

HETEROCYCLES, Vol. 65, No. 10, 2005, pp. 2329 - 2337

Received, 19th May, 2005, Accepted, 8th August, 2005, Published online, 12th August, 2005

## SYNTHESIS OF NEW TRIFLUOROMETHYL SUBSTITUTED 11H-ISOINDOLO[2,1-*a*]BENZIMIDAZOL-11-ONE DERIVATIVES

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**Abstract** - A convenient method has been developed for the synthesis of new trifluoromethyl-substituted 11H-isoindolo[2,1-*a*]benzimidazol-11-one derivatives from 3-nitro-5-trifluoromethyl-*o*-phenylenediamine and aromatic anhydrides on the surface of silica gel impregnated with ZnCl<sub>2</sub> under solvent free microwave irradiation conditions.

### INTRODUCTION

Although a large number of benzimidazole analogs have been synthesized, there still exists much scope for the synthesis of new benzimidazole derivatives possessing different pharmacophores.<sup>1-3</sup> Tricyclic<sup>4</sup> and tetracyclic<sup>5,6</sup> heterofused benzimidazoles are known to possess bronchodilator activity and also considered as potential candidates as plant growth regulators. Some of them are thoroughly evaluated as antitumor agents due to their structural resemblance with batracyclin 8-aminoisoindolo[1,2-*b*]quinazolin-12(10H)-one which exhibits antineoplastic activity<sup>5</sup> *in vivo* against marine leukemia P-388. Preeti and coworkers<sup>7</sup> used tetracyclic heterofused benzimidazoles as active synthons for 2-aryl-5-[2,1-(benzimidazol-2'-yl)phenyl]-1,3,4-oxadiazoles possessing antitubercular activity and antibacterial activity. The preparation of nonfluorinated isoindolo[2,1-*a*]benzimidazoles was reported from *o*-diamines and phthalic anhydride in refluxing ethanol,<sup>4</sup> *n*-amyl alcohol,<sup>5</sup> and acetic anhydride.<sup>6</sup>

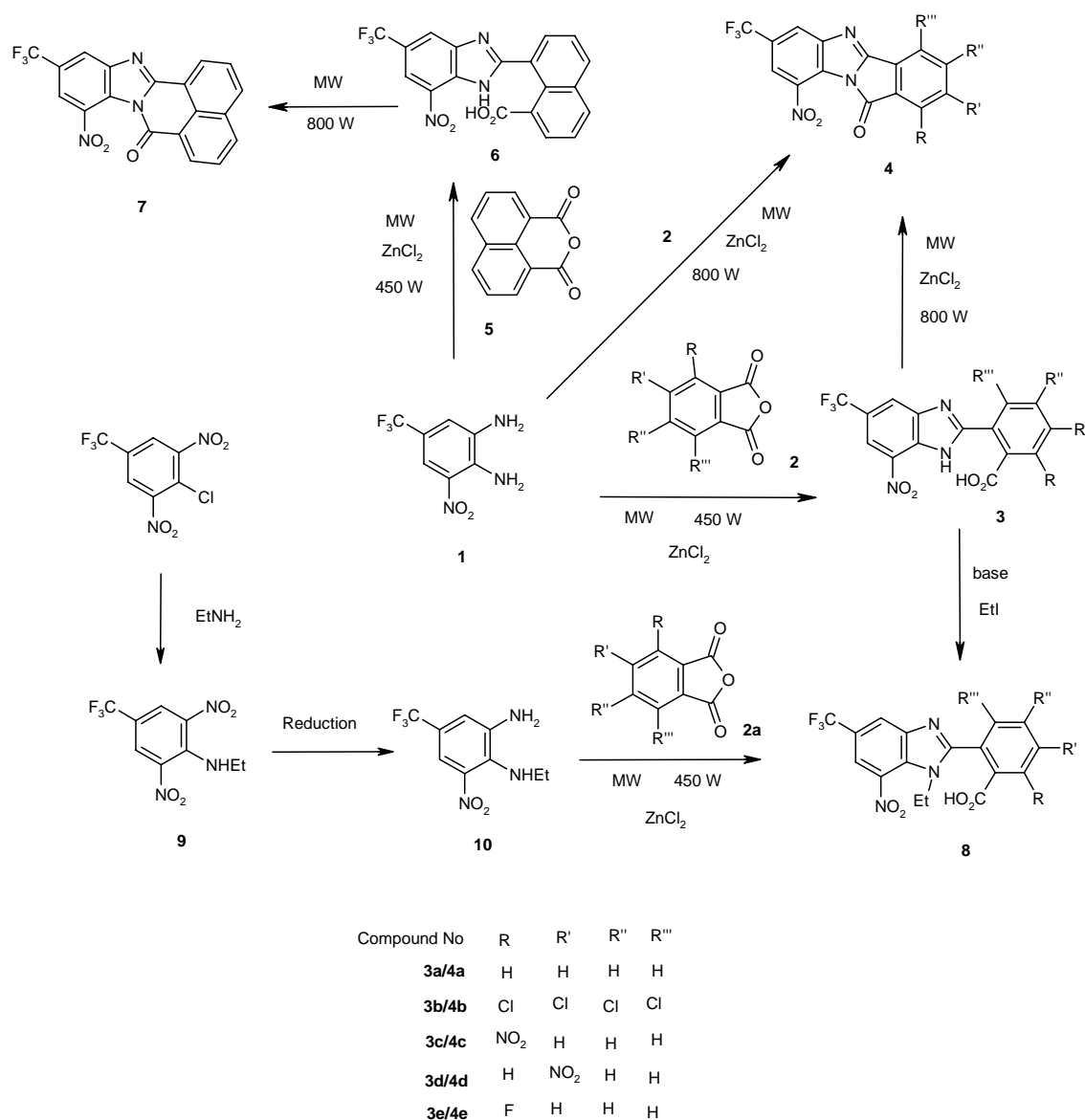
In view of our interest in the synthesis of fluorinated benzimidazoles<sup>8,9</sup> we have developed the most concise, effluent free and an efficient method for the synthesis of new trifluoromethyl substituted tetracyclic heterofused benzimidazoles using microwave irradiation in presence of catalytic amount of zinc chloride without the aid of any reagent or solvent. Incorporating trifluoromethyl group into a molecule can often lead to an enhancement in the biological activity and change in physiological properties.<sup>10</sup> These modifications are associated with increased stability and lipophilicity, while the steric distortion, compared to the parent compound is relatively small.

