ORGANIC LETTERS

2011
Vol. 13, No. 10
2742–2745

A Novel Supermolecular Tetrameric Vanadate-Selective Colorimetric and "Off–On" Sensor with Pyrene Ligand

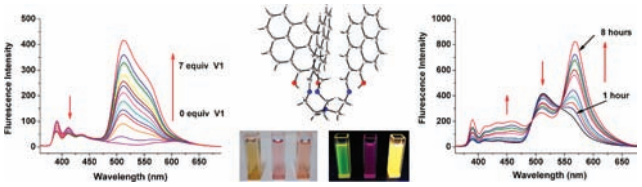
Ying Zhou,[†] Ji Young Jung,[‡] Hye Ryeong Jeon,[†] Youngmee Kim,[†] Sung-Jin Kim,[†] and Juyoung Yoon*[,†,‡]

Department of Chemistry and Nano Sciences and Department of Bioinspired Science (WCU), Ewha Womans University, Seoul 120-750, Korea

jyoon@ewha.ac.kr

Received April 1, 2011

ABSTRACT



Tris(2-((ethylimino)methyl)pyren-1-ol)amine (1) was synthesized and introduced as the first tetrameric vanadate fluorescence sensor, the entire binding of which was successfully accomplished in two steps with distinct colorimetric changes and "off-on" fluorescent enhancement.

The development of molecular recognition and sensing systems for anions has received considerable attention in recent years.[1] In contrast to the sensing of pyrophosphate or phosphate ions,[1a,2] which has been an especially active area of research because of their biological significance, the recognition of transition metal oxoanions, such as vanadate, has not been widely studied.[3] In fact, the significance of vanadate has been well documented in areas of biochemistry, medicine, and catalysis.[4] Most of these studies concentrated on the role of vanadate as a phosphate analogue, allowing it to act both as an inhibitor of phosphate-metabolizing enzymes as well as an activator of others.[5]

The main difficulty in studying the interaction of vanadate with organic ligands by way of fluorescent sensor is the tendency of V^V to hydrolyze, forming both mono- and polynuclear species in aqueous solution.[6] For example, aqueous solutions of vanadium salts often contain multiple species such as mono-, di-, tetra-, and pentanuclear compounds. Therefore, it is challenging to obtain a proper receptor to detect the binding of different vanadate species by colorimetric and fluorescent changes.

This paper reports tris(2-((ethylimino)methyl)pyren-1-ol)-amine (**1**) as a receptor of tetrameric vanadate to sense the

[†] Department of Chemistry and Nano Sciences.
[‡] Department of Bioinspired Science (WCU).

(1) (a) Martínez-Máñez, R.; Sancenón, F. *Chem. Rev.* **2003**, *103*, 4419. (b) Xu, Z.; Kim, S. K.; Yoon, J. *Chem. Soc. Rev.* **2010**, *39*, 1457. (c) Gale, P. A. *Chem. Soc. Rev.* **2010**, *39*, 3746. (d) Kim, S. K.; Sessler, J. L. *Chem. Soc. Rev.* **2010**, *39*, 3784. (e) Li, A.-F.; Wang, J.-H.; Wang, F.; Jiang, Y.-B. *Chem. Soc. Rev.* **2010**, *39*, 3729. (f) Xu, Z.; Chen, X.; Kim, H. N.; Yoon, J. *Chem. Soc. Rev.* **2010**, *39*, 127. (g) Caltagirone, C.; Gale, P. A. *Chem. Soc. Rev.* **2009**, *38*, 520. (h) Katayev, E. A.; Ustynyuk, Y. A.; Sessler, J. L. *Coord. Chem. Rev.* **2006**, *250*, 3004. (i) Chen, X.; Zhou, Y.; Peng, X.; Yoon, J. *Chem. Soc. Rev.* **2010**, *39*, 2120. (j) Zhou, Y.; Xu, Z.; Yoon, J. *Chem. Soc. Rev.* **2011**, *40*, 2222.

