Biradical Rearrangements during Intramolecular Cycloaddition of Double Bonds to Triplet Benzenes

Kung-Lung Cheng and Peter J. Wagner*

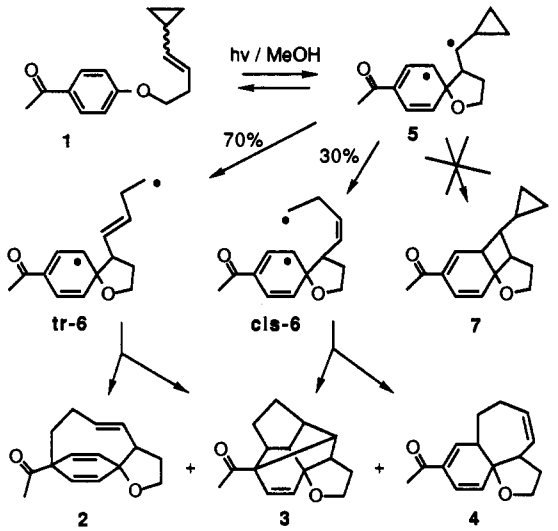
Chemistry Department, Michigan State University
East Lansing, Michigan 48824

Received April 21, 1994

We have reported that remote double bonds undergo photoinduced [2 + 2] ortho cycloaddition to acylbenzenes, which is followed by several thermal and photochemical electrocyclic rearrangements.[1,2] The initial bicyclo[4.2.0]octa-2,4-diene photoproduct thermally opens to a cyclooctatriene, which further photocyclizes to a bicyclo[4.2.0]octa-2,7-diene. The reactions show high regioselectivity for ring substituents[3,4] and high diastereoselectivity for tether substituents.[5] Efficient cis → trans isomerization of the double bond[1] occurs with $\Phi = 0.27$ and is thought to represent the cleavage of 1,4-biradical intermediates that is characteristic of other triplet [2 + 2] photocycloadditions[6,7] and of Norrish type II reactions.[8] The observed diastereoselectivity has also been explained in terms of conformational preferences during biradical formation and closure.[5] By incorporating a cyclopropylcarbinyl radical clock in this reaction, we have now confirmed the intermediacy of a 1,4-biradical, shown that it cyclizes very slowly, and observed what appears to be a rare tandem *biradical* cyclization process.

The rapid opening of cyclopropylcarbinyl radicals to allylcarbinyl radicals is well-known in free radical chemistry and has been widely used as a kinetic clock[9,10] and as a mechanistic probe for radical and biradical[11] intermediates. Such isomerization has been observed in the [2 + 2] photocycloadditions of enones[6,12,13] and of ketones[14] to double bonds, as well as in a host of other photogenerated biradicals.[15] We prepared the cyclopropyl-substituted *p*-(butenyloxy)acetophenone **1** as a 1.5:1 trans/cis mixture.[16] Methanol solutions of **1** were irradiated at wavelengths >290 nm.[17] Reaction progress was monitored by NMR, which showed that the cyclopropyl ring disappeared in parallel with the phenyl ring of **1**. Three primary products were formed, which were assigned the following isomeric structures: the para adduct **2**,[18] the polycyclic ketone **3**,[19] and the ortho adduct **4**.[20] At 100% conversion they were produced in the proportion of 5:3:1, respectively, with twice as much **2** at low conversion. A typical trans vinyl proton coupling constant (16 Hz), a pair of cis vinyl proton coupling constants typical of six-membered rings (11.1 and 10.2 Hz), and a pair of *W*-proton coupling constants (2.4 and 2.1 Hz) identify **2** as having a cyclohexa-1,4-diene skeleton and a ring containing a trans double bond. Unfortunately, **2** is quite unstable. It decomposed slowly just sitting and rapidly during chromatography and could not be isolated; so its structure is based on its nearly symmetric NMR spectrum as the major component in the mixture of products. The second major product was assigned as **3** by its simple AB quartet for vinyl protons, its ^{13}C-NMR DEPT spectrum, and its nonconjugated carbonyl.[21] The minor product was assigned as the tricyclic triene **4** from its five vinyl resonances with *J* values characteristic only of cis double bonds. Three of the vinyl signals are very similar to those in the bicyclo[4.2.0]octa-2,4-diene structures normally obtained in such systems.[5] No product with a cyclopropyl group and none of the characteristic vinyl resonances for **7** or its expected electrocyclic rearrangement products were ever evident during irradiation.

