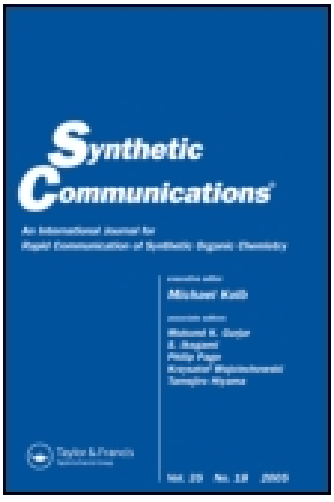

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Synthesis of *N*-Aryl-2-substituted Tetrahydrobenzimidazoles via Direct *N*-Arylation

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Abstract: A series of novel *N*-aryl-2-substituted tetrahydrobenzimidazoles has been synthesized via direct *N*-arylation of 2-substituted tetrahydrobenzimidazoles, which was accomplished by a medium aryl electrophile, 4-methylsulfonylfluorobenze, in the presence of 37% KF/Al_2O_3 and 18-crown-6 in fair yields under mild reaction conditions. Meanwhile, the hydrogenation of 2-phenylbenzimidazole was studied.

Keywords: *N*-arylation, hydrogenation, selective cyclooxygenase-2 inhibitors, tetrahydrobenzimidazole

INTRODUCTION

Selective cyclooxygenase-2 (COX-2) inhibitors have been demonstrated to be clinically effective anti-inflammatory and analgesic drugs with reduced gastrointestinal toxicity as compared to classic NSAIDs.[1] The most widely studied class is that of the compounds in which the pharmacophore is characterized by two aromatic moieties attached to adjacent atoms in a bridging heterocyclic five-membered ring.[2–4] For optimal COX-2 inhibitory

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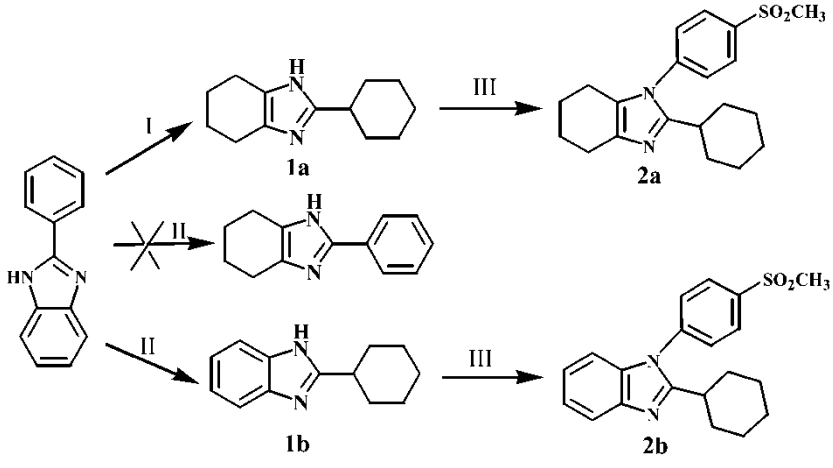
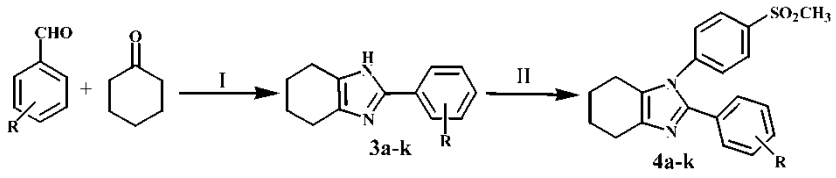
activity, one of the two aromatic rings is substituted in the *para*-position by a methylsulphonyl[2] or a sulfonamide group.[3,4] To find potent and selective cyclooxygenase-2 (COX-2) inhibitors with a safer profile, a series of novel *N*-arylation of 2-substituted tetrahydrobenzimidazoles containing a methylsulphonyl group in the *para*-position of *N*-aromatic ring has been designed in our anti-inflammatory program. Here we report the synthesis of these compounds (see Schemes 1 and 2). The preliminary COX-2 inhibitory activity data of some compounds are also given.

