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Effective Atomic Charges on Carbon Atoms in C–H Bonds are Reliable Predictors of Reactivity of Alcohols in Hydrogen-Abstraction Reactions

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Effective atomic charges on H-bearing carbon atoms are suggested as robust predictors of hydrogen-abstraction reactivity of alcohols. Mulliken partial charges and HOMO energy values are calculated at the RHF 6-31G(*d,p*) level for 17 monofunctional alcohols and for 13 difunctional alcohols, for which kinetic data are known. As found, the Mulliken charges on carbon atoms are strongly associated with the liability of the C–H bond to undergo hydrogen abstraction. An index of carbon positivity, $C_p = 10^x$, where x is the effective partial charge on the carbon atom, is proposed for convenient evaluation of the effect of the partial charge of the carbon atom on its reactivity in the hydrogen-abstraction reaction. The sum of all positivity indices, $C_{p\ total}$, is strongly associated with the hydrogen-abstraction rate constant of the alcohol and reflects a combined effect of the reactivity of the dominant hydrogen-abstraction channel and the number of H-bearing carbon atoms in the molecule. Thus, $C_{p\ total}$ is a crucial predictor of reactivity of alcohols in the hydrogen-abstraction reaction.

Ефективні атомові заряди на зв'язаних з Гідрогеном атомах Карбону запропоновано як надійні предиктори реакційної здатності спиртів у реакціях абстракції Гідрогену. Маллікенові часткові заряди та значення енергії НОМО обчислено на рівні RHF 6-31G(*d,p*) для 17 монофункціональних спиртів і для 13 дифункціональних спиртів, для яких відомі кінетичні дані. Виявлено, що Маллікенові заряди на атомах Карбону сильно пов'язані зі схильністю зв'язку C–H до абстракції Гідрогену. Для зручного оцінювання впливу часткового заряду атома Карбону на його реакційну здатність у реакції абстракції Гідрогену запропоновано індекс позитивності атомів Карбону $C_p = 10^x$, де x — ефективний частковий заряд на атомі Карбону. Сума всіх індексів позитивності $C_{p\ total}$ суттєво асоціюється з константою швидкості реакцій абстракції Гідрогену для спиртів і відображає комбінований вплив реакційної зда-

тності домінувального каналу абстракції Гідрогену та кількості зв'язаних з атомами Гідрогену атомів Карбону в молекулі. Таким чином, значення $C_{p\ total}$ є важливим предиктором реакційної здатності спиртів у реакції абстракції Гідрогену.

Эффективные атомные заряды на связанных с атомами водорода атомах углерода предложены в качестве надежных предикторов реакционной способности спиртов в реакциях абстракции водорода. Частичные заряды Малликена и значения энергии НОМО были рассчитаны на уровне RHF 6-31G(d,p) для 17 моnofункциональных спиртов и для 13 бифункциональных спиртов, для которых известны кинетические данные. Обнаружено, что заряды Малликена на атомах углерода тесно связаны со склонностью связи C–H к абстракции водорода. Индекс позитивности углерода $C_p = 10^x$, где x — эффективный частичный заряд на атоме углерода, предложен для удобной оценки влияния частичного заряда атома углерода на его реакционную способность в реакции абстракции водорода. Сумма всех индексов позитивности $C_{p\ total}$ тесно связана с константой скорости реакции абстракции водорода для спиртов и отражает совокупный эффект реакционной способности доминирующего канала абстракции водорода и числа связанных с атомами водорода атомов углерода в молекуле. Таким образом, $C_{p\ total}$ является важным предиктором реакционной способности спиртов в реакции абстракции водорода.

Key words: hydrogen abstraction, hydroxyl radical, Mulliken charges, reactivity of alcohols.

Ключові слова: абстракція Гідрогену, гідроксильний радикал, Маллікенові заряди, реакційна здатність спиртів.

Ключевые слова: абстракция водорода, гидроксильный радикал, заряды Малликена, реакционная способность спиртов.

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1. INTRODUCTION

The hydroxyl radical is one of the strongest biochemical oxidizing agents. Thus, understanding reactivity of the hydroxyl radical can help illuminate mechanisms of oxidative damage to biomolecules. The two types of reactions of the hydroxyl radical with organic molecules are addition and hydrogen abstraction. In the addition reactions, the strong electrophilic properties of the hydroxyl radical promote its binding to the sites of increased electron density in unsaturated or aromatic compounds, resulting in a free radical product. In the hydrogen-abstraction reactions, a free radical and the water molecule are produced. The rules governing the reactivity of the hydroxyl radical in hydrogen abstraction are less obvious com-

pared to those for the addition reactions. However, it can be assumed that information of reactivity in the hydrogen-abstraction reaction can be obtained from the electronic structure of the organic molecules that are oxidized by the hydroxyl radical.

In the hydrogen-abstraction reaction, a proton and an electron are abstracted in homolytic bond fission to combine with the hydroxyl radical into the water molecule. The bond polarity undoubtedly effects the process. In a polar bond, the electron pair is closer to the more electronegative atom thus making the electron less likely to follow the proton. Therefore, it can be assumed that the reaction is favoured from a non-polar bond rather than from a polar one. While the actual mechanism of hydrogen abstraction can be much more complicated and involve formation of hydrogen bonds between the hydroxyl radical and the organic compound in pre-reactive states [1], the simple mechanistic idea of the impact of bond polarity on its hydrogen-abstraction reactivity might be helpful for assessment of propensity of atoms in the molecule to be preferential targets in the reaction. Polarity of a chemical bond can be seen as distribution of electron density over the participating atoms and expressed as partial atomic charges. Important molecular properties such as dipole moments, polarizability, and, therefore, molecular reactivity depend on effective atomic charges [2].

