ORGANIC
LETTERS

2013
Vol. 15, No. 23
5920–5923

Novel Chemistry for the Selective Oxidation of Benzyl Alcohol by Graphene Oxide and N-Doped Graphene

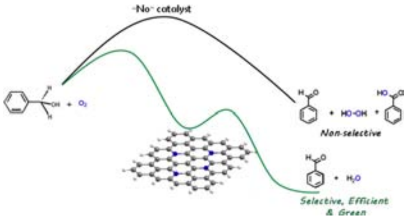
J. Vijaya Sundar and V. Subramanian*

Chemical Laboratory, CSIR-Central Leather Research Institute, Adyar, Chennai 600020, India

subuchem@hotmail.com, subbu@clri.res.in

Received August 15, 2013

ABSTRACT



A novel mechanism for the selective activation of benzyl alcohol by graphene oxide and N-doped graphene has been proposed using density functional theory based calculations. Interestingly, the proposed mechanism opens new avenues for graphene and its derivative-based catalysis.

In recent years, graphene and its functionalized forms have emerged as a promising material for various applications such as heterogeneous catalysis,[1−4] electron transport,[5,6] energy storage,[7,8] sensors,[9,10] and biomedical devices.[11,12] Interestingly, N-doped graphene (NG) acts as a catalyst for a variety of organic reactions such as selective oxidation of hydrocarbons,[13,14] aromatic alcohols,[15] and oxygen reduction reactions[16−18] in fuel cells. Moreover, such oxidative transformations occur in the aqueous phase with dioxygen as the ultimate oxidant and water as a byproduct.[15] Hence, usage of N-doped graphene as a catalyst is environmentally benign and highly selective compared to traditionally used transition-metal-based complexes and organic compounds.

In a seminal report, Bielawski and co-workers have elucidated that graphene oxide can catalyze oxidation of benzyl alcohol (BA) to benzaldehyde (BZ) with >90% conversion efficiency, using O_2 as terminal oxidant, without the formation of H_2O_2.[19] This study indicates that the conversion results in the reduction of epoxide to form reduced GO and chemically modified graphene (CMG). This reduction process is then followed by the release of water. However, the mechanism and the key intermediates controlling this reaction remain elusive.[19] In another computational study on benzyl alcohol oxidation by graphene oxide, Boukhvalov et al. have also highlighted that the epoxide plays a major role in the reaction.[20]

---

(1) Machado, B. F.; Serp, P. *Catal. Sci. Technol.* **2012**, *2*, 54–75.
(2) Dreyer, D. R.; Bielawski, C. W. *Chem. Sci.* **2011**, *2*, 1233–1240.
(3) Su, C.; Loh, K. P. *Acc. Chem. Res.* **2013**, *46*, 2275–2285.
(4) Pyun, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 46–48.
(5) Li, X.; Wang, X.; Zhang, L.; Lee, S.; Dai, H. *Science* **2008**, *319*, 1229–1232.
(6) Bai, J.; Duan, X.; Huang, Y. *Nano Lett.* **2009**, *9*, 2083–2087.
(7) Kamat, P. V. *J. Phys. Chem. Lett.* **2011**, *2*, 242–251.
(8) Wu, J.; Becerril, H. A.; Bao, Z.; Liu, Z.; Chen, Y.; Peumans, P. *Appl. Phys. Lett.* **2008**, *92*, 263302–263304.
(9) Lu, C. H.; Yang, H. H.; Zhu, C. L.; Chen, X.; Chen, G. N. *Angew. Chem., Int. Ed.* **2009**, *48*, 4785–4787.
(10) Schedin, F.; Geim, A. K.; Morozov, S. V.; Hill, E. W.; Blake, P.; Katsnelso, M. I.; Novoselov, K. S. *Nat. Mater.* **2007**, *6*, 652–655.
(11) Sun, X.; Liu, Z.; Welsher, K.; Robinson, J.; Goodwin, A.; Zaric, S.; Dai, H. *Nano Res.* **2008**, *1*, 203–212.
(12) Naldini, L.; Blömer, U.; Gallay, P.; Ory, D.; Mulligan, R.; Gage, F. H.; Verma, I. M.; Trono, D. *Science* **1996**, *272*, 263–267.
(13) Li, X.-H.; Chen, J.-S.; Wang, X.; Sun, J.; Antonietti, M. *J. Am. Chem. Soc.* **2011**, *133*, 8074–8077.
(14) Gao, Y.; Hu, G.; Zhong, J.; Shi, Z.; Zhu, Y.; Su, D. S.; Wang, J.; Bao, X.; Ma, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 1–6.
(15) Long, J.; Xie, X.; Xu, J.; Gu, Q.; Chen, L.; Wang, X. *ACS Catal.* **2012**, *2*, 622–631.
(16) Sidik, R. A.; Subramanian, N. P.; Kumaraguru, S. P.; Popov, B. N.; Anderson, A. B. *J. Phys. Chem. B* **2006**, *110*, 1787–1793.
(17) Qu, L.; Liu, Y.; Baek, J.-B.; Dai, L. *ACS Nano* **2010**, *4*, 1321–1326.
(18) Geng, D.; Chen, Y.; Chen, Y.; Li, Y.; Li, R.; Sun, X.; Ye, X.; Knights, S. *Energy Environ. Sci.* **2011**, *4*, 760–764.
(19) Dreyer, D. R.; Jia, H.-P.; Bielawski, C. W. *Angew. Chem., Int. Ed.* **2010**, *49*, 6813–6816.
(20) Boukhvalov, D. W.; Dreyer, D. R.; Bielawski, C. W.; Son, Y.-W. *ChemCatChem* **2012**, *4*, 1844–1849.

