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S-arylation of mercaptobenzimidazoles using Cu(I) catalysts—experimental and theoretical observations

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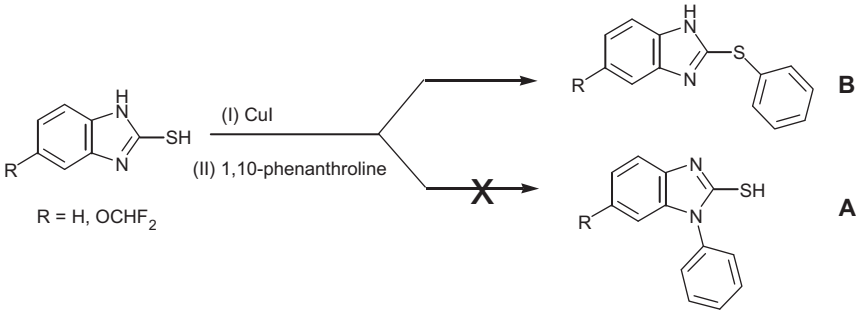
ABSTRACT

Substituted 2-mercaptobenzimidazoles (MBI) are an important class of bio-active and industrially important organic compounds. In this Letter, a new synthetic method is presented for the selective S-arylation of MBI with substituted aryl iodides using low cost copper (I) iodide and 1,10-phenanthroline as a catalytic system. The selective formation of S-arylated product was confirmed by several spectroscopic techniques and the vibrational spectrum was found to be in very good agreement with the theoretical spectrum calculated by density functional theory.

Substituted 2-mercaptobenzimidazole (MBI) molecules have drawn the attention of many synthetic chemists mainly for their wide range of biological activities (such as antiviral,[1] antibacterial,[2] antiulcerative,[3] antifungal,[4] and antitumor[5]) and industrial applications (such as corrosion inhibitor for copper,[6] steel plating,[7] antioxidant for plating rubber compounds,[8] and adsorbents for heavy metal ions[9]). Especially, a difluoromethoxy-substituted 2-thioarylbenzimidazole is an interesting compound, since it is used as a gastric acid secretion inhibitor.[10]

Several preparation methods are available in the literature for 2-thioarylbenzimidazoles.[11] However, there is no facile synthetic route for S-arylation of MBI. Generally, S-arylated benzimidazoles may be prepared either by coupling of MBI with iodonium salts[12] or by nucleophilic displacement of 2-(methylsulfonyl)-1*H*-benzimidazole with thiophenol in the presence of a base[13] or by the most often followed method, that is, reaction of N-protected 2-chlorobenzimidazoles with arylthiols.[14] However, these methods are rather unattractive, due to poor product yield (40–60%),



Scheme 1. S-arylation in MBI.

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Table 1
CuI-catalyzed S-arylation of FMBI (entries 1–10) and MBI (entries 11–13)

