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Original Article

Substituent Effects on the Relative Stabilities of Tautomers of 2-Butanone in the Gas Phase: A Theoretical PM3 and DFT Study

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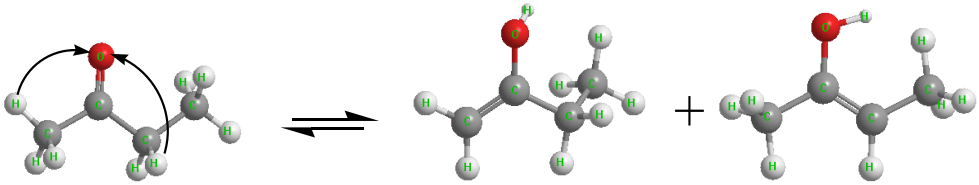
Abstract
This work presents a comprehensive theoretical study of the effects of substituents (X = F, OH, NH_2, CH_3, CN, CF_3) on the keto–enol tautomerism of 2-butanone. Using semiempirical PM3 and DFT (B3LYP/6-31G(d,p)) methods, we evaluated the relative stabilities of 2-butanone and its enol form, 2-buten-2-ol, in the gas phase. Thermodynamic parameters (ΔH, ΔG), isodesmic reaction enthalpies, and frontier molecular orbital (FMO) analyses were employed to investigate the influence of electron-donating and electron-withdrawing substituents at the α-carbon position. Our results indicate that 2-butanone is thermodynamically more stable than 2-buten-2-ol across all substituents. Electron-donating groups (EDGs) such as CH_3 and NH_2 exert a minor destabilization of the keto form, while electron-withdrawing groups (EWGs) like CN and CF_3 significantly reduce keto stability, favoring enolization. FMO analysis revealed that EWGs lower the HOMO-LUMO gap, indicating increased reactivity and a tendency to stabilize the enol tautomer. These insights provide a valuable framework for understanding substituent effects on tautomerism in aliphatic ketones.
Keywords. Keto–enol Tautomerism, PM3, DFT, Electron-Donating Groups, Electron-Withdrawing Groups.

Introduction

The study of tautomeric phenomena from both experimental and theoretical aspects has been developed in many areas of chemistry, biochemistry, and pharmacology [1-3]. These phenomena are often invoked to explain the chemical reaction mechanisms leading to the synthesis of organic molecules [4]. Keto-enol tautomerism is one of the most commonly studied forms of prototropic phenomena. This fundamental concept examines the migration of a proton between two constitutional isomers, the keto and enol tautomers [5-7]. The keto form is thermodynamically more stable than the enol form, but several factors, such as temperature, concentration, catalysts, the nature of the solvent, and substituent groups, can shift the equilibrium in favor of the enol [8-10]. In fact, understanding the effects of substituents has the greatest influence on the stability of tautomers. The nature of the substituent has a significant impact on the properties and interactions of molecules [11-14]. Interestingly, the work of Zou et al. studied the effect of substituents on the enol–dienol tautomerism of but-2-enal, examining how the electronic nature of the substituent affects this equilibrium [15].

It is well known that aliphatic carbonyl compounds with alpha hydrogens attached to the carbonyl group undergo keto-enol tautomerism [16-20]. Among different carbonyl compounds, ketones attract special attention due to their versatile properties as effective biofuels [21-23]. Methyl Ethyl Ketone [$CH_3COCH_2CH_3$], commonly known as 2-butanone, is the second member of the ketone series [24]. It is a colorless liquid, partially soluble in water, and is commonly used as a spark-ignition fuel or as an additive to reduce soot emissions. The enol forms of 2-butanone, also known as 2-buten-2-ol and 1-buten-2-ol, are referred to as tautomers. As shown in (Scheme 1), the first enol (2-buten-2-ol) forms from the shift of a hydrogen atom at the internal carbon atom in 2-butanone to the carbonyl oxygen, while the second enol (1-buten-2-ol) forms from the hydrogen shift at the terminal carbon atom in 2-butanone to the oxygen atom. The calculated heat of formation of 2-buten-2-ol (ΔH_f = -50.079 kcal/mol) is found to be less than that of 1-buten-2-ol (ΔH_f = -43.650 kcal/mol), suggesting that 2-buten-2-ol is the most stable enol. This agrees with published experimental results and theoretical calculations [20, 25-26]. Therefore, the present work focuses on 2-buten-2-ol, which is the most stable tautomer.



Scheme 1. Enolic forms of 2-butanone.

