Highly effective phosphate electrochemical sensor based on tetrathiafulvalene†

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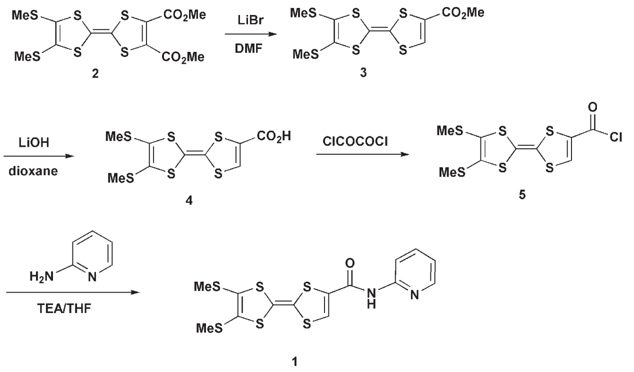
A neutral electrochemical chemosensor 1 based on TTF exhibited high selectivity for $H_2PO_4^-$ over a wide range of anions and the significant C–H···O hydrogen bonding between C=C–H of the TTF unit and $H_2PO_4^-$ played an important role in regulating the selectivity.

Over the past decades, anions in particular have received increasing attention as target analytes.[1] Fluorimetric, colorimetric, and electrochemical techniques have been utilized in a variety of approaches. Within the latter field, Beer's group has extensively studied the redox-responsive class of anion receptor based on transition-metal organometallic and coordination receptor systems.[2] The advantage of electrochemical detection is the stability and relative environmental insensitivity of electroactive labels compared with fluorophores that can quench or photo bleach. Although tetrathiafulvalene (TTF) is a strong π-electron donor, an ideal redox-active unit, and an organic neutral molecule,[3] only a few anion receptors incorporating TTF as the redox-active unit have been described in the literature. Becher *et al.* first reported the successful application of a mono-TTF calix[4]pyrrole as an electrochemical anion sensor.[4] Their results stimulate us to examine further the utility of TTF as an anion sensor.

In recent years, great efforts have been devoted to the design of new chemosensors for recognition of dihydrogen phosphate which is of biological and environmental significance.[5] However, due to the limitations in some systems, the inherent tetrahedral structure of phosphate ion is still a challenging problem for the design of effective receptors.

Neutral receptors of the amide type are particularly interesting; amide groups as a functional group are known to capture anions through hydrogen bonding between anions and the acidic hydrogen atoms on nitrogen atoms. So by combining an amide group with redox-active moiety TTF, we synthesized a relatively simple receptor **1**.

Scheme 1 shows a synthetic route for the receptor **1**. Reacting 1 equivalent of **5** with 4 equivalents of 2-aminopyridine, we obtained receptor **1** in 59% yield.‡ Compound **5** was prepared according to a protocol published by the Batail group.[6]



Scheme 1 Synthetic route for the receptor **1**.

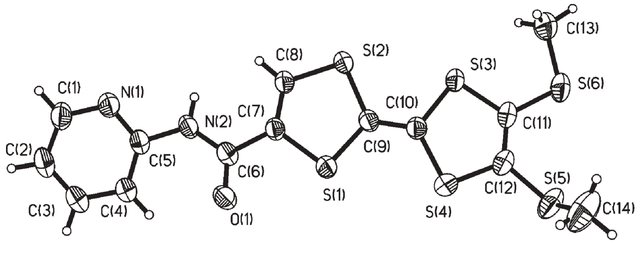


Fig. 1 Molecular structure of receptor **1** with 50% probability ellipsoids.

Single crystals of **1** were obtained by recrystallization in $CHCl_3$–CS_2 and the X-ray structure analysis was performed.§ Fig. 1 shows the molecular structure of **1** in the crystal. The TTF core has adopted a slight boat-shape conformation; the folding angles of the two C_3S_5 rings are 9.28° (left) and 1.65° (right) respectively, and the dihedral angle between the pyridine ring and the TTF core is about 14.76°. Intermolecular hydrogen bonds could be observed in the crystals between the N(2)–H(2), C=C–H of a TTF unit of one molecule and O(1) of an adjacent molecule (see Supporting Information). These hydrogen bonds may help us to understand the recognition behavior of receptor **1** toward anions studied in the following section.