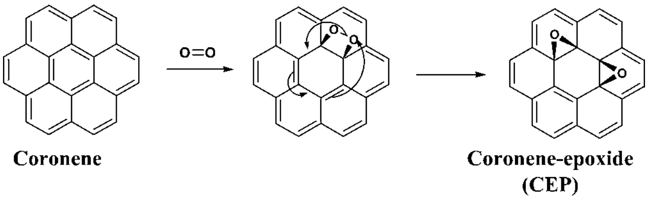
10.1021/ol402958h

Wang and co-workers have reported that N-doping of graphene enhances the aerobic oxidation of aromatic alcohols to aldehyde or ketone with $>99\%$ selectivity.[15] Further exploration revealed that graphitic nitrogen is actively involved in the catalysis, apart from the defects. For benzyl alcohol, the activation barrier of the reaction is found to be 13.4 ± 0.8 kcal/mol. Also, the same study indicates the absence of the formation of $OH^{\bullet}$, $O_2^{-\bullet}$, or H_2O_2.[15]

Ma and co-workers have investigated the aerobic oxidation of hydrocarbons, and they have indicated the immense role of graphitic nitrogen in catalysis.[14] They have demonstrated that the carbon atom which is ortho to nitrogen is "metal-like". It activates the dioxygen to form the reactive species, which may be "peroxide or epoxide"-like species, through spin and charge polarization. This finding provides a picture of the activation of dioxygen by graphitic nitrogen. Nevertheless, the structure of the reactive oxidant and the mechanism of the substrate oxidation without the formation of H_2O_2 have not completely unravelled.[14]

Epoxides have high reduction potentials (−2.3 V for stilbene oxide[21]), whereas the oxidation potential of benzyl alcohol is very low[22] (0.17 V), which makes the reduction of epoxide by benzyl alcohol highly unfavorable. Generally, acidification of epoxides opens up the ring to form hydroxyether, with monoalcohols.[23] Moreover, the possibility of acid−base reaction between benzyl alcohol and epoxide is ruled out by the pK_a of benzyl alcohol (15.4).[24] The above studies and arguments point out that the oxidation of benzyl alcohol by epoxide is dictated by a new mechanism. In this study, an attempt has been made to elucidate the reaction mechanism of oxidation of benzyl alcohol as catalyzed by coronene epoxide and N-substituted coronene using electronic structure methods. Previous studies have shown that coronene can be taken as a model for graphene.[25,26] Hence, in this study, the same has been considered as a model system. The calculations were carried out at M06-2X/6-311+g**//M06-2x/6-311g**[27−29] level of theory using the Gaussian 09[30] suite of programs. The solvent effect was included using polarizable continuum method[31] (PCM) at the same level of theory.

