ORGANIC
LETTERS

2012
Vol. 14, No. 22
5704–5707

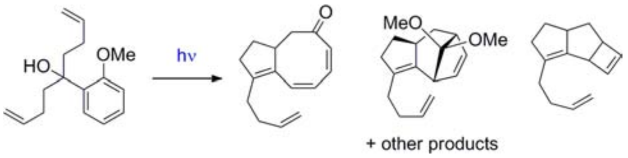
Investigating the Photochemical Properties of an Arenyl Dienol

Clive S. Penkett*,† **and Jason A. Woolford**†,‡,§

clive.penkett@googlemail.com

Received October 2, 2012

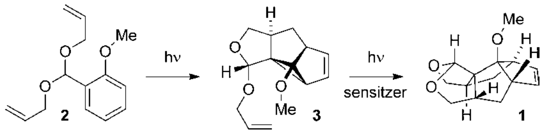
ABSTRACT



Upon irradiation with UV light, an arenyl dienol was transformed into linear and angular *meta* photocycloadducts and *ortho* derived photoadducts. Extended exposure to UV radiation resulted in the formation of other degradation products, which shed light on the chemical processes taking place. One of the linear *meta* photocycloadducts was thermally unstable and underwent further thermal and photochemical transformation, while the *ortho*-derived photocycloadducts ring-opened and eliminated methanol to afford a cyclooctadienone product.

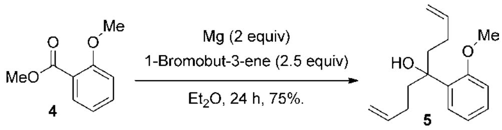
Organic photochemistry has a remarkable propensity for creating dramatic increases in molecular complexity starting from simple compounds.[1,2] A good example of this is the double [3 + 2] photocycloaddition reaction[3] which can assemble the fenestrane **1** in a one-pot procedure simply by irradiating the arenyl diene **2**. Further investigation of this reaction revealed that the efficiency of fenestrane formation could be improved by isolating the initially formed *meta* photocycloadduct[2] **3** and then irradiating **3** in the presence of a triplet sensitizer during a second step (Scheme 1). To our knowledge there has been very limited research into the photochemical properties of arenyl dienes, and hence we report some interesting observations involving the photochemistry of the arenyl dienol substrate **5**.

Scheme 1. Double [3 + 2] Photocycloaddition Reaction Involving Acetal **2**[3]



The photosubstrate **5** was prepared in 75% yield by the addition of 2 equiv of butenylmagnesium bromide to 2-methoxy methylbenzoate **4** (Scheme 2).

Scheme 2. Formation of Photosubstrate **5**



A solution of arenyl dienol **5** in cyclohexane was irradiated with 254 nm UV light using a 16 W low-pressure Hg vapor lamp until all the starting material had been

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† Research undertaken at Department of Chemistry, University of Sussex, Brighton BN1 9QJ, U.K.

‡ The chemistry herein has previously been described in Woolford, J. A. *The Double [3 + 2] Photocycloaddition Reaction*; Springer: 2011. ISBN 978-3-642-22859-9, a part of the Springer Theses Series, recognizing outstanding Ph.D. research and is presented with the kind permission of Springer Science+Business Media.

§ Present address: Department of Chemistry, Imperial College London SW7 2AZ, U.K.

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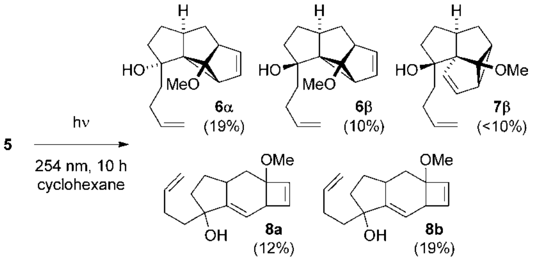
10.1021/ol302718p