For the present study, we chose alcohols as the model molecules for the hydrogen-abstraction reactions. We explored an association of known data for reactivity of alcohols in the hydrogen abstraction reaction with partial atomic charges and HOMO energy values calculated from the electronic structures of the molecules.

The aim of the study is to develop a convenient method to evaluate hydrogen-abstraction reactivity of alcohols based on effective atomic charges in the molecule.

2. EXPERIMENTAL METHODS

The *ab initio* calculations were performed with the quantum chemical program GAMESS [3, 4]. The starting geometries were obtained with a conformer search algorithm in the Avogadro 2.0.7.2 program [5]. The conformers of the lowest total energy were used for geometry optimization with a molecular mechanics method in the Avogadro. The obtained geometries were then *ab initio* optimized at the RHF 6-31G(*d,p*) level. The vibrational frequencies were not calculated; therefore, the resulting structures are local minima. The computations were carried out in the gas phase. Figures were generated in McMolPlt [6]. Data on rate constants of alcohol reactivity in the gas phase were taken from the review by Grosjean [8]. We calculated electronic structures at optimized geometry for 17 mono-

functional alcohols and for 13 difunctional alcohols including diols, hydroxyethers and hydroxycarbonyls of total thirty-three alcohols for which kinetic data are listed in the review by Grosjean [8]. We did not calculate the electronic structure of allyl alcohol that is an unsaturated alcohol, as its reaction with the hydroxyl radical is addition. Calculation results on 2-butanol are not included because data on its experimental rate constant are missing in the review. We also excluded CD₃OH. Statistical analysis was performed with the *R* software package. Statistical significance was set at $p = 0.05$.

3. RESULTS AND DISCUSSION

Partial atomic charges are essential for predicting various aspects of molecular reactivity. For the present study, we employed the Mulliken population analysis with the self-consistent field theory at the Hartree–Fock level using 6-31G(*d,p*) Pople basis set. The basis set is commonly used by many researchers to obtain reliable molecular geometry and energy in small and medium-size molecules. The combination of the procedure for charge density partitioning, choice of the Hamiltonian, and the choice of the basis set showed an agreement of being 2% close to the measured dipole moment of water and the respective charge on the oxygen atom [7].

Reactivity of Alcohols in Hydrogen-Abstraction Reactions. Alcohols preferentially undergo hydrogen abstraction from a C–H bond and to a very small extent from the O–H bond [8]. The hydrogen atom is more easily abstracted from tertiary C–H bonds than from secondary C–H bonds, and it is more easily abstracted from secondary C–H bonds than from primary C–H bonds. Therefore, *t*-butanol that only contains primary bonds reacts with hydroxyl radical more slowly than butan-1-ol. We wanted to see whether the reactivity properties could be related to the calculated molecular characteristics of the tested alcohols.

HOMO Localization and Energy Values. We analyzed energies and configurations of the highest occupied molecular orbitals (HOMO) in the alcohol molecules. The HOMO is the site in the molecule where the utmost frontier electron density is concentrated and is, therefore, the site of greatest nucleophilicity. Characteristics of the HOMO in the molecule are associated with its propensity to undergo preferential hydrogen abstraction by the strongly electrophilic hydroxyl radical. We found that the localization of the HOMO in the monohydric alcohols is similar for all alcohols under the study up to heptan-1-ol. The HOMO is centred on the oxygen atom in the hydroxyl group and incorporates the hydrogen atoms with highest electron density at the carbon atom bonded to the –OH group both in primary alcohols (Fig. 1) and in secondary alcohols (Fig. 2).

In *t*-butanol and other tertiary alcohols, the HOMO is associated with the oxygen atom of the hydroxyl group and the C-C bonds of the most positively charged carbon atom (Fig. 3). In this case, all the C-H bonds in the molecule are primary, and the HOMO does not involve the hydrogen atom with the highest electron density.

In octan-1-ol, the HOMO is spread along the carbon skeleton of the molecule and does not incorporate the -OH group (Fig. 4).

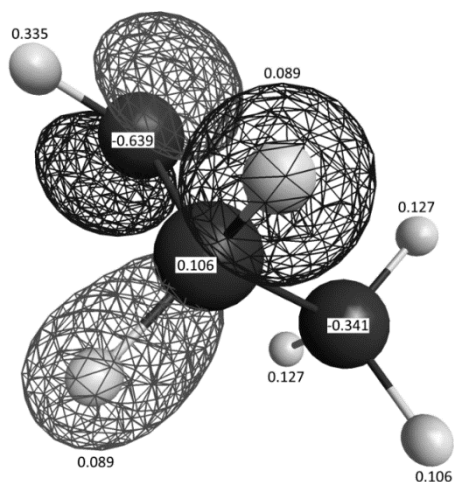


Fig. 1. Mulliken charges and localization of the HOMO in primary alcohols. Ethanol.

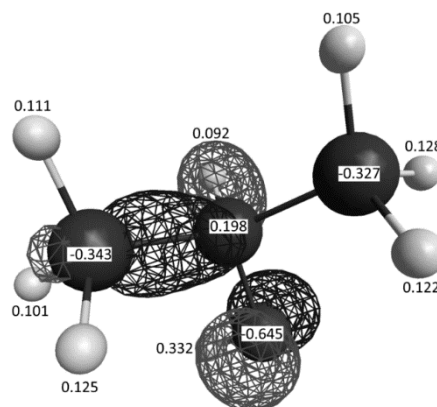


Fig. 2. Mulliken charges and localization of the HOMO in secondary alcohols. Propan-2-ol.

