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ORIGINAL PAPER

Transition-metal-free synthesis of imidazobenzothiazines via domino C-S/C-N bond formation

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Abstract The carbon-heteroatom bond formation is an important research field. Transition-metal-free synthesis of medicinally important heterocycles avoids products of transition metal contamination, and thus it is an environmentally friendly and cost-saving process. A transition-metal-free domino C-S/C-N formation for the synthesis of imidazobenzothiazines from 2-mercaptobenzimidazoles and 2-halobenzyl bromides is developed. The desired products were obtained in good to excellent yields. The mechanism of domino nucleophilic substitution (S_N2) and nucleophilic aromatic substitution (S_NAr) is proposed.

Keywords Green chemistry · Domino reaction · Imidazobenzothiazines · Coupling reaction · Transition-metal-free

Introduction

The carbon-heteroatom bond formation is one of the most important fields in organic chemistry. Numerous methods have been developed in last decades since Ullmann and Goldberg firstly reported the C-N cross-coupling reaction [1–3]. Most commonly palladium complexes and copper compounds are used as catalysts to promote the C-N and C-S coupling reaction. But disadvantages, for example, residual transition metal contaminant, seriously limit their applications. Therefore, to develop economical, transition-metal-free, and environmentally friendly cascade processes is drawing many chemists' attention. Early in 2001, Beller first reported a transition-metal-free intra- and intermolecular C-N coupling with aryl chlorides with primary and secondary amines as substrates [4]. Thereafter, a great number of C-X coupling reactions have been developed into transition-metal-free reactions [5–15].

Heterocycles bearing C-S and C-N bond, for example, imidazobenzothiazines, have been found with a broad range of uses in drugs, such as anti-inflammatory [16, 17], antimicrobial [18, 19], antitubercular [20–23], antifungal [24, 25], antagonist [26–30], and in functional material additives [31–33]. In the synthesis of these compounds, tandem C-S/C-N formation shows obvious advances over other methods due to their facile one-pot procedure [34–37]. In addition, recent advances in tandem reactions with C-X (X=N, S, O) coupling reactions show their great importance in both methodology development [37–42] and natural product synthesis [43]. However, these tandem reactions are always carried out in presence of transition metals. Therefore, development of transition-metal-free domino C-X (X=N, S, O) bond formation is of importance.

As part of our ongoing studies on C-S/C-N cascade coupling reaction (Scheme 1, equation A) [44–47] and C-X coupling reactions [48–50], we revisited tandem C-N/C-S bond formation to synthesize imidazobenzothiazines from 2-mercaptobenzimidazole and 2-iodobenzyl bromide (Scheme 1, equation B) [34], and discovered the transition-metal-free synthesis of imidazobenzothiazines (Scheme 1, equation C).

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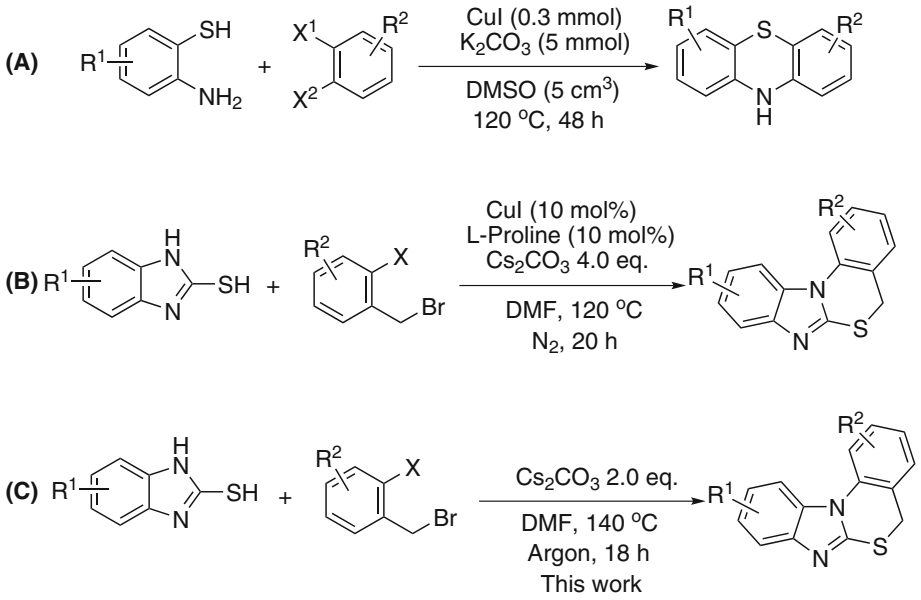
Scheme 1



Results and discussion

As a start, we choose 2-mercaptobenzimidazole and 2-iodobenzyl bromide as the model substrates to optimize reaction conditions, and the results are summarized in Table 1.

