On the photochemical reaction of pyridinium salts with nucleophiles

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Abstract

DFT calculations on the photochemical reaction of 1-*n*–*N*-butylpyridinium salt in water with hydroxide anion is in agreement with a singlet state process where the S_2 state at $\lambda = 253$ nm can be converted into a Dewar isomer (2-butyl-2-azabicyclo[2.2.0]hexa-2,5-dien-2-yl cation). The Dewar isomer can react with hydroxide anion giving the product, 6-*n*-butyl-6-azabicyclo[3.1.0]hex-3-en-2-ol.

Keywords Pyridinium salts · Photochemistry · Reaction with nucleophiles · Dewar isomer · Benzvalene isomer

1 Introduction

The photochemical reaction of methylpyridinium chloride in KOH yielded compound **1** (quantum yield of $\lambda = 0.1$) (Fig. 1) [1]. Recently, a very similar substrate (*N*–*n*-butyl bromide derivative) gave the analogues of **1** in 96% yield in a flow reactor able to give 3.7 g L^{-1} h^{-1} [2].

The reaction of *N*-phenylpyridinium perchlorate in methanol allowed the formation of the tetrahydropyridine derivatives, while the irradiation of *N*-allylpyridinium perchlorate in the same conditions gave a cyclopentene derivative [3]. Figure 1 collects the proposed mechanism for the formation of the observed product [3].

The described reaction can be extended to other substrates. In some cases, the aziridine deriving from the isomerization process can be isolated [4–6]. The reaction showed a good stereoselectivity and an interesting regioselectivity.

Selection of the reaction conditions can allow to separate the formation of the aziridine from its hydrolysis product [7].

The synthesis of aminocyclopentene derivatives through photochemical isomerization of pyridinium salts, coupled with a desymmetrization performed with acetylcholinesterase from *Electrophorus electricus* opened the possibility of

the use of this reaction in organic synthesis [8]. This way, this type of compounds has been used in the synthesis of (+)-mannostatin A [9, 10], (−)-allosamizoline aminocyclopentitol [11], 3-amino-3-deoxyaldopentoses [12], polyhydroxylated indolizidines [13, 14], (+)-castanospermine [14], trehazolin aminocyclitol [15], and (+)-lactacystin [16] (Fig. 1) [17].

The described reaction is probably one of the most interesting photoisomerizations of pyridine ring. However, a theoretical study able to confirm the proposed mechanism does not exist. The possible conversion of methylpyridinium cation to 6-azabicyclo[3.1.0]hex-3-en-2-yl cation has been discussed in a theoretical article [18]. In this paper, we want to report a DFT study on the photoisomerization reaction of *n*-butylpyridinium salt.

2 Results and discussion

In 2018 Siopa reported the conversion of 1-*n*–*N*-butylpyridinium bromide into 6-*n*-butyl-6-azabicyclo[3.1.0]hex-3-en-2-ol through irradiation in water in the presence of potassium carbonate in a flow reactor. The reaction showed a high efficiency. We performed a DFT study on 1-*n*–*N*-butylpyridinium cation to obtain a detailed description of the possible reaction pathways. *N*-methylpyridinium iodide showed an UV–Vis absorption spectrum in acetonitrile where peaks were at $\lambda = 340$ (352 kJ mol^{-1}) and 246 nm (486 kJ mol^{-1}); furthermore, shoulders have been observed at $\lambda = 264$, 259 and 254 nm (453, 462, and 453 kJ mol^{-1}, respectively) [19]. The UV–Vis spectrum of N-butylpyridinium chloride in