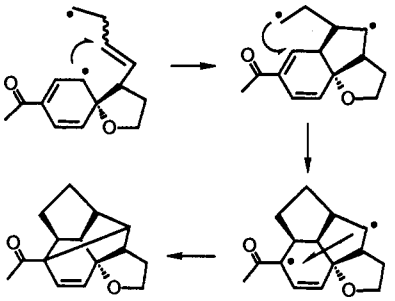
Scheme 1



(1) Wagner, P. J.; Nahm, K. *J. Am. Chem. Soc.* **1987**, *109*, 4404.
(2) Wagner, P. J.; Nahm, K. *J. Am. Chem. Soc.* **1987**, *109*, 6528.
(3) Wagner, P. J.; Sakamoto, M. *J. Am. Chem. Soc.* **1989**, *111*, 8723.
(4) Wagner, P. J.; Sakamoto, M.; Madkour, A. E. *J. Am. Chem. Soc.* **1992**, *114*, 7298.
(5) Wagner, P. J.; Cheng, K.-L. *Tetrahedron Lett.* **1993**, *34*, 907.
(6) Rudolph, A.; Weedon, A. C. *Can. J. Chem.* **1990**, *68*, 1590.
(7) Schuster, D. I.; Lem, G.; Kaprinidis, N. A. *Chem. Rev.* **1993**, *93*, 3.
(8) Wagner, P. J.; Kelso, P. A.; Kemppainen, A. E.; McGrath, J. M.; Schott, H. N.; Zepp, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 7506.
(9) Ingold, K. U.; Griller, D. *Acc. Chem. Res.* **1980**, *13*, 317.
(10) Newcomb, M.; Manek, M. B.; Glenn, A. G. *J. Am. Chem. Soc.* **1991**, *113*, 949.
(11) Wagner, P. J.; Liu, K.-C.; Noguchi, Y. *J. Am. Chem. Soc.* **1981**, *103*, 3837.
(12) Weedon, A. C.; Andrew, D.; Hastings, D.; Oldroyd, D. L.; Rudolph, A.; Wong, D. F.; Zhang, B. *Pure Appl. Chem.* **1992**, *64*, 1327.
(13) Becker, D.; Haddad, N.; Sahali, Y. *Tetrahedron Lett.* **1989**, *30*, 2661.
(14) Shimizu, N.; Ishawa, M.; Ishikura, K.; Nishida, S. *J. Am. Chem. Soc.* **1974**, *96*, 6456.
(15) Wagner, P. J. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 3, p 381.
(16) Reactant **1** was synthesized by the Wittig reaction of cyclopropanecarboxaldehyde with (3-hydroxypropyl)triphenylphosphonium chloride. The resulting alcohol was converted to its tosylate and then coupled with *p*-acetylphenolate anion. NMR analysis indicated a 1.5:1 trans/cis isomer ratio.
(17) Solutions 0.01 M in ketone were irradiated with a medium-pressure mercury arc filtered only by Pyrex. Product ratios were determined by NMR. Only three discrete product structures were apparent from low to high conversion. Their total yields initially were close to 100%, as determined by integration with respect to methyl benzoate internal standard, but decreased to ~70% as **2** slowly decomposed during reaction. Loss of **2** was shown to occur in the dark; but some photodecomposition could not be ruled out. The thermally stable **3** and **4** were stable to sufficient irradiation to completely react **1** and were isolated by chromatography on silica gel.
(18) **2**: ^{1}H NMR (CD_3OD) δ 1.87 (m, 2H), 2.03 (s, 3H), 2.07 (m, 2H), 2.20 (m, 2H), 2.31 (m, 1H), 3.94 (ddd, J = 15.4, 10.8, 9.1 Hz, 1H), 4.03 (ddd, J = 15.4, 8.5, 6.8 Hz, 1H), 5.03 (dd, J = 16.0, 9.3 Hz, 1H), 5.51 (dddd, J = 16.0, 11.5, 9.3, 2.8 Hz, 1H), 5.69 (dd, J = 11.1, 2.1 Hz, 1H), 5.74 (dd, J = 11.1, 2.4 Hz, 1H), 5.85 (dd, J = 10.2, 2.1 Hz, 1H), 5.94 (dd, J = 10.2, 2.4 Hz, 1H).
(19) **3**: ^{1}H NMR ($CDCl_3$) δ 1.49 (dddd, J = 12.6, 9.2, 6.2, 3.0 Hz, 1H), 1.59 (ddd, J = 12.3, 9.1, 3.0 Hz, 1H), 1.71 (ddd, J = 12.6, 9.1, 7.1 Hz, 1H), 2.02 (ddd, J = 9.7, 6.5, 1.9 Hz, 1H), 2.04 (dd, J = 1.6, 0.9 Hz, 1H), 2.07 (ddd, J = 12.3, 9.2, 7.1 Hz, 1H), 2.10 (dd, J = 6.2, 1.0 Hz, 1H), 2.16 (s, COMe), 2.19 (dd, J = 7.1, 6.5 Hz, 1H), 2.44 (ddt, J = 9.7, 9.1, 6.7 Hz, 1H), 2.55 (dd, J = 6.5, 1.0 Hz, 1H), 2.77 (ddd, J = 9.7, 1.9, 1.6 Hz, 1H), 3.95 (ddd, J = 11.7, 6.7, 6.5 Hz, 1H), 3.97 (dd, J = 11.7, 6.7 Hz, 1H), 5.52 (dd, J = 9.9, 1.6 Hz, 1H), 5.86 (dd, J = 9.9, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, DEPT) δ 24.5 (2°), 26.7 (2°), 27.8 (1°), 38.4 (2°), 44.4 (3°), 46.7 (3°), 47.0 (3°), 47.6 (3°), 54.9 (3°), 59.1 (4°), 60.8 (2°), 84.8 (4°), 128.2 (3°), 134.0 (3°), 210.2 (4°); IR 1709 cm^{-1}; MS m/z 230 (M^+).
(20) **4**: ^{1}H NMR ($CDCl_3$) δ 1.59 (m, 2H), 1.72 (dddd, J = 14.8, 7.2, 5.0, 3.6 Hz, 1H), 1.83 (dddd, J = 14.8, 8.6, 6.6, 2.2 Hz, 1H), 2.02 (m, 2H), 2.09 (s, Me), 2.28 (ddd, J = 6.6, 6.4, 3.6 Hz, 1H), 2.87 (qdd, J = 8.0, 2.2, 1.5 Hz, 1H), 3.90 (ddd, J = 13.7, 8.6, 5.0 Hz, 1H), 4.11 (ddd, J = 13.7, 7.2, 2.2 Hz, 1H), 5.16 (dd, J = 10.5, 6.4 Hz, 1H), 5.52 (dd, J = 10.3, 1.5 Hz, 1H), 5.63 (ddd, J = 10.5, 6.1, 2.0 Hz, 1H), 5.70 (d, J = 8.0 Hz, 1H), 6.26 (dd, J = 10.3, 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 25.4, 26.7, 30.9, 34.8, 46.7, 52.7, 68.0, 84.6, 124.7, 127.6, 133.4, 133.7, 133.9, 136.8, 199.0; IR: 1683 cm^{-1}; MS m/z 230 (M^+).
(21) Product **3** is a solid but has not yet provided crystals suitable for X-ray analysis. No other isomer makes sense both mechanistically and thermodynamically.