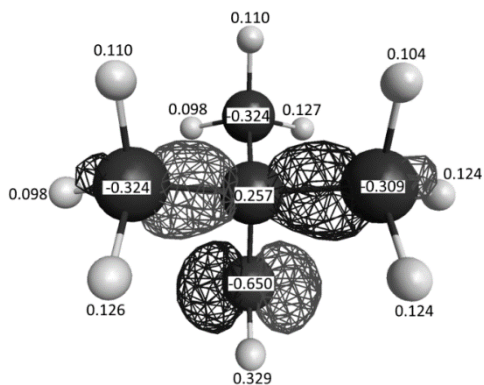


Fig. 3. Mulliken charges and localization of the HOMO in tertiary alcohols. *t*-butanol.

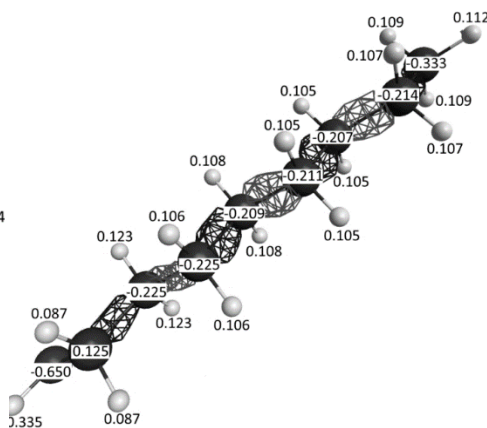


Fig. 4. Mulliken charges and localization of the HOMO in octan-1-ol.

The HOMO in diols is positioned on the both $-OH$ groups and both sets of hydrogen atoms with the highest electron density at the most positively charged carbon atoms as is in ethane-1,2-diol (Fig. 5) and in 2-hydroxyethylether (Fig. 6).

In the other hydroxyethers, the HOMO is centred on the ether oxygen atom and does not involve the $-OH$ group, as is in 2-ethoxyethanol (Fig. 7), and the charge of the oxygen atom in the $-OH$ group can be more negative than that of the ether oxygen.

In hydroxyacetaldehyde, the HOMO is associated with both the carbonyl and hydroxyl oxygen atoms and incorporates the hydrogen with the highest electron density bonded to the carbonyl carbon atom (Fig. 8) that has a high positive charge. However, it does not

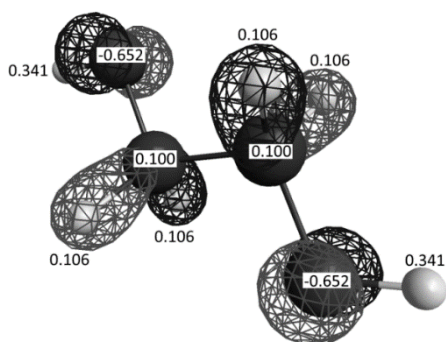


Fig. 5. Mulliken charges and localization of the HOMO in ethane-1,2-diol.

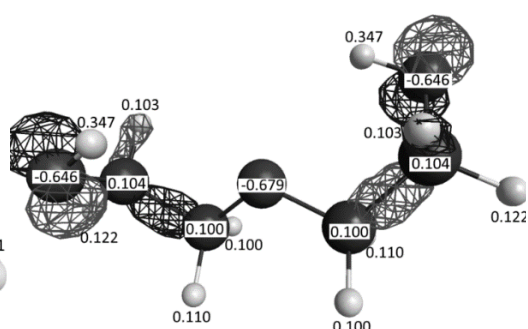


Fig. 6. Mulliken charges and localization of the HOMO in 2-hydroxyethylether.

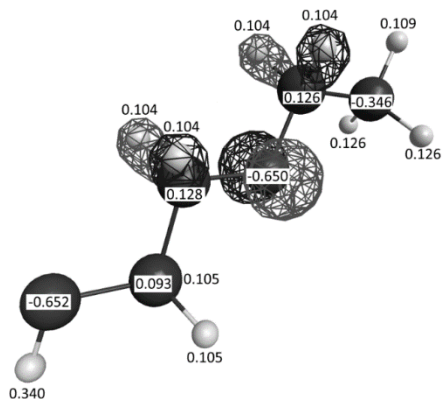


Fig. 7. Mulliken charges and localization of the HOMO in 2-ethoxyethanol.

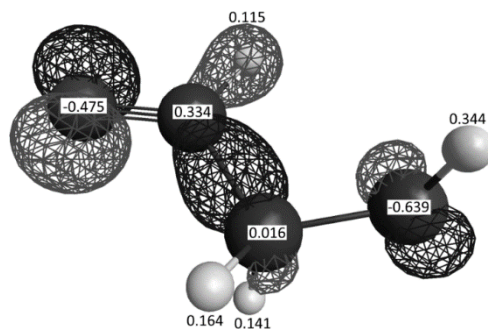


Fig. 8. Mulliken charges and localization of the HOMO in hydroxyacetaldehyde.

involve the hydrogen atoms in the secondary C-H bonds.

Similarly, such hydrogen atoms in the secondary C-H bonds are not associated with the HOMO in hydroxyacetone.