Firstly, we performed the reaction under the similar reaction conditions to the coupling reactions [44]. The expected product was obtained with high yield up to 85 % (Table 1, entry 1). CuBr, CuCl, $Cu(OAc)_2$, CuO, and $CuSO_4$ were found to be efficient catalysts for the tandem C-S/C-N reactions, while CuI gave the best result (Table 1, entries 1–7). In view of recent advances in transition-metal-free reactions [4–15], we intentionally performed this reaction without any copper salt as catalyst, and we surprisingly found that the desired product was also obtained (Table 1, entry 8). We then changed K_2CO_3 to Na_2CO_3, but lower yield was encountered (Table 1, entry 9).

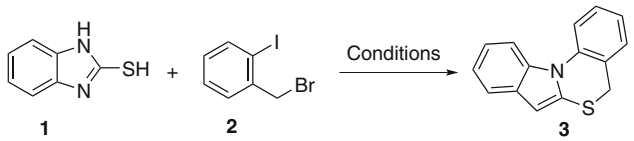
In account of the hydrogen atoms attaching to S and N are acidic rather than basic, we surmised that more basic base may benefit this reaction. So we tried K_3PO_4, KOH, and NaOH (Table 1, entries 10–12); however, the yield decreased. Fortunately, when we tried Cs_2CO_3 as a base, the yield increased to 52 % (Table 1, entry 13). After screening the amount of Cs_2CO_3, 2.0 equivalents were found to be the best one for this reaction (Table 1, entries 13–15).

Next, we studied the solvent influence. When performed in DMA, the yield went up to 54 %, and peaked in DMF at 57 % (entries 16, 17, and 18 vs. 13). We next increased the reaction temperature to 140 °C, and the yield sharply rose up to 83 % (Table 1, entry 19). But the yield did not increase any more when temperature was further raised to 150 °C (Table 1, entries 19 and 20). Both shortening and prolonging reaction time gave no positive effect on the yields (Table 1, entries 21 and 22).

With the optimized conditions at hand, other substrates were evaluated to examine the scope of the transition-metal-free C-S/C-N tandem reaction (Table 2). The results showed that all of the tested 2-mercaptobenzimidazoles could react with 2-halobenzyl bromides smoothly with good to excellent yields (Table 2). When 5-methyl-1*H*-benzo[*d*]imidazole-2-thiol was used, a pair of isomers of imidazobenzothiazine with 9- and 10-methyl groups was obtained with an excellent total yield of 90 % and with nearly 1:1 isomer ratio (Table 2, entry 2). All of the substituted 1*H*-benzo[*d*]imidazole-2-thiols **1** (5-Me, Cl, EtO, MeO, CF_3, and NO_2) afforded a pair of isomers with a ratio of about 1:1, respectively (Table 2, entries 2–7). Furthermore, we noticed that 1*H*-benzo[*d*]imidazole-2-thiol with electron-withdrawing groups gave lower yield (Table 2, entries 6 and 7), while these with electron-donating groups afforded higher yields (Table 2, entries 2–5).

On the contrary to the effects of electronic properties of substituents in 1*H*-benzo[*d*]imidazole-2-thiols on yields, 2-bromobenzyl bromide with an electron-withdrawing trifluoromethyl group reacted with 2-mercaptobenzimidazoles to afford pretty good yields (Table 2, entries 8–11). These 2-halobenzyl bromides with electron-donating groups (4,5-OCH_2O and 5-OCH_3) gave lower yields, no matter whether the substituents on 1*H*-benzo[*d*]imidazole-