The objective of this work is to perform theoretical calculations on the tautomerism of 2-butanone/2-buten-2-ol by evaluating the effects of substituents X (F, OH, NH_2, CH_3, CN, CF_3) (Scheme 2) on the relative stabilities of these two tautomers using the semiempirical PM3 (Parameterized Model Number 3) and the Density Function Theory (DFT) type

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(B3LYP) methods in the gas phase. This study uses PM3 and DFT calculations to examine the effects of electron-donating and electron-withdrawing substituents on the relative stabilities of these tautomers, focusing on thermodynamics, geometry, and molecular orbital properties.

(A) (B)

Scheme 2. X-substituted of (A) 2-butanone and (B) 2-buten-2-ol.

Methodology of the study

Computational Methods

The geometries of all parent and substituted tautomers were optimized using the PM3 semiempirical method and DFT with the B3LYP/6-31G(d,p) functional set in the MOPAC program, version 8.3 (2004) from Cambridge Soft Corporation [27-28]. Thermodynamic parameters, including enthalpy (ΔH), Gibbs free energy (ΔG), and dipole moments (μ), were calculated. Isodesmic reactions were analyzed to assess substituent stabilization effects, and FMO theory was applied to evaluate HOMO and LUMO energies and energy gaps (Eg).

Results and Discussion

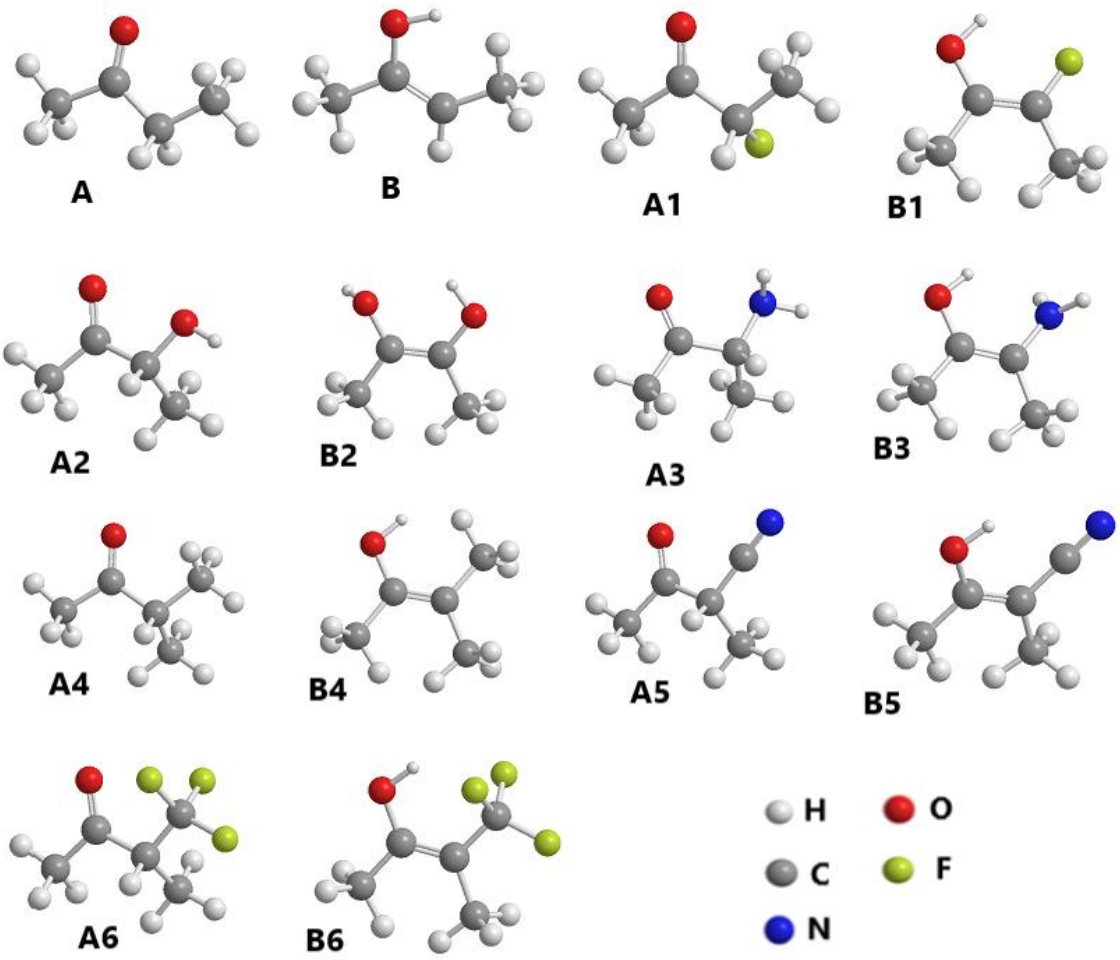

Figure 1. Molecular structures of the substituted 2-butanone (A) and 2-buten-2-ol (B).

