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# Tributylphosphine-catalyzed ring-opening reaction of epoxides and aziridines with acetic anhydride

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**Abstract**—Reactions of aziridines and epoxides with acetic anhydride catalyzed by an organophosphine provided the corresponding esters of β-amino alcohols and 1,2-diols in high yields, respectively. © 2003 Published by Elsevier Science Ltd.

Three-membered heterocyclic compounds such as epoxides and aziridines have become very popular in organic synthesis not only as building blocks, but also as synthetic intermediates.[1] The synthetic importance of aziridines and epoxides stems in large part from their facile and stereospecific nucleophilic ring opening with nucleophiles to furnish valuable 1,2-difunctional compounds.[2] For example, β-amino alcohols and 1,2-diols are useful intermediates in organic synthesis, and one of the most convenient ways to obtain these compounds is the ring-opening reactions of aziridines or epoxides by oxygen nucleophiles.[3] To date, alcohols and phenols are the most popular *O*-nucleophiles used in the ring opening reactions of epoxides and aziridines.[3a–d] However, the ether products were difficult to be converted into the corresponding free β-amino alcohols and 1,2-diols. In principal, the ring opening reactions using acid nucleophiles could provide β-amino alcohol esters and 1,2-diol esters, which were easier to be hydrolyzed,[4] but acidic or basic conditions were usually required to promote the reactions.

In previous studies,[5] we found that organophosphines remarkably promoted the ring opening reactions of aziridines and epoxides with various nucleophiles. Based upon these results, we envisioned that the activa-

**Table 1.** The tributylphosphine catalyzed ring opening of aziridines **1** with acetic anhydride


**1** **2** **3**

| Entry | Substrate | $R^1$ and $R^2$ | $R^3$ | Time (h) | Product[a] | Yield[b] |
|---|---|---|---|---|---|---|
| 1 | **1a** | $-(CH_2)_4-$ | Tosyl | 24 | **2a** | 85 |
| 2 | **1b** | $-(CH_2)_3-$ | Tosyl | 24 | **2b** | 80 |
| 3 | **1c** | Ph, H | Tosyl | 12 | **2c**, **3c** | 76 (65:35) |
| 4 | **1d** | $-(CH_2)_4-$ | -COPh | 24 | **2d** | 72 |
| 5 | **1e** | $-(CH_2)_4-$ | Boc | 48 | **2e** | 81 |
| 6 | **1f** | $-(CH_2)_5-$ | Tosyl | 48 | **2f** | 75 |
| 7 | **1g** | $n$-$C_4H_9$, H | Tosyl | 24 | **2g**, **3g** | 89 (>95:5) |

[a] In addition to the products **2** and **3**, a little amount of corresponding *N*-acylation products was isolated.
[b] Isolated yield based on aziridine.

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tion of anhydride with a catalytic amount of a phosphine will facilitate the ring opening of aziridines or epoxides under neutral conditions.[6–8]

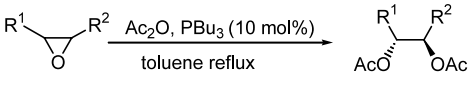
At the outset, we carried out the reaction of *N*-Tosyl aziridine **1a** with 2 equiv. of acetic anhydride in the presence of 10 mol% $Bu_3P$ in toluene at reflux and the ring-opened product was obtained in 85% yield (entry 1, Table 1). At lower temperature or in other solvents, such as $CH_3CN$, THF and $CH_2Cl_2$, more sluggish reactions were observed.

Various aziridines were used to test the catalytic ability of tributylphosphine in their ring-opening reactions with acetic anhydride (Table 1). In most cases, the corresponding β-amino alcohol esters were obtained in good to high yields. The reactivity of aziridines decreased along with the decrease of electron-withdrawing ability of the substituent on the nitrogen atom of aziridine. The reaction of phenyl substituted aziridine **1c** and the acyclic terminal aziridine **1g** predominantly occurred at the least-hindered carbon atom of substrates to give rise to the products in 65:35 and >95:5 ratio, respectively.

Tributylphosphine was also an effective catalyst for the reactions of epoxides with acetic anhydride to provide the corresponding 1,2-diol esters in high yields (Table 2). Control experiment showed that no reaction occurred in the absence of tributylphosphine. It was noted when 3-chloride epoxide **4g** was used as substrate, tributylphosphine did not react with carbon–chloride bond of substrate to form a phosphonium salt. The reaction provided 3-chloride-1,2-diol ester **5f** in high yield.

