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Synthesis of Benzo[4,5]imidazo[2,1-*b*]thiazole by Copper(II)-Catalyzed Thioamination of Nitroalkene with 1*H*-Benzo[*d*]imidazole-2-thiol

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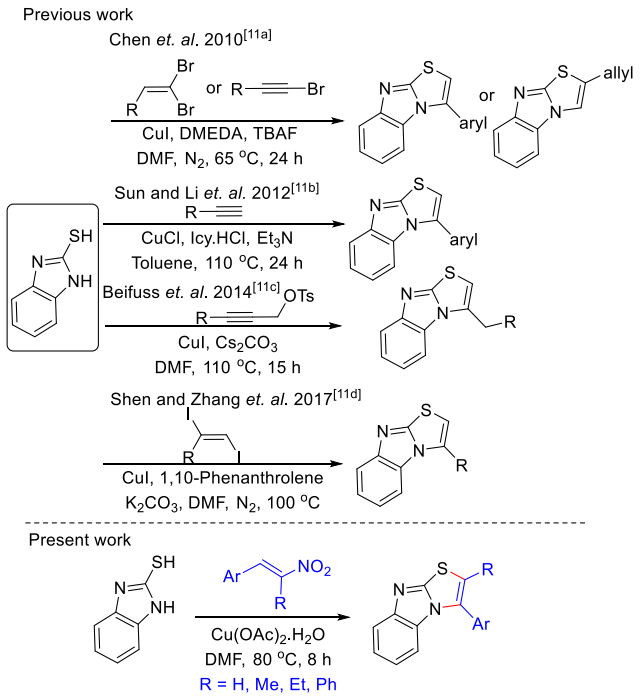
Abstract. A Copper(II)-catalyzed thioamination of *β*-nitroalkene with 1*H*-benzo[*d*]imidazole-2-thiol has been developed for the synthesis of benzo[4,5]imidazo[2,1-*b*]thiazole derivatives. A variety of *N*-fused benzoimidazothiazole derivatives are obtained in high yields through successive C-N and C-S bond formations. This protocol is also applicable to *β*-substituted *β*-nitroalkenes to afford 2,3-disubstituted benzoimidazothiazoles.

Keywords: *N*-fused benzoimidazothiazole; nitroalkene; regioselectivity; Michael addition; thioamination

Introduction

Imidazo[2,1-*b*]thiazole constitutes an important class of fused heterocycles because of their pharmacological activities such as calcium channel antagonistic,[1] acetylcholinesterase inhibitor,[2] SIRT1 activator[3] and also for their antifungal,[4] anti-inflammatory,[5] antitumor,[6] antidiabetic,[7] antitubercular activities[8] *etc*.[9] Particularly, benzo[4,5]imidazo[2,1-*b*]thiazole moiety offers promising immunomodulating and antimetastatic properties which have been studied extensively for drug development.[10] There are few synthetic methods for the construction of benzo[4,5]imidazo[2,1-*b*]thiazole which are based on coupling between 1*H*-benzo[*d*]imidazole-2-thiol and 1,1-dibromoalkenes/alkynes/*trans*-1,2-diiodoalkenes in presence of Cu-salts (Scheme 1).[11] However, these starting materials are not convenient to prepare and also most of reported methods afford 2-unsubstituted benzo[4,5]imidazo[2,1-*b*]thiazoles. Because of the significant biological aspects of benzo[4,5]imidazo[2,1-*b*]thiazole derivatives, new strategy for their preparation from readily accessible and less expensive precursors is desirable.

Owing to the ability to take part in a wide range of organic reactions and easy accessibility through nitro-aldol condensation, nitroalkenes have been used to synthesize a number of heterocycles[12] such as furan,[13a,14a,b] imidazole,[14c] pyridine,[13b] pyrimidine,[13c] indole,[13d] imidazopyridine,[13e,f,14d] *etc*[13g-k]. Notably, nitroalkene is bielectrophilic in nature and could serve as potential precursor to form heterocycles by reacting with binucleophiles *via* cascade hetero-Michael addition reaction.[14d] However, study for the coupling between nitroalkene and N, S –binucleophile to prepare thiazole moiety[15] *via* C-N and C-S bond formations is unexplored. In continuation of our ongoing program to explore the nitroalkene as bielectrophile to synthesize several heterocycles,[14] herein we disclose a Cu(II)-catalyzed coupling between nitroalkene and commercially available 1*H*-benzo[*d*]imidazole-2-thiol to afford imidazo[2,1-*b*]thiazoles (Scheme 1).

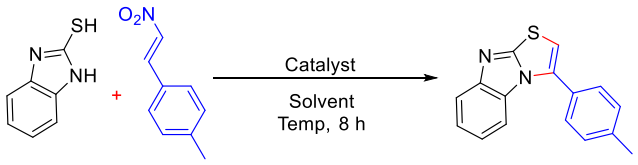


Scheme 1. Synthesis of benzo[4,5]imidazo[2,1-*b*]thiazoles.