Theoretical calculations were carried out with complete optimization of the geometries of 2-butanone, 2-buten-2-ol, and their derivatives at a temperature of 298.15 K in the gas (ε = 1.00) phase. The molecular structures of the optimized geometrical parameters are presented in (Figure 1).

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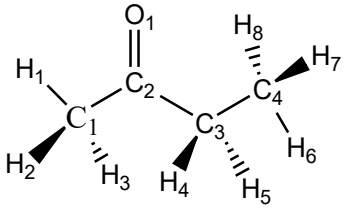
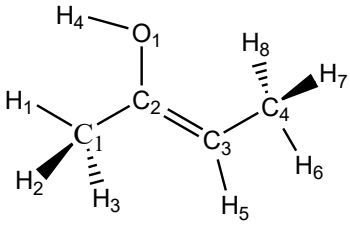
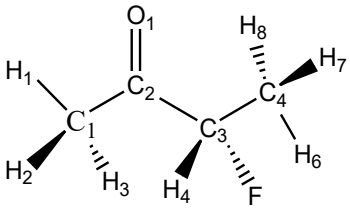
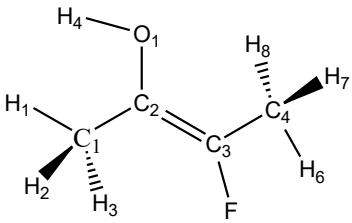
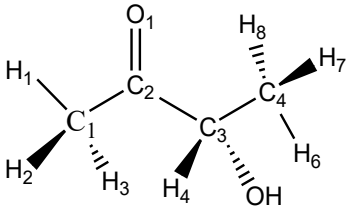
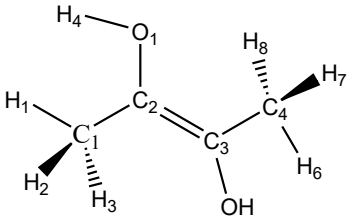
PM3 Calculations

(Table 1) displays the geometric parameters (bond lengths and bond angles) for the optimized compounds calculated in the gaseous state. All substituents (F, OH, NH_2, CH_3, CN, CF_3) cause some changes in the geometric parameters compared to the parent compound (without substitution), particularly where the substituent is attached.

The effect of substituents X on both parent structures shows that some C-C bonds have not been influenced. Thus, the dissimilarity in C-C bond lengths is not significant for all derivatives of the parent compounds. It is clear from (Table 1) that there is no variation in bond lengths between 2-butanone and its substituted derivatives, as well as their counterparts in the 2-buten-2-ol compounds. In Table 1, the effect of substituent X on bond angles is not significant. Fluctuations exist among many bond angles in all derivatives of both parent compounds. For the 2-butanone compounds, the bond angle C1-C2-C3 in molecule A2 has the maximum value of 117.833 degrees. For the 2-buten-2-ol compounds, the bond angle C1-C2-C3 in molecule B6 has the maximum value of 127.046 degrees.

Table 1. Optimized geometrical parameters calculated by PM3 for the substituted 2-butanone and 2-buten-2-ol in the gas phase.

Molecule & Structure		Bond Length (Å)		Bond Angle (°)	
A		C1-C2 C1-H1 C2=O1 C3-C2 C3-C4 C3-H4 C3-H5	1.507 1.098 1.218 1.514 1.510 1.109 1.109	C2-C1-H1 C1-C2-C3 C3-C2-O1 C4-C2-H5 C2-C3-C4	112.754 114.642 123.610 110.113 114.559
B		C1-C2 C1-H1 C2-O1 C3=C2 C4-C3 C3-H5 O1-H4	1.491 1.098 1.369 1.347 1.478 1.095 0.954	C2-C1-H1 C1-C2-C3 C3-C2-O1 C2-C3-C4 C4-C3-H5	111.369 123.692 124.521 124.418 116.200
A1		C1-C2 C1-H1 C2=O1 C2-C3 C3-C4 C3-F C3-H4	1.499 1.099 1.214 1.545 1.528 1.366 1.113	C2-C1-H1 C3-C2-O1 C2-C3-C4 C4-C3-F C1-C2-C3	110.031 120.007 109.088 110.863 111.256
B1		C1-C2 C1-H1 C2-O1 C3=C2 C4-C3 C3-F O1-H4	1.490 1.102 1.366 1.358 1.489 1.349 0.949	C2-C1-H1 C1-C2-C3 C3-C2-O1 C2-C3-C4 C4-C3-F	110.747 123.862 124.152 125.000 115.118
A2		C1-C2 C1-H1 C2-C3 C3-C4 C2-O1 C3-H4 C3-O	1.501 1.099 1.541 1.527 1.216 1.119 1.414	C2-C1-H1 C1-C2-C3 C3-C2-O1 C2-C3-H4 C4 - C2-O	110.000 117.833 119.713 109.533 112.364
B2		C1-C2 C1-H1 C2-C3 C2-O1 C4-C3 C3 -O O1-H4	1.489 1.098 1.358 1.371 1.491 1.381 0.953	C2-C1-H1 C1-C2-C3 C3-C2-O1 C2=C3-C4 O - C3-C4	110.884 124.657 123.243 135.783 117.254

