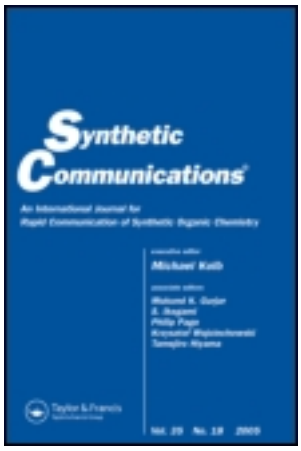

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A SIMPLE AND EFFICIENT METHOD FOR THE SYNTHESIS OF NOVEL TRIFLUOROMETHYL BENZIMIDAZOLES UNDER MICROWAVE IRRADIATION CONDITIONS*

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A SIMPLE AND EFFICIENT METHOD FOR THE SYNTHESIS OF NOVEL TRIFLUOROMETHYL BENZIMIDAZOLES UNDER MICROWAVE IRRADIATION CONDITIONS*

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ABSTRACT

The condensation of trifluoromethyl -*o*-phenylenediamines and aromatic aldehydes under microwave irradiation on metal halide supported alumina resulted exclusively trifluoromethyl-2-aryl benzimidazoles.

The benzimidazole nucleus is found in a variety of pharmaceuticals as cardiotonic agents,[1,2] potential antitumor agents[3] and antiulcer agents.[4] In particular the trifluoromethyl benzimidazoles[5–7] have importance as pesticidal and antibacterial compounds. Conventional methods on the synthesis of 2-aryl benzimidazoles involve the condensation of *o*-diamino aromatic compound and benzoic acid derivatives[8,9] in presence of

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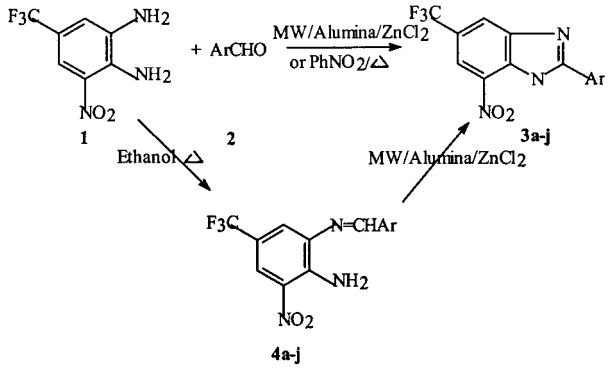
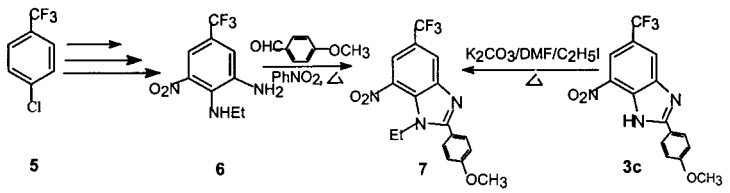
strong acidic medium or in high boiling solvents. In recent years there has been a considerable growth in interest on the synthesis of 2-aryl benzimidazoles by different methods viz., palladium catalysed reactions,[10] and solid phase reactions[11]. Further studies on the efficient synthesis of aryl benzimidazoles is of current interest because of their wide range of applications. As a continued interest on the synthesis of trifluoromethyl substituted molecules of biological interest,[12,13] we wish to report here for the first time a simple and convenient method of preparation of 2-aryl benzimidazoles using metal halide supported, solvent free solid phase reaction under microwave irradiation conditions.

