OXIDATIVE SYNTHESES AND RING OPENING OF OXAZOLINES AND RELATED COMPOUNDS BY AMMONIUM TRIBROMIDE

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Abstract – Oxidative syntheses and ring opening of oxazolines and related compounds with trimethylphenylammonium tribromide (phenyltrimethylammonium tribromide, PTAB) or pyridinium hydrobromide perbromide (PHPB) were summarized. PTAB and PHPB were effective for respective syntheses of oxazolines, dihydrooxazines, and 6-bromobenzothiazoles. PTAB was also available for the conversion of oxiranes to dioxanes in the presence of 1,3-propanediol. The oxidative ring opening of furans, oxazolines, and dioxanes to respective furanones, cyanomethyl esters, and hydroxypropyl esters with PTAB or PHPB was also described.

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1. INTRODUCTION

Trimethylphenylammonium tribromide (phenyltrimethylammonium tribromide, C₆H₅N⁺(Me)₃Br⁻, PTAB)¹ᵃ,¹ᵇ and pyridinium hydrobromide perbromide (C₅H₆N⁺Br₃⁻, PHPB)¹ᶜ,¹ᵈ are known to be convenient reagents for brominating the α-position of carbonyl compounds and for the addition of bromine to alkenes.²,³ As PTAB and PHPB have been much easier to handle and maintain the desired stoichiometry in comparison with bromine, the use of commercially available PTAB and PHPB has been more advantageous and attractive than that of bromine. PTAB-SbBr₃-Py (pyridine) was effective for oxidation of secondary alcohols to ketones.⁴ PHPB was also useful for the oxidative esterification of aromatic aldehydes and for the Tishchenko-like dimeric esterification of primary alcohols in water.⁵

Reaction of aldehydes with PTAB-NH₄OAc also afforded nitriles in good yields.⁷ Since oxidative syntheses of oxazolines and benzothiazoles with PTAB, PHPB have not been reported¹ᵇ,¹ᵈ we considered it interesting to find a convenient method for the syntheses of oxazolines and bromobenzothiazoles from aldehydes with PTAB and PHPB.⁸,⁹ Further, we were interested in the oxidative ring opening of alkoxyfurans,¹⁰ epoxides,⁶ dioxanes,¹¹ and oxazolines¹² to related products by PTAB or PHPB. This paper particularly describes the convenient reaction of aldehydes with PTAB or PHPB to oxazolines, dihydrooxazines, and bromobenzothiazoles. This review also presents the oxidative syntheses of furanones, dioxanes, cyanomethyl esters, and hydroxypropyl esters with PTAB or PHPB.

2. SYNTHESIS OF OXAZOLINES AND DIHYDROOXAZINES FROM ALDEHYDES

2-1. Synthesis of 2-Aryl-1,3-oxazolines from Aldehydes with PHPB in Water

Oxazolines are known to be important heterocycles for their biological activities⁸ᵃ,¹³ and for the synthesis of functional compounds as key intermediates.¹⁴,¹⁵ 2-Substituted 1,3-oxazoline derivatives have been well recognized as useful catalyst ligands in synthetic organic chemistry.¹⁵ Therefore, we were interested in convenient conversion of arylaldehydes to 2-aryl-1,3-oxazolines.

Though various useful methods for the syntheses of oxazolines have previously been reported, some of those methods involve disadvantages such as acidic conditions and the use of complex reagents in organic solvents. Investigating other convenient synthetic methods of oxazolines proved of value without using organic solvents in terms of economic benefit, environmental impact and safety. We reported the oxidation of alcohols to carbonyl compounds with PTPB. Further, Tishchienko-like dimeric esterification of primary aliphatic alcohols was reported with PTAB and PHPB in water. We also found that the
reaction of aldehydes and alcohols with PHPB in water afforded corresponding esters in previous papers.\textsuperscript{4,5}

\[
\text{ArCHO} + 2\text{-aminoethanol} \rightarrow \text{PHPB-H}_2\text{O} \rightarrow \text{Ar-N(O)}
\]

**Table 1.** Reaction of arylaldehydes and 2-aminoethanol with PHPB in H\textsubscript{2}O\textsuperscript{a}

<table>
<thead>
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<th>Run</th>
<th>Substrates</th>
<th>Oxazolines</th>
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</thead>
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<td>1b</td>
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<td>89</td>
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<tr>
<td>2</td>
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<td>2c</td>
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</tr>
<tr>
<td>3</td>
<td>1d</td>
<td>2d</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>1e\textsuperscript{b}</td>
<td>2e</td>
<td>81\textsuperscript{c}</td>
</tr>
<tr>
<td>5</td>
<td>1f\textsuperscript{b}</td>
<td>2f</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
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<td>2g</td>
<td>70\textsuperscript{d}</td>
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<table>
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<tr>
<td>8</td>
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<td>2i</td>
<td>85</td>
</tr>
<tr>
<td>9</td>
<td>1j</td>
<td>2j</td>
<td>58\textsuperscript{e}</td>
</tr>
<tr>
<td>10</td>
<td>1k</td>
<td>2k</td>
<td>92</td>
</tr>
<tr>
<td>11</td>
<td>1l</td>
<td>2l</td>
<td>72\textsuperscript{f}</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Substrates 1: 0.25 mmol; PHPB: 0.5 mmol; HO(CH\textsubscript{2})\textsubscript{2}NH\textsubscript{2}: 1.5 mmol; H\textsubscript{2}O: 6 mL; Temp: rt; Reaction time: 13-19 h.  
\textsuperscript{b} PHPB: 0.75 mmol.  
\textsuperscript{c} Recovered 1e: 16%.  
\textsuperscript{d} Hydroxyimine: 25%.  
\textsuperscript{e} Recovered 1j: 23%.  
\textsuperscript{f} Recovered 1l: 15%.

Therefore, we further studied preparing oxazolines 2 from aldehydes 1 and 2-aminoethanol with PHPB in H\textsubscript{2}O (Scheme 1).\textsuperscript{8a}
The reaction of aldehyde 1a and more than 2.0 molar equivalents of PHPB over 1a afforded oxazoline 2a in high yield. H2O and MeCN were more effective for the conversion of aldehyde to oxazoline than other solvents, hexane, MeOH, and CH2Cl2. H2O was particularly convenient and suitable for the conversion of 1a to 2a in view of the environmental impact and safety.

The reaction of various aromatic aldehydes under the same reaction conditions was carried out to elucidate the limitations and chemoselectivity for the conversion of aldehydes to 2-substituted 1,3-oxazolines by PHPB-H2O. The results are shown in Table 1.

The reaction of aldehydes 1b-1g expectedly took place to give the corresponding 1,3-oxazolines 2b-2g. p- and m-Tolualdehydes 1h and 1i were also converted to respective oxazolines 2h and 2i. The reaction of o-tolualdehyde 1j afforded a mixture of oxazoline 2j (58%) and recovered 1j (23%). Steric hindrance between formyl and methyl groups appeared to exert influence on the yield of 2j. 3,4-Dimethylbenzaldehyde 1k and 1-naphthaldehyde 1l were also converted to oxazolines 2k and 2l. In addition, the reaction of terephthalaldehyde 1m and isophthalaldehyde 1n with 3.0-4.0 molar equivalents of PHPB over dialdehydes 1m and 1n afforded the corresponding dioxazolines 2m and 2n in Scheme 2. On the contrary, phthalaldehyde was not converted to the corresponding dioxazoline under the same reaction conditions. The steric hindrance of two formyl groups in phthaldehyde inhibited generation of corresponding dioxazoline.

