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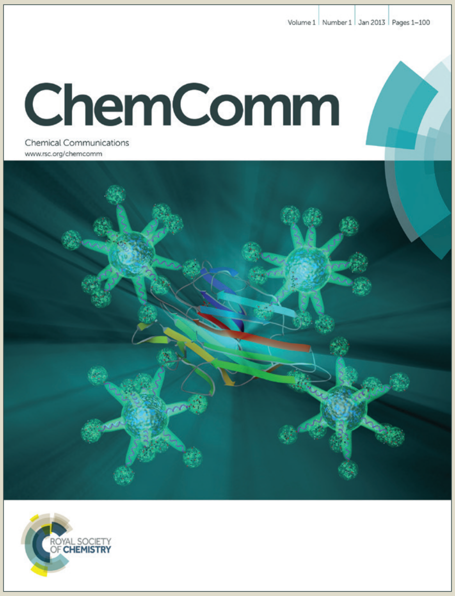

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ARTICLE TYPE

A Homolytic Oxy-Functionalization Mechanism: Intermolecular Hydrocarbyl Migration from M-R to Vanadate Oxo

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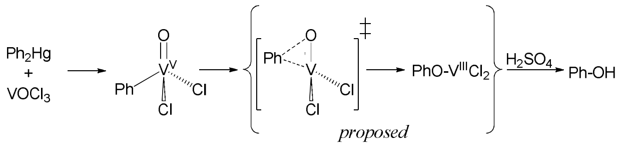
A new mechanism for generating C-O bonds from metal-hydrocarbyls involving homolytic, intermolecular migration of the hydrocarbyl group to a vanadium oxo is reported. Responsible for the C-O bond in phenol formed by the reaction of $OVCl_3$ with $HgPh_2$, it may provide air-regenerable metal oxo's a role in aerobic alkane oxidations.

The formation of carbon-oxygen bonds from metal-hydrocarbyl species is a central challenge to developing radical-free catalytic cycles for alkane functionalization. Several catalytic reactions have been developed in which alkane C-H bonds are activated by strongly electrophilic metals such as Pt^{II},[1] Hg^{II},[2] Pd^{II},[3] and Au^{III}[4] followed by reductive functionalization from $M^{\delta-}$-$R^{\delta+}$ intermediates. Unfortunately these systems are inhibited by water and alcohol products and can require oxidants stronger than O_2. Thus the high electrophilicity of these metals, which facilitates CH activation and reductive elimination, makes them commercially impractical. In contrast, the intramolecular migration of hydrocarbyl groups across metal-oxo bonds is a known mechanism for oxy-functionalizing hydrocarbyl groups on electropositive metals.[5] In a few experiments, direct evidence of such migrations (labeled as Intra-M^{2e} to indicate intramolecular migration that results in a two-electron reduction) has been shown.[5-6] Intra-M^{2e} was also proposed to be responsible for C-O bond formation in the generation of phenol from $OVCl_3$ and $HgPh_2$ in cyclohexane (Scheme 1).[7]

We studied this reaction with quantum mechanics (density functional theory, M06//B3LYP[8] see Supporting Information) including Poisson-Boltzmann implicit solvation.[9] Surprisingly, we find that the oxidation of V-Ph to V-OPh does *not* proceed through Intra-M^{2e} but rather through *intermolecular phenyl migration to a separate metal-oxo*. This is a new oxidation mechanism, Inter-M^{1e}, that leads to a one-electron reduction of both reactants, in contrast to previous (intra- and intermolecular) mechanisms that result in a two-electron reduction of either the M-R complex or oxidants.[5-6, 10]



Scheme 1 Mechanism for the formation of phenol by the reaction of Ph_2Hg and $VOCl_3$ proposed by Reichle et al.

