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Regular Article

Revisiting the Photo-Induced Paternò-Büchi Reaction Mechanism by MS-CASPT2 Method

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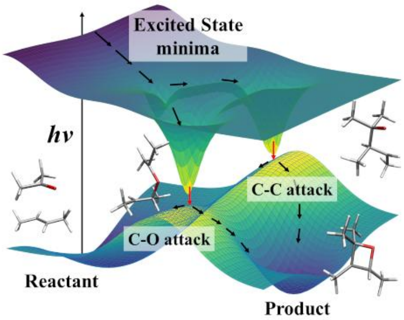
Abstract: The Paternò-Büchi (P-B) reaction can generate oxetane, which is of great value in organic synthesis and medicinal chemistry, but its mechanism remains controversial. In this work, we studied the mechanism of the P-B reaction between acetone and butene to form oxetane by using the method of multistate complete active space perturbation theory (MS-CASPT2). The calculation results establish that this reaction can occur on both singlet potential energy surfaces involving the S_0 and S_1 ($^1n\pi^*$) states, as well as on triplet potential energy surfaces containing the $^3n\pi^*$ and $^3\pi\pi^*$ states. The reaction pathways on both singlet and triplet states are energetically allowed. For the C-O attack pathway, there exist significant differences in structure and energy between the conical intersection point $(S_1/S_0)_x$-1 on the singlet reaction path and the intermediate $^3I_{CO}$ on the triplet reaction path. For the C-C attack pathway, the conical intersection point $(S_1/S_0)_x$-2 and the triplet intermediate $^3I_{CC}$ almost coincide, which means that the singlet and the triplet reaction paths go through a region where the energies of the four states (S_1, T_2, T_1, and S_0) are approximately degenerate. Our results have provided new insights into the mechanism of the P-B reaction.



Key words: Paternò-Büchi reaction, excited state, photochemistry, conical intersection.

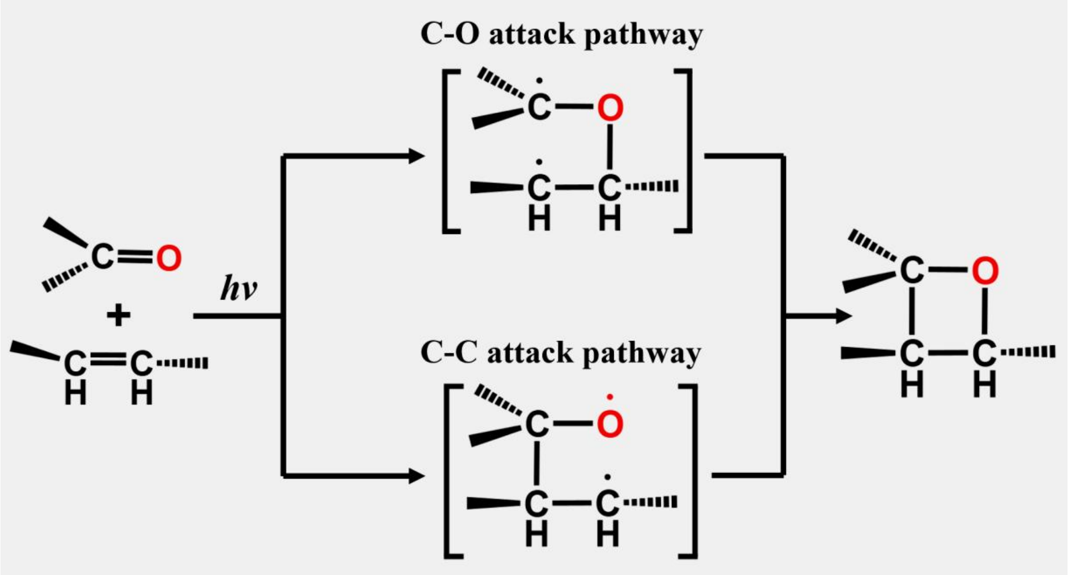
1. Introduction

The Paternò-Büchi (P-B) reaction, one of the [2+2] photocycloaddition reactions between a carbonyl compound and an alkene, is a flexible photochemical process that produces four-membered oxygen heterocycles oxetanes [1,2]. Oxetanes are found in the chemical structures of several natural and biologically active compounds [3], such as an antitumor drug paclitaxel [4], merrilactone possessing neurotrophic activity [5], and oxetanocin showing anti-HIV activity [6]. High regioselectivity and stereoselectivity in the P-B reaction can be obtained by proper adjusting the structures of the reactants [2]. In addition to its widespread applications in organic synthesis and medicine chemistry, the P-B reaction has significant value for locating the position of double bonds in alkenes, a topic of substantial interest in the field of lipidomics [7,8].

Although the P-B reaction has been known for more than a century [9,10], its mechanism continues to be an active area of research and debate. The mechanism of the Paternò–Büchi reaction presents several unresolved questions, including (1) Does the reaction take place in the singlet excited state (S_1 state) or the triplet excited state (T_1 state)? (2) Is the reaction concerted or stepwise? (3) Which intermediates are involved in the reaction? (4) What is the specific reaction pathway?