Table 1 Optimization of reaction conditions



Entry	Catalyst	Base	Solvent	*T*/°C	*t*/h	Yield/%[a]
1	CuI	K_2CO_3	DMSO	120	18	85
2	CuBr	K_2CO_3	DMSO	120	18	82
3	CuCl	K_2CO_3	DMSO	120	18	84
4	$Cu(OAc)_2$	K_2CO_3	DMSO	120	18	81
5	CuO	K_2CO_3	DMSO	120	18	82
6	$CuSO_4$	K_2CO_3	DMSO	120	18	82
7	Cu	K_2CO_3	DMSO	120	18	83
8	–	K_2CO_3	DMSO	120	18	47
9	–	Na_2CO_3	DMSO	120	18	31
10	–	K_3PO_4	DMSO	120	18	38
11	–	KOH	DMSO	120	18	35
12	–	NaOH	DMSO	120	18	35
13	–	Cs_2CO_3	DMSO	120	18	52
14[b]	–	Cs_2CO_3	DMSO	120	18	46
15[c]	–	Cs_2CO_3	DMSO	120	18	48
16	–	Cs_2CO_3	NMP	120	18	43
17	–	Cs_2CO_3	DMA	120	18	54
18	–	Cs_2CO_3	DMF	120	18	57
19	–	Cs_2CO_3	DMF	140	18	83
20	–	Cs_2CO_3	DMF	150	18	82
21	–	Cs_2CO_3	DMF	140	12	74
22	–	Cs_2CO_3	DMF	140	24	82

Reaction conditions: unless otherwise noted, all these cascade couplings were performed with 2.0 equiv. base under argon

[a] Yield after isolation

[b] Cs_2CO_3 was used in 1.0 equiv.

[c] Cs_2CO_3 was used in 3.0 equiv.

2-thiol were electron-donating or withdrawing (Table 2, entries 12–16). All of the reactions of substituted 1*H*-benzo[*d*]imidazole-2-thiols with 2-bromobenzyl bromides provided pairs of isomers (Table 2, entries 9–15). Lower yield encountered when 2,6-dichlorobenzyl bromide was used as a substrate (Table 2, entry 17). The reason probably is the lower activity of chloro atom on the aromatic ring. The simple 1*H*-imidazole-2-thiol also reacted smoothly with 2-iodobenzyl bromide but gave moderate yield (Table 2, entry 18).

Next, to explore the transition-metal-free tandem C-S/C-N reaction mechanism, the following control experiments were performed under the standard reaction conditions. We first chose benzyl bromide (1.0 mmol) to couple with 2-mercaptobenzimidazole (1.0 mmol) to make clear which H atom attached to S and N atoms in 2-mercaptobenzimidazole was first deprotonated by Cs_2CO_3. The result of only the C-S formation product obtained (Scheme 2, equation A), which implies that Cs_2CO_3 first deprotonates the S-attached H atom.

To figure out which carbon atom (C2 of the aromatic ring or benzylic carbon) is first to react with S or N heteroatom, we performed the reaction of 2-mercaptobenzimidazole (1.0 mmol) with benzyl bromide (1.0 mmol) and iodobenzene (1.0 mmol). That the only product 2-(benzylthio)-1*H*-benzo[*d*]imidazole was obtained demonstrates that the benzylic carbon was the first to react with thio group (Scheme 2, equation B). So the C-S bond is formed via a S_N2 pathway with the aid of Cs_2CO_3, and then an intramolecular nucleophilic aromatic substitution (S_NAr) affords the desired product.

Based on the above experimental data, a mechanism is proposed (Scheme 3). The first step is the double molecular nucleophilic substitution (S_N2) of 2-mercaptobenzimidazole and 2-iodobenzyl bromide with the aid of Cs_2CO_3. Then a small amount of S-(2-iodobenzylthio)benzimidazole is deprotonated by Cs_2CO_3 and the resulting strong benzoimidazole anion attacks iodobenzene via intramolecular S_NAr mechanism to afford the desired imidazobenzothiazines. The higher temperature and intramolecular proper spatial structure are necessary factors for this transformation.

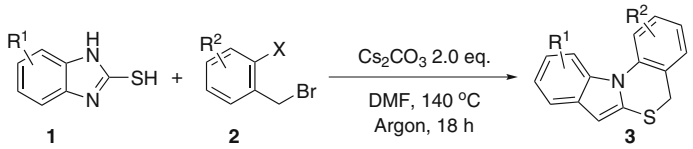
In conclusion, the first transition-metal-free domino C-S/C-N formation for the synthesis of imidazobenzothiazines from readily available 2-halobenzyl halides and 2-mercaptobenzimidazoles has been developed. The imidazobenzothiazines have potential application in biologically active compounds and functional material additives, so the facile cascade process without residual transition metal contamination has a good prospect in pharmaceutics and functional materials.

