Note

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Trans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxalane/HBr System as New, Effective, Mild and Non-toxic Reagent for Synthesis of 2-Aryl-1*H*-benzothiazoles and 2-Aryl-1-arylmethyl-1*H*-benzimidazoles

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Ttrans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxalane has been used as new, effective, solid, inexpensive and nontoxic oxidant for in situ generation of Br^+ from HBr. This system has been applied as catalyst for synthesis of 2-aryl-1*H*-benzothiazoles and 2-aryl-1-arylmethyl-1*H*-benzimidazoles at room temperature in excellent yields and high purity.

Keywords: Ttrans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxalane; 2-Aryl-1*H*-benzothiazoles; 2-Aryl-1-arylmethyl-1*H*-benzimidazoles; HBr.

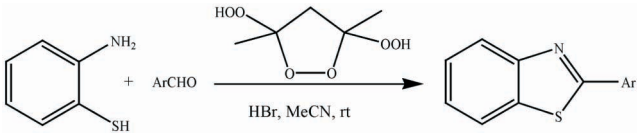
INTRODUCTION

2-Substituted benzothiazoles are an important class of compounds in medicinal and industrial chemistry.[1] Also, compounds with containing benzimidazoles core have been shown a wide range of biological properties.[2] Due to for importance of benzothiazoles, for synthesis of these compounds several methodologies have been reported.[3] Two major methods have been reported: 1. Condensation of 2-aminothiophenol with aldehydes. 2. Cyclization of thiobenzanilides.[4]

Several reagents have been used for catalyzes of this condensation that include DMSO/120 °C,[5a] ionic liquid 1-phenyl-3-methylimidazoliumbromide ([pmIm]Br),[5b] scandium triflate,[5c] silicagel,[5d] MnO_2/SiO_2,[5e] molecular iodine,[5f] molecular oxygen promoted by activated carbon,[5g] *p*-TSOH,[5h] SiO_2/graphite,[5i] electrochemical synthesis in methanol containing sodium acetate as supporting electrolyte,[5j] water/110 °C,[5k] carboxylic acid,[6] acid chlorides[7] or esters.[8]

Also, several sundry methods such as micro wave –mediated reaction of 2-aminothiophenol with β-chlorocinnamadehydes,[9] palladium-catalyzed Suzuki biaryl coupling of 2-bromobenzothiazoles with aryl bromides,[10] coupling of benzothiazoles with aryl bromides[11] and reaction of thiophenol with aromatic nitriles[12] have been used. Unfortunately, many of these procedures suffer from several defects such as using toxic and/or inexpensive catalysts,[3,4] the use of hazardous and carcinogenic organic solvent and multistep process for reaction.[5] So, founding of optimized methodology for synthesis of benzothiazoles is still important. On the other hand, the best method for preparation of benzimidazoles is condensation of 1,2-phenylenediamine with aldehydes. In recent years, several Lewis acids such as $Sc(OTf)_3$,[13] $Yb(OTf)_3$,[14] $In(OTf)_3$,[15] oxalic acid,[16] proline,[17] H_2O_2/HCl,[18] *p*-toluensulfonic acid-silica gel,[19] Caro's acid-silica gel,[20] acetic acid/MW,[21] H_2O_2/CAN,[22] ambelite IR-120,[23] K10,[24] oxone,[25] iodine,[26] $SiO_2/ZnCl_2$,[27] and SSA.[28] Recently, gem-dihydroperoxides have been used as new and effective oxidant.[29] Therefore, now, we have synthesized trans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxalane as new, solid and powerful oxidant for oxidation reactions.[30] In this work, for in situ generation of Br^+, we have used trans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxalane/HBr system. Br^+ as a powerful and effective Lewis acid has catalyzed the synthesis of benzothiazoles (Scheme I) and benzimidazoles (Scheme II). Although, in synthesis of benzimidazoles, tow products may be obtained, in this procedure, 2-aryl-1-arylmethyl-1*H*-benzimidazoles were obtained as only product (Scheme II).

Scheme I Synthesis of 2-arylbenzothiazoles



RESULTS AND DISCUSSION

For optimization test, benzaldehyde has been reacted with 2-aminothiophenol in different solvents. After optimi-

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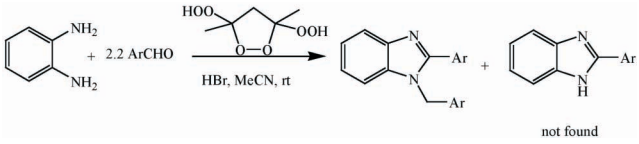
Scheme II Synthesis of 2-aryl-1-arylmethylbenzimidazoles

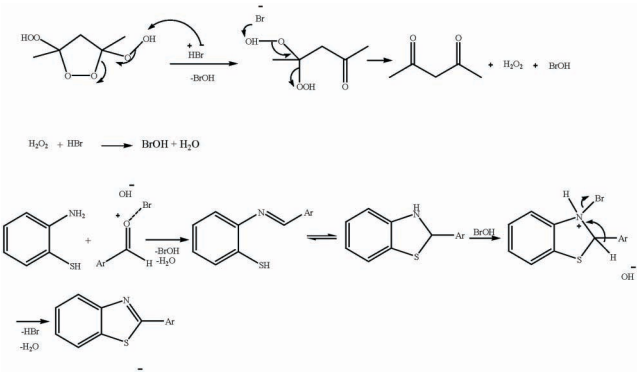


zation tests, MeCN has choose as the best solvent (Table 1, 91% yield, 22 minutes).