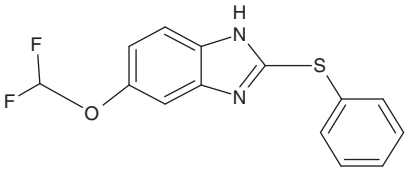
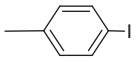
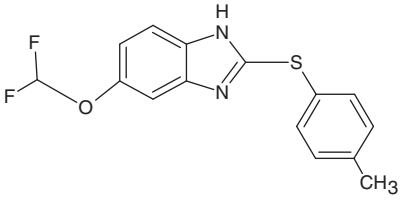
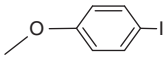
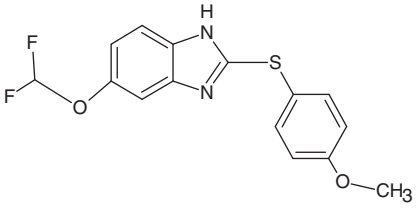
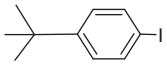
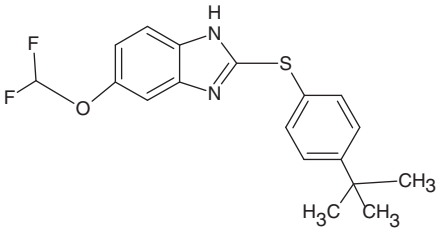
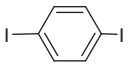
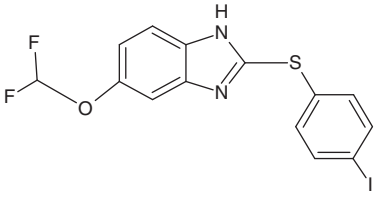
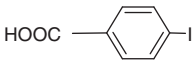
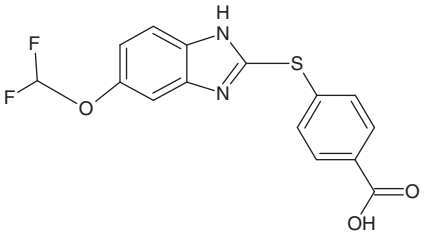
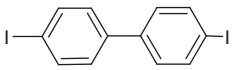
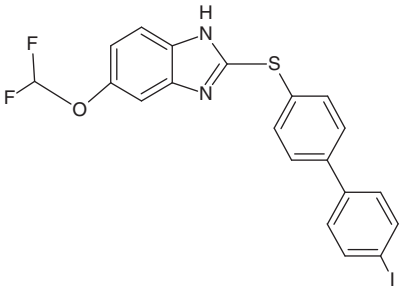
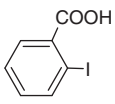
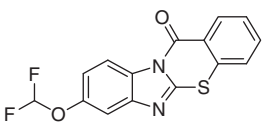
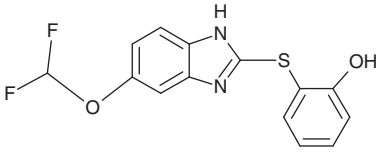
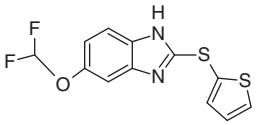
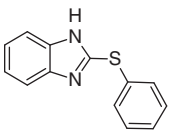
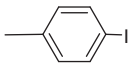
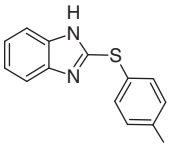
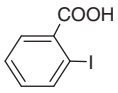
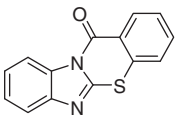
Entry	Aryliodide	Product[a]	Time(h)	Yield[b] (%)
1			22	84
2			24	87
3			22	88
4			24	88
5			24	89
6			22	83
7			24	81
8			24	72

Table 1 (*continued*)

Entry	Aryliodide	Product[a]	Time(h)	Yield[b] (%)
9			30	–
10			22	86
11			24	74
12			22	77
13			26	71

[a] The reactions were carried out with 1.0 equiv MBI (or) FMBI, 1.0 equiv aryliodides, 5 mol % CuI, 10 mol % 1,10-phenanthroline and 2.0 equiv K_2CO_3.
[b] Isolated yield after column chromatographic purification.

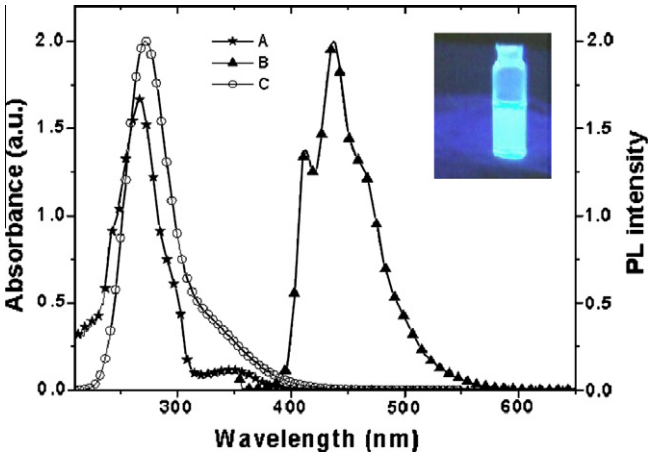
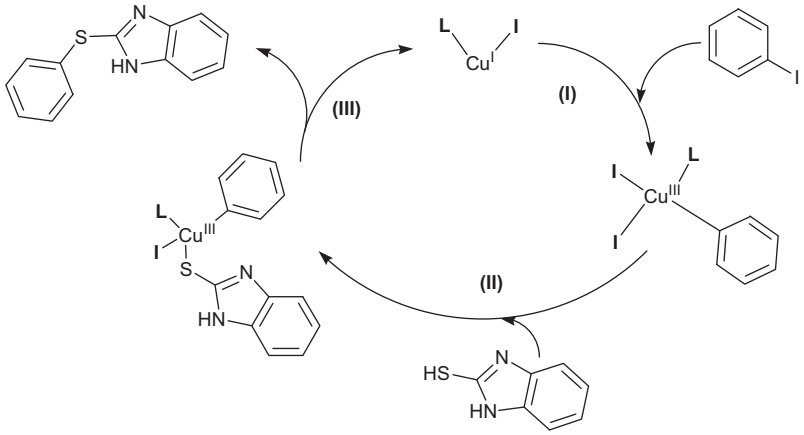