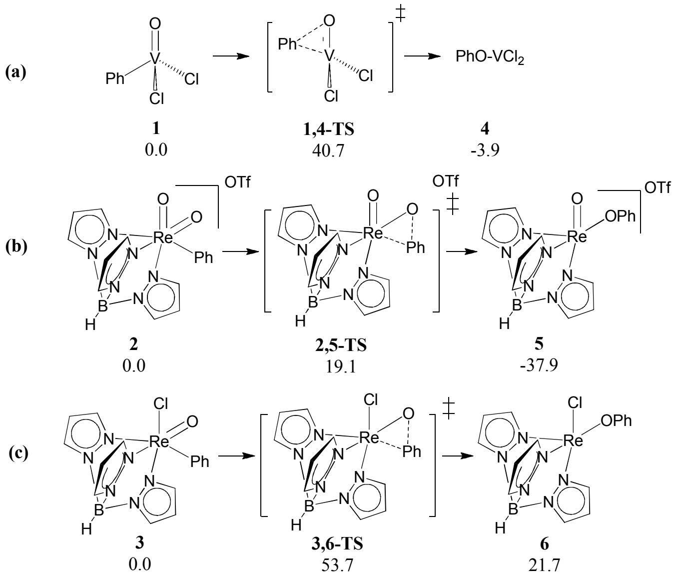


Fig. 1 The comparison of three intramolecular phenyl metal-to-oxo migrations (**Intra-M^{2e}**, free energies in kcal/mol, T=298K). The ground states of **1**,**4-TS**, **4**, and **6** are triplets.

First we studied Intra-M^{2e} rearrangement of $O{=}VCl_2Ph$ (**1**), a known intermediate generated by aryl transfer from $HgPh_2$ to $O{=}VCl_3$,[7] and compared the free energy surface to those of $[(HBpz_3)Re^{VII}O_2(Ph)]OTf$ (**2**) and $(HBpz_3)Re^{V}OPhCl$ (**3**) ($HBpz_3$ = hydrotris(1-pyrazolyl)borate, OTf = triflate). Intra-M^{2e} from Re^{VII} (**2**) is thermally accessible,[5c] whereas that from Re^{V} (**3**) is known to proceed photochemically.[5a, 5b] Indeed, we find that Intra-M^{2e} of **2** poses a much lower barrier (19.1 kcal/mol, Figure 1) than that of **3** (53.7 kcal/mol), consistent with the experiments. However, the barrier for **1** is calculated to be 40.7 kcal/mol, indicating that this reaction is not thermally accessible. This suggests that Intra-M^{2e} is not the pathway responsible for the oxidation of V-Ph to V-OPh. Indeed, Thiele et al. synthesized and isolated **1**, and found no formation of phenoxides when **1** decomposes.[11] In the experiments phenol was detected only when an excess of $OVCl_3$ was added to react with $HgPh_2$ ($OVCl_3/HgPh_2 > 2$).[7] Therefore, we considered the possibility that the unreacted $OVCl_3$ might serve as an oxidant and that V-Ph bonds are

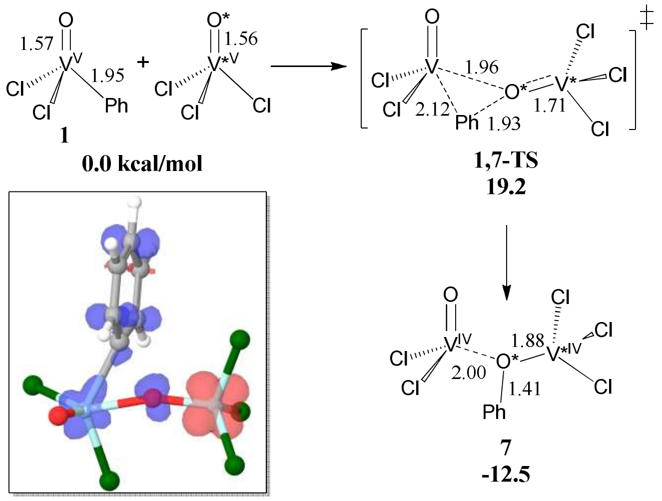


Fig. 2 The free energy surface of the phenyl intermolecular migration from $OVPhCl_2$ to the oxo of $O{=}VCl_3$ (kcal/mol). The polarized spin density in the transition state (red and blue showing up and down spin) is shown in the inset.

oxidized to V-OPh by transferring Ph intermolecularly from **1** to $OVCl_3$, similar to the oxidation of CH_3ReO_3 by OsO_4[10c] and the transfer of carbanions to $TpOs(N)Cl_2$.[12]