Experimental

All the reagents were purchased from Aldrich, Alfa Aesar, Aladdin, and Kelong chemical companies and used without further purification. KOH (99.999 %, metals basis), NaOH (99.99 %, metals basis), Na_2CO_3 (99.9999 %, metals basis), and K_2CO_3 (99.995 %, metals basis) were purchased from Aladdin Reagent Company and Cs_2CO_3 with a purity of 99.994 % (metals basis) was purchased from Alfa Aesar Company.

Purification of the synthesized compounds was carried out by flash column chromatography with silica gel (300–400 meshes). ^1H NMR and ^{13}C NMR spectra were recorded with DMSO-d_6 or $CDCl_3$ as solvent and TMS as an internal standard on a Bruker Avance-300 or 400

Table 2 C-S/C-N tandem reaction of 2-mercaptobenzimidazoles with 2-halobenzyl bromides under optimized conditions



Entry	R^1	R^2	X	Product	Yield/%[a]
1	H	H	I	**3a**	83
2	5-Me	H	I	**3b**	90
3	5-Cl	H	I	**3c**	85
4	5-EtO	H	I	**3d**	88
5	5-MeO	H	I	**3e**	79
6	5-CF_3	H	I	**3f**	72
7	5-NO_2	H	I	**3g**	61
8[b]	H	5-CF_3	Br	**3h**	87
9[b]	5-Me	5-CF_3	Br	**3i**	92
10[b]	5-Cl	5-CF_3	Br	**3j**	90
11[b]	5-EtO	5-CF_3	Br	**3k**	91
12	5-Me	4,5-OCH_2O	Br	**3l**	74
13	5-Cl	4,5-OCH_2O	Br	**3m**	75
14	5-EtO	4,5-OCH_2O	Br	**3n**	78
15	5-MeO	4,5-OCH_2O	Br	**3o**	67
16	H	5-OCH_3	Br	**3p**	77
17	H	6-Cl	Cl	**3q**	70
18[c]	–	H	I	**3r**	66

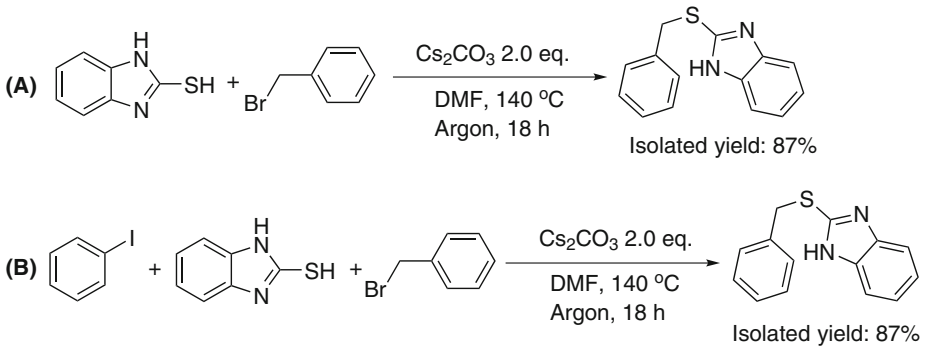
Reaction conditions: unless otherwise noted, all these cascade couplings were performed with 2.0 equiv. of base under argon protection

[a] Yield after isolation

[b] 1.0 equiv. Cs_2CO_3 was used

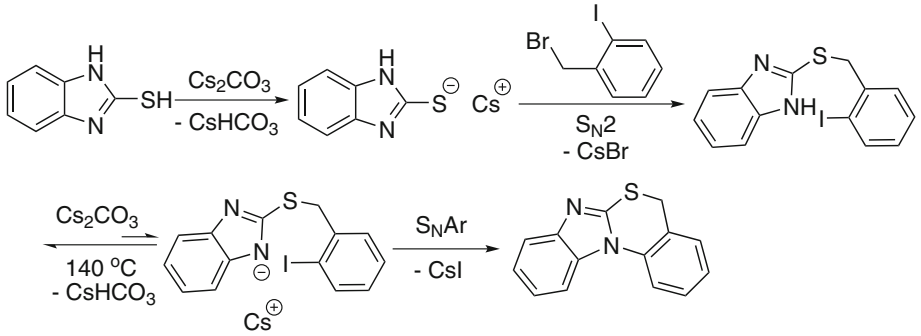
[c] 3.0 equiv. Cs_2CO_3 was used, starting material was 2-mercaptoimidazoline

