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Intramolecular photocycloaddition of olefin-tethered benzo[*a*]spiro[2,5]octa-1,4-dien-3-one derivatives

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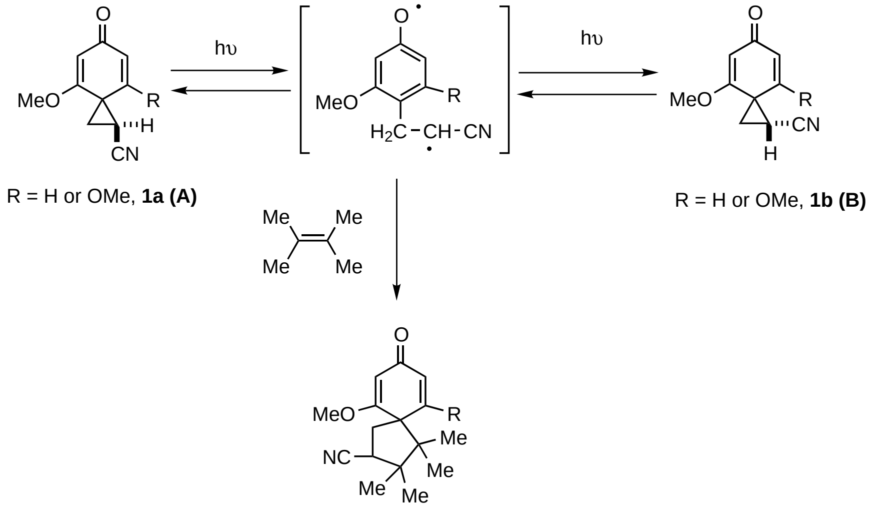
Abstract—Photolysis of benzo[*a*]spiro[2,5]octa-1,4-dien-3-one derivative **8a** afforded spiro-fused tetracycles **10** as a pair of diastereomers in 1.7:1 ratio. The photochemical process occurred by cycloaddition of the intermediate-sulfone stabilized biradical **9** to the tethered olefin. Photolysis of dienone **8b** gave only spiro-fused tetracycle **11** without bridged adduct **12**. © 2002 Elsevier Science Ltd. All rights reserved.

1,3-Biradical chemistry has emerged as one of the most attractive methodologies for creation of polycyclic carbocycles and heterocycles with one- or more five-membered rings.[1] The 1,3-biradical, commonly generated from homolytic cleavage of a cyclopropane ring or extrusion of N_2 on a diazene precursor, can undergo various transformations depending on reaction conditions and also substrates.[2] The Schuster research group has conducted detailed mechanistic studies on the photolysis of benzo[*a*]spiro[2,5]octa-1,4-dien-3-one, a model system for 1,3-diradical chemistry.[3] We are particularly interested in 1,3-biradical chemistry of this unique substrate when it incorporates an electron-withdrawing group on the cyclopropane ring. Recently, our research group demonstrated that the photolysis of spiro[2,5]octa-1,4-diene-3-one **1** as an 8:1 mixture of diastereomers **1a** (**A**) and **1b** (**B**) resulted in photo-isomerization to a photostationary state mixture **A** and **B** in a ratio of ∼1.6:1.[4] It is assumed that the mechanism of isomerization involves homolytic cleavage of the



R = H or OMe, **1a (A)**

R = H or OMe, **1b (B)**

R = OMe, **2**

Keywords: 1,3-biradical; photocycloaddition; isomeric interconversion.