## RESULTS AND DISCUSSION

The reaction of 3-nitro-5-trifluoromethyl-*o*-phenylenediamine (**1**)<sup>9</sup> with phthalic anhydride (**2**) in presence of anhydrous zinc chloride on silica gel support under controlled microwave irradiation by maintaining 450 W current resulted 2-arylbenzimidazoles (**3**). It is interesting to note that, the basicity of two amino functions present in the diamine (**1**) is not equal due to their position with reference to electron withdrawing groups in the ring. It is presumed that the reaction is initiated by the attack of the more basic amino group (*meta* to CF<sub>3</sub> and NO<sub>2</sub>) onto the carbonyl function of phthalic anhydride resulting in an open-chain amide by cleavage of anhydride. Cyclization of this amide by reacting with the other amino function present at *ortho* position, followed by dehydration furnished 2-arylbenzimidazole. The 2-arylbenzimidazoles (**3**) can exist in two possible positional isomers depending on the presence of hydrogen on either of the nitrogens of imidazole moiety. It is very difficult to differentiate these isomers based on spectral data. The possibility of assigning structure is based on forming H-bonding with the NO<sub>2</sub> group makes the H-atom to be present on the N-atom ortho to NO<sub>2</sub> group in the 2-arylbenzimidazole (**3**). The structure of **3** is further confirmed by converting it to ethylated derivative and synthesizing it by an unambiguous method to further confirm the structure of **3**.

The 2-arylbenzimidazole (**3**) is reacted with ethyl iodide using potassium carbonate as base to obtain the corresponding ethylated derivative (**8**). The authentic synthesis is designed starting from 3,5-dinitro-4-chlorobenzotrifluoride, reacted with ethylamine to furnish 3,5-dinitro-4-ethylaminobenzotrifluoride (**9**). Partial reduction of **9** gave 3-amino-4-ethylamino-5-nitrobenzotrifluoride (**10**). The condensation of *N*-ethyl diamine (**10**) with phthalic anhydride under specified microwave irradiation conditions (450 W) resulted in 1-ethyl-2-aryl-5-trifluoromethyl-7-nitrobenzimidazole (**8**). The mp of **8** and ethylated compound of **3** are exactly matching and the mixed mp is not depressed. The IR spectra of both ethylated **3** and **8** are superimposable. By confirming the structure of the compound (**8**), compound (**3**) is characterized as 2-aryl-5-trifluoromethyl-7-nitrobenzimidazole (Scheme-1).