1,2-Arylimidazoles can be prepared by cyclization of diarylamidines with strong electrophiles such as 3-bromo-1,1,1-trifluoroacetone and following dehydration,[5] but such methodology was ultimately proved to be ineffective for our target molecules because of the weak electrophilicity of 2-bromocyclohexanone. Because diaryl benzimidazoles can be easily synthesized by cyclization of *N*-phenyl-*o*-phenylenediamine with appropriate benzoyl chloride,[6] we wanted to prepare our target compounds by selective hydrogenation of diaryl benzimidazoles. However, the substituted benzene ring but not the fused one was first hydrogenated for 2-phenylbenzimidazole, as shown in Scheme 1. Hydrogenation of 2-phenylbenzimidazole, catalyzed by 5% Rh/C at 120°C under 100 $Kg \cdot cm^{-2}$ using 2 N HCl as solvent, gave 2-cyclo-hexanotetrahydrobenzimidazole **1a**. When decreasing the pressure to 50 $Kg \cdot cm^{-2}$ and using 50% acetic acid as solvent, 2-cyclohexanobenzimidazole **1b** was obtained.

We here report a new method for synthesizing the target compounds via direct *N*-arylation of 2-aryl tetrahydrobenzimidazoles **3**, which were prepared through the method described in the literature.[7] Traditional strategies for the



Scheme 1. (I) H_2, 5% Rh/C, 2 N HCl, 120°C, 100 $Kg \cdot cm^{-2}$; (II) H_2, 5% Rh/C, 50% HOAc, 120°C, 50 $Kg \cdot cm^{-2}$; (III) 4-methylsulfonylfluorobenze, DMSO, 37% KF/basic Al_2O_3, 18-crown-6, 120°C.



Scheme 2. (I) Excess $Cu(OAc)_2$, $NH_3 \cdot H_2O$, MeOH, reflux; (II) 4-methylsulfonyl fluorobenze, DMSO, 37% KF/basic Al_2O_3, 18-crown-6, 120°C.

construction of the *N*-arylimidazole moiety include the Ullmann coupling reaction[8] and nucleophilic aromatic substitution.[9] Unfortunately, the use of the Ullmann coupling reaction usually leads to difficult purification issues, with concomitant low yields. Nucleophilic aromatic substitution as an effective method for the *N*-arylation of imidazole notwithstanding, the method usually requires a strong base and is limited to aryl fluorides with strongly electron-withdrawing *ortho* and/or *para* groups. Strongly basic conditions tend to cleave the imidazole.[10] Furthermore, there is severe steric hindrance for the *N*-arylation of **3,** and 4-methylsulfonylfluorobenze is just a medium aryl electrophile. Therefore, an efficient method for the *N*-arylation of **3** is desired. W. J. Smith III has reported a novel and selective method for the *N*-arylation of indoles mediated by KF/Al_2O_3.[11] In our work, we modified the method to achieve the *N*-arylation of imidazoles. It was proved that all the object compounds were obtained in fairly good yields (50–60%) by intermediates **3** reacting with 4-methylsulfonylfluorobenze in the presence of 37% KF/Al_2O_3 and 18-crown-6 in DMSO at 120°C for 8 h.

To compare the new method (method A, based on Smith protocol) with traditional methods of nucleophilic aromatic substitution (method B, reaction conditions: NaH, DMSO, 120°C) and the Ullmann coupling reaction (method C, reaction conditions: anhydrous K_2CO_3, Cu power, DMF, 150°C), the latter two methods were also performed (see Table 1). Through method B, the purified yield was about 40%, but the reaction time was too long. No product was obtained by method C. In conclusion, the new method is a simpler and more expedient approach with short reaction time and fair yield for *N*-arylation of imidazoles and is even suitable for the *N*-arylation of imidazoles with bulky steric hindrance.

Because it was reported that the cyclohexyl group could substitute for the aromatic ring without a methylsulphonyl group in the *para*-position for some selective cyclooxygenase-2 (COX-2) inhibitors,[12] we also employed the new method to synthesize two novel compounds **2.**

Through the new method, a series of novel *N*-aryl-2-substituted tetrahydrobenzimidazoles has been synthesized. The structures of all compounds have been established by nuclear magnetic resonance (NMR), mass spectroscopy (MS), and elemental analysis.

