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Towards Structural-Functional Mimics of Acetylene Hydratase: Reversible Activation of Acetylene using a Biomimetic Tungsten Complex

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Abstract: *The synthesis and characterization of a biomimetic system that can reversibly bind acetylene (ethyne) is reported. The system has been designed to mimic catalytic intermediates of the tungstoenzyme acetylene hydratase. The thiophenyl-oxazoline ligand S-Phoz (2-(4′,4′-dimethyloxazolin-2′-yl)thiophenolate) is used to generate a bioinspired donor environment around the W center, facilitating the stabilization of W–acetylene adducts. The featured complexes [W(C_2H_2)(CO)(S-Phoz)$_2$] (**2**) and [WO(C_2H_2)(S-Phoz)$_2$] (**3**) are extremely rare from a synthetic and structural point of view as very little is known about W–C_2H_2 adducts. Upon exposure to visible light, **3** can release C_2H_2 from its coordination sphere to yield the 14-electron species [WO(S-Phoz)$_2$] (**4**). Under light-exclusion **4** re-activates C_2H_2 making this the first fully characterized system for the reversible activation of acetylene.*

Acetylene hydratase (AH) is unique among Mo- and W-dependent enzymes as it has the features of a redox-active enzyme but also catalyzes the net hydration reaction of acetylene (ethyne) to ethenol which then tautomerizes to acetaldehyde. The crystal structure of AH has been solved and shows a W^{IV} center surrounded by five sulfur donors: two molybdopterin moieties and a cysteine. The sixth coordination site is occupied by an oxygen ligand, which is believed to be water or alternatively a hydroxide.[1] The catalytic mechanism of AH is disputed. Electrophilic attack of H_2O on free C_2H_2, nucleophilic attack of H_2O on activated C_2H_2, electrophilic attack of Asp13 on activated C_2H_2, and nucleophilic attack by H_2O on activated C_2H_2 concerted with H^+ transfer to Asp13 have been suggested as entry points into the catalytic cycle.[1,2] Ethyne activation by coordination to a transition metal can not only lead to the desired AH-like hydration, but also to reduction to ethene as occurs with nitrogenase FeMo cofactors or to deprotonation and acetylide formation as typical in Reppe-type vinylations.[3] Thus, it is crucial to gain more detailed information on W adducts and their reactivity. However, from a synthetic point of view very little is known about monomeric metal–C_2H_2 adducts as they have remained largely elusive.

Modeling chemistry of AH is scarce. The chemistry of substituted acetylenes, primarily diphenylacetylene, has been studied extensively. However, only two systems which could qualify as structural models for AH have been reported, both of which were published prior to the crystallization of AH in 2007.[1] In the early 1980's, [W(C_2H_2)(CO)(dtc)$_2$] and [WO(C_2H_2)(dtc)$_2$] (dtc = S_2CNMe_2, S_2CNEt_2) were used to study alkynes as four-electron donors.[4,5] About 20 years later, the scorpionate complexes [Tp′WOI(C_2H_2)] and [Tp′WOI(C_2H_2)] (Tp′ = hydridotris(3,5-dimethylpyrazolyl)borate)] were used to examine vinyl– and vinylidene–tungsten bonding.[6–8] The only structural-functional model of AH was reported by Sarkar et al.[9,10] Originally [Et_4N]$_2$[WO(mnt)$_2$] (mnt = malonitrile) was designed to model W-dependent aldehyde ferredoxin oxidoreductase.[9] The complex was also found to perform approximately nine turnovers of acetylene hydration.[10] Mechanistic calculations suggest an adduct formation between [WO(mnt)$_2$] and C_2H_2.[11] However no adduct formation with C_2H_2 could be detected or intermediates of the catalytic cycle isolated; only oxidative addition of the strong electrophile dimethyl acetylenedicarboxylate could be demonstrated.

Herein we report the development of a new system with the bioinspired S-Phoz ligand (S-Phoz = 2-(4′,4′-dimethyloxazolin-2′-yl)thiophenolate)[12] which can stabilize W–ethyne adducts and with which we successfully demonstrate a photo-induced reversible activation of acetylene on a W^{IV} center.

