

## 2-Hydroxyphenyl-1,3-dimethylbenzimidazoles. Formal Two Hydrogen Atom-Donors for Photoinduced Electron Transfer Reactions

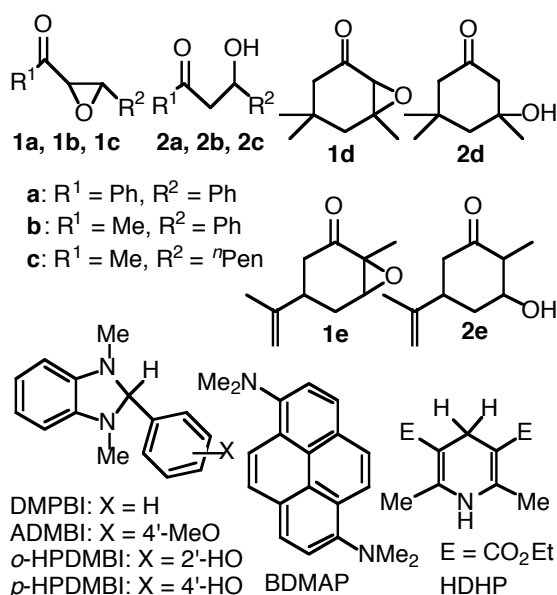
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Both 2-(2'-Hydroxyphenyl)-1,3-dimethylbenzimidazole and 2-(4'-hydroxyphenyl)-1,3-dimethylbenzimidazole were found to act as formal two hydrogen atom-donors for photoinduced electron transfer reactions of epoxy ketones and other carbonyl compounds.

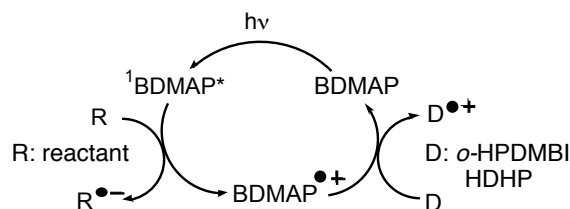
Electron transfer reactions have been often applied for the reductive transformation of organic molecules.<sup>1</sup> Several years ago, we first discovered that 1,3-dimethyl-2-phenylbenzimidazole (DMPBI) was an effective reagent for photoinduced reductive transformation of some carbonyl compounds as well as halides.<sup>2</sup> In these reactions, DMPBI acts as a formal single electron and one hydrogen atom transfer reagent. Therefore, addition of appropriate proton donors is necessary for the reduction of carbonyl compounds. Searching for a suitable proton donor and optimization of the quantity added to the reaction solution were often bothersome tasks to obtain the best yields of desired products. Therefore, it should be desirable to develop compounds that donate formally two hydrogen atoms to substrates to give their reduction products. After several attempts, we discovered that 2-hydroxyphenyl-1,3-dimethylbenzimidazoles (HPDMBI) acted reasonably well as formal two hydrogen atom-donors, that will be described below. The compounds studied are listed in Figure 1.



**Figure 1.**

We first ascertained that irradiation of epoxy ketone **1a** and DMPBI with a Pyrex-filtered light ( $\lambda > 280$  nm) in dry THF afforded *trans*-1,3-diphenyl-2-propen-1-one **3a** (not seen in

Figure 1) as a major product (35%) while the desired hydroxy ketone **2a** was obtained in low yield (20%).<sup>3</sup> Therefore, acetic acid or water was necessarily added to the reaction solution to give **2a** in good yields (> 90%). On the other hand, irradiation of **1a** with 2-(4'-hydroxyphenyl)-1,3-dimethylbenzimidazole (*p*-HPDMBI)<sup>4</sup> in THF for 1h gave **2a** in 86% based on the conversion of **1a** (49%). The relatively low conversion is probably due to interruption of light absorption by insoluble precipitates. Replacement of THF by MeOH solved this problem, namely, the yield of **2a** was 87% based on the conversion of **1a** (85%). It was then found that the corresponding *ortho*-isomer (*o*-HPDMBI)<sup>4</sup> worked even better to give **2a** (95%) without recovered **1a**.<sup>5</sup>



**Scheme 1.**

The above observation prompted us to conduct the reaction of alkyl carbonyl substituted epoxides such as **1b-1e**. Since these compounds less efficiently absorb the Pyrex-filtered light, we needed to employ a redox-sensitization condition using 1,6-bisdimethylaminopyrene (BDMAP)<sup>6</sup> as a visible light absorbing sensitizer and *o*-HPDMBI (Scheme 1). Oxidation potential of the singlet excited state of BDMAP is about -2.4 V vs SCE.<sup>2</sup> The results are presented in Table 1. In all cases studied, the yields of hydroxy ketones **2** were greater than 90% and the starting **1** were almost completely consumed. These results are better than those attained using a combination of 2-(4'-methoxyphenyl)-1,3-dimethylbenzimidazole (ADMBI)<sup>4</sup>-

