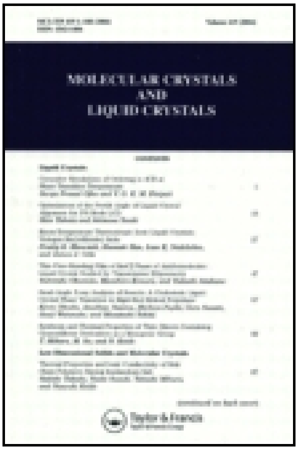

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Norrish Type I vs. Norrish-Yang Type II in the Solid State Photochemistry of CIS-2,6-DI(1-Cyclohexenyl)-Cyclohexanone: A Computational Study

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Norrish Type I vs. Norrish-Yang Type II in the Solid State Photochemistry of *CIS*-2,6-DI(1-Cyclohexenyl)-Cyclohexanone: A Computational Study

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*A computational study of the reaction mechanism for the solid state photolysis of cis-2,6-di(1-cyclohexenyl)cyclohexanone (**1**) was carried out using density functional theory. Compound **1** was designed to explore the competition between several possible pathways, but mainly to discern from α-cleavage/decarbonylation (Norrish type I), and γ-hydrogen abstraction followed by cyclization (Norrish type II- Yang). The triplet state reaction coordinates for the type I and II photochemistry were obtained computationally. While calculations predict that the type I reaction should be predominant in the triplet state due to lower barrier heights for the process, the observed reactivity in the solid state favored the type II process. By correlating the results from calculations and experiments with singlet/triplet sensitizers/quenchers, it was found that the observed reactivity takes place along the singlet manifold.*

Keywords: biradicals; computational studies; Norrish type I; Norrish-Yang type II

INTRODUCTION

Motivated by their potential in synthetic applications [1] and environmentally benign, solvent-free, green chemistry [2], increasing efforts have been aimed to the development of reactions in the solid state. In order for solid state reactivity to be generally useful, the factors

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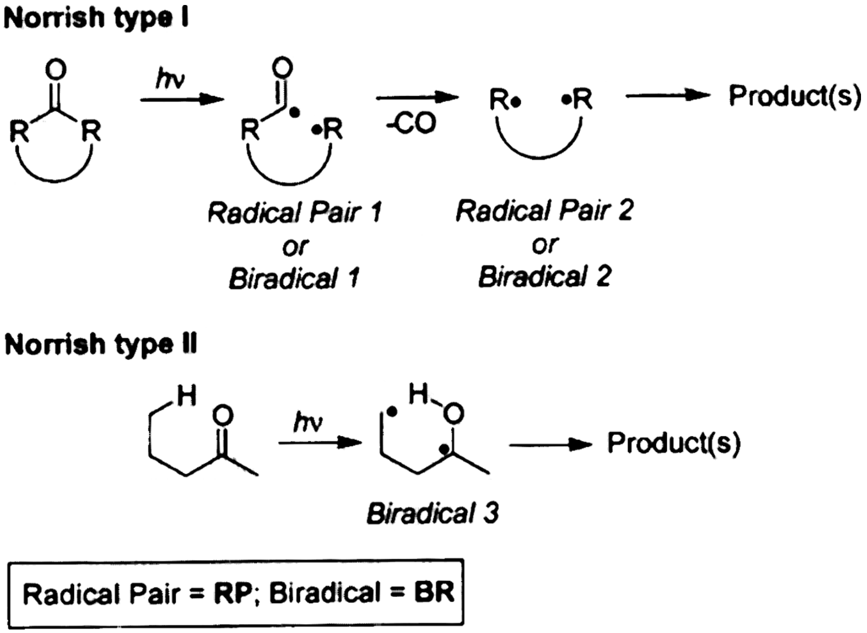
that control solid state reactivity must be well known [3], and the reactions employed must be versatile and efficient. Along these lines, we have devoted our efforts to the solid state photochemistry of ketones, focusing on Norrish type I and Norrish-Yang type II reactions (Scheme 1) [4,5]. The Norrish type I reaction is a photochemical process involving the cleavage of a ketone α-bond and the Norrish type-II reaction involves the transfer of a γ-hydrogen to the carbonyl oxygen to from a 1,4-hydroxy biradical (Biradical 3). The bond formation reaction following the Norrish type-II reaction yields a hydroxy-cyclobutanol in a process known as the Yang reaction.