This procedure is simple, effective, clean and non-toxic. The products were obtained in high yields (Table 2, 3). Also, products were obtained by aqua work-up in good purity. Thus, complex purification methods were not necessary.

In this work, we have used trans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxalane as new, powerful and solid oxidant to in situ generation Br^+ as a powerful Lewis acid to activation of carbonyl group. The suggested mechanism was shown in Scheme III.

Scheme III Suggested mechanism



As shown in Tables 2 and 3, both aldehydes with electron-withdrawing and electron-relaxing groups were reacted in this method in short times.

CONCLUSION

In summary, we have developed a facile and efficient method for synthesis of benzothiazoles and 2-aryl-1-arylmethyl-1H-benzimidazoles using trans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxalane/HBr system. The advantages of this method include (i) short reaction times, (ii) high yields, (iii) easy work-up, (iv) using a little amount of reagent, and (v) avoid of using of molecular bromine. Applying this system is easy, available, clean and effective.

Table 1. Selection of best solvent

Entry	Solvent	Time (min)	Yield (%)[a]
1	EtOH	25	85
2	$CHCl_3$	65	69
3	MeCN	22	91
4	CCl_4	70	52
5	THF	25	87

Table 2. Synthesis of 2-aryl-1*H*-benzothiazoles in optimized condition

Product[a]	Ar	Time (min)	Yield (%)[b]	m. p (°C)	
				found	Reported[55]
2a	C_6H_5	22	91	112-114	110-112
2b	4-MeC_6H_5	21	86	87-89	85-87
2c	2-MeC_6H_5	23	87	50-52	52-54
2d	2- $MeOC_6H_5$	30	83	100-102	99-102
2e	4- $MeOC_6H_5$	25	85	120-122	119-121
2f	2-ClC_6H_5	30	83	84-86	81-83
2g	4-ClC_6H_5	23	85	118-119	116-117
2h	2-OHC_6H_5	26	82	124-126	122-124
2i	4-OHC_6H_5	30	81	230-232	227-228
2j	2-$NO_2C_6H_5$	23	82	132-134	133-135
2k	3-$NO_2C_6H_5$	22	84	182-184	182-184
2l	4-BrC_6H_5	22	87	130-132	129-131
2m	4-FC_6H_5	24	85	96-98	98-100
2n	4-CNC_6H_5	25	86	166-168	165-166
2o	2-Furyl	40	77	102-104	100-103

[a] The products were characterized by their physical properties and spectral analysis and compared with authentic samples.
[b] Isolated yields.

Table 3. Synthesis of 2-aryl-1-arylmethyl-1*H*-benzimidazoles in optimized conditions

Entry	Ar	Time (min)	Yield (%)	m.p (°C)	
				found	Reported[45]
3a	C_6H_5	29	92	130-132	132-134
3b	4-MeC_6H_5	45	88	128-130	126-128
3c	4-$MeOC_6H_5$	38	83	132-134	130-131
3d	2- $MeOC_6H_5$	40	80	153-155	154-155
3e	2-ClC_6H_5	42	80	157-159	158-159
3f	4-ClC_6H_5	36	84	140-142	138-140
3g	2-OHC_6H_5	52	75	203-205	205-208
3h	4-OHC_6H_5	47	78	247-249	250-253
3i	2-$NO_2C_6H_5$	43	80	170-172	169-170
3j	4-$NO_2C_6H_5$	44	83	120-122	119-120
3k	4-CNC_6H_5	40	83	190-192	190-191
3l	4-$N(Me)_2C_6H_5$	35	90	254-256	254-256
3m	2-furyl	50	76	98-100	96-98

[a] The products were characterized by their physical properties and spectral analysis and compared with authentic samples.
[b] Isolated yields.

EXPERIMENTAL

All the chemicals were purchased from Merck Company. Melting points were measured by using the capillary tube method with an electro thermal 9200 apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Varian 200 MHz or JEOL FX 90 MHz spectrometer (DMSO-d6 solution). IR spectra were run from KBr disk on a PerkinElmer GX FT-IR spectrometer.

General procedure for synthesis of 2-aryl-1*H*-benzothiazoles

To a mixture of 2-aminothiophenole, aldehyde (1 mmol) and HBr (47%) (1.1 mmol) in MeCN (8 mL), was added trans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxalane (0.5 mmol) and stirred for appropriate time. The progress of reaction was followed by TLC. After completion of the reaction, 1 mL of Na_2SO_3 1 M was added and stirred for 10 minutes. Then, 15 mL of water was added. Benzothiazoles are not solvable in water, therefore, the participated products were filtrated and dried for obtain pure benzothiazoles (Table 2).

General procedure for synthesis of 2-aryl-1-arylmethyl-1*H*-benzimidazoles

To a mixture of 1,3-phenylenediamine (1 mmol), aldehyde (2.2 mmol), HBr (47%) (2 mmol) in MeCN (8 mL), was added trans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxalane (1 mmol) and stirred for appropriate time in room temperature. The progress of reaction was followed by TLC. After completion of reaction, the excess of peroxide and bromine was quenched with 1 mL of Na_2SO_3 1 M. Then 15 mL of water was added and stirred for some minutes in room temperature. Benzimidazoles are not solvable in water. So, participated solids were filtrated and dried for obtain pure 2-aryl-1-arylmethyl-1*H*-benzimidazoles (Table 3).

CAUTION

Trans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolan e as a peroxidic compound is potentially explosive and requires precautions in handling (shields, fume hoods, absence of transition metal salts and heating above room temperature).

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