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Lifetime of the 1,4-Biradical Derived from Alkyl Phenylglyoxylate Triplets: An Estimation Using the Cyclopropylmethyl Radical Clock

Shengkui Hu and D. C. Neckers*

Center for Photochemical Sciences,[1] Bowling Green State University, Bowling Green, Ohio 43403

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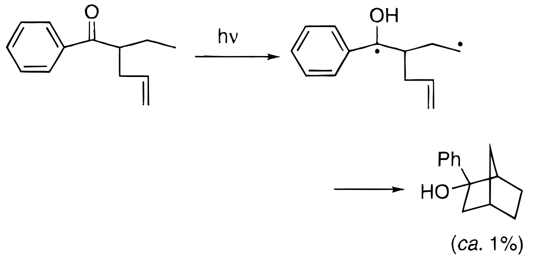
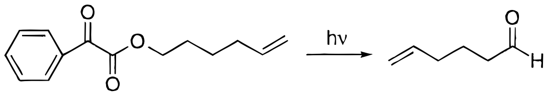
There have been several studies on the mechanism and synthetic utility of the photoreactions of alkyl phenylglyoxylates since they were originally proposed to undergo Norrish Type II photoreactions by one of us (Scheme 1).[2,3] No products resulting from cyclization of the intermediate 1,4-biradical have been observed, however. We reasoned[3] it to be because of the short lifetime of this biradical. It is known that an oxygen atom between the two radical sites accelerates the decay of 1,4-biradicals.[4] Nanosecond laser flash photolysis of alkyl phenylglyoxylates[3] reveals two transient decays with relatively long lifetimes and are attributed to the triplet excited state and mandelate radical. No transient absorption of the 1,4-biradical is detected because it may be too short-lived and escape detection, or its signal is blurred by that of two other transients. This study which follows was undertaken to assess the lifetime of the 1,4-biradical formed in phenylglyoxylate photoprocesses.

Free radical clocks capable of timing reaction intermediates within a very broad lifetime range are now available.[5] If one or both of the radical centers is attached to a group that can undergo rapid rearrangement, the lifetime of the biradical can be deduced from the product distribution and the radical rearrangement rate if the latter is assumed to be equal to that of an analogous monoradical. In a pioneering experiment, Wagner et al. measured the lifetime of the 1,4-biradical derived from a phenyl ketone triplet using the 5-hexenyl clock.[6] The trapping product, 2-phenyl-2-norbornanol was obtained, though in low yield, see eq 1.



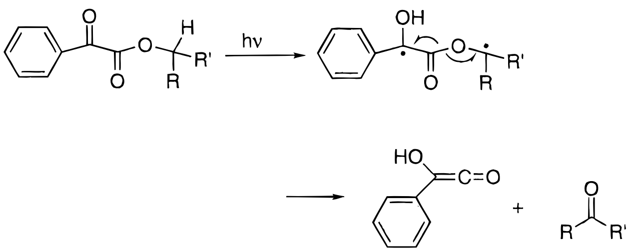
(1)

A similar attempt using 5-hexenyl radical clock to trap the 1,4-biradical derived from an alkyl phenylglyoxylate for synthetic purposes was unsuccessful. Instead, the Norrish Type II reaction proceeds normally, eq 2.[7] The 5-hexenylradical cyclization has a reported rate constant of 1×10^5 s^{-1},[5,8] so that a 1,4-biradical from a phenylglyoxylate cannot be trapped by the 5-hexenyl radical is understandable. This biradical is even shorter lived than the biradical from phenyl ketones. Radical clocks with higher rearrangement rates must be used in order to accomplish this purpose.



(2)

Scheme 1



Cyclopropylmethyl radicals with different substituents rearrange with rate constants ranging from 10^7 s^{-1} to 10^9 s^{-1}. These fast rearrangements are thus capable of monitoring short-lived 1,4-biradicals.[4d,9] We therefore incorporated cyclopropylmethyl groups in phenylglyoxylates in order to study the lifetime of the biradical formed upon Norrish Type II hydrogen abstraction. α-Keto esters **1a**−**c** were synthesized and photolyzed. The lifetime of the intermediate 1,4-biradical is successfully deduced from the relative amounts of products formed before and after the cyclopropylmethyl radical rearrangement as well as from its rearrangement rate.