However, the alcohols, which contain atoms other than carbon, hydrogen and oxygen, have different patterns of the HOMO localization. In 2-chloroethanol, the HOMO is centred on the chlorine atom that is much more positive than the oxygen atom of the -OH group. The hydrogen atoms involved in the HOMO have much lower electron density compared to the hydrogens in the CH₂ group, and the carbon atom associated with the HOMO has a smaller positive charge than that of the CH₂ group. However, hydrogen abstraction in halogenated ethanols occurs predominantly from the CH₂ group [9] that might be explained by the hydrogen bonding of the chlorine and hydrogens at the terminal carbon or by the higher electron density of the hydrogen atoms and more positive charge of the carbon atom in the CH₂ group. Similarly, in 2-(dimethylamino)ethanol, the HOMO is centred on the nitrogen atom that harbours less electron density than the oxygen atom in the hydroxyl group (Fig. 9).

Thus, we found that while, surprisingly, the HOMO is not always centred on the most negatively charged oxygen atom, it is always associated with the most positive carbon in the molecules of the alcohols, which only consist of carbon, hydrogen and oxygen atoms. When the most positive carbon is bonded to hydrogen atoms, they have higher electron density than the other hydrogens in the molecule and are involved in the HOMO.

We did not find any association between the HOMO energy values of the alcohols under the study and their hydrogen abstraction rate

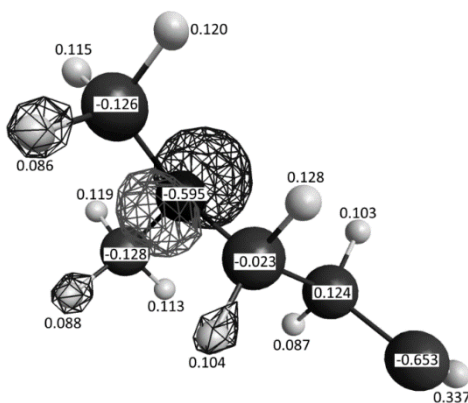


Fig. 9. Mulliken charges and localization of the HOMO in 2-(dimethylamino)ethanol.

constants. The absence of the association can be explained by the multifocal character of hydrogen abstraction as opposed to a specific localization of the HOMO in the alcohol molecule. Indeed, the HOMO energy values seem to depend more on the positions of the functional group than on the number of carbon atoms in the molecule. Thus, the six straight-chain monohydric primary alcohols from ethanol to heptan-1-ol under the study have very similar HOMO energy values: -0.434 and -0.433 Hartree, while the three straight-chain monohydric secondary alcohols from propan-2-ol to hexan-2-ol have HOMO energy values of -0.429 and -0.428 (Table).

We found a strong association of the HOMO energy value and the charge of the most positive C atom associated with the HOMO, with the Pearson correlation coefficient $r = 0.743$ ($p < 0.001$). Interestingly, the association was stronger than that for the charge of the oxygen atom, upon which the HOMO is centred, where the Pearson correlation coefficient is 0.494 ($p = 0.007$). Therefore, the results imply that, in the molecules of alcohols, which only consist of carbon, hydrogen and oxygen, the most positively charged carbon atom has a prominent role in the localization and energy of the HOMO.

Partial Atomic Charges and Reactivity. The poor reactivity of the O–H bond in the hydrogen-abstraction reaction may be related to the polarity of the O–H bond. Along with being stronger and shorter than the C–H bond, the O–H bond is much more polar compared to it; the charge on the oxygen atom is markedly negative and ranges from -0.634 in methanol to -0.669 in 4-hydroxy-4-methylpentan-2-one, with most frequently found charges between -0.649 and -0.652 (Table). The charges on hydrogen atoms in the O–H bond are highly positive and range from 0.329 in *t*-butanol to 0.363 in 4-hydroxy-4-methylpentan-2-one (Table). The negativity of the effective partial charge on the oxygen atom indicates that the electron density is concentrated close to it, and the electron cannot follow the proton in hydrogen abstraction easily.

For easier hydrogen atom transfer from a C–H bond, the electron pair should be closer to the hydrogen atom, thus increasing its electron density. The carbon atom in the bond consequently should have an increased positive charge. Therefore, among the carbon atoms in C–H bonds in the alcohol molecules, we may regard the most positively charged carbon as the principal target for hydrogen abstraction, as indeed we see from the HOMO localization.

We found a remarkably strong relationship between the calculated Mulliken charge of the carbon atom in a C–H bond and its reactivity. For ethanol, the Mulliken charge of 0.106 on C1 in a secondary C–H bond is much more positive than that on C2 in a primary C–H bond (Table), and it is the preferential place for hydrogen abstraction with $80 \pm 15\%$ yield of acetaldehyde [10].

TABLE. Electronic properties of alcohol molecules and kinetic data for the reaction of the alcohols with the hydroxyl radical.

	E_{HOMO}	Charge on O	Charge on H in O-H	Charges on H-bearing carbons		H_N^{total}	C_P^{total}	Rate constant $10^{-12} \text{ cm}^3 \times$ $\times \text{molecule}^{-1} \text{ s}^{-1}$
				Most positive carbon C_p	In secondary C-H bond			
1. methanol CH_3OH	-0.442	-0.634	0.336	-0.013		1.27	0.97	0.93 ± 0.04
2. ethanol $\text{CH}_3\text{CH}_2\text{OH}$	-0.434	-0.639	0.335	0.106		2.55	1.74	3.33 ± 0.23
3. propan-1-ol $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$	-0.434	-0.647	0.335	1.27				
4. propan-2-ol $\text{CH}_3\text{CHOHCH}_3$	-0.429	-0.645	0.332	0.125	-0.227	3.85	2.37	5.34 ± 0.29
5. butan-1-ol $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	-0.433	-0.649	0.335	1.33				
6. t-butanol $(\text{CH}_3)_3\text{COH}$	-0.424	-0.650	0.329	0.198		3.84	2.50	5.81 ± 0.34
7. pentan-1-ol $\text{CH}_3(\text{CH}_2)_3\text{CH}_2\text{OH}$	-0.433	-0.649	0.335	1.58	-0.222	5.12	2.99	8.31 ± 0.63
				1.33	-0.228			
				0.124		3.89	1.43	1.07 ± 0.08
				1.33				
				0.124	-0.225			
				1.33	-0.222			
					-0.212			
						6.41	3.61	10.8 ± 1.1

Continuation TABLE.