Results and Discussion

We commenced our study by reacting 1*H*-benzo[*d*]imidazole-2-thiol (**1a**) with (*E*)-1-methyl-4-(2-nitrovinyl)benzene (**2a**) in presence of 10 mol% $Cu(OAc)_2.H_2O$ in DMSO at 80 °C (Table 1, entry 1). Interestingly, the desired product **3aa** was isolated in 35% yield after 8 h. The structure was confirmed on the basis of ^1H NMR spectra in which the characteristic peak for thiazole (sp^2-H) is observed as singlet at 6.55 ppm and also by comparing with literature.[11a,b,d] In order to determine the optimal conditions, the reaction was screened with several solvents like MeCN, DMF, DMA, toluene, nitrobenzene, NMP, DCB and AcOH (Table 1, entries 2 to 9). Among them DMF was found to be the best to give the product **3aa** in 68% yield (Table 1, entry 3). Further increasing catalyst loading to 15%, the yield of **3aa** was improved to 87% (Table 1, entry 10). An almost similar result was obtained with 20 mol% of $Cu(OAc)_2.H_2O$ (Table 1, entry 11). Other metal acetates like $Zn(OAc)_2.2H_2O$ and AgOAc were employed as the catalyst, however these were not so effective like $Cu(OAc)_2.H_2O$ (Table 1, entries 12 and 13). Treatment with other common Cu salts such as $CuCl_2$, $CuBr_2$, $CuSO_4.5H_2O$ and $Cu(OTf)_2$ as catalyst were found to be less effective for this process (Table 1, entries 14 to 17). $FeCl_3$ was also tested but it did not produce any desired product (Table 1, entry 18). With increasing the reaction temperature to 100 °C, no observable change of the yield was noticed (Table 1, entry 19); but at lower temperature (60 °C), a much lower yield was obtained (Table 1, entry 20). Thus, a combination of 15 mol% $Cu(OAc)_2.H_2O$ in DMF at 80 °C for 8 h was found to be optimal reaction conditions for this thioamination process (Table 1, entry 10).

Table 1. Evaluation of the reaction condition.[a]



1a **2a** **3aa**

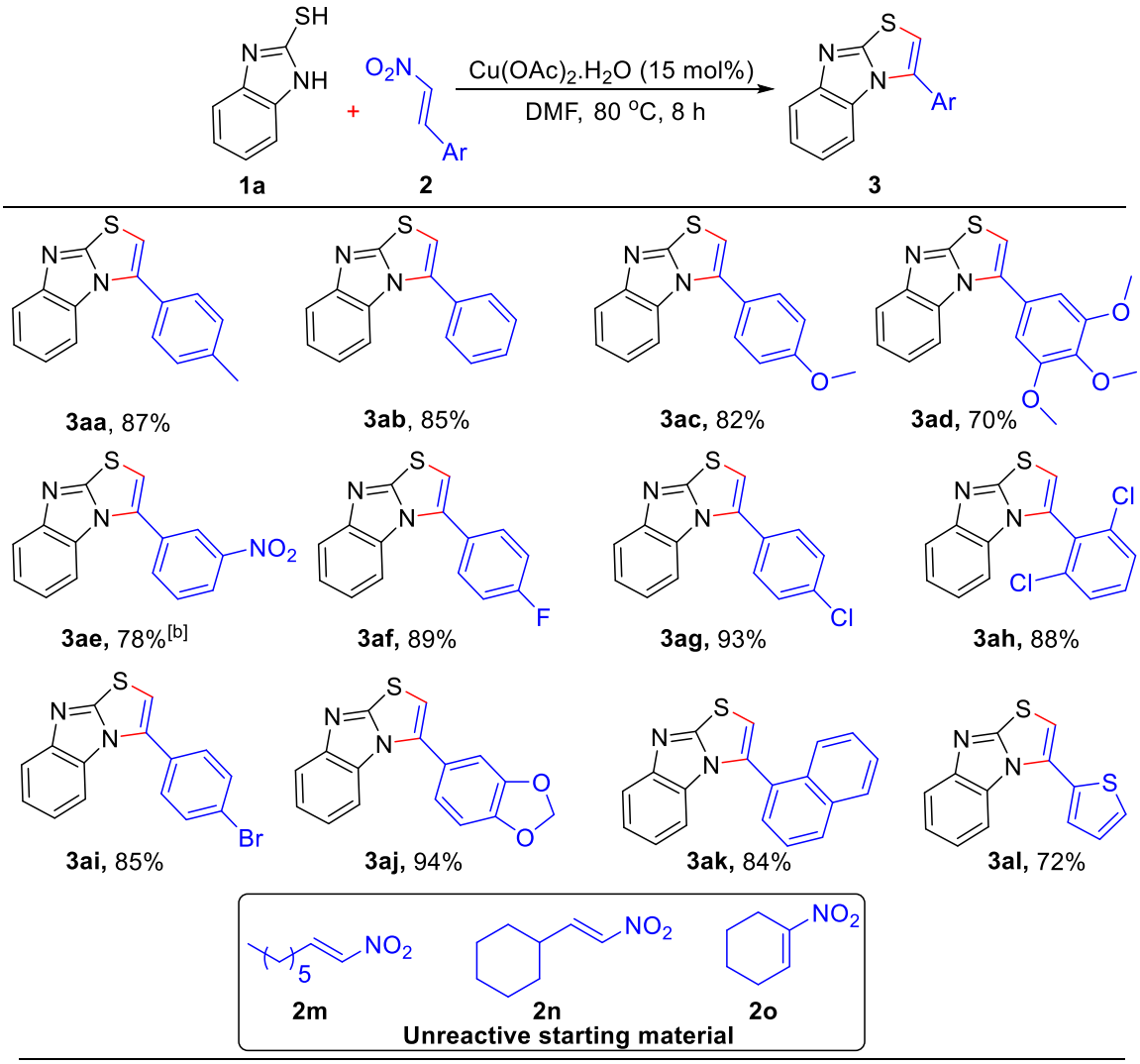
Entry	Catalyst (mol%)	Solvent	Temperature	Yield[b]
1	$Cu(OAc)_2.H_2O$ (10)	DMSO	80 °C	35%
2	$Cu(OAc)_2.H_2O$ (10)	MeCN	80 °C	Trace
3	$Cu(OAc)_2.H_2O$ (10)	DMF	80 °C	68%
4	$Cu(OAc)_2.H_2O$ (10)	DMA	80 °C	Trace
5	$Cu(OAc)_2.H_2O$ (10)	toluene	80 °C	ND[c]
6	$Cu(OAc)_2.H_2O$ (10)	$PhNO_2$	80 °C	36%
7	$Cu(OAc)_2.H_2O$ (10)	NMP	80 °C	Trace
8	$Cu(OAc)_2.H_2O$ (10)	DCB	80 °C	32%
9	$Cu(OAc)_2.H_2O$ (10)	AcOH	80 °C	52%
10	**$Cu(OAc)_2.H_2O$ (15)**	**DMF**	**80 °C**	**87%**
11	$Cu(OAc)_2.H_2O$ (20)	DMF	80 °C	87%
12	$Zn(OAc)_2.2H_2O$ (15)	DMF	80 °C	25%
13	AgOAc (15)	DMF	80 °C	21%
14	$CuCl_2$ (15)	DMF	80 °C	ND
15	$CuBr_2$ (15)	DMF	80 °C	ND
16	$CuSO_4.5H_2O$ (15)	DMF	80 °C	20%
17	$Cu(OTf)_2$ (15)	DMF	80 °C	27%
18	$FeCl_3$ (15)	DMF	80 °C	ND