Table 1. Comparison of the *N*-arylation methods

			Method A		Method B	
Entry	4	R	Time (h)	Yield (%)[a]	Time (h)	Yield (%)[a]
1	**a**	H	8	55	120	39
2	**b**	4-Me	8	55	120	41
3	**c**	4-Cl	8	57	120	42
4	**d**	3-Cl	8	53	120	40
5	**e**	2-Cl	8	50	120	38
6	**f**	2,5-Cl	8	52	120	35
7	**g**	2,4-Me	8	48	120	30
8	**h**	3,-4-Me	8	50	120	ND[b]
9	**i**	4-F	8	51	120	22
10	**j**	2,3-OMe	8	51	120	ND[b]
11	**k**	2-Me	8	71	120	ND

[a]The purified yield.
[b]ND means that the experiment was not done.

EXPERIMENTAL

Solvents were purified by standard procedures. Melting points were determined using a RY-1 apparatus and are uncorrected. NMR spectra were recorded on Varian Unity Inova 600-MHz or JNM-ECA-400 400-MHz instrument in the solvent indicated later. Chemical shift values are reported in parts per million (ppm) relative to that for tetramethylsilane (TMS) used as an internal reference standard. Spectral splitting patterns are designated as follows: s, singlet; br, broad; d, doublet; t, triplet; m, multiplet. Mass spectra were obtained using API3000 instruments. Elemental analysis was carried at the CarloErba-1106.

All reactions were monitored by thin-layer chromatography (TLC) on 25×75 mm glass sheets precoated with silica gel (GF254) to a thickness of 0.25 mm and viewed at 254 nm UV light.

2-Cyclohexanotetrahydrobenzimidazole 1a

To a solution of 4.85 g of 2-phenylbenzimidazole (25 mmol) in 50 mL of 2 N HCl, 5% rhodium on carbon (0.3 g) was added. The mixture was hydrogenated at 120°C under 100 $Kg \cdot cm^{-2}$ until the hydrogen was not absorbed in an autoclave. The catalyst was then removed by filtration and washed with water. The filtrate was evaporated to dryness and then dissolved with 30 mL of water. Then the solution was adjusted to pH 14 using 30% NaOH. The resulting precipitate was filtrated off, washed with water, and then dried to

give **1a** (5.1 g, 100% yield) as a white solid. Mp 266–267°C. ^{1}H NMR ($CDCl_3$) δ: 8.0–9.0 (1H, br, NH), 2.65 (1H, m), 2.54 (4H, br, CH_2), 2.02–2.05 (2H, d, $J = 12.32$ Hz, CH_2), 1.79–1.83 (5H, m, CH_2), 1.71 (1H, d, $J = 12.60$ Hz, CH_2), 1.21–1.54 (6H, m, CH_2). ESI-MS: 205.1 (M + 1). Anal. calc. for $C_{13}H_{20}N_2$ (204.16): C, 76.42; H, 9.87; N, 13.71; found: C, 76.58; H, 9.99; N, 13.85.

2-Cyclohexanobenzimidazole 1b

To a solution of 3.88 g of 2-phenylbenzimidazole (20 mmol) in 30 mL of 50% HOAc, 5% rhodium on carbon (0.2 g) was added. The mixture was hydrogenated at 120°C under 50 Kg · cm^{-2} for 1.5 h in an autoclave. The catalyst was then removed by filtration and washed with water. The filtrate was evaporated to about 20 mL, and then 30% NaOH was added until pH = 9. The resulting precipitate was filtrated and washed with water. Recrystallizing with ethanol gave **1b** (3.83 g, 95% yield) as a white solid. Mp 284–286°C. ^{1}H NMR (DMSO-d^6) δ: 12.11 (1H, br, NH), 7.44 (2H, d, $J = 8.6$ Hz, ArH), 7.09 (2H, d, $J = 8.6$ Hz, ArH), 2.83 (1H, m), 1.99–2.02 (2H, m, CH_2), 1.77–1.82 (2H, m, CH_2), 1.55–1.71 (3H, m, CH_2), 1.23–1.44 (3H, m, CH_2). ESI-MS: 201.0 (M + 1). Anal. calc. for $C_{13}H_{16}N_2$ (200.13): C, 77.96; H, 8.05; N, 13.99; found: C, 77.88; H, 7.99; N, 14.11.