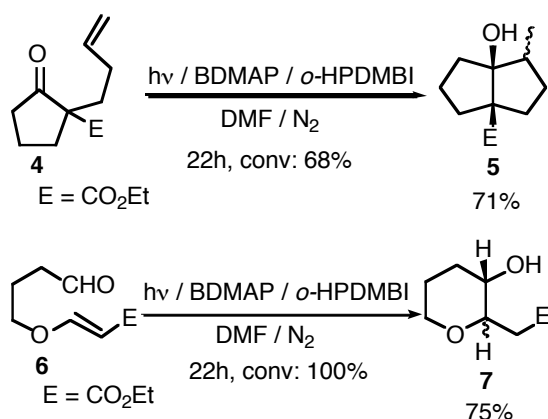
**Table 1.** BDMAP photosensitized reaction of alkyl carbonyl substituted epoxides **1** with *o*-HPDMBI in MeOH.<sup>a</sup>

exp	1	conv of 1 / %	yields of <b>2</b> <sup>b</sup> / %	
			<i>o</i> -HPDMBI	ADMBI-AcOH <sup>c</sup>
1	<b>1b</b>	100	93	83 (98)
2	<b>1c</b>	100	99	65 (69)
3	<b>1d</b>	99	93	80 (88)
4	<b>1e</b>	100	90	57 (60)

<sup>a</sup>**1** (0.40 mmol), *o*-HPDMBI (1.2 equiv vs **1**), BDMAP (0.05 equiv vs **1**),  $\lambda > 340$  nm, 3h. <sup>b</sup>Based on the conversion of **1**. <sup>c</sup>Solvent: DMF, numbers in parentheses represent the conversion of **1**.

acetic acid (also see Table 1). Determination of adequate quantity of acetic acid, which is often difficult, is required for the reaction with ADMBI since ADMBI is considered to be a two electron and one proton-donor.<sup>2c</sup> On the other hand, *o*-HPDMBI must act as an effective two electron and two proton-donor. It should be also noted that the BDMAP redox-sensitization method using *o*-HPDMBI appears to be superior to the previously reported PET method using excess triethylamine.<sup>7</sup>

We next conducted photoreactions of **1a** and **1d** with Hantzsch dihydropyridine (HDHP), a well-known formal two hydrogen atom donor.<sup>8</sup> As expected,<sup>9</sup> HDHP was also an effective reductant for the photoreaction of **1a** to give **2a** (92%) in MeOH. However, BDMAP photo-sensitized reaction of **1d** using HDHP resulted in 25% yield of **2d** based on 35% conversion of **1d** (compare to exp. 3 in Table 1). The difference in the efficiency of the reaction between *o*-HPDMBI and HDHP could be rationalized by considering the difference in their oxidation potentials ( $E_p^{ox}$ , V vs SCE): 0.31 for *o*-HPDMBI and 0.87 for HDHP. In the redox-sensitization cycle (see Scheme 1), the radical cation of BDMAP necessarily returns to its neutral form *via* single electron transfer (SET) with the co-present donor. Surveying the thermodynamics of these SET processes with *o*-HPDMBI as well as HDHP, the former is exothermic ( $\Delta G = -3.5$  kcal/mol) while the latter is endothermic ( $\Delta G = +9.5$  kcal/mol) accounting for the oxidation potential of BDMAP ( $E_p^{ox} = 0.46$  V vs SCE).



**Scheme 2.**

Finally, we briefly applied the above redox-sensitization method using *o*-HPDMBI to intramolecular ketone-olefin cyclization reactions.<sup>10</sup> Thus, BDMAP (0.10 equiv) photosensitized reaction of alkenyl ketone **4** with *o*-HPDMBI (1.2 equiv) produced the expected cyclization product **5** (73%) based on the consumed **4**. Then, we similarly conducted the cyclization reaction of vinyl ether tethering aldehyde **6** to obtain tetrahydropyran **7** that is a type of potentially useful intermediates for the synthesis of cyclic polyether natural products.<sup>11</sup> Then, we obtained **7** in 75% as a mixture of the stereo isomers (*anti* : *syn* = 57 : 43). Although both the yield and the stereoselectivity of **7** were modest, this photochemical method would be a unique alternative method to the previously reported methods employing metal reagents.<sup>12</sup>

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- Experimental procedure. A N<sub>2</sub> prepurged solution (4.0 mL) of epoxy ketone **1a** (0.40 mmol) and DMPBI or HPDMBI (0.48 mmol) in a Pyrex tube was irradiated with 500W Xe-lamp for 1h. In the case of redox-sensitization for **1b-1e**, a solution containing BDMAP (0.02 mmol), **1b-1e**, and HPDMBI or ADMBI similarly prepared as above was irradiated through a colored glass filter cutting the light below 340 nm for 3h. The photolysates were concentrated and then subjected to silica gel column or TLC separation. In the case using DMF as a reaction solvent, extraction of the photolysate with EtOAc was needed. BDMAP sensitized reactions of **4** and **6** with *o*-HPDMBI were similarly performed. The products **2**, **3**, **5**, and **6** were identified by their NMR and IR spectra. Oxidation products derived from HPDMBI, although not completely characterized yet, are considered to possess both benzimidazolium and phenoxide structures on the basis of their NMR and IR spectra.
- Both *p*-HPDMBI and *o*-HPDMBI were prepared by the reaction of the corresponding hydroxybenzaldehydes with *N,N'*-dimethyl-*o*-phenyldiamine. ADMBI was prepared similarly to the previously reported procedure for DMPBI.<sup>2</sup>
- The meta-isomer (*m*-HPDMBI) was not as effective as *o*-HPDMBI and *p*-HPDMBI. Preliminary experiments using *m*-HPDMBI revealed that the formation of **2a** (~70%) was always accompanied by that of **3a** (~20%) unlike *o*-HPDMBI and *p*-HPDMBI. Then, addition of acetic acid to the reaction solution containing *m*-HPDMBI significantly increased the yield of **2a** (89%).
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