doi:10.1246/cl.2011.1231
Published on the web October 8, 2011


# 1,8-Diazabicyclo[5.4.0]undec-7-ene-promoted Regioselective Elimination of Vicinal Dibromides Having an Adjacent *O*- and/or *N*-Functional Group

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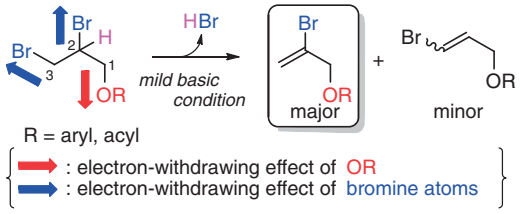
We have investigated the DBU-promoted HBr-elimination of vicinal dibromides having an adjacent *O*- and/or *N*-functional group under mild basic conditions. The elimination of 1-oxygen-functionalized 2,3-dibromopropanes was more regioselective than that of 1-nitrogen-functionalized 2,3-dibromopropanes. This observation suggests that the elimination selectivity is affected by the electronegativity of the neighboring heteroatoms themselves and not by the entire functional group.

2-Bromo-1-alkenes are extremely useful and versatile building blocks in organic synthesis. For example, 2-bromo-1-alkenes are used as substrates in preparing organometallic reagents such as vinyllithiums[1] and vinyl Grignard reagents,[2] coupling partners in a variety of transition-metal-catalyzed reactions, and precursors of $\alpha$-halo ketones[3] and heterocycles.[4]

Recently, Ohgiya, Nishiyama, et al. reported the regioselective hydrogen bromide-elimination of vicinal dibromides having an adjacent *O*-functional group under mild basic conditions.[5] They achieved the efficient systematic synthesis of 2-bromo-1-alkenes in high yields without the need for expensive reagents or laboratory equipment. According to their results and discussions, the high yield and regioselectivity were associated with the electron-withdrawing inductive effect of the oxygen substituent (OR), which enhances the acidity of the hydrogen at the C2 position, along with the electron-withdrawing inductive effects of both bromine atoms (Scheme 1).

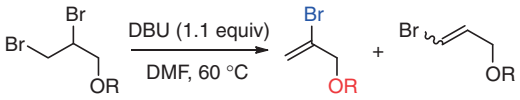
Indeed, electron-withdrawing aryloxy- and acyloxy groups (OR) showed the sufficient reactivity and regioselectivity.[5] In our recent work,[6] a wide variety of other *O*-functional groups such as benzyloxy- and silyloxy were also successfully utilized in controlling both the reactivity and regioselectivity of the elimination. We therefore started to evaluate the elimination reactivity and regioselectivity induced by the electron-withdrawing effect of the entire unit formed from the oxygen atom and its substituent (OR) (Table 1). Aryloxy- and acyloxy-substituted 2,3-dibromopropanes **1a**–**1f** gave good yields of **2a**–**2f**, as shown in the previous reports[5] (Entries 1–6). Furthermore, benzyloxy- (**1g**–**1i**), trityloxy- (TrO-, **1j**), benzyloxymethyloxy- (BOMO-, **1k**), and triisopropylsilyloxy- (TIPSO-, **1l**) substituted 2,3-dibromopropanes also gave excellent yields of **2g**–**2l** with satisfactory regioselectivities (Entries 7–12). It should be noted that not only electron-withdrawing acyl groups (Entries 3–6) but also the commonly used protecting groups, benzyl (Bn), *p*-methoxybenzyl (PMB), trityl (Tr), benzyloxymethyl (BOM), and triisopropylsilyl (TIPS) (Entries 7 and 9–12), could contribute to satisfactory selectivities in organic synthesis.

Next, the effects of the substituent of vicinal dibromides having both an electron-donating functional group ($R^1$ = triisopropylsilyl- or benzyl-) and an electron-withdrawing functional group ($R^2$ = *p*-nitrophenyl- or benzoyl-) were examined on the reaction yield and selectivity (Table 2). Treatment of the *syn*-dibromides **4a** and **4b** and the *anti*-dibromide **4c** with 1.1 equivalents of DBU gave respective mixtures of **5** and **6** with poor regioselectivity (2–1.6/1), whereas high stereoselectivities were attained for both **5** and **6** because of the highly stereospecific *trans*-elimination mechanism.[7] These results suggest that the acidity enhancement of hydrogens located at the bases of bromine atoms are associated with the electron-withdrawing effect of the neighboring *O*-functional groups (both $OR^1$ and $OR^2$). However, the observed regioselectivities were lower than those required for organic synthetic applications.




