

Communications

BF₃·OEt₂-Assisted Ring Opening of Epoxides with Ylides Derived from the Phosphoniosilylation Products of Enones

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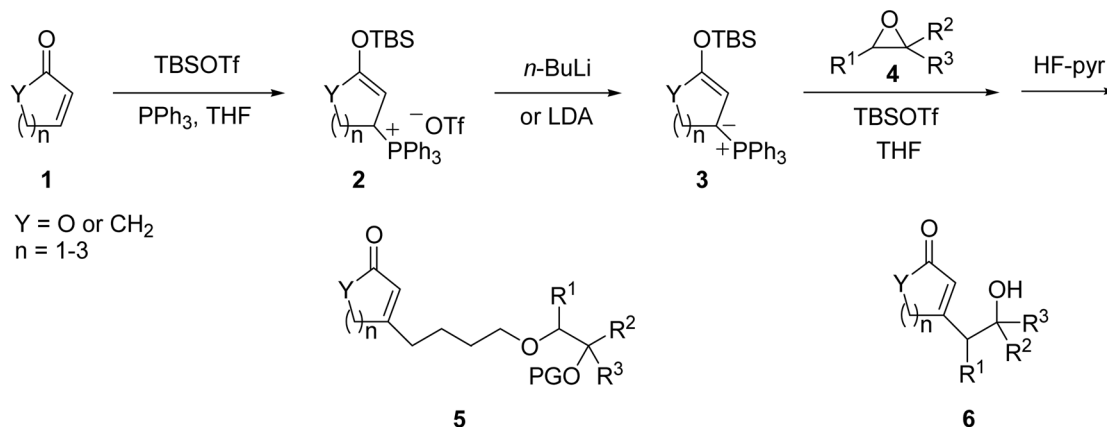
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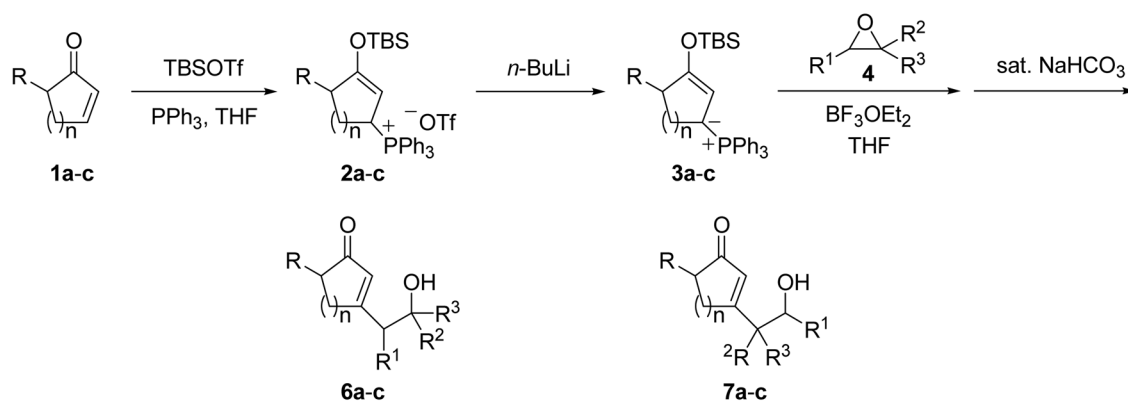
The dipole reversal process utilizing the phosphoniosilylation reaction of α,β -unsaturated carbonyl compounds with triphenylphosphine (Ph₃P) and *tert*-butyldimethylsilyl triflate (TBSOTf) has been successful for the various β -functionalizations of α,β -unsaturated carbonyl compounds.¹⁻⁴ Success of this method is due to the fact that the ylides derived from the phosphoniosilylation products can serve as acylvinyl anion equivalents to react with diverse electrophiles. Recently, we have studied the ring-opening reactions of epoxides with ylides **3** obtained from the phosphoniosilylation products **2** of α,β -unsaturated carbonyl compounds (Scheme 1).⁵ In the studies we have uncovered that TBSOTf-assisted ring-opening reactions of epoxides with ylides **3** in THF provide three-component coupling products **5** as a consequence of the participation of a reaction solvent, THF in the reaction. Although these results were very interesting, three-component products **5** were not our desired products. Thus, we needed to further investigate on the reactions of ylides **3** with epoxides **4** in order to secure the desired products **6**. Herein, we wish to report some of the results in these studies.

