

Charting the Reactivity Terrain of Benzophenones: A DFT-driven Exploration in Gas and Aqueous Environments

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ABSTRACT

Benzophenone and related derivatives are widely used bimolecular photoinitiators in the printing industry due to their low cost and high reactivity. Benzophenones are competent in initiating a chemical reaction to ultraviolet (UV) or visible light, which makes them valuable in UV curing applications. Chemical reactivity parameters of benzophenones are evaluated in the gas and aqueous phase using density functional theory (DFT) at B₃LYP/6-311++G(d, p) combination. Global reactivity descriptors such as chemical potential (μ), chemical hardness (η), softness (σ), electrophilicity (ω), and electronegativity (χ) provide a predictive framework for a molecule's reactivity without the need for experimental data. It is observed that substituted benzophenones are more reactive than benzophenone and chemical reactivity is improved in aqueous medium. Analogous to DFT, the approximations of Koopmans theorem can be used as a valid method for the prediction of reactivity of molecules in gas and aqueous phase. These descriptors help in understanding and rationalizing the mechanisms of chemical reactions, especially in terms of electron transfer processes. A link to the python+Tkinter code for the calculation of global reactivity parameters is Link (https://github.com/Manjeetkb/Reactivity_parameters.git).

Key words: Chemical hardness, Chemical potential, DFT, Electrophilic index, Global reactivity descriptors, Photoinitiators.

1. INTRODUCTION

Photoinitiators are a type of chemical compounds that absorb photons on irradiation with ultraviolet (UV) or visible light and form reactive species such as radicals, cations, or anions out of an excited state, which induce consecutive reactions [1-3]. Photoinitiated polymerization or photo cross cross-linking of monomers, oligomers, and polymers initiated by active species comprise the major industrial processes with a wide range of applications in printing, coating, adhesion, metal decoration, food packaging, and textile industry [4-8]. Benzophenone and its derivatives are widely used as photoinitiators due to their low cost, have strong absorption in short-wave UV region around 230–260 nm, and give good cure in low-viscosity coatings [9,10]. Benzophenone derivatives serve as versatile and effective UV photoinitiators, playing a crucial role in the initiation of photochemical reactions, particularly in the field of photopolymerization [11,12].

The distinctive chemical structure of benzophenone derivatives, characterized by a carbonyl group bridging two phenyl rings, imparts efficient UV absorption properties, making them pivotal in numerous industrial applications. The primary mechanism underlying the photoinitiation process involves Norrish Type I reactions. On exposure to UV light, benzophenone derivatives undergo homolytic cleavage of the C-O bond adjacent to the carbonyl group, generating radicals. These radicals initiate polymerization reactions by abstracting hydrogen atoms from monomers, leading to the formation of reactive species and the subsequent polymerization of various materials [3,9,11]. It is worth noting that the chemical reactivity of compounds is considered the benchmark in the selection of photoinitiators. The knowledge of chemical reactivity, stability, and electron-rich and electron-deficient sites of such industrially important compounds is useful in the study of various types of polymerization reactions in the gas phase as well as aqueous media [13,14].

Frontier molecular orbitals, namely, the highest occupied and lowest unoccupied molecular orbitals (HOMO-LUMO) gap and global reactivity descriptors such as chemical potential (μ), chemical hardness (η), softness (σ), electrophilicity (ω), and electronegativity (χ) provide a predictive framework for a molecule's reactivity without the need for experimental data [15,16]. These descriptors help in understanding and rationalizing the mechanisms of chemical reactions, especially in terms of electron transfer processes. These descriptors can be used to design molecules with specific reactivity profiles for applications in catalysis, material science, and drug design [17,18]. The quantitative nature of these descriptors allows for a systematic assessment of a molecule's reactivity, facilitating comparisons between different compounds. The HOMO-LUMO gap and global reactivity descriptors are essential tools in theoretical chemistry, providing valuable information about a molecule's reactivity, stability, and electronic properties. The chemical reactivity of a molecular system in an aqueous medium can be different from the gas phase [13]. For example, in an aqueous solution, the ionization potential (IP) of a molecule is typically higher than in the gas phase. This is because the surrounding water molecules can stabilize the cation that is formed when the molecule loses an electron. Similarly, the electron affinity (EA) of a molecule is usually lower in an aqueous solution than in the gas phase. This is because the water molecules can compete with the molecules for the electron.

