

Bisnitronyl nitroxides bridged by tetra(ethyleneoxy) sensing metal ions spectroscopically and electrochemically

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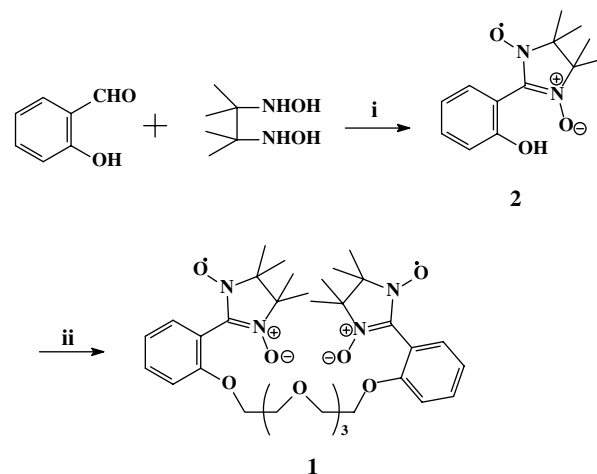
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Abstract—Compound **1** containing two nitronyl nitroxide units bridged by tetra(ethyleneoxy) was designed and synthesized for sensing metal ions, by taking the features of nitronyl nitroxides: a chromophore showing absorption in visible range, reversible oxidation/reduction and coordination to metal ions. The absorption spectrum of **1** was altered markedly upon mixing with a few rare earth metal ions and some transition metal ions. Moreover, the oxidation potential of **1** was shifted to more positive range in the presence of metal ions including Pb²⁺, Ba²⁺, and Ca²⁺. Thus, compound **1** can sense metal ions both spectroscopically and electrochemically.

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Nitronyl nitroxides were initially discovered by Ullman in 1970's and widely used as spin probes.¹ In 1991, *p*-nitrophenyl nitronyl nitroxide was found to be a bulk ferromagnet.² Since then, nitronyl nitroxides were intensively investigated for studies related to organic magnets. Because of their spin-related properties of nitronyl nitroxides, nitronyl nitroxides are introduced to calixarenes³ and crown ether frameworks⁴ to study molecular conformation change and sense metal ions with ESR as the output signal. Nitronyl nitroxides are also chromophores showing absorptions in visible range around 550 nm, and they are also electron donors that can be reversibly oxidized and reduced.⁵ For instance, the fluorescence of 2-nitronyl nitroxide pyrene was shown to be largely quenched and modulated by the combined actions of cysteine and CF₃COOH mimicking the performance of an 'AND' logic gate.⁶ It should also be mentioned that nitronyl nitroxides can be coordinated to metal ions under suitable conditions.⁷

Considering the unique properties of nitronyl nitroxide unit: a chromophore showing absorption in visible range, reversible oxidation/reduction and coordination to metal ions, a bisnitronyl nitroxides molecule (**1**, Scheme 1) was designed for sensing metal ions. The



Scheme 1. Synthesis of compound **1**. Reagents and conditions: (i) *p*-CH₃C₆H₄SO₃H (cat), HC(OCH₂CH₃)₃ (cat), CH₃OH, rt, 24 h, and PbO₂, 70%; (ii) tetraethylene glycol, DEAD, PPh₃/THF, 75%.

absorption spectrum of **1** changed markedly upon mixing with Gd³⁺, Er³⁺, Fe³⁺, and Cu²⁺. Moreover, the oxidation potential of **1** was anodically shifted in the presence of Pb²⁺ and even Ca²⁺ and Ba²⁺ which cannot induce any detectable change for the visible region of the absorption spectrum of **1**. Therefore,

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molecule **1** with two nitronyl nitroxides bridged by tetra(ethyleneoxy) can sense metal ions both spectroscopically and electrochemically.