We investigated this possibility and located a transition state in which phenyl migrates intermolecularly from $OVCl_2Ph$ to the oxo of $O{=}VCl_3$ (Figure 2 (a)). This reaction pathway poses a Gibbs free energy barrier of only 19.2 kcal/mol, consistent with the experiments, which show this to be a room-temperature reaction and absent of free radicals.[7] In the transition state **1,7-TS**, the phenyl carbon is 2.12 Å away from V and 1.93 Å away from O*, while V*=O* is elongated from 1.56 to 1.71 Å, and O* is loosely coordinated to V with a bond distance of 1.96 Å, longer than the normal V-O single bond length (1.76 Å). Importantly, this transition state is described by an open-shell singlet (OSS) wavefunction with two unpaired, antiferromagnetically coupled electrons. One localizes at the V* of the oxidant, while the other is delocalized among V, O*, and the phenyl carbon (Figure 2). The product **7** has R(V--O*) = 2.00, R(C-O) = 1.41, and R(V*-O*) = 1.88 Å. The tetrahedral coordination of both metals is maintained in the product. The wavefunction of the product is also described as an OSS state with two unpaired electrons localized at two V^{IV}. The triplet state of **7** is 0.1 kcal/mol uphill, suggesting there is slight superexchange interaction between the two metallic centers.

Significantly, comparing to Intra-M^{2e}, we find that the barrier of the Inter-M^{1e} oxidation (where "1e" denotes the one-electron change in oxidation states) is 21.5 kcal/mol lower. This can be rationalized by the relative stability of V^{IV} with respect to V^{V} and V^{III} evident in the Pourbaix diagrams of vanadium.[13] For illustration, the redox potentials of V^{IV}/V^{V} and V^{III}/V^{IV} couples in aqueous solution at pH = 0 (1.0 and 0.36 V vs NHE, respectively)[14] show that the comproportionation reaction $V^{V} + V^{III} \rightarrow 2\ V^{IV}$ is exergonic by 15 kcal/mol.

To investigate substrate scope, we considered the reaction of **1**-Me with $OVCl_3$ (Figure 3). In contrast to **1**, two transition states (TS) were located: the first (**1,7-TS**-Me) has a triangular V-C-O motif resembling **1,7-TS**, and the second (**1,7-TS'**-Me) has a linear V-C-O motif (including inversion of the methyl group) similar to the transition state for methyl transfer from $(CO)_5ReMe$ to SeO_2.[15] The most energetically favorable pathway is through **1,7-TS**-Me with a barrier of 27.3 kcal/mol, which is still 8.1 kcal/mol higher than that of **1**. This lower migratory aptitude of methyl is also observed in several other systems.[16] The reaction through **1,7-TS'**-Me poses a much higher barrier of 38.7 kcal/mol. This is presumably the result of forming the undercoordinated vanadium product $OVCl_2$.

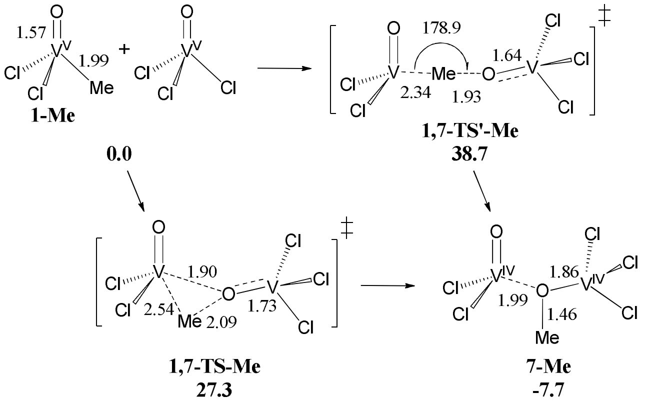


Fig. 3 The free energy surface of the intermolecular methyl migration from $VOMeCl_2$ to the oxo of $VOCl_3$ (free energies at 1M in kcal/mol,T=298K, bond lengths in Å).

The Inter-M^{1e} mechanism is unique compared to previous oxidation mechanisms. M-C bonds have been oxy-functionalized by:

(a) organometallic Baeyer-Villiger oxidations,[10a, 10b] in which the oxidation state of the metal in the M-R complex remains unchanged;

(b) electrophilic attack on carbon,[10c, 15] in which the oxidation state of the metal in the M-R complex remains unchanged, while the oxidant is reduced by two electrons;

(c) Intra-M^{2e},[5-6] in which the metal of the M-R complex is reduced by two electrons; or

(d) nucleophilic attack (or reductive elimination),[17] in which the metal in the M-R complex is formally reduced by two electrons.