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Global reactivity descriptors can generate vital data to make informed predictions about a molecule's behavior in various chemical reactions and guide the design of molecules with desired reactivity profiles. Using density functional theory (DFT), these reactivity descriptors can be obtained from IP, EA, and from HOMO-LUMO orbital energy based on Koopmans approximation [19]. These parameters offer quantitative measures that elucidate molecules' electronic structure and properties in response to external perturbations. Koopmans' approximation provides a simple yet effective method to estimate these descriptors from response functions based on orbital energies. The values of these descriptors can be calculated using various computational methods, such as DFT [17,19,20]. They can then be compared between different molecules or between the same molecule in different environments, such as the gas phase or an aqueous solution.

The present article is organized as follows: Section 2 describes and explores the mechanism underlying the generation of reactive species, which is the basis of photopolymerization or cross-linking reactions. Section 3 describes the computational scheme solicited to compute reactivity parameters. Obtained results including theoretical interpretation, approaches, and diverse applications of chemical reactivity descriptors based on HOMO-LUMO energy are presented in section 4. Finally, conclusions are given in section 5.

2. OVERVIEW

Benzophenone derivatives have been widely recognized and employed as UV photoinitiators in various industrial applications. These compounds play a crucial role in initiating photochemical reactions, particularly in the process of photopolymerization. Photopolymerization involves the use of UV light to induce chemical reactions that lead to the formation of polymers and coatings. Benzophenone derivatives are chosen for their ability to absorb UV radiation efficiently and initiate photochemical reactions, making them indispensable in diverse fields such as coatings, adhesives, dental materials, and packaging [4-6].

Benzophenone derivatives are characterized by the presence of the benzophenone moiety, which consists of two benzene rings linked by a carbonyl group. The general structure is shown as follows:



where *Ph* represents a phenyl group (C₆H₅).



Benzophenone derivatives function as photoinitiators through a process known as Norrish Type I photo-reaction. When exposed to UV light, benzophenone absorbs the energy and undergoes homolytic cleavage of the C-O bond adjacent to the carbonyl group. This results in the formation of two radicals:

These radicals then initiate the polymerization process by abstracting hydrogen atoms from monomers, leading to the generation of reactive species that propagate the polymerization reaction.

Applications of Benzophenone Derivatives as UV Photoinitiators:

- **Coatings and Adhesives:** Benzophenone derivatives are extensively used in UV-curable coatings and adhesives. The ability to induce rapid and controlled polymerization facilitates efficient curing, contributing to the production of coatings with enhanced durability and adhesives with improved bonding properties.
- **Inks and Printing:** UV-curable inks utilized in printing processes benefit from the use of benzophenone derivatives as photoinitiators. This enables quick drying and curing of inks during the printing process.

- **Dental Materials:** In dentistry, benzophenone derivatives find application in the fabrication of dental composites and adhesives. The precise control over the polymerization process ensures the development of durable and esthetic dental materials.
- **Photolithography:** Benzophenone derivatives play a crucial role in the photolithographic processes used in the semiconductor industry. They facilitate the patterning of photoresists on semiconductor wafers during the fabrication of microelectronic devices.
- **3D Printing:** UV-curable 3D printing technologies utilize benzophenone derivatives to enable layer-by-layer polymerization, allowing for the fabrication of intricate three-dimensional structures.

While benzophenone derivatives are valuable UV photoinitiators, some challenges need to be addressed. These may include issues related to the yellowing of materials on prolonged exposure to UV light, potential skin sensitization, and the need for continuous advancements in developing derivatives with enhanced performance [4]. Benzophenone derivatives have established themselves as indispensable components in UV photoinitiators, playing a pivotal role in the development of UV-curable materials across diverse industries. As research in materials science advances, the synthesis of novel benzophenone derivatives and the optimization of their properties continue to contribute to the evolution of UV photoinitiation technologies, opening new avenues for innovative applications and improved performance in various industrial sectors.