Exposing CH_2Cl_2 solutions of [W(CO)$_2$(S-Phoz)$_2$][12] (**1**) to a C_2H_2 atmosphere at 35 °C resulted in slow replacement of one CO ligand with ethyne to give the desired adduct [W(C_2H_2)(CO)(S-Phoz)$_2$] (**2**) in good yield (Scheme 1). Similar approaches have been previously used to coordinate C_2H_2 to W^{II} carbonyl complexes.[5,13] As side products, *cis*- and *trans*-polyacetylene (PA) are formed (identified by electron ionization mass spectrometry and IR spectroscopy). Subsequently under light exclusion the remaining CO ligand of **2** can be replaced by an oxo group using pyridine-*N*-oxide (Py*N*O) to afford [WO(C_2H_2)(S-Phoz)$_2$] (**3**) in high yield. The 5-coordinate 14-electron species [WO(S-Phoz)$_2$] (**4**) was obtained by irradiating solutions of **3** with visible light. On a small scale and in very dilute solutions, complete conversion of **3** into **4** is possible (see below). However, performing the reaction on a larger scale was unsuccessful as **4** not only forms in light, but also decomposes upon prolonged exposure (before reasonable conversion is reached). Throughout the synthetic route, reactivity is evidenced by distinct color changes of the product from orange-brown (**1**) via deep green (**2**), to pale yellow (**3**), and finally to intense purple (**4**).

The ^{1}H NMR spectra show that the synthesis of **2** yields one major isomer (> 95 %), which is believed to be in an N,N-

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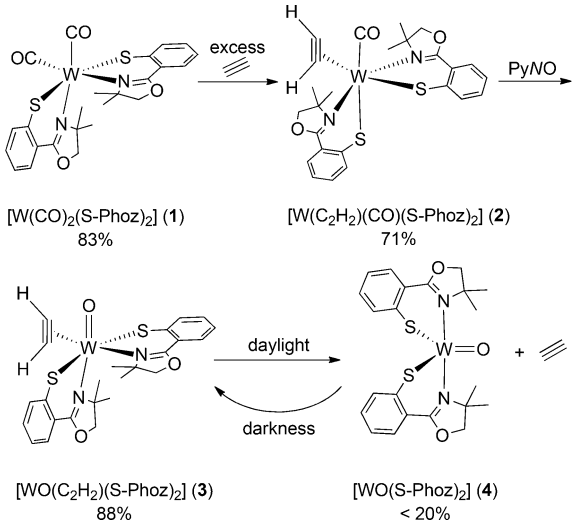

Scheme 1. Synthetic strategy for the preparation of complexes **2**–**4** and yields of the isolated products.

trans arrangement as reflected by the obtained molecular structure. Upon oxidation, isomerically pure S,S-*trans* **3** is obtained (see below). The photoinduced release of C_2H_2 from **3** results in the formation of the higher symmetric species **4**. In **2** successful activation of C_2H_2 is evidenced by two broad singlets for the acetylenic protons. Oxidation to **3** results in a significant upfield shift of the signals from $\delta = 12.22$ ppm and 11.57 ppm to approximately 10.5 ppm, indicating a drastic increase in acidity compared to free C_2H_2 which resonates at 1.96 ppm.[14] This is an important finding as deprotonation and nucleophilic attack are discussed as key steps in the mechanistic debate. The assignment of the C_2H_2 signals could be confirmed by HSQC cross peaks and by ^{183}W–^{13}C coupling in the ^{13}C NMR spectra (Table 1).

