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Synthesis and Reactivity of a Bio-inspired Dithiolene ligand and its Mo-oxo complex

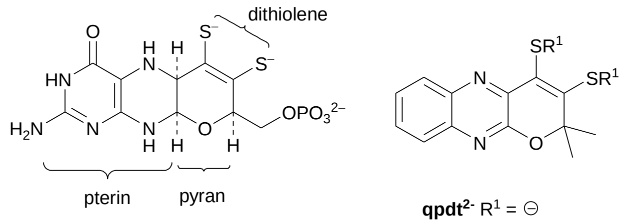
Jean-Philippe Porcher,[a] Thibault Fogeron,[a] Maria Gomez-Mingot,[a] Lise-Marie Chamoreau,[a] Yun Li*[a] and Marc Fontecave*[a]

Abstract: An original synthesis of the fused pyrano-quinoxaline dithiolene ligand, $qpdt^{2-}$, is discussed in detail. Specially, the most intriguing step was the introduction of the dithiolene function by the Pd-catalyzed carbon-sulfur coupling reaction. The corresponding $Mo^{IV}O$ complex $(Bu_4N)_2[MoO(qpdt)_2]$ (**2**) enjoyed reversible protonation in a strong acidic medium and remained stable under anaerobic conditions. Besides, **2** was found to be very sensitive towards oxygen forming a planar dithiin derivative. Moreover, the $qpdt^{2-}$ ligand in the presence of $[MoCl_4(t\text{BuNC})_2]$ formed an original tetracyclic structure. The products obtained from the unique reactivity of $qpdt^{2-}$ have been characterized by X-ray diffraction, mass spectrometry, NMR spectroscopy, UV-Vis spectroscopy and electrochemistry. The plausible mechanisms for the formation of these products are also enclosed.

Introduction

Six families of Mo or W containing enzymes (oxidoreductases, hydrolases, etc...)[1] have been discovered and characterized structurally by X-ray diffraction methods so far.[2] In general a single Mo/W ion is coordinated by molybdopterin (MPT, Figure 1), which is an unstable fused pyranopterin system containing a dithiolene chelate. During the catalytic cycle, the oxidation number of Mo/W varies from +4 to +6, while the MPT structure remains unchanged.

Several bioinorganic groups have focused their efforts on synthesizing Mo/W-dithiolene complexes as structural and functional analogues of these active sites. The pioneer work was launched by Holm's group[3] over 20 years ago and was followed by others.[4] We here report the synthesis of a new fused pyrano-quinoxaline dithiolene ligand, $qpdt^{2-}$, under its protected form **1** (Figure 1). To our knowledge, only very few examples of such dithiolene ligands have been reported so far. Recently, Basu *et al.* have developed the synthesis of an analogue of **1** and used it as a specific probe for Pb^{2+} detection.[5] However, this synthetic route required several delicate steps with moderate yields, especially for the pyran ring closure step. No Mo/W complex was reported in their work. Garner and co-workers have synthesized a tricyclic pyranopterin dithiolene ligand system (including the pyrimidine ring).[6] But they failed to complex a Mo/W ion. A Co complex was isolated and characterized instead. Burgmayer's group have reported the synthesis of the Mo^{IV}/Mo^{V} complexes Tp*MoO(pyrano-S_2BMOPP), where Tp* is tris(3,5-dimethylpyrazolyl)hydroborate and "pyrano-S_2BMOPP" is a tricyclic pyranopterin dithiolene chelate. The pyran ring is formed through a solvent-dependent spontaneous cyclization.[7]



MPT

qpdt²⁻ $R^1 = \ominus$
1 $R^1 = CH_2CH_2CO_2Et$

Figure 1. The structures of MPT, ligand $qpdt^{2-}$ and its protected form **1**.

In a previous communication we have shown that $qpdt^{2-}$ can be used to synthesize a $Mo^{IV}O$ complex $(Bu_4N)_2[MoO(qpdt)_2]$ (**2**, Figure 2). This complex acts as a remarkable catalyst for electro- and photo- reduction of protons into H_2 in organic solvents.[8] In the current study, we describe reactions of this complex in the presence of protons and oxygen. Finally, the reactivity of the dithiolene towards $[MoCl_4(t\text{BuNC})_2]$ is also reported. All these reactions illustrate the unique chemical reactivity of this original biomimetic complex.

Results and Discussion

1. Synthesis of the ligand

As regards the synthetic strategy, it seems that the great difficulty resides in the pyran ring closure step.[5] To circumvent this problem, we chose to first prepare the tricyclic skeleton, and to introduce the dithiolene function in a second stage. For this purpose, the bromo-enol **3** was synthesized. 2,3-dichloroquinoxaline (**4**), underwent a Sonogashira coupling followed by a pyran ring closure step with sodium methylate to afford methyl enol-ether **6**, according to a reported procedure.[9] After hydrolysis of **6** under acidic conditions, controlled mono-bromination of **7** at low temperature afforded **3** in 89 % yield (Scheme 1).

