

Substituent Effect in Photochemistry of β -Ethoxy- α -halopropiophenones

Sungsu Cho and Bong Ser Park*

Department of Chemistry, Dongguk University, Seoul 100-715, Korea

Photochemical reactivities of β -ethoxypropionophenones are changed dramatically by putting a halogen at a position to the carbonyl functionality. α -Bromo- β -ethoxypropionophenone gives C-Br bond cleavage products solely, but α -chloro- β -ethoxypropionophenone forms mainly the Yang photocyclization products upon irradiation. The different reactivities of two compounds can be explained by relative rates of C-X bond cleavage and δ -hydrogen abstraction.

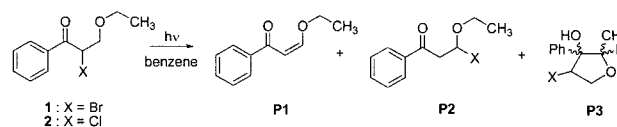
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We often encounter intriguing examples in which minor structure changes result in dramatic shift of chemical reactivities in organic chemistry. [1] One of the most recent examples showed that alpha substituted valerophenone followed completely different reaction routes upon photolysis depending on the alpha substituents; α -bromovalerophenone gives only the C-Br bond cleavage products, while α -chlorovalerophenone follows the classical Norrish/Yang reaction pathway predominantly. [2-3] When the substituents are sulphonates such as mesylate or tosylate, the reaction gives cyclopropyl derivatives *via* hydrogen abstraction/H-X elimination sequence. [4-5] Intrigued by the unique substituent effect, we extended our research interest to β -ethoxypropionophenone and how the alpha substituents altered its photochemical integrity. β -Ethoxypropionophenone is the simplest ketone that follows δ -hydrogen abstraction reaction upon photolysis. [6-7] We were curious about how the alpha substituents altered the photochemical integrity of the ketones. The oxygen bridge between the carbonyl group and δ -hydrogens being abstracted drew our special attention because the oxygen can lead to not only conformational changes in the excited ketone or/and the biradical intermediate but also shorten the life time of the biradical intermediate. [8-9] Thus α -bromo- β -ethoxypropionophenone (**1**) and α -chloro- β -ethoxypropionophenone (**2**) were prepared and their photochemical behaviors were investigated.

The ketones **1** and **2** were synthesized by bromination of β -ethoxypropionophenone using CuBr_2 on alumina and chlorination using SO_2Cl_2 , respectively. [10] Photolysis of the ketones was done using the output of Pyrex filtered light of a Hanovia medium pressure mercury arc lamp by hanging an NMR tube containing 0.02 M of the ketone in degassed benzene- d_6 near the lamp. The sample was monitored at regular intervals by ^1H NMR spectroscopy.

Photolysis of **1** gave cleanly a mixture of two products according to the ^1H NMR spectroscopy and TLC analysis. Large scale irradiation followed by separation of the photoproducts using column chromatography allowed us to identify the structure of each product. Two products isolated were *Z*-1-phenyl-3-ethoxypropenone (**P1**) and β -bromo- β -ethoxypropionophenone (**P2**). The product **P2** was unstable in alkaline condition and turned easily into a mixture of the product **P1** and the *E* isomer of **P1**, which supported our structure assignment further. The stereochemical assignment of **P1** could easily be made by the vicinal coupling constant of two vinylic protons, which was 4.4 Hz. [11]

The ^1H NMR spectrum taken after irradiation of **2** showed distinctive patterns of the tetrahydrofuranols as expected in addition to the presence of a small amount of **P1**. Two isomeric tetrahydrofuranols were formed in ca. 6 to 1 in favor of the *Z* isomer with a methyl doublet at 1.25 ppm over the *E* isomer with a methyl doublet at 0.86 ppm. The ratio was determined based on the integration of methyl doublets. As previously observed in a number of such products, the stereochemical assignment was made based on the fact that a methyl cis to the phenyl is significantly shielded relative to one trans. [12-13] Shown below is a summary of product distribution in the photolysis of **1** and **2**.



The common product, **P1**, from both **1** and **2** results from photo induced dehydrohalogenation as previously observed in photolysis of several ketones. [14-15] The fact that no reaction occurs in dark condition supports photochemical nature of this process. Another product from **1**, **P2**, is obtained by HBr trapping of **P1** in Michael type fashion. The trapping product, however, was not observed in photolysis of **2**, which may have been a consequence of the weaker nucleophilicity of

*To whom correspondence should be addressed.

E-mail : parkbs@dongguk.edu

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Table 1. Product Distribution of Photolysis of **1** and **2** in Benzene

Compounds	P1	P2	P3
1	50%	50%	-
2	19%	-	81%

chloride ions than that of bromide ions.

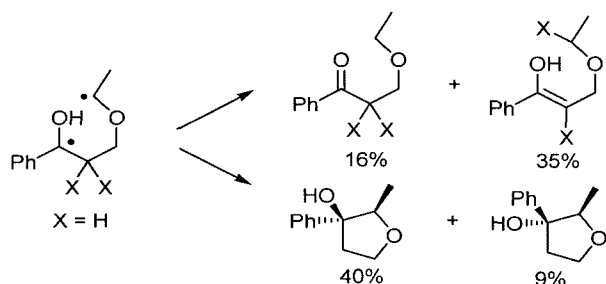
The product **P3** is a typical Norrish/Yang photocyclization product. Wagner studied photochemistry of β -ethoxypropio-phenone and reported that the ketone in benzene produced two tetrahydrofuranols in 4.4 to 1 ratio in favor of the *Z* isomer over the *E* isomer. The hydrogen abstraction rate, k_H , was measured to be $1.4 \times 10^7 \text{ s}^{-1}$. [16] In case of **2**, diastereoselectivities of the tetrahydrofuranol formation increased slightly compared to that from β -ethoxypropio-phenone. The increased diastereoselectivity may have resulted from the increase of barrier of conformational changes caused by Br or Cl substitution.

According to Scaiano's reports on photolysis of α -bromoacetophenone and α -chloroacetophenone, the C-X cleavage rate of the former is over $1 \times 10^{10} \text{ s}^{-1}$ while that of the latter is ca. $3 \times 10^6 \text{ s}^{-1}$. [17] These known kinetic values can explain our experimental results with **1** and **2** very nicely. In photolysis of **1**, the δ -hydrogen abstraction reaction is too slow to compete with the C-Br bond cleavage. In case of **2**, however, the hydrogen abstraction rate, $1.4 \times 10^7 \text{ s}^{-1}$, is 4-5 times as fast as that of C-Cl cleavage, $3 \times 10^6 \text{ s}^{-1}$, which is consistent with the ratio of **P3** to **P1** in our experiments. It means that the δ -hydrogen abstraction reaction rates of **1** and **2** are not much different from that of β -ethoxypropio-phenone.

In photolysis of β -ethoxypropio-phenone, it was observed that a large portion of the biradical intermediate can disproportionate as shown below. [16]

Thus it is interesting to note that no such analogues are not observed in photolysis of **1** and **2** where X = Br or Cl in the above picture. We are currently looking into this matter further with other structural analogues of **1** and **2**.

In summary, photochemical reactivities of β -ethoxypropio-phenones are changed dramatically by putting a halogen at α position to the carbonyl functionality. α -Bromo- β -ethoxypropio-phenone gives C-Br bond cleavage products solely, but α -chloro- β -ethoxypropio-phenone forms mainly the Yang photocyclization products upon irradiation. The different reactivities



of two compounds can be explained by relative rates of C-X bond cleavage and δ -hydrogen abstraction.

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