In a specified experiment, the reaction is mainly the condensation of 3-nitro-5-trifluoromethyl-*o*-phenylene diamine **1** and 4-methoxybenzaldehyde **2c** in presence of a catalytic amount of anhydrous zinc chloride. The reactants were adsorbed on alumina and subjected to microwave irradiation for a specified time to result product. The product is isolated by extraction with chloroform and purified by passing through a column of silicagel using *n*-Hexane : Chloroform (1 : 1) as eluents. Based on spectral data, it has been characterized as 2-(4-methoxyphenyl) -5-trifluoromethyl-7-nitrobenzimidazole **3c** (Scheme 1). This reaction has been extended to other substituted aromatic aldehydes and obtained the respective 2-arylbenzimidazoles. The structure of **3c** is confirmed after ethylation and comparing with an authentic sample prepared independently. Thus the 3-amine-5-nitro-4-ethylamino benzotrifluoride **6** is prepared from *p*-chloro benzotrifluoride **5** via nitration and amination by a known method[14] followed by controlled reduction using NaHS. The condensation of compound **6** with 4-methoxybenzaldehyde under thermal conditions obtained 1-ethyl-2 (4-methoxyphenyl)5-trifluoromethyl 7-nitrobenzimidazole **7**. Alternately the direct



Scheme 1.



Scheme 2.

ethylation of **3c** using ethyl iodide also gave **7** (Scheme 2). The compound **7** which was prepared independently by both the routes is found to be similar in their m.p. IR, ^{1}H NMR and Mass spectra.

In general the formation of benzimidazoles involve the initial formation of a Schiff's base **4** and its cyclisation followed by dehydrogenation to give the desired compound **3**. The intermediate Schiff's base 3-*N*′-arylidene-4-amino-5-nitrobenzotrifluoride **4a–j** is prepared by the reaction of diamine and aldehyde in ethanol with constant stirring at reflux temperature. The possibility of the formation of other isomer for **4** may be ruled out based on electronic factors. The nucleophilic attack of 3-amino group of compound **1** on to aldehyde is more possible as the lone pair electrons of 3-amino group is easily available for Schiff's base formation, whereas that of the 4-amine group is in conjugation with the trifluoromethyl group present at para position. The Schiff's base **4a–j** is subjected to microwave irradition in presence of $ZnCl_2$ on alumina to give corresponding benzimidazoles **3a–j**.

In order to compare the rate of reaction, yields of the products and substituent effect, the reactions were conducted under thermal conditions. However we found that the rate of reaction is fast, yields are high and substituents have no effect on the formation of products under microwave conditions (Table 1).

In conclusion the developed methods i.e., cyclisation of Schiffs base and also *o*-diamine condensation can be universally applied for the synthesis of variety of benzimidazoles. These compounds will become as active synthons for building tricyclic heterocycles.

EXPERIMENTAL

Melting points are determined in open glass capillaries on a Fisher Johnes melting point apparatus. IR spectra are recorded on FT-IR Schimadzu Perkin–Elmer 1310 infrared spectrophotometer. ^{1}H NMR spectra

Table 1. Synthesis of Substituted-2-aryl Benzimidazoles

			Time (min)		Yield (%)	
Entry	Ar	M.P. (°C)	Microwave	Thermal	Microwave	Thermal
3a	Phenyl	217	4	120	84	80
3b	4-Fluorophenyl	215	4	120	83	77
3c	4-Methoxyphenyl	245	4	120	72	64
3d	4-Methylphenyl	228	4	120	86	65
3e	4-Chlorophenyl	207	4	120	90	60
3f	4-(*N*,*N*-Dimethyl)phenyl	206	4	120	85	66
3g	4-Nitrophenyl	> 270	4	120	87	62
3h	4-Hydroxyphenyl	> 270	4	120	85	80
3i	Furyl	210	4	120	82	64
3j	Naphthyl	> 270	4	120	80	62

are recorded on Varian Gemini (200 MHz) spectrometer and TMS is used as internal standard. Mass spectra are recorded on a VG-micromass 7070H instrument at 70 eV. Elemental analysis were carried out on a Elemental Vario EL (Germany) apparatus.

Synthesis of Substituted 2-Aryl Benzimidazoles 3

General Procedure

Microwave Conditions

A mixture of diamine **1** (0.01 mole), aromatic aldehyde (0.01 mole) and anhydrous $ZnCl_2$ (0.001 mole) is adsorbed on alumina transferred in to a tube and subjected to microwave irradiation for 4 min in a domestic oven (600 watt, BPL BMD 700T) allowed to cool to room temperature. The products are extracted with chloroform and concentrated to get crude product. Then the products were purified by passing through a silicagel column using *n*-Hexane : Chloroform (1 : 1) as eluent.

