1,3-Dimethyl-2-phenylbenzimidazoline (DMPBI)–Acetic Acid: An Effective Reagent System for Photoinduced Reductive Transformation of α,β-Epoxy Ketones to β-Hydroxy Ketones

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Abstract: A combination of 1,3-dimethyl-2-phenylbenzimidazoline (DMPBI) and acetic acid has been utilized for photoinduced reductive transformation of α,β-epoxy ketones to β-hydroxy ketones. Study on photoreactions using several proton donors revealed that acetic acid is superior to other proton donors such as HCl, p-TsOH, MeOH, and water. 1,3-Dimethyl-2-phenylbenzimidazolium was produced in the reaction with acetic acid while N-benzoyl-N,N-dimethyl-o-phenylenediamine was formed in aqueous solvents. When THF solutions containing aryl carbonyl possessing α,β-epoxy ketones and DMPBI and acetic acid were irradiated (λ > 280 nm), β-hydroxy ketones were isolated in good to excellent yields. Photonsensitized conditions (λ > 340 nm) were employed for the reactions of alkyl carbonyl possessing α,β-epoxy ketones.

Key words: photoinduced electron transfer, 1,3-dimethyl-2-phenylbenzimidazoline, acetic acid, α,β-epoxy ketones, reductive ring opening, β-hydroxy ketones

During several decades of the last century, photoreactions of three-membered ring compounds gained much attention due to their interesting reactivities; among these compounds are epoxides.1 In particular, photoreaction of α,β-epoxy ketones were extensively investigated, which demonstrated that several types of photochemical processes are open to these compounds.2 Selectivity of the bond cleavage of epoxy rings such as C–O, C=O, C–C usually depends on the substitution and the nature of the reactive excited states. However, if a single electron is injected to carbonyl substituents to generate their radical anions (ketyl radicals), these intermediates would undergo selective C–O bond cleavage to give distonic radical anions followed by formal two-proton and single-electron transfer (SET) to become β-hydroxy ketones (Scheme 1). Therefore, irradiation of α,β-epoxy ketones in the presence of electron-donating compounds would become a new way to achieve this synthetically important process.3

About ten years ago, we first examined this concept by conducting photoreactions of several aromatic epoxy ketones in the presence of triethylamine and other electron donors.4 About the same time, Cossy and co-workers reported photoreactions of several aliphatic as well as aromatic epoxy ketones with triethylamine.5 In these experiments, while the yields of hydroxy ketones were modest, several problems were also encountered: other compounds such as β-diketones were the major products in some cases6 and the reactions could not be completed since prolonged irradiation caused decomposition of β-hydroxy ketones.5 Our subsequent mechanistic study demonstrated that selectivity of the reaction pathway either to produce β-diketones or β-hydroxy ketones depends on the nature of the radical cations of amines used.6 Now, we report herein a method to achieve photoinduced transformation of α,β-epoxy ketones to β-hydroxy ketones by using a combination of 1,3-dimethyl-2-phenylbenzimidazoline (DMPBI)7 and acetic acid, which is superior to the previously reported DMPBI-based method.8

Irradiation of trans-1,3-diphenyl-2,3-epoxypropane-1-one (chalcone epoxide) (trans-1a) with DMPBI (1.2–1.5 equivalents) in either aqueous THF or wet benzene produced 1,3-diphenyl-3-hydroxypropane-1-one (2a)8 (Scheme 2). It was already found that the yield of 2a was sensitive to the amount of water added: an appropriate amount of water (approx. 14 equivalents) was necessarily added to obtained 2a in a yield above 80% (Figure 1).8 Chalcone was a major product in dry solvents while substantial amounts of benzaldehyde as well as acetophenone, retro-aldol-fragmentation products, were formed in

Scheme 1

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the presence of large excess of water. On the basis of Scheme 1, one may anticipate that an efficient protonation to the anionic intermediate must be essential for the better yielding of 2a. This assumption led us to use acetic acid as a proton donor instead of water. Then, we found that the yield of 2a kept above 80% within a wider range of the amount of acetic acid used (1.3–70 equivalents) compared to that of water (Figure).

Therefore, it might be easier to optimize the reaction conditions determining the appropriate amount of a proton donor for a certain substrate by use of acetic acid rather than water. In these reactions, DMPBI is oxidized through sequential liberation of two electrons and one proton to the anionic intermediate must be essential for the better yielding of 2a. This assumption led us to use acetic acid as a proton donor instead of water. Then, we found that the yield of 2a kept above 80% within a wider range of the amount of acetic acid used (1.3–70 equivalents) compared to that of water (Figure).