	E_{HOMO}	Charge on O	Charge on H in O-H	Charges on H-bearing carbons			Rate constant $10^{-12} \text{ cm}^3 \times$ $\times \text{molecule}^{-1} \text{ s}^{-1}$	
				Most positive carbon C_p	In secondary C-H bond	In primary C-H bond		
8. pentan-2-ol $\text{CH}_3\text{CHOHCH}_2\text{CH}_2\text{CH}_3$	-0.428	-0.654	0.332	0.213 1.63 tertiary	-0.211 -0.229	-0.332 -0.346	6.43 3.76	11.8 ± 0.8
9. pentan-3-ol $\text{CH}_3\text{CH}_2\text{CHOHCH}_2\text{CH}_3$	-0.421	-0.653	0.338	0.206 1.61 tertiary	-0.214 -0.215	-0.337 -0.355	6.44 3.73	12.2 ± 0.7
10. 3-methylbutan-2-ol $(\text{CH}_3)_2\text{CHCHOHCH}_3$	-0.425	-0.650	0.334	0.212 1.63 tertiary	-0.133	-0.324 -0.329 -0.345	6.43 3.76	12.4 ± 0.7
11. cyclopentanol cyclo- $[(\text{CH}_2)_4\text{CH}]\text{OH}$	-0.423	-0.650	0.332	0.179 1.51	-0.222 -0.229 -0.225 -0.238		6.54 3.88	10.7 ± 0.7
12. hexan-1-ol $\text{CH}_3(\text{CH}_2)_4\text{CH}_2\text{OH}$	-0.433	-0.649	0.335	0.124 1.33	-0.205 -0.214 -0.225 -0.225	-0.333	7.68 4.23	12.4 ± 0.7
13. hexan-2-ol $\text{CH}_3\text{CHOH}(\text{CH}_2)_3\text{CH}_3$	-0.428	-0.655	0.332	0.213 1.63 tertiary	-0.213 -0.214 -0.222	-0.333 -0.346	7.70 4.37	12.1 ± 0.7

Continuation TABLE.

	E_{HOMO}	Charge on O	Charge on H in O-H	Charge Most positive carbon C_P	Charges on H-bearing carbons		$H_{N \text{ total}}$	$C_{P \text{ total}}$	Rate constant $10^{-12} \text{ cm}^3 \times \text{molecule}^{-1} \text{ s}^{-1}$
					In secondary C-H bond	In primary C-H bond			
14. heptan-1-ol $\text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{OH}$	-0.433	-0.649	0.335	0.124 1.33	-0.207 -0.209 -0.214 -0.225 -0.225	-0.333	8.95	4.85	13.6 ± 1.3
15. 2,4-dimethylpentan-2-ol $(\text{CH}_3)_2\text{COHCH}_2\text{CH}(\text{CH}_3)_2$	-0.416	-0.652	0.330	-0.140 0.72 tertiary	-0.181	-0.309 -0.321 -0.322 -0.328	7.73	3.30	11.4 ± 3.0
16. 3,5-dimethylhexan-3-ol $\text{CH}_3\text{CH}_2\text{COH}(\text{CH}_3)\text{CH}_2\text{CH}(\text{CH}_3)_2$	-0.412	-0.658	0.329	-0.138 0.73	-0.186 -0.216	-0.310 -0.321 -0.326 -0.345	9.04	3.88	13.6 ± 3.6
17. octan-1-ol $\text{CH}_3(\text{CH}_2)_6\text{CH}_2\text{OH}$	-0.430	-0.650	0.335	0.125 1.33	-0.207 -0.209 -0.211 -0.214 -0.225 -0.225	-0.333	10.22	5.47	14.4 ± 1.5
18. hydroxyacetaldehyde HOCH_2CHO	-0.415	-0.639	0.344	0.334 2.16	0.016		2.72	3.20	10.0

Continuation TABLE.

	E_{HOMO}	Charge on O	Charge on H in O-H	Charges on H-bearing carbons			Rate constant $10^{-12} \text{ cm}^3 \times \text{molecule}^{-1} \text{ s}^{-1}$	
				Most positive carbon C_p	In secondary C-H bond	In primary C-H bond		
19. hydroxyacetone $\text{CH}_3\text{C}(\text{O})\text{CH}_2\text{OH}$	-0.400	-0.641	0.342	0.028	-0.401	2.81	1.47	3.0 ± 0.3
20. 4-hydroxy-4-methylpentan-2-one $\text{CH}_3\text{C}(\text{O})\text{CH}_2\text{COH}(\text{CH}_3)_2$	-0.406	-0.669	0.363	-0.314	-0.310	5.43	1.83	4.0 ± 1.2
21. ethane-1,2-diol $\text{HOCH}_2\text{CH}_2\text{OH}$	-0.434	-0.652	0.341	0.49	-0.337	2.56	2.52	7.7 ± 1.1
		-0.652	0.341	secondary	-0.415			
22. propane-1,2-diol $\text{HOCH}_2\text{CHOHCH}_3$	-0.429	-0.652	0.341	0.100	0.110	3.88	3.30	12 ± 1
		-0.659	0.336	1.26				
23. 2-hydroxyethylether $\text{HOCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OH}$	-0.437	-0.646	0.347	0.194	-0.351	5.14	5.06	30 ± 2
		-0.646	0.347	1.56				
		-0.679		tertiary				
24. 2-methoxyethanol $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OH}$	-0.417	-0.652	0.341	0.104	0.100	3.82	3.56	12.5 ± 0.7
		-0.637		0.104				
		(ether)		1.27				
25. 2-ethoxyethanol $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_2\text{OH}$	-0.414	-0.652	0.340	0.123	-0.005	5.10	4.37	18.7 ± 2.0
		-0.650		1.23				
		(ether)		0.128				
				1.34				
				0.126				
				0.093				