(2) (a) Kim, S. K.; Lee, D. H.; Hong, J.-I.; Yoon, J. *Acc. Chem. Res.* **2009**, *42*, 23. (b) Samamoto, T.; Ojida, A.; Hamachi, I. *Chem. Commun.* **2009**, 141. (c) Lee, D. H.; Kim, S. Y.; Hong, J.-I. *Angew. Chem., Int. Ed.* **2004**, *43*, 4777. (d) Kim, M. J.; Swamy, K. M. K.; Lee, K. M.; Jagdale, A. R.; Kim, Y.; Kim, S.-J.; Yoo, K. H.; Yoon, J. *Chem. Commun.* **2009**, 7215. (e) Lee, H. N.; Swamy, K. M. K.; Kim, S. K.; Kwon, J.-Y.; Kim, Y.; Kim, S.-J.; Yoon, Y. J.; Yoon, J. *Org. Lett.* **2007**, *9*, 243.

(3) (a) Zhang, X.; Woggon, W. -D. *J. Am. Chem. Soc.* **2005**, *127*, 14138. (b) Ligtenbarg, A. G. J.; Hage, R.; Feringa, B. L. *Coord. Chem. Rev.* **2003**, *237*, 89.

(4) (a) Rhule, J. T.; Hill, C. L.; Judd, D. A. *Chem. Rev.* **1998**, *98*, 327. (b) Gorzsas, A.; Getty, K.; Andersson, I.; Pettersson, L. *Dalton Trans.* **2004**, *18*, 2873. (c) Gorzsas, A.; Andersson, I.; Pettersson, L. *Eur. J. Inorg. Chem.* **2006**, *18*, 3559. (d) Dornyei, A.; Marcao, S.; Pessoa, J. C.; Jakusch, T.; Kiss, T. *Eur. J. Inorg. Chem.* **2006**, *18*, 3614. (e) Kikushima, K.; Moriuchi, T.; Hirao, T. *Chem. Asian J.* **2009**, *4*, 1213. (f) Kikushima, K.; Moriuchi, T.; Hirao, T. *Tetrahedron Lett.* **2010**, *51*, 340. (g) Xiong, D.; Wu, M.; Wang, S.; Li, F.; Xia, C.; Sun, W. *Tetrahedron: Asymmetry* **2010**, *21*, 374.

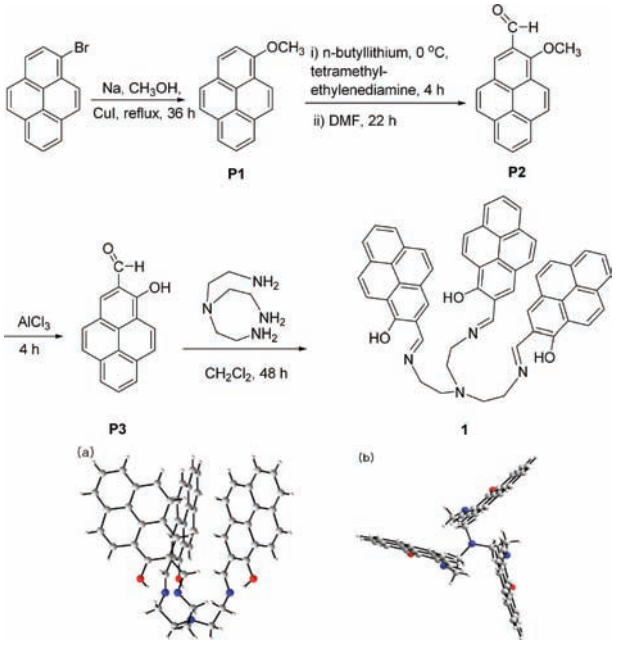
(5) (a) Yamaki, R. T.; Paniago, E. B.; Carvalho, S.; Howarth, O. W.; Kam, W. *J. Chem. Soc., Dalton Trans.* **1997**, 4817. (b) Zhang, X.; Meuwly, M.; Woggon, W. -D. *J. Inorg. Biochem.* **2004**, *98*, 1967. (c) Nica, S.; Pohlmann, A.; Plass, W. *Eur. J. Inorg. Chem.* **2005**, 2032.

(6) Hamilton, E. E.; Fanwick, P. E.; Wilker, J. J. *J. Am. Chem. Soc.* **2002**, *124*, 78.