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Fig. 1 The photochemical reaction of pyridinium salts in basic conditions. The possible mechanism. Some synthetic applications of the reaction
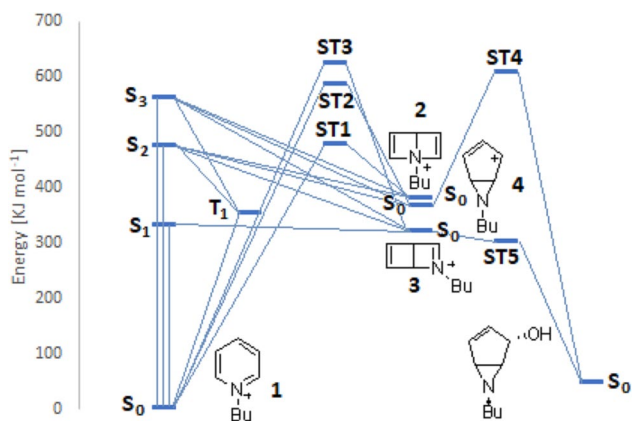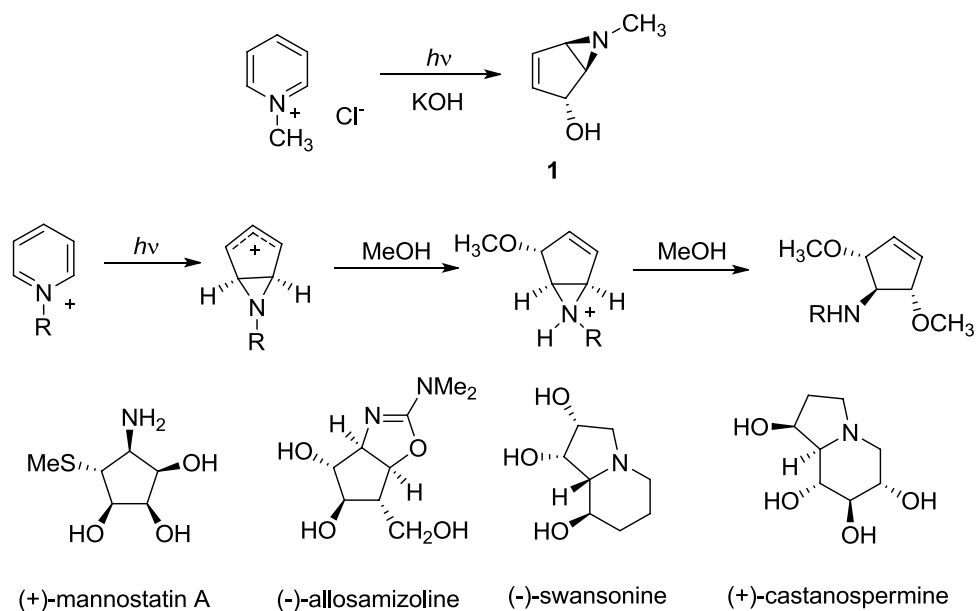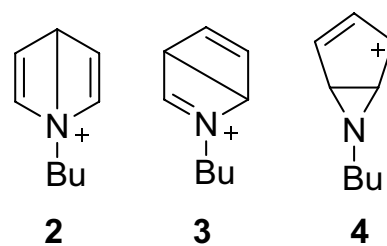

Fig. 2 Photochemical reaction of 1-*n*-butylpyridinium with hydroxide anion. ST: transition state

Fig. 3 Possible intermediate in the photochemical reaction of 1-*n*-butylpyridinium with hydroxide anion

methanol showed absorptions at $\lambda = 258$ and 216 nm (464 and 554 kJ mol^{-1}, respectively). TD-DFT calculations at B3LYP/6-311G + (d,p) level of theory in methanol gave an absorption at $\lambda = 396$ nm (302 kJ mol^{-1}), due to a π, π^* HOMO–LUMO transition but with low oscillator strength (0.0761), an absorption at $\lambda = 253$ nm (473 kJ mol^{-1}), due to a π,π^* NHOMO-LUMO transition, and one at $\lambda = 213$ nm (561 kJ mol^{-1}), due to a π, π^* HOMO-NLUMO transition.

The results of our calculations performed at DFT/B3LYP/6-311G+(*d,p*) level of theory on Gaussian 09 in water are reported in Fig. 2.

The population of S$_2$ and S$_3$ excited singlet states allows the formation of the triplet state. S$_1$ singlet excited state cannot allow the conversion to the corresponding triplet state. This feature allows us to exclude the participation of the triplet state to the reaction (see below).

The S$_2$ and S$_3$ singlet excited states can be converted into the Dewar isomers **2** and **3** (Fig. 3). They show energies of 381 and 319 kJ mol^{-1}, respectively. Furthermore, an electrocyclic ring closure reaction, directly allowing the formation of the carbocation **4** (Fig. 3), can be postulated. The cation **4** showed an energy of 365 kJ mol^{-1} (Fig. 2).