Thermal Conditions

A mixture of diamine **1** (0.01 mole), aromatic aldehyde (0.01 mole) were dissolved in nitrobenzene (6 mL) and heated at 160°C for 2 h.

The reaction mixture is cooled and diluted with pentane. The separated solid is filtered, washed with pentane, dried and recrystallised from chloroform to give substituted 2-aryl benzimidazoles **3**.

The spectral data of compounds **3a–j** are shown in below.

2-Phenyl-5-trifluoromethyl-7-nitrobenzimidazole(3a): ^{1}H NMR ($CDCl_3$) δ 10.9 (s, 1H, NH), 8.5 (s, 1H, Ar), 8. 4 (s, 1H, Ar), 8.2 (m, 2H, Ar), 7.6 (m, 3H, Ar), IR (KBr, cm^{-1}) 3384 (NH), 1645, 1524, 1338, 1290, MS (EI, *m*/*z*) M^+ 307, Analysis calcd. for $C_{14}H_8F_3N_3O_2$; C, 54.73; H, 2.62; N, 13.67. Found: C, 54.71; H, 2.60; N, 13.59.

2-(4–Fluorophenyl)-5-trifluoromethyl-7-nitrobenzimidazole(3b): ^{1}H NMR ($CDCl_3$) δ 13.2 (s, 1H, –NH), 8.6 (s, 1H, Ar–H), 8.5 (s, 1H, Ar–H), 8.2 (d, 2H, Ar–H), 7.2 (d, 2H, Ar–H), IR (KBr, cm^{-1}) 3394 (NH), 1645, 1524, 1339, 1291, MS (EI, *m*/*z*) M^+ 325 Analysis calcd. for $C_{14}H_8F_4N_3O_2$; C, 51.70; H, 2.16; N, 12.92. Found. C, 51.62; H, 2.20; N, 13.01.

2-(4–Methoxyphenyl)-5-trifluoromethyl-7-nitrobenzimidazole(3c): ^{1}H NMR ($CDCl_3$) δ 10.7 (s, 1H, -NH), 8.4 (s, 1H, Ar–H), 8.3 (s, 1H, Ar–H), 8.1 (d, 2H, Ar–H), 7.1 (d, 2H, Ar–H), 3.9 (s, 3H, -OCH_3) IR (KBr, cm^{-1}) 3390 (NH), 1645, 1524, 1339, 1291 MS (EI, *m*/*z*) M^+ 337 Analysis calcd. for $C_{15}H_{10}F_3N_3O_3$; C, 53.42; H, 2.98; N, 12.45. Found: C, 53.29; H, 2.99; N, 12.41.

2-(4-Methylphenyl)-5-trifluoromethyl-7-nitrobenzimidazole(3d): ^{1}H NMR ($CDCl_3$) δ 10.8 (s, 1H, -NH), 8.5 (s, 1H, Ar–H), 8.4 (s, 1H, Ar–H), 8.1 (d, 2H, Ar–H), 7.4 (d, 2H, Ar–H), 2.3 (s, 3H, -CH_3) IR (KBr, cm^{-1}) 3357 (NH), 1608, 1520, 1332, 1292, MS (EI, *m*/*z*) M^+ 321 Analysis calcd. for $C_{15}H_{10}F_3N_3O_2$; C, 56.08; H, 3.13; N, 13.08. Found: C, 55.98; H, 3.11; N, 13.10.

2-(4–Chlorophenyl)-5-trifluoromethyl-7-nitrobenzimidazole(3e): ^{1}H NMR ($CDCl_3$) δ 10.8 (s, 1H, -NH), 8.5 (s, 1H, Ar–H), 8.4 (s, 1H, Ar–H), 8.2 (d, 2H, Ar–H), 7.2 (d, 2H, Ar–H), IR (KBr, cm^{-1}) 3392 (NH), 1644, 1523, 1338, 1290, MS (EI, *m*/*z*) M^+ 341 Analysis calcd. for $C_{14}H_7ClF_3N_3O_2$; C, 49.21; H, 2.06; N, 12.30. Found: C, 49.41; H, 2.10; N, 12.28.