Upon scrutinizing the results from TBSOTf-assisted ring-opening reactions of epoxides with ylides in THF,⁵ we envisaged that the use of different solvents and/or Lewis acids might change the nature of ring-opening reactions of

epoxides with ylides **3**. To test these notions we first examined the TBSOTf-assisted epoxide ring-opening reaction using ylide **3b** derived from 2-cyclohexen-1-one **1b** and (2,3-epoxypropyl)benzene **4p** as model substrates in other solvents rather than THF. Initially this epoxide opening process was attempted in ether type solvents such as diethyl ether, DME, and *t*-butyl methyl ether. However, the results were not successful. The reactions were complicated by the involvement of these solvents in the ring-opening process as THF participates in the reaction process. The use of other solvents such as benzene, toluene, dichloromethane, and co-solvent system of these solvents and THF did not give satisfactory results, either. Therefore, the use of other Lewis acids than TBSOTf was next considered to promote the desired reaction. Various Lewis acids such as Ti(O*i*-Pr)₄, SnCl₄, BCl₃, Et₃Al, Et₂AlCl, BF₃·OEt₂ were tested in THF. Among them, the use of BF₃·OEt₂ gave the best result for the purpose. Upon further examining a variety of reaction solvents THF was mostly suitable. Thus, when the ylide **3b** was reacted with the model epoxide **4p** in the presence of BF₃·OEt₂ in THF at -78 °C, and the resulting intermediate was then treated with saturated aqueous NaHCO₃ solution at -78 °C to rt in the same reaction vessel, an epoxide opening product **6bp** was obtained in reasonable 62% yield together with some unidentifiable products.



Scheme 1



For **1-3** & **6-7**, **a**: $n = 1$, $R = \text{H}$; **b**: $n = 2$, $R = \text{H}$; **c**: $n = 2$, $R = \text{CH}_2\text{Ph}$

For **4-7**, **p**: $R^1=R^2 = \text{H}$; $R^3 = \text{CH}_2\text{Ph}$; **q**: $R^1=R^2 = \text{H}$; $R^3 = \text{CH}_2\text{CH}_3$; **r**: $R^1=R^2 = \text{H}$; $R^3 = (\text{CH}_2)_3\text{CH}_3$;

s: $R^1=R^2 = \text{H}$; $R^3 = \text{CH}_2\text{Cl}$; **t**: $R^1=R^2 = \text{H}$; $R^3 = (\text{CH}_2)_6\text{CH}=\text{CH}_2$; **u**: $R^2 = \text{H}$, $R^1 = R^3 = (\text{CH}_2)_4$;

v: $R^1=R^2 = \text{H}$; $R^3 = \text{Ph}$; **w**: $R^1 = \text{H}$, $R^2 = R^3 = \text{CH}_3$

Scheme 2

Encouraged by the successful epoxide ring-opening at the β -position of 2-cyclohexen-1-one **1b** with an epoxide **4p**, we have examined this four-step one pot process, *i.e.* (1) phosphoniosilylation with Ph_3P and TBSOTf, (2) ylide formation with $n\text{-BuLi}$, (3) epoxide opening reaction in the presence of $\text{BF}_3\cdot\text{OEt}_2$ and (4) desilylative elimination of Ph_3P , varying enones and epoxides (Scheme 2). We found that the epoxide ring-opening at the β -position of cyclic enones can be achieved successfully. The selected results are shown in Table 1 and demonstrate the efficacy and applicability of the process. This process works well in cyclopentenone and cyclohexenone series such as **1a-c**. With epoxides **4p-w** (entries 1-10) consisting of primary and secondary carbons, the alcohols **6a-c** were obtained as exclusive products in moderate to good yields (49-74%). The results indicate that the ring-opening reactions of epoxides **4** with ylides **3** in the presence of $\text{BF}_3\cdot\text{OEt}_2$ also proceed with high regioselectivities,⁶ similarly to the previously reported three-component coupling reactions of the ylides **3**, epoxides **4**, and THF in the presence of TBSOTf.⁵ Epoxides such as cyclohexene

Table 1. β -Epoxide Opening at the β -Position of Cyclic Enones in the presence of $\text{BF}_3\cdot\text{OEt}_2$

Entry	Starting material	Epoxide	Product ^a	Yield (%) ^b
1	1a	4p	6ap	65
2	1a	4r	6ar	73
3	1a	4s	6as	48
4	1b	4p	6bp	62
5	1b	4r	6br	72
6	1b	4s	6bs	49
7	1c	4p	6cp	62
8	1c	4q	6cq	74
9	1c	4s	6cr	62
10	1c	4w	6ct	64

^aAll products were characterized by ^1H NMR, ^{13}C NMR, IR, and mass spectroscopy. ^bOverall isolated yields.

oxide **4u**, styrene oxide **4v**, and 1,2-epoxy-2-methylpropane **4w** were also employed to the reaction sequence. However, the results attending this procedure were disappointing. Yields of products were very low (4-5%).⁶ Rather poorer results than those in three-component coupling process with these epoxides can be understood, considering the use of stronger Lewis acid $\text{BF}_3\cdot\text{OEt}_2$ in this process than TBSOTf used in the three-component coupling reaction process and the fact that epoxides can rearrange to carbonyl compounds under Lewis acidic conditions.⁷ Although acyclic enones, α,β -unsaturated lactones and esters were also tried to expand the applicability of this process, such efforts proved fruitless. Either no significant amounts or poor yields of products were obtained. Either lower reactivity of ylides or decomposition of epoxides and ylides might be responsible for such unsuccessful outcomes in those cases.

In summary, we have shown that epoxide opening reactions of ylides, derived from the phosphoniosilylation products of cyclic enones, can be successfully executed by the use of $\text{BF}_3\cdot\text{OEt}_2$ as a Lewis acid. The whole four-step one pot process provides an efficient tool for β -(2-hydroxy)alkylation of cyclic enones.

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