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ARTICLE

Iodine -Mediated C-N and C-S bond formation: Regioselective synthesis of benzo [4,5]imidazo[2,1-*b*] thiazoles.

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The development of new strategy involving iodine mediated reaction for the construction of C-N and C-S bond formation has been reported. This method features inexpensive catalyst, base free and metal free with simple procedure and short reaction time.

Introduction

The Oxidative C-H bond activation/functionalization has emerged as an effective tool for the construction of carbon-carbon and carbon-heteroatom bond formations by using transition metals as a catalyst.[1-2] Also there are metal free organic synthesis for the construction C-C and C-X bond formations are popular.[3] Iodine seems to be an excellent reagent owing to its characteristics such as ready availability, low cost and non-metallic nature. Moreover, molecular iodine has additional advantages as it has a lowest dissociation, no radioactivity and moderate redox potential.[4] The use of iodine in oxidative coupling reactions has been extensively explored. Specifically, molecular iodine has been extensively used for C-S[5] coupling reaction involving sulfonylating reagents such as DMSO, R-SO_2NHNH_2, R'SO_2Na and R_2S_2. Li *et al*.[6] reported iodine-mediated intramolecular cyclization of enamines via iodide intermediates.

Benzimidazo[2,1-b]thiazoles are privileged structures encountered in wide range of natural products and bioactive molecules. This class of compounds exhibits diverse biological activities such as antibacterial,[7] antitumor,[8] antidiabetic,[9] anti-inflammatory,[10] antitubercular,[11] anti-cardiovascular agents,[12] anti-neurodegenerative[13] and immunosuppressive activities.[14] A number of synthetic methods have been developed for the synthesis of benzimidazo[2,1-b]thiazoles including copper (I) catalyzed arylation,[15] Pd–Cu catalyzed heterocyclization[16] and carbene rearrangement of hypervalent bromanes.[17] During 2010 Chen[18] *et al*. developed a powerful copper (I) catalysed aminothiolation of 1,1-dihaloalkene and later, in 2012, Xiao[19] *et al*. established a new method for the synthesis of N-fused heterocycles *via* C-S coupling and 5-endo-dig cyclization reactions (scheme 1). Recently Gabriele[20] *et al* reported palladium-catalyzed carbonylative multicomponent synthesis of functionalized benzimidazothiazoles.

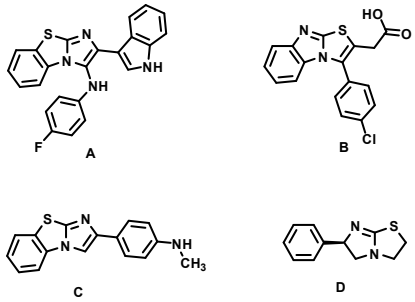

Figure 1. The representative examples of biological active imidazothiazoles.

However, there is no report available for the synthesis of benzimidazothiazoles starting from enamines. Enaminones are versatile synthons for organic synthesis and their chemistry received much attention in recent years. They are ambient in nature having the nucleophilicity of enamine and electrophilicity of enone finding applications as building blocks for the construction of large number of organic compounds.[21] Thus enaminones has been chosen as the starting material for the present investigation to get benzimidazothiazoles. The enamino ketones, (E)-1-(4-aryl)-3-(dimethylamino)-prop-2-en-1-ones, required for the present work, were prepared by the reported methods.[22] To the best of our knowledge, this is the first report for the simultaneous construction of C-N and C-S bonds in a single operation using molecular iodine (scheme 2).