**Scheme 1.**

**Table 1.** Regioselective elimination of vicinal dibromides having an oxygen functional group




1 2 3

| Entry | 1 | Time/h | 2 + 3 Yield/% [2/3][a] |
|---|---|---|---|
| 1 | **1a**: R = Ph | 1 | 88 [25/1] |
| 2 | **1b**: R = *p*-$BrC_6H_4$ | 0.5 | 87 [27/1] |
| 3 | **1c**: R = Bz | 1.3 | 85 [20/1] |
| 4 | **1d**: R = *p*-$BrC_6H_4C(O)$ | 1 | 95 [25/1] |
| 5 | **1e**: R = *p*-$MeOC_6H_4C(O)$ | 0.3 | 88 [22/1] |
| 6 | **1f**: R = Piv | 0.5 | 94[b] [25/1] |
| 7 | **1g**: R = Bn | 1 | 93 [11/1] |
| 8 | **1h**: R = *p*-$ClC_6H_4CH_2$ | 1 | 96 [12/1] |
| 9 | **1i**: R = PMB | 1 | 97 [13/1] |
| 10 | **1j**: R = Tr | 1 | 99 [10/1] |
| 11 | **1k**: R = BOM | 2 | 98 [15/1] |
| 12 | **1l**: R = TIPS | 1 | 96 [15/1] |

[a]Ratio of 2-bromo-1-alkene **2** and 1-bromo-1-alkene **3** was determined by $^1$H NMR. [b]Yield was determined by $^1$H NMR using 1,4-bis(trimethylsilyl)benzene as internal standard.

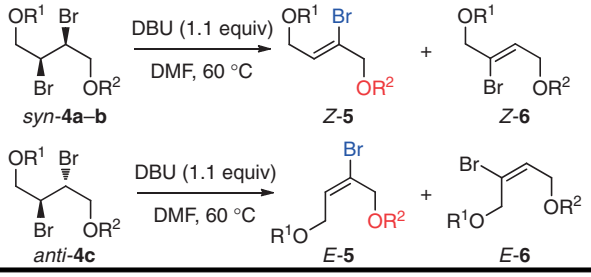
We also performed the DBU-promoted elimination of vicinal dibromides having an adjacent *N*-functional group (Table 3). Intriguingly, there was no noticeable difference in regioselectivity with substituents (R and R′) on the nitrogen, irrespective of the electron-withdrawing effect of R and/or R′.

All results (Tables 1–3) suggest that the elimination selectivity is more directly susceptible to the electronegativity of the heteroatoms (O and N) themselves rather than the electron-withdrawing effects of the substituents (R) on the heteroatoms.

To confirm the hypothesis, the eliminations of the vicinal dibromides **10** having both an *O*-functional group (electron-

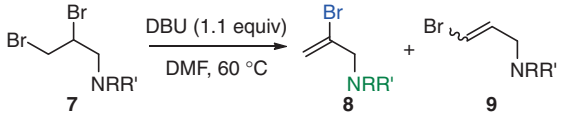
**Table 2.** DBU-promoted elimination of vicinal dibromides having both an electron-withdrawing *O*-functional group and an electron-donating *O*-functional group

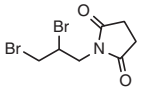
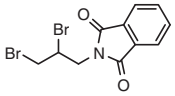



| Entry | 4 | | Time/h | 5 + 6 Yield/% [5/6][a] |
|---|---|---|---|---|
| 1 | *syn*-**4a**: | $R^1$ = TIPS<br>$R^2$ = *p*-$O_2NC_6H_4$ | 5.0 | 97 [1.6/1] |
| 2 | *syn*-**4b**: | $R^1$ = Bn<br>$R^2$ = *p*-$O_2NC_6H_4$ | 5.5 | 92 [2.0/1] |
| 3 | *anti*-**4c**: | $R^1$ = TIPS<br>$R^2$ = Bz | 2.5 | 80 [1.6/1] |

[a]Ratio of **5** and **6** was determined by $^1$H NMR.