The design of such photochemical reactions in the solid state must take several factors under consideration. Among these, the topochemical postulate and reaction cavity concept provide general guidelines to address the limited amount of motion in the solid state [6]. The molecularity of the reaction and the predisposition of reagents is also a very important issue. While bimolecular reactions must be "crystal engineered" to bring the two reactants together within bonding distances [7], unimolecular reactions may require specific molecular conformations [8]. The intrinsic photochemical reactivity and the



SCHEME 1

energetics of the reaction are also important as the molecules in crystals have limited forms of kinetic energy which can make it difficult to reach the transition state of many reactions. Theory and computational chemistry may be very helpful in that regard [9].

With particular interest on the energetics that dominate the photochemical decarbonylation of ketones (the Norrish type I reaction), we have found that ketones possessing α-/α′-substituents providing radical stabilizing energies (RSE) of ca. ≥12–15 kcal/mol are likely to undergo decarbonylation in the solid state [10,11]. The generation of biradicals and radical pairs in the solid state can lead to highly selective recombination, with retention of the stereochemistry from the ketone precursor. Thus, the reaction can be exploited as a synthetic tool by simple modification of the α-/α′-substituents, to cleave the carbonyl moiety and generate a new carbon-carbon bond (Fig. 1).

With the goal of understanding the factors that control photochemical reactivity in the solid state, the α,α′-dicyclohexenyl ketone **1** was selected to study the potential competition between the Norrish type I and Norrish type II-Yang (Norrish-Yang) reactions with each other and with other potential reaction pathways characteristic of α,β-unsaturated ketones [12], such as 1,3-acyl shifts and the oxadi-π-methane rearrangement (Scheme 2). In addition, ketone **1** is a crystalline compound [13], which should be suitable for structure-reactivity correlations in the solid state. Ketone **1** has two vinyl groups in the α-/α′-positions that can potentially stabilize by approximately 21 kcal/mol the biradical generated after α-cleavage and decarbonylation [14]. This value is well within the suggested lower limit of 12–15 kcal/mol. Furthermore, the ketone also has allylic hydrogens in the γ-position, which makes it susceptible to Norrish-Yang type II reaction [15]. With several photochemical options available for compound **1**, we focused on a computational investigation of the Norrish

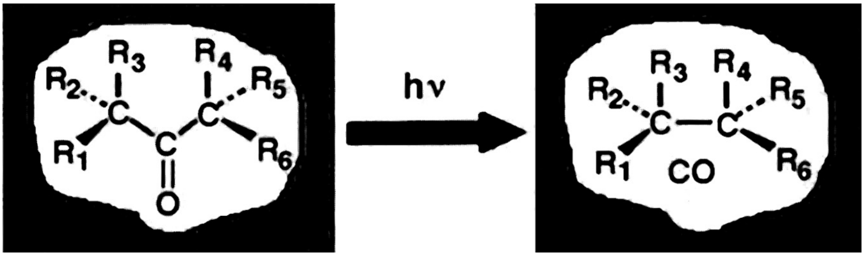
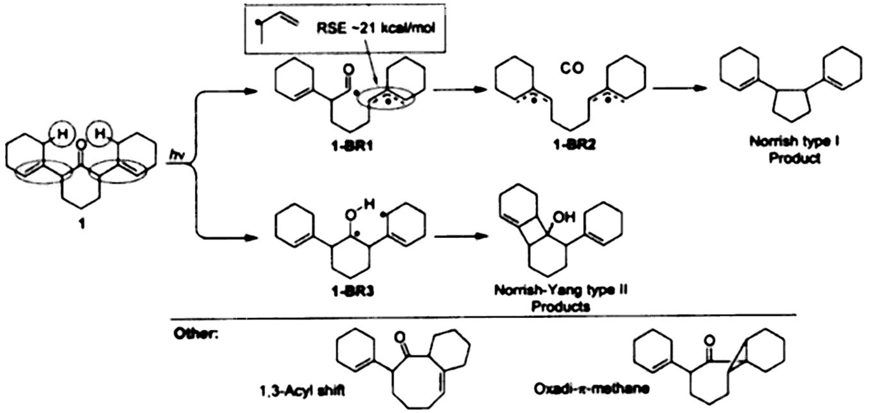