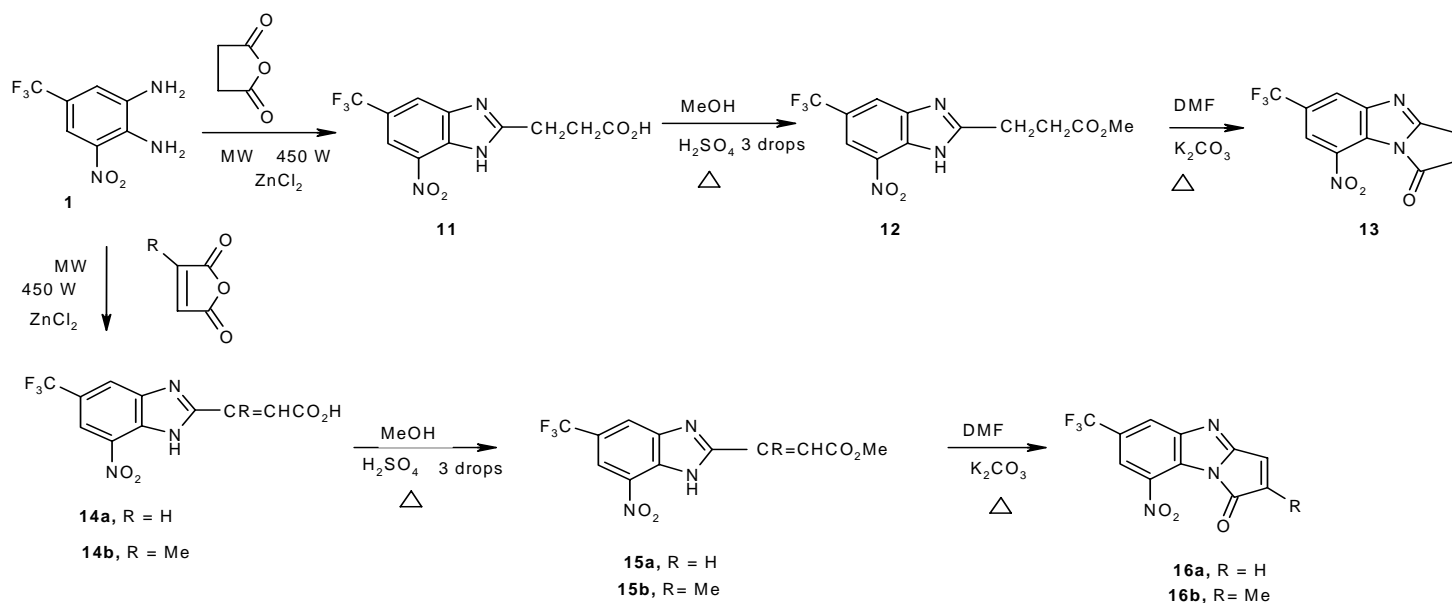
The presence of NH and carboxylic functions in 2-arylbenzimidazoles (**3**) can be conveniently utilized in making tetracyclic systems. 2-Arylbenzimidazole (**3**) on microwave irradiation in presence of catalytic amount of anhydrous zinc chloride at 800 W furnished a new compound. The NMR spectrum showed absence of NH and carboxylic acid proton, indicating the formation of cyclised product, characterized as isoindolobenzimidazole (**4**). The tetracyclic ring system (**4**) is also obtained directly by reacting the diamine (**1**) and phthalic anhydride (**2**) under microwave irradiation at 800 W in presence of zinc chloride. However non-fluorinated isoindolobenzimidazoles are also prepared from diamine and phthalic anhydride in refluxing ethanol<sup>4</sup> (yield 60%), in *n*-amyl alcohol<sup>5</sup> (yield 39%), and in acetic anhydride<sup>6</sup> (yield 29%). The condensation of diamine (**1**) with tricyclic anhydride (**5**) by MW irradiation at 450 W resulted in the corresponding 2-arylbenzimidazole, which on further exposure to 800 W microwave power gave pentacyclic derivative (**7**) (Scheme-1).