Compound **2** was prepared according to the reported procedure¹ by condensation of salicylaldehyde with 2,3-bis(hydroxylamino)-2,3-dimethylbutane, followed by oxidation with PbO₂. Compound **2** was transformed to compound **1** after reaction with tetraethylene glycol, PPh₃, and DEAD via Mitsunobu reaction⁸ in 76% yield.⁹

Compound **1** shows strong absorptions at 286, 330 nm and weak absorption at 550 nm (Fig. 1). Compound **1** contains tetra(ethyleneoxy) unit and two nitronyl nitroxides and thus may form complexes with metal ions as crown ether. It is expected that coordination with metal ions would alter its electronic structure and thus its absorption spectrum. Alkali metal ions, alkali earth metal ions, transition metal ions and several rare earth metal ions were tested. It was found that the absorption spectrum of **1** was changed markedly upon addition of a few rare earth metal ions. For instance, Figure 1 shows the absorption spectra of **1** in the presence of different amounts of Gd³⁺. Upon addition of Gd³⁺, the absorption intensity around 550 nm was gradually reduced, and concomitantly a new absorption around 401 nm emerged. Accordingly, the color of the solution of **1** varied gradually after addition of Gd³⁺ and the color change can be detected by naked-eye as displayed in Figure 2. Besides, the absorption bands at 286 and 330 nm were hypsochromically shifted and their intensities were slightly enhanced. Three isoabsorptive points at 337, 370, and 482 nm were clearly observed. The inset of Figure 1 shows the plot of the variation of absorbance at 401 and 558 nm versus the amount of Gd³⁺ added to the solution of **1**, implying that the 1:1 complex was formed between **1** and Gd³⁺. The corresponding binding constant was estimated to be $(2.867 \pm 0.1692) \times 10^4$ ($R = 0.99433$) by fitting the data to Benesi–Hildebrand equation. It is interesting to note that the absorption spectrum of **1** can be fully restored after addition of

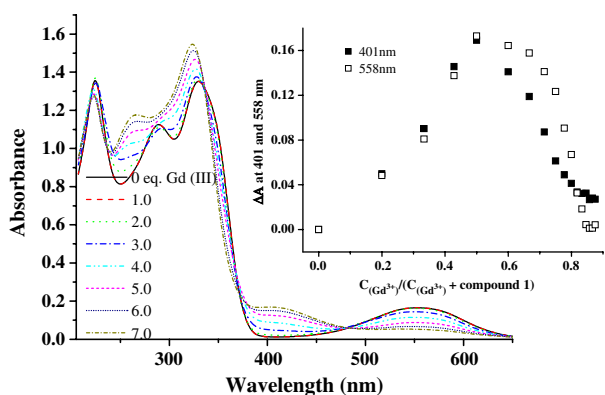


Figure 1. Absorption spectra of compound **1** in the presence of Gd³⁺ with increasing concentration (0, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0 $\times 10^{-4}$ M) in CH₃CN; the concentration of the compound **1** was 1.0×10^{-4} M in CH₃CN; Inset shows the Job plot for compound **1**–Gd³⁺ complex in CH₃CN solution.



Figure 2. Color changes observed for the solution of **1** (5.0×10^{-4} M) in the presence of different amounts of Gd³⁺ and pyridine in CH₃CN: from left to right: 0.0 equiv of Gd³⁺ + 0.0 equiv of pyridine, 1.0 equiv of Gd³⁺ + 0.0 equiv of pyridine, 2.0 equiv of Gd³⁺ + 0.0 equiv of pyridine, 3.0 equiv of Gd³⁺ + 0.0 equiv of pyridine, 4.0 equiv of Gd³⁺ + 0.0 equiv of pyridine, 4.0 equiv of Gd³⁺ + 4.0 equiv of pyridine.

4.0 equiv amount of pyridine to the solution of **1** containing Gd³⁺ (4.0 equiv). This is likely due to the coordination of Gd³⁺ with pyridine and thus compound **1** was released. This result again supports the fact that variation of the spectrum of **1** in the presence of Gd³⁺ is due to its coordination with Gd³⁺.¹⁰ Under the same conditions, addition of Er³⁺ to the solution of **1** led to similar absorption spectral changes as shown in Figure 3. In the presence of Dy³⁺ and Nd³⁺ obvious changes for absorption bands below 400 nm were observed, but the absorption band around 550 nm was kept almost unaltered (Fig. 3).¹¹

Among the tested transition metal ions including Zn²⁺, Cu²⁺, Ni²⁺, Co²⁺, Fe²⁺, Fe³⁺, and Mn²⁺, addition of Cu²⁺/Fe³⁺ to the solution of **1** can also cause detectable absorption spectral change (Fig. 4). Similarly, on the basis of the plot of the absorbance difference measured at 401 nm versus the amounts of Cu²⁺/Fe³⁺ it may be concluded that compound **1** also forms 1:1 complex with Cu²⁺/Fe³⁺. The corresponding binding constants for Cu²⁺ and Fe³⁺ were estimated to $(1.900 \pm 0.103) \times 10^3$ ($R = 0.99922$) and $(1.054 \pm 0.028) \times 10^3$ ($R = 0.99791$), respectively.