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†Electronic Supplementary Information (ESI) available: Copies of 1H- and 13C-NMR spectra of all compounds, ESI-Mass spectra for selected compounds and X-ray diffraction data for compounds SA-2 and SA-4. CCDC 1444119 and 1444118. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/x0xx00000x

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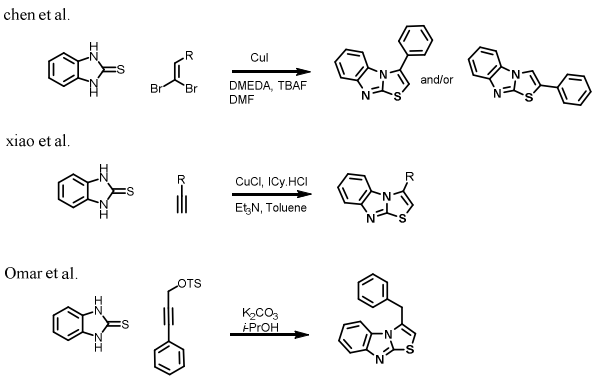
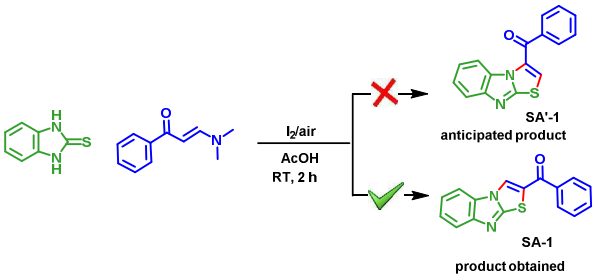


Scheme1. Previous approaches for the Synthesis of Imidazo [2,1-b]thiazoles.



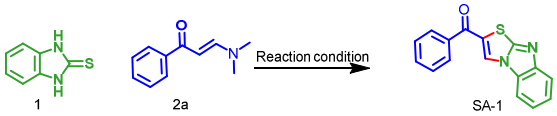
Scheme 2. Preparation of benzo[4,5]imidazo[2,1-b]thiazol-3-yl(phenyl)methanone.

Results and discussion

In continuation of our ongoing research for the development of new routes to access heterocyclic systems,[23] we started our investigation by employing of 2-mercaptobenzimidazole **1**(1.0 equiv), and (E)-1-(4-aryl)-3-(dimethylamino)-prop-2-en-1-one **2a**(1.0 equiv),as model substrates for the synthesis of benzo[4,5]imidazo[2,1-b]thiazole (**SA-1**) under various reaction conditions as depicted in Table 1. When the reaction was carried out in 5 mL of acetic acid at room temperature for 6 h, no product was formed (Table 1, entry 1). Further optimization revealed that the use of CuI (1.0 equiv) as a promoter in acetic acid at room temperature under open air for 12 h yielded 62% of the product (Table 1, entry 2). Here we expected SA'-1 as a product, because sulphur is strong nucleophile than nitrogen in 2-mercaptobenzimidazole, it can undergo thione-thiol tautomerization. There could be nucleophilic attack of (E)-3-(dimethylamino)-1-phenylprop-2-en-1-one with 1H-benzo[d]imidazole-2-thiol led to elimination of N,N-dimethylamine and then intramolecular cyclization may afford expected product SA'-1. Unfortunately the expected product SA'-1 was not formed. The product was unexpected SA-1 formed via nucleophilic substitution reaction and intramolecular oxidative cyclization followed by elimination of Me_2NH as a by-product was shown in scheme 2. The structure of SA-1 was undoubtedly assigned by spectral and single crystal X-ray data (Figures 2 and 3). Next we optimized equimolar amounts various copper reagents such as CuI, CuCl, CuBr, CuO, $Cu(OTf)_2$ and $Cu(OAc)_2$ as a promoter in acetic acid and DMF under atmospheric air. They were found to be less effective for this transformation (Table 1, entry 3-9).

Next we tried different oxidants such as $K_2S_2O_8$ (1.0 equiv) and oxone (1.0 equiv) in CH_3CN at room temperature, but unfortunately the desired product is not formed (Table 1, entry 10 and 11). With equimolar amount of iodine (Table 1, entries 12-18), this reaction worked well in acetic acid and acetonitrile, but not effective in other solvents such as toluene, dichloromethane, THF, DMF and ethanol. By simply stirring **1** and **2a** with iodine (1.0 equiv) in acetic acid at room temperature under open air for 2 h, the product was obtained in 92% yield (Table 1, entry 14). When the reaction was carried out with and without oxygen atmospheres, the yield of the reaction in absence of air atmosphere was apparently lower, which proved that O_2 air played an energetic role in the process. These optimized results indicate that one equivalent of iodine is necessary for the full conversion of the starting materials. When I_2 (0.5 equiv) was used, only 47% product was obtained even after 6 h (Table 1, entry 19).