3. COMPUTATIONAL METHOD

Using the B₃LYP/6-311++G(d, p) method including D3 dispersion correction, quantum mechanical calculations are performed on the Gaussian 16 code [21] for the evaluation of global reactivity descriptors. Reactivity properties in solvent (aqueous medium) are obtained using the PCM model. The PCM is a widely used computational method in chemistry to model the effects of a solvent on molecules. It treats the solvent as a homogeneous dielectric continuum rather than explicitly including individual solvent molecules. Molecular structures were obtained from PubChem and NIST databases and are geometrically relaxed. The vibrational frequency calculations confirmed that the stationary point was found, and no imaginary frequencies were present. The B₃LYP/6-311++G(d, p) method is a popular and powerful computational tool for obtaining global reactivity descriptors in chemistry. The B₃LYP functional [22] combines the Becke three-parameter exchange functional with the Lee-Yang-Parr correlation functional, providing a good balance between accuracy and computational cost. B₃LYP, a hybrid DFT functional, combining the strengths of the local density approximation and Hartree-Fock exchange. It provides accurate energies and geometries for a wide range of molecules and reactions. This is a double-zeta (6-311) basis set with diffuse functions (++) and polarization functions (G) for all atoms. This means it accurately represents both core and valence electrons, including lone pairs and polarized bonds. These functions are essential for capturing the behavior of electrons in outer orbitals, which are crucial for reactivity descriptors such as IP and EA. These functions allow the electron cloud to deform in response to an external electric field, important for accurate calculations of dipole moments and other reactivity-related properties. The D3 dispersion correction [23], also known as the Grimme dispersion correction, with Becke-Johnson damping [24] is added to the DFT calculations which is crucial for the description of Van Der Waals interactions and dispersion forces that are not adequately captured by standard DFT functionals. Compared to higher-level methods, B₃LYP/6-311++G(d, p) provides good accuracy at a reasonable computational cost, making it accessible to a wider range of researchers. This method can be applied to a diverse range of molecules and systems, from small organic molecules to large biomolecules and complex materials.

4. RESULTS AND DISCUSSION

Global reactivity descriptors are theoretical tools used to understand and predict the chemical reactivity of molecules. Using B₃LYP/6-311++G(d, p) DFT theory, these descriptors are computed, and the results are compared with the values obtained from Koopmans approximation. Both gas phase and aqueous phase results are presented. Table 1 shows the optimized structures of the selected compounds along with HOMO-LUMO orbitals.

Table 2 presents the energies of frontier molecular orbitals with the energy band gap of molecules in the gas and aqueous phase. Similarly, Tables 3-5 report chemical reactivity parameters in both gas and aqueous medium using Koopmans approximation, from IE and EA in the gas phase and aqueous medium, respectively. IE is the energy required to remove an electron from the HOMO of a molecule. A lower IE value indicates a molecule is more likely to be oxidized (lose an electron). Similarly, EA is the energy released when an electron is added to the LUMO of a molecule. A higher EA value indicates a molecule is more likely to be reduced (gain an electron). IE and EA of any molecule are computed as:

$$IE = E(N-1) - E(N) \quad (3)$$

$$EA = E(N) - E(N+1) \quad (4)$$

These parameters are discussed in detail in the preceding sections.

4.1. Global Reactivity Descriptors in Gas Phase

Global reactivity descriptors provide valuable insights into the electronic structure and chemical reactivity of a molecular system. These descriptors offer a comprehensive understanding of how a molecule or system may interact with its environment and participate in chemical reactions. The key global reactivity descriptors include the chemical potential (μ), global hardness (η), and global softness (σ). Here's what each descriptor reveals about the molecular system:

- **HOMO-LUMO Gap:** The HOMO-LUMO gap is the energy difference between the highest occupied and the lowest unoccupied molecular orbital. The HOMO-LUMO gap serves as a key indicator of a molecule's reactivity. A smaller gap suggests higher reactivity as it requires less energy to promote an electron from the HOMO to the LUMO, facilitating electron transfer in chemical reactions. The HOMO is often associated with electron-donating abilities, while the LUMO is associated with electron-accepting abilities. A smaller gap

Table 1: Optimized molecular structures of the selected benzophenone derivatives using B₃LYP/6-311++G (d, p) DFT theory. Frontier molecular orbitals (HOMO-LUMO) are also shown.