Scheme 1. Coronene Epoxide Formation from Dioxygen and Coronene



Dioxygen activation is the initial step in the catalytic pathway of GO. This activation step involves a complicated pathway. However, experiments have shown that the rate-determining step is the reaction between activated oxygen and benzyl alcohol.[15] Hence, no attempt has been made to study the activation of O_2, but such an activation process could be guessed to get an idea about the structure of the activated species. Scheme 1 illustrates an adduct formation between a carbon−carbon double bond and dioxygen, which then undergoes O−O bond cleavage to form coronene epoxide (CEP).

Once the epoxide (O1) is formed, the next step is the reduction of epoxide by benzyl alcohol. This reaction occurs by a proton (H^p) and a hydride (H^h) transfer from benzyl alcohol to coronene epoxide. Epoxides are well-known for their ability to accept a proton rather than hydride. Hence the OH group of benzyl alcohol is interacted with epoxide. Among the various possible modes of interaction, the most stable structure (EC_{EP}) is taken for further reaction (Figure 1a). Scheme 2 illustrates the entire pathway along with a description.

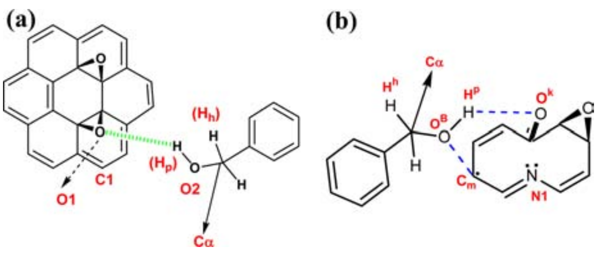


Figure 1. Schematic illustration of the formation of encounter complex (EC_{EP}) between (a) BA and CEP, (b) BA and N1-CK.

The transfer of H^p to O1 results in the rearrangement of π-bonds. This causes the carbon atom (C1), which is in the para-position to O1, to accept the hydride, leaving benzaldehyde as a product. Hence, the transfer of H^p to O1 and H^h to C1 is a concerted reaction with activation energy ($TS1_{EP}$) of 25.4 kcal/mol (Supporting Information Figure S6a).

The next step is the formation of water, through the combination of H^h (bonded to C1) and hydroxyl oxygen (O1). This occurs in two ways: (i) the direct recombination (DR) and (ii) the solvent (benzyl alcohol)-assisted recombination (SAR). In direct recombination, H^h interacts with O1 to form water with an activation energy of 65.1 kcal/mol. The solvent-assisted recombination occurs by the concerted transfer of H^h to the oxygen of benzyl alcohol and the hydrogen (bonded to the oxygen of benzyl alcohol)

---

(21) Boujlel, K.; Martigny, P.; Simonet, J. *J. Electroanal. Chem.* **1983**, *144*, 437–442.

(22) Dieckmann, G. R.; Langer, S. H. *J. Appl. Electrochem.* **1997**, *27*, 1–8.

(23) Jacobsen, E. N. *Acc. Chem. Res.* **2000**, *33*, 421–431.

(24) http://en.wikipedia.org/wiki/Benzyl_alcohol.

(25) Osuna, S.; Torrent-Sucarrat, M.; Solà, M.; Geerlings, P.; Ewels, C. P.; Van Lier, G. *J. Phys. Chem. C* **2010**, *114*, 3340.

(26) Bulat, F. A.; Burgess, J. S.; Matis, B. R.; Baldwin, J. W.; Macaveiu, L.; Murray, J. S.; Politzer, P. *J. Phys. Chem. A* **2012**, *116*, 8644–8652.

(27) Zhao, Y.; Truhlar, D. G. *Chem. Phys. Lett.* **2011**, *502*, 1–13.

(28) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257.