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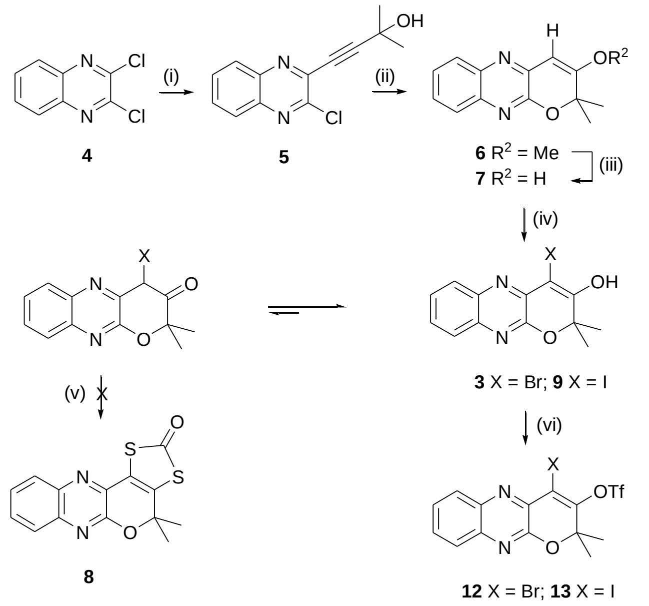
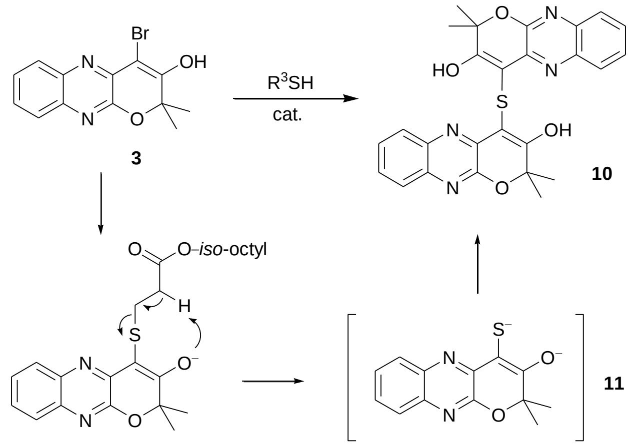


Scheme 1. Tentative formation of dithiocarbonate **8**. Reaction conditions: (i) HC≡CC(OH)Me_2, $PdCl_2(PPh_3)_2$ (3 %), CuI (6 %), *i*Pr_2NEt, THF, RT, 16 h (84 %); (ii) MeONa, MeOH, reflux, 1.5 h, (65 %); (iii) HCl (1 M), THF, RT, 16 h (95 %); (iv) for **3**: Br_2, CH_2Cl_2, 0 °C, 0.5 h (89 %); for **9**: I_2, CH_2Cl_2, 0 °C, 0.5 h (68 %); (v) a) *i*PrOC(S)SK; b) 70 % $HClO_4$; (vi) Tf_2O, *i*Pr_2NEt, CH_2Cl_2, RT, 89 % for **12** and 68 % for **13**.

In order to prepare the dithiocarbonate **8** as a protected dithiolene ligand, compound **3** was first treated with O-*iso*-propylxanthic acid potassium salt, a classical method for introducing a dithiocarbonate from an α-bromoketone.[10] Despite many attempts under different experimental conditions (reaction temperatures, solvents…), no nucleophilic substitution product was obtained. Only the starting compound **3** was detectable by ^{1}H NMR spectroscopy. The same results were obtained even when the iodo-enol **9** was employed as the starting reagent. It is likely that, in both **3** and **9**, the keto-enol equilibrium is strongly displaced towards the enol form, according to the ^{1}H NMR data (δ_{OH} = 8.42 ppm, 1H for **3** and δ_{OH} = 8.47 ppm, 1H for **9**, D_2O exchangeable for both protons) and therefore the substitution reaction by a S-nucleophile is disfavored.

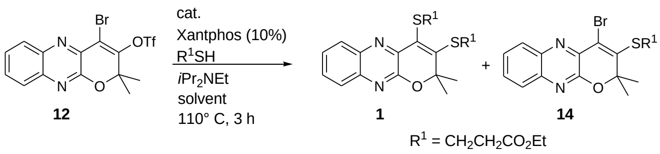
Itoh *et al.* have developed a general carbon-sulfur bond formation method *via* a palladium-catalyzed coupling reaction of aryl bromides/triflates and thiols.[11] In order to insert a thiol surrogate, we extended this methodology to the vinyl bromide function in **3**. Thioacetic acid and *iso*-octyl-3-mercaptopropionic acid were tested (Scheme 2). The dimerization product **10** was obtained in both cases. This result strongly suggests that a de-protection step assisted by the adjacent enolate occurred after thiol insertion, resulting in a highly nucleophile thiolene intermediate **11** (Scheme 2). However, what is remarkable is that a protected thiol could indeed replace a vinyl bromide under this condition.



Scheme 2. Formation of dimer **10**. Reaction conditions: $Pd(OAc)_2$ (2.5 %), Xantphos (5 %), *i*Pr_2NEt, 1,4-dioxane, 80 °C, 3 h; R^3SH = AcSH or $HSCH_2CH_2CO_2$(*iso*-octyl). Reaction yields = 77 % and 70 %, respectively.

We decided next to prepare the corresponding bromo-vinyl triflate **12** and iodo-vinyl triflate **13** under standard conditions (Tf_2O / *i*Pr_2NEt / CH_2Cl_2, Scheme 1). Both **12** and **13** were submitted to a double palladium-catalyzed cross-coupling reaction with two equivalents of $HSCH_2CH_2CO_2Et$. The iodo derivative **13** gave a complex mixture after the reaction.

