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Photoinduced Electron Transfer Reactions of α, β-Epoxy Ketones with 2-Phenyl-N,N-dimethylbenzimidazoline (PDMBI): Significant Water Effect on the Reaction Pathway

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Abstract: Irradiation of aroyl substituted epoxy ketones with 2-phenyl-N,N-dimethylbenzimidazoline in aqueous tetrahydrofuran or aqueous benzene produced the corresponding aldols in good to excellent yields. Changing the amount of water addedsignificantly influenced the product distribution. Copyright © 1996 Elsevier Science Ltd

Since selective transformation of α , β -epoxy ketones to β -hydroxy ketones (aldols) is recognized as a synthetically important process, various methods have been developed to achieve this objective.¹ Among them are the methods conducted under electron transfer conditions in which generation of a ketyl radical species of epoxy ketones is involved. The photoinduced electron transfer (PET) process is also known to be a useful way to generate ketyl radicals.² Thus, Cossy and coworkers have reported that irradiation of epoxy ketones with triethylamine produced the corresponding aldols in moderate to good yields.³ However, we have found that the major isolable products were β -diketones rather than aldols on the irradiation of certain aromatic epoxy ketones, such as chalcone epoxides, with triethylamine.⁴⁴ Apparently, there have been no generally acceptable electron donors for this photochemical transformation, particularly for aroyl substrates. Based on our mechanistic studies,⁴ we simply considered that compounds possessing both good electron-donating and hydrogen-donating properties should be promising candidates. Thus, 2-phenyl-N,N-dimethylbenzimidazoline (PDMBI)^{5,6} became attractive to us. Here, we first report that photoreactions of α , β -epoxy ketones with PDMBI in aqueous tetrahydrofuran or aqueous benzene produced β -hydroxy ketones in good yields (eq 1).⁷



When 1,3-diphenyl-2,3-epoxypropanone (1a) was irradiated in the presence of PDMBI in dry tetrahydrofuran, the desired 1,3-diphenyl-3-hydroxypropanone (2a) was found to be a minor component of the reaction mixture. Other products were 1,3-diphenylpropenone (3a), the major product, and a small amount of benzaldehyde (4a). After several attempts to find the best solvent systems, we have finally found that addition of water dramatically increased the yield of 2a.⁸ Other interesting observations were that 1) polar solvents such as acetonitrile and methanol were not effective even in the presence of water, 2) aqueous benzene operated quite well just as tetrahydrofuran did. These preliminary observations prompted us to look at the reaction profile influenced by changing the amount of water added. The results are shown in Figure 1 (the yields are based on the conversion of 1a). As mentioned above, **3a** was usually the major product for the reactions in



10 0

2

4

Figure 1. Effect of H2O amount on the photoreaction of 1a with PDMBI in THF

8

10

6

3**a**

12 H₂O volume / %

dry tetrahydrofuran.⁹ As the amount of water was increased to about 1% of the solution volume, the yield of **2a** dramatically increased to become greater than 85%. At the range of more than 2% of water content, the yield of **2a** gradually decreased and that of **4a** increased to a similar extent¹⁰ while the yield of **3a** was kept at less than 5%.

Next, we conducted photoreactions of other epoxy ketones 1b, 1c, 1d, and 1e with PDMBI in both aqueous tetrahydrofuran and aqueous benzene to determine the generality and the limitations of this photochemical method. As presented in Table 1, irradiation of aroyl substituted epoxy ketones 1a-1d with PDMBI produced the corresponding aldols in good to excellent yields. On the other hand, no formation of

Entry	1	R ¹	R ²	aq Solvent	Conv / %	2 / % ^{b)}
1	1a	Ph	Ph	THF	100	89
2	1a	Ph	Ph	Benzene	100	85
3	1 b	Ph	н	THF	97	74 (76)
4	1 b	Ph	Н	Benzene	100	84
5	1 c	Ph	<i>i</i> -Pr	THF	81	55 (68)
6	1 c	Ph	<i>i</i> -Pr	Benzene	97	74 (76)
7	1 d	Ph	n-Pr	THF	93	68 (73)
8	1 d	Ph	n-Pr	Benzene	97	67 (69)
9	1 e	Me	Ph	THF	34	0
10	1 e	Me	Ph	Benzene	13	0

Table 1. Photoreactions of epoxy ketones 1 with PDMBI in aqueous tetrahydrofuran and aqueous benzene a)

a) Conditions: 500 W Xe-Hg lamp (Pyrex); 1 h; N2; 1 (0.40 mmol), PDMBI (1.5 equiv), solvent (8 ml), H2O (0.1 ml).

b) Isolated yields by column chromatography (yields based on the conversion of 1).

aldol 2e was observed in the photoreaction of acetyl substituted epoxy ketone 1e with PDMBI. Under the irradiation conditions, acetyl chromophore less efficiently absorbs the incident light ($\lambda > 280$ nm) that could account for the lower reactivity of 1e.