For the current system we observe Inter-M^{1e} (Figure 2), in which both metals in the M-R complex and oxidant are formally reduced by one electron. This mechanism will prove useful if integrated as the C-O formation step in a complete catalytic cycle for hydrocarbon oxidation, and its electronic structure suggests advantages over known functionalization routes. Firstly, in a process in which the oxidant is to be regenerated by triplet dioxygen, the open shell character and oxidation potential of V^{IV} (1.0V vs NHE calculated for $O{=}V^{IV}Cl_3^{-1}(aq)$) offer kinetic and thermodynamic advantages over oxidants like $[PtCl_6^{2-}]$[18] and peroxides,[3a, 3b, 19] respectively. These advantages have already been demonstrated by known, air-regenerable catalysts based on vanadium, other metals and polyoxometalates.[20] Secondly, stoichiometric reactions involving the formal transfer of a hydrocarbyl *anion* to an oxidant have not been incorporated into catalytic cycles for alkane oxidation. These mechanisms have involved electropositive metals incompetent for CH activation (e.g. MTO and Grignard reagents) or strong oxidants (e.g. peracids, N_2O).[21] The electropositivity that promotes these reactions also makes catalysts based on such metals susceptible to unwanted oxidation prior to CH activation.[22] In contrast the Inter-M^{1e} mechanism requires the CH activation catalyst to be formally reduced by one electron, so we are now exploring its application to 'M-R' substrates of metals that are simultaneously competent for non-radical C-H activation and tolerant of more oxidizing conditions.

Instead of the expected intramolecular phenyl metal-to-oxo migration, we find that the oxy-functionalization of $VOPhCl_2$ proceeds through an intermolecular phenyl migration to the oxo of a separate $VOCl_3$. This mechanism can be verified experimentally by a pseudo first-order kinetic study, in which a high concentration of $VOCl_2Ph$[11] is reacted with controlled concentration of $VOCl_3$. The two electrons in the initial V-C bond are decoupled during the reaction, leading to two vanadium centers which have been reduced to the +4 state. Therefore, we categorize this as a new oxy-functionalization mechanism involving two one-electron reductions.

