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Tetrahedron Letters 47 (2006) 3431–3434

Tetrahedron Letters

A new crown ether annelated tetrathiafulvalene derivative with anthracene moiety as a sensor for Li^+ and $^1O_2$

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Received 13 December 2005; revised 9 March 2006; accepted 10 March 2006
Available online 29 March 2006

Abstract—A new crown ether annulated tetrathiafulvalene derivative with an anthracene moiety is shown to act as a dual-functional sensor for Li^+ and $^1O_2$, which may be useful in information processing at the molecular level.

Development of fluorescent methods for sensing chemical events in living cells is receiving growing interest because they are highly sensitive and fast responding.[1] To establish stable and suitable fluorescent probes is of critical importance for fluorescent images,[2] and the design of molecular and supramolecular systems should meet such demands for miniaturization and mass production of devices.[3] Generally, when ionic or molecular species combine with receptors, fluorescence emission changes and a minor variation can be detected accurately. Appropriate probes for fluorescent sensing often are based on the fluorophore–spacer–receptor archetype.[4]

Singlet oxygen ($^1O_2$), an electronically excited state of molecular oxygen, has unique reactivity toward organic compounds.[5] It is highly active in both biological and environmental processes as an oxidant.[6] However, the short lifetime of $^1O_2$ ($\sim$3 μs)[5c] presents a great challenge to the design of its sensor. When we considered this problem, the classical fluorophore anthracene came to our mind because its capability for $^1O_2$ capture (formation of endoperoxide) is also known.[1a,7] To further enhance the reactivity of anthracene unit to $^1O_2$ electron supply from elsewhere in a molecular assembly is needed. This consideration led us to the direction of joining an electron-rich tetrathiafulvalene (TTF) segment to the anthracene end group in our design for a singlet oxygen detector.[7d] TTF and its derivatives show fully reversible, two or multi-step oxidations and they are important as alternative electroactive units in the design of redox-responsive system. Recently, they have been more widely studied as versatile building blocks and redox-active components in cation sensors, molecular shuttles and switches, and photovoltaic materials.[8]

To tune the TTF and thereby influence the sensibility of the anthracene unit toward singlet oxygen is not simple. However, we conjectured that a potential solution lies in annulation of the dithiazole ring with crown ether because the ion binding at the crown ether site would perturb the electron density of the TTF. With this concept in mind we proceeded to build a 15-membered O, S-hybrid crown ether because it should be able to bind lithium ion.[9] Actually, sensors for lithium ions are active research targets,[10] because lithium has medical implications such as its calming effect on patients.[11] The investigations are also related to increasing applications in pharmacology.[12] Of course, new fluorescent chemosensors for Li^+ still require improvements for practical use.

Our objective is to construct a molecule featuring an annulated TTF that is sensitive to lithium ion and at the other end joined by a linker to anthracene for detection of $^1O_2$. This combination is new, although individual fluorescent chemosensors for alkali metal cations and $^1O_2$ are quite well documented.[1,2,4,9] Thus our initial target is 2-(2′-cyanoethylthio)-3-[{2-(9′-anthryloxy)-ethyl}thio]-6,7-bis(3′,6′,9′-trioxoundecylthio)-1,4,5,8-tetrathiafulvalene, and the ensuing experimental work indeed confirms our expectation, finding its ability to detect lithium ion and $^1O_2$, therefore a new dual-functional sensor for Li^+ and $^1O_2$ has become available.

Keywords: Tetrathiafulvalene; Fluorescent sensor; Anthracene; Electrochemical properties.

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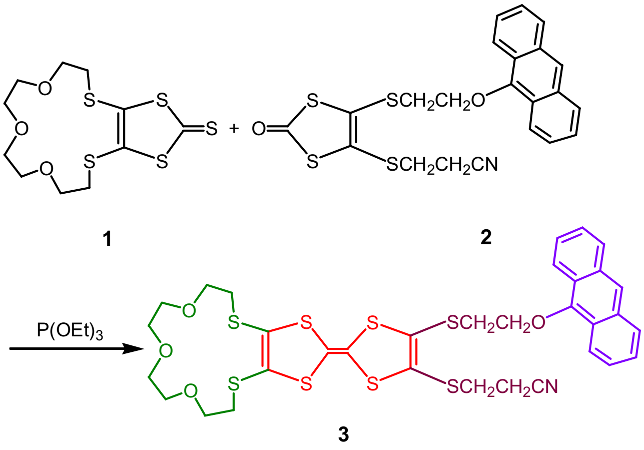
doi:10.1016/j.tetlet.2006.03.055



Scheme 1. Synthesis route of compound **3**.