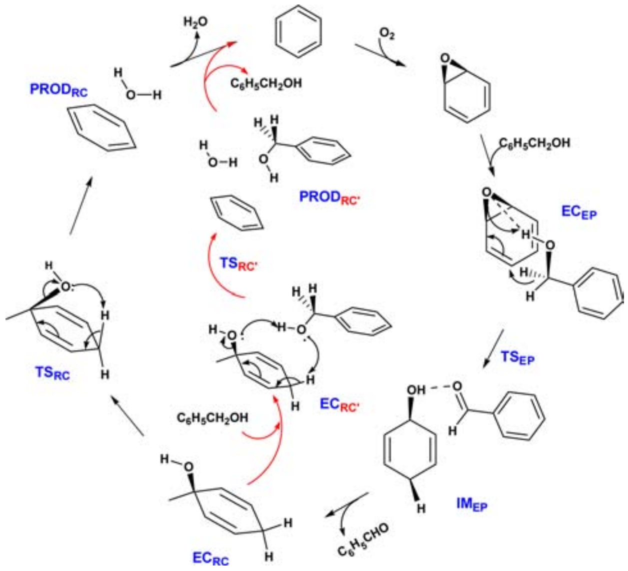
(29) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.

(30) Frisch, M. J.; et al. *Gaussian 09*, revision A.02; Gaussian, Inc.: Wallingford, CT, 2009.

(31) Miertuš, S.; Scrocco, E.; Tomasi, J. *J. Chem. Phys.* **1981**, *55*, 117.

to the hydroxyl group with an activation energy of 30.7 kcal/mol (Supporting Information Figure S6b). Comparison of the activation energies of both the recombination pathways indicates that the solvent-assisted recombination is the most feasible step.

Scheme 2. Reaction Mechanism for the Entire Pathway of Oxidation of Benzyl Alcohol by Coronene Epoxide

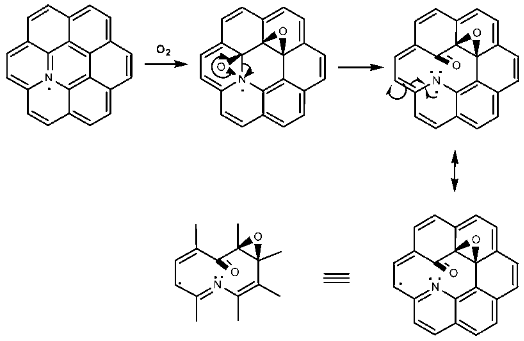


Further oxidation of benzaldehyde to acid by epoxide is schematically represented in the Supporting Information (Scheme S1). The reaction profile and optimized structures are given in Supporting Information (Figures S7 and S10). Mulliken charge analysis indicates that epoxide is negatively charged (−0.35, nucleophilic) and carbonyl carbon of benzaldehyde is positively charged (0.06, electrophilic). Hence, the reaction proceeds by the internal S_N2 attack of epoxide oxygen (O1) on the carbonyl carbon (C_α) of benzaldehyde. This leads to the transition state ($TS2_{BZ}$) with an activation energy of 34.4 kcal/mol. The intermediate ($IM1_{BZ}$) formed is more stable than EC_{BZ} by −14.9 kcal/mol. For the reaction to complete, the carbonyl hydrogen has to transfer to O1. This occurs through a transition state ($TS2_{BZ}$) with an activation energy of 45.4 kcal/mol. The above finding clearly reveals that the significant difference in the activation energies between the oxidation of benzyl alcohol to benzaldehyde and benzaldehyde to acid leads to the high selectivity in the conversion of benzyl alcohol to benzaldehyde. When compared to the previous study,[20] the present investigation provides a detailed concerted mechanism for proton and hydride transfer from benzyl alcohol to coronene epoxide and all possible regeneration reaction pathways.

Graphitic nitrogen substitution in coronene epoxide can be carried out in three distinct positions: N1, N2, and N3, as shown in Supporting Information (Figure S5). The calculations reveal that the formation of N1 is highly feasible when compared to other substitutions.