**Table 3.** Regioselective elimination of vicinal dibromides having an nitrogen functional group

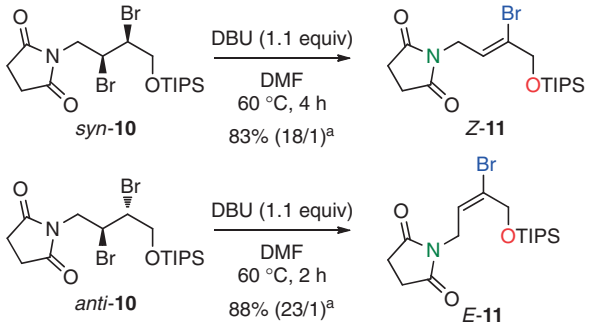



| Entry | 7 | | Time/h | 8 + 9 Yield/% [8/9][a] |
|---|---|---|---|---|
| 1 | **7a** | R = H<br>R′ = Boc | 2 | 89 [3.3/1] |
| 2 | **7b** | R = Bn<br>R′ = Bn | 3 | 79 [2.7/1] |
| 3 | **7c** | R = Ns[b]<br>R′ = Bn | 3 | 87 [3.5/1] |
| 4 | **7d** |  | 2 | 60 [1.3/1] |
| 5 | **7e** | R = Me<br>R′ = Ts | 2 | 99 [3.3/1] |
| 6 | **7f** |  | 2 | 84 [1.2/1] |

[a]Ratio of 2-bromo-1-alkene **8** and 1-bromo-1-alkene **9** was determined by $^1$H NMR. [b]Ns = 2-Nitrobenzenesulfonyl.

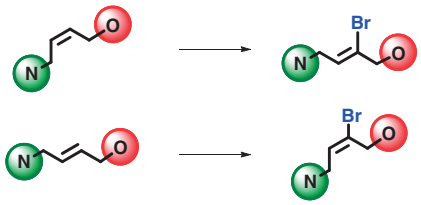
donating triisopropylsilyl) and an *N*-functional group (electron-withdrawing succinimide residue) were examined (Scheme 2). As expected, both *syn*- and *anti*-dibromides **10** gave the corresponding single isomers **11** in high yields and excellent regioselectivities and stereoselectivities. This elimination rule may, therefore, be applied to the effective synthesis of 2-bromo-4-amino-1-allylalcohol derivatives (Scheme 3).

In summary, we investigated the DBU-promoted hydrogen bromide elimination of vicinal dibromides having an *O*-functional group, both $OR^1$ ($R^1$ = electron-donating substituent) and $OR^2$ ($R^2$ = electron-withdrawing substituent) groups, an *N*-functional group, and both *O*-functional and *N*-functional groups. All results suggest that the elimination selectivity is subject to the electro-




[a]Selectivity was determined by $^1$H NMR.

**Scheme 2.**



**Scheme 3.**

negativity of the neighboring heteroatoms themselves rather than the electron-withdrawing effects of the entire functional group. A further investigation directed toward the utilization of this method and elucidation of the selectivity is in progress.

We thank Dr. Tadaaki Ohgiya (Manager, Organic Chemistry Department, Organic Chemistry Group 1, Tokyo New Drug Research Laboratories, Pharmaceutical Division, Kowa Co., Ltd.) for chemical discussions. This work was partly supported by the Sasakawa Scientific Research Grant from The Japan Science Society.

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6 One-pot reactions including DBU-promoted regioselective elimination: a) N. Kutsumura, K. Niwa, T. Saito, *Org. Lett.* **2010**, *12*, 3316. TBAF-promoted eliminations: b) N. Kutsumura, K. Kubokawa, T. Saito, *Synlett* **2010**, 2717. c) N. Kutsumura, K. Kubokawa, T. Saito, *Synthesis* **2011**, 2377.

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