Scheme-1

The methodology has been extended to aliphatic anhydrides to make it a general applicability for the synthesis of trifluoromethylated tetracyclic isoindolobenzimidazoles. The diamine is utilized with succinic anhydride admixed with zinc chloride under microwave irradiation furnished 2-alkylbenzimidazoles (**11**). The compound (**11**) did not cyclize further even or prolonged microwave irradiation at 800 W, remained unchanged. In order to get the cyclised compound, the carboxylic function of **11** is esterified to **12**. The ester underwent cyclization in presence of a base to furnish a tricyclic compound (**13**) in good yield. The NMR spectra of **13** showed the characteristic signal for methylenes as triplets and absence of ester methyl group. Based on spectral data it has been characterised as 8-nitro-6-trifluoromethyl-2, 3-dihydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazolyl-1-one (**13**). The reaction of diamine (**1**) with maleic anhydride resulted a regioselective ring open product 2-alkylbenzimidazole (**14**). The amino function of diamine attacked on the more reactive electron deficient carbonyl to yield the product (**14**) by ring opening regioselectively, such a selective reaction is known with an analogous molecule (*S*)-acetoxysuccinic anhydride.<sup>11</sup> The open chain

acid (**14**) is esterified to **15** and further cyclised to result the corresponding tricyclic system (**16**) in good yield (Scheme-2).



In conclusion, the synthesis of polycyclic trifluoromethylbenzimidazoles by a fast, cleaner, efficient and solventless method using microwave irradiation technique is described. The behavior of aliphatic anhydrides is also same but the latter cyclization part is by a chemical method. It involves easy workup and negligible effluent formation during the course of reaction.

## ACKNOWLEDGEMENTS

The authors are thankful to Dr. J. S. Yadav, Director, IICT and Shri. S. Narayan Reddy, Head, Fluoroorganic division, IICT, Hyderabad for their constant encouragement and financial support from industry-sponsored project.

## EXPERIMENTAL

General methods: <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> on Gemini 200 spectrometer, chemical shifts are reported in ppm relative to internal TMS (δ = 0.00 ppm). Melting points were recorded on VMP-AM melting point apparatus and are uncorrected. Elemental analyses were carried out on Elemental Vario EL (Germany) apparatus. IR spectra were recorded on FT-IR Shimadzu Perkin-Elmer 1310 infrared spectrophotometer. Electron Impact (EI) MS spectra were recorded on VG 7070 H ev instrument at 70 ev.

### General procedure for the synthesis of substituted 2-aryl-5-trifluoromethyl-7-nitrobenzimidazoles (**3**).

A mixture of 3-nitro-5-trifluoromethyl-*o*-phenylenediamine (**1**) (0.3 g, 1.3 mmol), aromatic anhydride (**2**) (1.3 mmol) and zinc chloride (17 mg, 0.13 mmol) was adsorbed uniformly on the surface of silica gel (2 g,

100-200 mesh) and irradiated in domestic microwave oven at 450 W in an open tube for 2-4 min. The solid was allowed to cool to rt and confined a silica gel column using *n*-hexane: chloroform (1:1) as eluent to furnish the title compound, in sufficiently pure form.

**2-[7-Nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]benzoic acid (3a)**

Yield 82%; mp 287.9 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3485, 3329, 1645, 1524, 1338, 1290;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 8.00-8.18 (4H, m), 8.36 (1H, s), 8.50 (1H, s), 13.18 (1H, br s); MS *m/z* 351(M<sup>+</sup>), 333, 307, 261; Anal. Calcd for C<sub>15</sub>H<sub>8</sub>N<sub>3</sub>O<sub>4</sub>F<sub>3</sub>: C, 51.29; H, 2.29; N, 11.96. Found: C, 51.24; H, 2.36; N, 12.02.

**2,3,4,5-Tetrachloro-6-[7-nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]benzoic acid (3b)**

Yield 79%; mp 256.7 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3480, 3375, 3083, 1724, 1540, 1292, 1119;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 8.38 (1H, s), 8.64 (1H, s), 13.21(1H, br s); MS *m/z* 489(M<sup>+</sup>), 445, 399; Anal. Calcd for C<sub>15</sub>H<sub>4</sub>N<sub>3</sub>O<sub>4</sub>Cl<sub>4</sub>F<sub>3</sub>: C, 36.84; H, 0.89; N, 8.77. Found: C, 36.89; H, 0.71; N, 8.58.

**2-Nitro-6-[7-nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]benzoic acid (3c)**

Yield 74%; mp 284.7 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3443, 2922, 1539, 1272;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 8.06-8.15 (3H, m), 8.37 (1H, s), 8.60 (1H, s), 13.20 (1H, br s); MS *m/z* 396 (M<sup>+</sup>), 378, 306; Anal. Calcd for C<sub>15</sub>H<sub>7</sub>N<sub>4</sub>O<sub>6</sub>F<sub>3</sub>: C, 45.47; H, 1.78; N, 14.14. Found: C, 45.38; H, 1.72; N, 14.09.