2-(4-*N*,*N*-Dimethylphenyl)-5-trifluoromethyl-7-nitrobenzimidazole(3f): ^{1}H NMR ($CDCl_3$) δ 10.6 (s, 1H, -NH), 8.4 (s, 1H, Ar–H), 8.2 (s, 1H, Ar–H), 8.0 (d, 2H, Ar–H), 6.8 (d, 2H, Ar–H), 3.1 (s, 6H, -CH_3) IR (KBr, cm^{-1}) 3350 (NH), 1606, 1520, 1330, 1291, MS (EI, *m*/*z*) M^+ 350 Analysis calcd. for $C_{16}H_{13}F_3N_4O_2$; C, 54.85; H, 3.74; N, 15.99. Found: C, 54.65; H, 3.42; N, 16.01.

2-(4–Nitrophenyl)-5-trifluoromethyl-7-nitrobenzimidazole(3g): ^{1}H NMR ($CDCl_3$) δ 12.4 (s, 1H, -NH), 8.5 (s, 1H, Ar–H), 8.4 (s, 1H, Ar–H), 8.1 (d, 2H, Ar–H), 7.4 (d, 2H, Ar–H), IR (KBR, cm^{-1}) 3390 (NH), 1645, 1520, 1339, 1290 MS (EI, *m*/*z*) M^+ 352 Analysis calcd. for $C_{14}H_7F_3N_4O_4$; C, 47.73; H, 2.00; N, 15.90. Found: C, 47.63; H, 2.02; N, 15.95.

2-(4–Hydroxyphenyl)-5-trifluoromethyl-7-nitrobenzimidazole(3h): ^{1}H NMR ($CDCl_3$) δ 13.0 (s, 1H, –NH), 9.9 (s, 1H, -OH), 8.4 (m, 4H, Ar–H), 6.9 (d, 2H, Ar–H), IR (KBr, cm^{-1}) 3390 (NH), 3310 (OH), 1645, 1523, 1340, 1292, MS (EI, m/z) M^+ 323 Analysis calcd. for $C_{14}H_8F_3N_3O_3$; C, 52.02; H, 2.49; N, 13.00. Found: C, 52.20; H, 2.51; N, 13.02.

2-Furyl-5-trifluoromethyl-7-nitrobenzimidazole (3i): ^{1}H NMR ($CDCl_3$) δ 13.1 (s, 1H, -NH), 8-.2 (d, 2H, Ar–H), 7.9 (s, 1H, Ar–H), 6.9 (s, 1H, Ar–H), IR (KBr, cm^{-1}) 3384 (NH), 1640, 1520, 1337, 1288. MS (EI, m/z) M^+ 297 Analysis calcd. for $C_{12}H_6F_3N_3O_3$; C, 48.49; H, 2.03; N, 14.13. Found: C, 49.51; H, 2.21; N, 14.41.

2-Napthyl-5-trifluoromethyl-7-nitrobenzimidazole (3j): ^{1}H NMR ($CDCl_3$) δ 10.9 (s, 1H, -NH), 8-.9 (d, 1H, Ar–H), 8.5 (d, 1H, Ar–H), 8.2 (d, 1H, Ar–H), 8.0 (m, 2H, Ar–H), 7.7 (m, 4H, Ar–H) IR (KBr, cm^{-1}) 3390 (NH), 1640, 1520, 1500, 1340, 1290, MS (EI, m/z) M^+ 357 Analysis calcd. for $C_{18}H_{10}F_3N_3O_2$; C, 60.50; H, 2.82; N, 11.76. Found: C, 60.41; H, 2.71; N, 11.80.

Synthesis of 3-*N*-Arylidene-4-amino-5-nitrobenzotrifluoride (4)

General Procedure

The diamine **1** (0.01 mole) and aromatic aldehyde (0.01 mole) were dissolved in ethanol (10 mL) and refluxed for 1.5 h. The reaction mixture is cooled to room temperature and the solvent is removed from the reaction mixture. The residual solid is purified by recrystallisation with dichloromethane and dried.