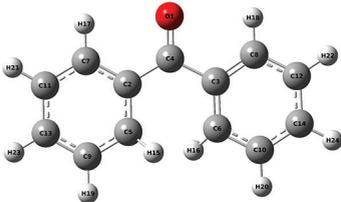
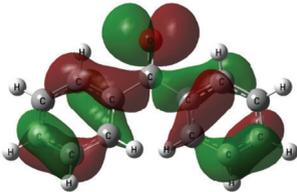
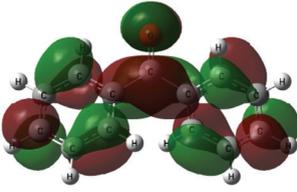
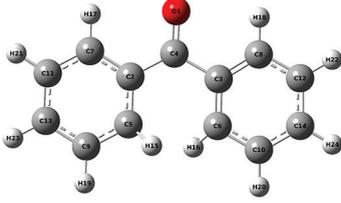
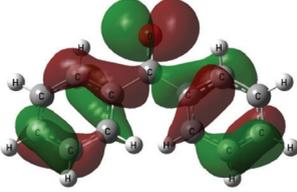
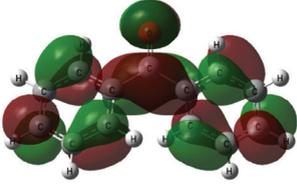
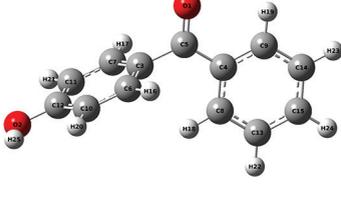
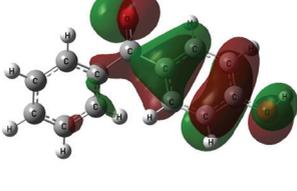
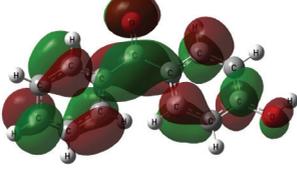
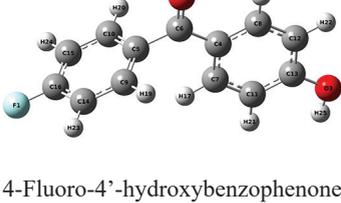
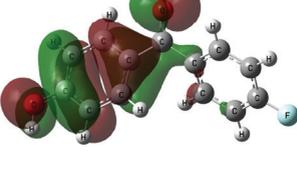
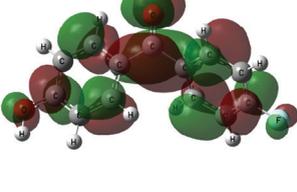
Molecule	HOMO	LUMO
 Benzophenone		
 Benzophenone-d ₁₀		
 4-hydroxybenzophenone		
 4-Fluoro-4'-hydroxybenzophenone		

Table 2: Computed HOMO-LUMO energy of molecules in the gas and aqueous phases.

Molecule	CAS no.	Gas phase			Aqueous		
		ϵ_{HOMO}	ϵ_{LUMO}	ΔE_{Gap}	ϵ_{HOMO}	ϵ_{LUMO}	ΔE_{Gap}
BZP	119-61-9	-7.00	-2.10	4.90	-7.22	-2.27	4.95
BZP-d10	22583-75-1	-7.00	-2.10	4.90	-7.22	-2.27	4.95
4-H-BZP	1137-42-4	-6.69	-1.96	4.72	-6.76	-2.14	4.62
4-F-4-H-BZP	25913-05-7	-6.79	-2.06	4.74	-6.78	-2.16	4.61
2-MBZP	131-58-8	-6.92	-2.04	4.88	-7.06	-2.22	4.84
2-HBZP	117-99-7	-6.68	-1.95	4.73	-6.71	-2.21	4.50
3-MBZP	643-65-2	-6.89	-2.04	4.85	-7.03	-2.24	4.79
4-MBZP	134-84-9	-6.88	-2.00	4.88	-7.06	-2.21	4.85
4-PBZP	2128-93-0	-6.97	-2.05	4.92	-7.13	-2.23	4.89
2-H-4-MBZP	131-57-7	-6.42	-1.79	4.63	-6.53	-2.10	4.42
M-2-BB	606-28-0	-6.98	-2.01	4.97	-7.32	-2.23	5.09
2,3,4-THBZP	1143-72-2	-6.40	-1.84	4.56	-6.41	-2.14	4.27
2,2-DH-4-MBZP	131-53-3	-6.27	-1.58	4.69	-6.55	-1.93	4.62
5-Cl-2-HBZP	85-19-8	-6.59	-2.55	4.03	-6.66	-2.57	4.09

Table 3: Global reactivity parameters of benzophenone derivatives from HOMO-LUMO energy (Koopmans approximation) in gas and aqueous environments.