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Notes and references

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1. (a) R. A. Periana, D. J. Taube, S. Gamble, H. Taube, T. Satoh and H. Fujii, *Science*, 1998, **280**, 560-564; (b) A. E. Shilov and G. B. Shul'pin, *Chem. Rev.*, 1997, **97**, 2879-2932; (c) J. A. Labinger and J. E. Bercaw, *Nature*, 2002, **417**, 507-514.
2. R. A. Periana, D. J. Taube, E. R. Evitt, D. G. Loffler, P. R. Wentrcek, G. Voss and T. Masuda, *Science*, 1993, **259**, 340-343.
3. (a) L. C. Kao, A. C. Hutson and A. Sen, *J. Am. Chem. Soc.*, 1991, **113**, 700; (b) M. Muehlhofer, T. Strassner and W. A. Herrmann, *Angew. Chem.-Int. Ed.,* 2002, **41**, 1745; (c) R. A. Periana, O. Mironov, D. Taube, G. Bhalla and C. J. Jones, *Science*, 2003, **301**, 814.
4. C. J. Jones, D. Taube, V. R. Ziatdinov, R. A. Periana, R. J. Nielsen, J. Oxgaard and W. A. Goddard, *Angew. Chem.-Int. Ed.*, 2004, **43**, 4626-4629.
5. (a) S. N. Brown and J. M. Mayer, *J. Am. Chem. Soc.*, 1994, **116**, 2219-2220; (b) S. N. Brown and J. M. Mayer, *Organometallics*, 1995, **14**, 2951-2960; (c) S. N. Brown and J. M. Mayer, *J. Am. Chem. Soc.*, 1996, **118**, 12119-12133.
6. J. L. Smeltz, P. D. Boyle and E. A. Ison, *J. Am. Chem. Soc.*, 2011, **133**, 13288-13291.
7. W. T. Reichle and W. L. Carrick, *J. Organomet. Chem.*, 1970, **24**, 419.
8. (a) Y. Zhao and D. G. Truhlar, *Theor. Chem. Acc.*, 2008, **120**, 215-241; (b) A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648; (c) C. T. Lee, W. T. Yang and R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785.
9. B. Marten, K. Kim, C. Cortis, R. A. Friesner, R. B. Murphy, M. N. Ringnalda, D. Sitkoff and B. Honig, *J. Phys. Chem.*, 1996, **100**, 11775-11788.
10. (a) B. L. Conley, S. K. Ganesh, J. M. Gonzales, W. J. Tenn, K. J. H. Young, J. Oxgaard, W. A. Goddard and R. A. Periana, *J. Am. Chem. Soc.*, 2006, **128**, 9018-9019; (b) S. M. Bischof, M. J. Cheng, R. J. Nielsen, T. B. Gunnoe, W. A. Goddard and R. A. Periana, *Organometallics*, 2011, **30**, 2079-2082; (c) B. L. Conley, S. K. Ganesh, J. M. Gonzales, D. H. Ess, R. J. Nielsen, V. R. Ziatdinov, J. Oxgaard, W. A. Goddard and R. A. Periana, *Angew. Chem. Int. Edit.*, 2008, **47**, 7849-7852; (d) M. J. Cheng, R. J. Nielsen, M. Ahlquist and W. A. Goddard, *Organometallics*, 2010, **29**, 2026-2033.
11. K. H. Thiele, W. Schumann, S. Wagner and W. Bruser, *Z. Anorg. Allg. Chem.*, 1972, **390**, 280-288.
12. T. J. Crevier, B. K. Bennett, J. D. Soper, J. A. Bowman, A. Dehestani, D. A. Hrovat, S. Lovell, W. Kaminsky and J. M. Mayer, *J. Am. Chem. Soc.*, 2001, **123**, 1059-1071.
13. M. Pourbaix, *Atlas of electrochemical equilibria in aqueous solutions* Pergamon Press, Oxford, New York, 1966.
14. G. Inzelt, in *Inorganic Electrochemistry*, eds. A. J. Bard and M. Stratmann, WILEY-VCH, 2006, vol. 7a. Liberation of phenol from **7** via hydrolysis (mimicking product work-up), was calculated to be highly exergonic (see ESI.)
15. W. J. Tenn, B. L. Conley, C. H. Hovelmann, M. Ahlquist, R. J. Nielsen, D. H. Ess, J. Oxgaard, S. M. Bischof, W. A. Goddard and R. A. Periana, *J. Am. Chem. Soc.*, 2009, **131**, 2466.
16. (a) H. C. Brown and C. J. Kim, *J. Am. Chem. Soc.*, 1968, **90**, 2082; (b) M. F. Hawthorne, W. D. Emmons and K. S. Mccallum, *J. Am. Chem. Soc.*, 1958, **80**, 6393-6398; (c) M. Stiles and R. P. Mayer, *J. Am. Chem. Soc.*, 1959, **81**, 1497-1503; and references 5, 10(b) and 10(d). We attribute this to the ability of both σ- and π-electrons on the *ipso* carbon to participate in bonding in the migration TS.
17. (a) M. Tilset and M. Lersch, *Chem. Rev.*, 2005, **105**, 2471-2526; (b) A. Vigalok, *Chem. Eur. J.*, 2008, **14**, 5102-5108.
18. (a) N. F. Goldshleger, A. A. Shteinman, A. E. Shilov and V. V. Eskova, *Zhur. Fizicheskoi Khim.*, 1972, **46**, 1353; (b) D. R. Weinberg, J. A. Labinger and J. E. Bercaw, *Organomet.*, 2007, **26**, 167.
19. C. Hammond, M. M. Forde, M. H. Ab Rahim, A. Thetford, Q. He, R. L. Jenkins, N. Dimitratos, J. A. Lopez-Sanchez, N. F. Dummer, D. M. Murphy, A. F. Carley, S. H. Taylor, D. J. Willock, E. E. Stangland, J. Kang, H. Hagen, C. J. Kiely and G. J. Hutchings, *Angew. Chem.-Int. Ed.*, 2012, **51**, 5129-5133.
20. (a) T. Hirao, M. Mori and Y. Oshiro, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2399; (b) U. Tatsuno, M. Tatsuda and S. Otsuka, *J. Chem. Soc. Chem. Comm.*, 1982, 1100; (c) J. T. Gleaves, J. R. Ebner and T. C. Kuechler, *Catalysis Reviews-Science and Engineering*, 1988, **30**, 49; (d) R. Neumann and A. M. Khenkin, *Chem. Commun.*, 2006, 2529.
21. (a) P. T. Matsunaga, J. C. Mavropoulos and G. L. Hillhouse, *Polyhedron*, 1995, **14**, 175-185; (b) T. M. Figg and T. R. Cundari, *Organometallics*, 2012, **31**, 4998-5004; (c) K. Kamaraj and D. Bandyopadhyay, *Organometallics*, 1999, **18**, 438-446.
22. O. A. Mironov, S. M. Bischof, M. M. Konnick, B. G. Hashiguchi, V. R. Ziatdinov, W. A. Goddard, M. Ahlquist and R. A. Periana, *J. Am. Chem. Soc.*, 2013, **135**, 14644-14658.