Table 1. Synthesis of **1** by a double Pd-catalyzed cross-coupling reaction



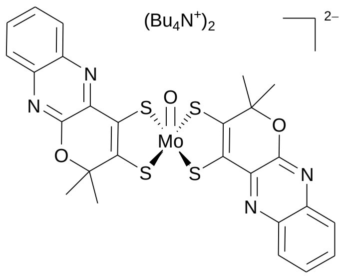
Entry	cat. (equiv.)	R^1SH (equiv.)	*i*Pr_2NEt (equiv.)	solvent	**1/14**[a]
1	$Pd(OAc)_2$ (0.1)	2.2	3	dioxane	no reaction
2	$Pd(dba)_2$ (0.1)	2.2	3	DMF	57/43
3	$Pd_2(dba)_3$ (0.05)	2.2	3	DMF	51/49
4	$Pd(dba)_2$ (0.1)	4	5	dioxane	58/42
5	$Pd_2(dba)_3$ (0.05)	4	5	dioxane	54/46
6	$Pd(dba)_2$ (0.1)	2.2	3	dioxane	75/25 (66/21)[b]
7	$Pd_2(dba)_3$ (0.05)	2.2	3	dioxane	88/12 (77/8)[b]

[a]The ratios are determined by ^{1}H NMR spectroscopy. [b]The yields correspond to isolated products.

However, starting with **12**, it was possible to isolate the protected dithiolene ligand **1**, along with the mono-substituted product **14** (Table 1). As expected, the vinyl triflate function was more reactive than the vinyl bromide one. In order to optimize the yield of **1**, different conditions (solvents, catalysts and the amount of the thiol) were tested. The results are listed in Table 1. The best result was obtained with $Pd_2(dba)_3$ (5 %) and Xantphos (10 %) in dioxane in the presence of 2.2 equiv. of $HSCH_2CH_2CO_2Et$ and 3 equiv. of *i*Pr_2NEt at 110 °C (entry 7). Under the same conditions, $Pd(dba)_2$ (10 %) gave a slightly lower yield of **1** (entry 6). $Pd(OAc)_2$ did not catalyze this reaction (entry 1). DMF is a less good solvent than 1,4-dioxane (entries 2 and 3). Finally, the isolated compound **14** could be again transformed to **1** in 75 % yield under the same conditions. Both **1** and **14** are fully characterized, especially by ^1H and ^{13}C NMR spectroscopy (Figure S1- S4, Supporting Information). Thus, we show for the first time that this cross coupling reaction leading to sulfurated compounds can be extended to functionalized vinyl derivatives.

2. Complexation and reactivity of 1 towards Mo^{4+} ion

1 was treated with *t*BuOK under anaerobic conditions to generate the dithiolene ligand $qpdt^{2-}$ (Figure 1). Due to its instability, this latter was not isolated and was directly reacted with $K_3Na[MoO_2(CN)_4].6H_2O$[12] to afford the square planar pyramidal, mononuclear complex $(Bu_4N)_2[Mo^{IV}O(qpdt)_2]$ (**2**, Figure 2) after cation exchange with Bu_4NBr.[8]



2 $(Bu_4N)_2[Mo^{IV}O(qpdt)_2]$

Figure 2. The Mo-oxo complex $(Bu_4N)_2[MoO(qpdt)_2]$ (**2**).

2.1. Reactivity of $(Bu_4N)_2[Mo^{IV}O(qpdt)_2]$ towards protons

Figure 3 shows the UV-Vis spectrum of 50 μM $(Bu_4N)_2[Mo^{IV}O(qpdt)_2]$ in CH_3CN with its three characteristic absorption bands at 322, 374 and 470 nm. The addition of increasing amounts of trifluoroacetic acid (TFA) resulted in drastic changes of the UV-visible spectrum. After addition of 1 equivalent of TFA, a first species was formed with a characteristic absorption at 592 and 440 nm. Further addition of TFA led to evolution of a second species with a main prominent absorption band at 564 nm and a shoulder at 510 nm and three small bands in the 300- 400 nm range. The mass spectrum of the species resulting from the reaction of **2** with 10 equivalents of TFA demonstrates a double protonation of complex **2** with a mass corresponding to $\{[MoO(qpdt)_2] + 2H^+\}$., nicely fitting with the theoretical spectrum, m/z = 663.9 (calcd. for $C_{26}H_{22}MoN_4O_3S_4$: m/z = 663.9629) (Figure S5). Thus, reaction of **2** with one equivalent of TFA quantitatively converts it into a mono-protonated species while a large excess of acid is required to displace the equilibrium towards the doubly protonated species.

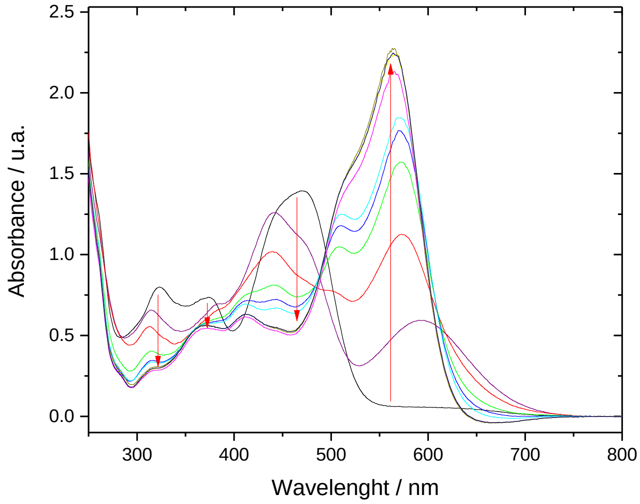


Figure 3. UV-Vis spectrum of 50 μM $(Bu_4N)_2[Mo^{IV}O(qpdt)_2]$ in acetonitrile (black curve). Additions of TFA: 1equiv. (purple), 2 equiv. (red), 3 equiv. (green), 4 equiv. (blue), 5 equiv. (light blue), 10 equiv. (magenta), 25 equiv. (yellow), 50 equiv. (dark yellow) and 100 equiv. (navy).