0002-7863/94/1516-7945$04.50/0

Scheme 2



The mechanism presented in Scheme 1 shows how all three products might arise by ring opening of the suspected initial 1,4-biradical **5** to a cis/trans mixture of the 1,7(9)-biradical **6**. The major product **2** is formed by para closure of **tr-6** as a 1,9-biradical. Such a para addition is similar geometrically to the photoaddition of a diene to benzene.[22] Minor product **4** is formed by ortho coupling of **cis-6** as a 1,7-biradical. It seems reasonable that **tr-6** would cyclize only to a nine-membered ring, given the strain a trans double bond would cause in **4**. It is not so evident why **cis-6** apparently cyclizes only to the seven-membered ring. The instability of **2** suggests that para coupling introduces significant ring strain. As a bicyclo[4.5.0]undecadiene, **4** is less strained than the bicyclo[4.2.0]octadienes normally formed by cyclization of biradicals like **5**; this fact presumably explains why **4** does not undergo significant further electrocyclic rearrangement as observed for the initial [2 + 2] photoadduct of most *o*- and *p*-(alkenyloxy)acetophenones.[1] We consider it highly unlikely that any of the observed products arise by secondary rearrangements of **7**, since none of the "usual" products were seen even at low conversion and since the cyclopropyl group is not on a double bond in the normal rearrangement products.

The formation of **3** can be explained, as shown in Scheme 2, by a tandem *biradical* cyclization process obeying the "rule of five", comparable to reported tandem radical[23,24] and biradical[25,26] cyclizations. The first step is a normally disfavored 5-endo cyclization, here greatly facilitated by the two frozen bonds of the spiro structure. Other modes of radical cyclization do not appear conformationally feasible. If we assume that **5** opens to **6** with the same 2.3:1 trans/cis ratio measured for the opening of 1-cyclopropylethyl radical,[27] we can conclude from the overall product ratio that **3** is formed from both **tr-6** and **cis-6**.

