

Hydrogen Abstraction by Alkoxy Radicals: Computational Studies of Thermodynamic and Polarity Effects on Reactivities and Selectivities

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Cite This: *J Am Chem Soc* 2022 144 6802 6812



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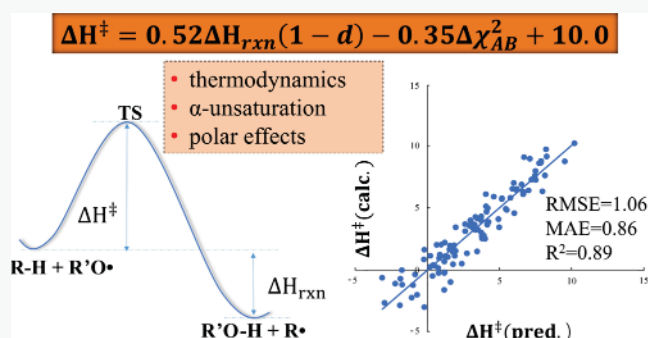
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ABSTRACT: Density functional theory calculations (B97X-D) are reported for the reactions of methoxy, *tert*-butoxy, trichloroethoxy, and triethoxy radicals with a series of 26 C–H bonds in different environments characteristic of a variety of hydrocarbons and substituted derivatives. The variations in activation barriers are analyzed with modified Evans–Polanyi treatments to account for polarity and unsaturation effects. The treatments by Roberts and Steel and by Mayer have inspired the development of a simple treatment involving the thermodynamics of reactions, the difference between the reactant radical and product radical electronegativities, and the absence or presence of α -unsaturation. The three-parameter equation ($\Delta H^\ddagger = 0.52 \Delta H_{\text{rxn}}(1-d) - 0.35 \chi_{\text{AB}}^2 + 10.0$, where $d = 0.44$ when there is α -unsaturation to the reacting C–H bond), correlates well with quantum mechanically computed barriers and shows the quantitative importance of the thermodynamics of reactions (dictated by the reactant and the product bond dissociation energies) and polar effects.



1 INTRODUCTION

The reactivities and selectivities of radicals in hydrogen abstraction reactions determine the utility of radical-induced C–H functionalization reactions.^{1–4} Understanding the reaction mechanisms, reactivities, and selectivities has been an important goal of physical organic and theoretical chemistry,⁵ and being able to predict these by empirical equations or theoretical calculations should assist the design and application of C–H functionalization reactions.^{6–10} Although density functional theory is now capable of accurate predictions of reaction rates, there is still a strong interest in quantitative understanding of factors that control these rates.

Many studies show that the reactivities and selectivities of C–H activation can be adjusted using the various nonmetal hydrogen atom transfer (HAT) radicals and catalysts.^{11–16} For example, Zuo et al. showed that gaseous alkanes could react in the presence of visible light, cerium salts, and alcohol catalysts under mild experimental conditions. They proposed that alkoxy radicals, $\text{RCH}_2\text{O}^\bullet$, are the active HAT agents.^{17–19} Zuo's work showed that the polarity of the alcohol catalysts influences the reactivities and selectivities with various hydrocarbons (Table 1). The reactivity and selectivity are both influenced by the structure of the alcohol catalyst, with the regioselectivity increasing from $\text{CCl}_3\text{CH}_2\text{OH}$ to CH_3OH , as the reactivity decreases.¹⁷ Similar phenomena were observed by MacMillan et al.,²⁰ who achieved selective sp^3 C–H

Table 1. Photocatalytic HAT Based Amination of Alkanes Catalyzed by Cerium Chloride and Alcohols

alkane	entry	cerium catalyst ^b	alcohol catalyst ^c	time (h)	yield (%)	1°/2°
propane	1	CeCl_3	$\text{CCl}_3\text{CH}_2\text{OH}$	9	70	1:1
	2	CeCl_3	$\text{CF}_3\text{CH}_2\text{OH}$	12	61	1:1
	3	CeCl_3	CH_3OH	19	39	1:3.9
butane	4	CeCl_3	$\text{CCl}_3\text{CH}_2\text{OH}$	6	76	1:1.7
	5	CeCl_3	$(\text{CH}_3)_2\text{CHOH}$	18	40	1:4
	6	CeCl_3	CH_3OH	18	72	1:8

^aData from ref 17. ^b CeCl_3 loading 0.5 mol % . ^cAlcohol catalyst loading 20 mol % .

alkylation via polarity-matched HAT to the quinuclidine radical cation, where the polarity of the substrate and the catalyst was shown to impact both the HAT reactivity and selectivity.

Received: January 11, 2022

Published: April 5, 2022



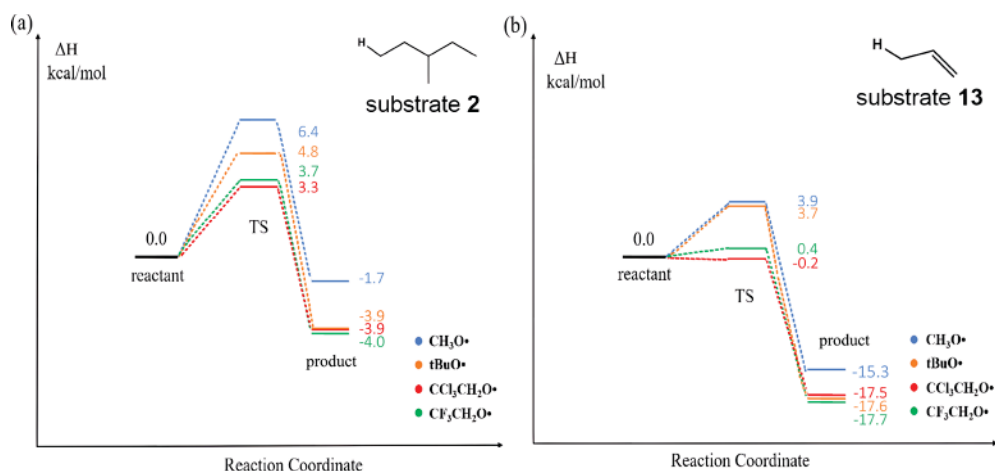


Figure 1. Energy diagram of HAT from the primary C(sp³)-H bond of (a) **2** in Table 2 and (b) **13** in Table 2 to alkoxy radicals in acetonitrile using U B97X-D/6-311++G(d, p)//U B97X-D/6-31G(d)/SMD(MeCN). All the energy terms are given in kcal/mol.