10.1021/ol200846a
Published on Web 04/22/2011

binding process by both distinct colorimetric and fluorescent changes for the first time. During the titration, **1** was *immediately* able to bind V1 (monomeric, VO_4^{3-}), V4 (tetrameric, $V_4O_{12}^{4-}$), and V5 (pentameric, $V_5O_{15}^{5-}$) simultaneously, and the color of the solution **1** changed from pink to yellow, with a strong yellow-green fluorescence. Interestingly, the equilibrium of oligomeric vanadates shifted toward V4 slowly, because **1** preferentially binds V4 over V1 and V5, and the situation reached the maxium point after 8 h of the addition of monovanadate. The color of solution **1** changed from yellow to orange, with a strong yellow fluorescence emission. Therefore, the entire sensing process of vanadate was successfully indicated by the colorimetric and fluorescent changes of **1** in two steps.

Scheme 1. Synthetic Route for Compound **1** and Crystal Structure of **1** (a) along the *b*-Axis and (b) along the *c*-Axis



Scheme 1 explains the synthetic route of compound **1**. Compounds **P1**–**P3** were synthesized with improved yield by a modification of the previously reported procedure.[7] The condensation of **P3** with tris(2-aminoethyl)amine produced the target compound **1**, which was rapidly purified by filtration, in a high yield of 70%. The structure of **1** was characterized by NMR spectroscopy and confirmed by X-ray crystallography. As shown in Scheme 1, a basket framework is formed in **1** by the introduction of tris(2-aminoethyl)amine group, and three hydroxyl groups face outward the center of the "basket" due to the steric effect.

The absorption and fluorescence properties of **1** were tested in DMSO. Compound **1** exhibited an major absorption band centered at 548 nm with three peaks at 350, 393, and 432 nm. As 0–3 equiv of $(n\text{-}Bu_4N)_2\cdot HVO_4$ (V1) was added to the solution of **1**, the peaks around 350 and 550 nm decreased while the peaks at 393 and 481 nm increased significantly, with two isosbestic points at 364 and 512 nm (Figure 1a). However, the increase did not stop after it reached the maximum point with 3 equiv of V1. The intensities of peaks at 393 and 481 nm increased slowly and finally stopped increasing 1 h after the addition (Figure 1a, inset). As shown in Figure 1b, the color of solution **1** *immediately* changed from pink to yellow when 3 equiv of $(n\text{-}Bu_4N)_2\cdot HVO_4$ was added and changed slowly from yellow to orange within 1 h.

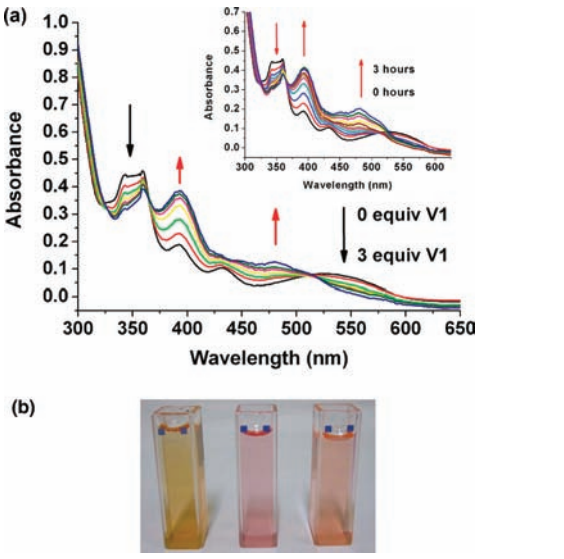


Figure 1. (a) UV–vis changes of **1** (1×10^{-5} M, DMSO) upon the addition of 3 equiv of $(n\text{-}Bu_4N)_2\cdot HVO_4$ after 5 min. Inset: UV–vis changes of **1** (1×10^{-5} M, DMSO) after addition of 3 equiv of $(n\text{-}Bu_4N)_2\cdot HVO_4$ for 1 h. (b) Pictures of compound **1** upon the addition of 7 equiv of $(n\text{-}Bu_4N)_2\cdot HVO_4$ after 5 min (left); compound **1** (middle); compound **1** upon the addition of 7 equiv of $(n\text{-}Bu_4N)_2\cdot HVO_4$ after 10 h (right).