Molecule	Gas phase					Aqueous				
	μ	η	σ	ω	χ	μ	η	σ	ω	χ
BZP	-4.5496	2.4524	0.2039	4.2201	4.5496	-4.7458	2.4764	0.2019	4.5475	4.7458
BZP-d10	-4.5496	2.4524	0.2039	4.2201	4.5496	-4.7458	2.4764	0.2019	4.5475	4.7458
4-H-BZP	-4.3229	2.3624	0.2117	3.9553	4.3229	-4.4527	2.3090	0.2165	4.2933	4.4527
4-F-4-H-BZP	-4.4240	2.3685	0.2111	4.1318	4.4240	-4.4689	2.3067	0.2168	4.3290	4.4689
2-MBZP	-4.4786	2.4405	0.2049	4.1094	4.4786	-4.6402	2.4209	0.2065	4.4471	4.6402
2-HBZP	-4.3131	2.3670	0.2112	3.9297	4.3131	-4.4563	2.2497	0.2223	4.4136	4.4563
3-MBZP	-4.4657	2.4232	0.2063	4.1149	4.4657	-4.6344	2.3951	0.2088	4.4835	4.6344
4-MBZP	-4.4404	2.4376	0.2051	4.0443	4.4404	-4.6338	2.4264	0.2160	4.4247	4.6338
4-PBZP	-4.5072	2.4600	0.2032	4.1289	4.5072	-4.6812	2.4466	0.2044	4.4784	4.6812
2-H-4-MBZP	-4.1084	2.3165	0.2148	3.6432	4.1084	-4.3159	2.2122	0.2260	4.2101	4.3159
M-2-BB	-4.4974	2.4843	0.2013	4.0709	4.4974	-4.7732	2.5462	0.1964	4.4740	4.7732
2,3,4-THBZP	-4.1198	2.2822	0.2191	3.7185	4.1198	-4.2721	2.1368	0.2340	4.2706	4.2721
2,2-DH-4-MBZP	-3.9258	2.3437	0.2133	3.3879	3.9258	-4.2384	2.3097	0.2165	3.8889	4.2384
5-Cl-2-HBZP	-4.5704	2.0169	0.2479	5.1784	4.5704	-4.6168	2.0470	0.2443	5.2065	4.6168

indicates a molecule's potential to donate or accept electrons easily. The HOMO-LUMO gap is related to a molecule's absorption spectrum, influencing its color and UV-vis absorption characteristics. It is observed that substituted benzophenone possesses lower gaps than benzophenone suggesting higher reactivity. 2,3,4-THBZP, 2-H-4-MBZP, 4-HBZP, and 2,2-DH-4-MBZP have higher reactivity than benzophenone in the gas phase. A much higher reactivity is observed in the aqueous phase for these molecules. However, the reactivity decreases for BZP, BZP-d10, M-2-BB, and 5-Cl-2-HBZP in aqueous medium, irrespective of other molecules. These reactivity patterns have established that the substituted benzophenone derivatives provide a better cure at high concentrations in low-viscosity coatings. Substituted benzophenones absorb in the

mid-UV range around 280–330 nm and are relatively more reactive than benzophenone.

- **Chemical Potential (μ):** The chemical potential represents the change in energy with respect to the number of electrons in the system. A higher chemical potential indicates a greater tendency for the system to gain electrons. The chemical potential is related to the electronegativity of the system; higher values suggest a stronger attraction for electrons. μ can be obtained as in equation (5) from the HOMO-LUMO energy using concepts of Koopmans approximation. Knowledge of the chemical potential helps understand the system's electron distribution and its ability to undergo electron transfer in chemical reactions. Based on the values molecules such as 5-Cl-2-HBZP, BZP, BZP-d10, 4-PBZP, and M-2-BB are among the best electron acceptors.

Table 4: Chemical reactivity descriptors from ionization energy and electron affinity computed using B₃LYP/6-311++G (d, p) in the gas phase.

Molecule	DFT (Gas phase)						
	IE	EA	<i>M</i>	η	σ	ω	χ
BZP	-8.68	-0.50	-4.5900	4.0900	0.1222	2.5756	4.5900
BZP-d10	-8.68	-0.50	-4.5900	4.0900	0.1222	2.5756	4.5900
4-H-BZP	-8.37	-0.38	-4.3750	3.9950	0.1252	2.3956	4.3750
4-F-4-H-BZP	-8.58	-0.47	-4.5250	4.0550	0.1233	2.5247	4.5250
2-MBZP	-8.56	-0.43	-4.4950	4.0650	0.1230	2.4852	4.4950
2-HBZP	-8.39	-0.35	-4.3700	4.0200	0.1244	2.3752	4.3700
3-MBZP	-8.51	-0.47	-4.4900	4.0200	0.1244	2.5075	4.4900
4-MBZP	-8.49	-0.44	-4.4650	4.0250	0.1242	2.4764	4.4650
4-PBZP	-8.55	-0.42	-4.4850	4.0650	0.1230	2.4742	4.4850
2-H-4-MBZP	-8.05	-0.23	-4.1400	3.9100	0.1279	2.1918	4.1400
M-2-BB	-8.63	-0.50	-4.5650	4.0650	0.1230	2.5633	4.5650
2,3,4-THBZP	-8.13	-0.32	-4.2250	3.9050	0.1280	2.2856	4.2250
2,2-DH-4-MBZP	-7.88	-0.04	-3.9600	3.9200	0.1276	2.0002	3.9600
5-Cl-2-HBZP	-8.33	-0.99	-4.6600	3.6700	0.1362	2.9585	4.6600

Table 5: Chemical reactivity descriptors from ionization energy and electron affinity computed using B₃LYP/6-311++G(d, p) in aqueous phase.