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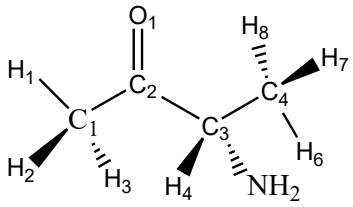
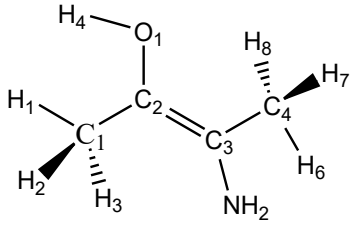
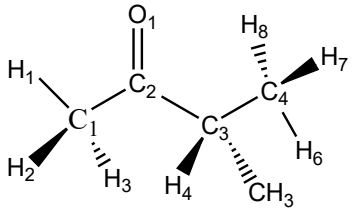
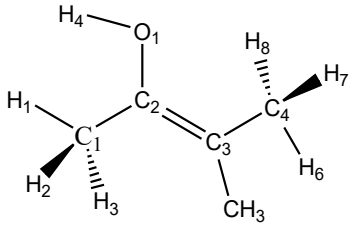
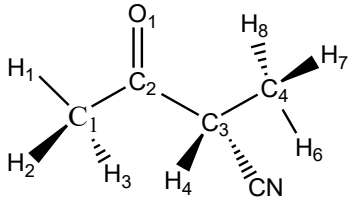
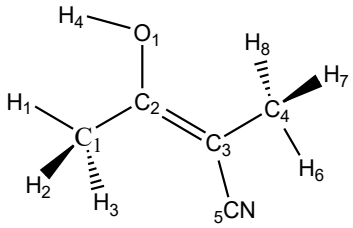
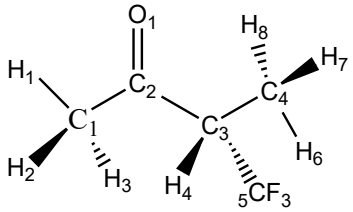
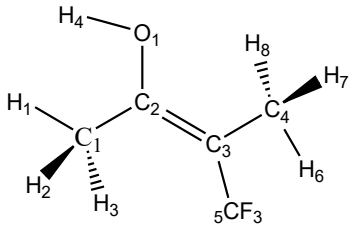
A3		C1-C2 C1-H1 C2-C3 C2-O1 C3-N C3-H4 C4-C3	1.509 1.098 1.544 1.215 1.482 1.508 1.523	C2-C1-H1 C1-C2-C3 O1-C2-C3 C2-C3-C4 C4-C3-N	109.470 116.067 121.965 109.900 108.800
B3		C1-C2 C1-H1 C2-C3 C3-C4 C3-N C2-O O1-H4	1.491 1.102 1.359 1.491 1.440 1.372 0.953	C2-C1-H1 C1-C2-C3 C2-C3-C4 O1-C2-C3 C4-C3-N	110.000 119.500 119.165 122.399 123.065
A4		C1-C2 C1-H1 C2-O1 C2-C3 C3-H4 C4-C3 C5-C3	1.505 1.098 1.216 1.529 1.118 1.519 1.520	C2- C1-H1 C1-C2-C3 C3-C2-O1 C1 -C3-C4 C2-C3-C5	110.063 116.757 121.148 111.172 109.932
B4		C1-C2 C1-H1 C2-C3 O1-C2 C4-C3 C5-C3 O1-H4	1.492 1.102 1.363 1.370 1.487 1.486 0.953	C2-C1-H1 C3-C2-O1 C1-C2-C3 C2-C3-C4 C4-C3-C2	111.080 124.098 125.210 123.190 114.492
A5		C1-C2 C1-H1 C2-O1 C2-C3 C3-C4 C3-C5 C3-H4	1.502 1.099 1.214 1.538 1.522 1.453 1.121	C2-C1-H1 C1-C2-C3 C3-C2-O1 C2-C3-C4 C4-C3-C2	110.338 117.624 119.770 110.309 110.814
B5		C1-C2 C1-H1 C2-O1 C3-C2 C4-C3 O1-H1 C3-C5	1.491 1.098 1.211 1.360 1.489 0.954 1.421	C2-C1-H1 C1-C2-C3 C3-C2-O1 C2-C3-C4 C4-C3-C5	111.832 125.240 123.415 124.224 114.880
A6		C1-C2 C1-H1 C2-C3 C2-O1 C3-C5 C4-C3 C3-H4	1.509 1.113 1.509 1.208 1.457 1.523 1.113	C2-C1-H1 C1-C2-C3 C3-C2-O1 C2-C3-C4 C5-C3-C4	109.470 116.067 121.965 109.900 109.510
B6		C1-C2 C2-C3 C1-H1 C3-C5 C4-C3 C2-O1	1.385 1.357 1.113 1.522 1.484 1.358	C2-C1-H1 C1-C2-C3 C3-C2-O1 C2-C3-C4 C5-C3-C4	110.000 127.046 125.643 122.846 115.298