Continuation TABLE.

	E_{HOMO}	Charge on O	Charge on H in O-H	Charges on H-bearing carbons			Rate constant $10^{-12} \text{ cm}^3 \times$ $\times \text{molecule}^{-1} \text{ s}^{-1}$
				Most positive carbon C_p	In secondary C-H bond	In primary C-H bond	
26. 2-butoxyethanol $\text{CH}_3(\text{CH}_2)_3\text{OCH}_2\text{CH}_2\text{OH}$	-0.429	-0.649 -0.661 (ether)	0.349	0.130 1.35 0.106 1.28 0.102 1.27 all secondary	-0.214 -0.230	-0.335	7.69 5.56 23.1 ± 0.9
27. 3-ethoxypropan-1-ol $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2)_2\text{CH}_2\text{OH}$	-0.413	-0.652 -0.640 (ether)	0.335	0.127 1.34	0.120 0.114 -0.244	-0.345	6.40 4.98 22.0 ± 1.3
28. 3-methoxybutan-1-ol $\text{CH}_3\text{CH}(\text{OCH}_3)\text{CH}_2\text{CH}_2\text{OH}$	-0.404	-0.650 -0.645 (ether)	0.336	0.204 1.60 tertiary	0.098 -0.227	-0.335	5.16 4.90 23.6 ± 1.6
29. 2-(dimethylamino)ethanol $(\text{CH}_3)_2\text{NCH}_2\text{CH}_2\text{OH}$	-0.348	-0.644	0.337	0.124 1.33	-0.023	-0.126 -0.128	5.12 3.78 90 ± 20
30. 2-chloroethanol $\text{ClCH}_2\text{CH}_2\text{OH}$	-0.434	-0.653	0.345	0.114 1.30	-0.298		2.83 1.81 1.4 ± 0.1

In secondary alcohols, the increased positive charge on the carbon atom in the tertiary C–H bond makes the hydrogen atom easier to be abstracted. In propan-2-ol, the Mulliken charge on C₂ is 0.198 (tertiary C–H bond), and it is the favoured place for hydrogen abstraction, forming acetone as the major product of the reaction [11]. Consistently, *t*-butanol that is a tertiary alcohol containing all primary C–H bonds with markedly negative charges on the carbon atoms (Table) has a rate constant of 1.07, comparable to the rate constant of methanol and much smaller than that of butan-1-ol. For hydroxyacetaldehyde, hydrogen abstraction proceeds mostly from the carbonyl carbon [12], being responsible for 78% of its hydrogen abstraction reactivity [13]. The charge on the carbonyl carbon is a strongly positive 0.334. Both hydroxyacetaldehyde and ethanol contain two carbon atoms but the hydrogen-abstraction rate constant for hydroxyacetaldehyde is three times higher than that for ethanol (Table) that is consistent with the significantly different charges on respective C1 atoms. Similarly, ethane-1,2-diol contains two carbon atoms, which are bonded to the hydroxyl groups and have markedly positive charges of 0.100. The hydrogen abstraction is thus strongly favoured at the both carbon atoms in ethane-1,2-diol, and the rate constant of the reaction is about two times higher than that of the ethanol (Table).

The charges on the carbon atoms in C–H bonds demonstrate great variability, ranging from a very negative –0.415 in a primary C–H bond of 4-hydroxy-4-methylpentan-2-one to a strongly positive 0.213 in the tertiary C–H bond in pentan-2-ol (Table).

For convenient evaluation of the effect of the partial charge of the carbon atom on its reactivity in the hydrogen-abstraction reaction, we introduce an index of carbon positivity, $C_p = 10^x$, where x is the effective partial charge on the carbon atom. Thus, for ethanol, we obtain carbon positivity indices of 1.28 and 0.46 for the carbon atoms in the secondary and primary C–H bonds, respectively. The C_p for the most reactive C₂ in propan-2-ol is 1.58, while the less reactive terminal carbons have C_p of 0.45 and 0.47.

With an increase of the number of carbon atoms where hydrogen abstraction is possible, the OH-reaction rate constants increase for the homologous series from methanol to octan-1-ol [14, 15]. For the multifocal hydrogen abstraction, the reactivity of the molecule depends not only on the charge of the most positively charged atom, but on the charges of all other carbon atoms in C–H bonds as well. For the alcohols in the study, we calculated $C_{p\ total}$ values, which are the sums of C_p of all carbon atoms in the molecule (Table). While for compounds with same number of carbon atoms the $C_{p\ total}$ reflects the different positivity of carbon atoms, as is in butan-1-ol and *t*-butanol or in ethanol and hydroxyacetaldehyde, with an increase of

the carbon chain length, the $C_{P\ total}$ indicates the combined effect of the positive charge of the carbon atom favoured in hydrogen abstraction and the increased number of atoms where the abstraction can occur. Excluding the results for 2-chloroethanol and 2-(dimethylamino)ethanol, which contain atoms other than carbon, hydrogen and oxygen, we found a highly significant correlation of the $C_{P\ total}$ and rate constants, with the Spearman's correlation coefficient of 0.939 ($p < 0.01$). Figure 10 shows the strong association of the $C_{P\ total}$ and the rate constants for the tested alcohols.