Table 1. Optimization of reaction conditions[a]



Entry	Promoter (1.0 equiv)	Solvent	Temp	Time	Yield (%)[b]
1	----[c]	AcOH	RT	6 h	NR[d]
2	CuI	AcOH	RT	12 h	62
3	CuI	AcOH	100 °C	12 h	57
4	CuI	DMF	100 °C	12 h	51
5	CuCl	DMF	100 °C	12 h	20
6	CuBr	DMF	100 °C	12 h	25
7	CuO	DMF	100 °C	12 h	NR
8	$Cu(OTf)_2$	DMF	100 °C	12 h	40
9	$Cu(OAc)_2$	DMF	RT	12 h	48
10	$K_2S_2O_8$	MeCN	RT	12 h	NR
11	Oxone[e]	MeCN	RT	12 h	NR
12	I_2	Toluene	RT	6 h	31
13	I_2	DCM	RT	6 h	55
14	**I_2**	**AcOH**	**RT**	**2 h**	**92**
15	I_2	MeCN	RT	2 h	81
16	I_2	DMF	RT	6 h	62
17	I_2	THF	RT	6 h	58
18	I_2	EtOH	RT	6 h	38
19	I_2 (0.5)	AcOH	RT	6 h	47

[a]Reaction conditions: 2-mercaptobenzimidazole (1.0 equiv), (E)-1-(4-aryl)-3-(dimethylamino)-prop-2-en-1-one 2 (1.0 equiv), promoter(1.0equiv) oxidant (1.0 equiv) under open air in 5 mL of solvent. [b]Isolated yield. [c]Reagent free reaction. [d]No reaction. [e]Chemical formula of oxone is $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$.

With the optimized conditions in hand, we extended the scope of the reaction using electron withdrawing and electron donating substituent in phenyl rings were converted to the corresponding products in moderate to good yields (Scheme 2, 78–92%; SA-1-14). The optimized conditions were also successfully applied to a hetero aryl enaminones, which generated the corresponding heterocyclic substituted products in moderate yields (71 and 77%; SA-15 and 16) respectively. In

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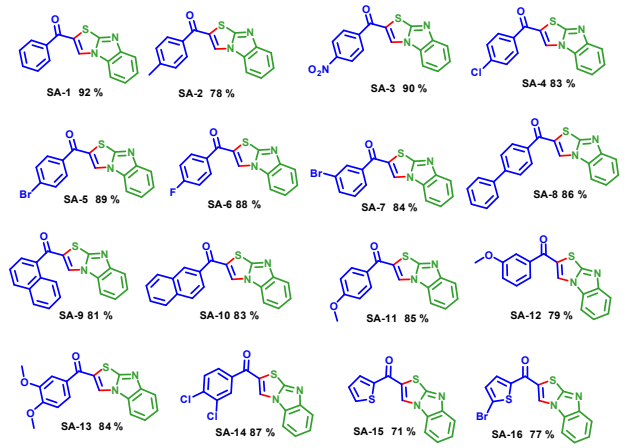
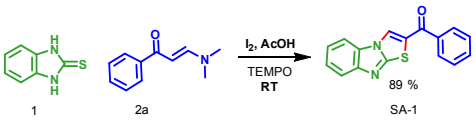
order to understand the mechanism of this reaction, the radical trapping experiments were tested (Scheme 3). TEMPO (2,2,6,6-tetramethylpiperidinooxy) was used as a radical scavenger. In the presence of TEMPO, SA-1 was observed in good yield (89%) and this result indicating that radical intermediates were not involved in this reaction.[24]

Table 2. Synthesized compounds SA-1-16[a]