The cyclic voltammogram of **2** in CH_3CN displays a reversible redox couple at -0.19 V *vs.* Ag/AgCl electrode that has been assigned to the Mo^{IV}/Mo^{V} couple.[8] Addition of TFA triggers a shift of the potential towards more positive potentials, with a slight loss of current intensity (Figure 4). This shift follows the same trend than that of the absorbance at 564 nm for the same number of equivalents in TFA (Figure 5). Similar results have been recently published by Dicks *et al.*[13] with simplified asymmetric ene-1,2-dithiolate Co complexes, $[(\eta^5\text{-}C_5H_5)Co\{SC(H)CRS\}]$ where [R= pyridine-3-yl or pyrazine-2-yl]. In this work, they observed that the presence of a 5 : 1 excess of TFA facilitated the reduction of the complexes, i.e. the reduction occurred at more positive potentials. This was attributed to the protonation of a pyrazine-2-yl ring N atom. Our previous DFT calculations showed that N atom of the central cycle of **2** is likely to be the first protonation site.[8] A second protonation on the same cycle can occur however less favorably because of electrostatic repulsion. These protonation events facilitate reduction of **2**, explaining the low overpotential observed during photo- and electro- proton reduction catalyzed by **2**.

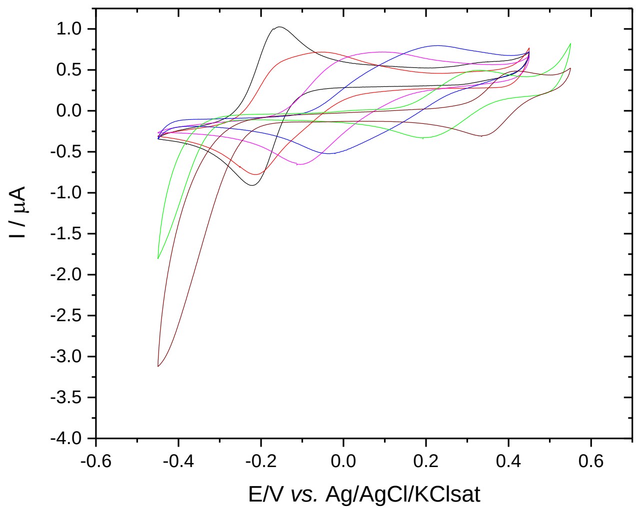


Figure 4. Cyclic voltammograms of 1 mM solutions of $(Bu_4N)_2[Mo^{IV}O(qpdt)_2]$ in 0.1 M TBAP in CH_3CN under Ar conditions in the presence of TFA: no acid (black), 1 mM (red), 3 mM (magenta), 5 mM (blue), 10 mM (green) and 25 mM (brown) TFA. Further additions of TFA have no effect on the CV. In all cases the third scan is represented. Scan rate 50 mV s^{-1}; glassy carbon electrode.

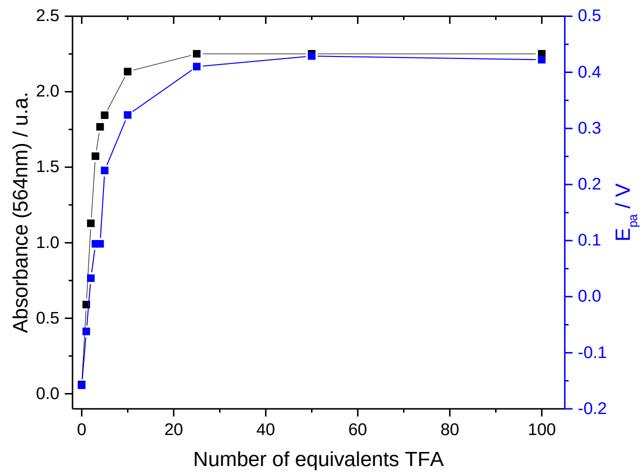


Figure 5. Plot of the absorbance of $(Bu_4N)_2[Mo^{IV}O(qpdt)_2]$ (black squares) at 564 nm and the corresponding anodic potential peak (blue squares) as a function of the number of equivalents of TFA.

Interestingly, the shift of 600 mV on the peak potential of the Mo^{IV}/Mo^{V} couple upon addition of 100 equivalents of TFA turned out to be reversed upon subsequent neutralization with base (triethylamine, Et_3N) (Figure S6). This reversibility was also observed by UV-visible spectroscopy (Figure S7). These data show that under anaerobic and strong acidic conditions, $(Bu_4N)_2[MoO(qpdt)_2]$ (**2**) is not degraded. It undergoes a reversible protonation process, which can be monitored by UV-visible spectroscopy and cyclic voltammetry.

2.2. Reactivity of $(Bu_4N)_2[Mo^{IV}O(qpdt)_2]$ towards O_2

In solution (CH_3CN or $CDCl_3$), complex **2** is sensitive to O_2. The yellow-green color turned almost instantaneously to orange under exposure to air. The oxidized product was isolated and characterized as the dithiin derivative **15**. Single crystals were obtained as orange plates by slow evaporation of an acetonitrile solution containing the crude product. An ORTEP diagram of the molecular structure of **15**[14] shown in Figure 6 reveals a highly conjugated molecule with nearly all the atoms in one plane.

