand) is similar to ours.[31]

Selectivity of HPBO to Li^+ in comparison to Na^+ and K^+. To determine whether the fluorescence change of HPBO was specific to Li^+, we repeated similar titration experiments with Na^+ and K^+, in the presence and absence of base. Without base, there was an overall enhancement in the fluorescence intensity of HPBO with Na^+ of ~25% compared to the overall enhancement due to Li^+; the 421 nm peak was absent and the overall spectral shape of HPBO remained unchanged. With base, a 2% increase in emission intensity was observed with Na^+ and no change in shape of the overall emission spectrum of the ligand occurred. The peaks characteristic of HPBO did not disappear, as with the Li^+ titration. There was no notable change in the emission spectrum of HPBO when titrated with K^+ either.

Fig. 5(a) shows the effect of Li^+, Na^+ and K^+ on the fluorescence spectrum of HPBO. In each case equal concentrations of one of the metal ions (1.2 mM) were added to a known volume of a 7.1×10^{-5} M solution of HPBO and base. A similar experiment was also conducted by monitoring the changes in absorbance spectrum of HPBO. As shown in Fig. 5(b), there was no change with Na^+ and K^+, but with Li^+ there was a decrease in the 300 nm absorbance peak accompanied by a new peak at 370 nm. Thus, in each case neither Na^+ nor K^+ affected the fluorescence, nor the absorbance spectra of HPBO, thus suggesting that HPBO can be used as a fluorescent sensor for Li^+ without interference from Na^+ and K^+.

NMR spectroscopy

A solution of HPBO in acetonitrile-d_3 was prepared and its ^1H NMR spectrum was measured. Addition of 1 equiv. of NEt_3 to the HPBO solution (0.38 M) resulted in a decrease in the intensity of the phenolic proton peak at 11.45 ppm. Addition of Li^+ (0.40 M) to the HPBO–base solution resulted in the disappearance of the phenolic proton peak. An increase in Li^+ concentration resulted in a shift of the entire spectrum upfield, indicating complex formation. The addition of Li^+ without base did not change the HPBO ^1H NMR spectrum.

We also investigated the HPBO–Li^+ complex by ^7Li NMR. An HPBO solution in acetonitrile-d_3 (1.0×10^{-4} M) was prepared and its ^7Li NMR was recorded with and without base; the signal at 0.00 ppm is due to the LiCl standard [Fig. 6(a)]. The ^7Li NMR spectrum of 1.0×10^{-4} M HPBO, with 1 equiv. of NEt_3, with Li^+ added to the solution showed two peaks, one at −1.795 ppm and one at 0.000 ppm [Fig. 6(b)]. The −1.795 ppm peak is similar to those found in complexes in which lithium ion is coordinated to N and O donor atoms from chelating ligands.[35] An increase in Li^+ concentration resulted in a downfield chemical shift of this peak [Fig. 6(c)]. We assign the −1.795 ppm peak to HPBO-bound Li^+, and the peak at 0.000 ppm to "free" (solvated) Li^+. Although the −1.795 ppm peak appeared as a single peak, peak expansion showed two closely spaced peaks separated by 0.005 ppm; possibly there are alternate conformers of the HPBO–Li^+ complex in solution.

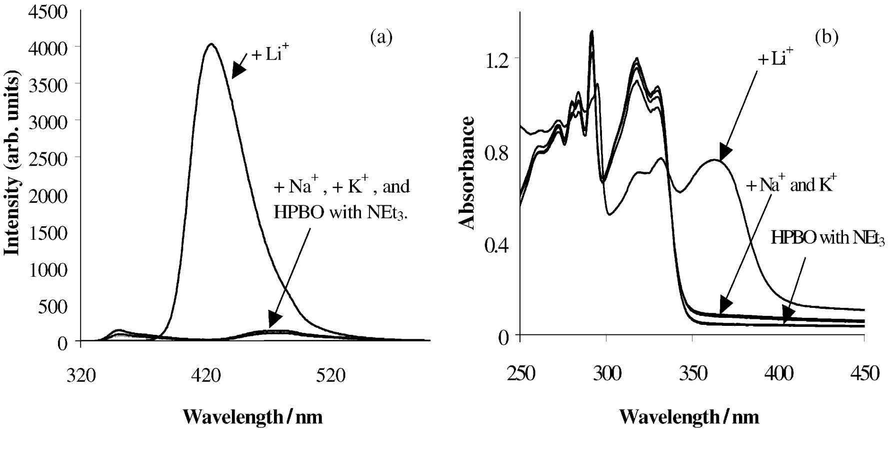
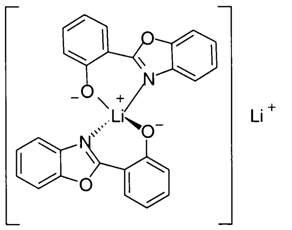


Fig. 5 Selectivity of HPBO for Li^+. (a) Fluorescence spectrum of HPBO (7.1×10^{-5} M) upon addition of Li^+, Na^+ or K^+ (all 1.2 mM) in the presence of base. (b) UV-Vis spectrum of HPBO (1.0×10^{-4} M) upon addition of Li^+, Na^+ or K^+ (all 0.16 M) in the presence of base.