19	$Cu(OAc)_2.H_2O$ (15)	DMF	100 °C	85%
20	$Cu(OAc)_2.H_2O$ (15)	DMF	60 °C	26%

[a] *Reaction conditions*: 0.3 mmol of **1a,** 0.3 mmol of **2a** and catalyst in 1.5 mL solvent at 80 °C for 8 h.
[b] Isolated yields.
[c] ND = Not detected.

After getting the optimized reaction conditions, the scope of *β*-nitroalkene (**2a-2o**) was examined, and the results are shown in Table 2. *β*-Nitroalkenes having both electron donating substituents like -Me, -OMe and electron withdrawing group like $-NO_2$ on the phenyl ring responded well to give the corresponding 3-substituted benzo[4,5]imidazo[2,1-*b*]thiazoles (**3aa**-**3ae**) with 78-87% yields. Different halogens like -F, -Cl and -Br containing *β*-nitroalkenes reacted very smoothly with 1*H*-benzo[*d*]imidazole-2-thiol to give the respective products in significant yields (**3af**-**3ai**). The position of substitution in the phenyl ring of *β*-nitroalkenes did not affect the yield of the reactions (**3ac**-**3ai**). Interestingly, *β*-nitroalkene bearing an acid sensitive dioxole unit also afforded the respective product (**3aj**) without any difficulties. Furthermore, (*E*)-1-(2-nitrovinyl)naphthalene and (*E*)-2-(2-nitrovinyl)thiophene provided good yields of the corresponding products (**3ak** and **3al**). However, the current methodology is not applicable for nitroalkenes having aliphatic substituents at *α*-position (**2m**, **2n** and **2o**).

Table 2. Substrate scope**:** Variation of *β*-nitroalkenes.[a]



[a] *Reaction conditions*: 0.3 mmol of **1a**, 0.3 mmol of **2** and 15 mol% $Cu(OAc)_2.H_2O$ in 1.5 mL DMF at 80 °C for 8 h.
[b] Reaction time 24 h.

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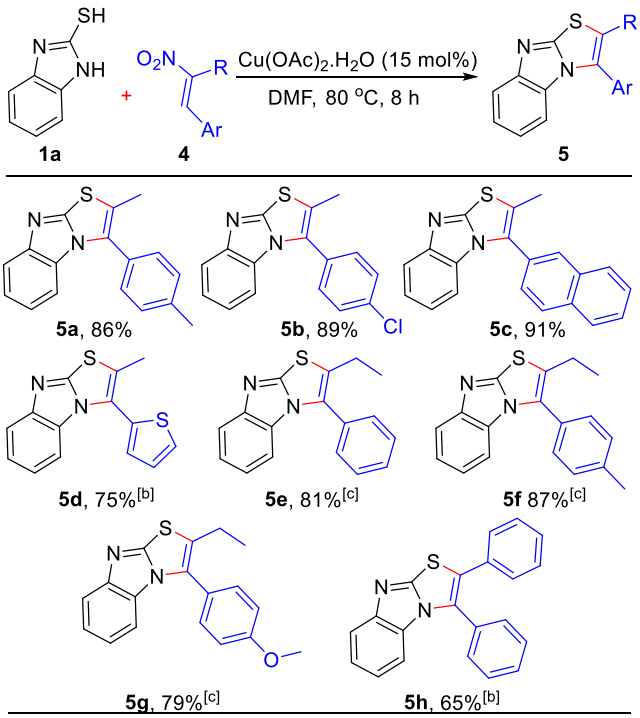
Moreover, *β*-substituted *β*-nitroalkene such as *β*-methyl *β*-nitroalkene, *β*-ethyl *β*-nitroalkene and *β*-phenyl *β*-nitroalkene derivatives were also successfully employed as the coupling partner with 1*H*-benzo[*d*]imidazole-2-thiol under the optimized reaction conditions (Table 3). In all the cases, cyclization occurred with good yields to furnish 3,4-disubtituted benzo[4,5]imidazo[2,1-*b*]thiazoles (**5a-5h**).