Time-resolved ^1H NMR spectra of pure **3** in CD_2Cl_2 were recorded to follow the photoinduced release of C_2H_2 from **3** and its reactivation by **4** (Figure 1). After 12 minutes of exposure to light, 90% of **3** had released its C_2H_2 (ratio **3** to **4** was 0.1:1.0). In the spectrum, the resonance signal of liberated acetylene integrates to sub-stoichiometric amounts, but the signal intensity clearly increases during irradiation. The reverse reaction was achieved by excluding light from the tube and is significantly slower. After 32 hours, more than 90% of **3** was recovered (ratio of **3** to **4** was 11.3:1.0) and free ethyne had been depleted. Minor decomposition (less than 10%) to HS-Phoz and $(S\text{-Phoz})_2$ were detected as a side reactions. The protonated ligand HS-Phoz and its disulfide $(S\text{-Phoz})_2$ were synthesized as reference materials to confirm the identity of the detected side products.

The ^1H NMR experiments clearly show that acetylene liberation can be controlled by visible light. The targeted release is achieved by simply irradiating the sample. In a closed system the liberated equivalent C_2H_2 can be successfully reactivated from the gas phase by light exclusion. Exposing isolated product **4** to a C_2H_2 atmosphere also leads to the recovery of **3** and the formation of PA. In the literature, reports on the reversible activation of acetylene are rare. $[MoO(S_2CNEt_2)_2]$, $[MoO(S_2CNMe_2)_2]$, cationic Co^{III} porphyrins, monolayer-dispersed Ni^{II} complexes, Pt^{IV} iodide complexes, and polymer-bound $[Mn(MeCp)(CO)_3]$ have been reported to reversibly coordinate acetylene.[15] However, in none of these cases stable adducts could be isolated.

Molecular structures of all compounds could be obtained using single-crystal X-ray diffraction analysis (see Figure 2 and Table 1).[21] All presented molecular structures are rare examples of their kind. To date, the only reported tungsten–acetylene structures have been $[W(C_2H_2)Cl_2(MeCN)_3]$-$[WOCl_4(MeCN)]$ and $[W(C_2H_2)(CO)(S_2CNEt_2)_2]$,[5,16] making complex **2** only the second example of a mononuclear adduct between C_2H_2 and a transition metal carbonyl complex. Additionally a handful of structures with metal carbonyl oligomers bridged by C_2H_2 in a mixed side-on/end-on arrangement exist. Typically those bridging C≡C bonds are longer than in **2**.[17] Structure **3** is the first reported metal–oxo–ethyne species. This is particularly interesting in view of AH as it is a W^{IV} center bearing C_2H_2 in a bioinspired environment and thus resembles proposed catalytic intermediates. Complex **4** is the first example of a trigonal-bipyramidal W^{IV}–oxo species. All other fivefold coordinated W^{IV}–oxo species are square pyramidal with the O atom as the top of the pyramid. Consequently all published biomimetic W^{IV}–oxo models with dithiolene ligands are square pyramidal. These complexes are typically $[WOL_2]$ dianions with two counterions such as $[NEt_4]^+$,[9,18] whereas in contrast our system is neutral.

The molecular structures of **2** and **3** show a significant loss of linearity in the bound C_2H_2. Similarly, the C≡C bond lengths in **2** and **3** (1.327(3) and 1.268(6) Å, respectively; Table 1) are significantly longer than that of free acetylene (1.186(4) Å[19]). The asymmetric coordination of the C_2H_2 moiety could indicate the presence of a partial negative charge on one acetylenic C atom, a slight polarization which potentially facilitates nucleophilic attack. The shorter C≡C

Table 1: Overview of the analytical data for complexes **2**–**4**.

	^1H NMR[a]	^{13}C NMR[a]		IR[b]			X-ray crystal structures[21]					
	δ(HC≡CH)	δ(C≡C)	J_{W-C}	ν(C≡O)	ν(C≡C)	ν(W=O)	C≡C[c]	W–C_2H_2[c]	C≡C–H[d]	W–CO[c]	C≡O[c]	W=O[c]
2	12.22	200.0	27	1889	1588	–	1.327(3)	2.0548(18)	122.7(15)	1.9623(18)	1.160(2)	–
	11.57	193.1	2		1566			2.0268(17)	146.9(16)			
3	10.60–10.47	152.9	14	–	1604	939	1.268(6)	2.094(4)	149(3)	–	–	1.724(3)
		151.6	19		1597			2.109(4)	143(4)			
4	–	–	–	–	–	934	–	–	–	–	–	1.707(3)

[a] Spectra recorded in CD_2Cl_2; chemical shifts (δ) given in ppm and coupling constants (J_{W-C}) given in Hz. [b] Values given in cm^{-1}. [c] Bond lengths, given in Å. [d] Angles, given in degrees (°).