Many empirical methods for estimating the activation energy have been developed. One of the most venerable is the Bell Evans Polanyi (BEP) correlation, also referred to more simply as the Evans Polanyi relationship or sometimes the Brønsted Evans Polanyi relationship.^{6,21,22} This relationship indicates that as a reaction becomes more exothermic, it becomes faster. The decrease in selectivity accompanying an increase in the reaction rate is expressed through related concepts such as the Hammond Postulate.²³ In 1982, Tedder proposed Evans Polanyi relationships for HAT reactions, showing a correlation between the rate and the reaction energy.⁸ Later, Mayer proved that this correlation is quite general.²⁴ In the past few decades, BEP-type relationships have become a widely used method for evaluating the activation energy of numerous reactions. Such an approach has contributed to the establishment of rate-determining steps in reaction mechanisms.^{25–30}

In 1956, Marcus proposed what is now known as the Marcus theory⁷ to explain the rates of electron transfer reactions. The Marcus theory is widely used to predict the reaction barriers from the reaction driving forces and intrinsic barriers. Mayer applied the Marcus cross relationship (MCR) to a wide range of HAT reactions and found that it holds very well with only a few outliers.³¹ Shaik et al. have explored HAT reactions,^{9,10,32–36} and they proposed several approximate equations based on the valence bond (VB) model (“VB state correlation diagrams” and “VB configuration mixing diagrams”) to predict and explain the reactivities and selectivities. Using the promotion energy gap G , the resonance energy of the transition state (T_S) B , and the reaction energy E_{rxn} , these equations give good correlations with high-level computational data and experimental data for many reactions and can be applied to different reaction types, not only H-abstractions. The VB model creates a natural bridge to the Marcus equation.^{33,35}

In addition to the thermodynamic effects, a number of studies showed that polar effects can play an important role in HAT processes.^{37–45} In the reactions of neutral free radicals, the term polar effect is used to describe the influence on the activation energy of any charge transfer which may occur on going from the reactant(s) to the transition state.⁴⁴ This has been interpreted by both VB and molecular orbital (MO) theories. In VB theory, an activation energy is lowered by the

contribution of a zwitterionic VB structure,⁴⁵ while in MO theory, the non-bonding MO of the transition state is stabilized when one terminus is more electronegative than the other.^{44,46} In 1994, Roberts and Steel indicated that along with the overall enthalpy change H_{rxn} , polar effects, steric and stereo-electronic effects, as well as the degree of unsaturation should also be taken into consideration when discussing the reactivity. They proposed a modified form of the Evans Polanyi equation (that we call here the “Roberts relationship”) to correlate and predict the activation energies for HAT reactions.⁴⁷ In previous work, we and others observed bimodal BEPs between activation barriers and bond dissociation energies (related to the reaction energy of a hydrogen abstraction) depending on whether the radical generated is adjacent only to saturated carbons (“saturated”) or is stabilized by resonance due to adjacent π bonds (“unsaturated”).^{39,48}

There have been reactivity and selectivity studies of related oxidants,^{6,9,13,40} such as dioxiranes^{49,50} and metal oxo species such as the iron- and manganese-oxo reagents popularized by White and Costas^{51,52} and Du Bois’s ruthenium-oxo catalysts.⁵³ Baran et al. have explored a variety of oxidants for selective syntheses.^{54–56} We have now explored reactivity relationships for various types of C–H bonds in hydrocarbons and heterosubstituted compounds in HAT to alkoxy radicals with differing polarities ($R-H + R'O \rightarrow R + R'OH$). Four radicals were investigated: methoxy ($CH_3O\cdot$), *tert*-butoxy ($tBuO\cdot$), and the more electronegative trichloroethoxy ($CCl_3CH_2O\cdot$) and trifluoroethoxy ($CF_3CH_2O\cdot$). We have explored the influence of thermodynamic, polarity, and unsaturation effects on the reactivity and selectivity. Our goal is to gain understanding and to develop a simple model to interpret and predict selectivities in terms of the reactivities (thermodynamics) and radical and substrate structures (electronegativity differences and unsaturation).

2 COMPUTATIONAL METHODS

The geometries of minima and transition states were optimized using unrestricted B97X-D with the 6-31G(d)^{57,58} basis set. The keyword “stable = opt” was set to guarantee the stability of the wavefunction. Frequency analyses were performed to verify that these structures correspond to energy minima or saddle points (transition states). Single-point energies with a more extensive basis set were carried out with U B97X-D/6-311++G(d, p) on the optimized geometries. The solvent effects of CH_3CN on the reaction were taken into account by

Table 2. C–H Bonds for HAT to Alkoxy Radicals Studied in This Work

1	2	3	4	5	6	7
8	9	10	11	12		
13	14	15	16	17	18	19
20	21	22	23	24	25	26

^aThe H abstracted is shown in each panel.