General Procedure for *N*-Arylation of Imidazoles

Method A

Under an N_2 atmosphere, 10% weight equivalent 18-crown-6, 1 weight equivalent 37% potassium fluoride absorbed onto basic alumina, and 4-methylsulfonylfluorobenze (5 mmol) in 20 mL DMSO were added successively to the 20-mL DMSO solution of **3** (5 m mol). The mixture was stirred and heated to 120°C until the reaction was completed, for about 8 h. The reaction progress was monitored by TLC. Then, the mixture was filtrated. The filtrate was poured into ice and stirred. The resulting precipitate was filtrated off and washed by water. The crude reaction mixture was purified by silica-gel column chromatography to give **4**.

Method B

Under an N_2 atmosphere, 5 m mol NaH (60% on mineral oil) were added to the solution of **3** (5 m mol) in 20 mL DMSO at 15°C. After stirring for 1 h, 4-methylsulfonylfluorobenze (5 m mol) was added. The resulting mixture was heated to 120°C and stirred until the reaction was completed. The reactive solution was poured into ice and stirred. The resulting precipitate

was filtrated off and washed by water. The crude reaction mixture was purified by silica-gel column chromatography to give **4**.

Data

1-(4-Methylsulfonylphenyl)-2-cyclohexanotetrahydrobenzimidazole (2a). White solid. Yield: 58%. Mp 230–232°C. ^{1}H NMR ($CDCl_3$) δ: 8.09 (2H, d, $J = 8.4$ Hz, ArH), 7.42 (2H, d, $J = 8.4$ Hz, ArH), 3.16 (3H, s, SO_2CH_3), 2.65 (2H, t, $J = 5.18$ Hz, CH_2), 2.44 (1H, m, CH), 2.26 (2H, t, $J = 5.76$ Hz, CH_2), 1.75–1.85 (10H, m, CH_2), 1.12–1.31 (4H, m, CH_2). ^{13}C NMR ($CDCl_3$): δ151.17, 141.47, 140.30, 135.36, 128.87, 128.04, 125.57, 45.72, 44.40, 35.83, 32.32, 26.18, 25.52, 23.94, 23.20, 22.93, 21.41. ESI-MS: 359 (M + 1). Anal. calc. for $C_{20}H_{26}N_2O_2S$, (358.12): C, 67.01; H, 7.31; N, 7.81; found: C, 66.84; H, 7.20; N, 7.50. Elution solvent for the column is petroleum ether/ethyl acetate (1:1, v/v); Rf = 0.62. The inhibitory rate to COX-2 is 26.36% at the concentration of 3 μmol/L.

1-(4-Methylsulfonylphenyl)-2-cyclohexanobenzimidazole (2b). White solid. Yield: 54%. Mp 166–168°C. ^{1}H NMR ($CDCl_3$) δ: 8.20 (2H, d, $J = 8.4$ Hz, ArH), 7.82 (1H, d, $J = 8.12$ Hz, ArH), 7.61 (2H, d, $J = 8.4$ Hz, ArH), 7.22–7.31 (2H, m, ArH), 7.00 (1H, d, $J = 8.12$ Hz, ArH), 3.21 (3H, s, SO_2CH_3), 2.67–2.72 (1H, m, CH), 1.82–1.89 (6H, m, CH_2), 1.19–1.35 (4H, m, CH_2). ESI-MS: 355.2 (M + 1). Anal. calc. for $C_{20}H_{22}N_2O_2S$ (354.14): C, 67.77; H, 6.26; N, 7.90; found: C, 67.30; H, 6.26; N, 7.52. Elution solvent for the column is petroleum ether/ethyl acetate (1 : 1, v/v); Rf = 0.58.

