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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, $C_6H_5N^+(Me)_3Br_3^-$, PTAB)[1a,1b] and pyridinium hydrobromide perbromide ($C_5H_6N^+Br_3^-$, 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-$SbBr_3$-Py (pyridine) was effective for oxaidation 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-NH_4OAc also afforded nitriles in good yields.[7]

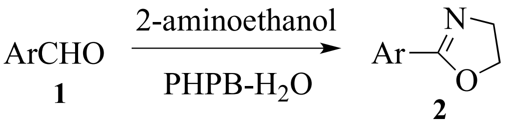
Since oxidative syntheses of oxazolines and benzothiazoles with PTAB, PHPB have not been reported,[1b,1d] we considered it interesting to find a convenient method for the syntheses of oxazolines and bromobenzothiazoles from aldehydes with PTAB and PHPB.[8,9] Further, we were interested in the oxidative ring opening of alkoxyfurans,[10] epoxides,[6] dioxanes,[11] and oxazolines[12] to related products by PTAB or PHPB. This paper particularly describes the convenient reaction of aldehydes with PTAB or PHPB to oxazolines, dihydooxazines, 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 activities[8a,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.[4,5]



1a: Ar = 4-bromophenyl
1b: Ar = 3-bromophenyl
1c: Ar = 4-chlorophenyl
1d: Ar = 3-chlorophenyl
1e: Ar = 2-chlorophenyl
1f: Ar = 4-nitrophenyl
1g: Ar = 2-nitrophenyl
1h: Ar = 4-methylphenyl
1i: Ar = 3-methylphenyl
1j: Ar = 2-methylphenyl
1k: Ar = 3,4-dimethylphenyl
1l: Ar = 1-naphthyl

2a: Ar = 4-bromophenyl
2b: Ar = 3-bromophenyl
2c: Ar = 4-chlorophenyl
2d: Ar = 3-chlorophenyl
2e: Ar = 2-chlorophenyl
2f: Ar = 4-nitrophenyl
2g: Ar = 2-nitrophenyl
2h: Ar = 4-methylphenyl
2i: Ar = 3-methylphenyl
2j: Ar = 2-methylphenyl
2k: Ar = 3,4-dimethylphenyl
2l: Ar = 1-naphthyl

Scheme 1

Table 1. Reaction of arylaldehydes and 2-aminoethanol with PHPB in H_2O[a]

Run	Substrates	Oxazolines		Run	Substrates	Oxazolines	
	1	**2**	(%)		**1**	**2**	(%)
1	**1b**	**2b**	89	7	**1h**	**2h**	87
2	**1c**	**2c**	95	8	**1i**	**2i**	85
3	**1d**	**2d**	90	9	**1j**	**2j**	58[e]
4	**1e**[b]	**2e**	81[c]	10	**1k**	**2k**	92
5	**1f**[b]	**2f**	95	11	**1l**	**2l**	72[f]
6	**1g**	**2g**	70[d]				

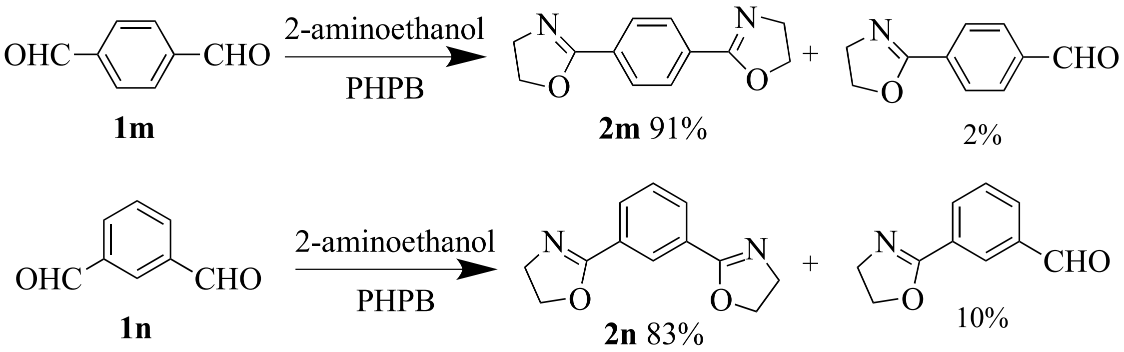
[a] Substrates **1**: 0.25 mmol; PHPB: 0.5 mmol; $HO(CH_2)_2NH_2$: 1.5 mmol; H_2O: 6 mL; Temp: rt; Reaction time: 13-19 h.
[b] PHPB: 0.75 mmol. [c] Recovered **1e**: 16%. [d] Hydroxyimine: 25%.
[e] Recovered **1j**: 23%. [f] Recovered **1l**: 15%.

Therefore, we further studied preparing oxazolines **2** from aldehydes **1** and 2-aminoethanol with PHPB in H_2O (Scheme 1).[8a]

The reaction of aldehyde **1a** and more than 2.0 molar equivalents of PHPB over **1a** afforded oxazoline **2a** in high yield. H_2O and MeCN were more effective for the conversion of aldehyde to oxazoline than other solvents, hexane, MeOH, and CH_2Cl_2. H_2O was particularly convenient and suitable for the conversion of **1a** to **2a** in view of the enviromental 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-H_2O. 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.