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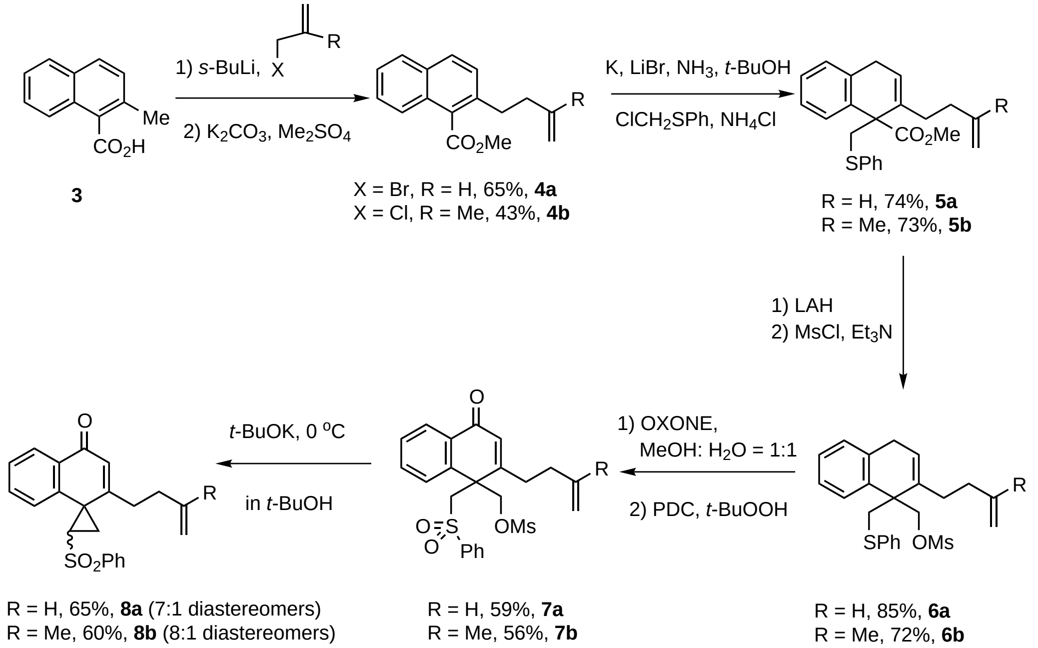
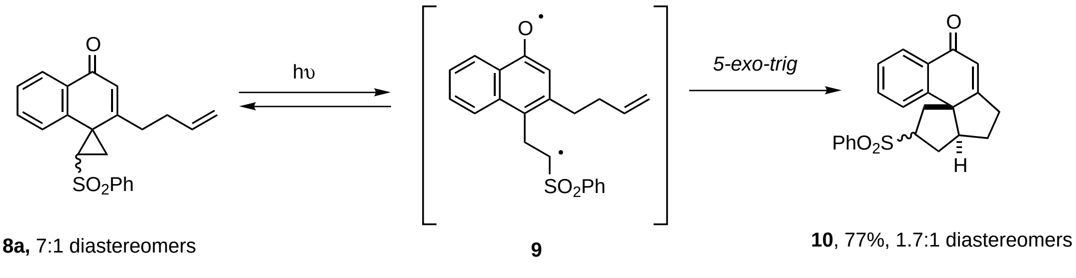


Scheme 1.

cyclopropane ring to give the intermediate nitrile-stabilized biradical. Photolysis of **1** ($R = OMe$) in the presence of tetramethylethylene gave spiro[4,5]deca-1,4-diene-3-one **2** by cycloaddition of the intermediate biradical. In an ongoing effort to develop and establish the synthetic value of this new method for construction of complex carbocyclic and heterocyclic ring systems, we describe here the synthesis and photochemical behavior of benzo[*a*]spiro[2,5]octa-1,4-dien-3-one derivatives **8a** and **8b**.

The synthesis of dienones **8a** and **8b** is shown in Scheme 1.[5] Metalation of 2-methyl-1-naphthoic acid **3** with 2.0 equiv. of *s*-BuLi and quenching the dianion with allylic bromide followed by esterification of the corresponding acid with potassium carbonate and dimethyl sulfate provided the ester **4a**. Birch reduction–alkylation of **4a** with chloro-methylphenylsulfide afforded the diene **5a**.[6] Reduction of **5a** with lithium aluminum hydride followed by mesylation of the corresponding alcohol gave the mesylate **6a**. Selective oxidation of the sulfide to sulfone was then accomplished by reaction of **6a** with OXONE in methanol–water solution (1:1) without over oxidation of the tethered olefin.[7] Treatment of the sulfone with pyridinium dichromate (PDC) and *t*-BuOOH in benzene provided the dienone **7a**.[8] Intramolecular cyclopropanation of the sulfone-stabilized anion generated from **7a** under the treatment with *t*-BuOK in *t*-BuOH at 0°C gave the spiro compound **8a** as a 7:1 mixture of two diastereomers.[9] Analogous synthesis afforded the dienone **8b** from **4b**.