Scheme 2



spectrometer (300 MHz, 400 MHz). All IR spectra were taken on a Bruker Tensor-27 infrared spectrometer with an OPUS workstation. Electrospray ionization mass spectra were recorded on an Agilent 1200 series LC/MS DVL instrument. Melting points were determined on an X-4 melting-point apparatus with microscope.

Scheme 3



*General procedure for C-S/C-N one-pot tandem reaction: 5H-benzimidazo[1,2-a][3, 1]-benzothiazine (**3a**)*

To an oven-dried test tube with ground joint with a magnetic stir bar, 150 mg 2-mercaptobenzimidazole (1.0 mmol), 650 mg Cs_2CO_3 (2.0 mmol), 297 mg 2-iodobenzyl bromide (1.0 mmol), and 5 cm^3 DMF were added. Then the sealed test tube was evacuated and backfilled with argon for three times. The test tube was put in a preheated oil bath at 140 °C, and the mixture was stirred at 140 °C for 18 h (see Table 2). After the test tube was cooled to room temperature, it was unfastened and 10 cm^3 water was added. The reaction mixture was extracted with 15 cm^3 ethyl acetate for three times. The combined organic layer was dried over anhydrous Na_2SO_4 and condensed in vacuo. The residue was purified by column chromatography on silica gel with petroleum ether and ethyl acetate (10:1 to 3:1 v/v) as an eluent to provide the desired product.

5H-Benzimidazo[1,2-a][3, 1]-benzothiazine (**3a**, $C_{14}H_{10}N_2S$)
Yield: 83 %; bright yellow solid; m.p.: 112–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) $\delta\delta = 7.83$ (m, 2H), 7.75 (m, 1H), 7.46 (m, 2H), 7.32 (m, 2H), 7.27 (m, 1H), 4.04 (s, 2H) (Ref. [34] 112–113 °C).

9- and 10-Methyl-5H-benzimidazo[1,2-a][3, 1]-benzothiazine, mixture of isomers (**3b**, $C_{15}H_{12}N_2S$)
Yield: 90 %; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) $\delta = 7.78$ (dd, $J = 11.4$ Hz, 8.2 Hz, 1H), 7.62 (dd, $J = 12.0$ Hz, 8.4 Hz, 1H), 7.48 (m, 1H), 7.41 (dd, $J = 11.0$ Hz, 4.4 Hz, 1H), 7.35 (d, $J = 7.5$, 1H), 7.22 (m, 1H), 7.11 (m, 1H), 3.98 (s, 2H), 2.49 (d, $J = 10.9$, 3H), ^{1}H NMR was found to be identical with the one described in Ref. [34].

9- and 10-Chloro-5H-benzimidazo[1,2-a][3, 1]-benzothiazine, mixture of isomers (**3c**, $C_{14}H_9ClN_2S$)
Yield: 85 %; white solid; m.p.: 157–158 °C; ^{1}H NMR (300 MHz, DMSO): $\delta = 7.98$ (m, 1H), 7.89 (m, 1H), 7.69 (dd, $J = 19.9$, 5.3 Hz, 1H), 7.58 (d, $J = 7.4$ Hz, 1H), 7.53 (d, $J = 7.9$ Hz, 1H), 7.37 (t, $J = 5.5$ Hz, 1H), 7.33 (d, $J = 1.9$ Hz, 1H), 4.31 (d, $J = 3.1$ Hz, 2H) ppm; ^{13}C NMR (75 MHz, DMSO): $\delta = 152.22$, 151.50, 144.36, 142.15, 134.32, 132.78, 131.06, 129.12, 128.37, 127.57, 126.13, 123.50, 122.84, 119.81, 118.22, 113.14, 111.77, 29.02 ppm; MS (ESI): $m/z = 273$ ($[M + H]^+$).