Figure 1. Normalized absorption and emission spectra of compound **8**. (A) Absorption spectrum in chloroform solution. (B) Emission spectrum in chloroform solution (λ_{exc} = 265 nm). (C) Absorption spectrum obtained from time dependent-DFT calculations. Inset: fluorescence of a solution of **8**.

lengthy protocols, commercial unavailability and stench of thiophenols. Instead of using 2-chlorobenzimidazole as a precursor, Teague et al.[15] used a reaction of 2-mercaptobenzimidazole (MBI) with activated aryl fluorides to obtain 2-arylthio-substituted benzimidazoles. However, this approach usually requires aryl fluorides activated by electron-withdrawing groups such as nitro groups, which limits the scope of the reaction. These limitations have led to an increased interest in developing a transition metal catalytic system for S-arylation of MBI with aryl halides.

Transition metal-catalyzed C–S bond formation between aryl halides and heterocyclic compounds has evolved as an important method for the synthesis of heterocyclic compounds.[16] Since sulfur-containing compounds have long been known to act as poisons of catalysts, the transition metal-catalyzed C–S cross coupling reaction is much less studied than the corresponding C–N and C–O coupling reactions.[17] In 1980, Migita et al.[18] first reported C–S bond formation using a palladium-catalyzed reaction. After that, considerable progress has been made in coupling of aryl halides with thiols, using Pd(0) and Ni(0) catalysts.[19] However, this approach is not attractive from an industrial perspective because Pd and Ni are expensive and toxic.[20] Later, Venkataraman[21] and Buchwald[22] reported C–S bond formation using the less expensive CuI catalyst. Using this catalyst, it is possible to S-arylate 2-mercaptobenzothiazoles (MBT)[23] through an intermolecular mechanism. However, in the case of MBI, both S-arylation and N-arylation may take place due to the existence of two tautomeric forms (thioketo and thiol).[24] Developing a catalytic system capable of selectively arylating the sulfur in MBI with aryl iodides through a simple procedure is, therefore, the subject of our research efforts. Interestingly, Reddy et al.[25] recently did not succeed to S-arylate MBI with aryl iodides using a nano-sized indium oxide catalyst.

In this Letter we describe our successful experiments to selectively S-arylate MBI with aryl iodides, using copper (I) iodide as a catalyst with 1,10-phenanthroline as a ligand (Scheme 1). The compounds were fully characterized with different spectroscopic techniques (IR, NMR, MS, etc.) to confirm the structures of the formed products. We also used theoretical calculations (Density Functional Theory; DFT) to obtain theoretical spectra (absorbance and IR) and compared them with experimental spectra to discriminate between N- and S-arylation. Modern computational chemistry methods offer a unique possibility for the synthetic organic chemist to generate optimized structures and from the structural and electronic properties make decisions as to which chemical transformations have occurred in the reactions under investigation.[26]



Scheme 2. Possible catalytic cycle.

The subject of this study was the development of a novel, simple C–S cross-coupling methodology between mercaptobenzimidazole and substituted iodobenzenes using commercially available low-cost copper catalysts. 5-Difluoromethoxy-2-mercapto-1*H*-benzimidazole (FMBI) and substituted iodobenzenes were used as the prototypical substrate combination for preliminary optimization of the reaction conditions. Among the various copper catalysts available, CuI was chosen due to its good stability.[22] Initially, we planned to perform the coupling reaction using CuI, ethylene glycol and K_2CO_3 in isopropyl alcohol to generate the final product, but due to the poor solubility of FMBI in isopropyl alcohol, we replaced isopropyl alcohol by DMF. However, the yield was very poor. Surprisingly, high yields were obtained by performing the coupling reaction in pure DMF in the presence of CuI, K_2CO_3 and 1,10-phenanthroline (without ethylene glycol) at 130–140 °C under a nitrogen atmosphere (see Table 1).[27] 1,10-Phenanthroline has been found to be one of the best ligands for Cu in these kinds of reactions.[23] Its possible role is to prevent aggregation, decomposition of intermediate copper complexes, and to improve the solubility of the intermediate copper complexes.[28]