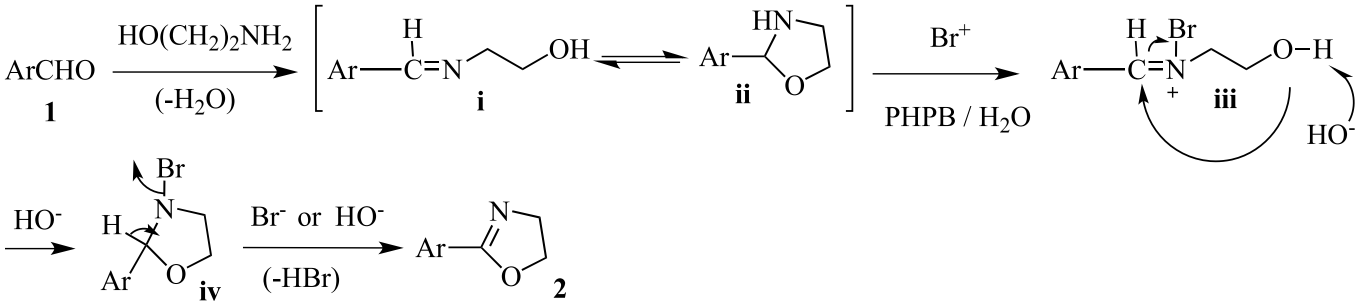
Scheme 2

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 hydoxyimine (ca. 20%) determined by ^{1}H 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-H_2O in the presence of the

2-aminoethanol system was chemoselective for the conversion of aromatic aldehydes to 2-substituted oxazolines. PHPB-H_2O 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.[8a,13d]

The conversion of aldehyde to oxazoline with PHPB-Py-H_2O proceeds by a plausible mechanism illustrated in eq. 1 and Scheme 3.[15p] First, the combination of PHPB and H_2O 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**.

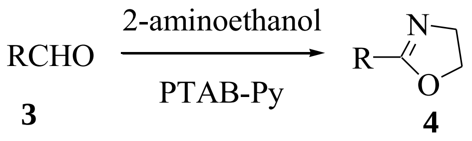
$PHPB + H_2O \longrightarrow HO^-Br^+ + HBr + [PyH]^+Br^-$ (eq. 1) PHPB: $[PyH]^+Br_3^-$; Py: pyridine



Scheme 3. Plausible reaction mechanism for oxazoline from aldehyde with PHPB-H_2O

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_2O. 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_2O. A mixture of oxazoline **3a** (73%) and pyridine-2-*N*-(2-hydroxylethyl)carboxamide (18%) was afforded with PTAB-H_2O in the presence of Py.



3a: R = 2-pyridyl
3b: R = 3-pyridyl
3c: R = 4-pyridyl
3e: R = 2-quinolyl
3f: R = 3-quinolyl
3g: R = 4-quinolyl
3d: R = 6-methyl-2-pyridyl

4a: R = 2-pyridyl
4b: R = 3-pyridyl
4c: R = 4-pyridyl
4e: R = 2-quinolyl
4f: R = 3-quinolyl
4g: R = 4-quinolyl
4d: R = 6-methyl-2-pyridyl

Scheme 4

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

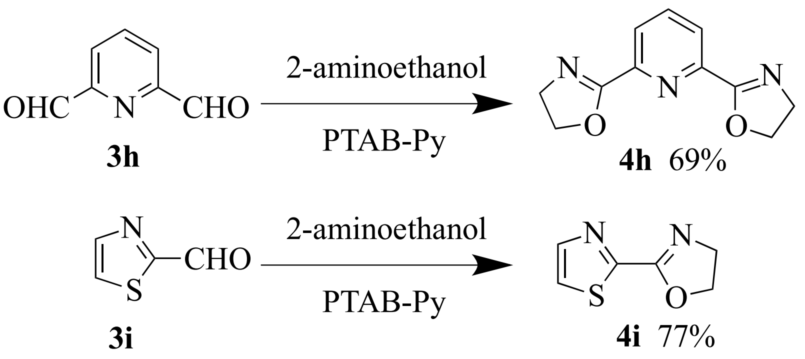
Run	Substrates 3	Oxazolines 4	(%)
1	**3a**[b]	**4a**	84
2	**3b**	**4b**	81
3	**3c**	**4c**	84
4	**3d**	**4d**	70
5	**3e**	**4e**	81
6	**3f**	**4f**	86
7	**3g**	**4g**	78

[a] **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. [b] MeCN was used instead of MeOH.

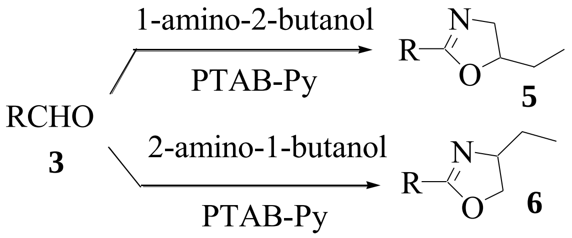
The yield of **4a** was generally low in H_2O because PTAB was less soluble in H_2O than other organic solvents. Therefore, the reaction of **3a** and 2-aminoethanol with PTAB-Py was carried out in organic solvents such as hexane, DMSO, and CH_2Cl_2. In hexane or DMSO, the reaction of **3a** and 2-aminoethanol with PTAB-Py afforded a mixture of **4a** and **3a.** As the yield of **4a** was low in CH_2Cl_2, 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 pyridincarbaldehydes and quinolinecarbaldehydes to respective 2-substituted 1,3-oxazolines.



Scheme 5



3a: R = 2-pyridyl
3b: R = 3-pyridyl
3c: R = 4-pyridyl
3d: R = 6-methyl-2-pyridyl
3g: R = 2-quinolyl
3h: R = 3-quinolyl
3i: R = 4-quinolyl

5a: R = 2-pyridyl
5b: R = 3-pyridyl
5c: R = 4-pyridyl
5d: R = 6-methyl-2-pyridyl
5g: R = 2-quinolyl
5h: R = 3-quinolyl
5i: R = 4-quinolyl

6a: R = 2-pyridyl
6b: R = 3-pyridyl
6c: R = 4-pyridyl
6h: R = 3-quinolyl
6i: R = 4-quinolyl