The absorption bands below 400 nm of **1** were changed upon addition of Ba²⁺ and Ca²⁺, but the absorption

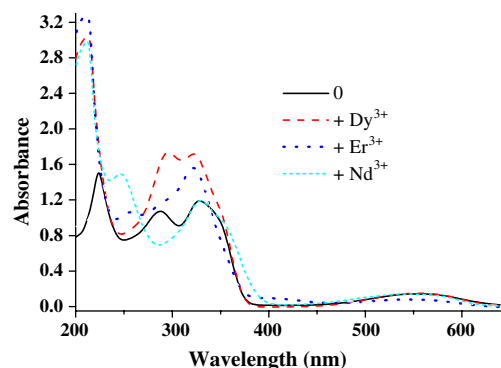


Figure 3. Absorption spectra of compound **1** in the presence of Dy³⁺ (5.0 equiv), Er³⁺ (5.0 equiv), and Nd³⁺ (5.0 equiv); the concentration of the compound **1** was 1.0×10^{-4} M.

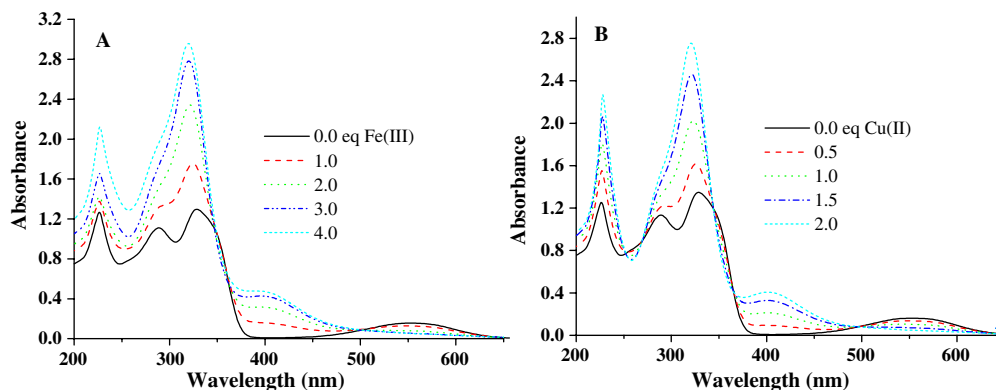


Figure 4. (A) Absorption spectra of compound **1** in the presence of increasing amounts of Fe(III) (0.0, 1.0, 2.0, 3.0, and 4.0 equiv); (B) absorption spectra of compound **1** in the presence of increasing amounts of Cu(II) (0.0, 0.5, 1.0, 1.5, and 2.0 equiv); the concentration of the compound **1** was 1.0×10^{-4} M.

band around 550 nm kept almost unchanged (see [Supplementary data](#)). However, alkali metal ions cannot induce any detectable absorption spectral change for compound **1**.¹²

As reported previously, nitronyl nitroxides can be reversibly oxidized and reduced.⁵ Coordination of **1** with metal ions would alter its electronic structure. Thus, it can be anticipated that the oxidation potential of **1** would be varied upon coordination with metal ions.

As indicated in [Figure 5A](#), compound **1** shows an oxidation potential ($E_{ox}^{1/2}$) of 0.72 V, implying that the two nitronyl nitroxides of **1** are simultaneously oxidized. Both the oxidation and reduction peak currents were gradually reduced after addition of Gd^{3+} to the solution of **1** ([Fig. 5A](#)). Similar to the absorption spectral change of **1** in the presence of Gd^{3+} , its cyclic voltammogram can be also restored after addition of pyridine as displayed in [Figure 5B](#), where the cyclic voltammograms of the solution of **1** containing 6.0 equiv of Gd^{3+} after addition of different amounts of pyridine are displayed.