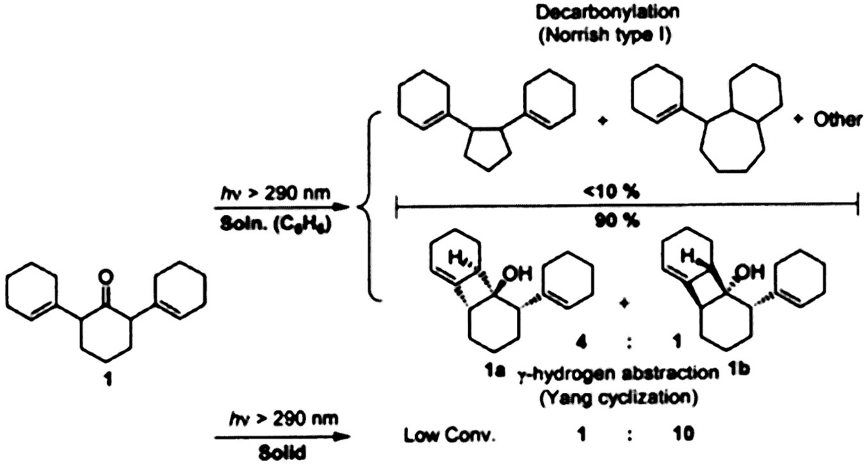
FIGURE 1 Stereospecific decarbonylation of a hexasubstituted ketone in the crystalline solid state.



SCHEME 2

type I and Norrish-Yang reactions in the triplet excited state in order to understand the experimental observations previously reported (vide infra) [16].

In benzene solution, the photolysis of **1** yields a mixture of products, which is dominated by the Norrish-Yang cyclization in ca. 90%. Decarbonylation products are present in smaller amounts of <10%. The Norrish-Yang cyclization products **1a** and **1b**, present in a 4 to 1 ratio, are shown in Scheme 3. Interestingly, low conversion photolysis of **1** in the solid state did not yield any decarbonylation products,



SCHEME 3

and only cyclization products were formed in an opposite ratio than that observed in solution. At high conversions, the ratio converged to 1:1, apparently due to decay of the crystal lattice. The X-ray structure of **1** revealed a conformation that is favorable for Norrish type II reactivity, according to the parameters described by Scheffer [17]. Thus, we investigated computationally the triplet state reaction coordinate to understand the thermochemical factors that determine the type I *vs.* type II chemoselectivity.

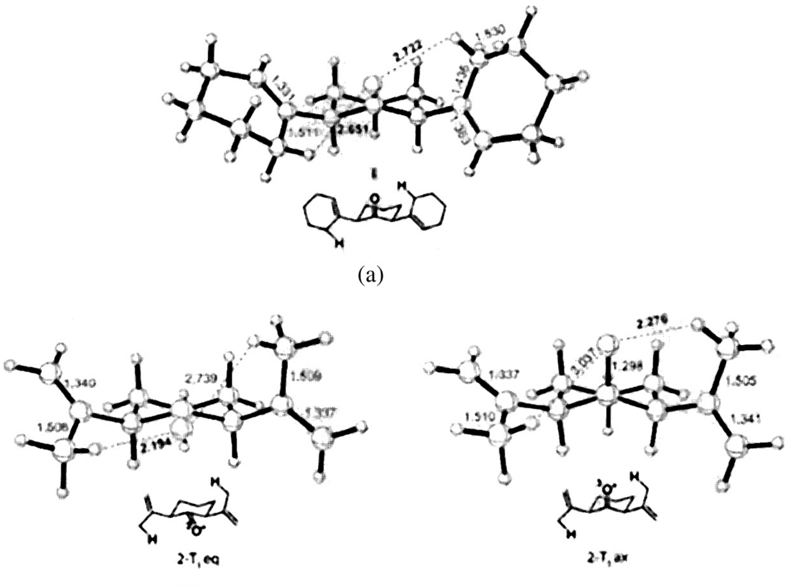
METHODS

Calculations were carried out with the Gaussian 03 suite of programs [18]. The energies and vibrational calculations were performed at the UB3LYP7/6-31G* level of theory [19] along the triplet manifold. The relative energies are inclusive of the scaled zero-point energy (ZPE) [20]. The frequency calculations were analyzed to confirm minimum energy structures and transition structures having the appropriate imaginary frequency for the reaction coordinates being analyzed.