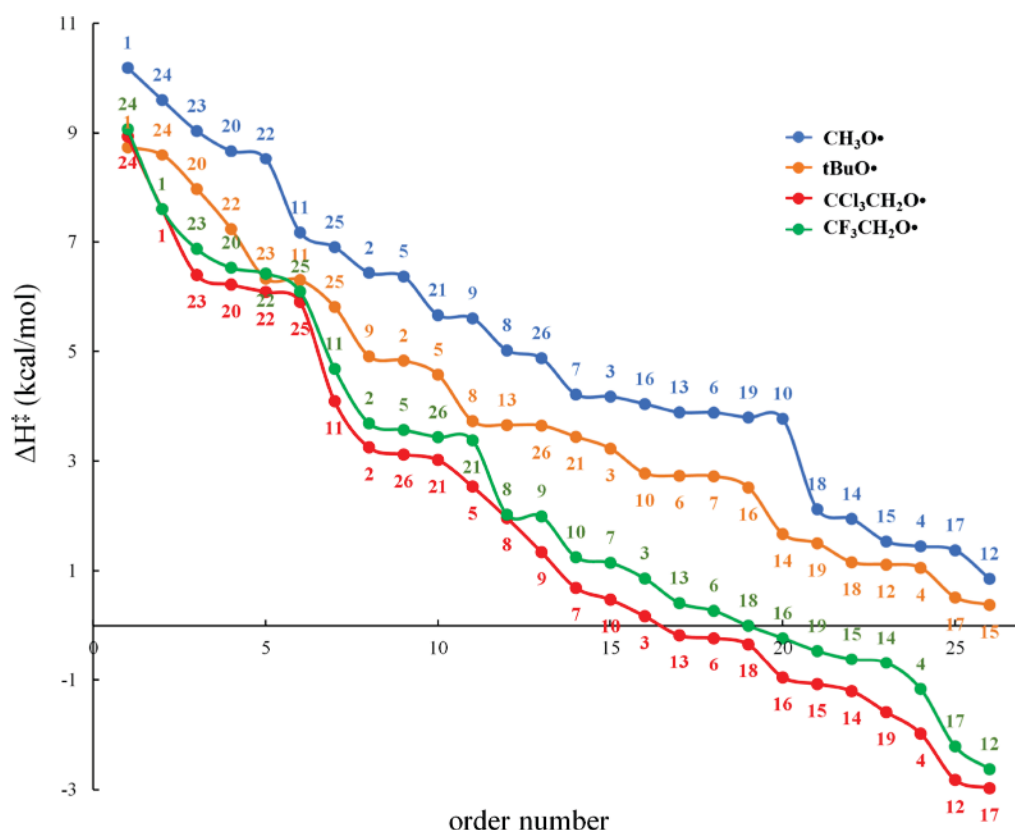


Figure 2. $\Delta H^\ddagger$ for HAT from the C–H bonds of the substrates shown in Table 2 to the four alkoxy radicals: $\text{CH}_3\text{O}^\bullet$ (blue), $t\text{BuO}^\bullet$ (orange), $\text{CCl}_3\text{CH}_2\text{O}^\bullet$ (red), and $\text{CF}_3\text{CH}_2\text{O}^\bullet$ (green). Calculations are based on U-B97X-D/6-311++G(d,p)//U-B97X-D/6-31G(d) with the SMD model in CH_3CN . Energies are given in kcal/mol.

using the solvation model based on density (SMD model).⁵⁹ All calculations were carried out with Gaussian 16.⁶⁰ The effectiveness of U-B97X-D for geometries and energies has been demonstrated by many studies.^{61,62}

3 RESULTS AND DISCUSSION

Figure 1a,b shows the enthalpy diagrams for reactions of substrates 2 (1° C–H of 3-methylpentane) and 13 (α C–H of propene) in Table 2, with the four alkoxy radicals ($\text{CH}_3\text{O}^\bullet$, $t\text{BuO}^\bullet$, $\text{CCl}_3\text{CH}_2\text{O}^\bullet$, and $\text{CF}_3\text{CH}_2\text{O}^\bullet$). They are selected as the representative “saturated” and “unsaturated” C–Hs, respectively. For both 2 and 13, HAT to $\text{CH}_3\text{O}^\bullet$ shows the lowest reactivity corresponding to the lowest reaction enthalpy. This

is consistent with the BEP relationship that is, the more exothermic the reaction, the lower the activation barrier. However, for the other three radicals, the BEP relationship did not hold anymore: the changes in reactivity are associated with very similar reaction enthalpies. The differences in the reaction enthalpy between 2 and 13 are greater than 13 kcal/mol, while the differences in the activation enthalpy are within 3.5 kcal/mol for all four radicals. This shows the important contribution of unsaturation. For 3-methylpentane, which was taken as the representative of primary, secondary, and tertiary “saturated C–Hs”, the activation energy decreases with the increase of exothermicity as expected from the BEP relationship or simple considerations of bond dissociation energies/

enthalpies (BDEs) (Tables S1–S4). The results confirm that unsaturation and polar effects are important factors for the reactivities in HAT processes.

In order to explore the reactivity prediction model for HAT to alkoxy radicals, we studied HAT using the four alkoxy radicals from all of the sp^3 C–Hs indicated in Table 2. Both “saturated” C–Hs (1–12 in Table 2) and “unsaturated” C–Hs (13–26 in Table 2, containing C–Hs α to $C=C$, $C=O$, CN, or benzene, so that delocalized radicals are generated) have been studied.

CH_3O , $tBuO$, CCl_3CH_2O , and CF_3CH_2O are the HAT agents. Tables S1–S4 present the activation energy (E), activation enthalpy (H), activation free energy (G), reaction enthalpy (H_{rxn}), reaction free energy (G_{rxn}), and C–H BDE (enthalpy) for HAT promoted by CH_3O , $tBuO$, CCl_3CH_2O , and CF_3CH_2O , respectively. While C–H BDEs range from 79.0 to 104.4 kcal/mol, H values range from 1.0 to 10.2 kcal/mol for CH_3O , 0.4 to 8.7 kcal/mol for $tBuO$, 3.0 to 8.9 kcal/mol for CCl_3CH_2O , and 2.6 to 9.1 kcal/mol for CF_3CH_2O . Overall, the reactivities for HAT to CCl_3CH_2O and CF_3CH_2O are similar and higher than those for $tBuO$. CH_3O is the least reactive radical (Figure 2). The structure–reactivity relationships for each H-abstracter and how reactivity is influenced by polar effects and unsaturation will be discussed.