We further examined the reaction of other carbonyl compounds such as nonanal, cyclooctanone, acetophenone, and benzophenone with PHPB and 2-aminoalcohol. The reaction of nonanal afforded a complex mixture of recovered nonanal (ca. 50%) and respective hydroxyimine (ca. 20%) determined by 1H NMR analysis of crude products. The reaction of cyclooctanone also took place to give a mixture of hydroxyimine (22%) and recovered cyclooctanone (70%). The reaction of acetophenone similarly afforded a mixture of hydroxyimine (67%) and acetophenone (23%). Benzophenone (92%) was recovered unchanged under the same reaction conditions. Consequently, PHPB-H2O in the presence of the
2-aminoethanol system was chemoselective for the conversion of aromatic aldehydes to 2-substituted oxazolines. PHPB-H\(_2\)O system in the presence of 2-aminoethanol was confirmed to be an alternative convenient procedure for the conversion of aromatic aldehydes to 2-substituted 1,3-oxazolines without overoxidation to carboxylic acid.\(^8\text{a,13d}\)

The conversion of aldehyde to oxazoline with PHPB-Py-H\(_2\)O proceeds by a plausible mechanism illustrated in eq. 1 and Scheme 3.\(^{15p}\) First, the combination of PHPB and H\(_2\)O generated HO'Br\(^+\), HBr, and pyridinium hydrobromide (PyHBr). Nitrogen of ii was attacked by Br\(^+\) and ii was led to ammonium bromide iii. Ammonium bromide iii attacked by HO was transformed into iv. Successive dehydrobromination of iv by HO' or Br' produced oxazoline 2.

\[
\text{PHPB} + \text{H}_2\text{O} \rightarrow \text{HO'Br}^+ + \text{HBr} + [\text{PyH}]^+\text{Br}^- \quad (\text{eq. 1})
\]

**Scheme 3.** Plausible reaction mechanism for oxazoline from aldehyde with PHPB-H\(_2\)O

2-2. Synthesis of 2-Heterocyclic 1,3-Oxazolines from Aldehydes with PTAB and Pyridine

Heterocyclic oxazolines are also useful for the synthesis of many functional compounds as key intermediates\(^{14,15}\) and ligands for excellent catalyst.\(^ {15}\) Many useful methods for the synthesis of heterocyclic oxazolines have been reported. We also carried out the synthesis of heterocyclic oxazolines. The reaction of 2-pyridinecarbaldehyde 3a and 6.0 molar ratio of 2-aminoethanol in the presence of 2.0 molar ratio of PHPB over 3a gave a mixture of 2-(oxazolin-2-yl)pyridine 4a and pyridine-2-N-(2-hydroxylethyl)carboxamide in H\(_2\)O. HBr was at least responsible for hydrolysis of oxazoline 4a to carboxamide. The yield of oxazoline 4a (67%) was not complete even in the presence of 2.0 molar ratio of Py over 3a for neutralizing HBr. We examined the reaction of 3a and 2-aminoethanol with PTAB instead of PHPB in H\(_2\)O. A mixture of oxazoline 3a (73%) and pyridine-2-N-(2-hydroxylethyl)carboxamide (18%) was afforded with PTAB-H\(_2\)O in the presence of Py.
Scheme 4

Table 2. Reaction of various aldehydes and 2-aminoethanol with PTAB-Py

<table>
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<th>Substrates</th>
<th>Oxazolines</th>
<th>Run</th>
<th>Substrates</th>
<th>Oxazolines</th>
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<td>3e</td>
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<td>6</td>
<td>3f</td>
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<td>3c</td>
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<td>3g</td>
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<tr>
<td>4</td>
<td>3d</td>
<td>4d 70</td>
<td></td>
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</tr>
</tbody>
</table>

<sup>a</sup> 3: 0.5 mmol; PTAB: 1.0 mmol; Py: 1.0 mmol; 2-aminoethanol: 3.3 mmol; MeOH: 6.0 mL; Temp: rt; Time: 21-23 h. <sup>b</sup> MeCN was used instead of MeOH.

The yield of 4a was generally low in H<sub>2</sub>O because PTAB was less soluble in H<sub>2</sub>O than other organic solvents. Therefore, the reaction of 3a and 2-aminoethanol with PTAB-Py was carried out in organic solvents such as hexane, DMSO, and CH<sub>2</sub>Cl<sub>2</sub>. In hexane or DMSO, the reaction of 3a and 2-aminoethanol with PTAB-Py afforded a mixture of 4a and 3a. As the yield of 4a was low in CH<sub>2</sub>Cl<sub>2</sub>, we tested the reaction of 3a and 2-aminoethanol with PTAB in other polar solvents such as MeOH and MeCN. In MeOH or MeCN, oxazoline 4a was expectedly obtained in good yields.

Consequently, we examined the reaction of various aldehydes and 2-aminoethanol with PTAB-Py under the same reaction conditions (Scheme 4). The results are shown in Table 2. The reaction of pyridinecarbaldehydes 3b, 3c, and 3d took place to give the corresponding 2-substituted 1,3-oxazolines 4b, 4c, and 4d. Quinolinecarbaldehydes 3e, 3f, and 3g were also converted to the corresponding (oxazolin-2-yl)quinolines 4e, 4f, and 4g. In addition, 2,6-pyridinedicarboxaldehyde 3h was converted to 2,6-bis(oxazolin-2-yl)pyridine 4h in Scheme 5. The reaction of 2-formylthiazole 3i similarly gave oxazoline 4i. Since oxazolines 4h and 4e have been well recognized as useful ligands such as Pybox and...
Quinox in synthetic organic chemistry, we demonstrated that PTAB-Py in MeOH or MeCN was an alternative method for conversion of pyridinecarbaldehydes and quinolinecarbaldehydes to respective 2-substituted 1,3-oxazolines.

To clarify the limitations of this method, we then investigated the reaction of aldehydes and 1-amino-2-butanol or 2-amino-1-butanol instead of 2-aminoethanol with PTAB-Py in Scheme 6. The results are summarized in Table 3. In the presence of 1-amino-2-butanol, the reaction of pyridinecarbaldehydes \(3a\), \(3b\), and \(3c\) afforded respective oxazolines \(5a\), \(5b\), and \(5c\). 6-Methyl-2-pyridinecarbaldehyde \(3d\) was also converted to oxazoline \(5d\). The reaction of quinolinecarbaldehydes \(3e\), \(3f\), and \(3g\) gave corresponding oxazolines \(5e\), \(5f\), and \(5g\).
Table 3. Reaction of various aldehydes and 1-amino-2-butanol or 2-amino-1-butanol with PTAB-Py

<table>
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</tr>
<tr>
<td>2</td>
<td>3b</td>
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</tr>
<tr>
<td>3</td>
<td>3c</td>
<td>5c</td>
<td>86</td>
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<tr>
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<tr>
<td>12</td>
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</table>

<sup>a</sup> 3: 0.5 mmol; PTAB: 1.0 mmol; Py: 1.0 mmol; 1-amino-2-butanol: 1.3-2.2 mmol; 2-amino-1-butanol: 2.2 mmol; MeOH: 6.0 mL; Temp: rt; Time: 21-23 h; MeOH: 6.0 mL; Temp: rt; Time: 18-23 h.

<sup>b</sup> MeCN was used instead of MeOH.

Scheme 7

Even in the presence of 2-amino-1-butanol, pyridinecarbaldehydes 3a, 3b, and 3c were similarly converted to corresponding oxazolines 6a, 6b, and 6c. Further, the reaction of quinolinecarbaldehydes 3f and 3g afforded respective oxazolines 6f and 6g. However, the yields of 6a and 6g were lower than those of isomers 5a and 5g. These results suggested that amino group of 2-amino-1-butanol hindered by ethyl and hydroxymethyl moieties resulted in less reactive than that of 2-aminoethanol and 1-amino-2-butanol.