9- and 10-Ethoxy-5H-benzimidazo[1,2-a][3, 1]-benzothiazine, mixture of isomers (**3d**, $C_{16}H_{14}N_2OS$)
Yield: 88 %; light yellow solid; m.p.: 112–113 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.81$ (d, $J = 8.1$ Hz, 1H), 7.61 (d, $J = 8.8$ Hz, 1H), 7.45 (t, $J = 7.8$ Hz, 1H), 7.39 (d, $J = 6.9$ Hz, 1H), 7.32 (d, $J = 2.2$ Hz, 1H), 7.26 (dd, $J = 8.0$, 7.0 Hz, 1H), 6.94 (dd, $J = 8.8$, 2.3 Hz, 1H), 4.10 (q, $J = 7.0$ Hz, 2H), 4.01 (s, 2H), 1.46 (t, $J = 7.0$ Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 155.99$, 150.64, 148.99, 144.90, 38.29, 135.39, 133.16, 128.85, 128.09, 125.67, 119.63, 117.78, 112.55, 111.79, 102.95, 97.25, 64.35, 30.52, 14.93 ppm; MS (ESI): $m/z = 283$ ($[M + H]^+$).

9- and 10-Methoxy-5H-benzimidazo[1,2-a][3, 1]-benzothiazine, mixture of isomers (**3e**, $C_{15}H_{12}N_2OS$)
Yield: 79 %; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.48$ (d, $J = 1.5$ Hz, 1H), 7.38 (dd, $J = 11.6$, 4.8 Hz, 1H), 7.30 (t, $J = 6.6$ Hz, 3H), 7.21 (m, 1H), 7.13 (d, $J = 1.4$ Hz, 1H), 3.99 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 143.48$, 140.55, 132.51, 132.16, 128.06, 127.04, 121.28, 119.31, 118.43, 118.00, 37.83, 28.68 ppm; MS (ESI): $m/z = 269$ ($[M + H]^+$).

9- and 10-(Trifluoromethyl)-5H-benzimidazo[1,2-a]-[3, 1]benzothiazine, mixture of isomers (**3f**, $C_{15}H_9F_3N_2S$)
Yield: 72 %; light yellow solid; m.p.: 132–134 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.32$ (d, $J = 8.1$ Hz, 1H), 7.17 (td, $J = 7.8$, 1.5 Hz, 1H), 7.04 (d, $J = 7.3$ Hz, 1H), 7.00 (s, 1H), 6.96 (d, $J = 8.1$ Hz, 1H), 6.85 (m, 2H), 6.28 (s, 1H), 4.05 (s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 143.38$, 141.84, 132.85, 130.05, 129.60, 129.00,

128.23, 127.64, 120.85, 119.69, 116.11, 115.63, 38.07 ppm; MS (ESI): $m/z = 307$ ($[M + H]^+$).

9- and 10-Nitro-5H-benzimidazo[1,2-a][3, 1]-benzothiazine, mixture of isomers (**3g**, $C_{14}H_9N_3O_2S$)
Yield: 61 %; light yellow solid; m.p.: 214-216 °C; ^{1}H NMR (300 MHz, $CDCl_3$) $\delta = 8.74$ (d, $J = 2.0$ Hz, 1H), 8.59 (d, $J = 2.0$ Hz, 1H), 8.25 (ddd, $J = 8.9$, 5.2, 2.2 Hz, 2H), 7.88 (d, $J = 9.0$ Hz, 1H), 7.80 (dd, $J = 17.0$, 8.5 Hz, 3H), 7.57 (m, 2H), 7.48 (d, $J = 6.8$ Hz, 2H), 7.38 (td, $J = 7.5$, 1.7 Hz, 2H), 4.11 (d, $J = 4.9$ Hz, 4H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 152.27$, 151.57, 144.82, 142.53, 135.10, 133.08, 131.25, 129.03, 128.27, 126.26, 125.71, 124.01, 123.25, 120.15, 119.60, 118.14, 111.70, 30.37 ppm; MS (ESI): $m/z = 284$ ($[M + H]^+$).