Initially both thermal and photochemical techniques were examined on **8a** to screen for the best reaction conditions. Pyrolysis of **8a** (7:1 diastereomeric mixture) dissolved in xylene in a sealed tube at 200°C afforded very complicated product mixtures. The product analyses revealed that the spiro-fused tetracycles **10** were formed with other cyclopropane ring-opened products. Direct irradiation of **8a** in dry benzene at room temperature at 366 nm for 1 h provided much cleaner product mixtures. Optimum results were obtained by addition of a drop of piperylene as a triplet quencher.[10] Thus, photolysis of **8a** in benzene for 2.0 h generated biradical species **9** which underwent intramolecular 1,3-biradical cycloaddition to the tethered olefin to provide spiro-fused tetracycles **10** (1.7:1 ratio of diastereomers) in 77% yield.[11] The diastereomers could easily be separated by flash column chromatography and were fully characterized. The mechanism of photocycloaddition most likely to involves: (1) homolytic cleavage of the cyclopropane ring to provide the intermediate sulfone-stabilized biradical **9**; (2) intramolecular cyclization of



the phenoxydiradical **9** to the tethered olefin via 5-*exo*-*trig* process to yield a new diradical; (3) subsequent ring closure of the diradical to give spiro-fused tetracycle **10**. The formation of the bicyclo[3.3.0]-product, in keeping with the 'rule of five', was predominant in the photocycloaddition pathway. Isomeric interconversion of spirooctadienone to the photo-stationary state was observed in the photolysis of spiro[2,5]octa-1,4-dien-3-one **1**.[4] We have also monitored the photochemical process of **8a** in *d*-benzene by ^{1}H NMR. Interestingly, isomeric interconversion of **8a** could be clearly seen while photocycloaddition of diasteromeric **8a** to form **10** was taking place. The results of the time-dependent diastereomeric interconversion of **8a** are graphically portrayed in Fig. 1. The ratio of two diastereomers of **8a** could be obtained by integration of the characteristic vinyl proton at δ 6.25 in one diastereomer and δ 6.07 in the other. It is assumed that isomerization of **8a** occurred through a phenolic diradical intermediate **9**. Photolysis of **8a** as a 7:1 mixture of diastereomers at the beginning of the reaction resulted in rapid isomerization until the diastereomeric ratio of **8a** became constant at ~1.6:1 after 1 h irradiation. The diastereomeric interconversion of **8a** was accompanied by the process of photocycloaddition of the diradical **9** to the tethered olefin for the formation of **10** as a pair of diastereomers (ratio: 1.7:1). This result suggests that the rate of addition of the diradical to olefin is not competitive with that of the diastereomeric interconversion of **8a**. The photoreaction was terminated after 2 h because most of the starting material **8a** disappeared and prolonged reaction time resulted in some decomposition.

Photolysis of the analog dienone **8b** (8:1 diastereomers) under the same conditions surprisingly afforded only spiro-fused adduct **11** without any bridged adduct **12**.[12] The structure of **12** was excluded by a decoupling ^{1}H NMR study. Irradiation of the methine proton appearing at δ 3.76 caused collapses of four upfield multiplets to two AB quartets resulting from geminal coupling in the two adjacent methylene groups. This result demonstrated that no 6-*endo*-*trig* cyclization process was involved in the photocycloaddition pathway, which suggested that the cycloaddition might proceed under kinetic control.

In summary, we have demonstrated that complex carbocyclic skeletons can be formed by intramolecular 1,3-biradical cycloaddition of olefin-tethered benzo[*a*]-spiro[2,5]octa-1,4-dien-3-one derivatives **8a** and **8b**. It is expected that remarkable diversity will be achieved

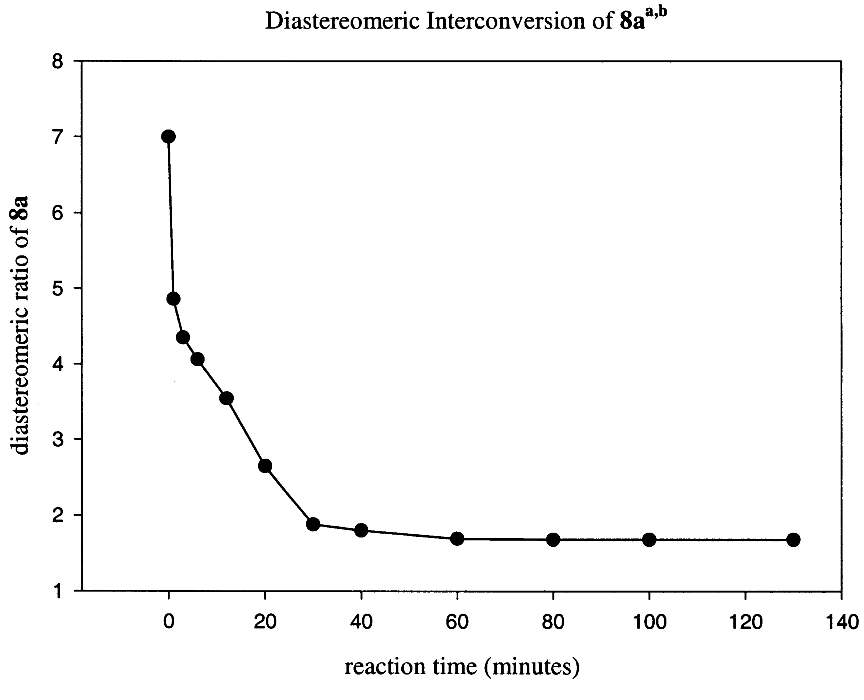
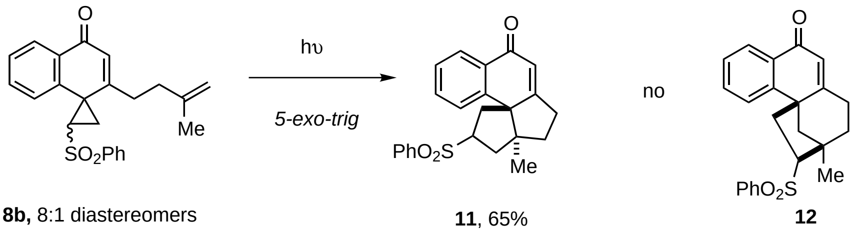