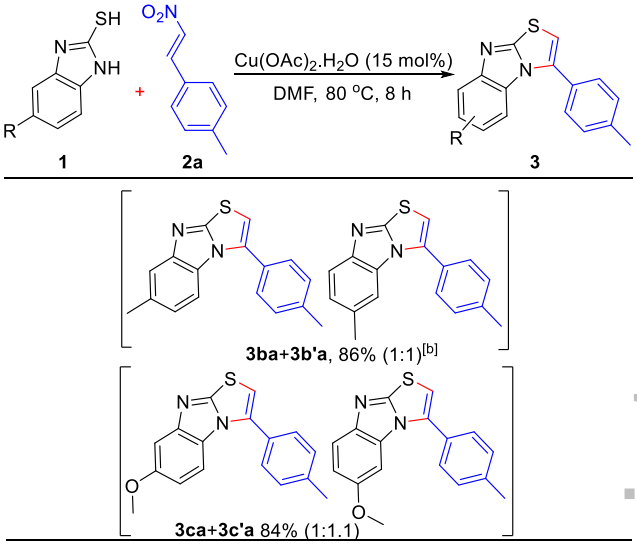
Table 3. Substrate scope: Reaction with *β*-substitute-*β*-nitroalkenes.[a]



[a] *Reaction conditions*: 0.3 mmol of **1a**, 0.3 mmol of **4** and 15 mol% $Cu(OAc)_2.H_2O$ in 1.5 mL DMF at 80 °C for 8 h.
[b] Reaction time 16 h.
[c] Reaction time 24 h.

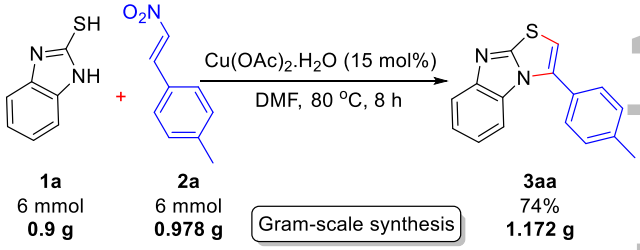
Next, the compatibility of this method with 1*H*-benzo[*d*]imidazole-2-thiols having substituents like -Me and -OMe on the phenyl ring as shown in Table 4 was studied. In both the cases mixture of two regioisomers (**3ba**+**3b'a**) and (**3ca**+**3c'a**) were isolated with almost equal ratios. However, benzo[*d*]imidazole-2-thiols having electron withdrawing substituents such as -Cl and $-NO_2$ on benzene ring were not suitable substrates for this annulation.

Table 4. Substrate scope: Variation of substituents on 1*H*-benzo[*d*]imidazole-2-thiol.[a]



[a] *Reaction conditions*: 0.3 mmol of **1**, 0.3 mmol of **2a** and 15 mol% $Cu(OAc)_2.H_2O$ in 1.5 mL DMF at 80 °C for 8 h.
[b] The isomeric ratio was determined by ^1H NMR.

Gram scale applicability of the present methodology was also demonstrated in Scheme 2. The reaction between 1*H*-benzo[*d*]imidazole-2-thiol (**1a**) and (*E*)-1-methyl-4-(2-nitrovinyl)benzene (**2a**) afforded the thiazole product in 74% (1.172 g, **3aa**) yield under the ordinary reaction set-up.



Scheme 2. Practical applicability of the present protocol.

On the basis of the literature report and our previous work,[14a,d] the probable mechanism of the present protocol is outlined in Scheme 3. Initially the intermediate **A** is formed *via* Michael addition of 1*H*-benzo[*d*]imidazole-2-thiol (**1a**) to (*E*)-1-methyl-4-(2-nitrovinyl)benzene (**2a**). Subsequently **B** intermediate is generated from the intermediate **A** through intramolecular cyclization *via* C-S bond formation in presence of $Cu(OAc)_2.H_2O$. Finally the product (**3aa**) was obtained by the elimination of water and HNO.[13h,14d] It is worthy to mention that initial Michael addition occurs through N-atom under the reaction conditions although S-atom is more nucleophilic than N-atom. It might be due to the complexation of S-atom with Cu(II)-catalyst.