To test the accuracy of our computational results, single-point energies were evaluated by unrestricted DLPNO-CCSD(T)/cc-pVTZ calculations based on the optimized structures with U-B97X-D/6-31G(d) using the ORCA 5.1.0 program.^{63–65} Figure 3 shows the plot of H

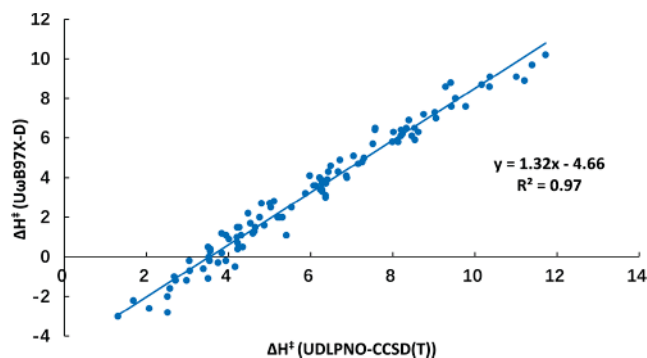


Figure 3. Plot of H calculated by unrestricted DLPNO-CCSD(T)/cc-pVTZ vs H calculated using U-B97X-D/6-311++G(d,p) based on the optimized structures with U-B97X-D/6-31G(d) for HAT from the C–H bonds of the substrates shown in Table 2 to the four alkoxy radicals. Energies are given in kcal/mol.

(DLPNO-CCSD(T)) versus H (U-B97X-D) based on the optimized structures with U-B97X-D/6-31G(d) for HAT from the C–H bonds of the substrates shown in Table 2 to the four alkoxy radicals, and Table S5 lists the H (DLPNO-CCSD(T)). The correlation is good, indicated by $R^2 = 0.97$. Additionally, we performed calculations for seven HAT reactions of HO , CH_3O , and $tBuO$ for which experimental data are available in Roberts and Steel's work⁴⁷ (see Table S6). U-B97X-D/6-311++G(d,p)//U-B97X-D/6-31G(d), UM062X/6-311++G(d,p)//UM062X/6-31G(d),⁶⁶ and UDLPNO-CCSD(T)/cc-pVTZ//U-B97X-D/6-31G(d) were tested. The calculations are listed in Table S6 along with E (exp). R^2 for E (U-B97X-D) versus E (exp), E (U-B97X-D) versus E (UM062X), and E (U-B97X-D) versus E (UDLPNO-CCSD(T)) are

0.94, 0.99, and 0.96, respectively (see Figure S1). All these results indicated that U-B97X-D is a reliable method to study the HAT reactions. Our subsequent discussions are based on the calculations by U-B97X-D. There are other composite methods such as (RO)CBS-QB3,^{39,67} Radom's G3(MP2)-RAD,⁶⁸ and G4(MP2)-6X⁶⁹ that have also been shown to be reliable for radical reactions.

3.1 BEP Correlation The BEP correlation relates the activation energy to the reaction enthalpy, eq 1

$$\Delta H^\ddagger = \gamma \Delta H_{rxn} + \xi \quad (1)$$

where H is the activation enthalpy of the reaction, H_{rxn} is the reaction enthalpy, and γ and ξ are parameters that are obtained from the linear regression analysis of the data.

Figure 4 shows a plot of H versus H_{rxn} for the reactions of sp^3 C–Hs with all four alkoxy radicals studied here.

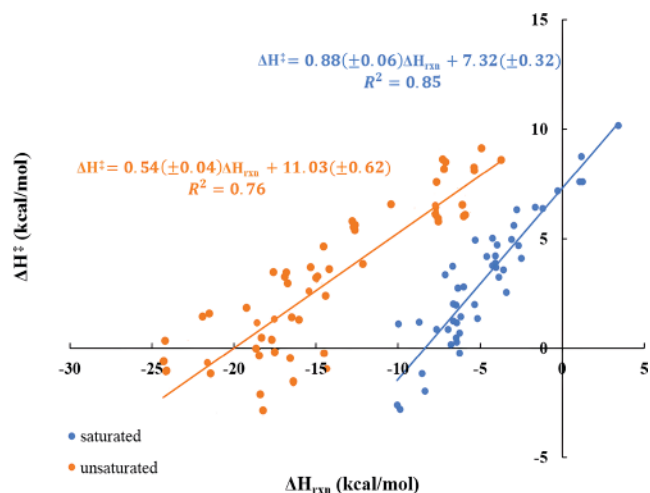


Figure 4. Plot of H vs H_{rxn} for HAT from the C–H bonds of the substrates shown in Table 2 to the four alkoxy radicals. Calculations are based on U-B97X-D/6-311++G(d,p)//U-B97X-D/6-31G(d) with the SMD model in CH_3CN . Energies are given in kcal/mol.

Although the correlation is rough, the “saturated” and “unsaturated” C–Hs display different behaviors as in our previous study of dioxirane reactions⁴⁸ and in a recent study from one of us of reactions involving the cumyloxy radical.³⁹ The linear relationship for the “saturated group” is reasonably good ($R^2 = 0.85$), while it is $R^2 = 0.76$ for the “unsaturated group”. The “intrinsic barrier” in Marcus language, where $H_{rxn} = 0$, is 7.3 kcal/mol for the saturated and 11.0 kcal/mol for the unsaturated compounds, while the “saturated” C–H is more sensitive to the H_{rxn} . These trends are discussed for cumyloxy in the recent paper.³⁹

Taking the polarity of the alkoxy radicals into account, we then inspected BEP plots for three categories of H-abstracting alkoxy radicals: (1) $tBuO$, (2) CH_3O , and (3) CCl_3CH_2O and CF_3CH_2O taken together as radicals displaying increased electronegativity. These three correlations are shown in Figure 5. All are improved as compared to the correlation for all four radicals (Figure 4). This is consistent with the idea that an intrinsic property of each radical is important, and we take this to be the radical electronegativity. For all radicals, the sensitivity of the activation barrier to the reaction exothermicity is larger for the saturated (0.7–0.9) than for the unsaturated C–H bonds (0.4–0.6), consistent with Bernasconi's principle of non-perfect synchronization (NPS).^{70–72}