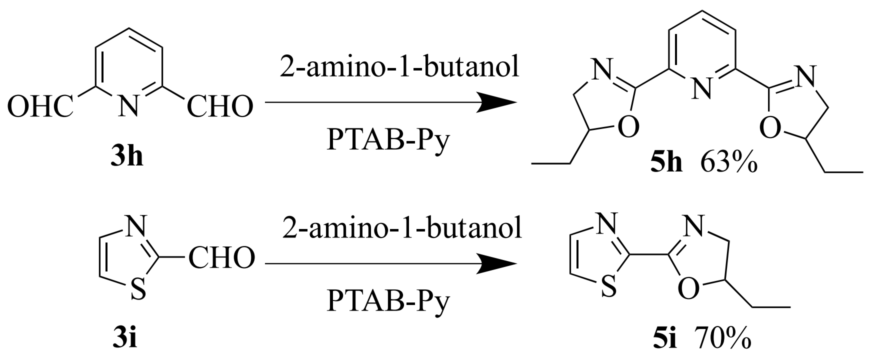
Scheme 6

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[a]

Run	Substrates **3**	Oxazolines	Yield (%)	Run	Substrate **3**	Oxazolines	Yield (%)
1	**3a**	**5a**	84	7	**3g**	**5g**	92
2	**3b**	**5b**	86	8	**3a**	**6a**	58
3	**3c**	**5c**	86	9	**3b**	**6b**	73
4	**3d**[b]	**5d**	75	10	**3c**	**6c**	73
5	**3e**	**5e**	83	11	**3f**	**6f**	75
6	**3f**	**5f**	81	12	**3g**	**6g**	55

[a] **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.
[b] MeCN was used instead of MeOH.



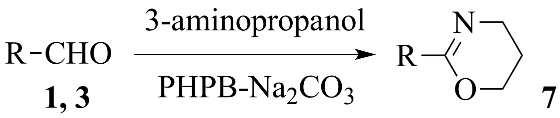
Scheme 7

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 hydoxymethyl 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 dioxazoline **5h** in Scheme 7. The reaction of 2-formylthiazole **3i** with1-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 iones.[16] In view of the previous synthesis of oxazolines from aldehydes and 2-aminoethanol with PHPB or PTAB,[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_2O (Scheme 8).



1a: R = 4-bromophenyl
1b: R = 3-bromophenyl
1c: R = 4-chlorophenyl
1d: R = 3-chlorophenyl
1f: R = 4-nitrophenyl
1h: R = 4-methylphenyl
1i: R = 3-methylphenyl
1k: R = 3,4-dimethylphenyl
1o: R = phenyl
3b: R = 3-pyridyl
3i: R = 4-quinolyl
7a: R = 4-bromophenyl
7b: R = 3-bromophenyl
7c: R = 4-chlorophenyl
7d: R = 3-chlorophenyl
7f: R = 4-nitrophenyl
7h: R = 4-methylphenyl
7i: R = 3-methylphenyl
7k: R = 3,4-dimethylphenyl
7o: R = phenyl
7p: R = 3-pyridyl
7q: R = 4-quinolyl

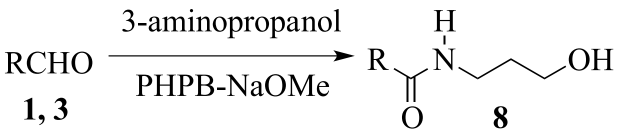
Scheme 8

The reaction of aldehyde **1a** 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_2CO_3 over **1a** resulted in a one-step construction of dihydrooxazine **7a** in water. The results of various dihydrooxazine synthesis with PHPB in the presence of Na_2CO_3 or Py are summarized in Table 4. The reaction of aromatic aldehydes afforded respective dihydrooxazines. The reaction of 3-pyridinecarbaldehydes **3b** and 4-quinolinecarbaldehyde **3i** gave corresponding dihydrooxazines **7p** and **7q**. On the other hand, the reaction of 2-pyridinecarbaldehyde or 2-quinolinecarbaldehyde was liable to give *N*-(3-hydoxypropyl)carboxamides with PHPB-Na_2CO_3 under the same reaction conditions. We suspected that 2-(2'-pyridydyl)-1,3-dihydrooxazine and 2-(2'-quinolinyl)-1,3-dihydrooxazine were easily hydrolyzed to *N*-(3-hydroxypropyl)carboxamides. Therefore, more strong base NaOMe than Na_2CO_3 was expected to give *N*-(3-hydroxypropyl)carboxamide. The reaction of 2-pyridinecarbaldehyde **3a** with PHPB and NaOMe in the presence of 3-aminopropanol afforded pyridine-2-*N*- (3-hydroxypropyl)carboxamide **8a** in Scheme 9.

Table 4. Reaction of electron-deficient arylaldehydes and 3-aminopropanol with PHPB[a]

Run	Substrates **1**	Additive	Time (h)	Products Yield (%)		Run	Substrates **1** or **3**	Additive	Time (h)	Products Yield (%)	
1	**1a**	Na_2CO_3	24	**7a**	87	7	**1i**	Py	14	**7i**	76
2	**1b**	Na_2CO_3	16	**7b**	83	8	**1k**	Na_2CO_3	15	**7k**	81
3	**1c**	Na_2CO_3	24	**7c**	81	9	**1o**	Py	14	**7o**	68
4	**1d**	Na_2CO_3	19	**7d**	80	10	**3b**	Na_2CO_3[b]	15	**7p**	74
5	**1f**	Py	46	**7f**	82	11	**3i**	Na_2CO_3[b]	15	**7q**	91
6	**1h**	Na_2CO_3	17	**7h**	70						

[a] Substrates: 0.25 mmol; 3-aminopropanol: 1.3 mmol; PHPB: 0.5 mmol; Additive: 1.5mmol; H_2O: 6 mL; Temp: rt. [b] Substrates: 0.5 mmol; 3-aminopropanol: 1.3 mmol; PHPB: 1.0 mmol; Na_2CO_3: 3.0 mmol; H_2O: 6 mL; Temp: rt.