Early in 1954, Büchi et al. proposed that the P-B reaction of benzaldehyde with 2-methyl-2-butene involves the most stable biradical intermediate formed by the triplet-state carbonyl compound reacting with the ground-state alkene [10-12]. This triplet state-involved mechanism was supported by multiple follow-up experiments [13-17] and calculations [18-20]. However, Turro et al. studied the P-B reaction between acetone and the trans-dicyanoethylene (t-DCE) and found this photocycloaddition does not proceed via the acetone triplet state but via a singlet complex of acetone and t-DCE [21,22]. Further investigation of Turro and Wriede on the photocycloaddition of acetone to 1-methoxy-l-butene revealed that both acetone singlets and acetone triplets are involved in oxetane formation based on kinetic analysis and quantum yield studies [23]. Robb and co-workers performed MC-SCF calculations on the P-B reaction between formaldehyde and ethylene and revealed the C-O attack and C-C attack pathways behave differently [24]. For the singlet reaction the C-C attack pathway is favored and it is concerted, while the C-O attack pathway is stepwise due to the S_0/S_1 conical intersection that located before the formation of the biradical intermediate. They also found the triplet biradicals have similar energies and structures to the singlets, and the triplet reaction pathways can be predicted by the most stable biradical rule [24]. The biradical intermediates in the P–B reaction of formaldehyde and ethylene were evaluated in view of the spin-orbital coupling (SOC) between the singlet and triplet states. The computed SOC value in the C-C attack course is two orders of magnitude larger than that in the C–O attack, indicating the C-C attack path is more possible [25]. Meanwhile, exploring the P-B reaction pathways of $H_2CO+C_2H_4$ with artificial force induced reaction (AFIR) method showed that the C–O–C–C biradical formation by C-O attack is more favorable than the O–C–C–C biradical formation by C-C attack [26]. Transient electronic and vibrational absorption spectroscopies on the photo-induced P−B reaction between benzaldehyde and cyclohexene also provided the evidence on the T_1 state of benzaldehyde that decays at a timescale of 80 ps through reaction with cyclohexene and the C−O bond formation to the biradical intermediate [27]. Conformational analysis of singlet-triplet state mixing in P-B radicals with MP2 and MCSCF methods by Kutateladze [28] supported the Griebeck model of ISC-controlled stereochemistry of P-B reactions [29]. In case of P-B reactions with electron-rich alkenes, photo-induced electron transfer (PET) from the alkenes to carbonyl compounds may occur, leading to the formation of radical-ion pair [30,31]. Frequently, P-B reactions involving a PET mechanism are more selective than those only via a biradical intermediate [32]. It is worth mentioning that most P-B reactions take place through the interaction of the excited-state carbonyl compounds with the ground-state alkenes, but the transposed P-B reaction was also obtainable where the excited-state alkene reacts with a ground-state carbonyl compound [33].

Given the significant importance of the P-B reaction and the debates surrounding its mechanism, we employed the MS-CASPT2 method in this study to investigate the mechanism of oxetane formation from the P-B reaction model system acetone and trans-butene under light irradiation (see **Scheme 1**). Both C-O attack and C-C attack pathways in singlet and triplet states were considered.



Scheme 1. Schematic diagram of the photoinduced P-B reaction between acetone and trans-butene.

2. Computational details

All the critical points (minima, transition states (TSs) and conical intersections (CIs)) and reaction pathways in this work were calculated by the MS-CASPT2 [34] method with the ANO-S-VDZP basis set [35]. On top of the optimized geometries vibrational frequencies were computed at the same theoretical level to confirm that the obtained structures were true minima or first-order saddle points. The intrinsic reaction coordinate (IRC) method [36,37] was used to search the two critical points connected by the TS, and the linear interpolation approach or constrained optimization was employed to explore the decay pathways that pass the intersection points. The decay pathways from the Franck-Condon point to the excited-state minima were traced with the minimum energy path (MEP) method. In MS-CASPT2 single-point calculations, five roots were computed with equal weights. An imaginary level shift [38] parameter of 0.2 a. u. and no ionization potential-electron affinity (IPEA) [39] were used. The spin-orbital coupling (SOC) strength between singlet and triplet states was calculated with atomic mean-field integrals by using one-electron operator.

The choice of orbitals in the active space is a key step in MS-CASPT2 calculations [40]. To keep line with previous computational studies [24,26,41] on the mechanism of the Paternò-Büchi reaction in model systems, we chose the (6,5) active space in this work. As shown in **Figure 1**, the (6,5) active space for the Franck-Condon (FC) structure of the reactant (acetone-butene complex) contains two pairs of π/π* orbitals locating on the C=O and C=C bonds and one in-plane non-bonding orbital of the oxygen atom.

To validate the choice of the active space, we performed TD-DFT calculations employing the B3LYP [42] and CAM-B3LYP [43] functionals with the 6-311+g(d,p) basis set [44,45]. The empirical D3 dispersion corrections [46] with the Becke-Johnson damping potential [47] were used to describe the weak interactions. The MS-CASPT2 calculations were performed with the OpenMolcas v25.06 software [48] and the TD-DFT calculations were performed with the Gaussian 16 software [49].