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Synthesis and Photochemistry of Spiro[2.5]octa-1,4-dien-3-ones. Reversible Biradical Formation and Biradical-Olefin Cycloaddition

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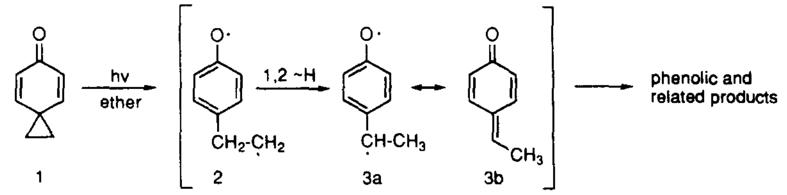
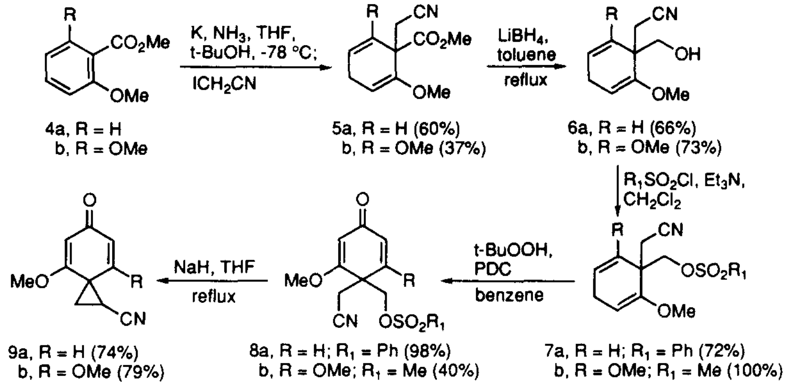
Abstract: Photolysis of the spiro[2.5]octa-1,4-dien-3-one **9a** results in photoisomerization via the nitrile-stabilized biradical **10**. Photolysis of dienone **9b** in the presence of tetramethylethylene gave spiro[4.5]deca-1,4-dien-3-one **12** by cycloaddition of the intermediate biradical **11** to tetramethylethylene. Copyright © 1996 Elsevier Science Ltd

The photolysis of spiro[2.5]octa-1,4-dien-3-one (**1**) in ether solution gives phenolic and related products by a mechanism that involves homolytic cleavage of the cyclopropane ring to give the intermediate biradical **2**.[1a-c] Isotopic labeling studies have revealed that an intramolecular 1,2-hydrogen atom rearrangement in **2** occurs to give **3a**.[1c] It was suggested that an important driving force for the unusual 1,2-hydrogen shift is transition state stabilization by formation of quinone methide **3b** in which all electrons are paired. Stereospecific and wavelength dependent photochemical rearrangements of 2,4-di-*t*-butylspiro-[2.5]octa-1,4-dien-3-ones to isolable quinone methides also have been reported.[1d] In this paper, we report the synthesis and preliminary photochemical study of spiro[2.5]octa-1,4-dien-3-ones **9a** and **9b**. We demonstrate that the formation of biradical **10** from **9a** is reversible and that biradical **11** can be intercepted by cycloaddition to tetramethylethylene.



The synthesis of dienone **9a** is shown in Scheme I.[2] Birch reduction of methyl 2-methoxybenzoate and alkylation of the resulting potassium enolate with iodoacetonitrile afforded the 1,4-cyclohexadiene **5a**. Selective reduction of the ester group in **5a** was accomplished with lithium borohydride in refluxing toluene. Alcohol **6a** was converted to the benzenesulfonate **7a**, from which the 2,5-cyclohexadien-1-one **8a** was obtained by bis allylic oxidation with *t*-butyl hydroperoxide and pyridinium dichromate (PDC) in benzene.[3] Intramolecular alkylation of the nitrile stabilized anion generated from **8a** and NaH in THF provided the spiro[2.5]octa-1,4-dien-3-one **9a** as an 8:1 mixture of two diastereomers **A** and **B**.[4] Analogous chemistry afforded the crystalline dienone **9b**[5] from methyl 2,6-dimethoxybenzoate **4b**.[6]

Scheme I

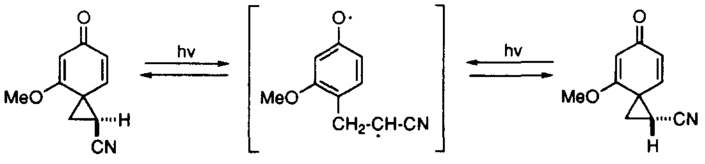


Photolysis of **9a** as an 8:1 mixture of diastereomers **A** and **B** resulted in rapid isomerization to a photostationary state mixture of **A** and **B** of ~1.6:1. Table I describes the progress of isomerization over a period wherein very little decomposition of **A** and **B** occurred. Prolonged irradiation resulted in extensive decomposition to an uncharacterized product mixture. It is assumed that the mechanism of isomerization (and eventual decomposition) involves homolytic cleavage of the cyclopropane ring to give the intermediate nitrile-stabilized biradical **10**.[1d]