1, 3

8

3a: R = 2-pyridyl
3d: R = 6-methyl-2-pyridyl
3g: R = 2-quinolyl
1h: R = 4-methylphenyl
1i: R = 3-methylphenyl
1o: R = phenyl

8a: R = 2-pyridyl
8d: R = 6-methyl-2-pyridyl
8g: R = 2-quinolyl
8h: R = 4-methylphenyl
8i: R = 3-methylphenyl
8o: R = phenyl

Scheme 9

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

Run	Substrates **3**	Time (h)	**8**	Yield (%)	Run	Substrates **1**	Time (h)	**8**	Yield (%)
1	**3a**	38	**8a**	90	4	**1h**	62	**8h**	75
2	**3d**	96	**8d**	89	5	**1i**	62	**8i**	73
3	**3g**	62	**8g**	67	6	**1o**	62	**8o**	75

[a] Substrates: 0.5 mmol; PHPB: 1.0 mmol; 3-Aminopropanol: 1.3 mmol; NaOMe: 4.0 mmol; H_2O: 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 Na_2CO_3 in H_2O was an alternative method for the synthesis of dihydrooxazines from aldehydes and 3-aminopropanol.

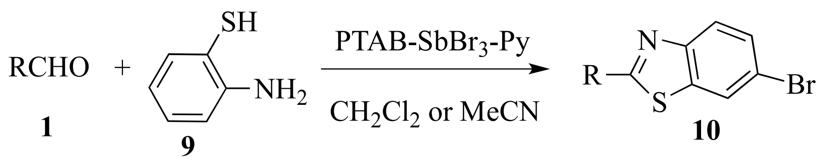
3. SYNTHESIS OF 2-ARYL-6-BROMO-1,3-BENZOTHIAZOLES FROM ARYLALDEHYDES AND 2-AMINOTHIOPHENOL WITH PTAB IN THE PRESENCE OF ANTIMONY(III) BROMIDE

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.[17,18] Many synthetic procedures of 2- or 6-substituted 1,3-benzothiazoles have been reported.[18,19] As 6-halogenated 1,3-benzothiazoles[19d] were useful as key intermediates for the syntheses of other intricate structure of 6-substituted 1,3-benzothiazoles,[17a] 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-$SbBr_3$-Py in CH_2Cl_2 in Scheme 10.[9]

The reaction of 4-bromophenylaldehyde **1a** and 2-aminothiophenol **9** with PTAB and Py in the presence of a catalytic amount of $SbBr_3$ in CH_2Cl_2 afforded 6-bromobenzothiazole **10a**. Of several other solvents



10a-e, 10h-l, 10o-v

1a: R = 4-bromophenyl
1b: R = 3-bromophenyl
1p: R = 2-bromophenyl
1c: R = 4-chlorophenyl
1d: R = 3-chlorophenyl
1e: R = 2-chlorophenyl
1o: R = phenyl
1h: R = 4-methylphenyl
1i: R = 3-methylphenyl
1j: R = 2-methylphenyl
1k: R = 3,4-dimethylphenyl
1q: R = 4-methoxyphenyl
1r: R = 3,4-dimethoxyphenyl
1l: R = 1-naphthyl
1s: R = 3-phenylpropyl
1t: R = 2-phenylpropyl
1u: R = octyl
1v: R = methyl

Scheme 10

Table 6. Reaction of various aldehydes and 2-aminothiophenol **9** with PTAB-SbBr$_3$ in CH$_2$Cl$_2$[a]

Run	Substrates **1**	Time	Products **10**		Run	Substrates **1**	Time	Products **10**	
	R	(h)	Yield (%)			R	(h)	Yield (%)	
1	**1a**	20	**10a**	82	8	**1h**	41	**10h**	65
2	**1b**	44	**10b**	82	9	**1i**	47	**10i**	84
3	**1p**	44	**10p**	67	10	**1j**	47	**10j**	79
4	**1c**	20	**10c**	82	11	**1k**	18	**10k**	89
5	**1d**	16	**10d**	82	12	**1q**	20	**10q**	88
6	**1e**	14	**10e**	81	13	**1r**	18	**10r**	77
7	**1o**	41	**10o**	90	14	**1l**	20	**10l**	68

[a] Substrates **1**: 0.25 mmol; 2-aminothiophenol **9**: 0.30 mmol; PTAB: 1.00 mmol; SbBr$_3$: 0.05 mmol; Py: 1.00 mmol; CH$_2$Cl$_2$: 6 mL; Temp: rt.

such as hexanae, 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-SbBr$_3$-Py 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.

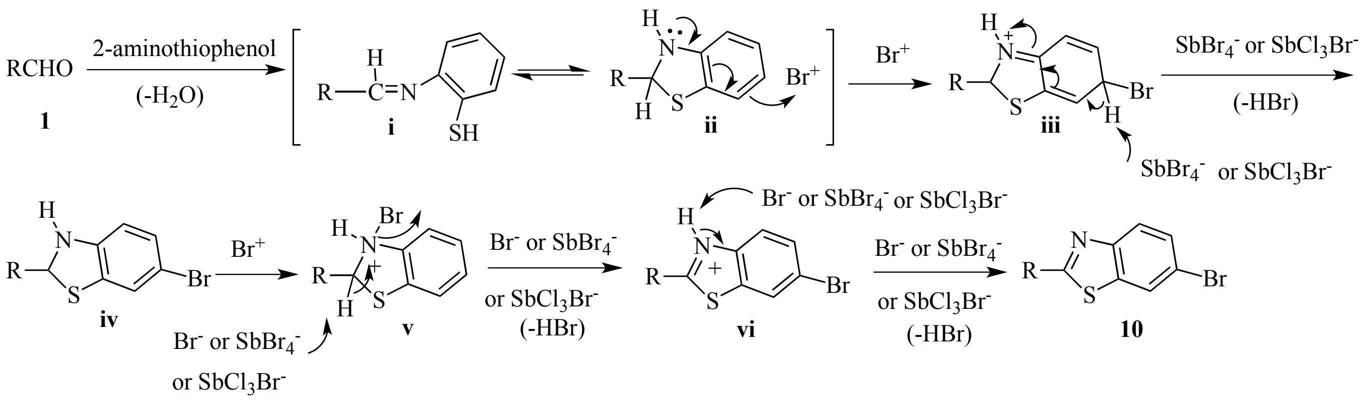
$$\text{PTAB: Ph(Me)}_3\overset{+}{\text{N}}\text{Br}_3{}^-$$