The relationship is exceptionally good for the monohydric alcohols, diols, hydroxyacetaldehyde and hydroxyketones tested under the study. Thus, the sum of all carbon positivity indices in the alcohol molecule that consists of carbon, hydrogen and oxygen exhibits a powerful association with its reactivity in hydrogen-abstraction reactions.

It may be assumed that the most positively charged carbon atom is bound to the hydrogen atom with the highest electron density, and the charges of hydrogen atoms differ for primary, secondary or tertiary bonds. Within the molecule, the hydrogen atom with the smallest positive charge is indeed bound to the most positive carbon. However, across the tested molecules, the charges of hydrogens in primary, secondary and tertiary C-H bonds show a significant overlap. The charges on the hydrogen atoms in secondary C-H bonds range from 0.086 in propan-1-ol to 0.164 in hydroxyacetaldehyde. Primary C-H bonds are least reactive in hydrogen abstraction within the molecule, the charge range is, however, not very different from that for the secondary bonds and spans from 0.093 in methanol to 0.149 in hydroxyacetone. The charges on hydrogen at-

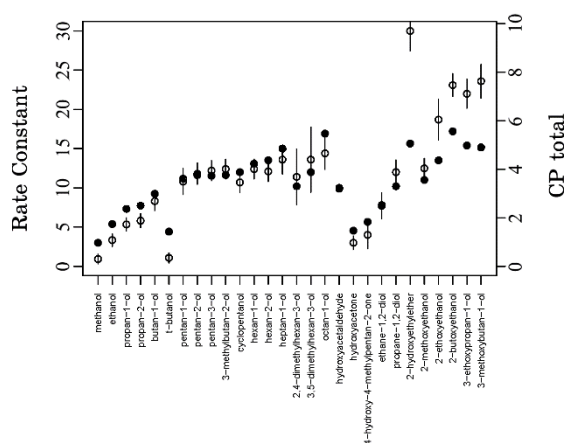


Fig. 10. Association of the sums of all carbon positivity indices $C_{P\ total}$ (gray dots) and the rate constants (black dots) for the tested alcohols.

oms in tertiary C–H bonds, which are most reactive in hydrogen abstraction, range from 0.088 to 0.122. Thus, the charges of the hydrogen atoms in the C–H bonds are less variable than those of the carbon atoms are, and do not show significant differences between the types of bonds. We averaged the charges on the hydrogen atoms bonded to the same carbon atom. For instance, the charges on the hydrogen atoms of 0.127, 0.106 and 0.127 bonded to the terminal carbon atom in ethanol (Fig. 1) have the average value of 0.120. Then, we transformed the averaged charge as the index of hydrogen negativity, $H_N = 1/x$, where x is the averaged charge of all hydrogens bonded to the same carbon atom. In this way, the smallest positive charge on the hydrogen atom in the molecule reflects the greatest propensity of the atom to be abstracted by the hydroxyl radical. We calculated the sums of the obtained values $H_{N\ total}$ for all carbon-bonded hydrogen atoms in the alcohol molecules (Table). The resulting indices show a strong relationship with the rate constants, with the Spearman's correlation coefficient of 0.693 ($p < 0.01$). The relationship is nonetheless weaker than that for the $C_{P\ total}$ indices for the carbon atoms in the molecules.

Linear Regression. We found that the $C_{P\ total}$ indices and the $H_{N\ total}$ indices had a highly significant linear relationship with the rate constants of the alcohols under the study. The coefficient of determination $r^2 = 0.873$; the correlation coefficient $r = 0.935$. While the present study is not aimed at the prediction of rate constants of alcohols in the hydrogen-abstraction reaction, it can be seen that the $C_{P\ total}$ of the hydrogen-bearing carbons and/or the $H_{N\ total}$ of the carbon-bonded hydrogens in the alcohol molecule may be valuable easy obtainable factors for prediction of rate constants using a QSAR approach. The $C_{P\ total}$ index is related to the sum of partial reactivities of each carbon in C–H bonds. Likewise, the group additivity method for prediction of rate constants regards the overall rate constant of a specific organic molecule as the sum of partial rate constants of each of its reactive sites [16]. In a QSAR study by Monod and Doussin, OH-oxidation rate constants of aliphatic organic compounds were estimated using the sum of the hydrogen-abstraction kinetic rates of each H-bearing function [17]. In the study, the partial rate constants were modulated with α - and β -neighbouring functions to account for the effect of the neighbouring atoms. In our study, the partial atomic charges on carbon atoms intrinsically reflect the effect of neighbouring atoms and thus do not need additional modulation. A QSAR study by Hatipoglu and Cinar reported a linear relationship between the logarithms of the rate constants of five straight-chain primary alcohols from methanol to pentan-1-ol, the HOMO energies, and the sums of Mulliken charges of the alpha carbon atom and the hydrogen atoms bonded to

it [18]. While the study also found most positively charged carbon atoms to be preferential sites for hydrogen abstraction, the approach does not account for the multifocal nature of the reaction that cannot be explained by the reactivity of the single site at the alpha carbon. Therefore, the $C_{p\ total}$ index is a potent predictor of the overall reactivity of alcohols in hydrogen-abstraction reactions. It accounts for the contribution of each H-bearing carbon atom to the reactivity. It also reflects the effects of neighbouring groups for each of the carbons and thus can be used for heterofunctional compounds.