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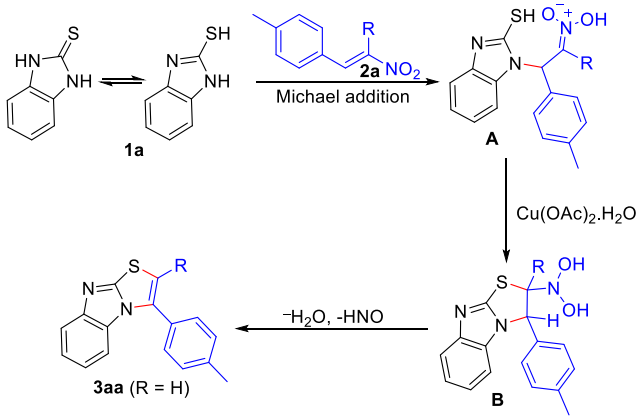

Scheme 3. Possible mechanistic pathway.

We have developed a new Cu(II)-catalyzed methodology for the synthesis of benzo[4,5]imidazo[2,1-*b*]thiazole derivatives by the reaction between 1*H*-benzo[*d*]imidazole-2-thiol and *β*-nitroalkene. This transformation shows broad substrate scope and a wide range of functional group tolerance. Moreover, starting materials are readily available. To the best of our knowledge there is no report on synthesis of benzo[4,5]imidazo[2,1-*b*]thiazole ring *via* 1,2-aminothiolation of *β*-nitroalkene which acts as a bielectrophile. We believe the present protocol is very convenient and will open the door to synthesize various heterocycles.

Experimental section

General Information: Reagents were purchased from commercial sources and used without further purification. ^{1}H and ^{13}C{^{1}H} NMR spectra were determined on 400 MHz spectrometer. ^{1}H NMR spectra were determined on 400 MHz spectrometer as solutions in $CDCl_3$. Chemical shifts are expressed in parts per million (δ) and the signals were reported as s (singlet), d (doublet), t (triplet), m (multiplet), q (quartet), dd (double doublet), dq (double quartet) and coupling constants (J) were given in Hz. ^{13}C{^{1}H} NMR spectra were recorded at 100 MHz in $CDCl_3$ solution. Chemical shifts as internal standard are referenced to $CDCl_3$ (δ = 7.26 for ^{1}H and δ = 77.16 for ^{13}C{^{1}H} NMR) as internal standard. TLC was done on silica gel coated glass slide. Commercially available solvents were freshly distilled before the reaction. All reactions involving moisture sensitive reactants were executed using oven dried glassware.

General Procedure for the Synthesis of Table 2 to Table 4: A mixture of 1*H*-benzo[*d*]imidazole-2-thiol (**1,** 0.30 mmol), *β*-Nitroalkene (**2**, 0.30 mmol) and $Cu(OAc)_2.H_2O$ (15 mol %, 9 mg, 0.045 mmol) in DMF (1.5 mL) was taken in a reaction tube and the reaction mixture was stirred at 80 °C for 8 h. After completion of the reaction it was allowed to cool at room temperature and extracted with ethyl acetate and water. The organic phase was dried over anhydrous Na_2SO_4. The crude residue was obtained after evaporating the solvent under reduced pressure and finally it was purified by column chromatography on silica gel (60-120 mesh) using petroleum ether/ethyl acetate = 9:1 as an eluent to afford the pure product.

3-(*p*-Tolyl)benzo[4,5]imidazo[2,1-*b*]thiazole (3aa):[11a,b,d] Yellow solid (69 mg, 87%), mp 118−120 °C (lit. mp 118−121 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 7.6 Hz, 2H), 7.32 (t, J = 8.4 Hz, 1H), 7.08-7.06 (m, 1H), 6.99-6.96 (m, 1H), 6.55 (s, 1H), 2.49 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.3, 148.6, 140.4, 134.4, 130.2, 129.7, 128.8, 126.5, 123.4, 120.4, 119.2, 111.8, 106.8, 21.6.

3-Phenylbenzo[4,5]imidazo[2,1-*b*]thiazole (3ab):[11a,b,d] Yellow solid (64 mg, 85%), mp 138−139 °C (lit. mp 138−140 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (d, J = 8.0 Hz, 1H), 7.67-7.64 (m, 2H), 7.59-7.56 (m, 3H), 7.32 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 7.06 (t, J = 8.0 Hz, 1H), 6.60 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.3, 148.7, 134.4, 130.2, 129.5, 129.1, 129.0, 128.4, 123.5, 120.6, 119.3, 111.8, 107.3.

3-(4-Methoxyphenyl)benzo[4,5]imidazo[2,1-*b*]thiazole (3ac):[11a,b] Yellow solid (69 mg, 82%), mp 148−149 °C (lit. mp 148−150 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 8.8 Hz, 2H), 7.31 (t, J = 8.4 Hz, 1H), 7.23 (d, J = 8.4 Hz, 1H), 7.09-7.06 (m, 3H), 6.52 (s, 1H), 3.92 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.0, 157.3, 148.6, 134.2, 130.4, 130.2, 123.4, 121.6, 120.4, 119.2, 114.4, 111.7, 106.5, 55.6.