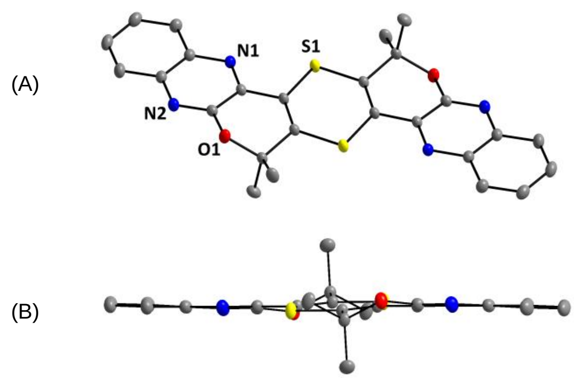
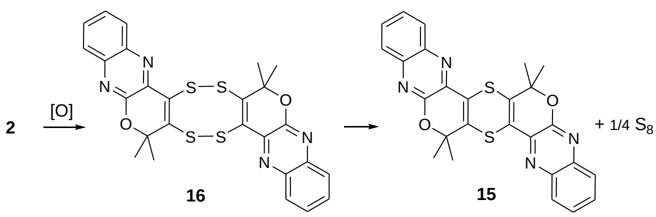


Figure 6. Crystal structure (ellipsoids drawn at 50 % probability) of **15** (A) with nearly all the atoms in one plane (B). Hydrogen atoms are omitted for clarity.

The proposed mechanism for the formation of **15** is depicted in Scheme 3. During the oxidative dimerization reaction, **2** first lost its metal ion to form the bis-disulfide **16**, then a rearrangement took place to give the more stable dithiin **15** by elimination of two sulfur atoms of the ligand. This hypothesis was confirmed by positive-ion electrospray mass spectra of **2** in acetonitrile solution upon exposure to air after 1 and 30 minutes, respectively. A peak at m/z = 549 (corresponding to [**16** + H]$^+$) in the first case (Figure S8), and another one at m/z = 485 (corresponding to [**15** + H]$^+$) in the second case (Figure S9), were observed. This mechanism is comparable to the previously reported one for the air oxidation of disodium dimercaptomaleodinitrile (Na_2mnt) giving tetracyano-1,4-dithiin as the product.[15] To our knowledge, it is the first time that the air oxidation product of a $Mo^{IV}(dithiolene)_2$ complex was structurally characterized.



Scheme 3. Formation of dithiin **15** from $[Mo^{IV}O(qpdt)_2]^{2-}$ under air oxidation.

2.3. Reactivity of qpdt^{2-} towards [$MoCl_4$(*t*BuNC)$_2$]

The de-protected ligand qpdt^{2-} was allowed to react with another Mo^{4+} reagent [$MoCl_4$(*t*BuNC)$_2$], in order to generate a new bis-dithiolene bis-isocyanide Mo^{IV} complex [Mo^{IV}(qpdt)$_2$(*t*BuNC)$_2$] (**17**, Scheme 4), by a previously reported procedure.[16] The starting [$MoCl_4$(*t*BuNC)$_2$] was generated *in situ* by [$MoCl_4$(CH_3CN)$_2$)] and an excess of *t*BuNC. However, no trace of **17** could be detected by electrospray mass spectroscopy. A new tetracyclic imino-thiazole derivative **18** was isolated instead. Single-crystal X-ray analysis of **18**[14] revealed a quite original tetracyclic structure with a C=S bond on the pyran ring (Figure 7).

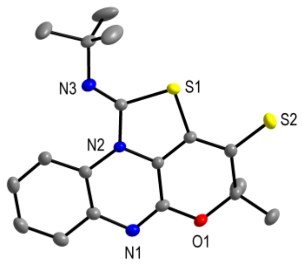
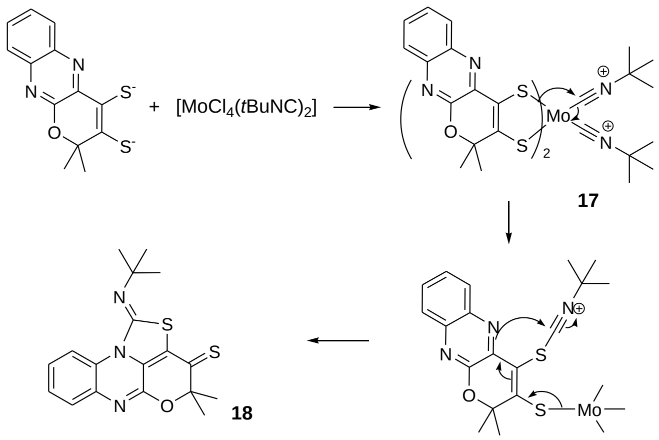


Figure 7. ORTEP representation of imino-thiazole **18** at 50 % probability. Hydrogen atoms are omitted for clarity.

In a separate experiment, the qpdt^{2-} ligand was treated with *t*BuNC in the absence of [$MoCl_4$(CH_3CN)$_2$)] and **18** was not observed by ^{1}H NMR spectroscopy. The proposed mechanism is outlined in Scheme 4. We suggest that due to the presence of the neighboring nitrogen atom, a rearrangement took place after the formation of complex [Mo(qpdt)$_2$(*t*BuNC)$_2$] **17**, leading to the original tetracyclic imino-thiazol **18**.



Scheme 4. A proposed mechanism for the formation of **18**.