**5-Nitro-2-[7-nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]benzoic acid (3d)**

Yield 77%; mp 282.7 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3455, 2922, 1539, 1272;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 8.22-8.34 (3H, m), 8.42(1H, s), 8.66(1H, s), 13.00 (1H, br s); MS *m/z* 396 (M<sup>+</sup>), 378, 306, 260; Anal. Calcd for C<sub>15</sub>H<sub>7</sub>N<sub>4</sub>O<sub>6</sub>F<sub>3</sub>: C, 45.47; H, 1.78; N, 14.14. Found: C, 45.36; H, 1.70; N, 14.10.

**2-Fluoro-6-[7-nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]benzoic acid (3e)**

Yield 72%; mp 291.9 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3454, 2934, 1602, 1211;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 8.15-8.25 (3H, m) 8.38 (1H, s), 8.60 (1H, s), 13.12 (1H, br s); MS *m/z* = 369 (M<sup>+</sup>), 351,325; Anal. Calcd for C<sub>15</sub>H<sub>7</sub>N<sub>3</sub>O<sub>4</sub>F<sub>4</sub>: C, 48.79; H, 1.91; N, 11.38. Found: C, 48.72; H, 1.89; N, 11.33.

**8-[7-Nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]-1-naphthoic acid (6)**

Yield 78%; mp 274.8 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3384, 1600, 1338, 1290;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 7.80-7.90 (3H, m), 8.00-8.12 (3H, m), 8.38 (1H, s), 8.44 (1H, s), 13.22 (1H, br s); MS *m/z* = 401(M<sup>+</sup>), 383, 357, 312; Anal. Calcd for C<sub>19</sub>H<sub>10</sub>N<sub>3</sub>O<sub>4</sub>F<sub>3</sub>: C, 56.86; H, 2.51; N, 10.47. Found: C, 56.83; H, 2.48; N, 10.40.

**General procedure for the synthesis of substituted 11*H*-Isoindolo[2,1-*a*]benzimidazol-11-one (4)**

**Procedure-A:** A mixture of diamine (**1**) (0.3 g, 1.3 mmol), aromatic anhydride (**2**) (1.3 mmol) and zinc chloride (17 mg, 0.13 mmol) was adsorbed on silica gel (2 g, 100-200 mesh) and subjected to microwave irradiation in an open tube at 800 W for 2-4 min. Passing through a silica gel column using *n*-hexane: chloroform (3:1) as eluent furnished the title compound (**4**).

**Procedure-B:** The compound (**3**) (0.5 mmol), zinc chloride (40 mg, 0.3 mmol) and catalytic amount of acetic acid (2 drops) was adsorbed on silica gel (2 g, 100-200 mesh) and subjected to microwave irradiation

at 800 W for 1-2 min. The solid was passed through a silica gel column using *n*-hexane: chloroform (3:1) as eluent to afford the title compound (**4**).

**9-Nitro-7-trifluoromethyl-11H-benzo[4,5]imidazo[2,1-*a*]isoindol-11-one (4a)**

Yield 80%; mp 184.5 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  1645, 1600, 1524, 1338;  $\delta_{\text{H}}(\text{CDCl}_3)$  7.95-8.10 (3H, m), 8.42 (1H, s), 8.58 (1H, s); MS  $m/z$  333( $\text{M}^+$ ), 307; Anal. Calcd for  $\text{C}_{15}\text{H}_6\text{N}_3\text{O}_3\text{F}_3$ : C, 54.06; H, 1.81; N, 12.61. Found: C, 54.00; H, 1.78; N, 12.58.

**1,2,3,4-Tetrachloro-9-nitro-7-trifluoromethyl-11H-benzo[4,5]imidazo[2,1-*a*]isoindol-11-one (4b)**

Yield 68%; mp 234.6 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  1648, 1602, 1555, 1291;  $\delta_{\text{H}}(\text{CDCl}_3)$  8.53 (1H, s), 8.66 (1H, s); MS  $m/z$  = 471( $\text{M}^+$ ), 425; Anal. Calcd for  $\text{C}_{15}\text{H}_2\text{N}_3\text{O}_3\text{Cl}_4\text{F}_3$ : C, 38.25; H, 0.42; N, 8.92. Found: C, 38.16; H, 0.47; N, 8.98.