Molecule	DFT (Aqueous)						
	IE	EA	<i>M</i>	η	σ	ω	χ
BZP	-7.10	-2.41	-4.7559	2.3428	0.2134	4.8273	4.7559
BZP-d10	-7.10	-2.41	-4.7559	2.3428	0.2134	4.8273	4.7559
4-H-BZP	-6.70	-2.29	-4.4927	2.2029	0.2270	4.5813	4.4927
4-F-4-H-BZP	-6.71	-2.30	-4.5060	2.2036	0.2269	4.6070	4.5060
2-MBZP	-6.97	-2.35	-4.6590	2.3114	0.2163	4.6954	4.6590
2-HBZP	-6.66	-2.34	-4.5003	2.1581	0.2317	4.6922	4.5003
3-MBZP	-6.93	-2.38	-4.6579	2.2758	0.2197	4.7667	4.6579
4-MBZP	-6.95	-2.35	-4.6512	2.2984	0.2175	4.7062	4.6512
4-PBZP	-7.04	-2.36	-4.7029	2.3388	0.2138	4.7282	4.7029
2-H-4-MBZP	-6.44	-2.25	-4.3437	2.0970	0.2384	4.4988	4.3437
M-2-BB	-7.21	-2.37	-4.7879	2.4210	0.2065	4.7344	4.7879
2,3,4-THBZP	-6.36	-2.28	-4.3187	2.0432	0.2447	4.5640	4.3187
2,2-DH-4-MBZP	-6.44	-2.07	-4.2530	2.1865	0.2287	4.1361	4.2530
5-Cl-2-HBZP	-6.59	-2.71	-4.6508	1.9416	0.2575	5.5700	4.6508

$$\mu = -\frac{1}{2}(IP + EA) = \frac{1}{2}(\epsilon_{LUMO} + \epsilon_{HOMO}) \quad (5)$$

- Global hardness (η): Global hardness measures the resistance of a system to changes in electron density when subjected to an external perturbation. High hardness indicates a stable system with strong electron–electron repulsion, suggesting low reactivity. Low hardness implies a more reactive system that readily adapts to changes in electron density. Hardness is related to the polarizability of the system; systems with high hardness are less polarizable. Chemical hardness can be obtained as below.

$$\eta = \frac{1}{2}(IP - EA) = \frac{1}{2}(\epsilon_{LUMO} - \epsilon_{HOMO}) \quad (6)$$

Based on the observed values of η BZP, BZP-d10, M-2-BB, and 4-PBZP are hard molecules and consecutively less reactive. 5-Cl-2-HBZP with η value 2.0169 is the most reactive among all investigated molecules.

- Global softness (σ): Global softness is the inverse of global hardness and represents the ease with which electron density can change in response to an external perturbation. High softness implies a system that readily undergoes changes in electron density, making it more reactive. Soft systems are often more polarizable and can easily adapt to electronic perturbations. Softness is related to the electrophilicity of a system; soft systems are more prone to acting as electrophiles in chemical reactions. A higher $\sigma = 0.2479$ of 5-Cl-2-HBZP indicates high reactivity. M-2-BB and 4-PBZP are less reactive than other molecules.

$$\sigma = \frac{1}{2\eta} \quad (7)$$

- Electrophilic Index (ω): A measure of a molecule's tendency to accept electrons. It is calculated as the square of the chemical potential divided by the chemical hardness. A higher ω value indicates a molecule is more electrophilic [25]. A much higher electrophilicity nature is observed in 5-Cl-2-HBZP, BZP, BZP-d10, 4-F-4-H-BZP, and 4-PBZP. This means these molecules are better electron acceptors.

$$\omega = \mu^2 \sigma \quad (8)$$

Global reactivity descriptors provide qualitative predictions of a system's reactivity in chemical reactions. Understanding these descriptors aids in the design of molecules with specific electronic and reactivity properties. Global reactivity descriptors contribute to the elucidation of reaction mechanisms, particularly in terms of electron transfer processes.

4.2. Global Reactivity Descriptors in Aqueous Medium

The effect of an aqueous medium on global reactivity descriptors compared to the gas phase can be multifaceted and vary depending on the specific descriptor and molecule. The specific effects on each descriptor depend on the individual molecule and its interactions with the aqueous environment [26,27]. Computational methods like DFT can be used to predict the behavior of specific molecules in aqueous media with greater accuracy [28,29]. The values of global reactivity descriptors can be significantly different for the same molecule in the gas phase and in an aqueous solution. This is because the solvent can interact with the molecule in various ways, such as through hydrogen bonding or electrostatic interactions. These interactions can affect the molecule's electronic structure and, consequently, its reactivity.