The fluorescence spectrum of **1** in DMSO exhibited characteristic emission bands of the pyrene monomer at 390, 410, 437 nm as well as a small peak at 607 nm, with a pink color emission. (Figure 2a) Upon titration with V1, the fluorescence of both of the monomer and the peak at 607 nm quenched while a peak at 508 nm, assigned to the emission of the pyrene excimer,[8] and a shoulder peak at 564 nm appeared, which confirmed the stacking of pyrene. With the addition of 7 equiv of V1 to solution **1**, the intensity of the major peak at 513 nm, with a 5 nm red-shift, increased significantly with 30-fold enhancement (Figure 2b). The solution fluorescence color changed from pink to yellow-green (Figure 2a). After it reached the maximum point,

(7) (a) Demerseman, P.; Einhorn, J.; Gourvest, J. F.; Royer, R. *J. Heterocycl. Chem.* **1985**, *22*, 39. (b) Zhou, Y.; Wang, F.; Kim, Y.; Kim, S.-J.; Yoon, J. *Org. Lett.* **2009**, *11*, 4442. (c) Zhou, Y.; Kim, H. N.; Yoon, J. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 125. (d) Zhou, Y.; Won, J.; Lee, J. Y.; Yoon, J. *Chem. Commun.* **2011**, *47*, 1997.

(8) (a) Xu, Z.; Singh, N. J.; Lim, J.; Pan, J.; Kim, H. N.; Park, S.; Kim, K. S.; Yoon, J. *J. Am. Chem. Soc.* **2009**, *131*, 15528. (b) Wang, F.; Nandhakumar, R.; Moon, J. H.; Kim, K. M.; Lee, J. Y.; Yoon, J. *Inorg. Chem.* **2011**, *50*, 2240.

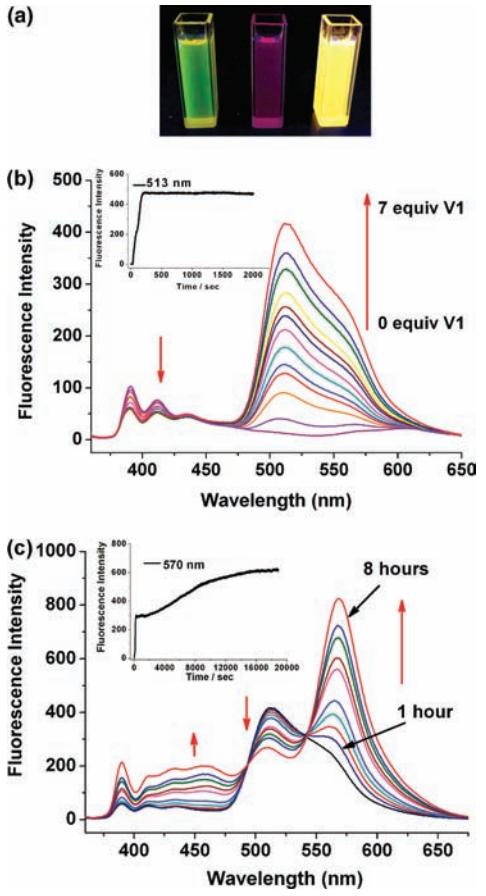


Figure 2. (a) Fluorescence pictures of compound **1** after the addition of 7 equiv of $(n\text{-}Bu_4N)_2 \cdot HVO_4$ for 5 min (left); compound **1** without $(n\text{-}Bu_4N)_2 \cdot HVO_4$ (middle); compound **1** after the addition of 7 equiv of $(n\text{-}Bu_4N)_2 \cdot HVO_4$ for 10 h (right). (b) Fluorescence changes of **1** (1×10^{-5} M, DMSO) upon the addition of 0−7 equiv of $(n\text{-}Bu_4N)_2 \cdot HVO_4$ (tested within 10 min), Inset: kinetics upon addition of 50 equiv of V1 to **1** in DMSO, excitation at 335 nm. (c) Fluorescence changes of **1** (1×10^{-5} M, DMSO) after adding of 7 equiv of $(n\text{-}Bu_4N)_2 \cdot HVO_4$ (tested from 1 to 9 h). Inset: kinetics upon addition of 50 equiv of V1 to **1** in DMSO, excitation at 335 nm, slit 1.5 nm/3 nm.

no additional V1 was added to the solution. As time progressed, the peak at 513 nm quenched (Figure S3 in Supporting Information), while the peak at 564 nm increased with 50-fold enhancement and an isosbestic point at 541 nm (Figure 2c). Eight hours later, the major peak finally red-shifted to 568 nm, and an orange-colored solution with a yellow emission was formed (Figure 2a).