$$\text{PTAB} + \text{SbBr}_3 \rightarrow \text{Ph(Me)}_3\overset{+}{\text{N}}\text{Br}^- + \text{SbBr}_5 \qquad \text{(eq. 2)}$$

$$\text{PTAB} + \text{SbCl}_3 \rightarrow \text{Ph(Me)}_3\overset{+}{\text{N}}\text{Br}^- + \text{SbCl}_3\text{Br}_2 \qquad \text{(eq. 3)}$$

$$\text{SbBr}_5 \longrightarrow \overset{\delta+}{\text{Br}}\text{-}\overset{\delta-}{\text{Br}}\text{---SbBr}_3 \longrightarrow \text{Br}^+ + \text{SbBr}_4{}^- \qquad \text{(eq. 4)}$$

$$\text{SbCl}_3\text{Br}_2 \longrightarrow \overset{\delta+}{\text{Br}}\text{-}\overset{\delta-}{\text{Br}}\text{---SbBr}_3 \longrightarrow \text{Br}^+ + \text{SbCl}_3\text{Br}^- \qquad \text{(eq. 5)}$$



Scheme 11. Plausible reaction mechanism for 2-aryl-6-bromobenzothiazole

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 $ZnBr_2$.

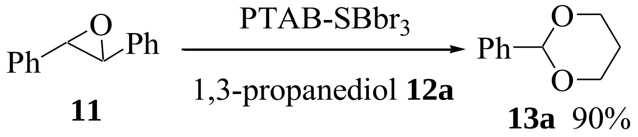
Since antimony can possess both Sb^{3+} and Sb^{5+}, the reaction of antimony halides $SbBr_3$ or $SbCl_3$ with PTAB afforded $SbBr_5$ and $SbCl_3Br_2$ (eq. 2, 3). $SbBr_5$ then generated Br^+ and $SbBr_4^-$ (eq. 4). Similarly, $SbCl_3Br_2$ generated Br^+ or $SbCl_2Br^-$ (eq. 5). In the present our studies of synthesis of 1,3-benzothaizole, 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 benzothiazoline **ii** by Br^+ causes selective bromination at 6-position of benzothiazole ring, and successively produces bromo derivative **iv** after loss of proton by $SbBr_4^-$ or $SbCl_3Br^-$. After brominating at N atom of thiazoline **iv** by Br^+, 6-bromobenzothaizole was formed via oxidative dehydrobromination. Loss of proton from the intermediate bromine-containing cation **vi** results in additional formation of $SbBr_3$ 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 $SbCl_3$ and $LiAlH_4$ was reported to be more effective for the conjugate reduction of 2-butene-1,4-diones. The combination of $SbBr_3$ and $NaBH_4$ was also useful for the reductive debromination of aromatic α-bromo ketones in comparison with those of $NaBH_4$ and other metal halides, $AlCl_3$, $CuCl_2$, $FeCl_3$.[22a,22b] In addition, $SbCl_3$-Bu_4NI in the presence of $Na_2S_2O_3$ 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 $SbBr_3$ 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-$SbBr_3$ system is expected to be an alternative method for the oxidative acetalization of oxiranes.

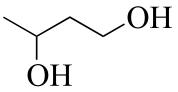
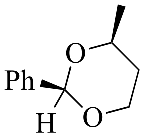
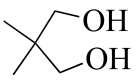
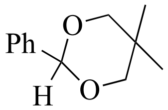
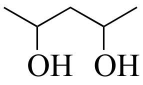
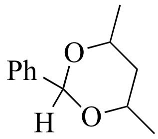
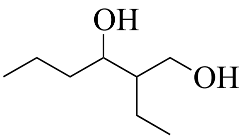
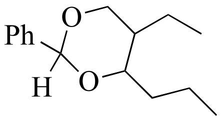
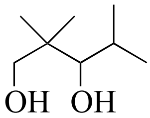
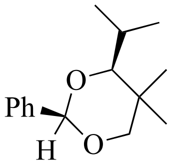
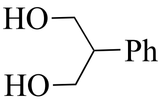
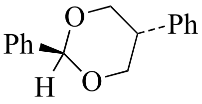
We carried out the transformation of *trans*-stilbene oxide **11** with PTAB-$SbBr_3$ in DMSO to 2-phenyl-1,3-dioxane **13a** (Scheme 12).[6]



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 $SbBr_3$ in DMSO. Both $SbBr_3$ 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-$SbBr_3$ 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-$SbBr_3$ in DMSO[a]

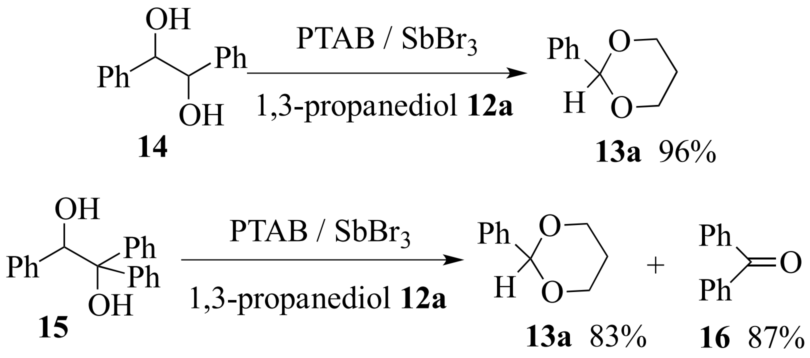
Run	1,3-diols **12**			Time	Products		Yields
	molar ratio / **11**			(h)	**13**		%
1		**12b**	6.0	43		**13b**	88
2		**12c**	4.0	39		**13c**	85
3		**12d**	6.0	40		**13d**	81
4		**12e**	4.0	39		**13e**	92
5		**12f**	2.5	46		**13f**	91
6		**12g**	2.0	46		**13g**	79

[a] Substrate **11**: 0.25 mmol; PTAB: 0.75 mmol; $SbBr_3$: 0.05 mmol; $PhCH_2(Et)_3NCl$: 0.25 mmol; DMSO: 8 mL; Temp: rt.