Both the β-amino alcohol ester **2a** and 1,2-diol ester **5b** were easily hydrolyzed to provide the corresponding β-amino alcohol and 1,2-diol in moderate yields (Eq. (1)).[9]

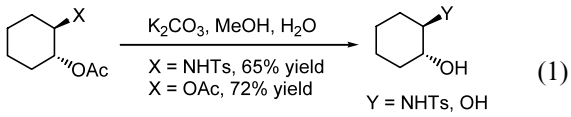
**Table 2.** The tributylphosphine catalyzed ring opening of epoxides **4** with acetic anhydride




**4** **5**

| Entry | Substrate | $R^1$ and $R^2$ | Product | Yield[a] |
|---|---|---|---|---|
| 1 | **4a** | Ph, H | **5a** | 98 |
| 2 | **4b** | $-(CH_2)_4-$ | **5b** | 92 |
| 3 | **4c** | $-(CH_2)_3-$ | **5c** | 94 |
| 4 | **4e** | *n*-$C_4H_9$, H | **5d** | 96 |
| 5 | **4f** | $CH_2{=}CHCH_2CH_2$, H | **5e** | 92 |
| 6 | **4g** | $ClCH_2$, H | **5f** | 96 |

[a] Isolated yield based on epoxide.




(1)

In our previous work,[5] we found that the organophosphine served as the nucleophile to attack aziridine or epoxide to form a phosphonium salt, which was supported by the corresponding signal at +34.4 ppm in the $^{31}P$ NMR spectrum. Vedejs also observed a signal at +32.9 ppm in the $^{31}P$ NMR spectrum of the mixture of $Bu_3P$ and acetic anhydride in $C_6D_6$ in the tributylphosphine-catalyzed acylation of alcohols by the anhydride.[7a] In our phosphine-catalyzed reactions of aziridines and epoxides with acetic anhydride, the $^{31}P$ NMR spectrum of the reaction mixture (0.1 mmol $Bu_3P$, 2 mmol $Ac_2O$ and 1 mmol aziridine **1a** in $C_6D_6$) showed a signal at +32.57 ppm as compared to the signal of tributylphosphine at −31.20 ppm. When 0.1 mmol of $Bu_3P$ and 1 mmol aziridine **1a** were mixed in $C_6D_6$ at 25°C, a signal at +34.74 ppm was observed ($Bu_3P$: −31.24 ppm). It is consistent with the direct attack of $Bu_3P$ at the aziridine to form the phosphonium salt. Under similar conditions, a signal at +32.53 ppm was recorded for the mixture of 0.1 mmol of $Bu_3P$ and 1 mmol acetic anhydride in $C_6D_6$ ($Bu_3P$: −31.24 ppm). According to the above evidence, a plausible mechanism was proposed (Scheme 1). Tributylphosphine activated anhydride, instead of the aziridine or epoxide, to form $R_3P^+C(O)CH_3$, $AcO^-$, which attacked the substrate to give the ring opening product with re-generation of $Bu_3P$ (Scheme 1).[10]

In conclusion, a new phosphine-catalyzed ring opening reaction of aziridines and epoxides with acetic anhydride has been developed, which provides a simple and convenient access to β-amino alcohols and 1,2-diols. Further investigations on the reactions by using organophosphines as the catalyst are underway.

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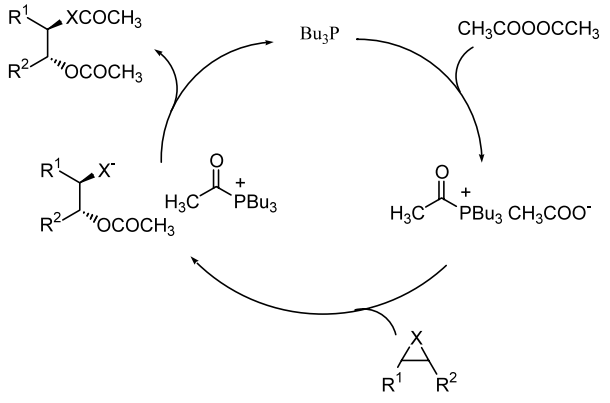


**Scheme 1.** A proposed mechanism.

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10. In the aziridine case, no signal of the hydrogen of amine was detected by $^1$H NMR after the reaction of aziridine **1a** with acetic anhydride. However, after work up and flash column chromatography, product **2a** was obtained in 85% yield. **2a**: Solid, mp: 118–120°C; $^1$H NMR ($CD_3Cl$) $\delta$ ppm; 1.10–1.50 (m, 4H), 1.51–1.71 (m, 2H), 1.75 (s, 3H), 1.86–1.98 (m, 1H), 1.99–2.15 (m, 1H), 2.45 (s, 3H), 3.15–3.29 (m, 1H), 4.51–4.61 (m, 1H), 4.86 (d, $J=7.6$ Hz, 1H, NH), 7.28–7.38 (m, 2H), 7.75 (d, $J=8.0$ Hz, 2H); EI-MS $m/z$ (%): 312 (($MH^+$) 10.15), 252 (40.11), 187 (73.40), 91 (100). Anal. for $C_{15}H_{21}NSO_4$. Calcd: C, 57.86; H, 6.80; N, 4.50. Found: C, 58.71; H, 7.04; N, 4.08.