RESULTS AND DISCUSSION

In order to minimize the computational cost, the model ketone **2** was used for the calculations (see Fig. 2). The ground state structure from the X-ray parameters is very similar to that of the computed structures of **2**. In the triplet state, the ketone pyramidalized in two ways where the oxygen can be in an axial, **2-T$_1$ ax**, or equatorial, **2-T$_1$ eq**, position (see Fig. 2B and C). Both structures are nearly isoenergetic (**2-T$_1$ ax** at 0.1 kcal/mol above **2-T$_1$ eq**) and interconvert by a barrier ca. 4.7 kcal/mol. Depending on the orientation of the carbonyl oxygen, different hydrogen atoms get in closer proximity for abstraction. In **2-T$_1$ ax**, the closet O···H distance lies at 2.28 Å whereas in **2-T$_1$ eq**, the closest distance is only 2.19 Å. Thus, we explored both pathways in the triplet state in order to fully understand the reaction and discern from any particular preference for reactivity in the triplet state.

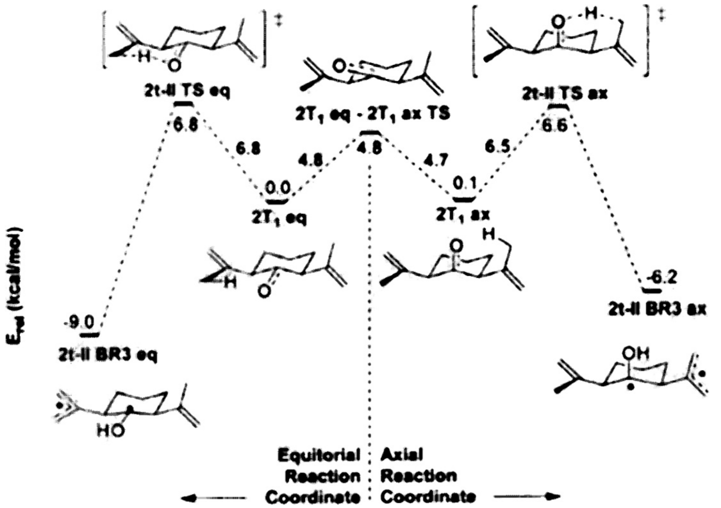
The reaction coordinate for the type II abstraction towards both available γ-hydrogens is shown in Scheme 4, including the interconversion of the two possible triplet minima. Both axial and equatorial reaction coordinates have γ-hydrogen abstraction transition structures that are nearly isoenergetic, with barrier heights of 6.8 kcal/mol in the equatorial conformer and 6.5 kcal/mol in the axial conformation. The resulting biradicals show that the equatorial conformer is more stable than the axial by 2.8 kcal/mol. Such reaction coordinate profile shows that the cyclohexanone does not show any noticeable



(a)

(b) (c)

FIGURE 2 Molecular representations of the X-ray structure of **1** (A), and the two triplet energy minima of **2** (B and C).