In the presence of $BiBr_3$, $CuBr_2$, $FeCl_3$, and $CoCl_2$ instead of $SbBr_3$, 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 $SbCl_3$ instead of $SbBr_3$ under the same reaction conditions. $SbBr_3$ and $SbCl_3$ 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-$SbBr_3$ 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-$SbBr_3$-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-$SbBr_3$ 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-$SbBr_3$ in 1,3-propanediol. To make sure the chemoselectivity for acetalization, we carried out the following experiments with PTAB-$SbBr_3$-DMSO in the presence of various alcohols. Benzaldehyde **1o** was acetalized to **13a** with PTAB-$SbBr_3$ 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-$SbBr_3$ in the presence of 1,3-propanediol. These results accounted for the chemoselective acetalization of aldehyde to 1,3-dioxane by PTAB-$SbBr_3$ in DMSO.

In the present study, we found that PTAB-$SbBr_3$ 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

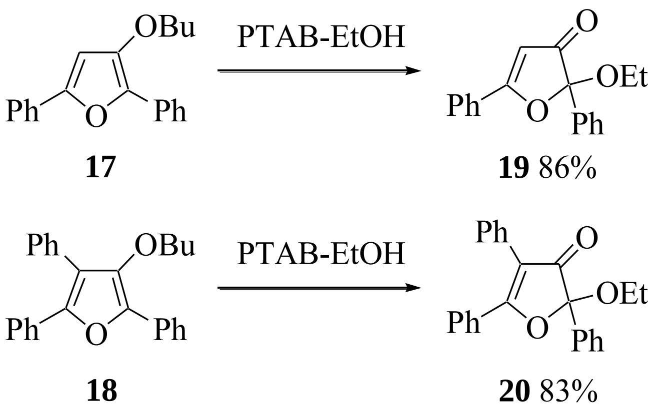
5-1. Transformation of 3-Alkoxyfurans to 2-Alkoxy-3(2*H*)-furanones or *cis*-2-Alkoxy-2-butene-1,4-diones with PTAB

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 furanes, 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.[24-29] Therefore, synthetic methods for the 3(2*H*)-furanone, 3-alkoxyfuran, and 2-alkoxy-2-butene-1,4-dione skeletons have been developed.[30-35] The classical approach to oxidative ring opening of furans with Br_2 in buffered methyl alcohol involves the preparation of the α,α-dimethoxydihydrofuran derivatives. Then, α,α-dimethoxydihydrofuran derivatives were hydrolyzed to enediones.[24a,30] However, enediones and furans have been known to isomerize to *tetra*-ring-opened *bis*(*trans*-enedione) or resinous substances under acidic conditions.[30c] Therefore, the effective methods for the synthesis of 3(2*H*)-furanones has been investigated.[31] In contrast, the transformation of 3-alkoxyfurans to 3(2*H*)-furanones has been little studied in comparison with conversion of furans to enediones or lactones.[30,32-35]

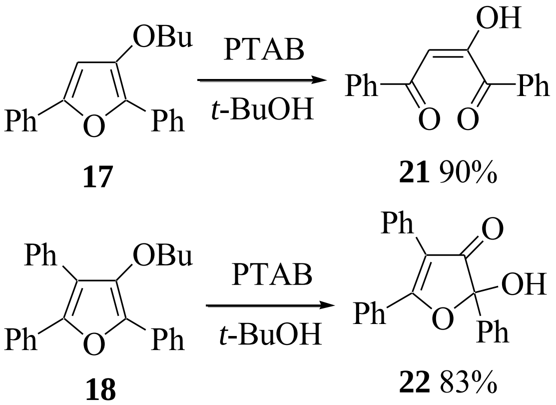
We studied an oxidative ring opening of 3-alkoxyfurans to 3(2*H*)-furanones or enediones with PTAB or PHPB. Both 3-alkoxy-2,5-diphenylfurans and 3-alkoxy-2,4,5-triphenylfurans were easily prepared from 1,4-diphenyl-2-butene-1,4-dione and 1,2,4-triphenyl-2-butene-1,4-dione. Therefore, we investigated 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*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*H*)-furanone **20**.[10a]



Scheme 14

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(2*H*)-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(2*H*)-furanone. We presumed bulky isopropoxyl group caused lower yield of 2-isopropoxy-3(2*H*)-furanone than that of 2-ethoxy-3(2*H*)-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 *t*-BuOH in Scheme 15.

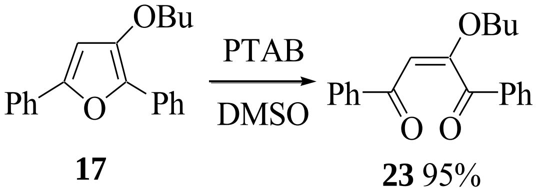


Scheme 15

The reaction of 3-butoxy-2,5-diphenylfuran **17** with an equivalent molar of PTAB over **17** in *t*-BuOH afforded 1,4-diphenyl-2-hydroxy-2-butene-1,4-dione **21**. 2-Butoxyenedione, 2-*t*-butoxyenedione, and 2-*t*-butoxy-3(2*H*)-furanone were not produced. Further, the reaction of 3-butoxy-2,4,5-triphenylfuran **18** with PTAB in *t*-BuOH took place to give 2-hydoxy-2,4,5-triphenyl-3(2*H*)-furanone **22**. 2-*t*-Butoxy-3(2*H*)-furanone, 2-butoxy-1,3,4-triphenyl-2-butene-1,4-dione, and 2-*t*-butoxy-1,3,4-triphenyl-2-butene-1,4-dione were not observed with PTAB in *t*-BuOH.[10b] These results indicated that PTAB in *t*-BuOH caused the cleavage of ethers to alcohols. We confirmed that bulky *t*-BuO$^-$ did not attack at 2-possition 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(2*H*)-furanone. Successive acetalization of 2-hydroxy-3(2*H*)-furanone by RO^- generated 2-alkoxy-3(2*H*)-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.