1-(4-Methylsulfonylphenyl)-2-phenyltetrahydrobenzimidazole (4a). Light yellow solid. Yield: 55%. Mp 214–216°C. ^{1}H NMR (DMSO-d^6) δ: 8.00 (2H, d, $J = 8.72$ Hz, ArH), 7.54 (2H, d, $J = 8.72$ Hz, ArH), 7.23–7.29 (5 H, m, ArH), 3.30 (3H, s, SO_2CH_3), 2.57 (2H, t, $J = 5.60$ Hz, CH_2), 2.38 (2H, t, $J = 5.60$ Hz, CH_2), 1.71–1.81 (4H, m, CH_2). ESI-MS: 353.0 (M + 1). Anal. calc. for $C_{20}H_{20}N_2O_2S$ (352.12): C, 68.16; H, 5.72; N, 7.95; found: C, 68.16; H, 5.66; N, 7.58. Elution solvent for the column is cyclohexane/$CHCl_3$/ethylenediamine (25:15:4, v/v/v); Rf = 0.55. The inhibitory rate to COX-2 is 26.19% at the concentration of 3 μmol/L.

1-(4-Methylsulfonylphenyl)-2-(4-methylphenyl)tetrahydrobenzimidazole (4b). White solid. Yield: 55%. Mp 204.5–207°C. ^{1}H NMR ($CDCl_3$) δ: 7.98 (2H, d, $J = 8.52$ Hz, ArH), 7.35 (2H, d, $J = 8.4$ Hz, ArH), 7.17 (2H, d, $J = 8.4$ Hz, ArH), 7.03 (2H, d, $J = 8.52$ Hz, ArH), 3.11 (3H, s, SO_2CH_3), 2.73 (2H, t, $J = 5.74$ Hz, CH_2), 2.42 (2H, t, $J = 5.74$ Hz, CH_2), 2.30 (3H, s, CH_3), 1.83–1.90 (4H, m, CH_2). ^{13}C NMR ($CDCl_3$) δ:145.76, 142.42, 139.67, 138.28, 137.41, 129.09, 128.73, 128.35, 127.92, 127.77, 127.22,

44.43, 24.17, 23.19, 23.02, 21.99. ESI-MS: 367.8 (M + 1, 2). Anal. calc. for $C_{21}H_{22}N_2O_2S$ (366.14): C, 68.82; H, 6.05; N, 7.64; found: C, 68.49; H, 5.87; N, 7.58. Elution solvent for the column is cyclohexane/$CHCl_3$/ethylenediamine (25:15:4, v/v/v); Rf = 0.61.

1-(4-Methylsulfonylphenyl)-2-(4-chlorophenyl)tetrahydrobenzimidazole (4c). Light yellow solid. Yield: 57%. Mp 201–203°C. ^{1}H NMR ($CDCl_3$) δ: 8.01 (2H, d, J = 8.4 Hz, ArH), 7.36 (2H, d, J = 8.4 Hz, ArH), 7.20–7.24 (4H, m, ArH), 3.12 (3H, s, SO_2CH_3), 2.72 (2H, t, J = 5.74 Hz, CH_2), 2.41 (2H, t, J = 5.74 Hz, CH_2), 1.81–1.88 (4H, m, CH_2). Anal. calc. for $C_{20}H_{19}ClN_2O_2S$ (386.09): C, 62.09; H, 4.95; N, 7.24; found: C, 62.39; H, 4.87; N, 7.14. Elution solvent for the column is petroleum ether/ethyl acetate/ethylenediamine (1 : 1.4 : 0.1, v/v/v); Rf = 0.37.

1-(4-Methylsulfonylphenyl)-2-(3-chlorophenyl)tetrahydrobenzimidazole (4d). Light yellow solid. Yield: 53%. Mp 197–199°C. ^{1}H NMR ($CDCl_3$) δ: 8.02 (2H, d, J = 8.4 Hz, ArH), 7.36–7.40 (3H, m, ArH), 7.22 (1H, d, J = 7.88 Hz, ArH), 7.14 (1H, t, J = 7.84 Hz, ArH), 7.05 (1H, d, J = 7.84 Hz, ArH), 3.12 (3H, s, SO_2CH_3), 2.74 (2H, t, J = 5.72 Hz, CH_2), 2.41 (2H, t, J = 5.72 Hz, CH_2), 1.84–1.90 (4H, m, CH_2). ^{13}C NMR ($CDCl_3$) δ: 144.01, 141.93, 140.25, 137.89, 134.42, 131.78, 129.57, 128.97, 128.72, 128.43, 128.34, 127.95, 126.23, 44.47, 24.11, 23.12, 22.92, 21.88. Anal. calc. for $C_{20}H_{19}ClN_2O_2S$ (386.09): C, 62.09; H, 4.95; N, 7.24; found: C, 62.56; H, 5.25; N, 6.78. Elution solvent for the column is petroleum ether/ethyl acetate/ethylenediamine (2 : 1 : 0.1, v/v/v); Rf = 0.57. The inhibitory rate to COX-2 is 8.74% at the concentrate of 3 μmol/L.