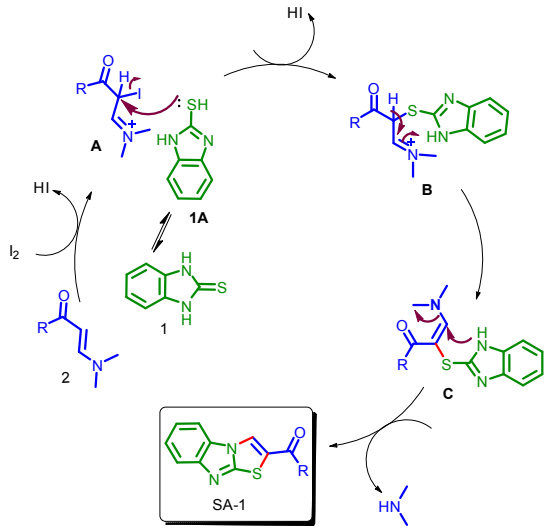


[a]Isolated yield.



Scheme 3 Control experiments.

The structures of all the synthesized compounds were confirmed by ^{1}H NMR, ^{13}C NMR, ESI-MASS and HRMS spectroscopic methods. The structures of compounds **SA-2** and **SA-6** were undoubtedly confirmed by X-ray diffraction analysis.[25] On the basis above results and literature report, a tentative mechanism is proposed for the formation of benzo[4,5]imidazo[2,1-b]thiazole (SA-1-16) as depicted in scheme 4. Initially the addition reaction between enaminones **2** and iodine leads to the formation of intermediate **A**.[26] The tautomeric thiol **1A** under acidic conditions undergoes nucleophilic substitution reaction affording intermediate **B** by the removal of HI molecule. This is followed by an intramolecular cyclization giving **C** and finally the removal of N,N-dimethylamine under acidic condition leads to the formation of the desired product benzo[4,5]imidazo[2,1-b]thiazole.



Scheme 4. Proposed mechanism for the formation of benzo[4,5]imidazo[2,1-*b*]thiazol-3-yl(phenyl)methanone.

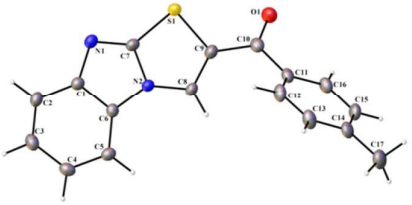


Figure 2. ORTEP diagram of SA-2.

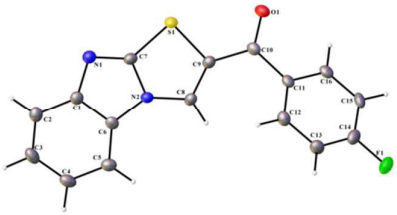


Figure 3. ORTEP diagram of SA-6.

Conclusions

We have developed a mild, novel and efficient iodine-mediated oxidative C-N and C-S bond reaction for the synthesis of substituted benzo[4,5]imidazo[2,1-b]thiazoles. The reaction is highly selective, metal and base free and shorter reaction time.

Experimental section

General methods

The melting points were measured in open capillary tubes and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker (Avance) 300 MHz NMR instrument using TMS as internal standard either $CDCl_3$ or DMSO-d^6 as solvent. Chemical shifts are given in parts per million (δ-scale) and the coupling constants are given in hertz (Hz). Silica gel-G plates (Merck) were used for thin layer chromatography (TLC) analysis with a mixture of petroleum ether (60-80 °C) and ethyl acetate as eluent. The single crystal X-ray data were collected on BRUKER GADDS X-ray (three-circle) diffractometer with Mo

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Ka(k= 1.5418 A˚) radiation. Elemental analyses were performed on a vario EL III CHNS elemental analyzer. Mass spectra were recorded in LCQ Fleet mass spectrometer, Thermo Fisher Instruments Limited, US. Electrospray ionization mass spectrometry (ESI-MS) analysis was performed in the positive ion and negative ion mode on a liquid chromatography ion trap.