Using these optimized reaction conditions, the coupling reactions were performed with various available substituted iodobenzenes and the observed product yields are generally good (>80%, see entries 1–7). Furthermore, we found that S-arylation using 2-iodobenzoic acid gave a highly fluorescent cyclized compound **8** in good yield. The structure was confirmed, among others, by the absence of –NH peaks in its IR and ^{1}H NMR spectra. For this cyclized compound **8**, the observed experimental and theoretical absorbance spectra are shown in Figure 1. The experimental (λ_{max} = 268 nm) and theoretical (λ_{max} = 270 nm) maxima match well. In addition, the experimental emission spectrum (λ_{em} = 438 nm) for this compound is also shown in Figure 1. S-arylation was not successful when 2-iodophenol was used (see entry 9). This may be due to the nucleophilicity of the –OH group[29] or due to its electron-donating properties which reduce its reactivity.[23] The coupling reaction is also feasible with 2-iodothiophene, a heterocyclic compound (see entry 10).

For comparison, we also performed the coupling reactions with unsubstituted MBI. However, the yields of the corresponding products were slightly lower (70–75%) than for the difluoromethoxy-substituted MBI's (see entries 11–13). The reason for the lower yields with unsubstituted MBI may lie in the absence of the electron-withdrawing difluoromethoxy group at C-5.[30] The cyclized product obtained by the reaction of unsubstituted MBI with 2-iodobenzoic acid (entry 13) also shows fluorescence (λ_{em} = 438 nm; see also Supplementary data Fig. S1).

We next investigated if increasing the amount of aryl iodide from 1 to 3 equiv using the same protocol would yield both S- and N-arylated products. However, only the formation of S-arylated products was observed. Even when the reaction time is increased from 24 to 52 h no N-arylation of the initial S-arylated product is observed. This can be understood from the mechanism of the copper-assisted nucleophilic substitution reaction. This mechanism follows three important steps; that is (I) an oxidative addition, (II) an intermediate step in which the thiol adds to the copper, and (III) the reductive elimination as shown in Scheme 2.[31] In the intermediate step, the –SH group predominantly attacks the copper complex as compared to the –NH, because sulfur is a more powerful nucleophile than nitrogen due to its nature, that is, large size, high polarizability and availability of more electron lone pairs. Furthermore, according to Pearson's Hard Soft Acid Base (HSAB) principle,[32] sulfur is softer as compared to nitrogen and thus favors interaction with copper, which is a soft metal atom. So, S-arylation will be preferred as compared to N-arylation.

In order to further confirm S-arylation, the vibrational properties of the products were investigated by a combined approach of FTIR measurements and density functional theory (DFT) calculations, since DFT has been successfully applied earlier to the description of the vibrational properties of many heterocyclic molecules.[33] Full geometry optimization of the S- and N-arylated products, together with the vibrational analysis of all possible isomers (Fig. 2) were carried out at the B3LYP/6-31G(d) level of theory using the GAUSSIAN 03 program.[34] It is important to mention here that calculation of the selected parameters of the neutral molecules in the gas phase requires much less calculation time than in the presence of solvent molecules; however, this did not result in significant differences between the calculated and experimental vibrational spectra.[35]

The substrates FMBI and MBI may exist in two tautomeric forms (thiol ⇌ thionine) and hence upon coupling with aryl iodides may yield either S- or N-arylated products as shown in Scheme 1. The calculated energies for 5- and 6-substituted S-arylated products are −1322.1090 and −1322.1094 a.u. whereas the calculated energy for N-arylated product is −1322.1102 a.u. Generally, vibrations above 3000 cm^{-1} are assigned to –NH and aromatic –CH stretching and vibrations at 645 and 621 cm^{-1} are assigned to symmetric and antisymmetric N–H out of plane bending modes. These peaks are easily recognized in the calculated vibrational spectra of the 5- and 6-substituted S-arylated product (Fig. 2B and C). However, the calculated spectrum of the N-arylated product does not show such peaks (Fig. 2A).