The synthetic procedure is shown in Scheme 1 (see also Supplementary data). Compound **3** was an unsymmetrical TTF derivative and prepared by the coupling of two distinct 1, 3-dithiole heterocycles.[13] The homo-coupling products that were formed together with the desired compound were removed by column chromatography. The pure product was an orange solid (30% yield) characterized by ^{1}H and ^{13}C NMR measurements (Fig. S1 and S2). After the addition of Li^+ ion in CH_3OH/CH_2Cl_2, ESI-mass spectral observation of a peak at 770.1 for $(M+Li^+)$ indicated the complexation of Li^+ ion to compound **3**. UV–vis absorption bands at 370 nm and 390 nm were assigned to the anthracene core, and the band around 330 nm was due to the absorption of TTF moiety (Fig. S3).

Two reversible single-electron redox waves ($E^1_{1/2} = 0.578$ V, $E^2_{1/2} = 0.773$ V) for compound **3** are shown in Figure 1. Reversible oxidation to its radical cation and then to the dication was indicated. Moreover, one irreversible oxidation peak at 1.148 V and one irreversible reduction wave at −1.892 V were also observed and they were ascribed to the oxidation and reduction of the anthracene unit, respectively.[14] Addition of 0.25 equiv $LiClO_4$ to the solution of sensor **3** led to the maximum positive shift (8 mV) of E^1_{ox}, while E^2_{ox} remained unchanged. It suggested the events of capture and release of Li^+ ion, and the electron density of the TTF moiety was changed. Differential pulse voltammetry of **3** (Fig. S4) upon the addition of Li^+ also confirmed the positive shift of the first half-wave potential peak. However, no obvious shift of the first oxidation peak was observed in the presence of Na^+ and K^+. This result indicated that compound **3** was responsive to Li^+, but not to other alkali metal cations. Good complexation selectivity of the receptor was achieved.

As shown in Figure 2, the triad **3** was a blue luminescent compound and exhibited a weak emission at 433 nm (excited at 396 nm) in THF/H_2O (v/v = 4:1), which was attributed to the effective photoinduced electron transfer (PET) between anthracene and TTF units.[14] Calculated from the Rehm–Weller equation,[16] the free energy (ΔG_{PET}) in this PET process was estimated as −0.56 eV, which confirmed that the PET from TTF to the anthracene unit was thermodynamically favorable.

No significant change in fluorescence intensity was observed when 1 equiv Li^+ ions was added to the above solution. After the addition of singlet oxygen ($^1O_2$), which was produced in situ from H_2O_2/NaOCl solution, the fluorescence was increased by 1.4 folds. The increase was due to oxidation of the TTF unit that prohibited the PET action.[7d,14] The maximum fluorescence emission (λ_{em}) was shifted to 418 nm and the excitation wavelength to 390 nm. According to the energy gap rule,[17]

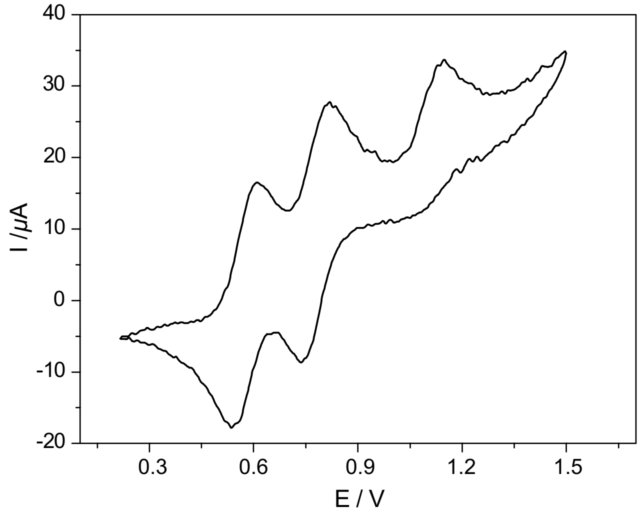


Figure 1. Cyclic voltammetry of compound **3**, with the concentration of 5×10^{-4} M, measured in CH_2Cl_2/CH_3CN (1:1, v/v) solution, *n*-Bu_4NClO_4 (0.1 M) as the supporting electrolyte, platinum as the working and counter-electrodes, Ag/AgCl as the reference electrode, at a scan rate of 50 mV/s.