As it is well-known, the solution of vanadate contains monovanadate in equilibrium with its oligomers. According to the changes in UV−vis and fluorescence spectra, it presumed that there are two steps for **1** to sense the vanadate ions and form the stable vanadate complexes.

The ^{51}V NMR titration of **1** was carried out, and the results proved the binding affinity of **1** toward V1, V4, and V5. The 2 mM vanadate stock solution shows three peaks at −527, −556, and −577 ppm, which can be assigned to monomeric (V1, VO_4^{3-}), dimeric (V2, $V_2O_7^{4-}$), and tetrameric (V4, $V_4O_{12}^{4-}$), respectively. With the addition of **1**, four different vanadate species,[9] V1 at −528 ppm, V2 at −558 ppm, V4 at −578 ppm, and pentameric (V5, $V_5O_{15}^{5-}$) at −585 ppm, appeared at the ^{51}V NMR (Figure 3). As **1** increased (equivalents of **1** are related to the concentration of V_1), the V1, V2 and V5 peaks disappeared, while the V4 peak became the major peak, indicating that the equilibrium of oligomeric vanadates shifts toward V4 during the titration. This scenario was achieved by reaching the maxium point by adding 1 equiv of **1**.

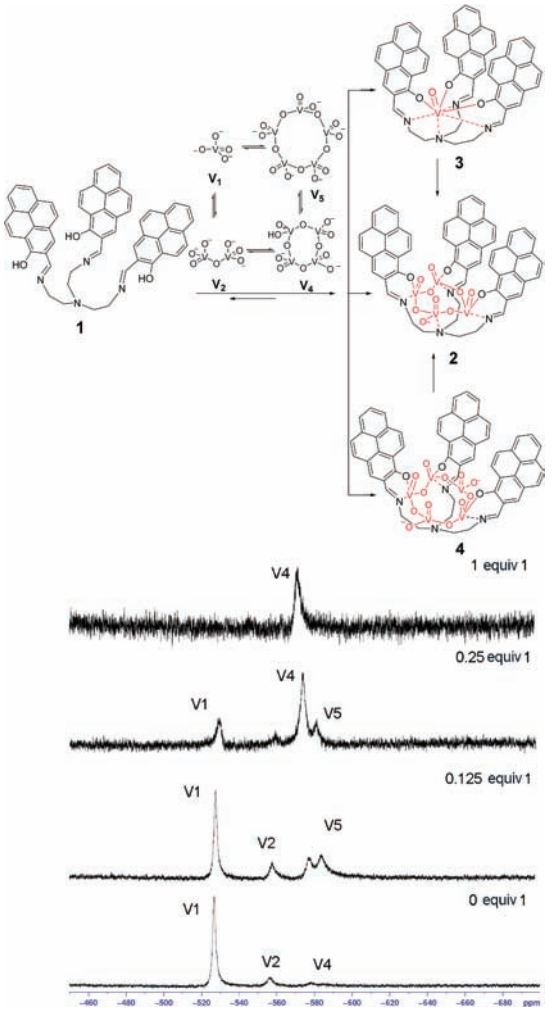


Figure 3. Proposed binding mechanism of compound **1** with different vanadate species and ^{51}V NMR spectra of vanadate (2 mM) with compound **1** (0.5 mM) in DMSO-d_6; equivalents of **1** are related to the concentration of V_1. NMR spectra explain preferential binding of **1** with V_4 over V_1 and V_5.