- IP: In general, solvation stabilizes the cation formed after ionization, making the removal of an electron more difficult. Hence, IP tends to increase in aqueous media. Small, highly charged molecules can experience stronger ion-dipole interactions with water, lowering their IP in aqueous media. The DFT computed values in the gas phase in Table 4 and the aqueous phase in Table 5 show that IP is higher in aqueous phase than gas phase. These computed values comply with the trend as discussed above.
- EA: Water molecules compete with the molecule for the electron, lowering the energy released when it is gained. Consequently, EA tends to decrease in aqueous media. Molecules with strong polarizability or specific interactions with water might see a slight increase in EA due to favorable stabilization effects. The reported EA values in Table 4 are higher than the values in Table 5. This shows that EA values in aqueous phase are lower than in the gas phase.
- Chemical hardness (effects). The reperfect of changes in IP ($\approx -\epsilon_{\text{HOMO}}$) and EA ($\approx -\epsilon_{\text{LUMO}}$) often leads to a higher energy gap between HOMO and LUMO, resulting in increased values in Table 5. This shows that EA P, BZP-d10, M-2-BB, and 5-Cl-2-HBZP increases in the aqueous phase while decreases in other molecules. Due to the increased band gap little change in 5. This shows that EA P, BZP-d10, M-2-BB, and 5-Cl-2-HBZP increases in phase. strong values in olecule lowering the band gap which in turn lower the stability but increases the reactivity, see Tables 2 and 3.
- Chemical potential (decreases in other molecules). Due to the increased band gap little change in 5. This shows that EA P, BZP-d10, M-2-BB, and 5desolvation during ionization or

interactions with water affecting orbital energies might show different trends. Computed HOMO-LUMO energies of the molecules show lowering trend in aqueous phase. Due to the lower values of orbital energies, during ionization ove lower values in aqueous phase.

- Electronegativity (χ): Electronegativity of a molecular system is computed as $\chi = -\mu$ from Koopmans approximation. Hence, increased χ values are observed in aqueous phase. However, specific interactions with water can influence orbital energies and modify the trend.
- Electrophilicity (ω): Due to the combined effects on μ and η , ω often decreases in aqueous media, indicating reduced electron-accepting ability. Molecules with minimal change in η and a significant decrease in μ might see an unexpected increase in ω . This trend for μ and η can be seen in Table 3. Equation (6) and (7) established that ω should increase in aqueous medium.

As a result of these solvation effects, molecules in aqueous solutions are generally more reactive than in the gas phase. However, the specific effect of the solvent on reactivity can vary depending on the nature of the molecule and the reaction being studied which is evident from the calculations of some molecules.

In summary, global reactivity descriptors offer a quantitative understanding of a molecular system's behavior in terms of electron distribution, reactivity, and response to external perturbations, making them invaluable tools in theoretical chemistry and molecular design.

4.3. Global Reactivity Descriptors: DFT versus Koopmans

Chemical reactivity parameters obtained through DFT means IE and EA values are utilized to obtain these parameters. While in the case of Koopmans approximation, reactivity descriptors are obtained through HOMO-LUMO energies. Koopmans theorem states that removing or adding an electron to a molecule does not significantly change the electronic structure of the remaining system. Such that IE and EA can be assumed fairly close to the HOMO and LUMO energies, respectively. Considering the above assumptions, the reported results in Tables 2-4 are in fairly close agreement in the gas phase while in perfect agreement in the aqueous phase. Figure 1 shows the variation of chemical potential in the aqueous phase from DFT and Koopmans approximation, which is almost identical and very close in the gas phase. This shows that the Koopmans theorem can be considered as a valid approximation for the computation of chemical potential in both gas and aqueous phase. Similarly, the electrophilic index for the investigated molecules shown in Figure 2 deviates by 30–40%

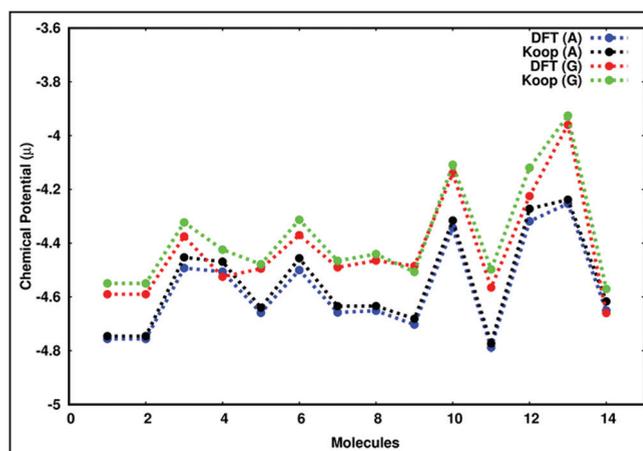


Figure 1: Chemical potential of benzophenones using DFT and Koopmans approximation in gas and aqueous phase.