The binding properties of **1** toward anions were evaluated using different methods including ^{1}H NMR and cyclic voltammetry (CV). The results showed that the receptor **1** has high affinity toward $H_2PO_4^-$.

^{1}H NMR experiments in $CDCl_3$ were performed to look into the anion binding properties. All counterions to the anions are tetrabutylammonium. Fig. 2 shows a partial ^{1}H NMR spectrum of **1**. When $H_2PO_4^-$ was added to the solution of **1**, dramatic changes occurred. Upon addition of 2 equivalents of $H_2PO_4^-$, the C=C–H of the TTF unit shifted downfield significantly ($\Delta\delta$ = 0.72 ppm), which suggested that the C=C–H of the TTF unit formed a strong

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† Electronic supplementary information (ESI) available: details of synthetic experimental, CV studies, ^{1}H NMR studies and X-ray crystallography. See http://dx.doi.org/10.1039/b509133k

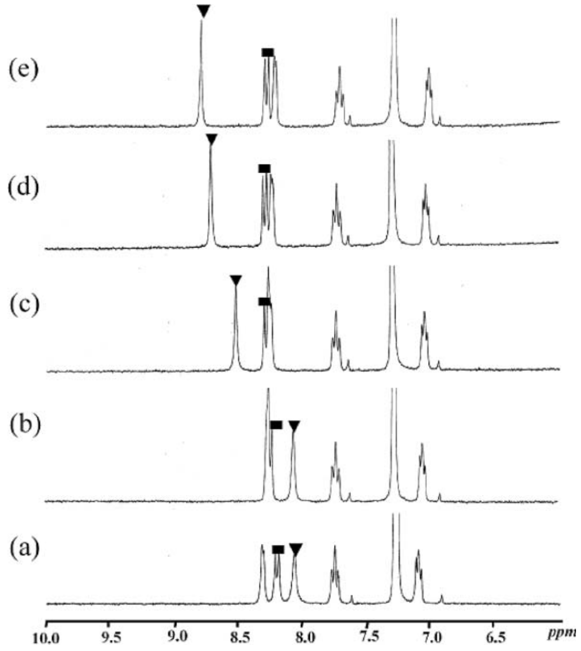

Fig. 2 Partial ^{1}H NMR spectra (300 MHz) recorded in $CDCl_3$: (a) free receptor **1**, (b) **1** + 0.5 equiv. $H_2PO_4^-$, (c) **1** + 1 equiv. $H_2PO_4^-$, (d) **1** + 1.5 equiv. $H_2PO_4^-$, (e) **1** + 2 equiv. $H_2PO_4^-$. ▼ C=C–H ■ α-H of pyridine group.

hydrogen bond with $H_2PO_4^-$; the α-H of pyridine[7] also showed a slight downfield shift ($\Delta\delta = 0.11$ ppm), which indicated that the N atom of pyridine participated in the formation of hydrogen bonding also. Unfortunately, the NH signal was not observed. However, when ^{1}H NMR experiments were performed in DMSO-d_6, the NH signal was observed but disappeared or broadened upon addition of $H_2PO_4^-$ (Supporting Information).

Determination of the stoichiometry and structure is essential for understanding the mechanism of a sensing system. The 2 : 1 complexation stoichiometry of the receptor **1** with $H_2PO_4^-$ could be determined by a continuous variation method (Job's method)[8] (Supporting Information). In addition, the result of computer modeling (LDA–DFT methods)[9] was consistent with observations in our case (Fig. 3). $H_2PO_4^-$ with four oxygens made the strongest complexes *via* six hydrogen-bonding interactions with two molecules of receptor **1**, which were believed to account for the high phosphate affinity observed for receptor **1**. The binding energy was obtained from the energy of the complex subtracted by the sum of energies of constituents ($\Delta E = -92.73$ kcal/mol). The interaction was very strong due to charged hydrogen bonds.

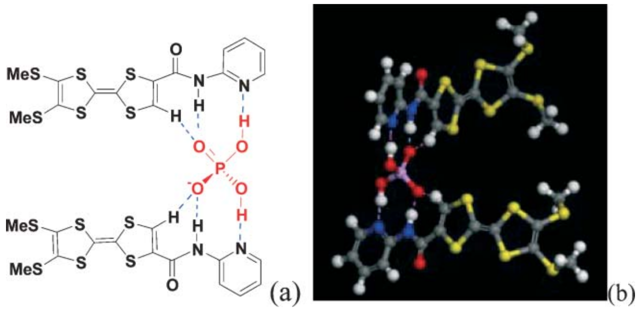

Fig. 3 (a) Schematic representation of the suggested multiple hydrogen bonding interactions; (b) computational optimized structure of $1_2{\cdot}H_2PO_4^-$.

