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CONTROL OF REGIOSELECTIVITY THROUGH RELIEF OF STERIC CROWDING IN THE DI-π-METHANE PHOTOREARRANGEMENT OF 9,10-ETHENOANTHRACENE DERIVATIVES

Jianxin Chen, Phani Raj Pokkuluri,
John R. Scheffer* and James Trotter*

Department of Chemistry, University of British Columbia
Vancouver, B.C., Canada V6T 1Z1

Abstract Product structures and quantum yields for the solution phase di-π-methane photorearrangement of the 9,10-ethenoanthracene derivatives 1-4 have been determined. The results are consistent with a model in which relief of steric crowding is the factor that governs regioselectivity.

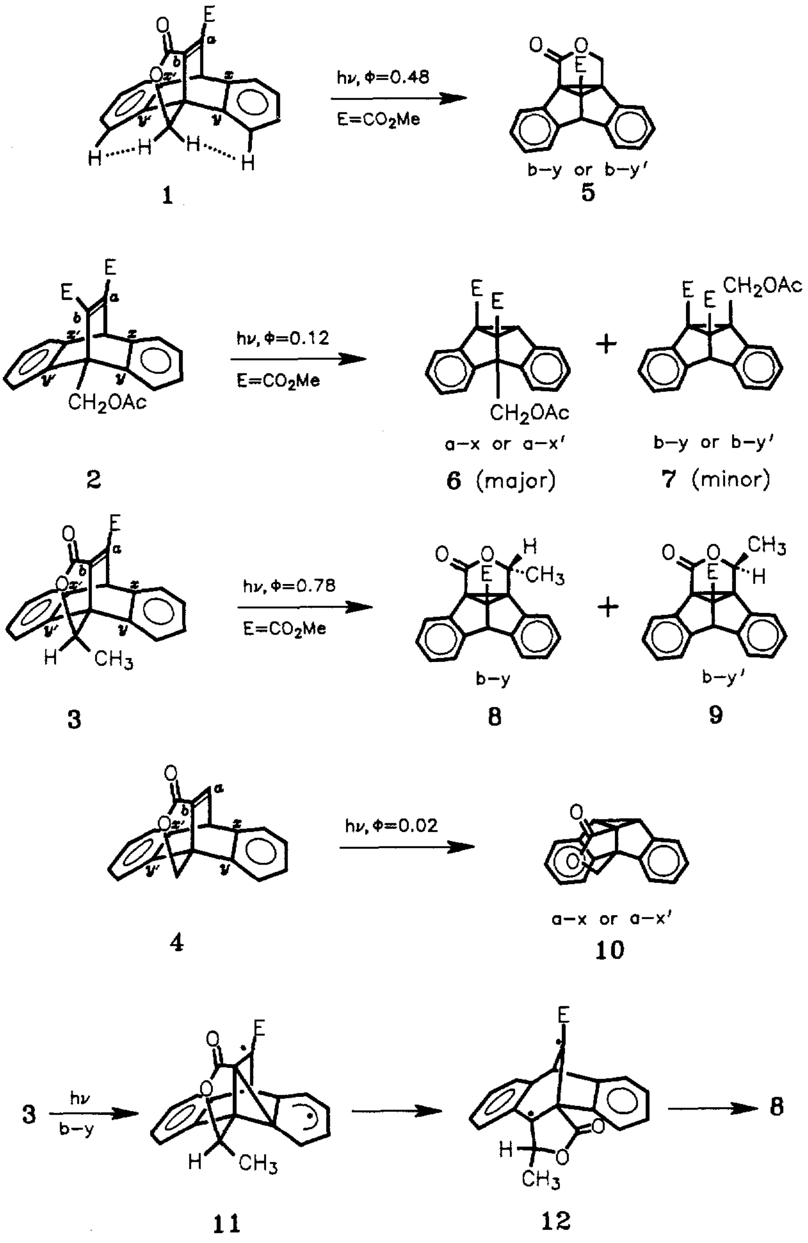
All other factors being equal, chemical reactions that relieve unfavorable non-bonded steric effects in proceeding from the ground state to the transition state are faster than their sterically unbiased counterparts. Thus, for example, sterically crowded tertiary derivatives undergo particularly facile S_N1 solvolysis reactions (B-strain),[1] and axial alcohols are oxidized more rapidly by chromic acid than their equatorial isomers.[2] In a recent publication,[3] we suggested without supporting evidence that the regioselectivity of the di-π-methane photorearrangement[4] of the lactone-ester 1 (Scheme) was governed by relief of the non-bonded repulsive interactions between the methylene hydrogen atoms of the lactone ring and the adjacent aromatic hydrogen atoms (dotted lines). This represents one of the few examples of which we are aware where relief of steric crowding was postulated as the controlling factor in an *excited state* reaction. In the present communication, we report experiments that corroborate this hypothesis. The approach taken was to see what effect both increasing and decreasing the steric crowding in compound 1 has on the photochemistry. To decrease the crowding, compound 2 was synthesized; in this case the unfavorable non-bonded interactions present in compound 1 can be relieved by rotation around the bond between the bridgehead carbon atom and the methylene group. The steric crowding was increased by replacing one of the methylene hydrogen atoms in the lactone ring by a methyl group (compound 3). Finally, in order to assess what role the vinyl ester substituent plays in these systems, lactone 4 (which lacks this group) was prepared and its photochemistry investigated.