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Substitution at the α-carbon caused significant changes in bond lengths and angles. EDGs (e.g., CH_3, NH_2) slightly lengthened the C=O bond in 2-butanone due to electron donation. EWGs (e.g., CN, CF_3) induced minor contractions of C=O bond, consistent with electron withdrawal.

Thermodynamic Analysis

Based on (Table 2), the enthalpy of 2-butanone (ΔHf = -57.509 kcal/mol) is less than that of 2-buten-2-ol (ΔHf = -50.079 kcal/mol), suggesting that 2-butanone is the more stable compound in the gas phase. Moreover, substituents X increase the stability of 2-butanone compared to 2-buten-2-ol. This is confirmed by thermodynamic calculations, which show a positive Gibbs free energy (Table 2). The ΔGr for the tautomerization is 8.507 kcal/mol, suggesting that enolization is not spontaneous.

Table 2. Calculated heats of formation (ΔHf, kcal/mol) and Gibbs free energies (ΔG, kcal/mol) for the parent and X-substituted 2-butanone (A) and 2-buten-2-ol (B).

	ΔH_{fA}	ΔH_{fB}	ΔG_A	ΔG_B	ΔGr
H	-57.509	-50.079	-81.851	-73.344	8.507
-F	-98.560	-93.719	-123.095	-118.418	4.677
-OH	-96.413	-91.533	-121.678	-117.009	4.669
$-NH_2$	-52.396	-49.625	-77.996	-74.673	3.323
$-CH_3$	-62.932	-58.955	-87.810	-85.955	1.855
-CN	-18.129	-15.239	-44.572	-41.464	3.108
$-CF_3$	-212.385	-207.343	-240.802	-235.506	5.296

$\Delta Gr = \Delta G_B - \Delta G_A$

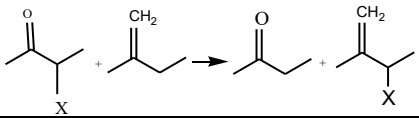
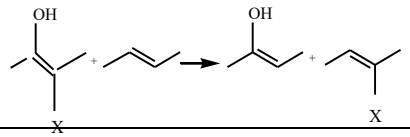
The introduction of substituents into the 2-butanone and 2-buten-2-ol system indicates that a positive value of ΔG_r can be obtained for all reactions. All substituents exhibit lower Gibbs free energies compared to the parent compounds, as shown in (Table 2), suggesting a destabilization of 2-butanone.

Calculated Gibbs free energy differences (ΔG) confirmed 2-butanone as more stable than 2 buten-2-ol under all conditions. However, EWGs markedly reduced keto stability (ΔG decreased by up to 3 kcal/mol), favoring enolization. This trend aligns with their strong inductive (−I) and mesomeric (−M) effects, enhancing α-hydrogen acidity.

The stabilization effect is often confirmed by isodesmic reactions [29-30]. A positive value of substituent stabilization energy (ΔH_{rxn}) indicates the stability of the reactant, while a negative value suggests a more stable product. It can be observed that the ΔH_{rxn} values (Table 3) for the isodesmic reactions of 2-butanone are lower than those for 2-buten-2-ol across all substituents, indicating that all substituents destabilize 2-butanone in comparison to 2-buten-2-ol.