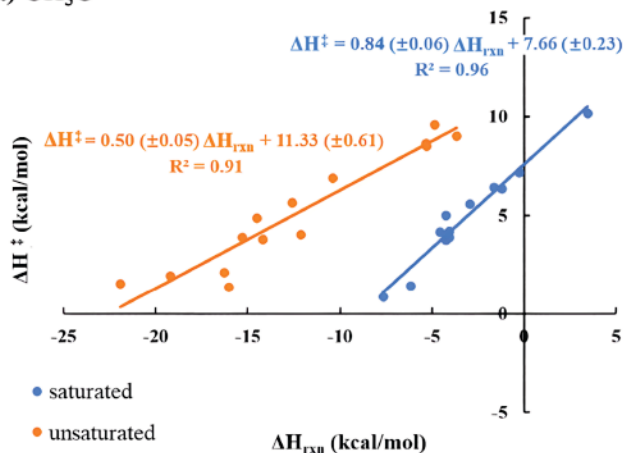
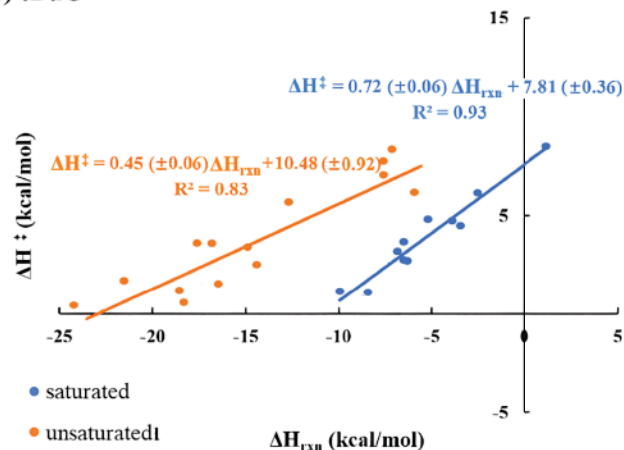
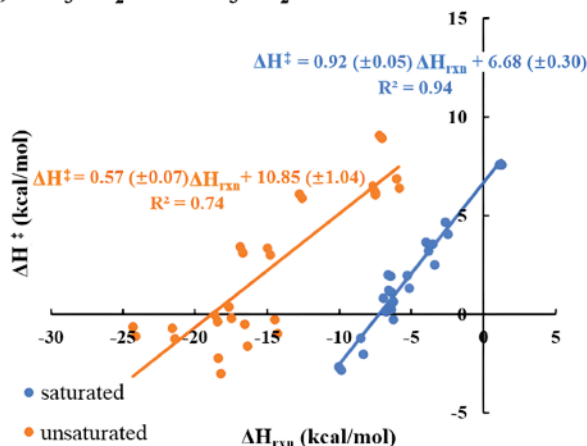
(a) $\text{CH}_3\text{O}\cdot$ (b) $t\text{BuO}\cdot$ (c) $\text{CCl}_3\text{CH}_2\text{O}\cdot$ & $\text{CF}_3\text{CH}_2\text{O}\cdot$ 

Figure 5. Plots of $\Delta H^\ddagger$ vs ΔH_{rxn} for HAT from the C–H bonds of the substrates shown in Table 2. (a) Graphical display of $\text{CH}_3\text{O}\cdot$. (b) Graphical display of $t\text{BuO}\cdot$. (c) Graphical display of $\text{CCl}_3\text{CH}_2\text{O}\cdot$ and $\text{CF}_3\text{CH}_2\text{O}\cdot$. Calculations are based on U–B97X-D/6-311++G(d,p)//U–B97X-D/6-31G(d) with the SMD model in CH_3CN . Energies are given in kcal/mol.

3.2 Marcus Cross Relationship The MCR is a corollary of the Marcus theory of electron transfer,⁷ and it was used effectively for HAT reactions by Mayer.³¹ According to the MCR, the rate constant for a HAT reaction ($\text{A} + \text{H} + \text{B} \rightarrow \text{A} + \text{BH}$) $k_{\text{AH/B}}$ can be estimated with eq 2

$$k_{\text{AH/B}} = \sqrt{k_{\text{AH/A}} k_{\text{BH/B}} K_{\text{eq}}} \quad (2)$$

$k_{\text{AH/A}}$ and $k_{\text{BH/B}}$ are the rate constants for the respective hydrogen-atom self-exchange reactions, controlled by the Marcus intrinsic barriers. The equilibrium constant K_{eq} can be obtained from the reaction driving force ΔG , which is related to the difference in free energies of reactions of AH and BH. This is the thermodynamic factor in the Marcus theory. MCR has the advantage that (in many cases) all of the parameters can be measured experimentally. Mayer proved that the MCR can predict within a factor of ~ 5 the rate constants for most organic and transition-metal-based HAT reactions, including those involving substrates with C–H, O–H, and N–H bonds.³¹

In this study, we treated the data in terms of the free energy, as in the usual formulation of the Marcus theory, rather than in terms of rates

$$\Delta G^\ddagger = \Delta G_{\text{int}}^\ddagger + \frac{\Delta G}{2} + \frac{(\Delta G)^2}{16\Delta G_{\text{int}}^\ddagger} \quad (3)$$

G_{int} is an average reaction barrier for self-exchange reactions ($\text{A} + \text{H} + \text{A} \rightarrow \text{A} + \text{A} + \text{H}$ and $\text{B} + \text{H} + \text{B} \rightarrow \text{B} + \text{B} + \text{H}$), and ΔG is the reaction free energy.

Activation free energies for self-exchange reactions (G_0) are listed in Table S7. Plots of the predicted activation free energies using eq 3 against those calculated based on transition state theory are shown in Figure 6. We note that (1) The activation barriers are systematically overestimated by MCR for all four alkoxy radicals. (2) The linear relationship between barriers obtained by the transition state theory and MCR is poor, especially for $\text{CCl}_3\text{CH}_2\text{O}\cdot$ and $\text{CF}_3\text{CH}_2\text{O}\cdot$ ($R^2 = 0.48, 0.52, 0.27, 0.29$ for $t\text{BuO}\cdot$, $\text{CH}_3\text{O}\cdot$, $\text{CCl}_3\text{CH}_2\text{O}\cdot$, and $\text{CF}_3\text{CH}_2\text{O}\cdot$, respectively). (3) The mean absolute error (MAE) and root mean square error (RMSE) increase with increasing electronegativity of the H-abstractors. All of these observations indicate that the polar effects should be taken into account when establishing the barrier prediction model and are not accounted for by intrinsic reaction barriers.