General experimental procedure for benzo[4,5]imidazo[2,1-*b*]thiazol-3-yl(phenyl)methanone SA-1-16. A mixture of 2-mercaptobenzimidazole 1 (1.0 equiv), (E)-1-(4-aryl)-3-(dimethylamino)-prop-2-en-1-one 2 (1.0 equiv), and iodine (1.0equiv) was added to 5 mL of acetic acid under open air at room temperature for 2 h. The completion of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured into water and workup with sodium thiosulfate and the solution was extracted with ethyl acetate. The combined organic phase was dried over Na_2SO_4 and then the solvent was removed. The crude sample was purified by column chromatography.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(phenyl)methanone (SA-1) White solid, mp; 142-44 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.22 (s, 1H), 7.86 (d, *J* = 8.1 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 2H), 7.57 (t, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 187.2, 156.7, 148.6, 137.0, 133.1, 130.0, 129.5, 129.0, 128.7, 125.1, 122.0, 122.0, 119.7, 110.8 ppm. MS m/z 279.1 $(M+1)^+$. Anal.Calcd for $C_{16}H_{10}N_2O_2S$: C, 69.05; H, 3.62; N, 10.07; found C, 69.01; H, 3.59; N, 10.04.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(p-tolyl)methanone (SA-2) White solid, mp; 155-57 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.21 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 3H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.42-7.34 (m, 3H), 7.26 (t, *J* = 7.5 Hz, 1H), 2.47 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 186.8, 156.7, 148.5, 144.0, 134.3, 130.2, 129.7, 128.8, 125.0, 121.9, 119.6, 110.7, 21.79 ppm. MS m/z 292.3560 $(M)^+$. Anal.Calcd for $C_{17}H_{12}N_2OS$: C, 69.84; H, 4.14; N, 9.58; found C, 69.81; H, 4.11; N, 9.54.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(nitrophenyl)methanone (SA-3) Yellow solid, mp; 190-92 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.73 (s, 1H), 8.54 (d, *J* = 8.1 Hz, 2H), 8.28 (s, 1H), 8.23 (d, *J* = 8.1 Hz, 2H), 7.82 (m, 2H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 185.6, 150.7, 128.5, 124.7, 123.3, 121.5, 120.1, 119.7, 117.6, 116.6, 114.2, 105.1, 104.6 ppm. MS m/z 323.03 $(M+1)^+$. Anal.Calcd for $C_{16}H_9N_3O_3S$: C, 59.44; H, 2.81; N, 13.00; found C, 59.41; H, 2.78; N, 12.97.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(4-chlorophenyl)methanone (SA-4) White solid, mp; 177-79 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.25 (s, 1H), 7.83-7.63 (m, 3H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 185.9, 156.6, 148.6, 139.5, 135.2, 130.0, 129.7, 129.5, 129.34, 125.4, 125.2, 122.1, 119.7, 110.8 ppm. MS m/z 313.18 $(M+1)^+$. Anal.Calcd for $C_{16}H_9ClN_2OS$: C, 61.44; H, 2.90; N, 8.96; found C, 61.41; H, 2.88; N, 8.93.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(4-bromophenyl)methanone (SA-5) White solid, mp; 208-10 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.64 (s, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 2H), 7.56-7.52 (m, 3H), 7.24 (t, *J* = 8.1 Hz, 1H) 7.10 (t, *J* = 8.1 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 185.6, 155.8, 147.2, 135.0, 131.7, 130.0, 129.2, 129.0, 127.4, 127.2, 124.7, 121.7, 118.5, 111.5 ppm. MS m/z 357.0 $(M+1)^+$. Anal.Calcd for $C_{16}H_9BrN_2OS$: C, 53.80; H, 2.54; N, 7.54; found C, 53.77; H, 2.51; N, 7.51.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(4-flurophenyl)methanone (SA-6) White solid, mp; 180-82°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.43 (s, 1H), 7.42-7.38 (m, 3H), 7.07 (d, *J* = 7.8 Hz, 1H) 6.79 (t, *J* = 7.8 Hz, 1H), 6.75 - 6.66 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 184.2, 164.1 (d, $^1J_{C\text{-}F}$ =251.8 Hz), 155.0, 146.8, 131.9, 130.4 (d, $^3J_{C\text{-}F}$ = 9 Hz), 128.7, 127.9, 126.8, 123.7, 120.7, 117.6, 114.8 (d, $^2J_{C\text{-}F}$ = 21.8 Hz), 111.1 ppm. MS m/z 297.13 $(M+1)^+$. Anal.Calcd for $C_{16}H_9FN_2OS$: C, 64.85; H, 3.06; N, 9.45; found C, 64.81; H, 3.03; N, 9.41.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(3-bromophenyl)methanone (SA-7) White solid, mp; 163-65 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.38 (s, 1H), 8.11(s, 1H), 7.91 (d, *J* = 7.8 Hz, 2H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.60 - 7.55 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 185.6, 138.8, 136.0, 131.6, 130.7, 129.8, 127.2, 125.6, 125.5, 123.3, 122.4, 119.8, 111.1 ppm. MS m/z 358.98 $(M+1)^+$. Anal.Calcd for $C_{16}H_9BrN_2OS$: C, 53.80; H, 2.54; N, 7.84; found C, 53.76; H, 2.51; N, 7.81.