3-(3,4,5-Trimethoxyphenyl)benzo[4,5]imidazo[2,1-*b*]thiazole (3ad): White solid (71 mg, 70%), mp 165-166 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (d, J = 8.0 Hz, 1H), 7.35-7.32 (m, 2H), 7.11 (t, J = 8.0 Hz, 1H), 6.85 (s, 2H), 6.63 (s, 1H), 3.92 (s, 3H), 3.89 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.4, 153.7, 124.1, 123.8, 123.2, 122.6, 120.8, 119.2, 115.1, 111.9, 109.6, 107.4, 106.3, 61.2, 56.5; Anal. Calcd for $C_{18}H_{16}N_2O_3S$: C, 63.51; H, 4.74; N, 8.23; Found C, 63.62; H, 4.68; N, 8.11%.

3-(3-Nitrophenyl)benzo[4,5]imidazo[2,1-*b*]thiazole (3ae): Yellow solid (69 mg, 78%), mp 134-135 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.86 (t, J = 2.0 Hz, 1H), 8.54 (t, J = 2.0 Hz, 1H), 8.49-8.47 (m, 1H), 8.39-8.37 (m, 1H), 8.31-8.29 (m, 1H), 7.98-7.95 (m, 1H), 7.76 (t, J = 8.0 Hz, 1H), 7.68-7.63 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 143.7, 139.2, 139.0, 136.2, 134.5, 134.2, 130.3, 130.2, 127.6, 125.6, 125.3, 123.5, 123.4, 122.9, 122.4; Anal. Calcd for $C_{15}H_9N_3O_2S$: C, 61.01; H, 3.07; N, 14.23; Found C, 61.23; H, 3.10; N, 14.16%.

3-(4-Fluorophenyl)benzo[4,5]imidazo[2,1-*b*]thiazole (3af):[11b,d] Yellow solid (72 mg, 89%), mp 173−174 °C (lit. mp 174−177 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (d, J = 8.0 Hz, 1H), 7.66-7.62 (m, 2H), 7.36-7.26 (m, 3H), 7.15 (d, J = 8.4 Hz, 1H), 7.09 (t, J = 7.2 Hz, 1H), 6.62 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 163.8 (d, J = 232 Hz), 157.2, 148.3, 132.8, 131.0 (d, J = 8 Hz), 125.5 (d, J = 3 Hz), 123.7, 120.8, 119.3, 116.4 (d, J = 22 Hz), 115.8, 111.6, 107.9.

3-(4-Chlorophenyl)benzo[4,5]imidazo[2,1-*b*]thiazole (3ag):[11a,d] Yellow solid (79 mg, 93%), mp 200-201 °C (lit. mp 199−202 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (d, J = 8.0 Hz, 1H), 7.62-7.54 (m, 4H), 7.34 (t, J = 8.4 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 7.10 (d, J = 8.0 Hz, 1H), 6.62 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.2, 148.7, 136.5, 133.0, 132.8, 130.2, 129.5, 127.8, 123.7, 120.8, 119.4, 111.6, 108.0.

3-(2,6-Dichlorophenyl)benzo[4,5]imidazo[2,1-*b*]thiazole (3ah): Yellow solid (84 mg, 88%), mp 184-186 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79 (d, J = 8.0 Hz, 1H), 7.57-7.49 (m, 3H), 7.31 (t, J = 8.4 Hz, 1H), 7.04 (t, J = 8.0 Hz, 1H), 6.78 (s, 1H), 6.68 (d, J = 8.0 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.1, 148.0, 137.2, 132.3, 128.6, 127.1, 125.5, 123.5, 121.1, 119.3, 110.5, 110.1, 106.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_9Cl_2N_2S$: 318.9858; found: 318.9861.

3-(4-Bromophenyl)benzo[4,5]imidazo[2,1-*b*]thiazole (3ai):[11a] Yellow solid (84 mg, 85%), mp 205-206 °C (lit.

mp 205-206 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.81 (d, J = 8.0 Hz, 1H), 7.73-7.71 (m, 2H), 7.55-7.52 (m, 2H), 7.34 (t, J = 7.2 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 7.10 (t, J = 8.4 Hz, 1H), 6.64 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.2, 148.5, 132.4, 131.8, 131.7, 130.4, 128.4, 124.7, 123.7, 120.8, 119.4, 111.6, 108.1.

3-(Benzo[*d*][1,3]dioxol-5-yl)benzo[4,5]imidazo[2,1-*b*]thiazole (3aj): White solid (83 mg, 94%), mp 171-172 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79 (d, J = 8.4 Hz, 1H), 7.47-7.41 (m, 1H), 7.34-7.28 (m, 2H), 7.14-7.11 (m, 1H), 7.09-7.08 (m, 1H), 6.54 (s, 1H), 6.14 (s, 1H), 6.10 (s, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.2, 149.3, 148.6, 148.2, 133.9, 130.1, 124.1, 123.5, 123.2, 120.6, 119.3, 116.2, 111.8, 108.9, 106.9, 101.9; Anal. Calcd for $C_{16}H_{10}N_2O_2S$: C, 65.29; H, 3.42; N, 9.52; Found C, 65.43; H, 3.31; N, 9.59%.