On the basis of the above observations, we applied the reagent system of DMPBI and acetic acid to the photoreactions of other epoxy ketones 1 (Scheme 2). When THF solutions containing 1 and DMPBI (1.2 equivalents) and acetic acid (6.6 equivalents) were irradiated by Pyrex-filtered light (λ > 280 nm) for 1 hour, most of hydroxy ketones 2 were isolated in good to excellent yields (Table 1). In the reactions of all chalcone epoxides 1a–g examined (entries 1–8), the yields of hydroxy ketones 2a–g were greater than those (average 84%) in the reactions using DMPBI and water.8b Both trans- and cis-epoxy ketones reacted similarly to produce comparable yields of hydroxy ketones (compare entries 1 and 2, and entries 9 and 10). In the reaction of dypnone epoxide 1h, the isolated yields of 2h were modest while substantial amounts of acetoephone (7–14%) were produced (entries 9 and 10). Since 1H NMR analysis of the crude reaction mixture of cis-1h demonstrated that only trace amounts of acetoephone existed, 2h probably partially decomposed to give acetoephone during column separation. It should be also noted that the yield of 2k was significantly improved from that (37%) in the reaction of 1k using DMPBI and water.8b

Our next interest was to develop the reaction conditions utilizing longer wavelengths, preferably visible light. Then, 1,6-bis(dimethylamino)pyrene (BDMAP)9 was chosen as a sensitizer since this yellow compound absorbs light above 340 nm, λmax = 373 nm (log ε = 4.35) and its end-absorption is close to 450 nm. Irradiation (λ > 360 nm) of BDMAP (0.05 equiv) with trans-1a and DMPBI (1.2 equivalents) and acetic acid (2.2 equivalents) for 1 hour completely consumed trans-1a and produced 2a in 89% yield, while the conversion of trans-1a (52%) and the yield of 2a (25%) were significantly low in the absence of BDMAP. A plausible mechanism is as follows. Under the above conditions, BDMAP first absorbs the incident light to become in the fluorescent excited state, which donates a single electron to DMPBI and water.8b Both trans- and cis-epoxy ketones reacted similarly to produce comparable yields of hydroxy ketones (compare entries 1 and 2, and entries 9 and 10). Since 1H NMR analysis of the crude reaction mixture of cis-1h demonstrated that only trace amounts of acetoephone existed, 2h probably partially decomposed to give acetoephone during column separation. It should be also noted that the yield of 2k was significantly improved from that (37%) in the reaction of 1k using DMPBI and water.8b
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Table 1  Photoreaction of Aryl Carbonyl Possessing Epoxy Ketones 1 with DMPBI–HOAc in THF

<table>
<thead>
<tr>
<th>Entry</th>
<th>I</th>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>Conv. (%)</th>
<th>Yield of 2 (%)</th>
<th>Bu₃SnH⁴</th>
<th>hv</th>
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ᵃ Isolated yields.
b Determined by ¹H NMR.
ᶜ The mixture of trans and cis (84:16) determined by ¹H NMR.
d Cited from ref. 3k.

Photoreactions of trans-1a with DMPBI: Typical Procedure
A solution of trans-1a (89.7 mg, 0.40 mmol) and DMPBI (107.7 mg, 0.48 mmol) in THF (8 mL) in the presence of HOAc (0.15 mL, 2.64 mmol) was purged with dry N₂ for 5 min followed by irradiation for 1 h. To the photolyserate was added H₂O (30 mL) followed

rification. Photoreactions were conducted in a Pyrex tube (1.5 cm diameter) immersed in a water bath with a 500-W Xe-lamp as a light source. Separation of photoreaction mixtures was performed by column chromatography with Wakogel C-200 silica gel and preparative TLC on 20 cm × 20 cm plates coated with Wakogel B-5F silica gel. Identification of photoproducts was mainly accomplished by their IR and NMR spectra. NMR spectra were measured in CDCl₃ with TMS as internal standard at 90 MHz, 200 MHz for ¹H NMR; 22.49 MHz and 49 MHz for ¹³C NMR. Mps are uncorrected.

1,3-Dimethyl-2-phenylbenzimidazoline (DMPBI)³,¹³
To a MeOH solution (80 mL) of 1,3-dimethyl-2-phenylbenzimidazoline iodide (2.1 g, 6 mmol) was slowly added NaBH₄ (567.5 mg, 15 mmol) under N₂ in an ice-water bath. The resulting mixture was stirred under N₂ at ambient temperature for 1 h followed by concentration, addition of H₂O (30 mL), and extraction with Et₂O (100 mL). The organic layer was treated with sat. Na₂SO₄, sat. NaCl, and anhyd MgSO₄. The crude product mixture obtained by concentration was subjected to silica gel column chromatography with benzene containing 1% Et₃N. The colorless solid obtained was washed with EtOH and subsequently recrystallized from EtOH to give colorless needles, 800.9 mg (60%, 3.57 mmol); mp 95–96°C (Lit.¹¹ mp 96°C). It should be noted that DMPBI sometimes decomposes in CDCl₃, which depends on the condition of CDCl₃. Therefore, CDCl₃ is recommended to be passed through a short alumina-column before the NMR experiment of DMPBI.