[1,1'-biphenyl]-4-yl(benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl)methanone (SA-8) Brown solid, mp; 157-59 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.41 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 2H), 7.92-7.87 (m, 3H), 7.83-7.73 (m, 3H), 7.64-7.51 (m, 4H), 7.43 (t, *J* = 7.5 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 186.9, 157.3, 148.9, 146.3, 139.9, 136.0, 130.6, 129.6, 129.4, 129.4, 128.8, 127.9, 127.6, 127.6, 125.4, 122.3, 120.0, 111.1 ppm. MS m/z 353.07 $(M-1)^-$.Anal.Calcd for $C_{22}H_{14}N_2OS$: C, 74.55; H, 3.98; N, 7.90; found C, 74.52; H, 3.95; N, 7.87.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(naphthalen-1-yl)methanone (SA-9) White solid, mp; 203-05 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.17 (s, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.95-7.93 (m, 1H), 7.83 (t, *J* = 7.5 Hz, 2H), 7.66 (m, 4H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 188.2, 134.4, 134.0, 133.0, 132.3, 130.4, 129.1, 128.6, 128.0, 127.3, 127.1, 126.6, 125.8, 125.1, 124.4, 122.7, 119.0, 111.2 ppm. MS m/z 329.11 $(M+1)^+$. Anal.Calcd for $C_{20}H_{12}N_2OS$: C, 73.15; H, 3.68; N, 8.53; found C, 73.12; H, 3.66; N, 8.50.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(naphthalen-2-yl)methanone (SA-10) White solid, mp; 212-14 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.43 (s, 1H), 8.33 (s, 1H), 8.06-8.03 (m, 2H), 7.97 (t, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.72-7.64 (m, 3H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H) ppm; ^{13}C NMR (75