The calculated theoretical spectrum of the S-arylated product matches well with the experimental vibrational spectrum (compound **1**). Together with the results from ^{1}H-NMR spectra, this clearly indicates that N-arylation is negligible and only S-arylated

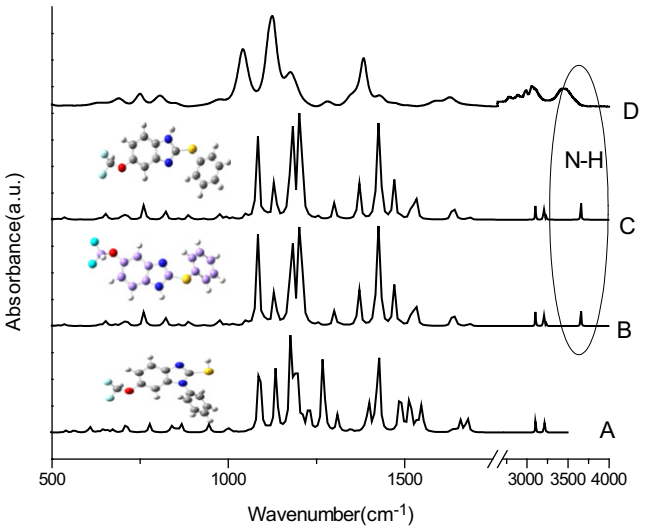


Figure 2. Vibrational spectra of arylated 2-mercaptobenzimidazole (entry 1): (A) calculated infrared absorption spectrum of N-arylated product; (B and C) calculated infrared absorption spectrum for 5- and 6-substituted S-arylated product; (D) experimental infrared absorption spectrum. (see inserts for DFT-optimized structures of the S and N-arylated product).

product is formed and isolated in the CuI-catalyzed coupling of (F)MBI with aryl iodides.

In summary, we have developed a useful and efficient procedure for the preparation of S-arylated 2-mercapto-benzimidazoles in good yield by a catalytic coupling reaction between (F)MBI and substituted aryl iodides using commercially available low cost copper (I) iodide with 1,10-phenanthroline as ligand. In addition to spectroscopic evidence, DFT calculations confirmed the formation of only S-arylated product. The synthetic method developed here efficiently yields new compounds that may find many applications in the fields of pharmaceutics, agrochemicals, and industrial science.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.04.078.