In addition, the reaction of 2,6-pyridinedicarboxaldehyde 3h in the presence of 1-amino-2-butanol took place to give dioxazine 5h in Scheme 7. The reaction of 2-formylthiazole 3i with 1-amino-2-butanol also afforded oxazoline 5i. Accordingly, we established in the present study that PTAB-Py in the presence of
the 2-aminoethanol or 1-amino-2-butanol was an alternative method for transformation of various aldehydes into 2-substituted 1,3-oxazolines in MeOH or MeCN.

### 2-3. Synthesis of 1,3-Dihydrooxazines from Aldehydes with PHPB in Water

Dihydrooxazines have been prepared by cycloaddition between N-acyl imines and alkenes, or 1,4-dipolar cycloaddition between olefins and aminomethyl ions.\textsuperscript{16} In view of the previous synthesis of oxazolines from aldehydes and 2-aminoethanol with PHPB or PTAB,\textsuperscript{8} we extended to the synthesis of the six-membered homologous dihydrooxazine 7 from aldehyde and 3-aminopropanol instead of 2-aminoethanol with PHPB in H\textsubscript{2}O (Scheme 8).

![Scheme 8](image)

The reaction of aldehyde 1\textsubscript{a} and 5.2 molar ratio of 3-aminopropanol with 2.0 molar ratio of PHPB in the presence of 6.0 molar ratio of Na\textsubscript{2}CO\textsubscript{3} over 1\textsubscript{a} resulted in a one-step construction of dihydrooxazine 7\textsubscript{a} in water. The results of various dihydrooxazine synthesis with PHPB in the presence of Na\textsubscript{2}CO\textsubscript{3} or Py are summarized in Table 4. The reaction of aromatic aldehydes afforded respective dihydrooxazines. The reaction of 3-pyridinecarbaldehydes 3\textsubscript{b} and 4-quinolinecarbaldehyde 3\textsubscript{i} gave corresponding dihydrooxazines 7\textsubscript{p} and 7\textsubscript{q}. On the other hand, the reaction of 2-pyridinecarbaldehyde or 2-quinolinecarbaldehyde was liable to give N-(3-hydroxypropyl)carboxamides with PHPB-Na\textsubscript{2}CO\textsubscript{3} under the same reaction conditions. We suspected that 2-(2'-pyridydyl)-1,3-dihydrooxazine and 2-(2'-quinoliny1)-1,3-dihydrooxazine were easily hydrolyzed to N-(3-hydroxypropyl)carboxamides. Therefore, more strong base NaOMe than Na\textsubscript{2}CO\textsubscript{3} was expected to give N-(3-hydroxypropyl)carboxamide. The reaction of 2-pyridinecarbaldehyde 3\textsubscript{a} with PHPB and NaOMe in the presence of 3-aminopropanol afforded pyridine-2-N-(3-hydroxypropyl)carboxamide 8\textsubscript{a} in Scheme 9.
### Table 4. Reaction of electron-deficient arylaldehydes and 3-aminopropanol with PHPB$^a$

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<th>Time (h)</th>
<th>Products</th>
<th>Yield (%)</th>
<th>Run</th>
<th>Substrates</th>
<th>Additive</th>
<th>Time (h)</th>
<th>Products</th>
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<td>Py</td>
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<td>7i</td>
<td>76</td>
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<td>2</td>
<td>1b</td>
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<td>16</td>
<td>7b</td>
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</table>

$^a$Substrates: 0.25 mmol; 3-aminopropanol: 1.3 mmol; PHPB: 0.5 mmol; Additive: 1.5 mmol; H$_2$O: 6 mL; Temp: rt.$^b$Substrates: 0.5 mmol; 3-aminopropanol: 1.3 mmol; PHPB: 1.0 mmol; Na$_2$CO$_3$: 3.0 mmol; H$_2$O: 6 mL; Temp: rt.

### Scheme 9

\[
\begin{align*}
RCHO & \xrightarrow{1, 3} \text{3-aminopropanol} \\
& \xrightarrow{\text{PHPB-NaOMe}} \text{H} \xrightarrow{\text{N}} \xrightarrow{\text{OH}} \text{8} \\
3a: R &= 2\text{-pyridyl} \\
8a: R &= 2\text{-pyridyl} \\
3d: R &= 6\text{-methyl-2-pyridyl} \\
8d: R &= 6\text{-methyl-2-pyridyl} \\
3g: R &= 2\text{-quinolyl} \\
8g: R &= 2\text{-quinolyl} \\
1h: R &= 4\text{-methylphenyl} \\
8h: R &= 4\text{-methylphenyl} \\
1i: R &= 3\text{-methylphenyl} \\
8i: R &= 3\text{-methylphenyl} \\
1o: R &= \text{phenyl} \\
8o: R &= \text{phenyl}
\end{align*}
\]

Scheme 9
Table 5. Reaction of aldehydes and aminoalcohol with PHPB-NaOMe

<table>
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<th>Yield (%)</th>
<th>Run</th>
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<td>8g 67</td>
<td>6</td>
<td>1o</td>
<td>62</td>
<td>8o 75</td>
</tr>
</tbody>
</table>

a Substrates: 0.5 mmol; PHPB: 1.0 mmol; 3-Aminopropanol: 1.3 mmol; NaOMe: 4.0 mmol; H₂O: 6.0 mL; Temp: rt.

We further examined the reaction of other aldehydes with PHPB-NaOMe under the same reaction conditions. The results are shown in Table 5. The reaction of 3-pyridinecarbaldehyde 3d or 2-quinolinecarbaldehyde 3g gave corresponding N-(3-hydroxypropyl)carboxamides 8d or 8g. In addition, the reaction of aromatic aldehydes such as tolualdehydes 1h, 1i, and benzaldehyde 1o afforded N-(3-hydroxypropyl)carboxamides 8h, 8i, and 8o. We demonstrated that the reaction of aldehydes in the presence of NaOMe took place to give respective N-(3-hydroxypropyl)carboxamides. Accordingly, we confirmed that PHPB and Py or Na₂CO₃ in H₂O was an alternative method for the synthesis of dihydrooxazines from aldehydes and 3-aminopropanol.

3. SYNTHESIS OF 2-ARYL-6-BROMO-1,3-BENZOTHIAZOLES FROM ARYLALDEHYDES AND 2-AMINOTHIOPHENOL WITH PTAB IN THE PRESENCE OF ANTIMONY(III) BROMIDE

We found that PTAB and PHPB were convenient reagents for synthesis of oxazolines and dihydrooxazines as previously described. In view of previous work, we further investigated whether PTAB and PHPB were similarly effective for the synthesis of 1,3-benzothiazoles.

On the other hand, 2- or 6-substituted 1,3-benzothiazoles are important biologically active compounds in medicinal chemistry. Many synthetic procedures of 2- or 6-substituted 1,3-benzothiazoles have been reported. As 6-halogenated 1,3-benzothiazoles were useful as key intermediates for the syntheses of other intricate structure of 6-substituted 1,3-benzothiazoles, we examined the alternative synthesis of 6-bromo-1,3-benzothiazoles from aldehydes and 2-aminothiophenol with PTAB or PHPB.