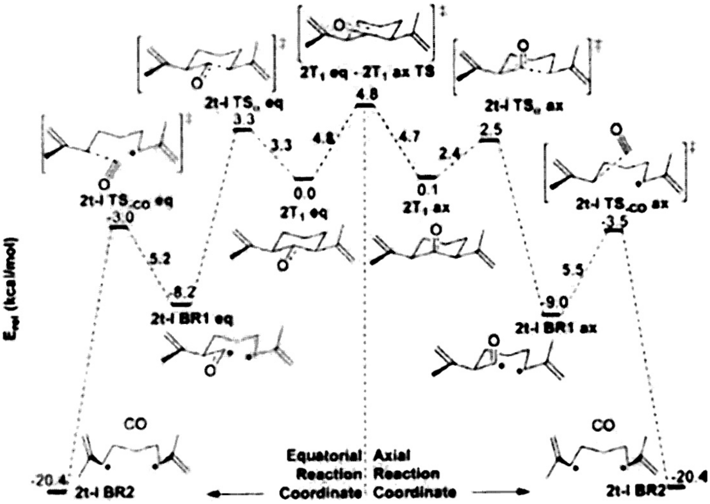


SCHEME 4

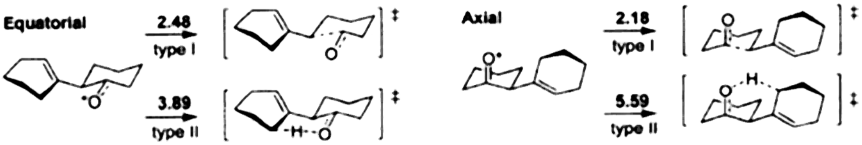
preference for either hydrogen abstraction. In the final outcome, it may be the cyclization path in the singlet biradical that may dictate the selectivity observed in solution.

Given the experimental preference for the Norrish-Yang type II γ-hydrogen abstraction in solution and in the solid state, the results of the triplet state reaction coordinate for Norrish type I reaction shown in Scheme 5 were very surprising. The reaction barriers for triplet state α-cleavage and decarbonylation are significantly lower than those for γ-Hydrogen abstraction, for both axial and equatorial conformers. In the axial reaction coordinate, α-cleavage is rather exothermic (−9.1 kcal/mol) to yield the biradical after overcoming a relatively small 2.4 kcal/mol barrier. The barrier for decarbonylation in the axial coordinate is also rather low at 5.5 kcal/mol, yielding a resonance stabilized biradical at −20.4 kcal/mol. The reaction coordinate along the equatorial conformation is very similar, with only a slightly larger barrier for α-cleavage at 3.3 kcal/mol, followed by decarbonylation after a 5.2 kcal/mol barrier height.

Given the discrepancy between experiment and the calculations for the simplified reaction model, we decided to analyze a model with a full cyclohexenyl group which might help account for the radical stability contributions of additional carbons in BR3 (Scheme 4). However, using the more complete model ketone did not change the outcome of the triplet state predictions summarized in Scheme 5. However, we must



SCHEME 5



SCHEME 6

note that the barrier height for the type II H-abstraction was considerably lower, especially in the case of the equatorial conformer. The relative activation barriers for Type-I and Type-II reactions for each conformer of the triplet cyclohexenyl-cyclohexanone are illustrated in Scheme 6.

The results from calculations depicted in Schemes 5 and 6 predict that Norrish type I photochemistry should prevail over type II reaction in the triplet state. These predictions also suggest that decarbonylation should be feasible in the solid state [4]. However, given that the experiments display a clear preference for the Norrish-Yang type II reaction in both media, it may be possible that the reaction takes place along the singlet excited state.

Evidence suggesting that reaction occurs along the excited singlet manifold was obtained from solution photolyses experiments carried out with quenchers and sensitizers. Reactions carried in isoprene as a solvent and as triplet quencher showed no effect on the reaction outcome. While it could be possible that the reaction could take place from a short-lived triplet state, experiments carried out with acetone as a triplet sensitizer resulted in complex product mixtures that excluded the Yang cyclization, suggesting that the latter reaction does proceeds via the singlet state.

CONCLUSIONS

Ketone **1** was chosen for its simple synthesis and to explore the effect of alkene groups on the solid state decarbonylation of ketones. Our previous work had shown that having such radical stabilizing groups should facilitate decarbonylation of ketones. However, the observed reactivity showed preference for the Norrish-Yang type II reaction. In order to test the validity of our model, we sought an explanation using computational chemistry. The results presented here suggest that the model still holds if the reaction proceeds along the triplet state. Computational and experimental evidence in the case of ketone **1** suggests that the photochemical reaction in solution and in crystals is very likely to proceed along the singlet manifold.

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