3-(Trifluoromethyl)-5H-benzimidazo[1,2-a][3, 1]-benzothiazine (**3h**, $C_{15}H_9F_3N_2S$)
Yield: 87 %; white solid; m.p.: 134–136 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.98$ (d, $J = 8.4$ Hz, 1H), 7.80 (m, 1H), 7.77 (d, $J = 1.6$ Hz, 1H), 7.75 (m, 1H), 7.71 (s, 1H), 7.37 (m, 2H), 4.11 (s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 172.23$, 154.63, 135.14, 133.83, 130.23, 129.36, 128.51, 126.38, 120.52, 117.17, 114.31, 77.36, 77.04, 76.72, 30.94 ppm; MS (ESI): $m/z = 307$ ($[M + H]^+$).

9- and 10-Methyl-3-(trifluoromethyl)-5H-benzimidazo-[1,2-a][3, 1]benzothiazine, mixture of isomers
(**3i**, $C_{16}H_{11}F_3N_2S$)
Yield: 92 %; light yellow solid; m.p.: 174–176 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.95$ (m, 1H), 7.74 (t, $J = 7.2$ Hz, 1H), 7.68 (d, $J = 6.2$ Hz, 1H), 7.63 (d, $J = 7.4$ Hz, 1H), 7.56 (d, $J = 14.0$ Hz, 1H), 7.17 (dd, $J = 7.3$, 5.1 Hz, 1H), 4.08 (s, 2H), 2.51 (d, $J = 11.1$ Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 150.18$, 149.52, 144.34, 142.09, 138.14, 133.89, 133.60, 132.61, 130.44, 126.13, 125.09, 124.58, 119.70, 119.17, 118.09, 111.41, 110.82, 29.64 ppm; MS (ESI): $m/z = 321$ ($[M + H]^+$).

9- and 10-Chloro-3-(trifluoromethyl)-5H-benzimidazo-[1,2-a][3, 1]benzothiazine, mixture of isomers
(**3j**, $C_{15}H_8ClF_3N_2S$)
Yield: 90 %; white solid; m.p.: 184–186 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.89$ (q, 1H), 7.78 (d, $J = 2.0$ Hz, 1H), 7.72 (t, $J = 5.1$ Hz, 2H), 7.66 (m, 1H), 7.32 (m, 1H), 4.11 (s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 151.61$, 144.91, 142.59, 137.64, 132.85, 131.00, 129.50, 126.23, 125.37, 124.55, 123.67, 120.40, 119.60, 118.13, 111.90, 111.51, 77.41, 76.98, 76.56, 29.64 ppm; MS (ESI): $m/z = 341$ ($[M + H]^+$).

9- and 10-Ethoxy-3-(trifluoromethyl)-5H-benzimidazo-[1,2-a][3, 1]benzothiazine, mixture of isomers
(**3k**, $C_{17}H_{13}F_3N_2OS$)
Yield: 91 %; white solid; m.p.: 165–168 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.92$ (m, 1H), 7.67 (m, 3H), 7.23 (d, $J = 2.3$ Hz, 1H), 6.96 (m, 1H), 4.12 (m, 4H), 1.47 (td, $J = 7.0$, 2.3 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 156.37$, 150.50, 148.66, 145.12, 138.30, 128.88, 127.78, 127.34, 126.74, 126.09, 125.19, 121.78, 119.99, 117.85, 113.02, 112.20, 111.66, 103.33, 97.42, 64.42, 64.04, 29.63, 14.79 ppm; MS (ESI): $m/z = 351$ ($[M + H]^+$).

9- and 10-Methyl-5H-benzimidazo[1,2-a]-1,3-dioxolo-[4,5-g][3, 1]benzothiazine, mixture of isomers
(**3l**, $C_{16}H_{12}N_2O_2S$)
Yield: 74 %; white solid; m.p.: 166–169 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.61$ (d, $J = 8.3$ Hz, 1H), 7.51 (s, 1H), 7.36 (d, $J = 9.2$ Hz, 1H), 7.13 (dd, $J = 8.3$, 4.0 Hz, 1H), 6.86 (s, 1H), 6.03 (d, $J = 4.0$ Hz, 2H), 3.92 (d, $J = 2.0$ Hz, 2H), 2.51 (d, $J = 9.9$ Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 147.84$, 144.93, 143.90, 141.65, 132.95, 130.51, 129.81, 124.58, 124.11, 119.32, 118.93, 118.61, 110.94, 110.39, 107.92, 101.83, 100.23, 29.59, 21.82, 21.34 ppm; MS (ESI): $m/z = 297$ ($[M + H]^+$).