We carried out the one pot synthesis of 6-bromo-1,3-benzothiazole 10 from aldehydes 1 and 2-aminothiophenol 9 with PTAB-SbBr₃-Py in CH₂Cl₂ in Scheme 10. The reaction of 4-bromophenylaldehyde 1a and 2-aminothiophenol 9 with PTAB and Py in the presence of a catalytic amount of SbBr₃ in CH₂Cl₂ afforded 6-bromobenzothiazole 10a. Of several other solvents
such as hexane, MeOH, DMSO and MeCN, MeCN also afforded 6-bromobenzothiazole 10a in good yield. In our further research for optimal reaction conditions, we found that the synthesis of 6-bromobenzothiazole 10a from 4-bromophenylaldehyde 1a and 2-aminophenol 9 with PTAB-SbBr₃-Py

**Scheme 10**

**Table 6.** Reaction of various aldehydes and 2-aminothiophenol 9 with PTAB-SbBr₃ in CH₂Cl₂

<table>
<thead>
<tr>
<th>Run</th>
<th>Substrates I</th>
<th>Time (h)</th>
<th>Products 10</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a: R = 4-bromophenyl</td>
<td>20</td>
<td>10a</td>
<td>82</td>
</tr>
<tr>
<td>2</td>
<td>1b: R = 3-bromophenyl</td>
<td>44</td>
<td>10b</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>1p: R = 2-bromophenyl</td>
<td>44</td>
<td>10p</td>
<td>67</td>
</tr>
<tr>
<td>4</td>
<td>1c: R = 4-chlorophenyl</td>
<td>20</td>
<td>10c</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>1d: R = 3-chlorophenyl</td>
<td>16</td>
<td>10d</td>
<td>82</td>
</tr>
<tr>
<td>6</td>
<td>1e: R = 2-chlorophenyl</td>
<td>14</td>
<td>10e</td>
<td>81</td>
</tr>
<tr>
<td>7</td>
<td>1o: R = phenyl</td>
<td>41</td>
<td>10o</td>
<td>90</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Run</th>
<th>Substrates I</th>
<th>Time (h)</th>
<th>Products 10</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>1h: R = 4-methylphenyl</td>
<td>47</td>
<td>10h</td>
<td>82</td>
</tr>
<tr>
<td>9</td>
<td>1i: R = 3-methylphenyl</td>
<td>47</td>
<td>10i</td>
<td>65</td>
</tr>
<tr>
<td>10</td>
<td>1j: R = 2-methylphenyl</td>
<td>47</td>
<td>10j</td>
<td>82</td>
</tr>
<tr>
<td>11</td>
<td>1k: R = 3,4-dimethylphenyl</td>
<td>18</td>
<td>10k</td>
<td>89</td>
</tr>
<tr>
<td>12</td>
<td>1q: R = 4-methoxyphenyl</td>
<td>20</td>
<td>10q</td>
<td>88</td>
</tr>
<tr>
<td>13</td>
<td>1r: R = 3,4-dimethoxyphenyl</td>
<td>20</td>
<td>10r</td>
<td>77</td>
</tr>
<tr>
<td>14</td>
<td>1l: R = octyl</td>
<td>20</td>
<td>10l</td>
<td>68</td>
</tr>
</tbody>
</table>

a Substrates I: 0.25 mmol; 2-aminothiophenol 9: 0.30 mmol; PTAB: 1.00 mmol; SbBr₃: 0.05 mmol; Py: 1.00 mmol; CH₂Cl₂: 6 mL; Temp: rt.
rest on the complemental function of PTAB, SbBr_3, and Py. We examined the reaction of various aldehydes and 2-aminothiophenol to elucidate the limitations of the PTAB-SbBr_3-Py system. The results are shown in Table 6. Various arylaldehydes such as bromobenzaldehydes, chlorobenzaldehyde, tolualdehydes, and 3,4-dimethylbenzaldehyde were found to be regioselectively converted to respective 6-bromobenzothiazoles. In addition, the reaction of naphthaldehyde also afforded 6-bromobenzothiazole. In contrast to arylaldehydes, the reaction of aldehydes such as 3-phenylpropanal _1s_, 2-phenylpropanal _1t_, nonanal _1u_, and acetaldehyde _1v_ afforded 6-bromobenzothiazoles in less satisfactory yields. As aliphatic aldehydes were easily brominated with PTAB, the reaction of aliphatic aldehydes afforded a complex mixture.

In addition, the reaction of _p_-chlorobenzaldehyde _1c_ and 2-aminothiophenol _9_ to examine the superiority of SbBr_3 was carried out with other metal halides such as SbCl_3, CuBr_2, NiBr_2, and ZnBr_2 under the same reaction conditions. Antimony halides SbBr_3, SbCl_3 were ascertained to be more effective for synthesis of 6-bromobenzothiazoles from arylaldehydes than those of CuBr_2, NiBr_2, and ZnBr_2.

Since antimony can possess both Sb^{3+} and Sb^{5+}, the reaction of antimony halides SbBr_3 or SbCl_3 with PTAB afforded SbBr_3 and SbCl_3Br_2 (eq. 2, 3). SbBr_3 then generated Br^+ and SbBr_4^- (eq. 4). Similarly, SbCl_3Br_2 generated Br^+ or SbCl_2Br^- (eq. 5). In the present our studies of synthesis of 1,3-benzothiazole, selective conversion of arylaldehydes to 6-bromobenzothiazoles by the combination of PTAB and SbBr_3 or SbCl_3 was supposed to proceed in Scheme 11. An electrophilic attack of aromatic ring on

---

**Scheme 11.** Plausible reaction mechanism for 2-aryl-6-bromobenzothiazole
benzothiazoline \( \text{ii} \) by \( \text{Br}^+ \) causes selective bromination at 6-position of benzothiazole ring, and successively produces bromo derivative \( \text{iv} \) after loss of proton by \( \text{SbBr}_4^- \) or \( \text{SbCl}_3\text{Br}^- \). After brominating at N atom of thiazoline \( \text{iv} \) by \( \text{Br}^+ \), 6-bromobenzothiazole was formed via oxidative dehydrobromination. Loss of proton from the intermediate bromine-containing cation \( \text{vi} \) results in additional formation of \( \text{SbBr}_3 \) as a catalyst.

4. CONVERSION OF AROMATIC EPOXIDES TO 2-ARYL-1,3-DIOXANE DERIVATIVES WITH PTAB IN THE PRESENCE OF ANTIMONY(III) BROMIDE

Several transformations of organic compounds with antimony halides as a catalyst have been developed.\(^{20,21}\) The combination of \( \text{SbCl}_3 \) and \( \text{LiAlH}_4 \) was reported to be more effective for the conjugate reduction of 2-butene-1,4-diones. The combination of \( \text{SbBr}_3 \) and \( \text{NaBH}_4 \) was also useful for the reductive debromination of aromatic \( \alpha \)-bromo ketones in comparison with those of \( \text{NaBH}_4 \) and other metal halides, \( \text{AlCl}_3 \), \( \text{CuCl}_2 \), \( \text{FeCl}_3 \).\(^{22a,22b}\) In addition, \( \text{SbCl}_3-\text{Bu}_4\text{NI} \) in the presence of \( \text{Na}_2\text{S}_2\text{O}_3 \) was also useful for the reductive ring-opening of 2,3-epoxy-1,4-butanedions to 2-hydroxy-1,4-butanediones.\(^{22c}\)

Similarly, the combination of PTAB and \( \text{SbBr}_3 \) was effective for synthesis of 6-bromobenzothiazoles described above. Therefore, there has been much interest in further applications for other organic synthesis with the combination of PTAB and antimony halides. As there are still continuing developments in the chemoselective acetalization of aldehyde and functional compounds,\(^{23}\) the PTAB-\( \text{SbBr}_3 \) system is expected to be an alternative method for the oxidative acetalization of oxiranes.