1-(4-Methylsulfonylphenyl)-2-(2-chlorophenyl)tetrahydrobenzimidazole (4e). White solid. Yield: 50%. Mp 163–164°C. ^{1}H NMR ($CDCl_3$) δ: 7.88 (2H, d, J = 8.44 Hz, ArH), 7.50 (1H, dd, J = 8.96 Hz, ArH), 7.24–7.30 (5H, m, ArH), 3.06 (3H, s, SO_2CH_3), 2.76 (2H, t, J = 5.60 Hz, CH_2), 2.50 (2H, t, J = 5.60 Hz, CH_2), 1.84–1.93 (4H, m, CH_2). Anal. calc. for $C_{20}H_{19}ClN_2O_2S$ (386.09): C, 62.09; H, 4.95; N, 7.24; found: C, 62.26; H, 5.08; N, 6.91. Elution solvent for the column is petroleum ether/ethyl acetate/ethylenediamine (1 : 1.4 : 0.1, v/v/v); Rf = 0.35.

1-(4-Methylsulfonylphenyl)-2-(2,5-chlorophenyl)tetrahydrobenzimidazole (4f). White solid. Yield: 52%. Mp 191–193°C. ^{1}H NMR ($CDCl_3$) δ: 7.92 (2H, d, J = 8.68 Hz, ArH), 7.56 (1H, d, J = 2.52 Hz, ArH), 7.26–7.30 (3H, m, ArH), 7.19 (1H, d, J = 8.68 Hz, ArH), 3.08 (3H, s, SO_2CH_3), 2.76 (2H, t, J = 5.76 Hz, CH_2), 2.49 (2H, t, J = 5.76 Hz, CH_2), 1.86–1.92 (4H, m, CH_2). ESI-MS: 421.2 (M + 1). Anal. calc. for $C_{20}H_{18}Cl_2N_2O_2S$ (420.05): C, 57.01; H, 4.31; N, 6.65; found: C, 57.00; H, 4.54; N, 6.48. Elution solvent for the column is petroleum ether/ethyl acetate/ethylenediamine (1 : 1.4 : 0.1, v/v/v); Rf = 0.30.

1-(4-Methylsulfonylphenyl)-2-(2,4-methylphenyl)tetrahydrobenzimidazole (4g). White solid. Yield: 48%. Mp 118–121°C. ^{1}H NMR ($CDCl_3$) δ: 7.87 (2H, d, $J = 8.40$ Hz, ArH), 7.20 (2H, d, $J = 8.4$ Hz, ArH), 7.04 (1H, d, $J = 7.56$ Hz, ArH), 6.93 (1H, s, ArH), 6.89 (1H, d, $J = 7.84$ Hz, ArH), 3.06 (3H, s, SO_2CH_3), 2.73 (2H, t, $J = 5.72$ Hz, CH_2), 2.28 (2H, t, $J = 5.72$ Hz, CH_2), 1.85–1.91 (4H, m, CH_2). Anal. calc. for $C_{22}H_{24}N_2O_2S$ (380.16): C, 69.44; H, 6.36, N, 7.36; found: C, 69.32; H, 6.44; N, 7.05. Elution solvent for the column is petroleum ether/ethyl acetate/ethylenediamine (1:1.4:0.1, v/v/v); Rf = 0.47.

