ORGANIC LETTERS

2004
Vol. 6, No. 26
4893−4895

Photoinduced [4 + 4] Cycloadditions of *o*-Quinones with Oxazoles

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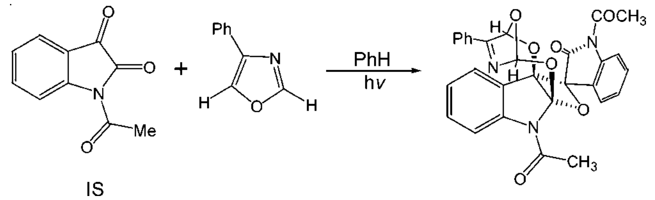
Received September 27, 2004

ABSTRACT



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Photocycloadditions of 9,10-phenanthraquinone (PQ) with oxazoles (1a and 1b) gave [4 + 4] products 2 with the O=C–C=O functionality in PQ and the 2-azadiene moiety in oxazole as 4π addends. Photoreactions of 1-acetylisatin (IS) with 1a, 1c, and 1d gave [4 + 4] product A, which underwent further [2 + 2] reactions with another ^{3}IS* to furnish 5. These regioselective and diastereoselective [4 + 4] photocycloadditions are rationalized by the intervening of the key conformers for ISC and bond formation of the most stable 1,6-diradical intermediates.

Photoinduced cycloadditions[1] and their thermal counterparts[2] provide one of the most efficient and versatile methods for the construction of carbo- and heterocycles of different ring sizes with high atomic economy. Also, study of the origin of the peri-, regio-, and stereoselectivity in these reactions have laid the foundation for our present understanding of the mechanisms of concerted and stepwise (via diradicaloid intermediate) reactions. In photoinduced cycloadditions, the [2 + 2] reactions, both between two C=C bonds leading to cyclobutanes[1b,3] and between C=O and C=C bonds giving oxetanes (the Paterno−Büchi reaction),[4] are the most commonly encountered and widely investigated, while higher order photocycloadditions[5] are less common. Photoinduced [4 + 4] cycloadditions[6] have mainly been found in (1) naphthalene[7] and anthracene[8] photodimerizations and their photocycloadditions with dienes[9,10] and (2) photodimerizations of 2-pyridones,[11] 2-pyrones,[12] and their photocycloadditions with dienes. All these known [4 + 4] photo-

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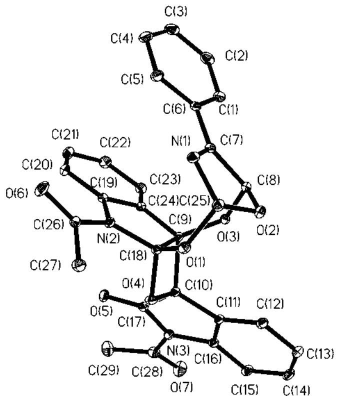
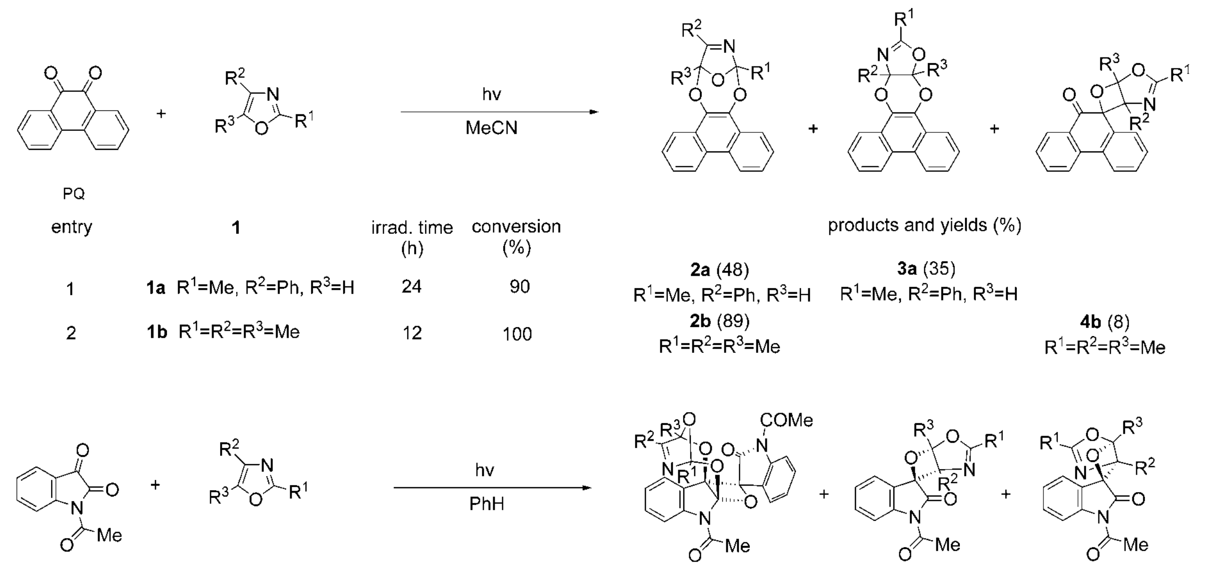