**1,9-Dinitro-7-trifluoromethyl-11H-benzo[4,5]imidazo[2,1-*a*]isoindol-11-one (4c)**

Yield 75%; mp 269.5 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  1654, 1600, 1553, 1299;  $\delta_{\text{H}}(\text{CDCl}_3)$  8.10-8.18 (3H, m), 8.38 (1H, s), 8.42 (1H, s); MS:  $m/z$  378( $\text{M}^+$ ), 332, 286; Anal. Calcd for  $\text{C}_{15}\text{H}_5\text{N}_4\text{O}_5\text{F}_3$ : C, 47.63; H, 1.33; N, 14.81. Found: C, 47.58; H, 1.38; N, 14.72.

**2,9-Dinitro-7-trifluoromethyl-11H-benzo[4,5]imidazo[2,1-*a*]isoindol-11-one (4d)**

Yield 76%; mp 268.0 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  1655, 1600, 1555, 1291;  $\delta_{\text{H}}(\text{CDCl}_3)$  8.35-8.50 (3H, m), 8.58 (1H, s), 8.66 (1H, s); MS  $m/z$  = 378( $\text{M}^+$ ), 332, 286; Anal. Calcd for  $\text{C}_{15}\text{H}_5\text{N}_4\text{O}_5\text{F}_3$ : C, 47.63; H, 1.33; N, 14.81. Found: C, 47.59; H, 1.34; N, 14.76.

**1-Fluoro-9-nitro-7-trifluoromethyl-11H-benzo[4,5]imidazo[2,1-*a*]isoindol-11-one (4e)**

Yield 71%; mp 252.4 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  1678, 1599, 1299;  $\delta_{\text{H}}(\text{CDCl}_3)$  7.98-8.20 (3H, m), 8.44 (1H, s), 8.58 (1H, s); MS  $m/z$  = 351( $\text{M}^+$ ), 305, 282; Anal. Calcd for  $\text{C}_{15}\text{H}_5\text{N}_3\text{O}_3\text{F}_4$ : C, 51.29; H, 1.43; N, 11.96. Found: C, 51.28; H, 1.52; N, 11.89.

**9-Nitro-11-trifluoromethyl-7H-benzo[*de*]benzo[4,5]imidazo[2,1-*a*]isoquinolin-7-one (7)**

Yield 72%; mp 298 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  1689, 1602, 1599, 1542, 1299;  $\delta_{\text{H}}(\text{CDCl}_3)$  8.15-8.35 (6H, m), 8.42 (1H, s), 8.66 (1H, s); MS:  $m/z$  383( $\text{M}^+$ ), 338, 259; Anal. Calcd for  $\text{C}_{19}\text{H}_8\text{N}_3\text{O}_3\text{F}_3$ : C, 59.53; H, 2.10; N, 10.96. Found: C, 59.48; H, 2.01; N, 10.89.

**1-Ethyl-2-substituted phenyl-5-trifluoromethyl-7-nitrobenzimidazole (8)**

**Procedure-A:** The compound (**10**) (0.35 g, 1.43 mmol), phthalic anhydride (**2a**) (207 mg, 1.4 mmol) and zinc chloride (19 mg, 0.14 mmol) were adsorbed on silica gel (2 g, 100-200 mesh) and exposed to microwave irradiation at 450 W for 2 min. The solid was purified by passing through a silica gel column using *n*-hexane: chloroform (1:1) as eluent afforded the title compound. (362 mg, Yield = 68%).

**Procedure-B:** To a solution of compound (**3a**) (0.5 g, 1.4 mmol) in dry dimethylformamide (4 mL), potassium carbonate (0.58 g, 4.2 mmol) and ethyl iodide (1.1 g, 7.1 mmol) were added and the mixture was heated at 75-80 °C for 15 h. The progress of the reaction monitored by TLC. The solvent was recovered under reduced pressure and the residue was treated with crushed ice. The separated solid was filtered, dried and

purified by silica gel column chromatography using *n*-hexane: chloroform (1:1) as eluent gave the title compound. (329 mg, Yield = 61%)

**2-[1-Ethyl-7-nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]benzoic acid (8)**

mp 244.9 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3489, 3000, 1594, 1548, 1334, 1299;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 1.44-1.48 (3H, t, J= 9 Hz), 4.14-4.16 (2H, q, J= 9 Hz), 7.82-7.95 (4H, m), 8.28 (1H, s), 8.32 (1H, s); MS *m/z* 379 (M<sup>+</sup>), 350, 333; Anal. Calcd for C<sub>17</sub>H<sub>12</sub>N<sub>3</sub>O<sub>4</sub>F<sub>3</sub>: C, 53.83; H, 3.18; N, 11.07. Found: C, 53.73; H, 3.10; N, 11.17.