3-*N*-Benzilidene-4-amino-5-nitro benzotrifluoride (4a): Yield 80% m.p. 124–127°C, ^{1}H-NMR ($CDCl_3$) δ 8.6 (s, 1H, Ar–H), 8.4 (s, 1H, –CH=N), 8.0 (d, 2H, Ar–H), 7.5 (m, 3H, Ar–H), 7.3 (s, 1H, Ar–H), 7.0 (s, 2H, $–NH_2$), IR (KBr, cm^{-1}) 3479, 3360 (NH_2), 1628, 1456, 1341, 1252. MS (EI, m/z) M^+ 309 Analysis calcd. for $C_{14}H_{10}F_3N_3O_2$; C, 54.37; H, 3.25; N, 13.58. Found: C, 54.39; H, 3.29; N, 13.64.

3-*N*-(4–Fluorobenzilidene)-4-amino-5-nitrobenzotrifluoride (4b): Yield 82% m.p. 134°C, ^{1}H NMR ($CDCl_3$) δ 8.6 (s, 1H, Ar–H), 8.35 (s, 1H, -CH=N), 8.0 (d, 2H, Ar–H), 7.4 (s, 1H, Ar–H),7.2 (d, 2H, Ar–H), 7.0 (s, 2H, $–NH_2$), IR (KBr, cm^{-1}) 3479, 3360 (NH_2), 1628, 1456, 1310, 1256, MS (EI, m/z) M^+ 327 Analysis calcd. for $C_{14}H_9F_4N_3O_2$; C, 51.38; H, 2.77; N, 12.84. Found: C, 51.42; H, 2.79; N, 12.71.

3-*N*-(4–Methoxybenzilidene)-4-amino-5-nitrobenzotrifluoride (4c): Yield 80% m.p. 85–87°C, ^{1}H NMR ($CDCl_3$) δ 8.5 (s, 1H, Ar–H), 8.3 (s, 1H, –CH=N), 7.9 (d, 2H, Ar–H), 7.4 (s, 1H, Ar–H) 7.0 (d, 2H, Ar–H), 7.1

(s, 2H, $-NH_2$), 3.9 (s, 3H, $-OCH_3$), IR (KBr, cm^{-1}) 3478, 3359 (NH_2), 1629, 1456, 1341, 1252 MS (EI, *m/z*) M^+ 339 Analysis calcd. for $C_{15}H_{12}F_3N_3O_3$; C, 53.10; H, 3.56; N, 12.38. Found: C, 53.21; H, 3.61; N, 12.42.

3-*N*-(4–Methylbenzilidene)-4-amino-5-nitrobenzotrifluoride (4d): Yield 70% m.p. 125–127°C, ^1H NMR ($CDCl_3$) δ 8.6 (s, 1H, Ar–H), 8.3 (s, 1H, -CH=N), 7.8 (d, 2H, Ar–H), 7.3 (d, 2H, Ar–H) 7.25 (s, 1H, Ar–H), 7.2 (s, 2H, $-NH_2$), 2.3 (s, 3H, $-CH_3$) IR (KBr, cm^{-1}) 3473, 3335 (NH_2), 1628, 1456, 1301, 1256 MS (EI, *m/z*) M^+ 323 Analysis calcd. for $C_{15}H_{12}F_3N_3O_2$; C, 55.73; H, 3.74; N, 12.99. Found C, 55.71; H, 3.76; N, 13.01.

3-*N*-(4–Chlorobenzilidene)-4-amino-5-nitrobenzotrifluoride (4e): Yield 78% m.p. 151–152°C, ^1H NMR ($CDCl_3$) δ 8.6 (s, 1H, Ar–H), 8.35 (s, 1H, -CH=N), 7.8 (d, 2H, Ar–H), 7.3 (d, 2H, Ar–H) 7.25 (s, 1H, Ar–H), 7.2 (s, 2H, $-NH_2$), IR (KBr, cm^{-1}) 3479, 3359 (NH_2), 1628, 1457, 1312, 1254 MS (EI, *m/z*) M^+343 Analysis calcd. for $C_{14}H_9ClF_3N_3O_2$; C, 48.92; H, 2.63; N, 12.22. Found C, 48.99; H, 2.67; N, 12.23.

