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Theory of Substituent Effects on the Regioselectivity of Di-π-methane Rearrangements of Dibenzobarrelenes

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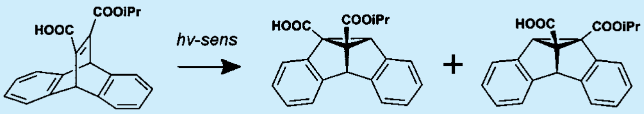
Ⓢ *Supporting Information*

ABSTRACT: The regioselectivities of the di-π-methane rearrangements of unsymmetrically substituted dibenzobarrelenes have been explored with DFT (UM06-2X). Regioselectivity depends on the intramolecular hydrogen bonding and originates from specific stabilization of the triplet biradical intermediates.



In 1966, Zimmerman and Grunewald described the photolysis of barrelene leading to semibullvalene.[1] Zimmerman et al. suggested that the stepwise mechanism involving the triplet state was quite general.[2] The reaction is particularly efficient for cyclic alkenes with a 1,4-diene structure, e.g., barrelene and benzobarrelenes. In these molecules, the di-π-methane (DPM) rearrangement is a triplet state reaction and requires the use of triplet sensitizers. Nonetheless, the DPM rearrangement of dibenzobarrelene diesters occurs without a sensitizer due the fact that they have an efficient intersystem crossing. Zimmerman et al. showed that cyclic 1,4-dienes tend to undergo concerted pericyclic reactions from the singlet excited state (S1), which in the case of barrelenes leads to the formation of cyclooctatetraenes when the samples are irradiated directly.[3,4] We previously described the triplet potential energy surface of the DPM rearrangement of dibenzobarrelene (DBB),[5] and have studied the dynamics on the triplet surface of this reaction.[6]

Garcia-Garibay, Scheffer, and Watson reported the regioselectivity of the disubstituted dibenzobarrelene shown in Figure 1.[7] The regioisomer **2** is the major product, although the regioselectivity is dependent on the concentration of the reactant. According to Garcia-Garibay et al., higher concentrations in benzene decrease regioselectivity, and the reaction in acetonitrile is even less regioselective. IR and UV spectroscopy showed **1** to have an intramolecular H-bond in benzene and to be H-bonded with solvent in the case of acetonitrile. In benzene, the ground state changes from intramolecular to intermolecular H-bonding as a function of increasing concentration.[7]

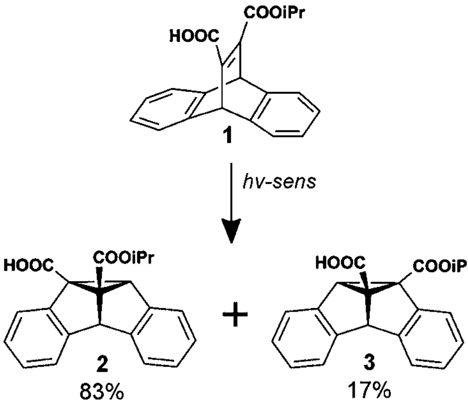


Figure 1. Regioselectiviy of the DPM rearrangement of the disubstituted DBB (0.001 M in benzene).[7]

The triplet (T_1) of the reactant, ^{3}**1***, can form 1,4-biradical **4a** or **4b**, a cyclopropane-containing intermediate that leads to a more stable triplet, **5a** or **5b**, via cleavage of the cyclopropane ring to recover aromaticity (Scheme 1). Both **5a** and **5b** are 1,3-biradicals stabilized by conjugation with one of the fused benzene rings.[1,2] After **5a** or **5b** is formed, the reaction decays to the ground state through an intersystem crossing channel to give the final product, dibenzosemibullvalene, **2** or **3**.[4,5] We suggested that, for the unsubstituted DBB, the biradical intermediate is sometimes skipped altogether, according to molecular dynamics simulations.[6]

We have explored the regioselectivity of the reaction of **1** by quantum chemistry methods. Electronic energies on the triplet state surface were calculated using the unrestricted DFT functional (U)M06-2X and a 6-31G(d) basis set.[8] Ground state energies were obtained at the M06-2X/6-31G(d) level of theory. The substituent effect on stabilization of a radical center is reflected in the value of the corresponding bond dissociation energy (BDE). It was calculated as the enthalpy difference at 298 K for the reaction on optimized geometries using B3LYP/6-31G(d,p).[9] All the calculations were performed with Gaussian09.[10]

The relative enthalpies from DFT (M06-2X) calculations of the conformers of 9,10-substituted dibenzobarrelene are shown in Figure 2, i.e., two conformers with intramolecular hydrogen bonding (Figure 2A and B) and two conformers without hydrogen bonding (Figure 2C and D).