For all substituents, the ΔH_{rxn} values of 2-buten-2-ol are more positive than those of the ketone. Therefore, thermodynamically, all substituents show an increase in the stability of 2-buten-2-ol. These results are confirmed by Gibbs free energy calculations (ΔG_r), which predict a shift in equilibrium toward 2-buten-2-ol compared to the parent compound. It can be seen from (Table 3) that the ΔH_{rxn} value of the isodesmic reaction for compound B3 is 2.132 kcal/mol, which is greater than that of compound A3 (ΔH_{rxn} = 0.619 kcal/mol), suggesting that CH_3 stabilizes compound B3 in the gas phase.

Table 3. Evaluation of the effects of substituents on substituted 2-butanone and 2-buten-2-ol via isodesmic reactions (ΔH_{rxn}, kcal/mol).

Isodesmic Reactions	F	OH	NH_2	CH_3	CN	CF_3
	-1.389	-0.006	2.244	0.619	-1.196	-1.030
	1.576	2.944	2.914	2.132	0.242	0.533

$\Delta H_r = \sum \Delta H_{product} - \sum \Delta H_{reactant}$

Electron densities

The F, OH, and NH_2 substituents are found to decrease the electron density at the carbon to which they are attached (C3) while increasing it on the adjacent carbons (C2 and C4), as shown in (Table 4). Therefore, these substituents act as electron-releasing groups [31]. The CH_3 substituent also exhibits weak electron-releasing properties. In contrast, the NO_2 and CF_3 substituents increase the electron density on the attached carbon (C3) and decrease it on the adjacent carbons (C2 and C4). Thus, these substituents act as electron-withdrawing groups [32]. The CN substituent is classified as a weak electron-withdrawing group.

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Table 4. Calculated electron densities of substituted 2-butanone (A) and 2-buten-2-ol (B) (see Table 1 for notation), obtained from PM3 in the gas phase.

	C1	C2	C3	C4	C5	O1	H1	H4	H5	O2	F1	N1
A	4.172	3.727	4.147	4.100		6.310	0.940	0.951	0.951			
B	4.067	3.941	4.293	4.043		6.242	0.951	0.798	0.882			
A1	4.165	3.745	3.979	4.139		6.295	0.924	0.946			7.144	
B1	4.067	3.968	4.123	4.056		6.223	0.943	0.796			7.100	
A2	4.158	3.722	3.968	4.149		6.513	0.922	0.935		6.307		
B2	4.053	3.973	4.128	4.063		6.234	0.945	0.805		6.228		
A3	4.166	3.715	4.136	4.136		6.308	0.932	0.920				5.030
B3	4.057	3.998	4.265	4.040		6.236	0.955	0.803				4.936
A4	4.177	3.722	4.128	4.113	4.106	6.312	0.932	0.913				
B4	4.074	3.939	4.261	4.042	4.047	6.243	0.943	0.799				
A5	4.169	3.723	3.981	4.110	4.157	6.292	0.924	0.896				
B5	4.085	3.873	4.162	4.037	4.071	6.229	0.933	0.791				
A6	4.175	3.716	4.173	4.112	3.654	6.286	0.921	0.881				
B6	4.128	3.822	4.379	4.038	4.038	6.229	0.910	0.788				

Orbital Energies

According to frontier molecular orbital (FMO) theory, the HOMO-LUMO interaction is primarily responsible for chemical reactivity [33]. E_{HOMO} is a quantum chemical parameter associated with the electron-donating ability of the molecule, while a high value of E_{LUMO} indicates a tendency for the molecule to have low energy in its empty molecular orbitals [34].

(Table 5) presents the frontier molecular orbital energies (HOMO and LUMO), as well as the interfrontier energy gaps (Eg) for X-substituted (A) 2-butanone and (B) 2-buten-2-ol. As shown in (Table 5), the introduction of substituents into 2-butanone (A) and 2-buten-2-ol (B) affects their orbital energies (HOMO and LUMO) compared to the parent compounds. An exception is noted for the NO_2 substituent, which causes a significant change.

Table 5. Calculated frontier orbitals (HOMO and LUMO in eV) of X-substituted (A) 2- butanone and (B) 2-buten-2-ol.

	HOMO	LUMO	Eg
A	-10.660	0.825	11.485
B	-9.146	1.073	10.219
A1	-10.921	0.440	11.361
B1	-9.234	0.634	9.868
A2	-10.656	0.758	11.414
B2	-8.747	0.991	9.738
A3	-9.684	0.756	10.440
B3	-8.254	0.997	9.251
A4	-10.568	0.829	11.397
B4	-8.903	1.017	9.920
A5	-11.134	0.218	11.352
B5	-0.127	1.502	1.629
A6	-11.288	0.142	11.430
B6	-9.981	0.037	10.018

Eg = LUMO – HOMO

The data in (Table 5) reveal that the Eg value for the parent compound 2-butanone (A) is -10.660 eV, compared to -9.146 eV for 2-buten-2-ol (B). This indicates that 2-buten-2-ol (B) is more stable than 2-butanone (A) by 1.266 eV. All substituents show that the energy gaps Eg (LUMO–HOMO) of substituted 2-butanone are less than those of 2-buten-2-ol, which suggests a decrease in the stabilization of 2-buten-2-ol. These results support the thermodynamic and isodesmic reaction calculations in the gas phase.