Because Fe^{3+} and Cu^{2+} are redox active, the studies of their effects on the cyclic voltammogram of **1** were not performed. Interestingly, the oxidation potential of **1** was shifted to more positive range in the presence of Pb^{2+} as shown in [Figure 6](#). For example, the potential of oxidation peak was changed to 0.91 V after addition of 1.0 equiv of Pb^{2+} . Ba^{2+} and Ca^{2+} can also cause the positive shift of the oxidation potential of **1** as shown in [Figure 7](#). But, Li^+ , Na^+ , K^+ , and Cs^+ cannot induce any variation of the oxidation potentials of **1**. The different effects of metal ions on the oxidation potential of **1** are probably due to their different binding constants with **1**.

For comparison, the analogue of **1** with one nitronyl nitroxide (compound **3**, see [Supplementary data](#)) unit was synthesized. Similar absorption spectral changes were observed for compound **3** in the presence of Gd^{3+} , Fe^{3+} , Cu^{2+} , Pb^{2+} , and Ba^{2+} (see [Supplementary data](#)). This can be understood by considering the fact that it is also possible to form complexes between **3**

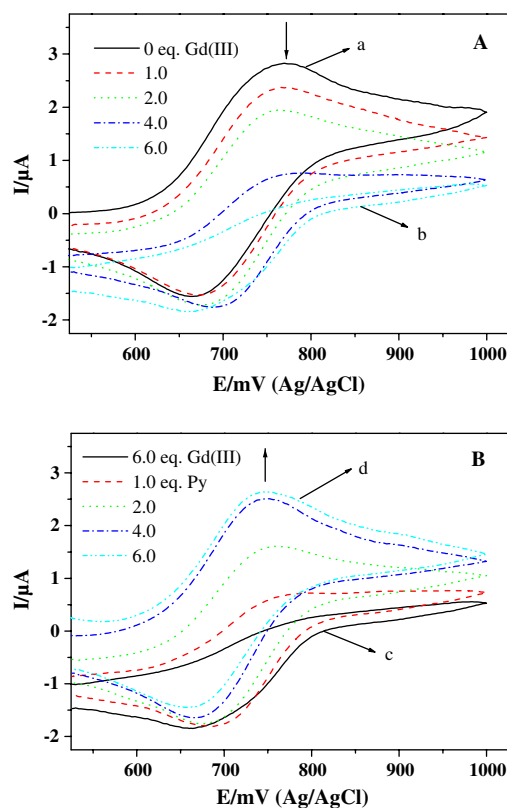


Figure 5. (A) Cyclic voltammograms of **1** (5.0×10^{-4} M) in the presence of increasing amounts $Gd(CF_3COO)_3$: (a) 0.0 equiv of Gd^{3+} , (b) 6.0 equiv of Gd^{3+} ; (B) cyclic voltammograms of the solution of **1** (5.0×10^{-4} M) containing 6.0 equiv of Gd^{3+} after addition of increasing amounts of pyridine: (c) 0.0 equiv of pyridine, (d) 6.0 equiv of pyridine; all experiments were performed in CH_3CN at 298 K with $n-Bu_4NPF_6$ (0.1 M) as supporting electrolyte, and the scanning rate was 20 mV/s.

and suitable metal ions through the oxygen atoms of the tetra(ethyleneoxy) and nitronyl nitroxide units.

By taking advantage of the features of nitronyl nitroxides: a chromophore showing absorption in visible range, reversible oxidation/reduction and coordination to metal ions, compound **1** containing two nitronyl nitr-

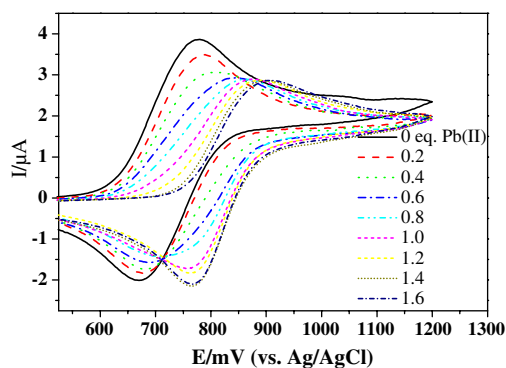


Figure 6. Cyclic voltammograms of **1** (5.0×10^{-4} M) in the presence of increasing amounts of $\text{Pb}(\text{ClO}_4)_2$; all experiments were carried out in CH_3CN at 298 K with $n\text{-Bu}_4\text{NPF}_6$ (0.1 M) as supporting electrolyte and scanning rate was 20 mV/s.

