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Communications to the Editor

New Photorearrangements of 2-Cyclopentenones. The Genesis and Fate of Cyclopropylcarbinyl Biradical Intermediates

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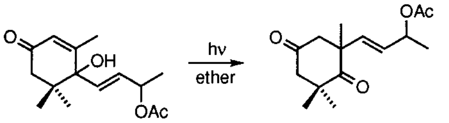
Ultraviolet light has long been known[1] to transform 2-cyclopentenones into their corresponding triplet excited states.[2] The readiness with which these energetic intermediates enter into [2 + 2] cycloaddition with alkenes and alkynes has played a significant role in the development of synthetic and mechanistic organic chemistry.[3] So dominant has been the pursuit of this specific process[4] that other studies of cyclopentenone photochemistry have languished. The sensitized photoaddition of methanol across the double bond,[5] the photorearrangement of select derivatives,[6] and the operation of intramolecular hydrogen abstraction processes[7] have commanded modest attention. These processes are clearly also triggered by activation of the conjugated double bond. Only a select few documented examples of Norrish type 1 cleavage have been reported.[8] In these systems, the high level of α-substitution totally redirects reaction toward generation of the 1,5-biradical.

In connection with the development of a possible photochemical synthetic entry to ingenol,[9] we initiated an investigation into the response of enantiomerically pure tetracyclic systems such as **1** to photoactivation. MM3 calculations had demonstrated that the most stable conformation of **1** has the C10−C11 bond particularly well stereoaligned with the cyclopentenone π-cloud (Figure 1). By analogy to the reasonably efficient photoinduced 1,2-shift reported for vomifoliol acetate and related compounds (eq 1),[10] we expected that **1** would give rise to **2** (Scheme 1). However, none of this enedione was seen.



(1)

Instead, irradiation resulted in the conversion to two products in which the structural features of ring C had been preserved. The fate of ring B was to experience contraction to the cyclohexene level. Most dramatic were the connectivity modifications in ring A. Although both **3** and **4** were observed to be formed in both dioxane and benzene, the more polar solvent was particularly conducive to lactone formation as in **3**, whereas benzene favored conversion to the spiro enone **4**. Photorearrangement proceeded more slowly in the latter medium. The structural assignments to **3** and **4**, which were initially based on detailed ^{1}H, ^{13}C, and 2D NMR studies at 500 MHz, received ultimate corroboration following X-ray crystallographic analysis. In view

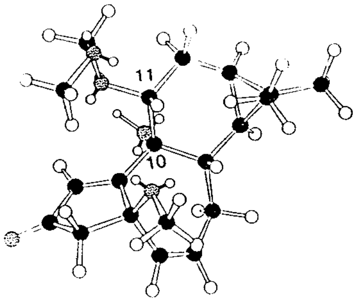
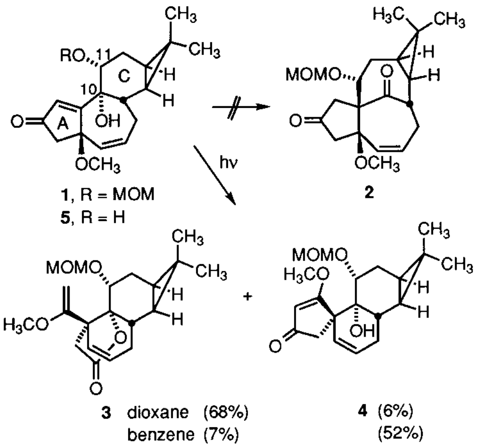


Figure 1. Lowest energy conformation of **1** as computed by MM3. The relative stereoalignment of the C10−C11 bond is of particular interest.

Scheme 1



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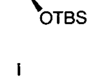
[11] Ketone **1** was prepared by sequential addition of the organocerate derived from (+)-cyclopentenyl bromide **i** to (+)-norcaranone **ii** (Paquette, L. A.; O'Neil, S. V.; Guillo, N.; Zeng, Q.; Young, D. G. *Synlett* **1999**, 1857) desilylation, perruthenate oxidation, and ring-closing metathesis.