1-(4-Methylsulfonylphenyl)-2-(3,4-methylphenyl)tetrahydrobenzimidazole (4h). White solid. Yield: 50%. Mp 240–241°C. ^{1}H NMR ($CDCl_3$) δ: 7.98 (2H, d, $J = 8.4$ Hz, ArH), 7.36 (2H, d, $J = 8.4$ Hz, ArH), 7.30 (1H, s, ArH), 6.91 (1H, d, $J = 7.84$ Hz, ArH), 6.76 (1H, dd, $J = 7.84$ Hz, ArH), 3.11 (3H, s, SO_2CH_3), 2.73 (2H, t, $J = 5.74$ Hz, CH_2), 2.42 (2H, t, $J = 5.74$ Hz, CH_2), 2.21 (3H, s, CH_3), 2.17 (3H, s, CH_3), 1.83–1.89 (4H, m, CH_2). Anal. calc. for $C_{22}H_{24}N_2O_2S$ (380.16): C, 69.44; H, 6.36; N, 7.36; found: C, 69.40; H, 6.32; N, 7.36. Elution solvent for the column is petroleum ether/ethyl acetate/ethylenediamine (1:1.6:0.08, v/v/v); Rf = 0.41.

1-(4-Methylsulfonylphenyl)-2-(4-fluorophenyl)tetrahydrobenzimidazole (4i). White solid. Yield: 51%. Mp 211–213°C. ^{1}H NMR ($CDCl_3$) δ: 8.01 (2H, d, $J = 8.4$ Hz, ArH), 7.36 (2H, d, $J = 8.4$ Hz, ArH), 7.28–7.32 (2H, m, ArH), 6.95 (2H, t, $J = 8.68$ Hz, ArH), 3.12 (3H, s, SO_2CH_3), 2.75 (2H, t, $J = 5.74$ Hz, CH_2), 2.41 (2H, t, $J = 5.74$ Hz, CH_2), 1.84–1.90 (4H, m, CH_2). Anal. calc. for $C_{20}H_{19}FN_2O_2S$ (370.12): C, 64.85; H, 5.17; N, 7.56; found: C, 64.83; H, 5.48; N, 7.38. Elution solvent for the column is petroleum ether/ethyl acetate/ethylenediamine (1:1:0.06, v/v/v); Rf = 0.41.

1-(4-Methylsulfonylphenyl)-2-(2,3-methyloxyphenyl)tetrahydrobenzimidazole (4j). White solid. Yield: 51%. Mp 211–213°C. ^{1}H NMR ($CDCl_3$) δ: 7.85 (2H, d, $J = 8.68$ Hz, ArH), 7.26 (2H, d, $J = 8.68$ Hz, ArH), 7.05 (2H, m, ArH), 6.91 (1H, m, ArH), 3.77 (3H, s, OCH_3), 3.49 (3H, s, OCH_3), 3.04 (3H, s, SO_2CH_3), 2.73 (2H, t, $J = 5.74$ Hz, CH_2), 2.46 (2H, t, $J = 5.74$ Hz, CH_2), 1.83–1.89 (4H, m, CH_2). Anal. calc. for $C_{22}H_{24}N_2O_4S$ (412.15): C, 64.06; H, 5.86; N, 6.79; found: C, 64.21; H, 6.02; N, 6.97. Elution solvent for the column is petroleum ether/ethyl acetate/ethylenediamine (1:1.4:0.1, v/v/v); Rf = 0.27.

1-(4-Methylsulfonylphenyl)-2-(2-methylphenyl)tetrahydrobenzimidazole (4k). White solid. Yield: 71%. Mp 204–207°C. ^{1}H NMR ($CDCl_3$) δ: 7.87 (2H, d, $J = 8.4$ Hz, ArH), 7.21 (2H, d, $J = 8.4$ Hz, ArH), 7.07–7.18 (4H, m, ArH), 3.06 (3H, s, SO_2CH_3), 2.74 (2H, t, $J = 5.74$ Hz, CH_2), 2.50 (2H, t, $J = 5.74$ Hz, CH_2), 2.10 (3H, s, CH_3), 1.86–1.92 (4H, m, CH_2). Anal. calc. for $C_{21}H_{22}N_2O_2S$ (366.14): C, 68.82; H, 6.05; N, 7.64; found: C, 69.09; H,

5.87; N, 7.58. Elution solvent for the column is petroleum ether/ethyl acetate/ethylenediamine (1:1.4:0.1, v/v/v); Rf = 0.57.

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