Reaction substrates were prepared according to the literature procedures: 1a-o,³⁶,¹⁴,¹¹ 1p,³⁶ 2a-o,³⁶,⁶,¹⁴ All photoproducts are known: 2a-o,³⁶,⁶,¹⁴ 2p,³⁶ 1,6-Bis(dimethyl-amino)pyrene (BDMAP) was prepared by the reported procedure.¹² THF was distilled from NaN₃ benzophenone under N₂. Benzene was treated with H₂SO₃, 5% NaOH, CaCl₂, and then distilled with CaH₂. H₂O for the reaction was obtained through an ion-exchange column. HOAc, anhyd DMF, and other solvents and reagents were purchased and used without further purification.
by extraction with Et<sub>2</sub>O (50 mL). The organic layer was treated with H<sub>2</sub>O, sat. NaHCO<sub>3</sub>, sat. NaCl, and anhyd MgSO<sub>4</sub>. The crude product mixture obtained by concentration of the extract was subjected to column chromatography (CH<sub>2</sub>Cl<sub>2</sub> followed by CH<sub>2</sub>Cl<sub>2</sub>–EtOAc, 5:1) to give 2a (87.3 mg, 0.39 mmol). Reactions using various amounts of acetic acid as well as reactions of cis-1a and 1b–l were performed by essentially same procedure.

Oxidized Products from DMPBI

In the reaction of trans-1a (89.7 mg, 0.40 mmol), DMPBI (107.7 mg, 0.48 mmol), and HOAc (0.03 mL, 0.52 mmol) in benzene (8 mL), an insoluble solid appeared during irradiation (1 h). This was filtered and washed with benzene to give a colorless solid (78.9 mg, 0.28 mmol) which was identified as 1,3-dimethyl-2-phenylbenzimidazolium acetate (4) by comparing its IR and 1H NMR spectra with those of the known iodide. 1H NMR analysis of the reaction mixture obtained by concentration of the filtrate revealed that some amount of the acetate existed with unreacted DMPBI: imidazolium acetate (38.8 mg, 0.14 mmol) and DMPBI (10.5 mg, 0.05 mmol). Column separation of this reaction mixture gave 2a (77.2 mg, 0.34 mmol).

Total yield of imidazolium acetate was 95% based on the consumed DMPBI (about 100% based on the conversion of trans-1a).

Imidazolium Acetate 4

Mp 60.5–61°C.

IR (KBr): ν = 1572, 1404 (-CO<sub>2</sub>–) cm<sup>-1</sup>.

1H NMR: δ = 4.05 (s, 6H, 2N-Me), 7.65–7.88 (m, 7H, 4H of benzimidazolium ring and m,p-3H of 2-Ph), 7.91–7.99 (m, 2H, o-2H of 2-Ph).

For comparison, imidazolium iodide: 1H NMR: δ = 4.02 (s, 6H, 2×N-Me), 7.67–7.85 (m, 7H, 4H of benzimidazolium ring and m,p-3H of 2-Ph), 8.02–8.09 (m, 2H, o-2H of 2-Ph).

BDMAP Photosensitized Reaction of 1m with DMPBI; Typical Procedure

A solution of 1m (64.9 mg, 0.40 mmol) and DMPBI (244.3 mg, 1.00 mmol), and BDMAP (5.8 mg, 0.02 mmol) in DMF (4 mL) in the presence of HOAc (0.15 mL, 2.64 mmol) was purged with dry N<sub>2</sub> for 5 min followed by irradiation through Toshiba UV-37 filtered light for 10 h. To the photolysate was added H<sub>2</sub>O (30 mL), followed by extraction with EtOAc (50 mL). The extract was treated with H<sub>2</sub>O, sat. NaHCO<sub>3</sub>, sat. NaCl, and anhyd MgSO<sub>4</sub>. The crude product mixture obtained by concentration of the extract was subjected to column chromatography (CH<sub>2</sub>Cl<sub>2</sub> followed by CH<sub>2</sub>Cl<sub>2</sub>–EtOAc, 5:1) to give 2n (42.5 mg, 0.26 mmol) and unreacted 1m (19.4 mg, 0.12 mmol). Reaction conditions for 1n–p were essentially the same as above except for the amount of HOAc (0.30 mL, 5.28 mmol) and the irradiation time (12 h). Modified reaction conditions were employed for trans-1a: DMF (8 mL), HOAc (0.05 mL, 0.88 mmol), Toshiba L-39 filtered light, 1 h.

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