Based on the results obtained and our related studies,^{11,4} the reaction mechanism depicted in Scheme 1 is proposed. The photoexcited state of 1 is considered to be efficiently quenched by PDMBI.¹¹ The formed anion radical 6 would abstract the proton from PDMBI" or undergo epoxy ring-opening. The ketyl radical 7 undergoes C α -O bond cleavage to give the oxy radical 8 that is subsequently reduced by I' to the anion 9. The anion 9 easily undergoes retro-aldol fragmentation to produce aldehvde 4 and ketone 5. On the other hand, the opened anion radical 10 abstracts the proton from PDMBI" to give the 6-keto radical 11 that is reduced by I' to the anion 12. The anion 12 is expected to easily give the enone 3. Therefore, effective protonation of the anions 9 and 12 would give the aldol 2 in good yields. In any case, two electrons and two protons are required to convert 1 to 2. Since PDMBI donates two electrons and one proton,⁶ additional proton sources have to be added into the reaction solutions. Apparently, water acts as an effective proton donor in the above reaction systems. However, increasing the amount of water should also change the medium polarity. A highly polar medium prefers a free ion radical species rather than ion radical pairs.² In the former case, effective proton and electron transfers do not occur between the intermediates in Scheme 1 and PDMBI derived radicals (PDMBI⁺ and I). Particularly, a large amount of water may be able to protonate 6 to give 7 and finally 8 that undergoes radical retro-aldol fragmentation¹¹ since subsequent electron transfer from I' would not be effective.

In summary, we have found that 2-phenyl-N,N-dimethylbenzimidazoline is an effective amine to photochemically convert aroyl substituted epoxy ketones to aldols. Since various imidazoline derivatives could be designed and synthesized from readily available starting materials,⁵ such compounds are expected to be useful reductants for various PET processes. This methodology is currently under investigation in our laboratory.

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- 7. Epoxy ketones 1, hydroxy ketones 2, and enones 3 were fully characterized by their spectral data.^{11.4} Since isolation of volatile benzaldehyde4a was difficult, its yield was determined by 'H-NMR analysis of the crude reaction mixture. Although isolation and characterization of the oxidized products from PDMBI have not been completed yet, among the compounds detected was N-methyl-N-(2-N'-methylanilino)benzamide, a ring-opened form of 2-hydroxy-PDMBI, that is probably formed through the reaction of imidazolium ion and hydroxy ion (see Scheme 1).
- 8. We similarly conducted photoreactions of 1 a with other commonly used amines for PET reactions² and found that neither triethylamine nor tribenzylamine was effective to obtain 2 a in high yields.
- 9. Using dry tetrahydrofuran (distilled from Na-benzophenone) for the reactions, we found that the yields of 2a irregularly changed on several entries. Lower yields of 2a appeared to result from the greater formation of 3a. We think that such tricky results indicate that accidental contamination of water (moisture) would influence the product distribution and this could not be easily avoided in the usual preparative experiments.
- 10. Since 4a seems to be the retro-aldol fragmentation product from the β -hydroxy carbonyls, the other fragment, acetophenone, should exist in the reaction mixture. This was confirmed by ¹H-NMR analysis of the concentrated photolysate. Qualitatively, the amount of acetophenone changed in a similar way to that of 4a upon changing the amount of water added.
- PDMBI was found to be a highly electron donating amine: the oxidation potential was measured as +0.32 V (Ep^{exvs} SCE; 100 mV/s). Therefore, electron transfer from PDMBI to the excited triplet state of 1a would be highly exothermic since the reduction potential of 1 was reported as -1.70 V (Ep^{red}vs SCE; 100 mV/s)⁴⁴ and the triplet energy of 1a is estimated as 71 kcal/mol.^{11b} b) Dewar, D. J.; Sutherland, R. G. J. Chem. Soc., Perkin Trans 2, 1977, 1522-1526.

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