A suggested structure for the HPBO–Li$^+$ complex

Our absorption and fluorescence spectroscopic titration results suggest a 2 : 1 HPBO : Li$^+$ stoichiometry, which is feasible, since Li$^+$ prefers tetrahedral coordination.[35] However, Kim *et al.* reported a 1 : 1 HPBO : Li$^+$ stoichiometry based on elemental analysis.[33] How can these data be reconciled?

A possible explanation is the formation of a 2 : 2 HPBO–Li$^+$ complex. In this model, Li$^+$ coordinates to two HPBO anion ligands, resulting in the negatively charged 2 : 1 HPBO : Li$^+$ complex, with another Li$^+$ ion as a solvated counterion, as represented by **3**. This formulation is consistent with our ^{7}Li NMR data.



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Structure **3** seems contradictory to the results from the absorption and fluorescence titrations we performed. However, absorption spectroscopy and fluorescence spectroscopy detect only the Li$^+$ coordinated to the ligands, which causes the absorbance peak at 370 nm and the emission peak at 421 nm. ^{7}Li NMR, of course, can detect both kinds of lithium. Our 2 : 2 stoichiometry, with an additional solvated Li$^+$ counterion, is consistent with Kim *et al.'s* data for their "unidentate" complex.[33] A single-crystal X-ray structure of the complex, which is in progress, is needed to determine with more certainty the coordination of Li$^+$ to the HPBO ligand.

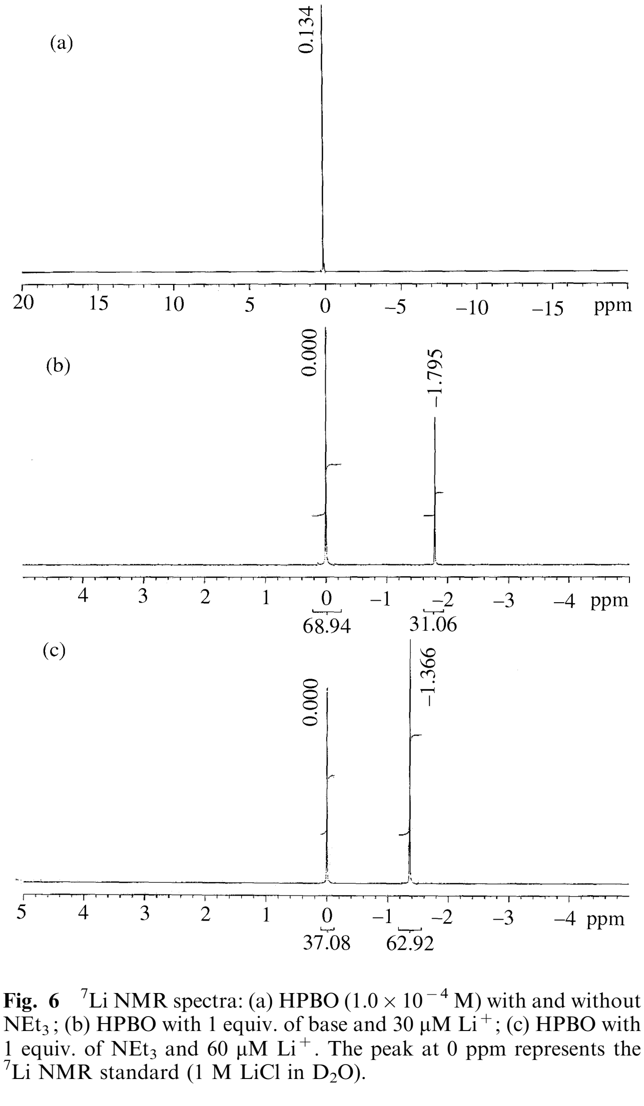

Fig. 6 ^{7}Li NMR spectra: (a) HPBO (1.0×10^{-4} M) with and without NEt_3; (b) HPBO with 1 equiv. of base and 30 μM Li$^+$; (c) HPBO with 1 equiv. of NEt_3 and 60 μM Li$^+$. The peak at 0 ppm represents the ^{7}Li NMR standard (1 M LiCl in D_2O).

Conclusion

We have demonstrated that HPBO is an excellent ligand to selectively monitor Li$^+$ concentrations in alkaline media. The ligand is commercially available, and lithium ion detection is feasible by both fluorescence and absorption spectroscopies. Submicromolar concentrations of lithium ion are detectable by fluorescence. We suggest that the complex consists of two HPBO anions tetrahedrally coordinated to one Li$^+$, and an additional solvated Li$^+$ as an associated counterion.

Acknowledgements

We thank Dr Perry Pellechia for his assistance with the ^{7}Li NMR studies, and Mr Bob Murphy for assistance with the Maple programming. This work was funded by the Department of Energy and EPSCoR.

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