Figure 1. X-ray structure of **5c**.

cycloadditions are between two dienes to give eight-membered carbocycles. Carbonyl compounds constitute another major type of substrates in photocycloadditions. Monoketones and aldehydes with $n\pi^*$ excited state take part in [2 + 2] reactions with alkene to give oxetanes.[4] At the same time, photocycloaddition of cyclic and acyclic α-dicarbonyl compounds with alkenes take place by [2 + 2] and [4 + 2] modes. Therefore, triplet excited benzil[13] and phenylglyoxylate[14] react with alkenes to give α-ketooxetanes and, less frequently, dihydrodioxines. Also, in photoreactions with alkenes, 1-acetylisatin (IS) gives α-ketooxetanes,[15] and phenanthrenequinone (PQ) gives α-ketooxetanes and dihydrodioxines (the Schönberg product).[16,17] To our knowledge, the only known [4 + 4] photocycloaddition involving a heterodiene is that between PQ and 1,3-diphenylisobenzofuran.[18] On the other hand, photo [4 + 4] cycloadditions between two heterodienes have not been reported. Photoinduced [4 + 4] cycloadditions involving any azadiene are also unknown. We report here photoinduced [4 + 4] cycloadditions of two *o*-quinones, PQ and IS, with oxazole, in which the α-dicarbonyl functionality (O=C−C=O) in *o*-quinones and the 2-azadiene moiety (C=N−C=C) in oxazoles serve as 4π addends.

Irradiation of PQ with 2-methyl-4-phenyloxazole (**1a**) in acetonitrile by selective excitation of PQ with light of wavelength longer than 400 nm followed by silica gel flash chromatography of the reaction mixture gave the [4 + 4] cycloadduct **2a** (48%) and the [2 + 4] adduct **3a** (35%). The structures of **2a** and **3a** are based on spectral and analytical data and are unambiguously confirmed by X-ray crystallographic analysis. Control experiments showed that **2a** and **3a** cannot be interconverted either by irradiation under the above photolysis conditions or by refluxing in a benzene solution. It is noted that although oxazoles take part in thermal Diels−Alder reactions as dienes with electron-deficient alkenes,[19] they have only behaved as 2π addends in photoinduced cycloadditions.[20] Similar photolysis of PQ with **1b** furnished the [4 + 4] adduct **2b** (89%) and a [2 + 2] oxetane product **4b** (8%) (Figure 2).



entry	1	irrad. time (h)	conversion (%)	products and yields (%)		
1	**1a** R^1=Me, R^2=Ph, R^3=H	24	90	**2a** (48) R^1=Me, R^2=Ph, R^3=H	**3a** (35) R^1=Me, R^2=Ph, R^3=H	
2	**1b** R^1=R^2=R^3=Me	12	100	**2b** (89) R^1=R^2=R^3=Me		**4b** (8) R^1=R^2=R^3=Me
3	**1a** R^1=Me, R^2=Ph, R^3=H	24	100	**5a** (9) R^1=Me, R^2=Ph, R^3=H	*anti*-**6a** (77) R^1=Me, R^2=Ph, R^3=H	
4	**1b** R^1=R^2=R^3=Me	12	100		*anti*-**6b** (54) R^1=R^2=R^3=Me	*syn*-**6b** (41) R^1=R^2=R^3=Me
5	**1c** R^1=R^3=H, R^2=Ph	12	100	**5c** (97) R^1=R^3=H, R^2=Ph		
6	**1d** R^1=R^3=H, R^2=*p*-ClPh	48	100	**5d** (64) R^1=R^3=H, R^2=*p*-ClPh	*anti*-**6d** (13) R^1=R^3=H, R^2=*p*-ClPh	*syn*-**6d** (8) R^1=R^3=H, R^2=*p*-ClPh

Figure 2.

Photoinduced reactions of IS with **1a** in benzene furnished **5a** (9%) and **6a** (77%). While **6a** is a spirooxetane with *anti* configuration by [2 + 2] cycloaddition, **5a** is obviously formed by secondary photocycloaddition of ^{3}IS* with a primary [4 + 4] product **A** (Figure 3). The structures of **5a** and **6a** are also established by X-ray crystallographic analysis. Photolysis of IS with **1c** gave a 2:1 (isatin/**1c**) cycloadduct **5c** (Figure 1) as the only product in 97% yield. Similar irradiation of IS with **1d** afforded the 2:1 product **5d** (64%) and a pair of diastereomeric oxetane products (*anti*-**6d** and *syn*-**6d**). However, in photoreactions of IS with **1b**, no [4 + 4] product was found and the oxetane diastereomers *anti*-**6b** and *syn*-**6b** are formed in 95% total yield.