To identify the time influence in the binding mode, the ^{51}V NMR of 2 mM vanadate stock solution with 0.5 mM 1 was tested at different time points: 2 min, 2 h, 8 h, and 24

(9) (a) Aureliano, M. *J. Inorg. Biochem.* **2000**, *80*, 141. (b) Bhattacharyya, S.; Martinsson, A.; Batchelor, R. J.; Einstein, F. W. B.; Tracey, A. S. *Can. J. Chem.* **2001**, *79*, 938. (c) Mba, M.; Pontini, M.; Lovat, S.; Zonta, C.; Bernardinelli, G.; Kündig, P. E.; Licini, G. *Inorg. Chem.* **2008**, *47*, 8616.

h after the addition (Figure 4). The results showed that, in the presence of **1**, the V4 and V5 peaks increased immediately and the peak of V2 decreased significantly. This implies that **1** binded V1, V4, and V5 at the same time, in other words, compounds **2**, **3**, and **4** coexist at the first stage (Figure 3). As the three hydroxyl groups of **1** turned from facing outside to facing inside to bind V1, V4, and V5, it could explain the increase of the fluorescence peak at 508 nm, assigned to the emission of the pyrene excimer in addition to a shoulder peak at 564 nm. Eight hours later, V2 disappeared and V1 and V5 decreased dramatically, which suggested compound **1** mainly binds V4 and creates an equilibrium of oligomeric vanadates that slowly shifts toward V4 (Figure 3). This corresponded to the increase of the fluorescence peak at 564 nm and the fluorescent color change from yellow-green to yellow. Both fluorescence and ^{51}V NMR titration indicated 1:1 complex final formation between **1** with V4 ($V_4O_{12}^{4-}$), as even the binding interaction of **1** to V4 ($K_a = 2.43\times 10^4\ M^{-1}$) was slightly weeker than that of **1** to V5 ($K_a = 3.14\times 10^5\ M^{-1}$) in the first step.[10]

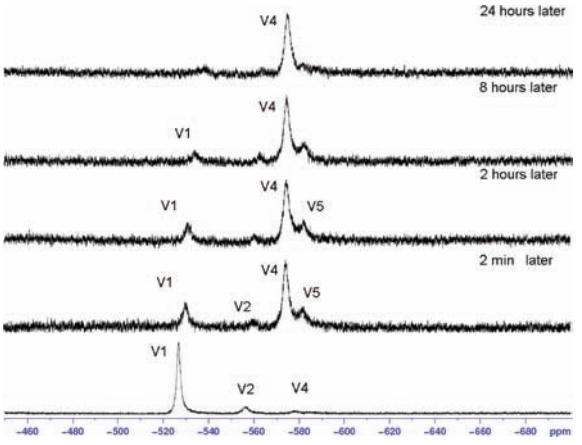


Figure 4. ^{51}V NMR spectra of vanadate (2 mM) with **1** (0.5 mM) in DMSO-d_6.

In conclusion, tris(2-((ethylimino)methyl)pyren-1-ol)-amine (**1**) was synthesized as a receptor for tetrameric vanadate, and for the first time, the entire binding process was successfully accomplished by the distinct colorimetric and "off−on" fluorescent changes of **1** in two steps. First, **1** *immediately* binds V1, V4, and V5 simultaneously. The color of solution **1** changed from pink to yellow, emiting a strong yellow-green fluorescence with 30-fold enhancement. Then, the equilibrium of oligomeric vanadates shifted toward V4 slowly because **1** preferentially binds to V4, and the situation reached the maxium point 8 h after the addition of monovanadate. The color of solution **1** changed from yellow to orange, with a 50-fold enhancement of yellow fluorescence emission. The entire sensing process of vanadate (V4, $V_4O_{12}^{4-}$) was successfully detected by the colorimetric and fluorescent changes of **1** in two steps. The good selectivity and unique fluorescence changes of **1** toward V4, coupled with visual detection by the naked eye, has proven **1** to be a promising candidate for practical applications as a good probe. Work toward this goal is currentlly underway in our laboratory.

Acknowledgment. This work was supported from the National Research Foundation (NRF) (2010-0018895), the Converging Research Center Program through the Ministry of Education, Science and Technology (2010K001202) and WCU program (R31-2008-000-10010-0). Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on a Jeol JMS 700 high resolution mass spectrometer.

Supporting Information Available. Experimental procedures and characterization data of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

(10) (a) Association constants were obtained using the computer program ENZFITTER, available from Elsevier-BIOSOFT, 68 Hills Road, Cambridge CB2 1LA, U.K. (b) Conners, K. A. *Binding Constants, The Measurement of Molecular Complex Stability*; Wiley: New York, 1987.