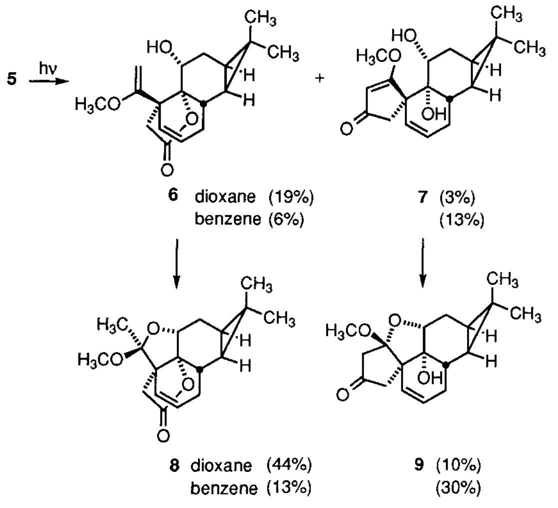


i

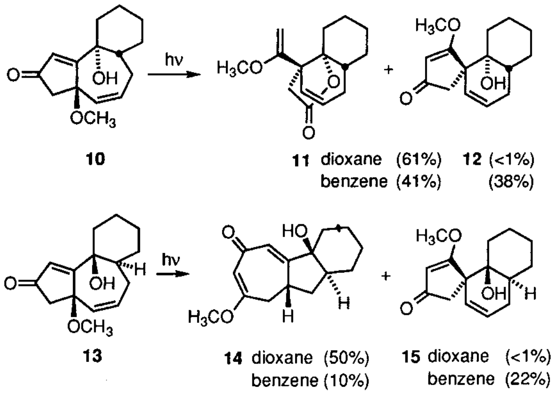
ii

10.1021/ja994081e CCC: $19.00

Scheme 2



Scheme 3

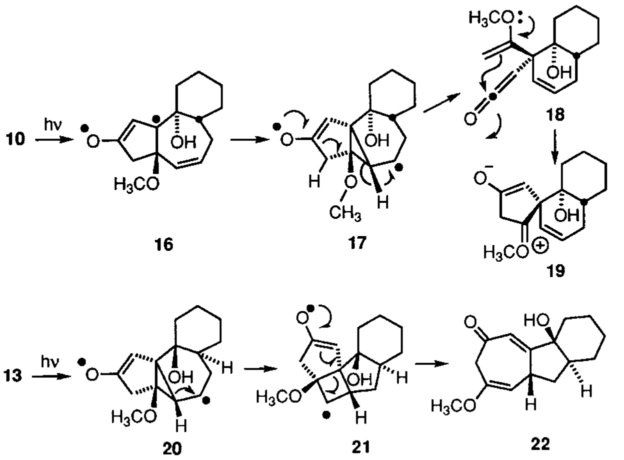


of our detailed knowledge of the structure of **1**,[11] the absolute configurations of **3** and **4** can be specified as shown in Scheme 1.

A comparable pattern of photoisomerization is exhibited by the related diol **5**. However, the availability of a second, strategically positioned hydroxyl group lends itself predominantly to the occurrence of secondary reactions (Scheme 2). Nice illustrations of these phenomena are the cyclizations of **6** and **7** to **8** and **9**, respectively, on standing at room temperature as neat samples or in solution over periods of several hours. Advantage was taken of the crystallinity of **9** to confirm its structure by X-ray diffraction. Monitoring of the progress of this photorearrangement suggests that **6** and **7** are primary photoproducts.[12] The actual yields of isolated products reported are for a representative run. For the reasons cited above, the proportions of **8** and **9** increase with time at the expense of **6** and **7**.

The differing response of diastereomers **10** and **13** provides added mechanistic enlightenment (Scheme 3). The absolute configurations of the three stereogenic centers in **10** are identical to those resident in **1** and **5**. The primary photoproducts in this instance are expectedly analogous to those described earlier. For **13**, however, the trans ring fusion across rings B and C is reversed, lactonization is no longer feasible, and a significant modification of conformational features in **13** relative to **10** is clearly evident. These changes are reflected in the fact that photolysis of **13** in dioxane delivers the cycloheptadienone **14**. The structural assignments to **11** and **14** have been corroborated by X-ray crystallography, thereby also defining those of their precursors.

Scheme 4



Our proposed mechanism for these excited-state events begins with excitation to the triplet state in every instance (see **16**, Scheme 4). This initial event is followed by 3-exo cyclization to generate cyclopropylcarbinyl biradicals, exemplified by **17** and **20**. The formation of these highly reactive species can be anticipated since 3-exo cyclizations have rate constants approximating 1000 s^{-1}.[13,14] The formation of these intermediates enhances ring strain and allows the operation of several processes involving fracture of the three-membered ring. For **17**, this involves fragmentation to ketene **18** and thermal cyclization to spirocycle **19**. In contrast, **20** favors expansion to the cyclobutyl radical **21** en route to **22**. The cyclization/migration **20** → **21** advanced here carries some analogy in the migrations of β-ester radicals that result in lactone ring contractions[15] and related expansions.[16]

In conclusion, we have discovered unprecedented photoisomerization reactions of 2-cyclopentenones suitable in scope and efficiency for preparative purposes.

Acknowledgment. The authors are indebted to the Eli Lilly Co. and Hoechst Marion Roussel for financial support, to Robin Rogers and Judith Gallucci for the X-ray crystallographic analyses, to Marty Newcomb for commentary, and to John Hofferberth for the MM3 calculations.

Supporting Information Available: X-ray crystallographic details for **3**, **4**, **9**, **11**, and **14** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) A third primary photoproduct formed to the extent of 13% in dioxane and 38% in benzene currently remains unidentified.

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