The total quantum yield for formation of compounds **3** and **4** was measured as 0.21.[28] On the basis of product ratios, the quantum yield for formation of **2** drops from 0.50 to 0.26 between 10 and 100% conversion. Assuming 100% efficient formation of 1,4-biradical **5** from the triplet ketone, we conclude that about 70% of the 1,4-biradicals **5** undergo rearrangement and only 30% revert to the starting ketone. Since the rate constant for opening of the model 1-cyclopropylethyl radical to the allylcarbinyl radical is known to be 7×10^7 s^{-1},[30] we can estimate that reversion of biradical **5** to **1** has a rate constant of $\sim 3 \times 10^7$ s^{-1} and coupling to **7** has a value of $\leq 3 \times 10^6$ s^{-1}. The low cyclization:reversion ratio for **5** is similar to that found for many 1,4-biradicals, including several that intervene in enone cycloadditions;[31] the reasons are unclear, given that both processes require similar biradical conformations. Our earlier measurements indicated a roughly 50:50 cyclization/reversion ratio;[1] the cyclopropyl group may disfavor cyclization sterically. If **5** did not rearrange, it would have a lifetime in the 35-ns range measured for many other 1,4-biradicals.[32-34] In contrast, the 1,7(9)-biradical **6** could be much longer lived, since it apparently undergoes what may be a relatively slow endo 4-pentenyl radical cyclization.[35]

The 1,4-biradical **5** behaves like a monoradical in undergoing rearrangement and tandem cyclization.[36] In terms of possible synthetic potential, the tandem cyclization illustrates both the main advantage and drawback of biradical *vs* radical rearrangements: final trapping occurs exclusively by intramolecular coupling and thus is very clean; however, such coupling may interfere with internal monoradical cyclizations more than does traditional bimolecular trapping.[23,37]

Acknowledgment. This work was supported by NIH Grant No. GM39821. The NMR spectrometers used were partially funded by NSF Grant CHE88-00770 and NIH Grant RR047550.

(22) Yang, N. C.; Chen, M. J.; Chen, P.; Mak, K. T. *J. Am. Chem. Soc.* **1982**, *104*, 853.
(23) Curren, D. P.; Rakiewicz, D. M. *Tetrahedron* **1985**, *41*, 3943. Curran, D. P.; Kuo, S. C. *J. Am. Chem Soc.* **1986**, *108*, 1106.
(24) Beckwith, A. L. J.; Roberts, D. H.; Schiesser, C. H.; Alex, W. *Tetrahedron Lett.* **1985**, *26*, 3349.
(25) Liu, R. S. H.; Hammond, G. S. *J. Am. Chem. Soc.* **1964**, *86*, 1892.
(26) Andemichael, Y. W.; Huang, Y.; Wang, K. W. *J. Org. Chem.* **1993**, *58*, 1651.
(27) Beckwith, A. L.; Moad, G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1473.
(28) Degassed methanol solutions 0.01 M in **1** were irradiated at 313 nm in parallel with valerophenone actinometers.[29] Yields of **3** and **4** at ≤10% conversion were determined by GC analysis relative to known concentrations of dialkyl phthalate internal standards. Yields of **2** were deduced by NMR integration.
(29) Wagner, P. J.; Kochevar, I. E.; Kemppainen, A. E. *J. Am. Chem. Soc.* **1972**, *94*, 7489.
(30) Ingold, K. U.; Browry, V. W.; Lusztyk, J. *J. Am. Chem. Soc.* **1991**, *113*, 5687.
(31) Hastings, D. J.; Weedon, A. C. *J. Am. Chem. Soc.* **1991**, *113*, 8525.
(32) Caldwell, R. A.; Majima, T.; Pac, C. *J. Am. Chem. Soc.* **1982**, *104*, 629.
(33) Scaiano, J. C. *Acc. Chem. Res.* **1982**, *15*, 252.
(34) Kaprinidis, N. A.; Lem, G.; Courtney, S. H.; Schuster, D. I. *J. Am. Chem. Soc.* **1993**, *115*, 3324.
(35) Lusztyk, J.; Maillard, B.; Deycard, S.; Lindsay, D. A.; Ingold, K. U. *J. Org. Chem.* **1987**, *52*, 3509.
(36) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, p 779.
(37) Boger, D. L.; Mathvink, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4003.