The ground state conformer A, with intramolecular hydrogen bonding between the acid and the carbonyl oxygen of the ester, is the most stable. The conformer B, H-bonded to the ester oxygen

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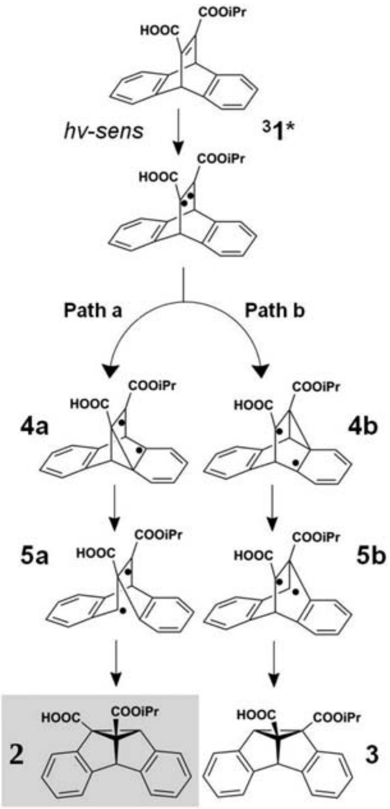
Scheme 1



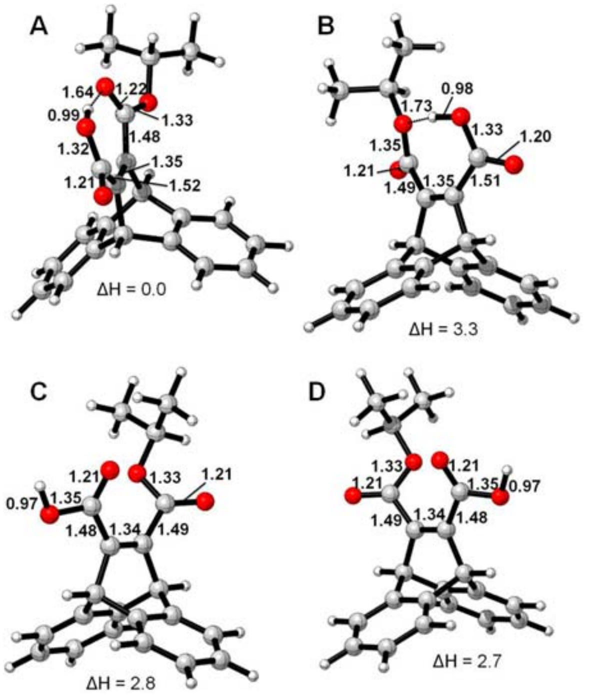


Figure 2. Relative enthalpies of H-bonded (A and B) and non-H-bonded (C and D) conformers of DBB. Energies in kcal/mol.

instead, is 3.3 kcal/mol higher in energy. The two conformers without the intramolecular hydrogen bonding (C and D in Figure 2) have similar energies, 2.7−2.8 kcal/mol higher than conformer A. The di-π-methane reactions of conformer A and the non-H-bonded geometry, D, were evaluated.

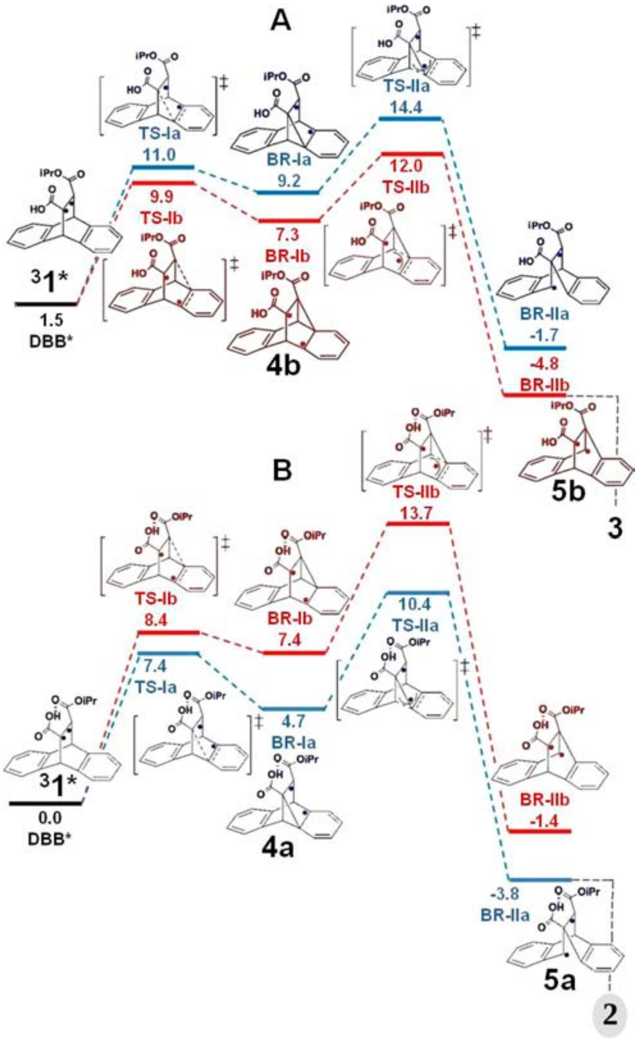


Figure 3. Energy profiles of the DPM rearrangement on the triplet state for the non-H-bonded (A) and H-bonded (B) geometries of DBB. The acid bridging pathway is in blue; the ester bridging pathway is in red. Energies in kcal/mol.