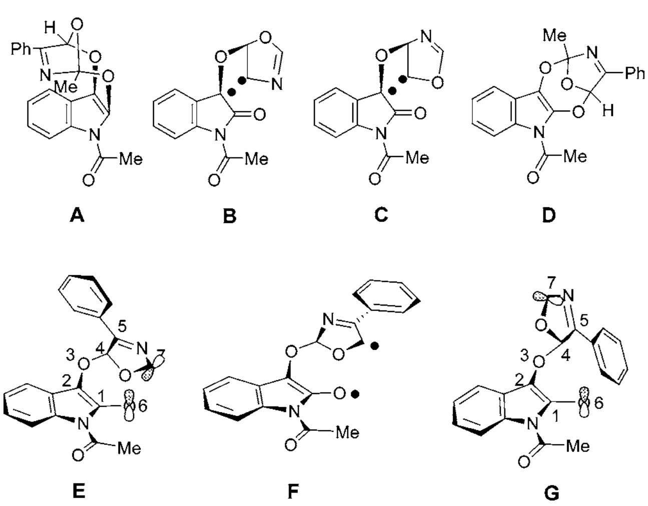


Figure 3.

The [2 + 2] photocycloadditions of PQ and IS with **1** are regiospecific, with all the oxetane products (**4**, **6**) having an acetal structure. This can be rationalized by the intervening of the most stable 1,4-diradical intermediate in the Paterno–Büchi reaction,[4] which in this case is **B** rather than **C**.[15,21] Regioselectivity in the oxetane formation in **5** from ^{3}IS* and **A** is similarly based on the intervening of the more stable 1,4-diradical intermediate.

The [4 + 4] photocycloadditions of IS with the oxazoles **1** are not only highly regioselective to give only one primary product **A** without its regioisomer **D** but also stereoselective. Crystallographic analyses of **5a**, **5c**, and **5d** showed that all these 2:1 products have the same steric configuration as indicated for **5c** in Figure 1, with the oxazole ring being *syn* with the isatin framework. To rationalize the regioselectivity and diastereoselectivity, we calculated the heat of formation of the possible diradical intermediates by DFT method at the UB3LYP-6-31G* level. In possible conformations of the diradical **B**, two gauche conformations are found to be energy minima. Conformation **G**, where the phenyl at C^5 is pointing downward (dihedral angles: C^1–C^2–O^3–C^4 −37°, C^2–O^3–C^4–C^5 154°) represents the global minimum. Conformation **E** in which the phenyl at C^5 points upward (dihedral angles: C^1–C^2–O^3–C^4 −36°, C^2–O^3–C^4–C^5 −41°) is a local minimum, 4.02 kcal/mol higher than **G**. In both **E** and **G**, there is effective overlap between the *n*-orbital at oxygen atom (atom O^3 in formulas **E** and **G**) and the σ^* orbital of the C^4–O bond in oxazole, and this anomeric interaction furnishes an additional stereoelectronic stabilizing effect to these conformers. Also, in **E** and **G**, the isatin framework and the oxazole ring are nearly perpendicular to each other so that the *p*-orbitals at the two radical centers (O^6 and C^7) are nearly orthogonal to each other, which is suitable for rapid intersystem crossing.[22] ISC in **G** would be followed by C–O bond cleavage to reverse the diradical to the starting materials (IS and **1**) because of the large interradical distance (IRD, 5.17 Å). In contrast, ISC from **E** with a small IRD (2.81 Å) by inward rotation of the *p*-orbital at C^7 results in bond formation to give the primary [4 + 4] product **A** with the experimentally found *syn* configuration. This inward rotation of the *p*-orbital at C^7 also benefits from the secondary orbital interaction between the phenyl at C^5 and the isatin π-system. Also, in this conformation, diradical **E** is 4.25 kcal/mol more stable than the regioisomeric 1,6-diradical **F**.

In summary, we have found a new type of [4 + 4] photoadditions between two heterodienes, in which the α-dicarbonyl moiety (O=C–C=O) in the quinones PQ and IS and the 2-azadiene (C=N–C=C) in oxazole serve as 4π addends. These [4 + 4] cycloadditions display high regioselectivity and stereoselectivity, which are rationalized by the intervening of the key ISC conformations of the thermodynamically most stable diradical intermediates.

Acknowledgment. This work was supported by the National Natural Science Foundation of China (NSFC, 20272024) and the SRFDP (20010284033). Partial support by the Modern Analytical Center at Nanjing University is also gratefully acknowledged.

Supporting Information Available: Experimental details, spectroscopic data for all new compounds, and X-ray crystallographic data for **2a** and **5c** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

OL048028T

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