Table I. Photolysis of **9a** (Photointerconversion of Diastereomers **A** and **B**)[a]

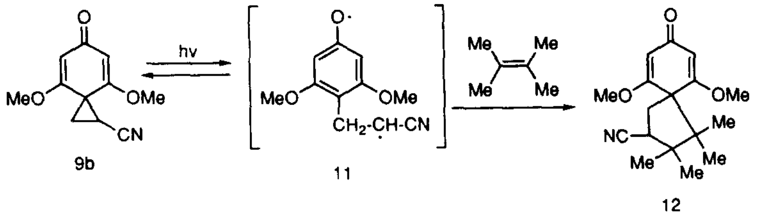
entry	period of photolysis (min)	ratio of diastereomers **A** and **B**[b]
1	0	8.1
2	10	4.5
3	18	2.7
4	35	2.1
5	65	1.8
6	132	1.7
7	164	1.6

[a] Photolysis of a 8.6 x 10^{-3} M solution of **9a** in $CDCl_3$ in a Pyrex NMR tube (5 mm diameter). The light source was a Hanovia 450-W medium pressure mercury arc lamp fitted with a uranyl glass filter. [b] Diastereomer **A** and **B** distribution determined by ^1H NMR analysis.

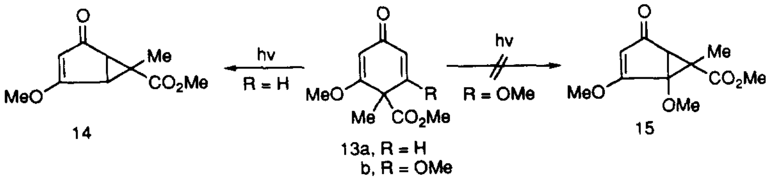


9a(A) 10 9a(B)

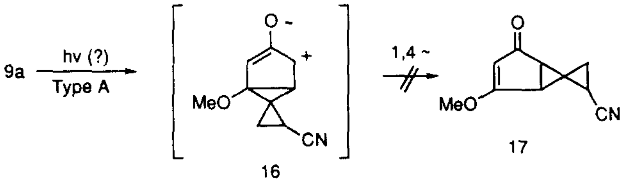
Dienone **9b** appeared to be photostable to irradiation in $CDCl_3$ solution for periods of up to 23 h. However, irradiation of a solution of 31 mg of **9b** in 3 mL of a 2:1 mixture of benzene and tetramethylene (purged with N_2 prior to photolysis) for 46 h and chromatographic separation of the photoreaction mixture on silica gel provided unreacted **9b** (19%) and spiro[4.5]deca-1,4-dien-3-one **12** (10% yield).[7] It is thought that spirocycle **12** is produced by cycloaddition of the transient biradical **11** to tetramethylethylene.[8]



The absence of competing type A photochemistry from **9a** is noteworthy.[9] It has been shown that the closely related 3-methoxy-2,5-cyclohexadien-1-one **13a** undergoes efficient photorearrangement to bicyclohexenone **14**; by contrast, the 3,5-dimethoxy analogue **13b** was found to be photostable (366 nm).[10]



Type A photoreactivity for **9a** may be precluded because of ring strain[1b] associated with the spiropentane unit in the hypothetical intermediate zwitterion **16** and/or bicyclohexenone **17**. On the other hand, the orthogonality[11] of the spirocyclopropane ring to the dienone unit in **9a** and **9b** may result in an overriding efficiency for homolytic cleavage of the three-membered ring.

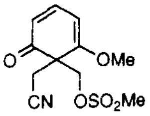


The formation of **12** is particularly remarkable in that three contiguous quaternary centers are generated by way of a bimolecular event involving a transient intermediate. Although the chemical yield for formation of **12** is modest, intermolecular cycloadditions with less sterically demanding diylophiles may prove to be more efficient. As with other tandem processes, the synthetic value of this new method for construction of spiro[4.5]deca-1,4-dien-3-ones may ultimately reside in the intramolecular modification. In anticipation of future synthetic applications of the cycloaddition process, we were pleased to find no evidence for 1,2-hydrogen atom rearrangements in hypothetical biradicals **10** and **11**.

Acknowledgment. This work was supported by the National Institutes of Health (GM 26568).