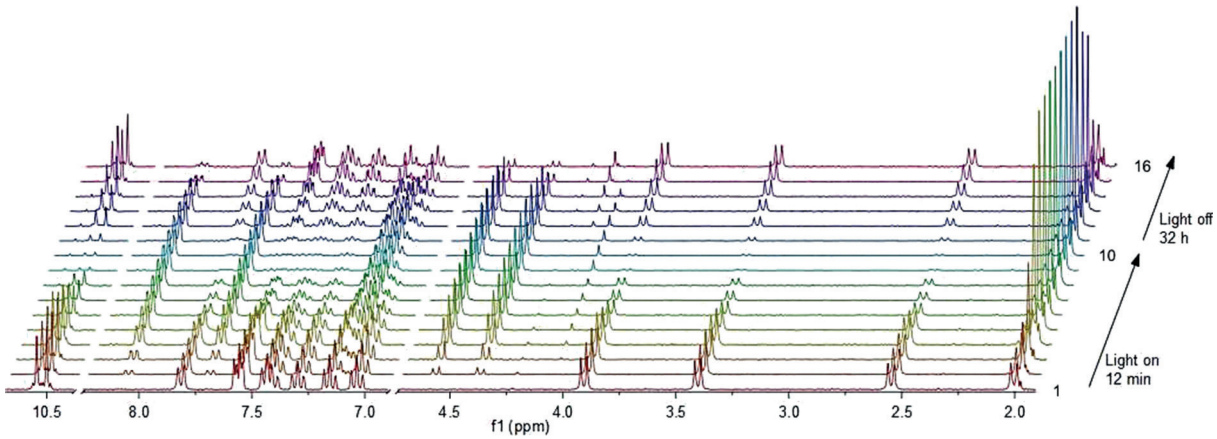

Figure 1. ^{1}H NMR study of the reversible activation of C_2H_2. Scans 1–10: photoinduced dissociation of C_2H_2 to yield **4**. Scans 11–16: re-activation of C_2H_2 to regenerate **3**.