We carried out the transformation of trans-stilbene oxide \( 11 \) with PTAB-\( \text{SbBr}_3 \) in DMSO to 2-phenyl-1,3-dioxane \( 13a \) (Scheme 12).\(^6\)

\[
\text{Ph} \quad \text{O} \quad \text{Ph} \quad \text{PTAB-SBbr}_3 \quad \text{1,3-propanediol 12a} \quad \text{Ph} \quad \text{O} \quad \text{O} \\
11 \quad \text{13a} \quad 90\%
\]

Scheme 12

The reaction of trans-stilbene oxide \( 11 \) and 7.0 molar ratio of 1,3-propanediol \( 12a \) with 3.0 molar ratio of PTAB over \( 11 \) predominantly afforded 2-phenyl-1,3-dioxane \( 13a \) in the presence of a catalytic amount of \( \text{SbBr}_3 \) in DMSO. Both \( \text{SbBr}_3 \) and PTAB in the presence of 1,3-propanediol were confirmed to be essential for the oxidative conversion of epoxide \( 11 \) to 1,3-dioxane \( 13a \). DMSO also turned out to be the most useful solvent for the conversion of epoxide \( 11 \) to 1,3-dioxane \( 13a \) in various solvents. In addition, more than 2.0 molar equivalents of PTAB over epoxide \( 11 \) were necessary for conversion of \( 11 \) to \( 13a \). On the other hand, the reaction of cis-stilbene oxide with PTAB-\( \text{SbBr}_3 \) in the presence of 1,3-propanediol
afforded a mixture of 13a (9%) and hydrobenzoin (60%). The reaction of cis-stilbene oxide even at 55 °C for 2 h was not favorable for obtaining 1,3-dioxane 13a (45%). On the contrary, the reaction of trans-4-chlorostilbene oxide gave a mixture of 2-phenyl-1,3-dioxane 13a (81%) and 2-(4-chlorophenyl)-1,3-dioxane (81%) under the same reaction conditions. Consequently, trans-epoxides were more smoothly oxidized and converted to corresponding 1,3-dioxanes by this method than cis-epoxide isomers.

Table 7. Conversion of trans-stilbene oxide 11 to various 1,3-dioxanes 13 with PTAB-SbBr3 in DMSO

<table>
<thead>
<tr>
<th>Run</th>
<th>1,3-dios 12</th>
<th>Time</th>
<th>Products</th>
<th>Yields</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12b</td>
<td>6.0</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>12c</td>
<td>4.0</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>12d</td>
<td>6.0</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>12e</td>
<td>4.0</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>12f</td>
<td>2.5</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>12g</td>
<td>2.0</td>
<td>46</td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Conversion of trans-stilbene oxide 11 to various 1,3-dioxanes 13 with PTAB-SbBr3 in DMSO

<table>
<thead>
<tr>
<th>Run</th>
<th>1,3-dios 12</th>
<th>Time</th>
<th>Products</th>
<th>Yields</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12b</td>
<td>6.0</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>12c</td>
<td>4.0</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>12d</td>
<td>6.0</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>12e</td>
<td>4.0</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>12f</td>
<td>2.5</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>12g</td>
<td>2.0</td>
<td>46</td>
<td></td>
</tr>
</tbody>
</table>

In the presence of BiBr3, CuBr2, FeCl3, and CoCl2 instead of SbBr3, the reaction of 11 predominantly took place to give hydrobenzoin. In contrast, 1,3-dioxane 13a was obtained in 90% yield in the presence of SbCl3 instead of SbBr3 under the same reaction conditions. SbBr3 and SbCl3 were effective for the
conversion of stilbene oxide 11 to 1,3-dioxane 13a with PTAB in DMSO.

To test limitations and chemoselectivity of this acetalization to dioxane, we investigated the reaction of trans-stilbene oxide 11 and various 1,3-propanediols 12b-12g with PTAB-SbBr3 in DMSO. The results are shown in Table 7. Respective 1,3-dioxane derivatives 13b-13f were expectedly afforded under the same reaction conditions. The reaction of 11 and 2-phenyl-1,3-propanediol 12g gave 1,3-dioxane 13g. We confirmed that the system PTAB-SbBr3-DMSO in the presence of various 1,3-diols was useful for oxidative transformation of aromatic epoxides to respective 2-aryl-1,3-dioxanes.

We further performed the reaction of aromatic 1,2-diols 14 and 15 with PTAB-SbBr3 to examine the application of this method for other organic compounds in Scheme 13. The reaction of meso-hydrobenzoin 14 in the presence of 1,3-propanediol 12a gave 1,3-dioxane 13a. In addition, the reaction of 1,1,2-triphenyl-1,2-ethanediol 15 afforded the 1,3-dioxane 13a and benzophenone 16.

### Scheme 13

Moreover, we established that the reaction of 14 in the presence of various 1,3-diols 12b-12g took place to give corresponding 1,3-dioxanes 13b-13g. Similarly, the reaction of 1,1,2-triphenyl-1,2-ethanediol 15 afforded the respective 1,3-dioxanes 13b-13g and benzophenone 16. These results suggested that aldehyde was predominantly acetalized to 1,3-dioxanes with PTAB-SbBr3 in 1,3-propanediol. To make sure the chemoselectivity for acetalization, we carried out the following experiments with PTAB-SbBr3-DMSO in the presence of various alcohols. Benzaldehyde 1o was acetalized to 13a with PTAB-SbBr3 in the presence of 1,3-propanediol, while benzophenone 16 was not acetalized. Further, the reaction of benzaldehyde 1o in the presence of both methanol and 1,3-propanediol gave only 1,3-dioxane 13a without benzaldehyde dimethylacetal. Accordingly, we presumed that benzaldehyde dimethylacetal was easily transformed to 1,3-dioxane 13a with PTAB-SbBr3 in the presence of 1,3-propanediol. These results accounted for the chemoselective acetalization of aldehyde to 1,3-dioxane by PTAB-SbBr3 in DMSO.

In the present study, we found that PTAB-SbBr3 in the presence of 1,3-propanediol was an oxidative
method for the transformation of aromatic epoxide and 1,2-ethanediol to 1,3-dioxanes without overoxidation to carboxylic acid in DMSO. We also showed that this system was an alternative mild and chemoselective procedure for acetalization of aldehydes to 1,3-dioxanes without dehydrating.

5. OXIDATIVE RING OPENING OF FURANES, OXAZOLINES, AND DIOXANES

5-1. Transformation of 3-Alkoxyfurans to 2-Alkoxy-3(2\text{H})-furanones or \textit{cis}-2-Alkoxy-2-butene-1,4-diones with PTAB

In the course of studies of oxidative syntheses of oxazolines, dihydrooxazines, 6-bromobenzothiazoles, and 1,3-dioxanes with PTAB or PHPB described above, we were interested in oxidative ring opening reaction of furans, oxazolines, and dioxanes with PTAB or PHPB.

On the other hand, novel antibiotics, antitumors, and antiinsection such as roseophilin, jatrophone, eremantholide, geiparvarine, and thiersinine possess 3-furanone, 2-butene-1,4-dione, and 3-alkoxyfuran moieties, respectively.\textsuperscript{24-29} Therefore, synthetic methods for the 3(2\text{H})-furanone, 3-alkoxyfuran, and 2-alkoxy-2-butene-1,4-dione skeletons have been developed.\textsuperscript{30-35} The classical approach to oxidative ring opening of furans with Br\textsubscript{2} in buffered methyl alcohol involves the preparation of the \(\alpha,\alpha\)-dimethoxydihydrofuran derivatives. Then, \(\alpha,\alpha\)-dimethoxydihydrofuran derivatives were hydrolyzed to enediones.\textsuperscript{24a,30} However, enediones and furans have been known to isomerize to \textit{tetra}-ring-opened \textit{bis}(\textit{trans}-enedione) or resinous substances under acidic conditions.\textsuperscript{30c} Therefore, the effective methods for the synthesis of 3(2\text{H})-furanones has been investigated.\textsuperscript{31} In contrast, the transformation of 3-alkoxyfurans to 3(2\text{H})-furanones has been little studied in comparison with conversion of furans to enediones or lactones.\textsuperscript{30,32-35}

We studied an oxidative ring opening of 3-alkoxyfurans to 3(2\text{H})-furanones or enediones with PTAB or PHPB. Both 3-alkoxy-2,5-diphenylfurans and 3-alkoxy-2,4,5-triphenylfurans were easily prepared from 1,4-diphenyl-2-butene-1,4-dione and 1,2,4-triphenyl-2-butene-1,4-dione. Therefore, we investigated the ring opening of 3-butoxy-2,5-diphenylfuran 17 and 3-butoxy-2,4,5-triphenylfuran 18 as representative furans to alkoxyfuranones with PTAB in Scheme 14.