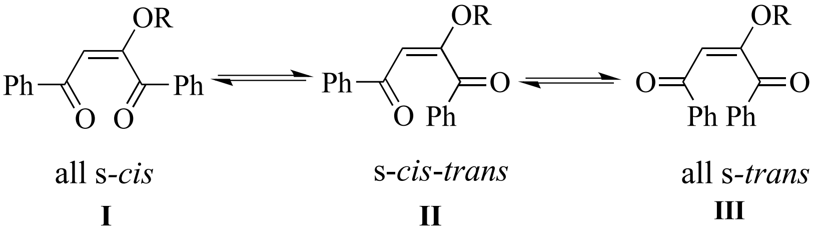
Scheme 16

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 CH_2Cl_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 Bu_4NBr 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.[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 alkoxyl group.[36-38]

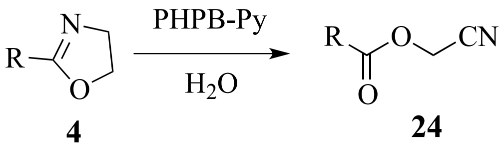
cis-2-Alkoxy-1,4-diphenyl-2-butene-1,4-diones can exist as the all s-*cis* conformer **I** illustrated in Scheme 17.[39] A conformational equilibrium among all s-*cis* **I**, s-*cis*-*trans* **II**, and all s-*trans* **III** can be attained in *cis*-2-alkoxy-1,4-diphenyl-2-butene-1,4-diones. As the equilibrium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



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.



4a: R = 2-pyridyl **4d**: R = 6-methyl-2-pyridyl **24a**: R = 2-pyridyl **24d**: R = 6-methyl-2-pyridyl

4b: R = 3-pyridyl **4g**: R = 2-quinolyl **24b**: R = 3-pyridyl **24g**: R = 2-quinolyl

4c: R = 4-pyridyl **4i**: R = 4-quinolyl **24c**: R = 4-pyridyl **24i**: R = 4-quinolyl

Scheme 18

Table 8. Reaction of various oxazolines with PHPB-Py[a]

Run	Substrates **4**	Time (h)	Products **24**	Yield (%)	Run	Substrates **4**	Time (h)	Products **24**	Yield (%)
1	**4b**	18	**24b**	90	4	**4g**	22	**24g**	93
2	**4c**	15	**24c**	59	5	**4i**	22	**24i**	90
3	**4d**	17	**24d**	93					

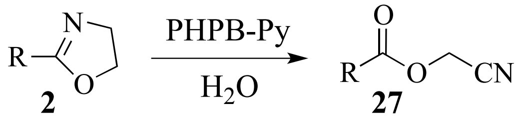
[a] **4**: 0.5 mmol; PHPB: 2.0 mmol; Py: 2.0 mmol; H_2O: 6.0 mL; Temp: rt.

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 H_2O.[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(amino)ester dendorimers.[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 NH_4OAc instead of Py, the reaction of 1,3-oxazoline **4a** with 3.0 molar ratio of PHPB in H_2O 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 CH_2Cl_2. These results indicated that the reaction of **4a** with PHPB in aprotic solvent such as CH_2Cl_2 predominantly produced *N*-bromoethylcarboxamide **26**.[46] In contrast to solvents such as hexane, MeOH, MeCN, and CH_2Cl_2, we confirmed that H_2O 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-H_2O 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-Py[a]



2a: R = 4-bromophenyl
2b: R = 3-bromophenyl
2c: R = 4-chlorophenyl
2d: R = 3-chlorophenyl
2h: R = 4-methylphenyl
2i: R = 3-methylphenyl
2o: R = phenyl

27a: R = 4-bromophenyl
27b: R = 3-bromophenyl
27c: R = 4-chlorophenyl
27d: R = 3-chlorophenyl
27h: R = 4-methylphenyl
27i: R = 3-methylphenyl
27o: R = phenyl

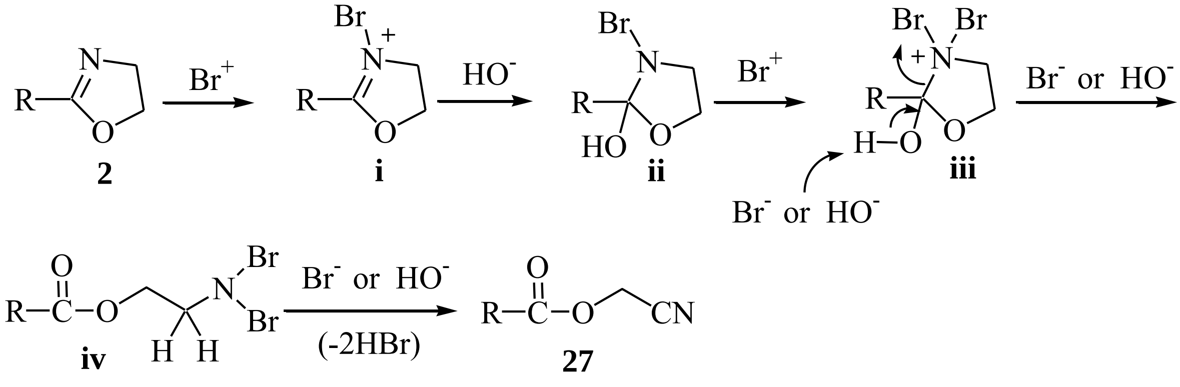
Run	Substrates **2** R	Time (h)	Products **27**	Yield (%)	Run	Substrates **2** R	Time (h)	Products **27**	Yield (%)
1	**2a**[b]	23	**27a**	94	5	**2h**	22	**27h**	90
2	**2b**	22	**27b**	93	6	**2i**	21	**27i**	93
3	**2c**	22	**27c**	94	7	**2o**	21	**27o**	93
4	**2d**[c]	16	**27d**	90					