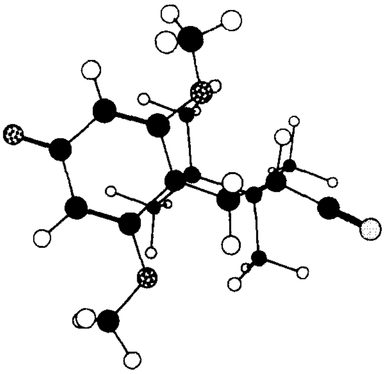
References and Notes

1. (a) Schuster, D. I.; Polowczyk, C. J. *J. Am. Chem. Soc.* **1964**, *86*, 4502. (b) Schuster, D. I.; Polowczyk, C. J. *J. Am. Chem. Soc.* **1966**, *88*, 1722. (c) Schuster, D. I.; Krull, I. S. *J. Am. Chem. Soc.* **1966**, *88*, 3456. (d) Pirkle, W. H.; Smith, S. G.; Koser, G. F. *J. Am. Chem. Soc.* **1969**, *91*, 1580.
2. Satisfactory combustion analyses or high resolution mass spectra were obtained for most of the new compounds reported in this paper; low resolution molecular ions were observed for all new compounds.
3. Schultz, A. G.; Taveras, A. G.; Harrington, R. E. *Tetrahedron Lett.* **1988**, *29*, 3907.
4. **9a** (8:1 mixture of diastereomers **A** and **B**): ^{1}H NMR (200 MHz, CDCl$_3$) δ (major diastereomer) 1.87 (dd, 1 H, J = 7 Hz, J = 5 Hz), 2.20 (dd, 1 H, J = 9 Hz, J = 5 Hz), 2.65 (dd, 1 H, J = 9 Hz, J = 7 Hz), 3.74 (s, 3 H), 5.81 (s, 1 H), 6.51 (s, 2 H); ^{1}H NMR (CDCl$_3$) δ (minor diastereomer) 1.80 (m, 1 H), 2.21 (m, 1 H), 2.41 (dd, 1 H, J = 7 Hz, J = 5 Hz), 3.84 (s, 3 H), 5.90 (d, 1 H, J = 1 Hz), 6.02 (d, 1 H, J = 10 Hz), 6.39 (dd, 1 H, J = 10 Hz, J = 1 Hz).
5. **9b** (mp 140-142 °C from ethyl acetate and hexane): ^{1}H NMR (CDCl$_3$) δ 2.06 (dd, 1 H, J = 9.7 Hz, J = 4.5 Hz), 2.24 (dd, 1 H, J = 7.4 Hz, J = 4.5 Hz), 2.49 (dd, 1 H, J = 9.7 Hz, J = 7.4 Hz), 3.70 (s, 3 H), 3.80 (s, 3 H), 5.68 (br s, 1 H), 5.75 (br s, 1 H).
6. A by-product from the oxidation of **7b** to give **8b** (mp 153-154 °C) was the 2,4-cyclohexadien-1-one **18** (mp 102.5-103.5 °C) obtained by flash chromatography on silica gel and crystallization from ethyl acetate and hexane.



18 (18%)

7. **12** (viscous oil): ^{1}H NMR (CDCl$_3$) δ 0.85 (s, 3 H), 0.98 (s, 3 H), 1.06 (s, 3 H), 1.22 (s, 3 H), 2.29 (dd, 1 H, J = 13 Hz, J = 6 Hz), 2.66 (t, 1 H, J = 13 Hz), 3.11 (dd, 1 H, J = 13 Hz, J = 6 Hz), 3.70 (s, 3 H), 3.73 (s, 3 H), 5.45 (br s, 1 H), 5.48 (br s, 1 H); IR (CHCl$_3$) 2927, 2857, 2243, 1649, 1262, 1372, 1238, 1213 cm^{-1}; chemical ionization mass spectrum, m/z (relative intensity) 290 (M$^+$ + 1, 57), 206 (84), 197 (30), 167 (100), 124 (28). The energy minimized (MacroModel-MM2, version 3.0) structure of **12** shown below is compatible with the experimentally determined ^{1}H NMR data. The sharply defined triplet is assigned to the methylene proton anti to the proton at the carbon atom bearing the cyano group. The calculated coupling constant for this relationship is 12 Hz while that for the second methylene proton/methine proton relationship is 5 Hz (MacroModel). Decoupling studies involving irradiation of the methine proton appearing at δ 3.11 caused a collapse of the upfield multiplets to the AB quartet resulting from geminal coupling in the methylene group.



8. For related examples of cyclopentane construction by cycloaddition of diyls to diylophiles, see: Little, R. D. *Chem. Rev.* **1996**, *96*, 93.
9. Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1962**, *84*, 4527.
10. Schultz, A. G.; Lavieri, F. P.; Macielag, M.; Plummer, M. *J. Am. Chem. Soc.* **1987**, *109*, 3991.
11. For a discussion of UV spectra of spiro[2.5]octa-1,4-dien-3-ones, see: Baird, R.; Winstein, S. *J. Am. Chem. Soc.* **1963**, *85*, 567.

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