Conclusions

We have developed an unprecedented efficient method to synthesize a bio-inspired dithiolene ligand which is closely related to the biological molybdopterin ligand. The corresponding Mo-oxo complex, which nicely mimics the active site of Mo-enzymes, with Mo being bis-coordinated by this ligand was also obtained.[8] Investigation of the reactivity of the Mo-dithiolene assembly towards protons, oxygen and isocyanides led to new reactions and original products, which have been spectroscopically and structurally characterized. This provides new insights into Mo-dithiolene chemistry which might have some biological relevance.

Experimental Section

General methods

All starting materials were commercially available and were used without further purification. Solvents were purified by an MBRAUN SPS-800 Solvent Purification System. All reactions were carried out under air atmosphere unless specified. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-III 300 NMR spectrometer (300 MHz for ^{1}H, 75 MHz for ^{13}C) at room temperature. High-resolution mass spectra (HRMS) were recorded on a LCT Premier XE mass spectrometer using ESI (electrospray ionization) at Institut de Chimie des Substances Naturelles in Gif-sur-Yvette. Mass spectra (MS) were recorded on an Applied Biosystems QSTAR pulsar I mass spectrometer using ESI (electrospray ionization) at Muséum National d'Histoire Naturelle (Paris). Flash chromatography was performed on Grace Reverlis® x2 with corresponding cartridges. UV-Vis spectra were recorded using a Cary 100 UV-Vis spectrophotometer instrument (Agilent). Voltammetric measurements were performed using a SP 300 Bio-Logic potentiostat (Bio-Logic Science Instruments SAS). All measurements were conducted using a three electrode system. A platinum wire, a glassy carbon (1 mm diameter) and a saturated Ag/AgCl/KCl saturated electrode were used as a counter and reference electrodes, respectively. Cyclic voltammograms were recorded in anhydrous acetonitrile (Sigma) containing 0.1 M tetrabutylammonium perchlorate (TBAP, Sigma) in anaerobic conditions at room temperature.
Synthesis of **3**, **7** and **12** were reported earlier.[8]

4-(3-chloroquinoxalin-2-yl)-2-methylbut-3-yn-2-ol (5). Under an Ar atmosphere, to a solution of 2,3-dichloroquinoxaline (10 g, 50.2 mmol) in dry THF (45 mL) were added CuI (619 mg, 3.26 mmol) and $PdCl_2(PPh_3)_2$ (1.056 g, 1.51 mmol). *i*Pr_2NEt (16.6 mL, 95.38 mmol) was slowly added *via* a syringe to give an orange suspension. 2-methylbut-3-yn-2-ol (4.217g, 50.2 mmol) was then slowly added to the mixture *via* a cannula needle. The suspension was stirred at room temperature overnight and led to a dark orange suspension. The reaction mixture was concentrated *in vacuo* and extracted with CH_2Cl_2 three times. The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. Purification of the crude product by flash chromatography over silica gel using EtOAc : cyclohexane (1 : 4) as an eluent gave a brown oil (10.452 g, 84 %). ^{1}H NMR ($CDCl_3$) *δ* 8.11 (m, 1H, Ar), 8.02 (m, 1H, Ar), 7.86 – 7.74 (m, 2H, Ar), 2.39 (s, 1H, D_2O exchangeable, OH), 1.74 (s, 6H, CH_3). This spectrum was identical to the previously reported one.[9]

3-Methoxy-2,2-dimethyl-2H-1-oxa-9,10-diaza-anthracene (6). Under an Ar atmosphere, sodium hydride (60 % in mineral oil, 8.48 g, 212 mmol) was added in small portions to methanol (66 mL) at 0° C. The white suspension was allowed to stir for 10-15 minutes at room temperature until no more gas evolvement could be observed. A solution of **5** (10.452 g 42.4 mmol) in 17 mL of methanol was slowly added *via* a cannula needle. The green/dark suspension was stirred at 80 °C for 1.5 h. MeOH was evaporated under reduced pressure. The usual work-up with EtOAc gave a crude product, which was purified by flash chromatography over silica gel (eluting with EtOAc : cyclohexane, 15 : 85). 5.951 g (58 %) was obtained. ^{1}H NMR ($CDCl_3$) *δ* 7.86 (m, 1H, Ar), 7.78 (m, 1H, Ar), 7.52 (m, 2H, Ar), 5.95 (s, 1H, CH), 3.67 (s, 3H, CH_3), 1.67 (s, 6H, CH_3). This spectrum was identical to the previously reported one.[9]

4-iodo-2,2-dimethyl-2H-1-oxa-9,10-diaza-anthracen-3-ol (9). Under an Ar atmosphere, a solution of I_2 (111 mg, 0.438 mmol) in dry CH_2Cl_2 (1 mL) was added dropwise to a solution of **8** (100 mg, 0.438 mmol) in dry CH_2Cl_2 (1.5 mL) *via* a syringe at 0° C. A suspension gradually formed. After 30 min, the reaction mixture was neutralized by careful addition of an aqueous solution of $NaHCO_3$. The usual work-up with CH_2Cl_2 gave a crude product, which was purified by flash chromatography over silica gel (eluting with THF : CH_2Cl_2, 5 : 95). A yellow powder (106 mg, 68 %) was obtained. ^{1}H NMR ($CDCl_3$): *δ* 8.47 (bs, 1H, D_2O exchangeable, OH); 7.59 (d, *J*=8.0 Hz, 1H, Ar), 7.42 – 7.20 (m, 3H, Ar), 1.70 (s, 6H, 2 CH_3). ^{13}C NMR ($CDCl_3$): *δ* 187.31 (C), 151.50 (C), 138.45 (C), 133.75 (C), 128.18 (CH), 127.24 (C), 125.46 (CH), 125.67 (CH), 114.79 (CH), 86.81 (C), 70.55 (C), 27.29 (2 CH_3). HRMS: *m/z* calcd. for $C_{13}H_{12}IN_2O_2$ [M + H]$^+$: 354.9944; found: 354.9951.