[a] Substrates **2**: 0.5 mmol; PHPB: 1.5 mmol; Py: 1.5 mmol; H_2O: 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-H_2O 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-H_2O proceeds by a plausible mechanism illustrated in eq. 1, eq. 6, and Scheme 19. The combination of PHPB and H_2O 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]

$HBr + Py \longrightarrow PyHBr$ (eq. 6)



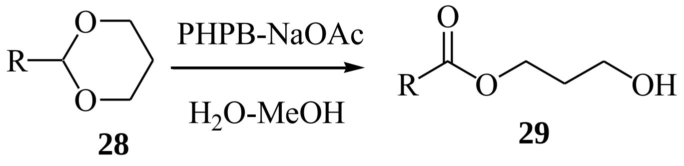
Scheme 19

In the present study, we confirmed that PHPB-Py-H_2O 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 regent 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 H_2O.[5] Therefore, we then investigated whether the oxidative ring opening of 1,3-dioxanes to esters with PHPB.

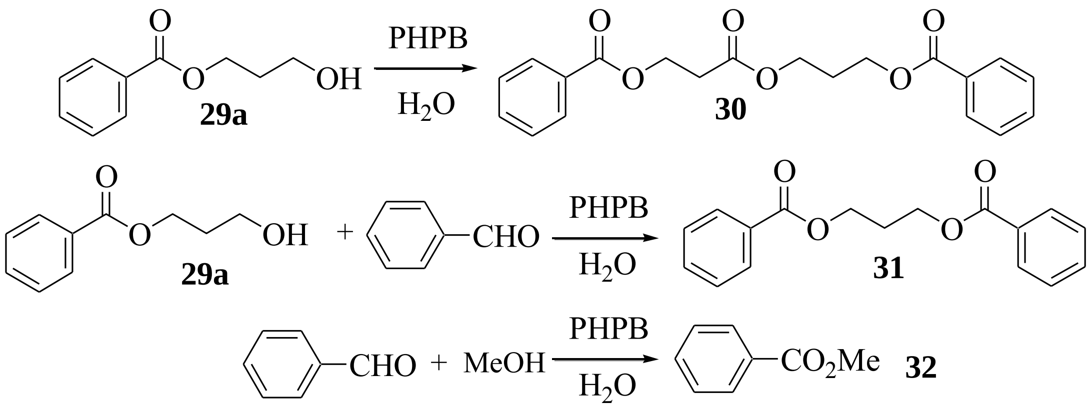
On the other hand, 1,3-dioxanes are widely used protective groups for carbonyl compounds and vicinal diols.[47] In addition, the oxidation of 1,3-dioxanes provides important hydoxypropyl esters for serving as cross-linking agents for polyesters and fungicides.[48] Direct conversion of open-chain acetals, 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 H_2O (Scheme 20).[11]



28a: R = phenyl
28b: R = 4-bromophenyl
28c: R = 3-bromophenyl
28d: R = 2-bromophenyl
28e: R = 4-chlorophenyl
28f: R = 3-chlorophenyl
28g: R = 2-chlorophenyl
28h: R = 4-methylphenyl
28i: R = 3-methylphenyl
28j: R = 2-methylphenyl
28k: R = 2-phenylethyl
28l: R = 1-phenylethyl
29a: R = phenyl
29b: R = 4-bromophenyl
29c: R = 3-bromophenyl
29d: R = 2-bromophenyl
29e: R = 4-chlorophenyl
29f: R = 3-chlorophenyl
29g: R = 2-chlorophenyl
29h: R = 4-methylphenyl
29i: R = 3-methylphenyl
29j: R = 2-methylphenyl
29k: R = 2-phenylethyl
29l: R = 1-phenylethyl

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]



Scheme 21

As we previously reported the mild oxidation of secondary alcohol with PTAB in MeOH,[4] we examined the reaction of **28a** in MeOH as a co-solvent. In H_2O-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.

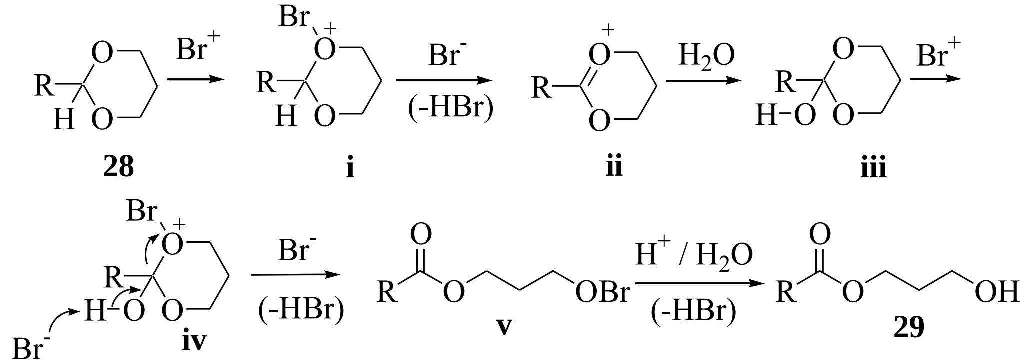
Table 10. Reaction of dioxanes with PHPB-NaOAc[a]

Run	28	Time (h)	29	Yield (%)	Run	28	Time (h)	29	Yield (%)
1	**28b**	17	**29b**	87	7	**28h**	19	**29h**	78
2	**28c**	19	**29c**	86	8	**28i**	19	**29i**	84
3	**28d**	24	**29d**	52[b]	9	**28j**	17	**29j**	80
4	**28e**	45	**29e**	83	10	**28k**	17	**29k**	93
5	**28f**	17	**29f**	94	11	**28l**	17	**29l**	93
6	**28g**	24	**29g**	51[c]					

[a] **28**: 0.5 mmol; PHPB: 1.0 mmol; NaOAc: 1.5 mmol; H_2O: 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 hydoxypropyl 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 substitutent 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 **291**.



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.[11] 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 H_2O 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 H_2O .

We demonstrated that the system PHPB-NaOAc in H_2O-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.

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