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MHz, $CDCl_3$) δ: 191.8, 161.2, 152.7, 140.1, 138.9, 137.2, 135.2, 134.5, 133.7, 133.5, 132.6, 132.0, 129.8, 129.5, 126.8, 123.6, 117.2 ppm. MS m/z 329.09 $(M+1)^+$. Anal.Calcd for $C_{20}H_{12}N_2OS$: C, 73.15; H, 3.68; N, 8.53; found C, 73.11; H, 3.65; N, 8.50.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(4-methoxyphenyl)methanone (SA-11) White solid, mp; 161-63 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.25 (s, 1H), 7.91(d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 1H), 3.92 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ:185.6, 163.7, 156.5, 148.4, 131.0, 130.2, 129.5, 124.9, 124.5, 121.9, 119.5, 114.2, 110.8, 55.6 ppm. MS m/z 309.13 $(M+1)^+$. Anal.Calcd for $C_{17}H_{12}N_2O_2S$: C, 66.22; H, 3.92; N, 9.08; found C, 66.18; H, 3.89; N, 9.04.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(3-methoxyphenyl)methanone (SA-12) White solid, mp; 170-72 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.29 (s, 1H), 8.01 (s, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.44 (broad, 2H), 7.29 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 3.97 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ:185.6, 153.6, 149.6, 130.0, 129.7, 125.0, 124.5, 123.2, 121.9, 119.7, 113.3, 110.7, 110.3, 56.2 ppm. Anal.Calcd for $C_{17}H_{12}N_2O_2S$: C, 66.22; H, 3.92; N, 9.08; found C, 66.18; H, 3.89; N, 9.04.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(3,4-methoxyphenyl)methanone (SA-13) White solid, mp; 127-29 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.29 (s, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.44 (broad, 2H), 7.29 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 4.00 (s, 3H), 3.97 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ:185.7, 156.8, 153.6, 149.7, 148.5, 130.1, 129.8, 129.6, 125.0, 124.5, 123.3, 122.0, 119.7, 111.3, 110.8, 110.3, 56.3, 56.3 ppm. MS m/z 339.30 $(M+1)^+$. Anal.Calcd for $C_{18}H_{14}N_2O_3S$: C, 63.89; H, 4.17; N, 8.28; found C, 63.86; H, 4.15; N, 8.25.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(3,4-dichlorophenyl)methanone (SA-14) Yellow solid, mp; 127-29 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.26 (s, 1H), 7.96 (s, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.72 - 7.64 (m, 3H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 184.7, 156.6, 148.8, 137.8, 136.7, 133.9, 131.2, 130.6, 129.6, 129.4, 127.7, 125.6, 125.4, 122.3, 120.0, 110.9 ppm. Anal.Calcd for $C_{16}H_8Cl_2N_2OS$: C, 55.35; H, 2.32; N, 8.07; found C, 55.31; H, 2.30; N, 8.04.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(thiophen-2-yl)methanone (SA-15) Yellow solid, mp; 185-87 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.52 (s, 1H), 7.96 (d, *J* = 3.9 Hz, 1H), 7.80 (t, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 7.8 Hz,1H), 7.44 (t, *J* = 7.8 Hz,1H), 7.35 (t, *J* = 7.8 Hz,1H), 7.28(m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 177.6, 156.5, 148.6, 141.3, 134.2, 132.9, 129.6, 129.3, 128.5, 125.1, 123.8, 122.1, 119.7, 110.9 ppm. MS m/z 285.0 $(M+1)^+$. Anal.Calcd for $C_{14}H_8N_2OS_2$: C, 62.85; H, 3.23; N, 8.93; found C, 62.82; H, 3.20; N, 8.90.

benzo[4,5]imidazo[2,1-*b*]thiazol-2-yl(5-bromothiophen-2-yl)methanone (SA-16) Yellow solid, mp; 178-80 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.47 (s, 1H), 8.89 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 4.2 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 4.2 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.3, 156.3, 148.7, 142.9, 133.0, 131.6, 129.6, 128.5, 125.3, 123.8, 123.4, 122.2, 119.9, 110.9 ppm. MS m/z 364.9 $(M+1)^+$. Anal.Calcd for $C_{14}H_7BrN_2OS_2$: C, 46.29; H, 1.94; N, 7.71; found C, 46.26; H, 1.92; N, 7.68.

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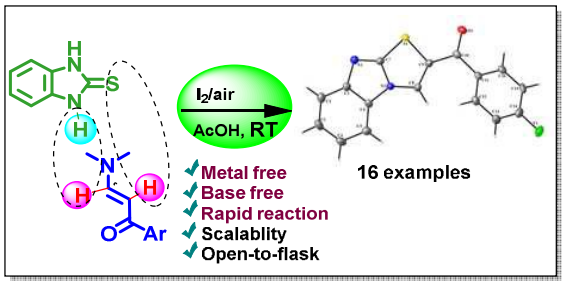

Regioselective synthesis of benzo[4,5]imidazo[2,1-b]thiazole derivatives via amination (C-N) and intramolecular cyclization (C-S) reaction in presence molecular iodine. This method features inexpensive catalyst, base free and metal free with simple procedure and short reaction time.