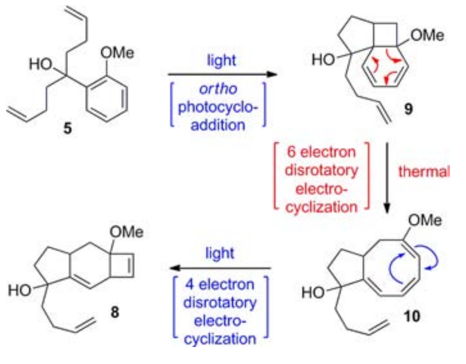
consumed. TLC analysis of the crude photolysis residue identified the formation of five major products, which were separated by flash column chromatography. Initially yields were difficult to establish due to a high number of impurities, some of which arose from the instability of the linear *meta* adducts toward acid induced fragmentation. This complicated flash column chromatography on a larger scale, but the acid induced degradation could be combated by adding 0.1% triethylamine during initial silica slurry formation and yields were eventually determined to be 19%, 10%, < 10%, 12%, and 19% for **6α**, **6*β***, **7*β***, **8a**, and **8b** respectively with an irradiation time of 10 h for 1.84 g of **5** (Scheme 3).

Scheme 3. Principal Photoadducts Generated from **5**



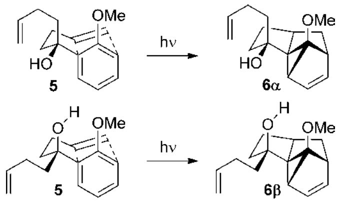
Only three *meta* photocycloadducts were formed upon initial irradiation; two linear forms **6α** and **6*β*** (with α and *β* oriented hydroxyl groups respectively) and one angular form **6*β*** (with a *β* hydroxyl group). Two other tricyclic compounds **8a** and **8b** were isolated, which were formed by intramolecular *ortho* cyclization[4] of one alkene across the arene ring, then a thermally induced six-electron electrocyclic disrotatory ring-opening, and finally a photochemically induced four-electron electrocyclic disrotatory ring-closure (Scheme 4).

Scheme 4. Formation of *Ortho*-Adduct **8** from **5**



The origin of the high diastereoselectivity during intramolecular *meta* photocyclization is a well-established process,[2c] when there is a methyne C–H group on the tether adjacent to the aromatic ring (see **3** being prepared from **2**). However the diastereoselectivity is less clearly defined when there are two groups of similar bulkiness situated on the tethering chain adjacent to the aromatic ring. A hydroxyl group created considerably more steric bulk than a hydrogen atom, which meant that both diastereoisomers of the linear *meta* adduct (**6α** and **6*β***) were formed to a significant degree (Scheme 5). Aside from the steric bulk argument a case could be made that a hydrogen-bonding interaction during the photocycloaddition of alcohol **5** would favor the formation of **6*β***; however Cornelisse[5] has shown this not to be the case with his study on 5-(2′-methoxyphenyl)-pent-1-ene derivatives. It was interesting that only one angular *meta* adduct (**7*β***) was formed during the primary irradiation step and we only managed to isolate it in a pure form by separately irradiating purified **6*β*** to give **7*β*** in 10% yield. This favorable photolytic interchange between **6*β*** and **7*β*** may partly explain the greater prevalence of **6α** over **6*β***, although **6*β*** was also found to be thermally unstable.

Scheme 5. Different Conformations of **5** Leading to **6α** and **6*β***



The diastereomeric assignment of the linear *meta* photocycloadducts **6α** and **6*β*** was highly significant to any subsequent chemical transformations that were to be undertaken. Unfortunately unambiguous confirmation could not be provided using ROESY correlation spectra, and hence the stereochemical assignment was based on a stereoelectronic analysis of the chemical reactivities of the two diastereoisomers (Scheme 6). It was noted that the *β*-hydroxy substituted analogue **6*β*** underwent thermal degradation at an accelerated rate compared to the α-hydroxy variant **6α**. This greater instability was attributed to stereoelectronic factors[6] relating to subtle structural differences between **6α** and **6*β***. Acetal photoadduct **3** and alcohol photoadduct **6α** both showed little sign of decomposition after being dissolved for several days in (mildly acidic) deuterated chloroform that had not been neutralized by passing through neutral alumina; however a