At a 1:1 molar ratio of 3-butoxy-2,5-diphenylfuran 17 and PTAB in EtOH, 2-ethoxy-3(2\text{H})-furanone 19 was obtained. The reaction of 3-butoxy-2,4,5-triphenylfuran 18 with PTAB in ethyl alcohol similarly gave 2-ethoxy-3(2\text{H})-furanone 20.\textsuperscript{10a}
To clarify the limitations and chemoselectivity for ring opening of alkoxyfurans to furanones by PTAB and alcohols, we further investigated the reaction of 3-alkoxy-2,4,5-triphenylfurans to 2-alkoxy-3(2H)-furanones with PTAB in various alcohols. In isopropyl alcohol, steric hindrance of the isopropoxy group exerted an influence on the yields of 2-isopropoxy-3(2H)-furanone. We presumed bulky isopropoxyl group caused lower yield of 2-isopropoxy-3(2H)-furanone than that of 2-ethoxy-3(2H)-furanones \[19\] or \[20\]. To validate to steric effect of alcohol, we investigated that the oxidation of 3-alkoxy-2,5-diphenylfuran and 3-alkoxy-2,4,5-triphenylfuran with PTAB in \(\text{t-BuOH}\) in Scheme 15.

The reaction of 3-butoxy-2,5-diphenylfuran \[17\] with an equivalent molar of PTAB over \[17\] in \(\text{t-BuOH}\) afforded 1,4-diphenyl-2-hydroxy-2-butene-1,4-dione \[21\]. 2-Butoxyenedione, 2-\(\text{t-BuO}\)-butoyenedione, and 2-\(\text{t-BuO}\)-3(2H)-furanone were not produced. Further, the reaction of 3-butoxy-2,4,5-triphenylfuran \[18\] with PTAB in \(\text{t-BuOH}\) took place to give 2-hydroxy-2,4,5-triphenyl-3(2H)-furanone \[22\]. 2-\(\text{t-BuO}\)-butoy-3(2H)-furanone, 2-butoxy-1,3,4-triphenyl-2-butene-1,4-dione, and 2-\(\text{t-BuO}\)-butoxy-1,3,4-triphenyl-2-butene-1,4-dione were not observed with PTAB in \(\text{t-BuOH}\).\[10\] These results indicated that PTAB in \(\text{t-BuOH}\) caused the cleavage of ethers to alcohols. We confirmed that bulky \(\text{t-BuO}\) did not attack at 2-possession of...
hemiacetal carbon of hydroxyfuranone and 2-hydroxyl group of cis-enedione.

In various alcohols such as MeOH, EtOH, iso-PrOH, and iso-BuOH, 3-alkoxy-2,5-diphenylfurans and 3-alkoxy-2,4,5-triphenylfurans turned out to be converted to corresponding 2-alkoxy-3(2H)-furanones with PTAB. We assumed that polar protic solvents promoted cyclization of cis-alkoxyenediones to 2-alkoxy-3(2H)-furanones as follows. cis-Alkoxyenediones derived from alkoxyfurans with PTAB were converted to cis-hydroxyenediones by the cleavage of ethers. Then, the cyclization of cis-hydroxyenedione by RO\(^-\) gave 2-hydroxy-3(2H)-furanone. Successive acetalization of 2-hydroxy-3(2H)-furanone by RO\(^-\) generated 2-alkoxy-3(2H)-furanone.

On the other hand, the ring opening of furans to enediones was achieved by using oxidative reagents such as pyridinium chlorochromate (PCC), \(m\)-chloroperbenzoic acid (\(m\)CPBA), magnesium monoperoxyphthalate, dioxirane, and methyltrioxorhenium/urea hydrogen peroxide.\(^{33-35}\) Further, a simple and convenient procedure for conversion of furans to cis- and trans-enediones was reported using Mo(CO)\(_6\)/cumyl hydroperoxide.\(^{35g}\) Therefore, we subsequently considered it interesting to examine other oxidative ring opening of 3-alkoxyfurans to alkoxyenediones with PTAB.

\[
\begin{array}{c}
\text{Ph} \quad \text{O} \quad \text{Bu} \\
\text{O} \\
\text{Ph} \\
\text{PTAB} \\
\text{DMSO} \\
\text{17} \\
\end{array}
\xrightarrow{\text{catalyst}}
\begin{array}{c}
\text{Ph} \quad \text{O} \quad \text{Bu} \\
\text{O} \\
\text{Ph} \\
\text{23} \\
\text{95\%} \\
\end{array}
\]

We carried out the oxidation of 3-butoxy-2,5-diphenylfuran \(17\) to cis-2-butoxyenedione \(23\) with PTAB in DMSO (Scheme 16).\(^{10}\) At the 1:1 molar ratio of \(17\) and PTAB, butoxyfuran \(17\) was transformed to cis-butoxyenedione \(23\) in THF-DMSO (\(v/v\) 2:1). In DMSO the reaction of \(17\) with an equal maolar equivalent of PTAB took place to give \(23\), whereas only in THF a mixture of cis-enedione \(23\) and recovered \(17\) was afforded. In \(\text{CH}_{2}\text{Cl}_2\) or DME the reaction of \(17\) similarly gave a mixture of \(17\) and \(23\) under the same reaction conditions. Consequently, we established that DMSO was an effective solvent for the oxidative ring opening of alkoxyfurans to alkoxyenediones with PTAB. Further, butoxyfuran \(17\) was recovered with \(\text{Bu}_4\text{NBr}\) or KBr in DMSO. We ascertained that PTAB was essential for the ring opening of alkoxyfurans to alkoxyenediones. The optimum conditions for obtaining cis-alkoxyenediones are needed to use DMSO as a solvent and an equal molar equivalent of PTAB over alkoxyfuran.

To test the limitation and chemoselectivity for oxidative ring opening of furans to enediones with PTAB, we then carried out the reaction of various 3-alkoxy-2,5-diphenylfurans with PTAB in THF-DMSO or DMSO. We found that the reaction of 3-alkoxyfurans with PTAB in THF-DMSO afforded respective
cis-2-alkoxyenediones without producing resinous substances. On the contrary, 2,5-diphenylfuran, 2,3,5-triphenylfuran, and 3-acetyl-2,5-diphenylfuran were recovered unchanged with PTAB in DMSO. These results indicated that an electron density on furan ring of 3-alkoxy-2,5-diphenylfurans was enriched by medium electron releasing of 3-alkoxy moieties. Accordingly, oxidative ring opening of alkoxyfurans to alkoxyenediones with PTAB more easily proceeded than that of 2,5-diphenylfuran, 2,3,5-triphenylfuran, and 3-acetyl-2,5-diphenylfuran. In the present study, we confirmed that the oxidation system PTAB in DMSO was an effective for ring opening of 3-alkoxyfurans to cis-alkoxyenediones. We demonstrated that PTAB in DMSO provided an alternative simple procedure for ring opening of 3-alkoxyfurans to cis-2-alkoxy-2-butene-1,4-diones as well as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) reported in the previous paper.\textsuperscript{10b,36}