Also, substitution at the N1 position results in the breaking of the N−C bond and rearrangement of the epoxide

Scheme 3. Schematic Illustration for the Formation of Reactive Oxygen Species



to form a "ketone-like" structure (N1-KC) as illustrated in Scheme 3. Figure 1b depicts the structure of N1-KC with nomenclature. The steric environment in the coronene ring restricts the conjugation of "ketonic oxygen" (O^k) with nearby sp^2-hybridized carbons, which could possibly lead to the reactivity of O^k.

In the course of this rearrangement, the unpaired electron located on N1, perpendicular to the plane of the ring, migrates to the meta-position (C^m), as depicted in Supporting Information (Figure S14). This spin density on C^m can activate benzyl alcohol through spin-induced polarization. The initial step of oxidation of benzyl alcohol by N1-KC can take place by the abstraction of either a hydroxyl proton (H^p) (P1) or C_α-hydrogen (H^h) (P2). Both abstractions lead to different reaction pathways.

The pathway leading to the product by hydroxyl proton abstraction (P1) is illustrated in Supporting Information (Scheme S3) along with a description. The reaction profile and optimized structures are presented in Figure 2 and Supporting Information (Figure S11). All spin density isosurfaces are given in Supporting Information (Figure S14).

The initial step in P1 is the abstraction of H^p by O^k from the hydroxyl group of benzyl alcohol. The activation barrier ($TS1_N$) for the transfer of H^p is 9.1 kcal/mol. This involves the spin polarization of hydroxyl oxygen (O^B) of benzyl alcohol by C^m, leading to the spin separation in the O−H bond. As a consequence, α and β spins on O^h and C^m combine to form an O^B−C^m bond. As a result, H^p is transferred to O^k with a net spin density, which then leads to the restoration of the C−N bond through spin delocalization. In $TS1_{N1}$, spin density is transferred from C^m to N1 through a cyclic rearrangement of electrons. Neither the reactant (EC_{N1}) nor the intermediate ($IM1_{N!}$) shows any localized spin density leading to a radical. $IM1_{N1}$ directly cannot undergo any further reaction because of improper orientation of H^h. Hence, the structure is rotated with respect to the coronene ring to allow possible interaction between H^h and O^k to form $IM2_{N1}$. All attempts to find a rotational transition state between $IM1_{N1}$ and $IM2_{N1}$ are in vain. In the next step, the C^m−O^B bond breaks through $TS2_{N1}$ to form $IM3_{N1}$, resulting in high spin density on O^B (Supporting Information (Figure S10)). The activation energy for this bond breakage is 19.6 kcal/mol. It could be noted that IM3$_{N1}$ has a net spin density of about 0.9 and hence acts as a radical. The formation of such a radical intermediate is already observed through spin trapping experiments.[15] The final step is the transfer of H^h to O^k with subsequent coronene$-O^k$ bond breakage, resulting in the product, water and benzaldehyde. This occurs through TS3$_{N1}$ with an activation energy of 18.3 kcal/mol. Spin density analysis shows that this transfer is radical in nature.

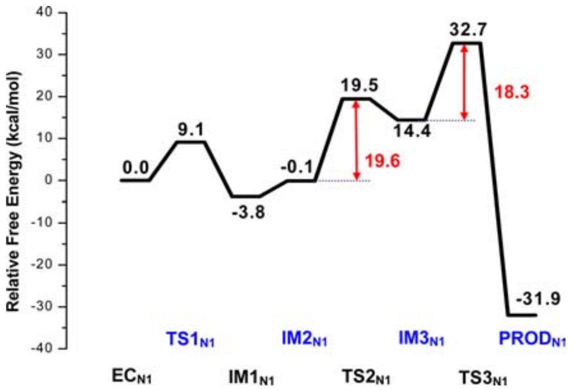


Figure 2. Reaction profile for the oxidation of BA with N1-CK.

Apart from IM3$_{N1}$, all other minima in this reaction sequence do not indicate any radical nature of the unpaired electron. This mechanism shows that the oxidation of benzyl alcohol occurs by two one-electron reductions of the activated oxygen species.