Results

Phenylglyoxylates **1a**−**c** were irradiated in dilute (0.005 M) benzene solution to avoid competition from intermolecular hydrogen abstraction processes.[3] As shown in Scheme 2, if biradical **2** undergoes no rearrangement, normal Norrish Type II products **3**−**5** derive. When R_1 and R_2 are something other than hydrogens, two different rearrangements can occur to biradical **2**. Rearrangement A leads to 1,7-biradical **6** while rearrangement B leads to 1,7-biradical **7**. Rearrangement A is preferred over B since **6** is more stable than **7**. It is thus expected that the resulting lactone **8** will be the major rearrangement product.

Compound **8c** has been reported before[7] as a labile product (25% yield) when photolysis of **1c** is carried out

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[1] Contribution No. 297 from the Center for Photochemical Sciences.

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(7) Kraus, G. A.; Wu, Y. *J. Am. Chem. Soc.* **1992**, *114*, 8705−8707. If alkenes of proper electron density are situated properly, the intramolecular釆Paternó−Büchi reaction dominants. For a timely paper on the interplay of Norrish Type II and Paternó−Büchi reactions of phenylglyoxylate, see Hu, S.; Neckers, D. C. *J. Org. Chem.*, in press.

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Scheme 2

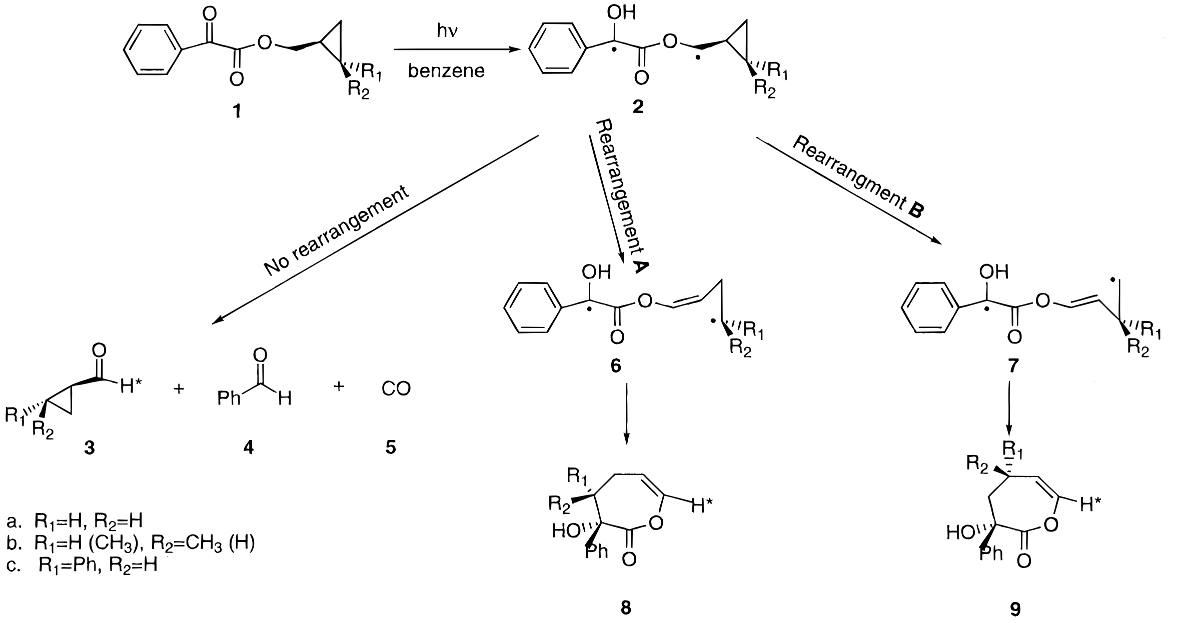

Table 1. Quantum Yields of Disappearance of 1 and Relative Amount of Products

1	Φ^a	3	8	9
1a	0.88	0.79	1^b	
1b	0.87	0.49	0.57	0.39
1c		0.04	0.62	0.38

[a] Quantum yield of the disappearance of **1**. [b] **8a** and **9a** are the same.

to about 70% completion.[10] In addition to **8c**, we also observed **9c** in the photolysis mixture obtained from of **1c**.[11] The relative amounts of **3c**, **8c**, and **9c** are obtained by repeated integration of the representative peaks (peaks of H*s in Scheme 2) in the ^{1}H NMR spectrum from a reaction mixture obtained in C_6D_6. The relative amounts of products from the photolysis of **1a** and **1b**[12] are similarly obtained, see Table 1. In all cases, NMR spectra of the reaction mixtures give material balances better than 95%. We were able to purify **8(9)a** through repeated short, quick silica gel chromatography[13] even though all seven-membered ring lactones such as **8** and **9** have proven to be quite labile under chromatographic conditions.