**General procedure for the preparation of 1*H*-benzo[*d*]pyrrolo[1,2-*a*]imidazolyl-1-ones.**

**Preparation of 3-[7-Nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]propanoic acid (11) and (14).**

A mixture of diamine (**1**) (1.3 mmol), aliphatic anhydride (1.3 mmol) and zinc chloride (17 mg, 0.13 mmol) adsorbed on silica gel (2 g, 100-200 mesh) and subjected to microwave irradiation in an open tube at 450 W for 1-2 min. The reaction mixture was purified by passing through a silica gel column using *n*-hexane:chloroform (1:1) as eluent to afford the title compounds (**11**) and (**14**).

**3-[7-Nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]propanoic acid (11)**

Yield 84%; mp 202.9 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3485, 3373, 3095, 1713, 1540, 1300;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 2.72-2.78 (2H, t, J = 9 Hz), 2.82-2.88 (2H, t, J= 9 Hz), 8.09 (1H, s), 8.29 (1H, s), 13.24 (1H, s); MS *m/z* 303 (M<sup>+</sup>), 258,74; Anal. Calcd for C<sub>11</sub>H<sub>8</sub>N<sub>3</sub>O<sub>4</sub>F<sub>3</sub>: C, 43.58; H, 2.66; N, 13.86. Found: C, 42.73; H, 2.10; N, 12.17.

**3-[7-Nnitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]propenoic acid (14a)**

Yield 82%; mp 229.4 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3482, 3371, 3103, 2924, 1717, 1539, 1345;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 5.96 (1H, d, J = 7 Hz), 7.27 (1H, d, J = 7 Hz), 8.34 (1H, s), 8.39 (1H, s), 13.22 (1H, s); MS *m/z* 301 (M<sup>+</sup>), 257,211; Anal. Calcd for C<sub>11</sub>H<sub>6</sub>N<sub>3</sub>O<sub>4</sub>F<sub>3</sub>: C, 43.87; H, 2.01; N, 13.95. Found: C, 42.73; H, 2.10; N, 13.17.

**2-Methyl-3-[7-nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]propenoic acid (14b)**

Yield 79%; mp 279.4 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3471, 3359, 3104, 1716, 1639, 1344, 1118;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 1.95 (3H, s), 7.70 (1H, s), 8.37 (1H, s), 8.40 (1H, s), 13.20 (1H, s); MS *m/z* 315 (M<sup>+</sup>), 270,224; Anal. Calcd for C<sub>12</sub>H<sub>8</sub>N<sub>3</sub>O<sub>4</sub>F<sub>3</sub>: C, 45.73; H, 2.56; N, 13.33. Found: C, 44.73; H, 2.39; N, 13.17.

**Preparation of Methyl 3-[7-nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]propanoate (12) and (15).** The acid compound (**11**) (484 mg, 1.6 mmol) was dissolved in methanol (5 mL) and 3, 4 drops of sulfuric acid was added. Then mixture was refluxed for 6 h. After completion of reaction, the solvent was removed under reduced pressure and the residue was treated with crushed ice. The separated solid was filtered, dried and purified by silica gel column chromatography using *n*-hexane: chloroform (1:1) as eluent gave the title compounds (**12**) and (**15**).

**Methyl 3-[7-nitro-5-trifluoromethyl-1*H*-benzo[*d*]imidazol-2-yl]propanoate (12)**

Yield 68%; mp 245.7 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$ : 3385, 1695, 1684, 1600, 1540, 1345;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 2.62-2.68 (2H, t, J= 10 Hz), 3.00-3.10 (2H, t, J= 10 Hz), 3.58 (3H, s), 8.28(1H, s), 8.31(1H, s) 13.2 (1H, br s); MS *m/z* 303 (M<sup>+</sup>), 258,74; Anal. Calcd for C<sub>12</sub>H<sub>10</sub>N<sub>3</sub>O<sub>4</sub>F<sub>3</sub>: C, 43.58; H, 2.66; N, 13.86. Found: C, 42.79; H, 2.11; N, 12.19.