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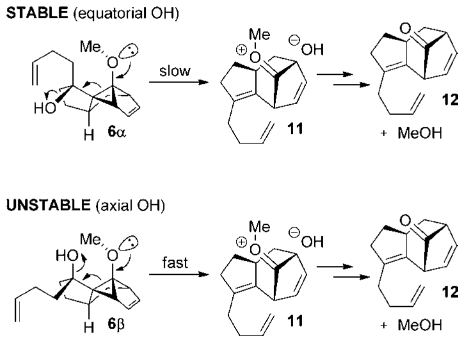
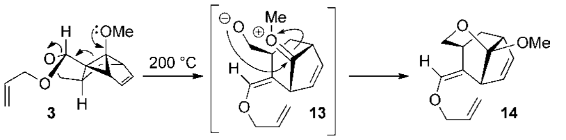
considerable proportion of **6*β*** decomposed after sitting for a few hours in the same solvent. The key difference was related to the orientation of the C–O bond of the hydroxyl moiety with respect to the C–C bond of the cyclopropane ring in the linear *meta* photoadduct framework of **6α** and **6*β***. If the C–O bond of the hydroxyl moiety and the C–C bond of the cyclopropane ring were aligned in a *syn*-periplanar fashion, the methoxy lone pair would assist in the fragmentation of the cyclopropane ring and cause the elimination of hydroxide. The insipient oxonium ion **11** would then be hydrolyzed by the hydroxide ion to give ketone **12** and a molecule of methanol. Compound **6α** was relatively stable due to there being near orthogonal orbital alignment with the pseudoequatorial C–O bond of its hydroxyl group and the adjacent cyclopropane bond, which would hinder any fragmentation/elimination process. By contrast compound **6*β*** was unstable due to there being almost *syn*-periplanar orbital alignment between the pseudoaxial C–O bond of the hydroxyl group and the C–C bond of the cyclopropane. A similar degradation process would not be possible in the angular case for **7*β***.

Scheme 6. Comparison of Thermal Stability of **6α** and **6*β***



Further evidence to substantiate the theory that cleavage of similar pseudoequatorial C–O bonds in related compounds was a disfavored process (see compound **6α**) was provided by the thermolysis reaction of acetal **3**.^{3b} Like compound **6α**, acetal **3** had a pseudoequatorial substituent that was attached *via* a C–O bond. Indeed there were two C–O bonds attached at the cyclopropylcarbinyl position of **3** in the form of an acetal and hence there was a choice of two bonds that in principle could break when acetal **3** was heated to 200 °C. Neither of the acetal C–O bonds of **3** had *syn*-periplanar orbital alignment with the C–C bond of the cyclopropane; hence it was comparatively stable at room temperature. When bond fragmentation did finally occur after heating to 200 °C, it was the C–O bond situated in the ring rather than the C–O bond residing in a pseudoequatorial position that broke preferentially and gave rise to the tricyclic acetal **14** (Scheme 7).

Scheme 7. Thermally Induced Transformation of **3** into **14**^{3b}



One of the key challenges often facing synthetic organic photochemistry is that photochemical processes often lead to multiple products that are themselves photochemically or thermally reactive. Irradiation of **5** beyond its total consumption (up to 36 h) resulted in the creation of additional minor products, although many of these remained uncharacterized due to an inability to separate them from polymeric degradation material. It was however possible to isolate three compounds, **15**, **16**, and **17**, albeit in very low yield, which provided an insight into the chemical processes that were taking place in the reaction vessel (Figure 1).

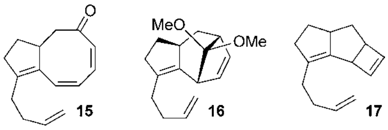
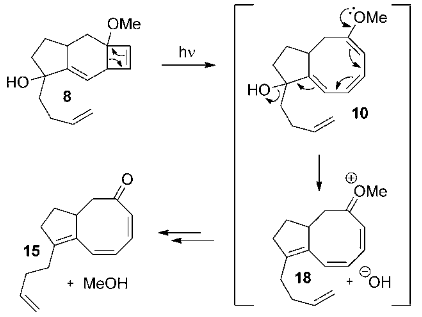


Figure 1. Degradation products **15**, **16**, and **17**.