Thioether compound 10. Under an Ar atmosphere, in a 50 mL Schlenk flask, a mixture of **3** (50 mg, 0.163 mmol), Xantphos (9.5 mg, 0.163 μmol) and $Pd(OAc)_2$ (1.8mg, 8.15 μmol) in dry 1,4-dioxane (1 mL) was degassed under Ar for 30 min. *i*Pr_2NEt (57 μL, 0.326 mmol) and thioacetic acid (14 μL, 0.196 mmol) were then added. The brownish mixture was gently degassed under Ar for 10 min and kept at 80° C for 3 h. The reaction mixture was evaporated to dryness. The usual work-up with CH_2Cl_2 gave a crude product, which was purified by flash chromatography over silica gel (eluting with THF : cyclohexane, 5 : 95) to give **10** as a yellow powder (37 mg, 77 %). ^{1}H NMR ($CDCl_3$): *δ* 12.50 (s, 2H, D_2O exchangeable, 2 OH), 7.74-7.60 (m, 4H, Ar), 7.52-7.44 (m, 2H, Ar), 7.43-7.33 (m, 2H, Ar), 1.78 (s, 6H, 2 CH_3), 1.57 (s, 6H, 2 CH_3). ^{13}C NMR ($CDCl_3$) *δ* 192.42 (C), 152.60 (C), 141.11 (C), 134.48 (C), 128.46 (C), 128.42 (CH), 127.24 (CH), 126.07 (CH), 116.63 (CH), 94.93 (C), 86.88 (C), 27.15 (4 CH_3). HRMS: m/z calcd. for $C_{26}H_{23}N_4O_4S$ [M + H]$^+$: 487.1440; found: 487.1425.

Trifluoro-methanesulfonic acid 4-iodo-2,2-dimethyl-2H-1-oxa-9,10-diaza-anthracen-3-yl ester (13). Under an Ar atmosphere, to a solution of **3** (155 mg, 0.438 mmol) and *i*Pr_2NEt (115 µL, 0.657 mmol) in dry CH_2Cl_2 (3 mL) was added at 0 °C dropwise triflic anhydride (161 mg, 0.569 mmol). After 20 minutes at room temperature, water (1 mL) was added and the usual work-up with CH_2Cl_2 gave a crude product, which was purified by flash chromatography over silica gel (eluting with CH_2Cl_2) the yield a white powder (135 mg, 64 %). ^{1}H NMR ($CDCl_3$): *δ* 8.14 (dd, *J* = 1.0, 8.0 Hz, 1H, Ar), 7.90 (dd, *J* = 1.0, 8.0 Hz, 1H, Ar), 7.71 (m, 2H, Ar), 1.79 (s, 6H, 2 CH_3). ^{13}C NMR ($CDCl_3$) *δ* 157.38 (C), 151.21 (C), 141.31 (C), 140.52 (C), 137.21 (C), 131.61 (CH), 129.18 (CH), 128.32 (CH), 127.23 (CH), 118.50 (q, $J_{C,F}$ = 321.4 Hz, CF_3), 94.73 (C), 82.18 (C), 26.05 (2 CH_3). HRMS: *m/z* calcd. for $C_{14}H_{11}F_3IN_2O_4S$ [M + H]$^+$: 486.9436; found: 486.9475.

3,4-bis-(Ethoxycarbonyl-ethylsulfanyl)-2,2-dimethyl-2H-1-oxa-9,10-diaza-anthracen (1) and 3-(4-Bromo-2,2-dimethyl-2H-1-oxa-9,10-diaza-anthracen-3-ylsulfanyl)-propionic acid ethyl ester (14). Under an Ar atmosphere, in a 250 mL Schlenk flask, a mixture of **12** (3 g, 6.83 mmol), Xantphos (395 mg, 0.683 mmol) and $Pd(dba)_2$ (393 mg, 0.683 mmol) in dry 1,4-dioxane (60 mL) was degassed under Ar for 30 min. *i*Pr_2NEt (3.6 mL, 20.5 mmol) and $HSCH_2CH_2CO_2Et$ (1.9 mL, 15 mmol) were then added. The brownish mixture was gently degassed under Ar for 10 min. and kept at 110° C for 3.5 h. The reaction mixture was evaporated to dryness. The usual work-up with CH_2Cl_2 gave a crude product, which was purified by flash chromatography over silica gel (eluting with AcOEt : cyclohexane 5 : 95). **1** (a brown oil, 2.08 g, 64 %) and **14** (a brown oil, 535 mg, 19 %) were obtained.