**Methyl-3-[7-nitro-5-trifluoromethyl-1H-benzo[d]imidazol-2-yl]propenoate (15a)**

Yield 65%; mp 279.7 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$ : 3371, 3103, 2924, 1690, 1639, 1539;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 3.63 (3H, s), 5.98 (1H, d, J= 7 Hz), 7.17(1H, d, J= 7 Hz), 8.37(1H, s), 8.58(1H, s) 10.09 (1H, br s); MS m/z 315 (M<sup>+</sup>), 300, 271, 269; Anal. Calcd for C<sub>12</sub>H<sub>8</sub>N<sub>3</sub>O<sub>4</sub>F<sub>3</sub>: C, 45.73; H, 2.56; N, 13.33. Found: C, 44.79; H, 2.41; N, 12.19.

**Methyl 2-methyl-3-[7-nitro-5-trifluoromethyl-1H-benzo[d]imidazol-2-yl]propenoate (15b)**

Yield 68%; mp 289.7 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3359, 1689, 1540, 1344, 1244;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 1.89 (3H, s), 3.73 (3H, s), 7.49 (1H, s), 8.37(1H, s), 8.59(1H, s) 10.9 (1H, br s); MS m/z 329 (M<sup>+</sup>), 297,283; Anal. Calcd for C<sub>13</sub>H<sub>10</sub>N<sub>3</sub>O<sub>4</sub>F<sub>3</sub>: C, 47.43; H, 3.06; N, 12.76. Found: C, 48.79; H, 3.21; N, 12.19.

**Preparation of 8-nitro-6-trifluoromethyl-2,3-dihydro-1H-benzo[d]pyrrolo[1,2-a]imidazolyl-1-one (13) and (16).** The ester compound (12) (317 mg, 1.0 mmol) was dissolved in DMF (5 mL) and potassium carbonate (414 mg, 3.0 mmol) was added. The mixture was heated at 100 °C for 4-5 h. After completion of reaction, the solvent was removed under reduced pressure and the residue was treated with water. The separated solid was filtered, dried and purified by silica gel column chromatography using *n*-hexane:chloroform (3:1) as eluent furnished the title compounds (13) and (16).

**8-Nitro-6-trifluoromethyl-2,3-dihydro-1H-benzo[d]pyrrolo[1,2-a]imidazolyl-1-one (13)**

Yield 72%; mp 210.7 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  3091, 1692, 1548, 1332, 1099;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 2.83-2.91 (2H, t, J= 10 Hz), 3.02-3.10 (2H, t, J= 10 Hz), 8.39(1H, s), 8.57(1H, s); MS m/z 285 (M<sup>+</sup>), 239; Anal. Calcd for C<sub>11</sub>H<sub>6</sub>N<sub>3</sub>O<sub>3</sub>F<sub>3</sub>: C, 46.33; H, 2.12; N, 14.73. Found: C, 45.79; H, 2.11; N, 13.19.

**8-Nitro-6-trifluoromethyl-1H-benzo[d]pyrrolo[1,2-a]imidazolyl-1-one (16a)**

Yield 68%; mp 194.7 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  1690, 1539, 1345, 1126;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 6.83 (1H, d, J= 7 Hz), 8.59(1H, s), 8.62 (1H, s), 8.98(1H, d, J= 7Hz); MS m/z 283 (M<sup>+</sup>), 237; Anal. Calcd for C<sub>11</sub>H<sub>4</sub>N<sub>3</sub>O<sub>3</sub>F<sub>3</sub>: C, 46.66; H, 1.42; N, 14.84. Found: C, 45.79; H, 1.21; N, 13.19.

**2-Methyl-8-nitro-6-trifluoromethyl-1H-benzo[d]pyrrolo[1,2-a]imidazolyl-1-one (16b)**

Yield 68%; mp 194.7 °C (chloroform);  $\nu_{\max}/\text{cm}^{-1}$  1692, 1639, 1539, 1345,1298, 1167, 1118;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 2.21 (3H, s), 8.60(1H, s), 8.63 (1H, s), 8.74(1H, s); MS m/z 297 (M<sup>+</sup>), 282,251; Anal. Calcd for C<sub>12</sub>H<sub>6</sub>N<sub>3</sub>O<sub>3</sub>F<sub>3</sub>: C, 48.50; H, 2.03; N, 14.14. Found: C, 47.79; H, 2.21; N, 13.29.

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