The structure of cis-alkoxyenediones were determined on the basis of spectral data and NOE experiments. The stereochemistries of cis-alkoxyenediones were confirmed by the respective values of NOEs (11-18\%) observed between olefin proton and adjacent proton of oxygen atom on alkoxy group.\textsuperscript{36-38}

cis-2-Alkoxy-1,4-diphenyl-2-butene-1,4-diones can exist as the all s-cis conformer I illustrated in Scheme 17.\textsuperscript{39} A conformational equilibrium among all s-cis I, s-cis-trans II, and all s-trans III can be attained in cis-2-alkoxy-1,4-diphenyl-2-butene-1,4-diones. As the equilibrium distribution of the conformations I-III depends on the bulkiness of substituent at 1- and 4-positions,\textsuperscript{40} bulky 1,4-diphenyl substituents displace the equilibrium to all-cis form I.

\begin{equation}
\text{Ph} \quad \text{Ph} \quad \text{OR} \quad \text{O} \quad \text{O} \quad \text{Ph} \quad \text{Ph}
\end{equation}

\begin{equation}
\text{OR} \quad \text{O} \quad \text{O} \quad \text{Ph} \quad \text{Ph} \quad \text{OR}
\end{equation}

\text{all s-cis I} \quad \text{s-cis-trans II} \quad \text{all s-trans III}

\text{Scheme 17}

5-2. Conversion of 2-Substituted 1,3-Oxazolines to Cyanomethyl Esters with PHPB and Pyridine

We demonstrated that PTAB was an alternative effective regent for oxidative ring opening of furans to furanones and 2-butene-1,4-diones. Therefore, PHPB or PTAB was expected to be useful for an oxidative ring opening of other compounds. We then investigated whether the oxidative ring opening of 1,3-oxazolines to esters or amides with PTAB or PHPB.
We studied the ring opening reaction of oxazoline 4 to cyanomethyl ester 24 in Scheme 18. The reaction of 2-(2’-pyridyl)-1,3-oxazoline 4a with 3.0-4.0 molar ratio of PHPB-Py gave cyanomethyl ester 24a in H2O. 12, 41 On the other hand, cyanomethyl esters have been known to be reactive enough to undergo transesterification, amidation, and aminoacylation in organic syntheses. 42 Aminoacylation of RNA derivatives such as 5’-phospho-2’-deoxyribocytidyl riboadenosines (pdCpA)42c,43 was achieved in high yield by transesterification of the active cyanomethyl esters. 41 Similarly, the reaction of active cyanomethyl ester intermediates afforded tertiary amine-bearing esters 44 and poly(aminoo)ester dendrimers. 42e, 45 Therefore, we further studied the ring opening of oxazolines to cyanomethyl esters in detail. In the presence of 3.0 molar ratio of NaOMe, NaOAc, or NH4OAc instead of Py, the reaction of 1,3-oxazoline 4a with 3.0 molar ratio of PHPB in H2O took place to give N-hydroxyethylamide 25. Hydrolysis of oxazoline 4a afforded hydroxyamide 25. Hard acids and bases such as H+, MeO-, AcO- proceeded the conversion of oxazoline 4a to N-hydroxyethylamide 25. PHPB and Py were ascertained to need 3.0-4.0 molar equivalents over 4a for obtaining 24a without generating 25. Moreover, we found that the reaction of 4a with PHPB-Py afforded N-bromoethylcarboxamide 26 in CH2Cl2. These results

![Scheme 18](image-url)
indicated that the reaction of 4a with PHPB in aprotic solvent such as CH₂Cl₂ predominantly produced N-bromoethylcarboxamide 26.⁴⁶ In contrast to solvents such as hexane, MeOH, MeCN, and CH₂Cl₂, we confirmed that H₂O was the most suitable for ring opening of oxazoline to cyanomethyl ester with PHPB-Py. We further examined the reaction of other oxazolines with PHPB-Py to elucidate the limitations for conversion of oxazolines to cyanomethyl esters. The results are shown in Table 8. The respective reaction of 2-(3'-pyridyl)-1,3-oxazoline 4b and 2-(4'-pyridyl)-1,3-oxazoline 4c took place to give corresponding cyanomethyl esters 24b and 24c. 2-(6'-Methyl-2'-pyridyl)-1,3-oxazoline 4d was similarly converted to cyanomethyl esters 24d. 2-(2'-Quinolinyl)-1,3-oxazoline 4g and 2-(4'-quinolinyl)-1,3-oxazoline 4i were also converted to corresponding cyanomethyl esters 24g and 24i. Accordingly, we demonstrated that PHPB-Py-H₂O was useful for the ring opening of various oxazolines to cyanomethyl esters.

Further, we investigated the ring opening of aromatic oxazolines to clarify the chemoselectivity by this method. The results are summarized in Table 9.

Table 9. Reaction of aromatic oxazolines with PHPB-Pya

<table>
<thead>
<tr>
<th>Run</th>
<th>Substrates 2</th>
<th>Time (h)</th>
<th>Products 27</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>23</td>
<td>27a</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>2b</td>
<td>22</td>
<td>27b</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>2c</td>
<td>22</td>
<td>27c</td>
<td>94</td>
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<tr>
<td>4</td>
<td>2d</td>
<td>16</td>
<td>27d</td>
<td>90</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Run</th>
<th>Substrates 2</th>
<th>Time (h)</th>
<th>Products 27</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>2h</td>
<td>22</td>
<td>27h</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>2i</td>
<td>21</td>
<td>27i</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>2o</td>
<td>21</td>
<td>27o</td>
<td>93</td>
</tr>
</tbody>
</table>

a Substrates 2: 0.5 mmol; PHPB: 1.5 mmol; Py: 1.5 mmol; H₂O: 6.0 mL; Temp: rt.

b 2a: 0.5 mmol; PHPB: 2.0 mmol; Py: 2.0 mmol. c 2d: 0.5 mmol; PHPB: 1.0 mmol; Py: 1.0 mmol.
The reaction of 2-(4’-bromophenyl)-1,3-oxazoline 2a and 2-(3’-bromophenyl)-1,3-oxazoline 2b gave corresponding cyanomethyl esters 27a and 27b. The reaction of 2-(4’-chlorophenyl)-1,3-oxazoline 2c and 2-(3’-chlorophenyl)-1,3-oxazoline 2d afforded corresponding esters 27c and 27d. 2-(4’-Methylphenyl)-1,3-oxazoline 2h and 2-(3’-methylphenyl)-1,3-oxazoline 2i were also converted to respective cyanomethyl esters 27h and 27i. 2-Phenyl-1,3-oxazoline 2o was similarly converted to ester 27o. The present results suggested that the ring opening of aromatic oxazolines to cyanomethyl esters with PHPB-Py-H2O was not rested on electron donating or withdrawing substituents on aromatic ring. We herein demonstrated that PHPB-Py-H2O was also convenient for preparation of cyanomethyl esters from aromatic oxazolines.

The above mentioned observations suggest that the ring opening of oxazolines to cyanomethyl esters with PHPB-Py-H2O proceeds by a plausible mechanism illustrated in eq. 1, eq. 6, and Scheme 19. The combination of PHPB and H2O generated HO’Br+, HBr, and pyridinium hydrobromide (PyHBr). Then, nitrogen of oxazoline 2 was attacked by Br+ and lead to ammonium bromide i. Ammonium bromide i attacked by HO’ was transformed into ii. Successive bromination of ii by Br+ gave intermediate iii. Oxidative esterification step was proposed to enable for feasible route (iii → iv) in Scheme 19. Finally, dehydrobromination of iv by HO’ or Br’ produced cyanomethyl ester 27. Py neutralized an additional formation of HBr (eq. 6).12

![Scheme 19](image)

In the present study, we confirmed that PHPB-Py-H2O was an alternative oxidative procedure for the ring opening of various oxazolines to cyanomethyl esters without generating respective N-hydroxyethylcarboxamides, N-bromoethylcarboxamides, and carboxylic acids.
5-3. Conversion of Aromatic 1,3-Dioxanes to Aromatic Hydroxypropyl Esters with PHPB and Sodium Acetate

We showed that PHPB was an alternative reagent for oxidative ring opening of 1,3-oxazolines to cyanomethyl esters. Moreover, we previously reported convenient oxidative methods for esterification of aldehydes with PHPB in H₂O.⁵ Therefore, we then investigated whether the oxidative ring opening of 1,3-dioxanes to esters with PHPB.