FMO results revealed that EWGs (Electron-withdrawing groups) lowered HOMO energies and slightly raised LUMO energies, leading to a reduced HOMO-LUMO gap (ΔE). This indicates increased chemical softness and a tendency to stabilize the enol tautomer. In contrast, EDGs (Electron-donating groups) increased ΔE, supporting keto predominance. (Figure 2) illustrates the conceptual effects of EDGs and EWGs on HOMO and LUMO levels for both tautomers. This conceptual diagram is supported by recent DFT studies showing that EDGs (e.g., $–NH_2$, $–CH_3$, $–OCH_3$) raise HOMO (and to a lesser extent

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LUMO) and generally increase the ΔE gap, while EWGs (e.g., $–NO_2$, $–CF_3$, –F) lower both HOMO and LUMO, with a preferential lowering of LUMO, thus reducing the HOMO–LUMO gap [35-37].

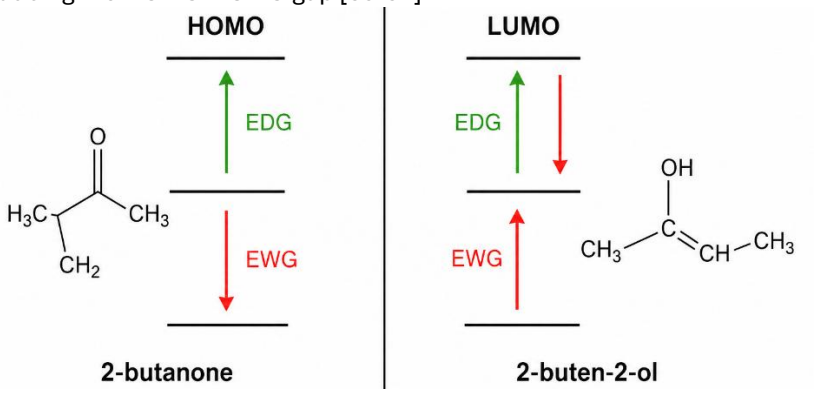

Figure 2. Schematic representation of the effect of EDG and EWG groups on HOMO-LUMO energy levels in 2-butanone and 2-buten-2-ol tautomers.

The HOMO-LUMO energy gaps (Eg) provide insight into the electronic reactivity of both tautomers [38]. For 2-butanone, EWGs lower the HOMO energy (more negative) and slightly raise the LUMO energy, reducing the gap (Eg), which implies higher chemical softness and reactivity. For 2-buten-2-ol, the opposite trend is observed with some EWGs, which increase the energy gap and thus decrease reactivity. This pattern suggests that EWGs may modulate the electronic reactivity of the enol tautomer by altering its frontier molecular orbital energies and reducing the HOMO–LUMO gap. However, the thermodynamic preference between the keto and enol forms must be assessed independently from the calculated ΔG_r values [39].

DFT calculations

Density Function Theory (DFT) type (B3LYP) calculations have been performed in the gas phase with complete optimization of geometrical parameters first on the parent compounds (2-butanone and 2-buten-2-ol) and then on the substituted 2-butanone and 2-buten-2-ol.The calculated enthalpy (H_A) of 2-butanone (H_A = -229.391958 Hartrees) is less than that of 2-buten-2-ol (H_B = -229.363518 Hartrees) (Table 6), which suggests that 2-butanone is more stable.

Table 6. Calculated entropy S (cal/mol.K), enthalpy H (Hartrees) and μ (Debye) of the substituted 2-butanone and 2- buten-2-ol,obtained from the DFT in the gas phase.