Results

Compounds 1 and 3 were prepared by Diels-Alder addition of dimethyl acetylenedicarboxylate to 9-hydroxymethyl- and 9-(1-hydroxyethyl)anthracene respectively. Under the reaction conditions (170°C, neat), lactonization of the initially formed adducts was virtually complete. Use of the acetate of 9-hydroxymethylanthracene as the diene afforded adduct 2, and lactone 4 was prepared by an *intra*molecular Diels-Alder reaction of the propiolate ester of 9-hydroxymethylanthracene. All new compounds were fully characterized by spectroscopic methods and elemental analysis.

As reported earlier[3], lactone 1 reacts photochemically to form di-π-methane regioisomer 5 (Scheme), the result of initial b-y or b-y' vinyl-benzo bridging; none of the alternative regioisomer resulting from a-x or a-x' bridging could be detected in solution, although small amounts of this product *were* formed in the solid state. In the present study, we found that compound **2**, the open chain analogue of **1**, photorearranges with a very different regioselectivity. In this case, compound **6**, the product of a-x or a-x' bridging, is the major regioisomer (90%) in acetone, benzene or acetonitrile. Photoproducts **6** and **7** were isolated and identified by spectroscopic methods. Particularly informative were the ^1H NMR spectra, in which the aliphatic methine hydrogen of **6** appeared as a singlet at δ = 4.39 and that of **7** at δ = 5.11. We and others

Scheme



have shown that such chemical shift differences are general for compounds of this type.[3,5] Lactone **4** exhibited similar (a-x or a-x') di-π-methane regioselectivity. Irradiation of this material in a variety of solvents invariably led to compound **10** (Scheme) as the sole isolable photoproduct. Once again proton NMR, which clearly indicates a plane of symmetry (the photoproduct resulting from b-y or b-y' bridging lacks symmetry), was instrumental in assigning the structure.