3-(Naphthalen-1-yl)benzo[4,5]imidazo[2,1-*b*]thiazole (3ak): White solid (76 mg, 84%), mp 205-206 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.11 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.71-7.69 (m, 1H), 7.63 (t, J = 8.0 Hz, 2H), 7.56 (t, J = 8.0 Hz, 1H), 7.42 (t, J = 8.4 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H), 6.81-6.79 (m, 1H), 6.77 (s, 1H), 6.28 (d, J = 8.0 Hz, 1H), ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.0, 148.6, 133.7, 132.2, 132.1, 131.0, 130.2, 129.1, 128.8, 127.7, 127.0, 126.8, 125.5, 125.2, 123.4, 120.7, 119.0, 111.5, 108.7; Anal. Calcd for $C_{19}H_{12}N_2S$: C, 75.97; H, 4.03; N, 9.33; Found C, 75.76; H, 3.90; N, 9.47%.

3-(Thiophen-2-yl)benzo[4,5]imidazo[2,1-*b*]thiazole (3al):[11a,b] White solid (55 mg, 72%), mp 95-96 °C (lit. mp 94−95 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (d, J = 8.4 Hz, 1H), 7.67-7.62 (m, 2H), 7.35-7.31 (m, 1H), 7.29 (d, J = 8.8 Hz, 1H), 7.17 (d, J = 7.6 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.59 (s, 1H), ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.5, 146.1, 131.09, 131.01, 123.6, 120.7, 119.8, 119.5, 116.6, 116.5, 116.3, 111.5, 107.5.

2-Methyl-3-(*p*-tolyl)benzo[4,5]imidazo[2,1-*b*]thiazole (5a): White solid (72 mg, 86%), mp 168−169 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.74 (d, J = 8.0 Hz, 1H), 7.43-7.37 (m, 4H), 7.27-7.23 (m, 1H), 6.97 (t, J = 7.6 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 2.50 (s, 3H), 2.32 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 155.1, 148.0, 140.1, 130.2, 129.8, 125.6, 123.0, 120.3, 119.5, 119.4, 119.0, 111.3, 110.6, 21.6, 13.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}N_2S$: 279.0950; found: 279.0953.

3-(4-Chlorophenyl)-2-methylbenzo[4,5]imidazo[2,1-*b*]thiazole (5b): Yellow solid (80 mg, 89%), mp 183−1853 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.8 Hz, 1H), 7.03-6.99 (m, 1H), 6.86 (d, J = 8.0 Hz, 1H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 155.0, 147.8, 136.3, 131.6, 131.5, 130.0, 129.6, 128.7, 127.0, 123.3, 120.6, 119.2, 111.1, 13.3; Anal. Calcd for $C_{16}H_{11}ClN_2S$: C, 64.32; H, 3.71; N, 9.38; Found C, 64.17; H, 3.78; N, 9.31%.

2-Methyl-3-(naphthalen-2-yl)benzo[4,5]imidazo[2,1-*b*]thiazole (5c): Yellow solid (86 mg, 91%), mp 150−152 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.07-7.98 (m, 3H), 7.94-7.92 (m, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.66-7.59 (m, 3H), 7.27-7.22 (m, 1H), 6.93-6.89 (m, 1H), 6.83 (d, J = 8.0 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 155.1, 148.1, 133.7, 133.2, 130.3, 130.1, 129.0, 128.9, 128.4, 128.1, 127.5, 127.2, 127.0, 125.9, 123.0, 120.4, 120.0, 119.1, 111.3, 13.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{15}N_2S$: 315.0950; found: 315.0948.

2-Methyl-3-(thiophen-2-yl)benzo[4,5]imidazo[2,1-*b*]thiazole (5d): Yellow solid (61 mg, 75%), mp 107-108 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.69 (d, J = 8.4 Hz, 1H), 7.58 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.27-7.19 (m, 3H), 6.96 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 154.3, 147.8, 131.0, 130.1, 129.1, 127.8, 123.4, 123.1, 121.7, 120.6, 119.1, 111.0, 109.5, 13.6; Anal. Calcd for $C_{14}H_{10}N_2S_2$: C, 62.19; H, 3.73; N, 10.36; Found C, 62.02; H, 3.70; N, 10.48%.

2-Ethyl-3-phenylbenzo[4,5]imidazo[2,1-*b*]thiazole (5e): Yellow solid (68 mg, 81%), mp 132-134 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.74 (d, J = 8.4 Hz, 1H), 7.59-7.56 (m, 3H), 7.53-7.49 (m, 2H), 7.26-7.22 (m, 1H), 6.96-6.92 (m, 1H), 6.76 (d, J = 8.0 Hz, 1H), 2.68 (q, J = 7.6 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 155.1, 147.8, 132.6, 130.3, 130.0, 129.2, 128.8, 128.3, 127.4, 123.0, 120.4, 118.9, 111.2, 21.2, 15.8; Anal. Calcd for $C_{17}H_{14}N_2S$: C, 73.35; H, 5.07; N, 10.06; Found C, 73.11; H, 5.13; N, 10.08%.

2-Ethyl-3-(*p*-tolyl)benzo[4,5]imidazo[2,1-*b*]thiazole (5f): Yellow oil (76 mg, 87%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.75 (d, J = 8.0 Hz, 1H), 7.42-7.37 (m, 4H), 7.25-7.23 (m, 1H), 6.99-6.94 (m, 1H), 6.82 (d, J = 8.0 Hz, 1H), 2.68 (q, J = 7.6 Hz, 2H), 2.51 (s, 3H) 1.26 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 155.2, 148.0, 140.2, 130.2, 129.9, 125.8, 124.3, 123.0, 120.3, 119.0, 116.6, 111.3, 109.5, 21.6, 21.3, 15.9; Anal. Calcd for $C_{18}H_{16}N_2S$: C, 73.94; H, 5.52; N, 9.58; Found C, 74.08; H, 5.47; N, 9.51%.