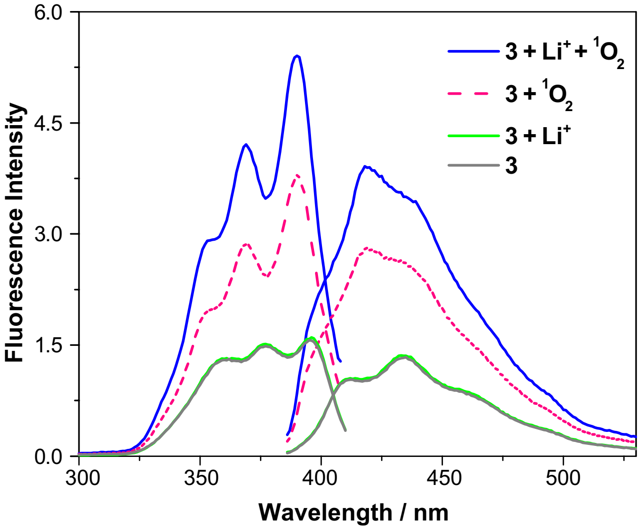


Figure 2. Fluorescence spectra of compound **3** (4×10^{-6} M), performed at room temperature in 50 mM sodium phosphate buffer (pH = 7) containing 80% THF as a co-solvent; $^1O_2$ was chemically generated and added from the H_2O_2/NaOCl (1 mM/10 mM) system in neutral and alkaline media.[7d,15]

the decreasing emission wavelength could be ascribed to decrease in internal conversion as the energy gap between the excited and ground state increased.

Interestingly, after the addition of 1 equiv of Li^+ to the above system, fluorescence was twice the intensity of that induced by singlet oxygen alone. This may be due to further restriction of PET since the oxidation potential of the receptor was raised by cation entry,[18] as evidenced by the above electrochemical and ESI-MS studies. The results clearly proved that our synthesized compound **3** was not only a probe for $^1O_2$, but also a good sensor for Li^+. Furthermore, the presence of $^1O_2$ triggered the detection of Li^+ ion.

Synthetic multistate and/or multifunctional systems may serve as models in unraveling the chemical basis of complex biological processes, and for the fabrication of devices at molecular-level directly related to signal generation, transfer, conversion, storage, and detection.[19,20]

In conclusion, we have shown that triad **3** is a new dual-functional sensor and may be useful for molecular optoelectronics or information processing at the molecular level. Further work on homologous crown moieties and more studies on their physical and chemical properties are under way in our laboratory.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (20531040 and 90501002). J.-L.Z. thanks the Program for New Century Excellent Talents in University of China (NCET-04-0469). The authors would like to thank the referees for their valuable comments and suggestions to improve the manuscript.

Supplementary data

Supplementary data (synthesis and additional characterization data for compound **3**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.03.055.

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13. Under a nitrogen atmosphere, the reaction mixture of **1** (0.534 g, 1.5 mmol) and **2** (0.682 g, 1.5 mmol) in 15 mL of freshly distilled $P(EtO)_3$ was heated at 110 °C for 1.5 h. Then, the solution was cooled to −20 °C and 40 mL of MeOH was added. Orange precipitate was obtained and purified by a short silica column. Yield 30%. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 2.62 (2H, s), 2.96 (6H, s), 3.39–3.71 (14H, m), 4.39 (2H, s), 7.39–7.46 (4H, m), 7.93 (2H, d, $J = 8.1$ Hz), 8.18 (1H, s), 8.27 (2H, d, $J = 8.1$ Hz); ^{13}C

NMR (500 MHz, $CDCl_3$, ppm): δ 18.38, 29.33, 31.00, 35.56, 35.94, 69.54, 70.28, 71.08, 73.41, 76.55, 76.80, 117.84, 122.61, 123.16, 124.96, 125.14, 125.50, 125.98, 128.93, 132.76, 150.61. ESI-MS: m/z 770.1 ($M+Li^+$). Anal. Calcd for $C_{33}H_{33}S_8O_4N$: C, 51.87; H, 4.35. N, 1.83; Found: C, 51.78; H, 4.23. N, 1.68.

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