In the case of lactone **3** there are four possible di-π-methane photoproducts, but of these only two, compounds **8** (77%) and **9** (23%), were formed in solution. The former is the result of b-y bridging and the latter is formed *via* b-y' bridging. Their structures were assigned on the basis of their spectra, including nOe difference measurements which established the relative configuration of the carbon to which the methyl group is attached in each case. To lend further credence to the structural assignments, the *un*observed (a-x and a-x') regioisomers were synthesized independently and shown to be different from compounds **8** and **9**.[6]

Discussion

There is general agreement that 1,3-diradicals such as **12** (Scheme) are key intermediates in the di-π-methane photorearrangements of 9,10-ethenoanthracene derivatives.[4,7] These may be visualized as being formed either through the intermediacy of cyclopropyldicarbinyl diradicals such as **11**, the result of vinyl-benzo bridging,[4,7a] or by direct 1,2-migration of the aryl group to the vinyl carbon.[7b] In the latter case, species **11** presumably represents a non-minimum point on the 1,2-shift hypersurface.[7a] For symmetrically substituted 9,10-ethenoanthracene derivatives, the four bridging modes are mechanistically degenerate and lead to the same photoproduct. In the case of compound **3**, however, there are four *different* 1,3-biradicals possible, and several factors must be considered in deciding which is likely to be favored. The first of these concerns the question of odd electron stabilization by ester carbonyl *vs* lactone carbonyl. The lactone carbonyl group, while presumably electronically equivalent to its non-cyclic counterpart, is in the present instance fixed in an orientation that is favorable for resonance stabilization of an adjacent radical. This might have been expected to favor a-x or a-x' bridging, but in fact no products corresponding to these pathways were formed in solution in the case of lactone-esters **1** and **3**; such a product *is* favored for compound **4**, however, where radical stabilization effects clearly determine regioselectivity.

A second factor to be considered concerns the electronic nature of the bridgehead substituent. Previous studies of the di-π-methane photorearrangement of a series of 9-substituted 9,10-ethenoanthracene derivatives by Iwamura et al.[5a] and Paddick et al.[5b] have established that there is a rough correlation between regioselectivity and the electronegativity of the bridgehead substituent. Alkyl substituents (methyl, isopropyl, *tert*-butyl) all favor a-x/a-x' bridging, a result that was rationalized as being due to electronic destabilization of the alternative bridging modes.[5] In the present instance, compound **2** is seen to conform to this reactivity profile, a result that is reasonable in view of the essential alkyl group nature of the CH_2OAc substituent. In striking contrast, compounds **1** and **3** react differently; tying back the CH_2OAc group in the form of a lactone ring reverses the reaction regioselectivity.

The most obvious consequence of this structural perturbation is restriction of the rotational freedom of the bridgehead methylene group and the introduction of fixed non-bonded interactions between the methylene hydrogens and the adjacent aromatic hydrogen atoms. As shown by X-ray crystallography, these contacts occur at H···H distances of 2.43 and 2.06 Å in the solid state, values that are at, and well below, the sum of the van der Waals radii (2.40 Å) for two hydrogen atoms. Clearly, the steric crowding in the methylated lactone **3** should be even worse, and will be particularly severe on the side of the methyl group. Thus, if relief of steric crowding is responsible for the reaction regioselectivity, the predominant photoproduct should be the one that most effectively alleviates the unfavorable CH_3···H interaction. Molecular models reveal that this is exactly the case. As depicted in the Scheme, b-y bonding leads to diradical **12** in which the CH_3···H interaction is relieved completely, and this intermediate goes on to form the major product **8**. In contrast, b-y' bonding affords minor photoproduct **9**, and this pathway leaves the CH_3···H interaction partially intact (to visualize this, imagine a CH_3/H interchange in diradicals **11** and **12**). It should be noted that pathways b-y and b-y' are both sterically favored over a-x and a-x', because the latter reaction modes do not relieve the H···H and CH_3···H interactions in **3** to any appreciable extent. As a result, no photoproducts from these paths are formed.

The reaction quantum yields for compounds **1-4** show an interesting variation with structure that supports the interpretation presented above. In the case of compounds **1-3**, the quantum yields are proportional to the steric crowding; the most highly strained compound, **3**, has the highest quantum yield ($\Phi = 0.78$), with lower values of 0.48 and 0.12 for compounds **1** and **2**, respectively. The quantum yield for **4** is lowest of all (0.02), possibly reflecting the fact that the steric crowding and radical stability effects work *against* one another in this molecule.

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