Figure 1. ^{a}Photolysis of 6.0×10^{-3} M solution of **8a** in benzene in a Pyrex NMR tube. The light source was a Hanovia 450-W medium pressure mercury arc lamp fitted with a uranyl glass filter. ^{b}The sample was irradiated for the indicated time. At each time interval, the light was shut down and a ^{1}H NMR of the sample was recorded to determine the diastereomeric ratio of **8a**.



by simple changes in tethered-olefin position and composition.

Acknowledgements

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9. *Selected data for **8a** (7:1 mixture of diastereomers).* ^{1}H NMR (500 MHz, *d*-benzene) major diasteromer: 7.96 (d, J=9.3 Hz, 1H), 7.37 (m, J=8.1 Hz, 1H), 6.96 (t, J=8.6 Hz, 1H), 6.89 (m, J=6.4 Hz, 2H), 6.78 (m, 2H), 6.61 (t, J=8.3 Hz, 2H), 6.07 (s, 1H), 5.35 (m, 1H), 4.83 (d, J=9.8 Hz, 1H), 4.76 (d, J=17.5 Hz, 1H), 2.84 (t, J=6.8 Hz, 1H), 2.62 (t, J=7.6 Hz, 1H), 1.60 (m, 2H), 1.58 (t, J=6.6 Hz, 1H), 1.35 (m, 1H), 1.20 (m, 1H); minor diastereomer: 8.21 (d, J=8.1 Hz, 1H), 7.42 (m, 2H), 7.05 (m, 1H), 6.98 (m, 3H), 6.75 (m, 2H), 6.25 (s, 1H), 5.60 (m, 1H), 4.96 (d, J=9.5 Hz, 1H), 4.92 (d, J=17.5 Hz, 1H), 2.63 (t, J=6.8 Hz, 1H), 2.50 (t, J=7.0 Hz, 1H), 2.42 (t, J=6.9 Hz, 1H), 1.95 (m, 1H), 1.90 (t, J=6.5 Hz, 1H), 1.38 (m, 1H), 1.17 (m, 1H). IR (film, cm^{-1}) 1654, 1312, 1151. MS (CI) 365, (M^{+}+1, 100).
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12. *Selected data for **11***: the stereochemistry at the carbon next to SO_2Ph has not yet been determined. ^{1}H NMR (*d*-benzene) δ 7.82 (d, J=7.5 Hz, 1H), 7.79 (d, J=6.8 Hz, 1H), 7.21 (m, 1H), 7.10 (t, J=7.1 Hz, 2H), 6.98 (m, 2H), 6.90 (m, 2H), 6.60 (s, 1H), 3.76 (m, J=7.6 Hz, 1H), 2.45 (dd, J=16.4, 8.0 Hz, 1H), 2.19 (dd, J=15.6, 7.8 Hz, 1H), 2.05 (dd, J=8.5, 5.1 Hz, 1H), 1.87 (m, J=7.4 Hz, 1H), 1.70 (dd, J=13.7, 3.7 Hz, 1H), 1.56 (dd, J=15.6, 6.8 Hz, 1H), 1.50 (dd, J=13.9, 7.1 Hz, 1H), 1.38 (t, J=5.4 Hz, 1H), 0.45 (s, 3H).