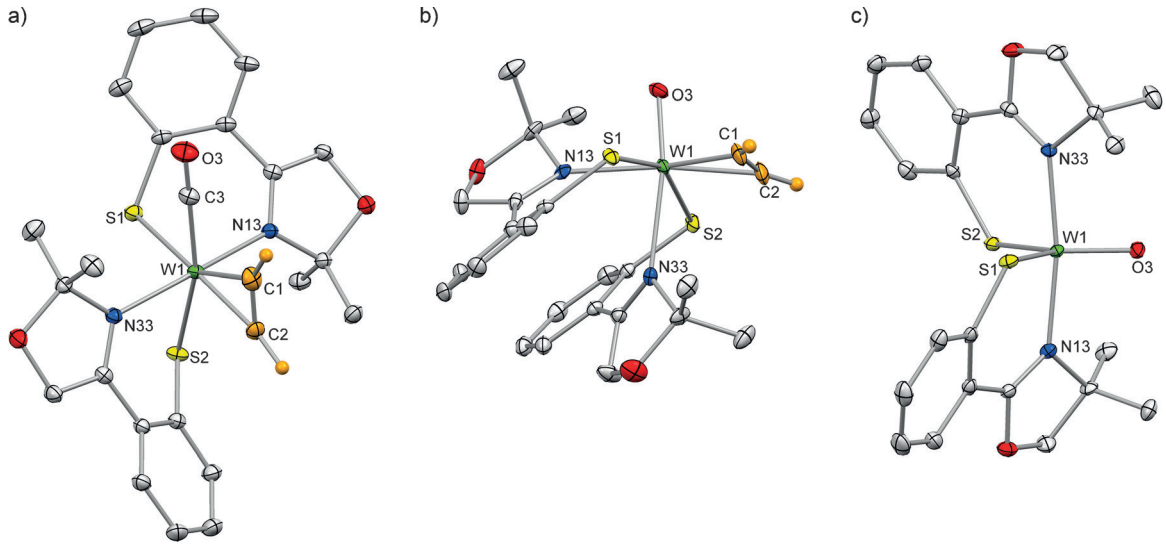

Figure 2. Molecular structures of a) **2**, b) **3**, and c) **4** showing the atomic numbering scheme.[21] Probability ellipsoids are set at 50% level.

distance and greater distance to the W center in **3** compared to **2** indicates that the oxidation reduces the ability of the W center for π backbonding, which is in good agreement with photoinduced dissociation occurring in **3**. The C≡C bond in **2** is significantly longer than in $[W(C_2H_2)(CO)(S_2CNEt_2)_2]$ (C≡C 1.29(1) Å[5]), indicating a tighter coordination of the acetylene within our system.

Complex **2** shows a parallel arrangement of the CO and acetylene ligands (Figure 2a), whereas **3** is characterized by a perpendicular orientation of the oxo group and the C_2H_2 (Figure 2b). This indicates that the system performs a 90° alkyne rotation to ensure ideal orbital overlap, as previously reported by Templeton and co-workers.[6,7] The crystallized isomers of **2** and **3** differ in the arrangement of ligands. A N,N-*trans* arrangement is found in complex **2**, whereas **3** features an S,S-*trans* geometry. This variation in the ligand arrangements within the complexes further shows the high flexibility and adaptability of our ligand system, features which we have also recently observed for related Pd^{II} complexes.[20]

We have successfully developed and fully characterized a new, biomimetic system which can not only stabilize tungsten–acetylene adducts, but is also capable of the reversible activation of acetylene. Release and activation of acetylene can be easily controlled by visible light. The reported species are possible intermediates in the catalytic cycle of acetylene hydratase and will be important to further our understanding of AH.

Keywords: acetylene hydratase · bioinorganic chemistry · S ligands · small-molecule activation · tungsten

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[1] G. Seiffert, G. M. Ullmann, A. Messerschmidt, B. Schink, P. M. H. Kroneck, O. Einsle, *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 3073–3077.