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27. *General procedure for CuI-catalyzed coupling of aryl iodides with (F)MBI*: CuI (0.05 equiv), 1,10-phenanthroline (0.1 equiv) and K_2CO_3 (2 equiv) were placed in an oven-dried screw-capped test tube with Teflon-lined septum that was filled with nitrogen. About 2.5 mL of dry DMF was then added at room temperature. Now the corresponding aryl iodide (1.0 mmol) was added followed by MBI or FMBI (1.0 equiv) and the tube was placed in the preheated oil bath at 140 °C and the reaction mixture was magnetically stirred for 22 h. After complete disappearance of iodobenzene (the progress of the reaction was followed by TLC), the reaction mixture was allowed to cool to room temperature. Then water was added and the reaction mixture was extracted with ethyl acetate. After removal of the solvent in vacuum, the crude residue was purified by column chromatography.
5- (or 6-) (Difluoromethoxy)-2-(phenylsulfanyl)-1H-benzimidazole (**1**). Light yellow colored solid product. ^{1}H NMR (300 MHz, $CDCl_3$/TMS; ppm) δ 6.21 (d, 1H, J = 1.8 Hz), 6.45 (d, 1H, J = 1.5 Hz), 6.70 (d, 1H, J = 1.5 Hz), 6.97–7.00 (m, 2H); 7.12–7.25 (m, 2H), 7.35–7.42 (m, 1H); 7.45–7.48 (m, 2H); 10–13 (br s, 1H). ^{13}C NMR (300 MHz, $CDCl_3$; ppm) δ 113.6, 115.6, 116.2, 119.7, 128.9, 129.5, 129.6, 133.0, 138.0, 146.7, 150.6. IR (KBr disc, cm^{-1}) 3438, 3062, 2984, 2888, 2786, 1879, 1628, 1427, 1383, 1280, 1176, 1124, 1041, 976, 806, 749, 688, 621, 540, 493, 443. GC–MS (EI, m/z): 293.1 [M$^+$]. Anal. Calcd for $C_{14}H_{10}F_2N_2OS$: C, 57.53; H, 3.45; N, 9.58; S, 10.97. Found: C, 57.27; H, 3.52; N, 9.62; S, 10.88.
5- (or 6-) (Difluoromethoxy)-2-[(4-methylphenyl)sulfanyl]-1H-benzimidazole (**2**). Brown colored oily product. ^{1}H NMR (400 MHz, $CDCl_3$/TMS; ppm) δ 1.97 (s, 3H) 6.17 (s, 1H), 6.36 (s, 1H), 6.55 (s, 1H), 6.8–6.9 (m, 2H), 7.07 (s, 1H), 7.23 (d, 1H, J = 8.8 Hz), 7.29 (d, 2H, J = 8.0 Hz), 9.89 (br s, 1H). ^{13}C NMR (400 MHz, $CDCl_3$; ppm) δ 21.46, 105.0, 112.2, 119.4, 125.2, 130.5, 130.8, 134.2, 155.3, 164.2. IR (KBr disc, cm^{-1}) 3446, 3038, 2959, 2918, 2791, 2688, 1614, 1507, 1487, 1440, 1411, 1336, 1278, 1232, 989, 812, 736, 639, 621, 532, 488, 430. GC–MS (EI, m/z): 307.3 [M$^+$]. Anal. Calcd for $C_{15}H_{12}F_2N_2OS$: C, 58.82; H, 3.95; N, 9.14; S 10.47. Found: C, 58.80; H, 3.88; N, 9.18; S, 10.50.
5- (or 6-) (Difluoromethoxy)-2-[(4methoxyphenyl)sulfanyl]-1H-benzimidazole (**3**). Dark brown colored oily product. ^{1}H NMR (400 MHz, $CDCl_3$/TMS; ppm) δ 3.50 (s, 3H), 6.29 (s, 1H), 6.47 (s, 1H), 6.58 (d, 1H, J = 8.0 Hz), 6.93–6.96 (m, 1H), 7.17 (d, 1H, J = 4.0 Hz),7.33 (d, 1H, J = 8.0 Hz), 7.44 (d, 2H, J = 8.0 Hz), 10.49 (br s, 1H). ^{13}C NMR (400 MHz, $CDCl_3$; ppm) δ 55.04, 105.9, 115.0, 116.5, 118.5, 136.7, 137.0, 139.6, 146.5, 153.2, 160.6. IR (KBr disc, cm^{-1}) 3420, 3075, 2943, 2780, 1888, 1670, 1628, 1591, 1492, 1443, 1402, 1343, 1289, 1255, 1176, 1130, 1029, 987, 829, 772, 646, 617, 534, 499, 439. GC–MS (EI, m/z): 323.3 [M$^+$]. Anal. Calcd for $C_{15}H_{12}F_2N_2O_2S$: C, 55.89; H, 3.75; N, 8.69; S, 9.95. Found: C, 55.93; H, 3.78; N, 8.67; S, 9.92.
2-[(4-tert-Butylphenyl)sulfanyl]-5-(or 6-) (difluoromethoxy)-1H-benzimidazole (**4**). Colorless solid product. ^{1}H NMR (300 MHz, $CDCl_3$/TMS; ppm) δ 1.26 (s, 9H), 6.21 (s, 1H), 6.46 (s, 1H), 6.71 (s, 1H), 6.96 (d, 1H, J = 1.8 Hz), 6.99 (d, 1H, J = 1.8 Hz), 7.263 (s, 1H), 7.39 (d, 1H, J = 8.4 Hz), 7.54 (d, 2H, J = 8.4 Hz); 9.9 (br s,1H). ^{13}C NMR (300 MHz, $CDCl_3$; ppm) δ 31.05, 34.7, 99.6, 99.8, 103.7, 116.6, 119.7, 127.1, 128.0, 129.5, 133.0, 146.7, 150.6, 153.2. IR (KBr disc, cm^{-1}) 3436, 3028, 2960, 2862, 2796, 2695, 2358, 1624, 1465, 1428, 1389, 1352, 1267, 1183, 1127, 1034, 821, 651, 622, 556. Anal. Calcd for $C_{18}H_{18}F_2N_2OS$: C, 62.05; H, 5.21; N, 8.04; S, 9.20. Found: C, 62.11; H, 5.18; N, 8.01; S, 9.15.
5- (or 6-) (Difluoromethoxy)-2-[(4-iodophenyl)sulfanyl]-1H-benzimidazole (**5**). Light yellow colored solid product (yield: 89%). ^{1}H NMR (300 MHz, $CDCl_3$/TMS; ppm) δ 6.26 (s, 1H), 6.51 (s, 1H), 6.76 (s, 1H), 7.01–7.04 (m, 1H), 7.12–7.15 (m, 1H), 7.26 (d, 1H, J = 2.1 Hz), 7.38–7.43 (m, 1H), 7.55 (s, 1H), 9.5–11.5 (br s, 1H). ^{13}C NMR (300 MHz, $CDCl_3$; ppm) δ 93.9, 115.7, 116.2, 119.9, 128.0, 128.6, 133.7, 137.9, 138.9, 140.9, 150.3. IR (KBr disc, cm^{-1}) 3438, 3042, 2776, 1627, 1594, 1564, 1445, 1361, 1346, 1276, 1123, 1040, 997, 948, 857, 805, 720, 668, 632, 532, 476, 432. GC–MS (EI, m/z): 418 [M$^+$]. Anal. Calcd for $C_{14}H_9F_2IN_2OS$: C,