3-*N*-(4–*N*, *N*-Dimethylbenzilidene)-4-amino-5-nitrobenzotrifluoride (4f): Yield 80% m.p. 114–115°C ^1H NMR ($CDCl_3$) δ 8.4 (s, 1H, Ar–H), 8.2 (s, 1H, -CH=N), 7.8 (d, 2H, Ar–H), 7.3 (s, 1H, Ar–H), 7.0 (s, 2H, NH_2), 6.8 (d, 2H, Ar–H), 3.0 (s, 6H, $-CH_3$) IR (KBr, cm^{-1}) 3470, 3331 (NH_2), 1628, 1457, 1300, 1250 MS (EI, *m/z*) M^+ 352 Analysis calcd. for $C_{16}H_{15}F_3N_4O_2$; C, 54.54; H, 4.29; N, 15.90. Found C, 54.61; H, 4.31; N, 16.10.

3-*N*-(4–Nitrobenzilidene)-4-amino-5-nitrobenzotrifluoride (4g): Yield 70% m.p. 180–181°C, ^1H NMR ($CDCl_3$) δ 8.9 (s, 1H, Ar–H), 8.4 (s, 1H, -CH=N), 8.3 (m, 2H, Ar–H), 8.2 (d, 2H, Ar–H) 7.6 (s, 1H, Ar–H), 7.4 (s, 2H, $-NH_2$), IR (KBr, cm^{-1}) 3479, 3360 (NH_2), 1628, 1456, 1310, 1252 MS (EI, *m/z*) M^+354 Analysis calcd. for $C_{14}H_9F_3N_4O_4$; C, 47.46; H, 2.56; N, 15.81. Found C, 47.42; H, 2.52; N, 15.72.

3-*N*-(4–Hydroxybenzilidene)-4-amino-5-nitrobenzotrifluoride (4h): Yield 78% m.p. 175–177°C, ^1H NMR ($CDCl_3$) δ 9.9 (s, 1H, -OH) 8.7 (s, 1H, Ar–H), 8.2 (s, 1H, -CH=N), 7.7 (d, 2H, Ar–H), 7 (s, 2H, $-NH_2$), 6.9 (d, 2H, Ar–H) IR (KBr, cm^{-1}) 478, 3359 (NH_2), 3330, 1629, 1450, 1302, 1257, MS (EI, *m/z*) M^+325 Analysis calcd. for $C_{14}H_{10}F_3N_3O_3$; C, 51.69; H, 3.09; N, 12.91. Found C, 51.67; H, 3.12; N, 12.93.

3-*N*-Furylidene-4-amino-5-nitrobenzotrifluoride (4i): Yield 68% m.p. 162–164°C, ^1H NMR ($CDCl_3$) δ 8.5 (s, 1H, Ar–H), 8.4 (s, 1H, -CH=N), 7.7 (d, 1H, Ar–H), 7.3 (s, 1H, Ar–H)7.1 (m, 2H, Ar–H), 6.7 (s, 2H, $-NH_2$), IR (KBr, cm^{-1}) 3475, 3360 (NH_2), 1630, 1450, 1336, 1250 MS (EI, *m/z*) M^+299 Analysis calcd. for $C_{12}H_8F_3N_3O_3$; C, 48.17; H, 2.69; N, 14.04. Found C, 48.23; H, 2.71; N, 14.05.