Fig. 4 shows a comparison of the ^{1}H NMR spectrum of **1** upon addition of 2 equivalents of F^-, AcO^-, HSO_4^-, $H_2PO_4^-$. In the case of F^-, AcO^-, the C=C–H of the TTF unit showed a significant upfield shift, which could be the result of an electrostatic effect. In the case of HSO_4^-, C=C–H and α-H of pyridine showed a slight downfield shift ($\Delta\delta = 0.05$ ppm and $\Delta\delta = 0.17$ ppm respectively).

Cyclic voltammetry (CV) was employed to evaluate the recognition properties of receptor **1**. Upon addition of AcO^-, F^-, Cl^-, Br^-, E_1^{ox}, E_2^{ox} showed no obvious changes (Supporting Information). On the other hand, the progressive addition of $H_2PO_4^-$ to the solution of **1** caused clear modifications in the CVs (Fig. 5). It could be observed that two new oxidation peaks appeared besides the original oxidation peaks of receptor **1**. And the peak current of these new waves increased gradually on increasing the amount of the $H_2PO_4^-$, meanwhile the peak current of the original waves decreased gradually and disappeared when 2 equiv. of $H_2PO_4^-$ were added. These two new oxidation peaks should correspond to the disappeared original waves, the first oxidation peak cathodically shifted by 100 mV from that of the free receptor, and the second oxidation peak positively shifted by 158 mV from that of the free receptor. The appearance of the first new oxidation peak could be explained by a strong propensity for delocalization of the negative charge from the binding site C=C–H···$H_2PO_4^-$ to the TTF core.[4] The computer modeling also proved this hypothesis; the results indicated that about 20% of the negative charge was delocalized to the TTF core, and the HOMO energy of the complex was increased by about 2.1 eV compared

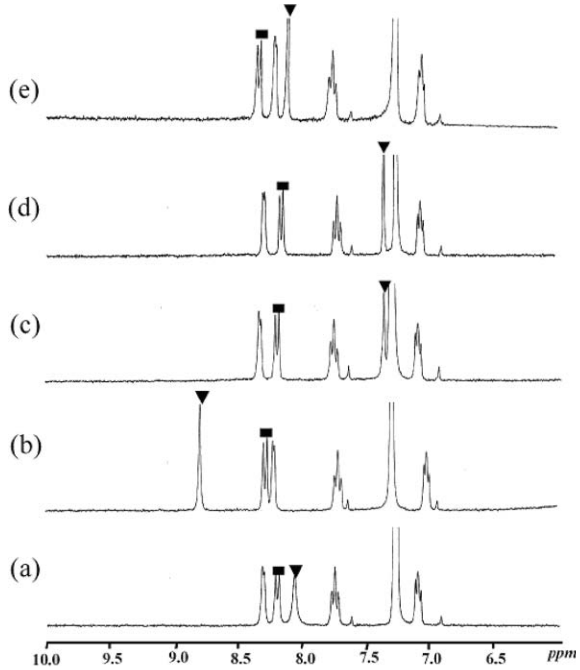

Fig. 4 Partial ^{1}H NMR spectra (300 MHz) recorded in $CDCl_3$: (a) free receptor **1**; (b) **1** + 2 equiv. of $H_2PO_4^-$; (c) **1** + 2 equiv. of F^-; (d) **1** + 2 equiv. of AcO^-; (e) **1** + 2 equiv. of HSO_4^-. ▼ C=C–H ■ α-H of pyridine group.