It has previously been demonstrated that one can safely assume that 1,4-biradicals undergo radical rearrangement at rates similar to their analogous model radicals.[8] We thus assume **2a** rearranges to **6(7)a** with the rate of the cyclopropylmethyl radical rearrangement. The latest data for the rate constant of such a rearrangement is 9.4×10^7 s^{-1} [14] with the trans/cis ratio of the resulting alkene radical being 2.2.[15] So the rate constant of **2a** rearranging to *cis*-**6(7)a** is 2.9×10^7 s^{-1} and only the *cis*-1,7-biradical can cyclize to the corresponding seven-membered ring lactone. Considering the **3a**/**8(9)-a** ratio of 0.79:1, the total rate constant for the decay of **2a** to products is 5.4×10^7 s^{-1}. Taking this number and the quantum yield of disappearance of **1a** as 0.88, i.e., 12% of **2a** disproportionates to **1a**, the total biradical decay rate of **2a** can be calculated to be 6.1×10^7 s^{-1}, which reflects a lifetime of 16 ns for **2a**. The *cis*- and *trans*-2-methylcyclopropylmethyl radicals rearrange to primary and secondary radicals with rate constants ranging from 2.8×10^8 s^{-1} to 1.0×10^9 s^{-1}.[16] Taking an average rate constant of 4.0×10^8 s^{-1} for the model 2-methylcyclopropylmethyl radical rearrangement and the product ratio of **3b**/(**8b**+**9b**), the lifetime of biradical **2b** is estimated to be 5 ns. The rate constant of the model 2-phenylcyclopropylmethyl radical rearrangement is reported to be greater than 1×10^{11} s^{-1}.[17] The lifetime of **2c** was not estimated because of the lack of a definite rate constant for this model, though the very small ratio of **3c**/(**8c**+**9c**) agrees with the expectation of a fast rearrangement of **2c**.

No product was observed from the disproportionation of the biradicals **6** and **7**. The triplet decay rate for **1a** was measured by nanosecond laser flash photolysis and showed no significant change when compared with that of other alkyl phenylglyoxylates,[3] indicating no significant change in the facility of triplet γ-hydrogen abstraction results from the introduction of a cyclopropyl group.

As expected, the lifetime of biradical **2** is shorter than are those of 1,4-biradicals without oxygen in their skeleton (τ = 35−40 ns[18]). We find the lifetimes of **2** are

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(10) Wu, Y. Ph D. Dissertation, Iowa State University.

(11) Besides the H* peak for **8c** at 5.74 ppm (dt, J_1 = 8 Hz, J_2 = 2 Hz), there is a distinct H* peak from **9c** at 5.91 ppm (ddd, J_1 = 8 Hz, J_2 = 1.6 Hz, J_3 = 1.2 Hz). The trans relationship between the two phenyl groups is derived from an X-ray structure determination in an earlier study.[7]

(12) H* peaks for **8b** (mixture of diastereoisomers): 6.16 ppm (ddd, J_1 = 8 Hz, J_2 = 2.8 Hz, J_3 = 2 Hz), 6.26 ppm (ddd, J_1 = 7.6 Hz, J_2 = 2.4 Hz, J_3 = 2 Hz). H* peaks for **9b** (mixture of diastereoisomers): 5.88 ppm (dd, J_1 = 6 Hz, J_2 = 2.4 Hz), 6.08 ppm (dd, J_1 = 8 Hz, J_2 = 2.4 Hz).

(13) Column chromatography was performed under a pressure of air. The elution solvent is hexanes/ethyl acetate = 10:1. The longer the compound is in contact with silica gel, the more it decomposes.

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close to those of other biradicals with oxygen in the skeleton,[19] such as the Paternó–Büchi (pre-oxetane) biradicals ($\tau = 1.5-4$ ns[4b]).