2-Ethyl-3-(4-methoxyphenyl)benzo[4,5]imidazo[2,1-*b*]thiazole (5g): Yellow semi solid (73 mg, 79%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.73 (d, J = 8.4 Hz, 1H), 7.60-7.56 (m, 1H), 7.37 (dd, J = 7.6 Hz, 2.0 Hz, 1H), 7.25-7.21 (m, 1H), 7.15-7.09 (m, 2H), 6.96-6.92 (m, 1H), 6.69 (d, J = 8.4 Hz, 1H), 3.70 (s, 3H), 2.65 (dq, J = 7.6 Hz, 2.4 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 158.5, 155.3, 147.9, 132.3, 131.9, 127.6, 122.7, 121.0, 120.2, 118.8, 111.3, 110.8, 109.6, 55.6, 21.4, 15.6; Anal. Calcd for $C_{18}H_{16}N_2OS$: C, 70.10; H, 5.23; N, 9.08; Found C, 70.36; H, 5.16; N, 9.01%.

2,3-Diphenylbenzo[4,5]imidazo[2,1-*b*]thiazole (5h):[11d] White solid (64 mg, 65%), mp 195-197 °C (lit. mp 196-197 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.81 (d, J = 8.4 Hz, 1H), 7.59-7.55 (m, 5H), 7.32-7.27 (m, 6H), 6.99 (t, J = 8.0 Hz, 1H), 6.74 (d, J = 8.4 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 154.7, 147.6, 131.4, 130.6, 130.4, 130.3, 129.5, 129.1, 128.87, 128.83, 128.47, 128.44, 123.6, 123.4, 120.8, 119.0, 111.5.

6-Methyl-3-(*p*-tolyl)benzo[4,5]imidazo[2,1-*b*]thiazole compound with 7-methyl-3-(*p*-tolyl)benzo[4,5]imidazo[2,1-*b*]thiazole (1:1): (3ba+3b'a):[11d] Yellow solid (72 mg, 86%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.66 (d, J = 8.4 Hz, 1H), 7.57 (s, 1H), 7.54-7.52 (m, 4H), 7.38-7.35 (m, 4H), 7.14 (d, J = 8.4 Hz, 2H), 7.05 (s, 1H), 6.88 (d, J = 8.8 Hz, 1H), 6.52-6.51 (m, 2H), 2.50 (s, 3H), 2.49 (s, 3H), 2.47 (s, 3H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 157.2, 156.8, 149.1, 148.4, 140.4, 133.2, 129.75, 129.72, 128.83, 128.80, 126.7, 124.9, 121.8, 119.1, 118.7, 117.1, 111.8, 111.3, 106.6, 106.4, 21.9, 21.7, 21.67, 21.64; Anal. Calcd for $C_{17}H_{14}N_2S$: C, 73.35; H, 5.07; N, 10.06; Found C, 73.21; H, 5.16; N, 10.01%.

6-Methoxy-3-(*p*-tolyl)benzo[4,5]imidazo[2,1-*b*]thiazole compound with 7-methoxy-3-(*p*-tolyl)benzo[4,5]imidazo[2,1-*b*]thiazole (1:1.1): (3ca+3c'a): Yellow solid (74 mg, 84%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (d, J = 9.2 Hz, 1H), 7.52 (d, J = 8.0 Hz, 4H), 7.35 (d, J = 7.6 Hz, 4H), 7.28-7.26 (m, 1H), 7.12 (d, J = 8.8 Hz, 1H), 6.96 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 6.74-6.67 (m, 2H), 6.52 (s, 2H), 3.85 (s, 3H), 3.68 (s, 3H), 2.47 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 164.3, 157.4, 156.8, 154.5, 145.9, 140.4, 134.4, 134.1, 131.4, 129.7, 129.6, 129.4, 128.9, 128.7, 126.5, 119.4, 112.2, 111.9, 110.3, 106.9, 106.4, 101.3, 55.9, 55.8, 22.0, 21.6; Anal. Calcd for $C_{17}H_{14}N_2OS$: C, 69.36; H, 4.79; N, 9.52; Found C, 69.47; H, 4.71; N, 9.61%.

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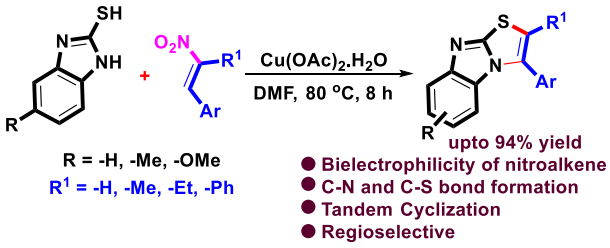
UPDATE

Synthesis of Benzo[4,5]imidazo[2,1-*b*]thiazole by Cu(II)-catalyzed Thioamination of Nitroalkene with 1*H*-Benzo[*d*]imidazole-2-thiol



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