40.19; H, 2.17; N, 6.70; S, 7.67. Found: C, 40.17; H, 2.20; N, 6.66; S, 7.69.

4-{[5- (or 6-) (Difluoromethoxy)-1H-benzimidazol-2-yl]sulfanyl}benzoic acid (**6**). Colorless solid product. ^{1}H NMR (300 MHz, $CDCl_3$/TMS; ppm) δ 6.45 (s, 1H), 6.70 (s, 1H), 6.95–7.04 (m, 1H), 7.34–7.47 (m, 2H), 7.75 (s, 1H), 7.96 (d, 2H, J = 8.1 Hz). ^{13}C NMR (300 MHz, $CDCl_3$; ppm) δ 94.6, 106.1, 112.8, 115.3, 115.7, 116.2, 119.7, 129.8, 134.0, 137.0, 138.4, 139.2, 146.8, 149.5, 162.6. IR (KBr disc, cm^{-1}) 3445, 3181, 2921, 2441, 1881, 1646, 1594, 1492, 1390, 1357, 1273, 1172, 1114, 1100, 1041, 854, 803, 762, 646, 628, 513, 448. Anal. Calcd for $C_{15}H_{10}F_2N_2O_3S$: C, 53.57; H, 3.00; N, 8.33; S, 9.53. Found: C, 53.55; H, 3.00; N, 8.37; S, 9.56.

5- (or 6-) (Difluoromethoxy)-2-[(4′-iodobiphenyl-4-yl)sulfanyl]-1H-benzimidazole (**7**). Colorless solid product. ^{1}H NMR (400 MHz, DMSO-d_6/TMS; ppm) δ 7.05–7.09 (m, 1H), 7.2–7.23 (m, 1H),7.35 (s, 1H), 7.42–7.58 (m, 3H), 7.62–7.65 (m, 2H), 7.73–7.8 (m, 2H), 7.84–7.9 (m, 2H), 13 (br s, 1H). ^{13}C NMR (400 MHz, DMSO-d_6; ppm) δ 94.2, 94.3, 114.2, 116.8, 119.3, 127.6, 128.6, 128.7, 132.1, 137.7, 137.8, 138.4, 138.9, 168.9. IR (KBr disc, cm^{-1}) 3437, 3061, 2788, 2705, 2598, 1902, 1590, 1470, 1385, 1287, 1175, 1114, 1042, 996, 802, 641, 622, 540, 484. GC–MS (EI, m/z): 368.4 [M−I]$^+$. Anal. Calcd for $C_{20}H_{13}F_2IN_2OS$: C, 48.60; H, 2.65; N, 5.67; S, 6.49. Found: C, 48.56; H, 2.64; N, 5.69; S, 6.47.