The S$_1$ excited singlet state can be converted only into the Dewar isomer **3**. It is noteworthy that the reverse reaction, the formation of 1-*n*-butylpyridinium salt, is not thermally allowed reaction considering the high transition state energies. Thus, the conversion of **2** into the starting material requires to pass a transition state at 97 kJ mol^{-1}, while the conversion of **3** requires 304 kJ mol^{-1} and the conversion of **4** into the starting material requires 120 kJ mol^{-1} to occur.

The most stable intermediate is the Dewar isomer **3**. The Dewar isomer **2** cannot be converted into the final product **1**. It is noteworthy that the conversion of **4** into **1** through a reaction with hydroxide anion requires a very high transition state energy (341 kJ mol^{-1}). The structure of the transition state is reported in Fig. 4.
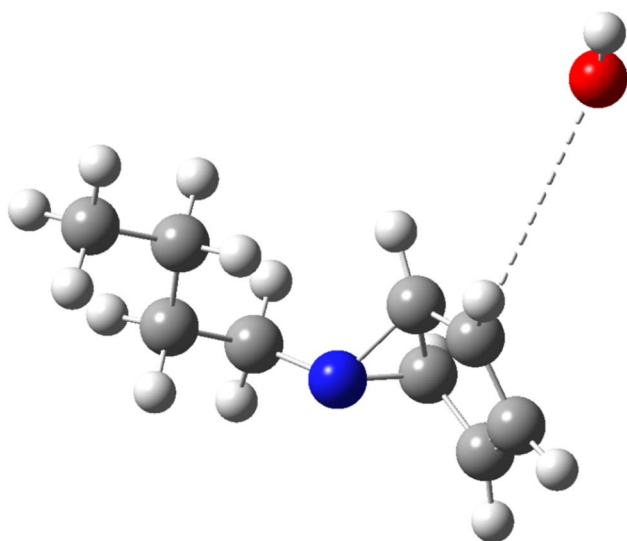
Fig. 4 Transition state in the conversion **4→1**

On the other hand, the direct conversion of the Dewar isomer **3** into **1**, through a nucleophilic attack of hydroxide anion to C-5 of the Dewar isomer **3**, can give the final product without a transition state. Our data seems to be in agreement with a mechanism involving a reaction of the Dewar isomer **3** instead of the benzvalene cation **4** as reported in the previous work in this field.

Furthermore, the when the reaction is performed in a flow reactor, fluorinated ethylene propylene tubing was used in a Rayonet reactor at 254 nm [2]. However, this material is not completely transparent [20]. The material is not transparent for wavelength < 300 nm and shows a transmittance around 4% at 371 nm when a 2 mm thick sample was irradiated. On the basis of these data, also considering that in Siopa's article thinner tubes were used, the flow reaction can occur only from S_1 or S_2 excited singlet state, and these singlet states allow the selective formation of the Dewar isomer **3**. Considering that the Rayonet lamps at 254 nm do not have emission at 396 nm, only the S_2 singlet state can be responsible of the reaction.

In conclusion, we have shown that the photochemical reaction of pyridinium salts in the presence of hydroxy anion can be explained on the basis of the selective formation of the Dewar isomer **3**, while the formation of the benzvalene cation **4** cannot be confirmed by theoretical consideration.

3 Materials and methods

Gaussian09 has been used for the discussions about the computed geometries [21]. All the computations were based on the Density Functional Theory (DFT) [22] and Time-Dependent DFT (TD-DFT) [23, 24] using the B3LYP hybrid xc functional [25]. Geometry optimizations and TD-DFT results from the Gaussian09 program have been obtained at the B3LYP/6-311G + (*d*,*p*) level of approximation. Geometry optimizations were performed with default settings on geometry convergence (gradients and displacements), integration grid and electronic density (SCF) convergence. Redundant coordinates were used for the geometry optimization as produced by the Gaussian09 program. Analytical evaluation of the energy second derivative matrix w.r.t. Cartesian coordinates (Hessian matrix) at the B3LYP/6-311G + (*d*,*p*) level of approximation confirmed the nature of minima on the energy surface points associated to the optimized structures. The transition states were calculated in S_0 state.

Declarations

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