4. CONCLUSIONS

The principal conclusions of the present study are as follow.

1. A mechanistic interpretation of hydrogen abstraction as a homolytic bond fission strongly effected by the polarity of the bond can help understand reactivity of alcohols in the hydrogen abstraction reaction.

2. The HOMO localization and energy are more strongly associated with the charge of the most positively charged carbon atom than with the charge of the oxygen atom, upon which the HOMO is centred. The calculated Mulliken charges on carbon atoms are related to the bond polarity and strongly associate with the propensity of the C–H bond to undergo hydrogen abstraction.

3. The positivity index C_p reliably reflects hydrogen-abstraction reactivity of the C–H bond in alcohols that do not contain atoms other than carbon, hydrogen and oxygen. The largest C_p in the molecule indicates the dominant channel for hydrogen abstraction in most cases.

4. The sum of all positivity indices $C_{p\ total}$ is strongly associated with the rate constant of the alcohol in hydrogen-abstraction reactions and reflects a combined effect of the reactivity of the dominant hydrogen-abstraction channel and the number of the H-bearing carbon atoms in the molecule, accounting for the multifocal character of the reaction. $C_{p\ total}$ is a potent predictor of reactivity of alcohols in the hydrogen-abstraction reaction.

REFERENCES

1. W. Sun, L. Yang, L. Yu, and M. Saeys, *J. Phys. Chem.*, **A113**: 7852 (2009); <https://doi.org/10.1021/jp8090792>.
2. D. C. Young, *Computational Chemistry. A Practical Guide for Applying Techniques to Real-World Problems* (New York: Wiley-Interscience: 2001), p. 99.
3. M. W. Schmidt, K. K. Baldrige, J. A. Boatz, S. T. Elbert, M. S. Gordon,

- J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis, and J. A. Montgomery, *J. Comput. Chem.*, **14**: 1347 (1993); <https://doi.org/10.1002/jcc.540141112>.
4. M. S. Gordon and M. W. Schmidt, *Advances in Electronic Structure Theory: GAMESS a Decade Later*. In: *Theory and Applications of Computational Chemistry: the First Forty Years* (Eds. C. E. Dykstra, G. Frenking, K. S. Kim, and G.E. Scuseria) (Amsterdam: Elsevier: 2005), p. 1167.
 5. M. D. Hanwell, D. E. Curtis, D. C. Lonie, T. Vandermeersch, E. Zurek, and G. R. Hutchison, *J. Cheminform.*, **4**: 17 (2012); <https://doi.org/10.1186/1758-2946-4-17>.
 6. B. M. Bode and M. S. Gordon, *J. Mol. Graphics Mod.*, **16**: 133 (1998); [https://doi.org/10.1016/S1093-3263\(99\)00002-9](https://doi.org/10.1016/S1093-3263(99)00002-9).
 7. F. Martin and H. Zipse, *J. Comput. Chem.*, **26**, No. 1: 97 (2005); <https://doi.org/10.1002/jcc.20157>.
 8. D. Grosjean, *J. Braz. Chem. Soc.*, **8**, No. 4: 433 (1997); <http://dx.doi.org/10.1590/S0103-50531997000500002>.
 9. J. A. Seetula, *Phys. Chem. Chem. Phys.*, **2**: 3807 (2000); <https://doi.org/10.1039/B001350L>.
 10. W. P. L. Carter, K. R. Darnall, R. A. Graham, A. M. Winer, and J. N. Pitts Jr., *J. Phys. Chem.*, **83**: 2305 (1979); <https://doi.org/10.1021/j100481a001>.
 11. T. Ohta, H. Bandow, and H. Akimoto, *Int. J. Chem. Kinet.*, **14**, No. 2: 173 (1982); <https://doi.org/10.1002/kin.550140207>.
 12. R. Atkinson and S. M. Aschmann, *Environ. Sci. Technol.*, **29**: 528 (1995); <https://doi.org/10.1021/es00002a032>.
 13. H. Niki, P. D. Maker, C. M. Savage, and M. D. Hurley, *J. Phys. Chem.*, **91**, No. 8: 2174 (1987); <https://doi.org/10.1021/j100292a038>.
 14. T. J. Wallington and M. J. Kurylo, *Int. J. Chem. Kinet.*, **19**, No. 11: 1015 (1987); <https://doi.org/10.1002/kin.550191106>.
 15. L. Nelson, O. Rattigan, R. Neavyn, H. Sidebottom, J. Treacy, and O. J. Nielsen, *Int. J. Chem. Kinet.*, **22**, No. 11: 1111 (1990); <https://doi.org/10.1002/kin.550221102>.
 16. E. S. C. Kwok and R. Atkinson, *Atmos. Environ.*, **29**: 1685 (1995); [https://doi.org/10.1016/1352-2310\(95\)00069-B](https://doi.org/10.1016/1352-2310(95)00069-B).
 17. A. Monod and J. F. Doussin, *Atmos. Environ.*, **42**: 7611 (2008); <https://doi.org/10.1016/j.atmosenv.2008.06.005>.
 18. A. Hatipoglu and Z. Cinar, *J. Mol. Struct.: THEOCHEM*, **631**: 189 (2003); [https://doi.org/10.1016/S0166-1280\(03\)00248-3](https://doi.org/10.1016/S0166-1280(03)00248-3).