On the other hand, 1,3-dioxanes are widely used protective groups for carbonyl compounds and vicinal diols.⁴⁷ In addition, the oxidation of 1,3-dioxanes provides important hydroxypropyl esters for serving as cross-linking agents for polyesters and fungicides.⁴⁸ Direct conversion of open-chain acetals, dioxanes, and dioxolanes to corresponding esters can be mediated by a variety of reagents such as ozone, molecular oxygen-Co(II), hypochlorous acid, potassium permanganate, N-hydroxyphthalimide in electrochemical oxidation, and tert-butylhydroperoxide in the presence of Pd(II), Ru(III), or pyridinium dichromate (PDC).⁴⁹,⁵⁰ We further examined the oxidative ring opening of 1,3-dioxanes 28 to hydroxypropyl esters 29 with PHPB and NaOAc in H₂O (Scheme 20).¹¹

Scheme 20

The reaction of 28a with 2.0 molar ratio of PHPB over 28a in the presence of 3.0 molar ratio of NaOAc, afforded a mixture of hydroxypropyl benzoate 29a and triester 30. We presumed that excess amounts of PHPB over 28a produced triester 30 by Tishchenko-like dimeric esterification of 29a in Scheme 21.¹¹
As we previously reported the mild oxidation of secondary alcohol with PTAB in MeOH, we examined the reaction of 28a in MeOH as a co-solvent. In H2O-MeOH, the reaction of 28a with 2.0 molar ratio of PHPB and 3.0 molar ratio of NaOAc expectedly afforded hydroxypropyl ester 29a without producing triester 30. In the present study, we ascertained that NaOAc and co-solvent MeOH suppressed deacetalization of 28a and Tishchenko-like dimeric esterification of 29a respectively. Moreover, diester 31 and methyl benzoate 32 were not afforded. Excess molar NaOAc over 28a was effective only for neutralizing the acidic conditions.

To elucidate the limitations for ring opening of 1,3-dioxanes to hydroxypropyl esters, we examined the reaction of other dioxanes with PHPB-NaOAc. The results of dioxanes are shown in Table 10.

Table 10. Reaction of dioxanes with PHPB-NaOAc

<table>
<thead>
<tr>
<th>Run</th>
<th>28</th>
<th>Time (h)</th>
<th>29</th>
<th>Yield (%)</th>
<th>Run</th>
<th>28</th>
<th>Time (h)</th>
<th>29</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>17</td>
<td>29b</td>
<td>87</td>
<td>7</td>
<td>28h</td>
<td>19</td>
<td>29h</td>
<td>78</td>
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<td>2</td>
<td>28c</td>
<td>19</td>
<td>29c</td>
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<td>29f</td>
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<td>11</td>
<td>28l</td>
<td>17</td>
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<td>93</td>
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<tr>
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<td>51</td>
<td></td>
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</tr>
</tbody>
</table>

*a 28: 0.5 mmol; PHPB: 1.0 mmol; NaOAc: 1.5 mmol; H2O: 4.0 mL; MeOH: 2.0 mL; Temp: rt. b 2-Bromobenzaldehyde; 31%. c 2-Chlorobenzaldehyde; 30%.
2-(4-Bromophenyl)-1,3-dioxane 28b, 2-(3-bromophenyl)-1,3-dioxane 28c, and 2-(2-bromophenyl)-1,3-dioxane 28d were similarly converted to respective hydroxypropyl esters 29b, 29c, and 29d. The reaction of 2-(4-chlorophenyl)-1,3-dioxane 28e, 2-(3-chlorophenyl)-1,3-dioxane 28f, and 2-(2-chlorophenyl)-1,3-dioxane 28g gave respective hydroxypropyl esters 29e, 29f, and 29g. The reaction of both 2-(2-bromophenyl)-1,3-dioxane 28d and 2-(2-chlorophenyl)-1,3-dioxane 28g possessing ortho halogen substituent of aryl moieties, afforded 29d and 29g in lower yields than those of 29b, 29c, 29e, and 29f. These results suggested that deacetalization of 28d and 28g proceeded faster than that of ring opening to hydroxypropyl ester to relieve the steric interaction between acetal and bulky halogen substituents on aryl moieties. The reaction of dioxanes 28h, 28i, and 28j also gave respective esters 29h, 29i, and 29j. In the present study, the ring opening of aromatic 1,3-dioxanes to hydroxypropyl esters by PHPB-NaOAc was not rested on electron donating or withdrawing substituents on aromatic ring. Moreover, 2-(2-phenylethyl)-1,3-dioxane 28k and 2-(1-phenylethyl)-1,3-dioxane 28l were similarly converted to corresponding esters 29k and 29l.

![Diagram](image)

**Scheme 22.** Plausible reaction mechanism for 1,3-dioxane 28 to 3-hydroxypropyl ester 29

The above mentioned observations suggested that the ring opening of 1,3-dioxane 28 to hydroxypropyl ester 29 with PHPB-NaOAc proceeded as follows illustrated in Scheme 22. The reaction of PHPB and NaOAc generated Br⁺, AcO⁻, NaBr, and pyridinium hydrobromide. Then, oxygen of dioxane was attacked by Br⁺. Dehydrobromination of i by Br⁻ afforded ii. Hemiacetalization of ii by H₂O produced intermediate iii. Oxidative esterification step was proposed to enable for feasible route (iii → iv → v). Finally, hydroxypropyl ester 29 was produced by H⁺ or H₂O.

We demonstrated that the system PHPB-NaOAc in H₂O-MeOH provides an alternative oxidative method for ring opening of 1,3-dioxanes to hydroxypropyl esters.
6. CONCLUSION

We herein showed that PTAB and PHPB were useful for oxidative syntheses of various compounds such as oxazolines, dihydrooxazines, bromobenzothiazoles, and dioxanes. We also demonstrated that PTAB and PHPB were alternative oxidative reagents for the ring opening of oxiranes, alkoxyfurans, oxazolines, and dioxanes to respective dioxanes, furanones, cyanomethyl esters, and hydroxypropyl esters. We presumed that those oxidative reactions proceeded via bromination of substrates by Br⁺ in Schemes 3, 11, 19, and 22. Brominated intermediates were successively oxidized to corresponding compounds by dehydrobromination with Br⁻, OH⁻, or RO⁻.

As α-position of aliphatic carbonyl compounds have been brominated with PTAB or PHPB, each of those oxidative reactions was not applicable to the synthesis of aliphatic compounds. Accordingly, PTAB or PHPB were particularly effective for oxidative synthesis of aryl compounds. We established that PTAB and PHPB were convenient reagents for oxidative syntheses and ring opening of oxazolines and related compounds under the mild reaction conditions.

REFERENCES AND NOTES


41. Preliminary reports were presented by S. Sayama at the 95th Annual Meeting of Chemical Society of Japan, Funabashi, Japan, March, 2015 (ab., p. 1555) and the 45th Congress of Heterocyclic Chemistry, Tokyo, Japan, September, 2015 (ab., p. 67).


45. (a) J.-P. Genet, S. Thorimbert, and A.-M. Touzin, *Tetrahedron Lett.*, 1993, **34**, 1159; (b) P. Wipf and


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