The second pathway (P2) occurs by the direct interaction of benzyl alcohol with O^k through a $C-H^\alpha$ bond. The reaction pathway for P2 is shown in Supporting Information (Scheme S4). The optimized geometries and reaction profile are represented in Supporting Information (Figures S7 and S11). The activation energy for the transfer of H^α to O^k is 29.7 kcal/mol. Spin density analysis indicates the radical formation on C_α and O^k atoms. The intermediate formed (IM1) is rotated to form IM2$_{N2}$, so that H^p interacts with O^k through a H-bond. In the next step, H^p is transferred to O^k through TS2$_{N2}$ with an activation energy of 17.9 kcal/mol to form water and benzaldehyde. This transfer results in net spin relocation from C_α to the N1 atom, leading to two one-electron transfer reactions. Comparing P1 and P2, it could be possible to show that P1 is the minimum energy pathway based on the following arguments: (i) the rate-determining step in P1 (TS2$_{N1}$) has an activation barrier of 19.7 kcal/mol, whereas the same in P2 is 29.7 kcal/mol (TS1$_{N2}$), and (ii) the experimentally observed intermediate is $C_6H_5CH_2O^\bullet$ (IM3$_{N1}$) rather than $C_6H_5C^\bullet(OH)$ (IM1$_{N2}$) as observed in P2.

Benzaldehyde oxidation to benzoic acid is then studied to unravel the selectivity of N-doped graphene. N1-KC is taken and interacted with benzaldehyde with similar conformation as that of coronene epoxide. The first step in the reaction is the lone pair attack of O^k on the C_α atom with an activation energy of 17.8 kcal/mol. This attack is followed by the transfer of C_α-hydrogen to O^k. This transfer takes place through TS2 with barrier height of 45.8 kcal/mol. The reaction profile is given in Supporting Information (Figure S7). Again, the selectivity arises due to a large difference in activation energy between benzyl alcohol oxidation and benzaldehyde oxidation (26.3 kcal/mol).

Generally, overoxidation of aldehyde to acid by metal oxidants arises due to the initial hydration of the carbonyl group. Then, condensation with the oxidant takes place, leading to the electron transfer from carbonyl hydrogen to the metal center. Hence, the barrier height for the reaction is low. However, the oxidation of benzyl alcohol by GO/N-doped graphene results in atom transfer reaction, which leads to high barrier height, and the same recation is responsible for the selectivity in the reaction.

In summary, the present DFT study provides a complete mechanism for the aerobic oxidation of alcohol by graphene oxide and N-doped graphene using model systems. In GO catalysis, the epoxide acts as a proton acceptor and a sp^2-hybridized carbon, which is para to epoxide, and behaves as a hydride acceptor. Such a peculiar mechanism is new to the chemistry of epoxide. This reaction pathway could reduce the overall barrier height of the reaction through the rearrangement of delocalized electrons of graphene. In the case of NG, the model provides a great deal of information about the initial activated oxygen species formed by dioxygen. This species contains a C=O group and catalyzes the reaction in a way similar to that of $Fe^{IV}=O$ in enzymes. The delocalization of the unpaired electron of the N-atom, on the ring, plays a major role in directing this activated oxygen to abstract hydrogen from benzyl alcohol as a radical. Such a spin-polarized activation mechanism of benzyl alcohol is not yet reported. This mechanism highly reduces the overall barrier height of the reaction and makes it ideal and novel for the oxidation of alcohols. Above all, the study provides the basis for the selectivity in benzyl alcohol oxidation. The rate-determining step for the oxidation of benzaldehyde involves a hydride transfer with high activation barrier height. This result could be very useful in controlling the selectivity of the reaction. Even though the model has limitations, it can provide useful information about the oxidation chemistry of graphene oxide and N-doped graphene.

Acknowledgment. The authors acknowledge the Multi-Scale Simulation and Modeling (MSM) project (CSC0129) funded by CSIR. J.V.S. thanks the Council of Scientific and Industrial Research (CSIR), New Delhi, for a research fellowship.

Supporting Information Available. Computational details, optimized geometries with relevant charge and spin density values and spin density isosurfaces. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.