9- and 10-Chloro-5H-benzimidazo[1,2-a]-1,3-dioxolo-[4,5-g][3, 1]benzothiazine, mixture of isomers
(**3m**, $C_{15}H_9ClN_2O_2S$)
Yield: 75 %; white solid; m.p.: 196–198 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.71$ (dd, $J = 8.4$, 1.9 Hz, 1H), 7.63 (dd, $J = 8.6$, 3.0 Hz, 1H), 7.29 (dd, $J = 5.0$, 2.5 Hz, 1H), 7.25 (d, $J = 2.1$ Hz, 1H), 6.87 (s, 1H), 6.07 (d, $J = 3.4$ Hz, 2H), 3.95 (d, $J = 1.0$ Hz, 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 152.15$, 151.45, 147.56, 145.07, 144.01, 141.80, 132.69, 130.96, 128.56, 127.48, 123.30, 122.70, 119.66, 119.35, 118.04, 112.95, 111.57, 108.22, 102.02, 100.60, 100.29, 29.28 ppm; MS (ESI): $m/z = 317$ ($[M + H]^+$).

9- and 10-Ethoxy-5H-benzimidazo[1,2-a]-1,3-dioxolo-[4,5-g][3, 1]benzothiazine, mixture of isomers
(**3n**, $C_{17}H_{14}N_2O_3S$)
Yield: 75 %; white solid; m.p.: 217–220 °C; ^{1}H NMR (300 MHz, $CDCl_3$) $\delta = 7.60$ (dd, $J = 8.8$, 1.5 Hz, 1H), 7.25 (m, 2H), 6.93 (m, 1H), 6.86 (d, $J = 2.2$ Hz, 1H), 6.05 (d, $J = 2.4$ Hz, 2H), 4.11 (m, 2H), 3.93 (d, $J = 1.7$ Hz, 2H), 1.46 (td, $J = 7.0$, 2.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 155.93$, 147.95, 145.03, 144.61, 138.08, 133.07, 129.79, 119.71, 112.59, 111.48, 108.01, 103.01, 101.90, 100.10, 96.86, 64.21, 29.27, 14.86 ppm; MS (ESI): $m/z = 327$ ($[M + H]^+$).

9- and 10-Methoxy-5H-benzimidazo[1,2-a]-1,3-dioxolo-[4,5-g][3, 1]benzothiazine, mixture of isomers (**3o**, $C_{16}H_{12}N_2O_3S$)
Yield: 67 %; bright yellow crystals; m.p.: 96–98 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.36$ (d, $J = 1.4$ Hz, 1H), 7.10 (t, $J = 3.3$ Hz, 2H), 6.79 (d, $J = 14.2$ Hz, 2H), 6.01 (s, 2H), 5.91 (s, 1H), 4.22 (s, 1H), 3.90 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 148.60$, 147.24, 146.95, 138.74, 134.56, 127.46, 116.67, 112.01, 108.15, 101.80, 62.56, 18.12 ppm; MS (ESI): $m/z = 313$ ($[M + H]^+$).

3-Methoxy-5H-benzimidazo[1,2-a][3, 1]-benzothiazine (***3p***)
Yield: 77 %; bright white solid; m.p.: 102–104 °C (Ref. [34] 102-103 °C).

4-Chloro-5H-benzimidazo[1,2-a][3, 1]-benzothiazine (**3q**, $C_{14}H_9ClN_2S$)
Yield: 70 %; bright white solid; m.p.: 166–167 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.75$ (dd, $J = 1.9$, 3.6 Hz, 3H), 7.43-7.28 (m, 4H), 4.25 (s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 150.57$, 144.03, 136.78, 132.89, 129.11, 126.70, 124.46, 123.70, 123.18, 119.65, 116.75, 111.33, 26.79 ppm; MS (ESI): $m/z = 273$ ($[M + H]^+$).

5H-Imidazo[1,2-a][3,1]benzothiazine (***3r***)
Yield: 66 %; yellow oil; ^{1}H NMR was found to be identical with the one described in Ref. [34].

2-(Benzylthio)-1H-benzimidazole (***3s***)
Yield: 61 %; white solid; m.p.: 183–185 °C (Ref. [51] 184–185 °C).

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