3.3 Roberts–Steel Relationship Equation 4 shows the form of the Roberts–Steel relationship, as we call it, which

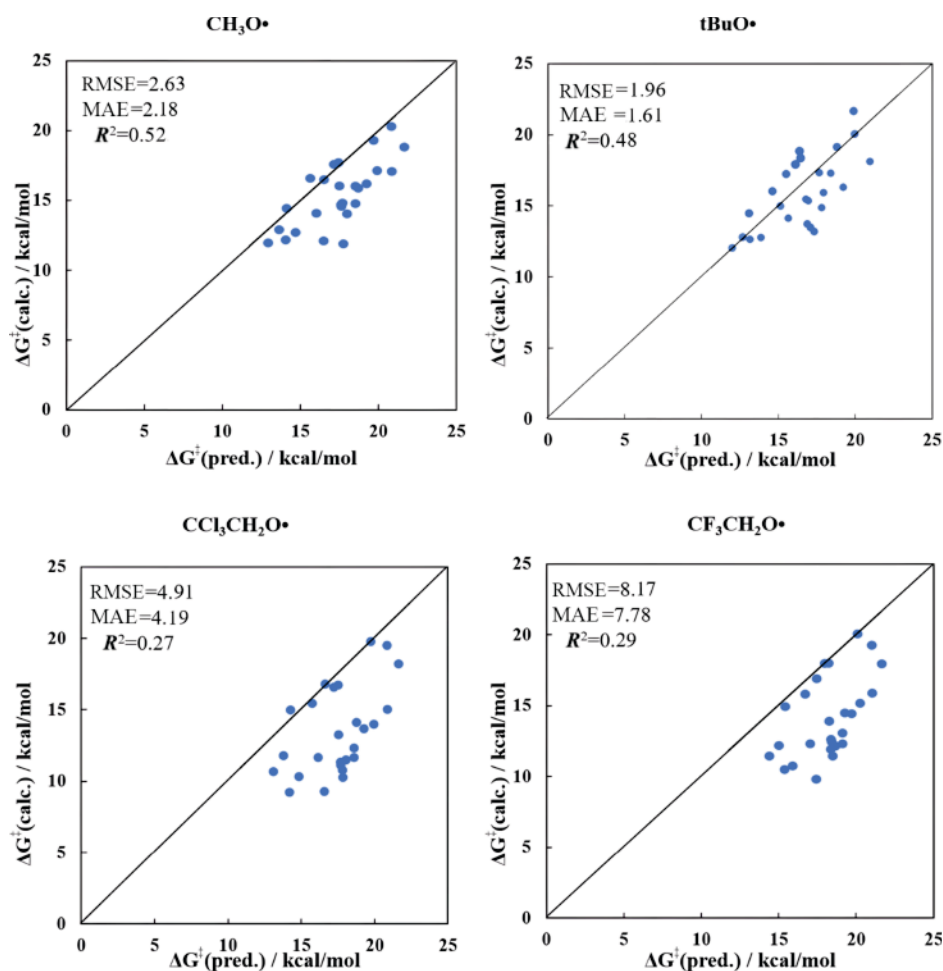


Figure 6. Plots of the predicted activation energies using MCR ($\Delta G^\ddagger(\text{pred.})$) against those calculated for the HAT reactions ($\Delta G^\ddagger(\text{calc.})$). The straight line corresponds to $\Delta G^\ddagger(\text{pred.}) = \Delta G^\ddagger(\text{calc.})$. Energies are given in kcal/mol.

contains the contribution of the strengths of A–H and B–H bonds, which form and break during the reaction (f), the enthalpy of reaction (H_{rxn} , basically the same as the BEP relationship), along with polar effects (χ_{AB}^2), unsaturation effects (d), and the structure factor (S_{X}). E_0 , α , β , and γ are parameters obtained from the least-squares regression.

$$\Delta H^\ddagger = E_0 f + \alpha \Delta H_{\text{rxn}}(1 - d) + \beta \Delta \chi_{\text{AB}}^2 + \gamma(S_{\text{A}} + S_{\text{B}}) \quad (4)$$

The f term is related to the energy required to stretch the A–H and B–H bonds, calculated from the BDEs, D_{AH} and D_{BH} of the reactant and the product, and D_{H_2} of H_2 eq 5

$$f = \frac{D_{\text{AH}} D_{\text{BH}}}{D_{\text{H}_2}^2} \quad (5)$$

The higher these dissociation energies, the higher the activation barrier, and the denominator makes this a dimensionless quantity.

The d -term represents unsaturation effects when there is α -unsaturation (e.g., $\text{C}=\text{C}$, $\text{C}=\text{O}$, CN , or benzene) with respect to the reacting C–H bond and is an empirical constant (see Table 3). According to Roberts's work,⁴⁷ d has two values: 0.44 for “unsaturated” C–Hs and 0.0 for “saturated” C–Hs. This means that the breaking of the “unsaturated” C–H bonds is 0.56 times as sensitive as the breaking of “saturated” C–H bonds to the energy of reaction. This was noted earlier in our

work on Bernasconi's principle of NPS in dioxirane reactions that also involve C–H bond breaking and transient radical formation.⁴⁸

The polar effect can be understood in terms of the interactions between the Frontier MOs of the reacting partners or charge-transfer interaction in the transition state using the VB model (which attempts to give a simple picture of the transition state itself). It is quantified by the Mulliken-type electronegativity: χ_{AB} is the electronegativity difference between the radicals A and B in HA and HB. The Mulliken-type electronegativity⁷³ of the radical X is defined in eq 6

$$\chi_{\text{X}} = \frac{\text{IE}_{\text{X}} + \text{EA}_{\text{X}}}{2} \quad (6)$$

IE and EA are the vertical ionization energy and vertical electron affinity of X, respectively, so that χ of a radical is the average of its IE and EA (or when computed, the negative of the average of the highest occupied molecular orbital and lowest unoccupied molecular orbital energies).

