PRF # 58693-DNI3

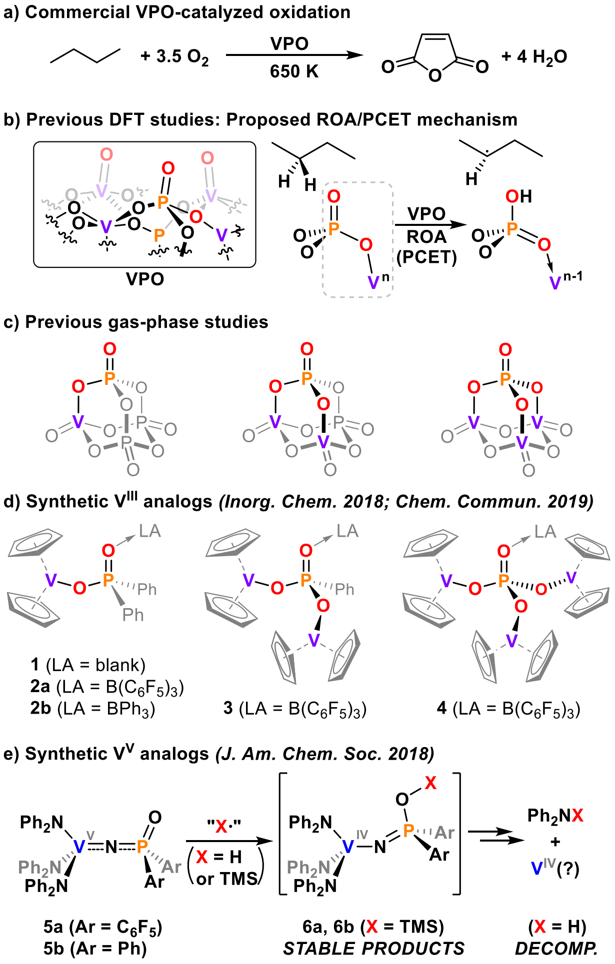
Project Title: Investigating the Proposed Reduction-Coupled Oxo Activation Mechanism for Hydrocarbon C-H Functionalization

Principle Investigator: Gabriel Ménard, Chemistry and Biochemistry, UC Santa Barbara

Co-PI: None

Introduction:

C–H bond activation is an attractive avenue for the transformation of inexpensive and abundant feedstocks into value-added commodity chemicals. At the industrial level, for example, the DuPont "butox" process catalyzes the partial oxidation of *n*-butane to maleic anhydride via a heterogeneous vanadium phosphorus oxide (VPO) catalyst (Scheme 1a).[1-3] While most research assigned the vanadyl (V=O) centers as the reactive sites for butane C–H bond activation, recent DFT studies by Goddard *et al.* suggest that the catalyst support P=O bonds – tethered to neighboring vanadyls – may instead be responsible, reacting by a cooperative proton-coupled electron transfer (PCET) mechanism with neighboring high-valent V centers (Scheme 1b), and termed in some reports reduction-coupled oxo activation (ROA).[4-6] This proposed reactivity has been partially supported by gas-phase studies reported by Schwarz *et al.*[7-10] investigating heteronuclear cluster ions, $[V_xP_{4-x}O_{10}]^{\bullet+}$ (x = 0-4), which have been reported to promote the homolytic C–H bond activation of methane (Scheme 1c).[8-9] Together, this unusual C–H reactivity mediated by an "innocent" main group center (P=O) stands in significant contrast to the decades of research on noble metal-mediated C–H bond activation chemistry[11] and may offer a new pathway to catalyzing these difficult transformations.


a) Commercial VPO-catalyzed oxidation

b) Previous DFT studies: Proposed ROA/PCET mechanism

c) Previous gas-phase studies

d) Synthetic V^III analogs *(Inorg. Chem. 2018; Chem. Commun. 2019)*

e) Synthetic V^V analogs *(J. Am. Chem. Soc. 2018)*

Scheme 1. a) Dupont's commercial oxidation of butane to maleic anhydride on the vanadium phosphorus oxide (VPO) surface catalyst. **b)** Previous DFT studies proposing an alternative reduction-couple oxo activation (ROA) mechanism for C–H activation at P=O linkages. **c)** Previous gas-phase studies on P=O mediated methane C–H activation. **d)** Sample of our reported V^{III}-based molecular mimics. **e)** First experimental support for the ROA mechanism using our V^{V} molecular mimics.

Research Progress:

In order to probe this possible new main-group mediated C–H bond functionalization chemistry, we have synthesized a suite of molecular mono- or multi-metallic VPO model complexes of the general formula, $(R_xV^n\text{-}L)_yP(O)Ar_{(3-y)}$ where the complexes with R_x = Cp_2, n = +3, L = O, y = 1, 2, 3, Ar = Ph are shown in Scheme 1d (compounds **1**-**4**).[12] A follow-up paper with a longer linker, L = $O(O)C(C_6H_4)$ (y = 1, 3), and maintaining the vanadocene metal centers was also reported (not shown).[13] All complexes were thoroughly characterized by a suite of spectroscopic (NMR, EPR, UV-Vis), magnetic (Evans, SQUID), electrochemical (CV), and structural (XRD) techniques. Their reactivities were also probed using, for instance, common H-atom donors (HADs), such as TEMPO-H, 1,4-cyclohexadiene, and others, in order to assess their possible ROA-type reactivity at the P=O centers similar to the previously proposed reactivity (Scheme 1b-c). Unfortunately, no ROA-type reactivity was observed.

We subsequently modified our V centers to incorporate higher-valent V^V centers (R_x = $(Ph_2N)_3$, n = +5, L = N, y = 1, Ar = Ph, C_6F_5; compounds **5a**-**5b**, Scheme 1e).[14] These molecules were again thoroughly characterized. We subsequently investigated C–H functionalization mediated by the terminal P=O bonds, analogous to the ROA mechanism (Scheme 1a). Our results indicated that these linkages may be reactive; however, ligand lability (ie. protonation of Ph_2N^-) precluded us from unambiguously making that assignment (Scheme 1e). We therefore turned to a hydrogen atom surrogate, trimethylsilyl radical (TMS•). Exposure of **5a** or **5b** to this TMS• donor resulted in the formation of the reduced PO–TMS linked products, **6a** or **6b**, with concurrent reduction of V^V to V^{IV} (Scheme 1e). This is, to the best of our knowledge, the first condensed phase experimental support for the proposed ROA mechanism.[14]

Career Impact:

The impact of this grant on graduate students has been substantial. Four of my current ten graduate students have been in part supported for varying periods of time by this grant. In addition, several undergraduate students – mentored by those graduate students – have also participated in this project. One of my graduate students also attended and presented at the Inorganic Reaction Mechanisms Gordon Research Conference (GRC) and Seminar this year thanks to the funding provided by this award.

This grant has also significantly impacted my career. In the first year alone, we have published three papers[12-14] on this chemistry in well respected journals. Moreover, we currently have two more papers ready to be submitted. In addition, I have been invited to several national and international department colloquia, as well as this year's Organometallics GRC, where I have extensively discussed this chemistry.

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