8- (or 9-) (Difluoromethoxy)-12H-benzo[e]benzo[4,5]imidazo[2,1-b][1,3]thiazin-12-one (**8**). Light brown colored solid product. ^{1}H NMR (400 MHz, $CDCl_3$/TMS; ppm) δ 6.41 (d, 1H, J = 8.8 Hz), 6.59 (d, 1H, J = 8.0 Hz), 6.78 (d, 1H, J = 8.0 Hz), 7.20–7.30 (m, 1H), 7.50–7.58 (m, 1H), 7.69–7.74 (m, 1H), 8.43 (s, 1H), 8.56–8.63 (m, 1H). ^{13}C NMR (300 MHz, $CDCl_3$; ppm) δ 109.5, 116.7, 118.8, 119.1, 122.4, 126.0, 127.3, 131.4, 131.5, 132.0, 132.3, 132.4, 134.1, 159.5, 165.9. IR (KBr disc, cm^{-1}) 3196, 2964, 2920, 2851, 1694, 1593, 1465, 1436, 1391, 1350, 1259, 1161, 1107, 1041, 804, 734, 680, 649, 612, 482, 465. GC–MS (EI, m/z): 318 [M$^+$]. Anal. Calcd for $C_{15}H_8F_2N_2O_2S$: C, 56.60; H, 2.53; N, 8.80; S, 10.07. Found: C, 56.62; H, 2.54; N, 8.81; S, 10.10.

5- (or 6-) (Difluoromethoxy)-2-(thiophen-2-ylsulfanyl)-1H-benzimidazole (**10**). Colorless solid product. ^{1}H NMR (400 MHz, $CDCl_3$/TMS; ppm) δ 6.48 (s, 1H), 6.66 (s, 1H), 6.85–6.88 (m, 1H), 6.99–7.02 (m, 1H), 7.22–7.26 (m, 1H), 7.34–7.4 (m, 2H), 9.83 (br s, 1H). ^{13}C NMR (400 MHz, $CDCl_3$; ppm) δ 106.2, 115.0, 115.6, 116.3, 118.9, 124.7, 128.2, 132.9, 136.9, 137.7, 146.7, 151.6. IR (KBr disc, cm^{-1}) 3440, 3080, 2850, 2789, 1626, 1588, 1486, 1398, 1352, 1284, 1176, 1125, 1041, 981, 850, 807, 713, 669, 646, 624, 571, 474. Anal. Calcd for $C_{12}H_8F_2N_2OS_2$: C, 48.31; H, 2.70; N, 9.39; S, 21.50. Found: C, 48.29; H, 2.72; N, 9.42; S, 21.49.

2-[(4-Methylphenyl)sulfanyl]-1H-benzimidazole (**12**). Colorless solid product. ^{1}H NMR (400 MHz, $CDCl_3$/TMS; ppm) δ 2.34 (s, 3H), 7.17–7.19 (m, 4H), 7.26 (s, 2H), 7.44–7.51 (m, 2H), 10.5 (br s, 1H). ^{13}C NMR (400 MHz, $CDCl_3$; ppm) δ 21.2, 122.4, 125.7, 130.7, 134.0, 139.9, 149.7. IR (KBr disc, cm^{-1}) 3441, 3040, 2953, 2920, 2860, 2789, 2695, 1619, 1510, 1491, 1441, 1406, 1349, 1268, 1235, 980, 804, 736, 636, 616, 527, 480, 432. Anal. Calcd for $C_{14}H_{12}N_2S$: C, 69.97; H, 5.03; N, 11.66; S, 13.34. Found: C, 69.95; H, 5.03; N, 11.69; S, 13.33.

12H-Benzo[e]benzo[4,5]imidazo[2,1-b][1,3]thiazin-12-one (**13**). Colorless solid product. ^{1}H NMR (400 MHz, $CDCl_3$/TMS; ppm) δ 7.26 (s, 1H), 7.42–7.58 (m, 3H), 7.69–7.78 (m, 2H), 8.63 (t, 2H, J = 8.0 Hz). ^{13}C NMR (400 MHz, $CDCl_3$; ppm) δ 116.1, 118.5, 122.7, 124.2, 125.9, 127.1, 131.4, 131.9, 132.4, 133.9, 142.5, 146.3, 171.0. IR (KBr disc, cm^{-1}) 3241, 2922, 2852, 1693, 1627, 1595, 1545, 1513, 1474, 1445, 1351, 1335, 1307, 1279, 1257, 1208, 956, 886, 745, 680, 620, 584, 557, 485, 445, 418. Anal. Calcd for $C_{14}H_8N_2OS$: C, 66.65; H, 3.20; N, 11.10; S, 12.71. Found: C, 66.68; H, 3.18; N, 11.14; S, 12.69.

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