The structure factor, S_{X} , represents the changes of the reactant's and the product's radical structures during the reaction, which are given as empirical constants for given radical types by Roberts and Steel. Generally speaking, the transition state geometries of the radical moieties, A and B, are different from those in the reactant states. According to

Table 3. Computed Data for the Radicals A and B Involved in the HAT Reaction

radical (X)	$D_{\text{HX}}/\text{kcal}\cdot\text{mol}^{-1}$	IE/eV	EA/eV	χ/eV	d	S_X
1	104.4	9.76	0.15	4.80	0	0.6
2	99.3	8.15	0.41	3.87	0	0.6
3	96.4	7.42	0.61	3.41	0	0.6
4	94.8	6.95	0.58	3.18	0	0.6
5	99.8	8.06	0.27	3.90	0	0.6
6	96.9	7.42	0.50	3.46	0	0.6
7	96.9	7.42	0.50	3.46	0	0.6
8	96.7	7.57	0.28	3.65	0	0.6
9	98.0	7.92	0.24	3.84	0	0.6
10	96.7	7.85	0.41	3.72	0	0.6
11	100.7	8.47	0.13	4.17	0	0.6
12	93.3	6.94	0.85	3.05	0	0.6
13	85.6	8.10	0.28	4.19	0.44	0.6
14	81.7	7.48	0.03	3.75	0.44	0.6
15	79.0	7.12	0.06	3.59	0.44	0.6
16	88.8	7.27	0.69	3.98	0.44	0.6
17	84.9	6.88	0.52	3.70	0.44	0.6
18	84.7	6.58	0.41	3.49	0.44	0.6
19	86.8	7.76	0.33	4.04	0.44	0.6
20	95.6	9.92	1.39	5.65	0.44	0.6
21	88.3	9.07	1.10	5.08	0.44	0.6
22	95.6	9.83	1.42	5.63	0.44	0.6
23	97.2	9.80	1.31	5.55	0.44	0.6
24	96.1	10.33	1.51	5.92	0.44	0.6
25	90.5	9.34	1.12	5.23	0.44	0.6
26	86.4	8.62	0.91	4.77	0.44	0.6
CH ₃ O	100.9	12.59	1.22	6.91		2.5
<i>t</i> BuO	103.2	8.55	3.91	6.23		2.5
CCl ₃ CH ₂ O	103.1	12.45	2.45	7.45		2.5
CF ₃ CH ₂ O	103.3	13.09	2.43	7.76		2.5
H ₂	101.7					

Roberts's work,⁴⁷ the values are 0.6 and 2.5 for alkyl and alkoxy radicals, respectively. As noted above, the parameters E_0 , α , β , and γ are determined from a multiple regression analysis of the data. The terms related to the Roberts relationship in this study are listed in Table 3, D_{HX} , IE, EA, and χ were computed here since many of these data are not known experimentally.

χ_{AB} values are listed in Table S9.

Instead of using the Roberts relationship directly, we have developed a simplified form (eq 7) containing the reaction enthalpy (H_{rxn}), the unsaturation term d , and the polar effect described by a Mulliken-type electronegativity χ_{AB} .

$$\Delta H^\ddagger = \alpha \Delta H_{\text{rxn}}(1 - d) + \beta \Delta \chi_{\text{AB}}^2 + \delta \quad (7)$$

This simplified Roberts relationship obtained from linear regressions of the data computed here is displayed in eq 8

$$\Delta H^\ddagger = 0.52 \Delta H_{\text{rxn}}(1 - d) - 0.35 \Delta \chi_{\text{AB}}^2 + 10.0 \quad (8)$$

There is now a good linear relationship between predicted and calculated activation energies. $R^2 = 0.89$ for the whole series, including all radicals and substrates studied here (see Figure 7). The MAE and RMSE are 0.86 and 1.06, respectively, so that the error in the barriers is on average about 1 kcal/mol, corresponding to better than a 1 order of magnitude accuracy of rates at room temperature. There is little improvement of eq 8 by including the f term and structure factor S_X from the original Roberts relationship (see Figures S2–S3). We also tried other combinations of these factors. $H = 0.23 H_{\text{rxn}} - 0.44 \chi_{\text{AB}}^2 + 9.77$ as obtained when

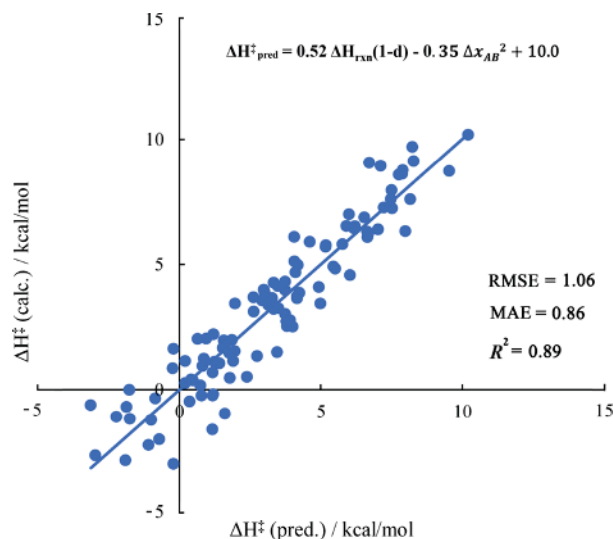


Figure 7. Plot of the predicted activation energies from a simplified Roberts–Steel relationship, eq 8 against those calculated quantum mechanically for the HAT reactions. Energies are given in kcal/mol.

both the f and d terms were removed, $R^2 = 0.85$ was obtained, see Figure S4. With equation $H = 0.72 H_{\text{rxn}}(1 - d) + 7.97$ where χ_{AB}^2 was removed further, $R^2 = 0.59$ was obtained, see Figure S5. The electronegativity factors are clearly important.

Interestingly, the coefficient α , the Evans–Polanyi slope, is 0.52 when including the unsaturation factor d into the H_{rxn}

term. This value is close to 0.5, which is frequently the case for simple BEP plots. This slope, 0.5, is also the slope of the Marcus equation as long as H_{rxn} is not too large. The d value derived by Roberts and Steel of 0.44 means that only about 1/2 (actually 0.56) of the exothermicity shows up in the transition state, and this is consistent with Bernasconi's Principle of NPS. The coefficient of 0.35 for χ_{AB}^2 means that as the difference in electronegativity increases, the activation barrier decreases by about 1/3 of that value. This is consistent with the polarity-matching effects, large polarity differences lead to lower barriers.³⁷

The polarity-matching concept (see Figure 8) is that the activation energy decreases as the electronegativity differences

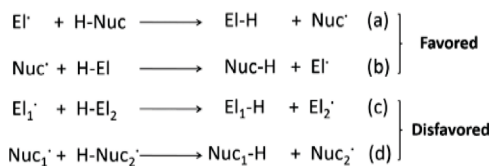


Figure 8. Scheme of polarity-matching effects in HAT reactions.

between the H-abstractor and the product radical increase. If El and Nuc represent electrophilic and nucleophilic radicals, respectively, the reactions (a,b) should be favored because of polar effects, while reactions (c,d), where the polarity of the two radicals is similar, will be disfavored.