Experimental Section

Benzene (Aldrich) was dried over sodium under argon. Other chemicals were obtained from Aldrich and used as received. NMR spectra were recorded on a Varian Unity Plus 400 NMR spectrometer. Chemical shifts are in ppm with TMS as an internal standard. GC/MS were taken on Hewlett-Packard 5988 mass spectrometer coupled to a HP 5880A GC. Infrared spectra were taken with a Galaxy Series 6020 FTIR spectrometer. Thin layer chromatography was performed with Whatman silica gel-coated TLC plates. Products are isolated by flash column chromatography using Aldrich silica gel (60 Å, 70–270 mesh). HRMS were obtained from the University of Illinois at Urbana–Champaign. General procedures for irradiating samples, isolating photoreaction products, quantum yield measurement, and nanosecond laser flash photolysis were reported earlier.[3]

Cyclopropylmethyl benzoylformate (1a) is obtained by esterification of benzoylformic acid using cyclopropylmethanol and DCC in 91% yield. The synthesis and purification procedure has been described earlier.[3] **1a**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.40 (m, 2H), 0.65 (m, 2H), 0.88 (m, 1H), 4.23 (d, $J = 7.2$ Hz, 2H), 7.53 (m, 2H), 7.65 (m, 1H), 8.01 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 3.61, 9.73, 71.08, 128.84, 129.97, 132.49, 134.82, 163.98, 186.47. IR (neat) 3087.05, 3009.88, 2955.85, 1736.47, 1690.15, 1597.55, 1200.09, 1176.94, 984.00. MS 55 (82.9), 77 (47.4), 105 (100), 204 (M$^+$, 0.03). HRMS *m/e* calculated: 204.0786, measured: 204.0787.

***cis,trans*-(2′-Methylcyclopropyl)methyl benzoylformate (1b)** is obtained by DCC esterification procedure using *cis,trans*-(2-methylcyclopropyl)methanol in 90% yield.[3] **1b**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.41 (m, 1H), 0.55 (m, 1H), 0.81 (m, 1H), 0.99 (m, 1H), 1.01 (d, $J = 6$ Hz, 3H), 4.23 (m, 2H), 7.52 (m, 2H), 7.66 (m, 1H), 8.02 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 11.85, 12.11, 18.08, 18.16, 70.63, 128.83, 129.94, 132.49, 134.81, 164.07, 186.56. IR (neat) 3071.62, 3006.02, 2955.85, 2870.96, 1728.75, 1694.02, 1597.55, 1296.56, 1200.09, 984.00. MS 41 (43.9), 69 (100), 77 (40.3), 105 (74.7), 173 (M$^+$ − 45, 0.1). HRMS *m/e* calculated: 218.0943, measured: 218.0942.

***trans*-(2′-Phenylcyclopropyl)methyl benzoylformate (1c)** is a known compound.[10] *trans*-(2-Phenylcyclopropyl)methanol was synthesized by LiAlH$_4$ reduction of *trans*-2-phenyl-1-cyclopropanecarboxylic acid. Esterification of benzoylformic acid produces **1c** in 80% yield.[3]

3-Hydroxy-3-phenylcycloheptene-6-lactone (8(9)a): ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.85 (m, 1H), 2.28 (m, 1H), 2.38 (m, 1H), 2.58 (m, 1H), 4.34 (s, 1H), 4.85 (m, 1H), 6.13 (dt, $J_1 = 7.6$ Hz, $J_2 = 2$ Hz, 1H), 7.25 (m, 5H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 22.99, 33.71, 71.56, 111.87, 125.75, 128.55, 128.64, 136.03, 137.91, 172.26. MS 77 (48.8), 105 (100), 120 (88.6), 158 (17.1), 176 (M$^+$ − 28, 12.5). HRMS *m/e* calculated: 204.0786, measured: 204.0787.

3-Hydroxy-3,4-diphenylcycloheptene 6-lactone (8c) is obtained in the photolysis of **3c** in agreement with an earlier study.[10]

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Supporting Information Available: ^{1}H and/or ^{13}C NMR (APT) spectra for all new compounds **1a**, **1b**, **8(9)a** (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(19) For an explanation of the short lifetime of biradicals with oxygen in their skeleton, see ref 4a.