	S	H	μ
A	72.785	-229.392	3.024
B	71.905	-229.363	1.345
A1	74.198	-327.129	2.140
B1	74.920	-327.129	1.332
A2	75.183	-303.526	22.185
B2	75.411	-303.519	19.705
A3	80.096	-283.967	4.703
B3	79.992	-283.963	2.358
A4	73.780	-268.207	2.928
B4	76.383	-268.180	1.757
A5	74.028	-320.421	3.050
B5	76.053	-320.412	1.484
A6	84.844	-561.578	6.057
B6	85.673	-561.565	3.727

Thermodynamic calculations

This is supported by the calculated Gibbs free energy (G_A) of 2-butanone (G_A = -229.425 Hartrees) and that of 2-buten-2-ol (G_B = -229.397 Hartrees) (Table 7), where $G_B > G_A$. The Gibbs free energy (ΔG_r) for the tautomerization ($\Delta G_B - \Delta G_A$) is ΔG_r = 0.0280 Hartrees (17.570 kcal/ mol), indicating that 2-butanone is thermodynamically more stable than 2-buten-2-ol and is therefore expected to predominate in the gas phase.

The DFT calculations consistently indicate that 2-butanone remains more stable than 2-buten-2-ol for all the investigated substituents, although the magnitude of the keto–enol free-energy difference varies depending on the substituent. Electron-donating groups (EDGs) such as CH_3 and NH_2 decrease ΔGr to 9.413 and 2.510 kcal/mol, respectively, relative to the unsubstituted system (17.570 kcal/mol), indicating a relative stabilization of the enol tautomer. The electron-withdrawing

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(EWGs) substituents also modify the keto–enol equilibrium, with F, CN, and CF_3 giving ΔGr values of 16.315, 5.020, and 7.530 kcal/mol, respectively. Among the investigated substituents, NH_2 produces the lowest ΔGr, corresponding to the greatest relative stabilization of the enol form. This is consistent with the established effect of electron-withdrawing substituents, which can withdraw electron density and increase the acidity of the α-hydrogen, thereby facilitating enolization [40].

Table 7. Calculated Gibbs free energies ΔG (kcal/mol) of substituted 2-butanone and 2-buten-2-ol obtained from DFT calculations.

	G_A (Hartrees)	G_B (Hartrees)	ΔG_r (kcal/mol)
H	-229.425	-229.397	17.570
-F	-327.190	-327.164	16.315
-OH	-303.562	-303.554	5.020
$-NH_2$	-284.005	-284.001	2.510
$-CH_3$	-268.231	-268.216	9.413
-CN	-320.456	-320.448	5.020
$-CF_3$	-561.618	-561.606	7.530

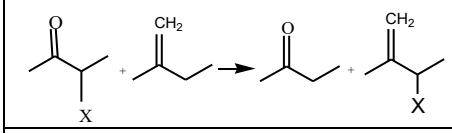
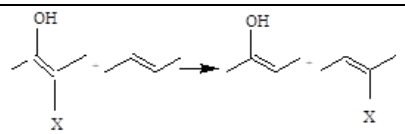
$\Delta Gr = G_B - G_A$ *(1 Hartrees = 627.5095 kcal.mol^{-1})*

Isodesmic reactions calculations

Isodesmic reactions reinforced the thermodynamic findings. Enol forms were more stabilized relative to the keto form in the presence of EWGs. EDGs had minimal effect.

The calculated isodesmic reactions in (Table 8) show that all ΔH_{rxn} values of 2-buten-2-ol are more positive than those of 2-butanone, suggesting that all substituents stabilize the 2-buten-2-ol. These results support thermodynamic calculations.

Table 8. Evaluation of substituent effects on the substituted 2-butanone and 2-buten-2-ol via isodesmic reactions (ΔH_{rxn} kcal/mol), obtained from DFT in the gas phase (ε = 1).

Isodesmic Reactions	F	OH	NH_2	CH_3	CN	CF_3
	0.213	2.259	4.657	1.403	-1.900	6.697
	3.152	2.423	5.353	2.846	-1.847	8.877

$\Delta H_{rxn} = \sum \Delta H_{product} - \sum \Delta H_{reactant}$

Isodesmic reaction enthalpies confirm substituent effects [41]. All EWGs yield positive ΔH_{nxn} values for 2-buten-2-ol, suggesting its stabilization relative to 2-butanone. CH_3 shows modest effects due to hyperconjugation.

Conclusions

This theoretical study highlights the profound impact of substituents on the relative stabilities of 2-butanone and 2-buten-2-ol. The PM3 and DFT analyses reveal that EWGs such as CN and CF_3 destabilize 2-butanone significantly and favor enol formation, while EDGs (NH_2, CH_3) have a moderate effect, slightly stabilizing the enol tautomer. Geometrical changes (bond lengths, angles), Gibbs free energies, and frontier orbital energies all consistently point to a substituent-driven modulation of keto-enol equilibria. These findings provide valuable insights for predicting tautomeric preferences in substituted ketones and can guide the design of molecules with desired reactivity and stability profiles.

Conflict of interest. **Nil**

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