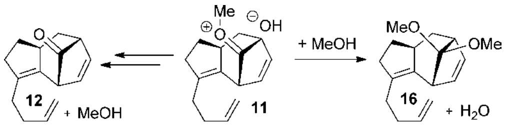
The bicyclic trienone compound **15** was probably the product of a decomposition pathway involving the *ortho* addition compounds **8a** and **8b**. We ascertained that this decomposition pathway was not thermal, because adducts **8a** and **8b** showed limited thermal decomposition even when heated above 200 °C for several hours. This suggested that the process was occurring through a photolytic reopening of the cyclobutene ring to give the methyl trienol ether **10**, which then eliminated the tertiary alcohol moiety and was hydrolyzed to **15** (Scheme 8). The existence of eight-membered ring intermediates has long been postulated to occur during the *ortho* mode of cycloaddition;^{4} however isolation of such structures has proved very difficult. Although not generated directly from the primary photolysis stage, compound **15** revealed that isolating such intermediates may be possible by careful choice of substrate.

Scheme 8. Proposed Mechanism for Formation of **15**

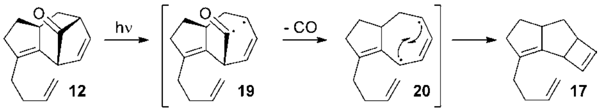


It is likely that compounds **16** and **17** were both obtained from the common intermediate **11**, which could be

Scheme 9. Formation of Ketone **12** and Acetal **16**



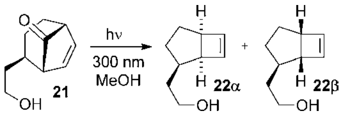
Scheme 10. Norrish Type I Process Involving Ketone **12**



derived from the decomposition of compounds **6α** and **6*β*** (Scheme 6). Oxonium ion **11** would either undergo hydrolysis to give ketone **12** and eliminate a molecule of methanol or combine with a molecule of methanol to give acetal **16** and eliminate a molecule of water (Scheme 9). For the formation of acetal **16** to be a viable process, a source of methanol was required, and this would have been supplied during the generation of trienone **15** and ketone **12**.

Although there was much evidence for the existence of ketone **12** within the reaction mixture, it was not possible to isolate it as a pure sample. This was probably due to it being rapidly converted to other compounds, before a significant concentration had accumulated. The existence of tricyclic [4.5.5] ring system **17** provided a clue to the most likely decomposition pathway for ketone **12**, which involved a Norrish Type I photochemical reaction.[7] Absorption of a photon of UV light would cause the excitation of the carbonyl moiety ($n \rightarrow \pi^*$) of ketone **12**, which would be followed by α-bond cleavage to give diradical **19**, extrusion of carbon monoxide, and finally radical–radical recombination to afford **17** (Scheme 10).

Scheme 11. De Keukeleire's Norrish I Observation[8]



De Keukeleire[8] reported a similar example of this Norrish I chemistry in the case of cyclopentenone derivative **21** (Scheme 11). Interestingly two diastereomers (**22α** and **22*β***) were formed, although we only managed to isolate one (**17**) and its stereochemistry could not be unambiguously defined using ROESY correlation spectra.

In summary, we have shown how the arenyl dienol **5** generated two linear *meta* photoadducts (**6α** and **6*β***), one angular *meta* photoadduct (**7*β***), and two *ortho* derived photoadducts (**8a** and **8b**). The two linear *meta* photoadducts demonstrated markedly different thermal stability, with one (**6*β***) readily undergoing fragmentive elimination of methanol to give ketone **12**. Although it could not be isolated, ketone **12** revealed its existence by the presence of acetal **16** and the Norrish I elimination product **17**. One further cyclooctadienone compound (**15**) was identified from the reaction mixture as being a ring-opened product of the *ortho* derived photoadducts **8** that had eliminated a molecule of methanol.

Acknowledgment. The authors would like to dedicate this paper to Professor Philip Parsons of Imperial College London in celebration of his 60th birthday. This work was supported by the EPSRC, and we thank Dr. Iain Day of Sussex University for NMR support.

Supporting Information Available. Complete experimental procedures, full characterization including ^{1}H, ^{13}C NMR spectra and where relevant COSY or DQF-COSY, multiplicity-edited HSQC, standard HMBC, and ROESY correlation spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.