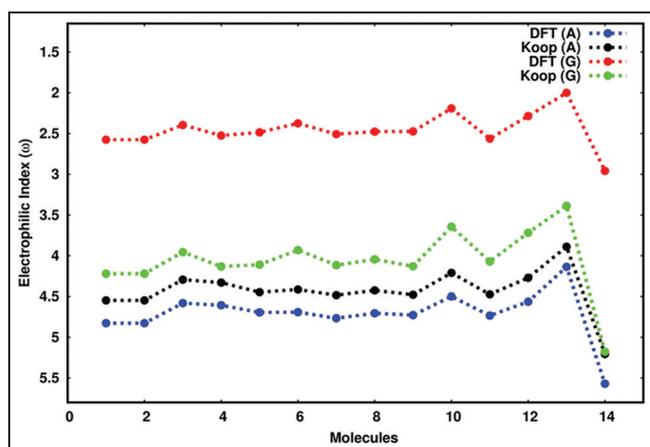


Figure 2: Electrophilic index of benzophenones using DFT and Koopmans approximation in gas and aqueous phase.

in the gas phase. While in the aqueous phase, the electrophile index obtained by DFT deviates by just 1–6% from the electrophile index obtained from the Koopmans approximation. Likewise, the Koopmans approximation underestimates chemical hardness by ~30% the DFT values. On the other hand, Koopmans approximation evaluates similar descriptors fairly perfectly alongside DFT results in aqueous phase.

These results have established that the Koopmans approximation can be used as a valid method for the prediction of the reactivity of molecules in aqueous phase while with a fairly acceptable margin in the gas phase. A Python and Tkinter-based code (GitHub: https://github.com/Manjeetkb/Reactivity_parameters.git) is provided to compute these parameters on the fly from HOMO and LUMO energies, see [30].

5. CONCLUSIONS

Chemical reactivity of benzophenone derivatives is predicted using B₃LYP/6-311++G(d, p) DFT theory in gas and aqueous phase. Global reactivity descriptors derived from DFT response functions are considered valid and powerful tools for the prediction of molecular reactivity. Parameters such as chemical potential (μ) hardness (η), softness (σ), electrophilic index (ω), and electronegativity (χ) based on response functions offer valuable insights into the behavior and reactivity of molecules and various reaction mechanisms such as photopolymerization. These properties in aqueous medium can be different from the gas phase. It has been observed that substituted benzophenones absorb in the mid UV range around 280–330 nm and is relatively more reactive than benzophenone. Due to the lower HOMO-LUMO energy gap, molecules such as 2,3,4-THBZP, 5-Cl-2-HBZP, 4-H-BZP, and 2-H-4-MBZP are more reactive than BZP. The chemical reactivity increases in the aqueous medium except BZP, BZP-d10, M-2-BB, and 5-Cl-2-HBZP due to the increased interactions with water molecule. Results from the Koopmans approximation show that 5-Cl-2-HBZP, BZP, and BZP-d10 have greater tendency to gain electrons, while 4-PBZP and M-2-BB have high stability and as a result low reactivity. Conversely, 4-PBZP and M-2-BB have a low chemical softness index. A higher electrophilic index of 5-Cl-2-HBZP indicates its better electron-accepting tendency compared to other investigated molecules. This comparative analysis has shown that the Koopmans approximation can be regarded as a valid approximation for the calculation of reactivity parameters. While not a definitive tool for replicating experimental results or supplanting existing theories, Koopmans' theorem offers valuable guidance for future research pursuits.

Understanding the differences in global reactivity descriptors between the gas phase and aqueous medium can be helpful for predicting the

behavior of molecules in different environments. The present research would be vital in designing new drugs, catalysts, and developing new materials with specific chemical properties that are effective in aqueous environments. Overall, benzophenone derivatives are a versatile and effective class of photoinitiators with a wide range of applications. Continued research is likely to lead to the development of new derivatives with even better properties.

6. DECLARATIONS

6.1. Ethical Approval

Not applicable.

6.2. Competing Interests

Not applicable.

6.3. Authors' Contributions

Not applicable.

6.4. Funding

Not applicable.

6.5. Availability of Data and Materials

Data are available on request from the author.

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*Bibliographical Sketch



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