This simplified Roberts relationship also echoes one of the VB equations proposed by Shaik,³³ eq 9.

$$\Delta E_{\text{VB}}^\ddagger \approx 0.5\Delta E_{\text{rxn}} + 0.3G_0 - B_{\text{AHB}} \quad (9)$$

where E_{rxn} is the reaction energy, G_0 is the average promotion gap (estimated by the sum of the vertical bond strengths of the bonds under activation in the forward and reverse directions), and B_{AHB} is the transition-state resonance energy estimated by $B_{\text{AHB}} = \frac{1}{4}(\text{BDE}_{\text{A-H}} + \text{BDE}_{\text{B-H}})$ and is related to the Bernasconi factor in our equation. The influence of χ_{AB}^2 in the simplified Roberts relationship is replaced by G_0 here, as these two terms have similar absolute coefficients (0.35 and 0.3, respectively).^{33,35} The VB and simplified Roberts Steel approach provide a similar accuracy and alternate ways of conceptualizing the factors controlling the reactivity.

3.4 Distortion/Interaction Analysis The distortion/interaction activation strain analysis that was proposed by Houk and Ess⁷⁴ was also used to explore the origins of reactivity in these HAT reactions. In this model, the activation energy (E) is divided into distortion energy (E_{d}) and interaction energy (E_{int}). The former is the energy required

to distort the two reactants to their geometries in the transition state without interacting. The interaction energy refers to the intermolecular interaction between the two distorted fragments. It can be written in terms of the following eq 10

$$\Delta E^\ddagger = \Delta E_{\text{d}}^\ddagger + \Delta E_{\text{int}}^\ddagger \quad (10)$$

where E is the electronic energy.

Activation energies (E), distortion energies (E_{d}), and interaction energies (E_{int}) for HAT reactions promoted by the four alkoxy radicals are listed in Tables S8–S11. The position of the TS is related to thermodynamic factors (exergonic = early; endergonic = late), and these are reflected in distortion and interaction energies. Both are low for early transition states and high for late transition states. Figure 9 shows the rather poor correlations between the activation energies and distortion ($R^2 = 0.75$) or interaction energies ($R^2 = 0.56$), respectively. Although in general these both increase as the TS becomes later and the E increases, the modified Roberts relationship gives a satisfactory and detailed insight into the factors controlling the reactivity.

4 CONCLUSIONS

We have studied the origins of reactivity and selectivity of HAT from sp^3 C–H bonds to different alkoxy radicals. The BEP, MCR, and Roberts relationship were applied to explore the reactivity prediction model. A simplified Roberts relationship which contains the reaction energy, unsaturation and polar effects works reasonably well, with $R^2 = 0.89$ and MAE and RMSE values of 0.9 and 1.1 kcal/mol, respectively. The average errors in activation energies are about 1 kcal/mol in this correlation. This relatively simple relationship shows that the reactivities and selectivities for different alkoxy radicals are related to (1) BDEs of the C–Hs being abstracted and the OHs being formed—the difference between these is H_{rxn} , the basis of the BEP relationship, and the thermodynamic factor (as G_{rxn}) in the Marcus equation; (2) the difference in electronegativity between the alkoxy radical and the alkyl radical formed in the reaction indicating that ionic contributions to the transition state wavefunction are stabilizing; (3) whether or not the carbon centered radical generated in the reaction is localized (saturated) or delocalized (unsaturated). While higher-order effects not included in our three-parameter equation account for precision greater than the 1 kcal/mol average error, the main features causing a 10 kcal/mol range in barriers are included in these three factors.

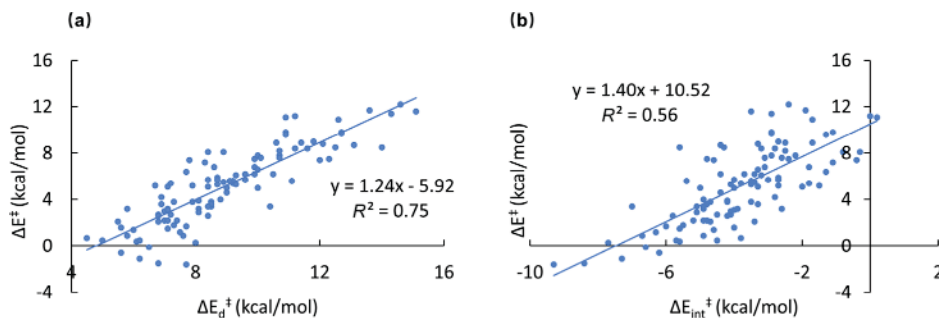


Figure 9. (a) E vs E_{d} . (b) E vs E_{int} . Energies are given in kcal/mol.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jacs.2c00389>.

Additional computational results; E , H , G , H_{rxn} , and G_{rxn} for H-abstraction promoted by four radicals; BDE (enthalpy) and activation free energy for self-exchange reactions; G calculated with MCR; difference in electronegativities of the moieties A and B (χ_{AB}); E , E_{d} , and E_{int} for H-abstraction catalyzed by four radicals; benchmark calculations with UDLPNO-CCSD(T), UM062X method and experiments; plot of the predicted activation energies using various simplified Roberts relationships against those calculated for the HAT reactions; and Cartesian coordinates of all computed structures (PDF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We are grateful to the National Science Foundation (CHE-1764328 to K.N.H.) and the Shanghai Sailing Program (no. 20YF1416000 to F.L.) for financial support of this research. CPU time was partially provided by the Supercomputer Center of East China Normal University (ECNU Public Platform for Innovation no. 001).

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