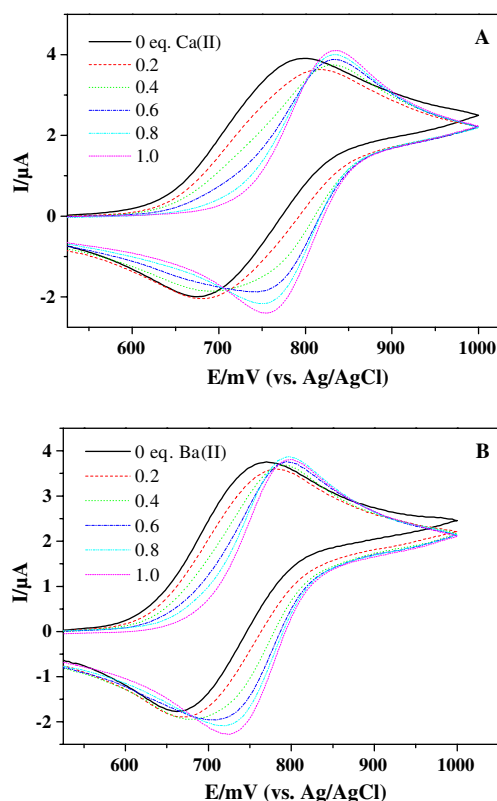


Figure 7. Cyclic voltammograms of compound **1** (5.0×10^{-4} M) in the presence of increasing amounts of Ca^{2+} (A) and Ba^{2+} (B).

oxide units bridged by tetra(ethyleneoxy) was designed for sensing metal ions. The absorption spectrum of **1** was altered markedly upon mixing with a few rare earth metal ions and some transition metal ions. Moreover, the oxidation potential of **1** was shifted to more positive range in the presence of metal ions including Pb^{2+} , Ba^{2+} , and Ca^{2+} . Thus, compound **1** can sense metal ion both spectroscopically and electrochemically. The present results will add new merits to the chemistry of nitronyl nitroxides. Further investigations include the optimization of the linker that connects two nitronyl

nitroxides and design new bisnitronyl nitroxides for selectively sensing metal ions.

Acknowledgements

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Supplementary data

Synthesis and characterization of compounds **1** and **3**; the absorption spectra of **1** in the presence of Pb^{2+} , Ba^{2+} , and Ca^{2+} ; the absorption spectra of **3** in the presence of Gd^{3+} , Fe^{3+} , Cu^{2+} , Pb^{2+} , Ba^{2+} , and Ca^{2+} . Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.03.061.

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- Characterization data for compound **1**: IR: 1366 cm^{-1} (for nitronyl nitroxide); EPR: nine lines (acetonitrile 1.0×10^{-4} mol/L), $\alpha_{\text{N}} = 0.35\text{ mT}$, $g = 2.0066$; TOF: 656 (M^+), 657 ($\text{M}+\text{H}^+$); HR-FABMS: Anal. Calcd for $\text{C}_{34}\text{H}_{48}\text{O}_9\text{N}_4$: 656.3421; found: 656.3415.
- Coordination complexes of nitronyl nitroxide with Gd^{3+} were reported previously: (a) Lescop, C.; Luneau, D.; Bussière, G.; Triest, M.; Reber, C. *Inorg. Chem.* **2000**, *39*, 3740–3741; (b) Lescop, C.; Luneau, D.; Rey, P.; Bussière,

- G. M.; Reber, C. *Inorg. Chem.* **2002**, *41*, 5566–5574, For compound **1**, the oxygen atoms of tetra(ethyleneoxy) and two nitronyl nitroxide units may be the coordination sites.
11. It seems that the complexes formed between compound **1** and $\text{Gd}^{3+}/\text{Er}^{3+}$ may have different structures compared to those of **1** with $\text{Dy}^{3+}/\text{Nd}^{3+}$. Further investigations are needed to understand such different spectral variation behavior.
 12. This is likely due to the fact that compound **1** cannot form stable complexes with alkali metal ions.