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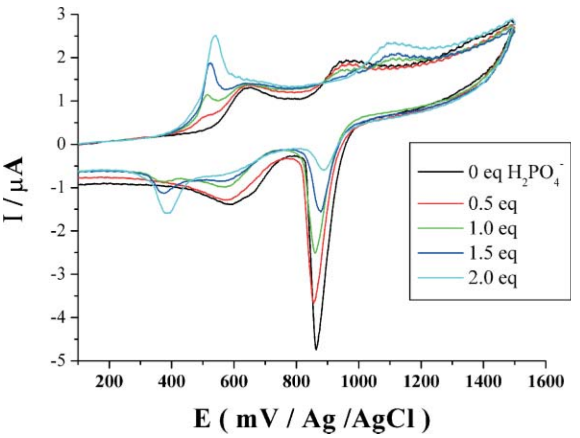

Fig. 5 Cyclic voltammograms of the receptor **1** (1.67×10^{-4} M) recorded in CH_2Cl_2 at 298 K with n-Bu_4NClO_4 (0.1 M) as the supporting electrolyte in the presence of increasing amounts of n-$Bu_4NH_2PO_4$.

with that of the free receptor. As a consequence, the **1**–$H_2PO_4^-$ complex is either easier to oxidize or harder to reduce than the free redox-active receptor. Upon complexation with $H_2PO_4^-$, two TTF units would likely provide a pseudo-tetrahedral cleft to hold $H_2PO_4^-$ *via* hydrogen bonding. As a consequence, a di-TTF complex was formed which is attributed to the positive shift of the second oxidation.[10] As far as HSO_4^- is concerned, it is more acidic than $H_2PO_4^-$ and may protonate the pyridine group, so the CV looked more complex. However, it did not affect the electrochemical recognition of $H_2PO_4^-$ with high selectivity.

To test the practical applicability of **1** as a $H_2PO_4^-$ selective electrochemical chemosensor, competition experiments were carried out. Receptor **1** (1.67×10^{-4} M) was treated with 1.5 equiv. $H_2PO_4^-$ in the presence of background anions (1.5 equiv.) (Supporting Information). The results showed that the background anions demonstrated little or no obvious interference with the detection of $H_2PO_4^-$.

We also tested the effect of the pH on the selectivity of **1**. Upon addition of Bu_4NOH, the successive deprotonations of $H_2PO_4^-$ led to the formation of HPO_4^{2-}, PO_4^{3-}, respectively (Supporting Information). The new E_1^{ox} disappeared when the concentration of Bu_4NOH was increased up to 2 equiv. This phenomenon implied that **1** showed high selectivity towards $H_2PO_4^-$.

In conclusion, we have presented a neutral and simple electrochemical sensor based on TTF, which effectively and selectively recognized $H_2PO_4^-$ over various anions. Especially, these binding phenomena can be detected by electrochemical means. The C=C–H moiety of the TTF unit played an important role in regulating the affinity to the anion through the hydrogen bonding. So the receptor **1** may be considered as a potential $H_2PO_4^-$ selective electrochemical sensor.

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Notes and references

‡ Selected data for new compound **1**: ^1H NMR (DMSO-d_6) δ 11.00 (s, NH, 1H), 8.38 (d, J = 3.27 Hz, 1H), 8.13 (s, C=C–H, 1H), 7.97 (d, J = 10.05 Hz, 1H), 7.82 (t, J = 7.59, 7.68 Hz, 1H), 7.17 (t, J = 5.73, 5.46 Hz, 1H), 2.50 (s, 6H) ppm. ^{13}C NMR: δ 158.2, 151.8, 148.5, 138.8, 133.7, 128.5, 127.3, 126.7, 120.6, 114.95, 113.2, 107.1, 18.99 ppm. MS *m*/*z*: 416 [M^+].

§ Crystal data for **1**: brown block ($0.68 \times 0.49 \times 0.40$ mm), $C_{14}H_{12}N_2OS_6$, MW = 416.62, monoclinic, space group $P2(1)/c$, a = 10.683(2), b = 16.387(3), c = 10.065(2) Å, V = 1761.7(6) $Å^3$, T = 293 K, μ = 0.779 mm^{-1}, Z = 4, 3989 reflections measured, 3989 unique (R_{int} = 0.000). Final R indices [$I > 2\sigma(I)$]: $R1$ = 0.0399, $wR2$ = 0.1051. R indices (all data): $R1$ = 0.0537, $wR2$ = 0.1106. CCDC 277407. See http://dx.doi.org/10.1039/b509133k for crystallographic data in CIF or other electronic format.

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7 The X-ray crystal structure of compound **1** showed that the intramolecular C(4)–H···O hydrogen bonded distance was 2.34.

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