1: ^{1}H NMR ($CDCl_3$): *δ* 8.06 (dd, *J* = 1.5, 8.0 Hz, 1H, Ar), 7.83 (dd, *J* = 1.5, 8.0 Hz, 1H, Ar), 7.66 (m, 1H, Ar), 7.59 (m, 1H, Ar), 4.17 (q, *J* = 7.0 Hz, 2H, CH_2), 4.10 (q, *J* = 7.0 Hz, 2H, CH_2), 3.33 (t, *J* = 7.0 Hz, 2H, CH_2), 3.31 (t, *J* = 7.0 Hz, 2H, CH_2), 2.67 (t, *J* = 7.0 Hz, 2H, CH_2), 2.62 (t, *J* = 7.0 Hz, 2H, CH_2), 1.74 (s, 6H, CH_3), 1.27 (t, *J* = 7.0 Hz, 3H, CH_3), 1.21 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$): *δ* 171.53 (C=O), 171.13 (C=O), 153.71 (C), 152.82 (C), 140.83 (C), 139.72 (C), 138.12 (C), 133.41 (C), 130.39 (CH), 129.086 (CH), 127.54 (CH), 127.21 (CH), 85.35 (C), 60.91 (CH_2), 60.72 (CH_2), 34.76 (CH_2), 34.34 (CH_2), 32.53 (CH_2), 28.67 (CH_2), 25.57 (CH_3), 14.18 (CH_3), 14.12 (CH_3). HRMS: *m/z* calcd. for $C_{23}H_{29}N_2O_5S_2$ [M + H]$^+$: 477.1518; found: 477.1540.

14 : ^{1}H NMR ($CDCl_3$): *δ* 8.09 (dd, *J* = 1.3, 8.2 Hz, 1H, Ar), 7.84 (dd, *J* = 1.3, 8.2 Hz, 1H, Ar), 7.65 (m, 2H, Ar), 4.20 (q, *J* = 7.1 Hz, 2H, CH_2), 3.43 (t, *J* = 7.2 Hz, 2H, CH_2), 2.72 (t, *J* = 7.2 Hz, 2H, CH_2), 1.79 (s, 6H, CH_3), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$): *δ* 171.08 (C=O), 153.10 (C), 148.67 (C), 141.47 (C), 139.89 (C), 136.80 (C), 130.88 (CH), 129.24 (CH), 127.75 (CH), 127.07 (CH), 126.07 (C), 86.31 (C), 61.01 (CH_2), 34.26 (CH_2), 31.18 (CH_2), 28.13 (CH_3), 14.19 (CH_3). HRMS: *m/z* calcd. for $C_{18}H_{20}BrN_2O_3S$ [M + H]$^+$: 423.0378, 425.0358; found: 423.0383, 425.0369.

Dithin compound 15. A solution of $(Bu_4N)_2$ [MoO(qpdt)$_2$] (**2**) (30 mg) in CH_3CN (2 mL) was allowed to be in contact with air under the fume hood without stirring. After 3 days, orange crystals suitable for X-ray diffraction were obtained (6 mg, 47 %). UV−vis (CH_3CN) λ_{max} (ε_M) 472 (840), 393 (13080), 342 (11120) sh, 321

(12620). ^{1}H NMR ($CDCl_3$): δ 8.07 (dd, J = 1.5, 8.0 Hz, 1H, Ar), 7.84 (dd, J = 1.5, 8.0 Hz, 1H, Ar), 7.64 (m, 2H, Ar), 1.89 (s, 6H, 2 CH_3). ^{13}C NMR ($CDCl_3$): δ 152.71 (C), 143.87 (C), 140.92 (C), 139.56 (C), 135.82 (C), 130.36 (CH), 128.87 (CH), 127.69 (CH), 127.30 (CH), 122.67 (C), 83.54 (C), 28.18 (2 CH_3). HRMS: *m/z* calcd. for $C_{26}H_{21}N_4O_2S_2$ $[M + H]^+$: 485.1106; found: 485.1102.

Imino-thiazol compound 18. The experience was carried out thoroughly under an Ar atmosphere by using Schlenk flasks and all solutions were degassed prior to use. To a suspension of $[MoCl_4(CH_3CN)_2]$[17] (50 mg, 0.155 mmol) in anhydrous THF (10 mL) was added *t*BuNC (141 μL, 1.25 mmol). After 15 min., [$MoCl_4$(*t*BuN*C*)$_2$] was formed *in situ* as a pink solution. Meanwhile and in a separate Schlenk flask, to a solution of **1** (148 mg, 0.31 mmol) in anhydrous THF (3 mL) was added NaH (50 mg, 60 % in mineral oil, 1.24 mmol) at 0° C. After 15 min. at room temperature, the dark red solution was slowly transferred to the [$MoCl_4$(*t*BuN*C*)$_2$] solution *via* a cannula needle. The color turned to dark brown immediately. The reaction was allowed to stir at room temperature for 1 night. Evaporation of THF *in vacuo* gave a crude product, which was purified by flash chromatography over silica gel (eluting with CH_2Cl_2) to furnish a red solid (71 mg, 64 %). Single crystals were grown by slow evaporation of CH_2Cl_2 containing the product. UV−vis (CH_3CN) λ_{max} (ε_M) 524 (11800), 494 (8720), 452 (3620) sh, 423 (1820) sh, 300 (3620). ^{1}H NMR ($CDCl_3$): δ 9.78 – 9.47 (m, 1H, Ar), 7.70 – 7.59 (m, 1H, Ar), 7.51 – 7.34 (m, 2H, Ar), 1.94 (s, 6H, 2 CH_3), 1.49 (s, 9H, 3 CH_3). ^{13}C NMR ($CDCl_3$): δ 208.89 (C=S), 152.93 (C), 145.81 (C), 137.22 (C), 128.39 (C), 127.87 (CH), 127.51 (CH), 127.16 (CH), 123.03 (C), 121.23 (C), 118.28 (CH), 96.42 (C), 56.18 (C), 31.07 (2 CH_3), 27.49 (3 CH_3). HRMS: *m/z* calcd. for $C_{18}H_{20}N_3OS_2$ $[M + H]^+$: 358.1048; found: 358.1061.

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[14] CCDC 1430930 and 1430931 contain the supplementary crystallographic data for **15** and **18**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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