3-*N*–Napthylidene-4-amino-5-nitrobenzotrifluoride (4j): Yield 60% m.p. 162–164°C, ^1H NMR ($CDCl_3$) δ 9.2 (s, 1H, Ar–H), 9 (d, 1H, Ar–H), 8.4 (s, 1H, Ar–H), 8.2 (d, 1H, Ar–H) 8.1 (d, 1H, Ar), 7.9 (d, 1H, Ar–H), 7.7

(m, 3H, Ar–H), (s, 2H, -NH_2), IR (KBr, cm^{-1}) 3476, 3335 (NH_2), 1628, 1456, 1310, 1250 MS (EI, *m*/*z*) M^+359 Analysis calcd. for $C_{18}H_{12}F_3N_3O_2$; C, 60.17; H, 3.36; N, 11.69. Found C, 60.07; H, 3.32; N, 11.70.

Preparation of Substituted 2-Arylbenzimidazoles 3 from Schiff's Base 4

General Procedure

Schiff's base **4** (10 mmole) and anhydrous zinc chloride (1 mmole) are adsorbed on alumina and heated for 1 min in microwave oven. The solid is allowed to cool to 30°C and extracted with ethanol. The solvent is removed and the solid residue was passed through column of silica gel using chloroform as eluant to give the corresponding 2-aryl benzimidazoles **3**.

Preparation of 3-Amino-4-ethylamino-5-nitrobenzotrifluoride (6)

General Procedure

To a mixture of sodium sulphide nonahydrate (2.6 g, 10 mmole) and sodiumbicarbonate(0.85 g 10 mmole) is dissolved in distilled water (20 mL) and methanol (30 mL) is added to it. The separated sodium carbonate is separated by filtration and filtrate is preserved. To the filtrate a solution of 3,5-dinitro-4-ethylaminobenzotrifluoride (1.4 g, 5 mmole) in methanol (10 mL) is added and heated at 70°C for 10 min. The methanol is removed and the residue is poured on to ice. The separated solid is filtered, dried and recrystallised in aq. methanol to give the compound **6**.

M.p. 111°C ^{1}H NMR ($CDCl_3$) δ 7.7 (s, 1H Ar–H), 7 (s, 1H, Ar–H), 6.1 (1H, -NH), 4 (s, 2H, -NH_2), 3.2 (q, 2H, -CH_2), 1.2 (t, 3H, -CH_3) MS (EI, *m*/*z*) M^+ 249 Analysis calcd. for $C_9H_{10}F_3N_3O_2$; C, 43.37; H, 4.04; N, 16.86. Found C, 43.29; H, 4.01; N, 16.53.

1-Ethyl-2-(4-methoxyphenyl)-5-trifluoromethyl-7-nitrobenzimidozole 7

Method 1: The compound **6** (60 mg, 0.25 mmoles) and 4-methoxybenzaldehyde (80 mg 0.58 mmole) were dissolved in nitrobenzene (6 mL) and heated at 170°C for 2 h. The reaction mixture is cooled and diluted with pentane. The separated solid is filtered, washed with pentane dried and

purified by passing through a column of silica gel using dichloromethane as eluant to give the compound **7**.

Method 2: To a solution of 2-(4-methoxyphenyl) -5-trifluoromethyl -7-nitro benzimidazole (100 mg 0.3 mmole) in dry dimethylformamide (5 g) potassium carbonate (500 mg 3.6 mmole) and ethyliodide (80 mg 0.5 mmole) is added and the mixture is heated at 110°C for 20 h. The progress of the reaction is monitored by TLC. The reaction mixture is poured on to crushed ice. The separated solid is filtered, dried to give **7**.

M.p. 181°C ^{1}H NMR ($CDCl_3$) δ 8.4 (s, 1H, Ar–H), 7.9 (s, 1H, Ar–H), 7.8 (d, 2H, Ar–H), 7 (d, 2H, Ar–H), 4.2 (Q, 2H, -CH_2), 3.9 (s, 3H, -OCH_3), 1.6 (t, 3H, CH_3) IR (KBr, cm^{-1}) 1643, 1520, 1335, 1290 MS (EI, m/z) M^+ 365 Analysis calcd. for $C_{17}H_{14}F_3N_3O_3$; C, 55.89; H, 3.86; N, 11.50. Found C, 55.70; H, 3.81; N, 11.55.

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