[2] a) M. A. Vincent, I. H. Hillier, G. Periyasamy, N. A. Burton, *Dalton Trans.* **2010**, *39*, 3816 – 3822; b) S. Antony, C. A. Bayse, *Organometallics* **2009**, *28*, 4938 – 4944; c) R.-Z. Liao, W. Thiel, *J. Comput. Chem.* **2013**, *34*, 2389 – 2397; d) R.-Z. Liao, J.-G. Yu, F. Himo, *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 22523 – 22527.
[3] a) Z. Wang in *Comprehensive Organic Name Reactions and Reagents* (Ed.: Z. Wang), Wiley, Hoboken, NJ, **2010**; b) R. Y. Igarashi, P. C. Dos Santos, W. G. Niehaus, I. G. Dance, D. R. Dean, L. C. Seefeldt, *J. Biol. Chem.* **2004**, *279*, 34770 – 34775; c) H.-I. Lee, M. Sørlie, J. Christiansen, T.-C. Yang, J. Shao, D. R. Dean, B. J. Hales, B. M. Hoffman, *J. Am. Chem. Soc.* **2005**, *127*, 15880 – 15890.
[4] J. L. Templeton, B. C. Ward, G. J.-J. Chen, J. W. McDonald, W. E. Newton, *Inorg. Chem.* **1981**, *20*, 1248 – 1253.
[5] L. Ricard, R. Weiss, W. E. Newton, G. J.-J. Chen, J. W. McDonald, *J. Am. Chem. Soc.* **1978**, *100*, 1318 – 1320.
[6] T. W. Crane, P. S. White, J. L. Templeton, *Inorg. Chem.* **2000**, *39*, 1081 – 1091.
[7] T. W. Crane, P. S. White, J. L. Templeton, *Organometallics* **1999**, *18*, 1897 – 1903.
[8] M. B. Wells, P. S. White, J. L. Templeton, *Organometallics* **1997**, *16*, 1857 – 1864.
[9] S. K. Das, D. Biswas, R. Maiti, S. Sarkar, *J. Am. Chem. Soc.* **1996**, *118*, 1387 – 1397.
[10] J. Yadav, S. K. Das, S. Sarkar, *J. Am. Chem. Soc.* **1997**, *119*, 4315 – 4316.
[11] Y.-F. Liu, R.-Z. Liao, W.-J. Ding, J.-G. Yu, R.-Z. Liu, *J. Biol. Inorg. Chem.* **2011**, *16*, 745 – 752.
[12] L. M. Peschel, J. A. Schachner, C. H. Sala, F. Belaj, N. C. Mösch-Zanetti, *Z. Anorg. Allg. Chem.* **2013**, *639*, 1559 – 1567.
[13] H. G. Alt, *J. Organomet. Chem.* **1977**, *127*, 349 – 356.
[14] R. J. Abraham, M. Reid, *J. Chem. Soc. Perkin Trans. 2* **2001**, 1195 – 1204.
[15] a) Y. Kurimura, Y. Takagi, E. Tsuchida, *J. Macromol. Sci. Part A* **1987**, *24*, 419 – 430; b) E. A. Maatta, R. A. D. Wentworth, W. E. Newton, J. W. McDonald, G. D. Watt, *J. Am. Chem. Soc.* **1978**, *100*, 1320 – 1321; c) S. A. Mitchenko, *Kinet. Catal.* **1999**, *40*, 248 – 252; d) J.-i. Setsune, M. Ikeda, Y. Ishimaru, T. Kitao, *Chem. Lett.* **1989**, 667 – 670; e) J. Setsune, S. Ito, H. Takeda, Y. Ishimaru, T. Kitao, M. Sato, H. Ohya-Nishiguchi, *Organometallics* **1997**, *16*, 597 – 605; f) R. T. Yang, R. Foldes, *Ind. Eng. Chem. Res.* **1996**, *35*, 1006 – 1011; g) E. A. Maatta, R. A. D. Wentworth, *Inorg. Chem.* **1979**, *18*, 524 – 526.
[16] M. Kersting, A. El-Kholi, U. Müller, K. Dehnicke, *Chem. Ber.* **1989**, *122*, 279 – 285.
[17] a) G. Conole, M. Kessler, M. J. Mays, G. E. Pateman, G. A. Solan, *Polyhedron* **1998**, *17*, 2993 – 3004; b) W. I. Bailey, M. H. Chisholm, F. A. Cotton, L. A. Rankel, *J. Am. Chem. Soc.* **1978**, *100*, 5764 – 5773; c) M. Ganesan, K.-Y. Shih, P. E. Fanwick, R. A. Walton, *Inorg. Chem.* **2003**, *42*, 1241 – 1247.
[18] a) C. A. Goddard, R. H. Holm, *Inorg. Chem.* **1999**, *38*, 5389 – 5398; b) H. Sugimoto, R. Tajima, T. Sakurai, H. Ohi, H. Miyake, S. Itoh, H. Tsukube, *Angew. Chem. Int. Ed.* **2006**, *45*, 3520 – 3522; *Angew. Chem.* **2006**, *118*, 3600 – 3602; c) Y. Hasenaka, T.-a. Okamura, M. Tatsumi, N. Inazumi, K. Onitsuka, *Dalton Trans.* **2014**, *43*, 15491 – 15502.
[19] R. K. McMullan, Å. Kvick, P. Popelier, *Acta Crystallogr. Sect. B* **1992**, *48*, 726 – 731.
[20] L. M. Peschel, C. Holzer, L. Mihajlović-Lalić, F. Belaj, N. C. Mösch-Zanetti, *Eur. J. Inorg. Chem.* **2015**, 1569 – 1578.
[21] CCDC 1404553 (**2**), 1404554 (**3**), and 1404555 (**4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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