The energy profiles of the triplet states (Figure 3A and 3B) show that the regioselectivity is determined by TS-II. This is different from the parent system, where the first transition state is highest in energy.[5,6] The first step has an energy of activation similar to that of the parent system (Figure S1), but both intermediates and second transition state are significantly higher in energy, presumably due to the fact that one of the substituents can no longer stabilize a radical center in Iab, TS-IIab, or IIab.

The first step leads to the shallow intermediate **4**, which can revert to DBB* (^{3}**1***), or can decay to ground state **1**. Once **4** is passed, the reaction proceeds to the most stable intermediate on the triplet surface, **5**. Reversion will be slow due to the barrier of ~10−14 kcal/mol (TS-IIab). The intersystem crossing channel to the ground state surface is expected to be faster.

The energetically lower pathway (Figure 3B; in blue) proceeds via bridging at the carbon containing the carboxylic acid and gives the racemic pair of **2** as the main product. The other pathway (Figure 3B; in red) proceeds via the bridging at the carbon containing the isopropyl ester, that is 3.3 kcal/mol higher and gives **3** as a minor product.

In contrast to the H-bonded conformer, the non-H-bonded conformer of DBB (Figure 3A) shows the opposite regioselectivity, since the energetically lower pathway on the triplet state (Figure 3A; in red) favors bridging on the carbon containing the ester instead of the acid group. As a consequence, **3** is the main product and **2** is the minor product.

The reaction gives **2** as major product. This pathway involves the acid/ester hydrogen bonding. As mentioned above, in the work by Garcia-Garibay et al.,[7] **2** is the main product with a product ratio of 2:3 in diluted concentrations using benzene as solvent (Figure 1).

A noteworthy aspect of our results is the destabilization of the second barrier (TS-II). This becomes the regioselectivity-determining step, when compared to the parent reaction without substituents (Figure S1), on which the first barrier is the highest.[5] As described earlier, this has to do with the fact that the substituents do not stabilize one of the radical centers in TS-IIab, but stabilize both in the alkene triplet state.

We evaluated whether an ester or an acid is better able to stabilize the substituted radical center in TS-IIab. In the lowest energy TS-II (TS-IIa in Figure 3B), the hydrogen-bonded ester stabilizes the radical center. To determine the intrinsic stabilization of radicals, we computed the bond dissociation energies (BDEs) for small models. The BDEs for the acid and ester models, including the hydrogen-bonding interaction, are 72.2 and 70.5 kcal/mol, respectively (Figure 4). Acid and ester groups have a stabilizing effect on a radical intermediate at an adjacent carbon, as it is expected for electron-attracting groups. The 1.7 kcal/mol difference, where the ester radical is preferred over the acid radical, is in agreement with TS-IIb being higher in energy than TS-IIa in Figure 3B (13.7 kcal/mol compared to 10.4 kcal/mol); i.e., the radical stabilization by the substituent controls the regioselectivity.

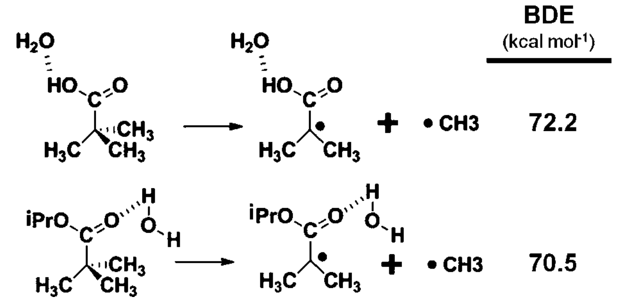


Figure 4. Calculated bond dissociations energies (BDE).

In summary, substituent effects change the rate-determing step from TS-I to TS-II. For the acid−ester substituted DBB, the regioselectivity originates mostly from DBB with an intramolecular H-bonding interaction between the acid and ester substituents, favoring **2** as the major product.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Optimized geometries and energies of all computed species and full authorship of ref 10. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Zimmerman, H. E.; Grunewald, G. L. *J. Am. Chem. Soc.* **1966**, *88*, 183.

(2) Zimmerman, H. E.; Binkley, R. W.; Givens, R. S.; Sherwin, M. A. *J. Am. Chem. Soc.* **1967**, *89*, 3932.

(3) Hixon, S. S.; Mariano, P. S.; Zimmerman, H. E. *Chem. Rev.* **1973**, *73*, 531.

(4) Frutos, L. M.; Sancho, U.; Castaño, O. *Org. Lett.* **2004**, *6*, 1229.

(5) Matute, R. A.; Houk, K. N. *Angew. Chem., Int. Ed.* **2012**, *51*, 13097.

(6) Jimenéz-Osés, G.; Liu, P.; Matute, R. A.; Houk, K. N. *Angew. Chem., Int. Ed.* **2014**, *53*, 8664.

(7) Garcia-Garibay, M. A.; Scheffer, J. R.; Watson, D. G. *J. Org. Chem.* **1992**, *57*, 241.

(8) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215.

(9) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(10) Frisch, M. J. et al. *Gaussian 09*, revision A.1; Gaussian, Inc.: Wallingford, CT, 2009.