

Short Note

## ***N*-(2-Chloro-5-cyanophenyl)-4,4,4-trifluorobutanamide**

**Karikere Ekanna Manojkumar<sup>1</sup>, Swamy Sreenivasa<sup>1,\*</sup>, Govindaiah Shivaraja<sup>1</sup> and Tadimety Madhu Chakrapani Rao<sup>2</sup>**

<sup>1</sup> Center for Advanced Materials, Department of Chemistry, Tumkur University, Tumkur-572103, India

<sup>2</sup> Tadimety Aromatics Pvt. Ltd, Hirehalli Industrial Area, Tumkur-572168, India

\* Author to whom correspondence should be addressed; E-Mail: drsreenivasa@yahoo.co.in.

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**Abstract:** *N*-(2-Chloro-5-cyanophenyl)-4,4,4-trifluorobutanamide (**3**) was synthesized by reacting 4,4,4-trifluorobutanoic acid (**1**) with 2-amino-4-chlorobenzonitrile (**2**) in the presence of triethylamine and propylphosphonic anhydride in ethyl acetate. Characterization of the compound was done by IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, LC-MS and CHN analysis.

**Keywords:** *N*-(2-chloro-5-cyanophenyl)-4,4,4-trifluorobutanamide; propylphosphonic anhydride; 4,4,4-trifluorobutanoic acid; 2-amino-4-chlorobenzonitrile.

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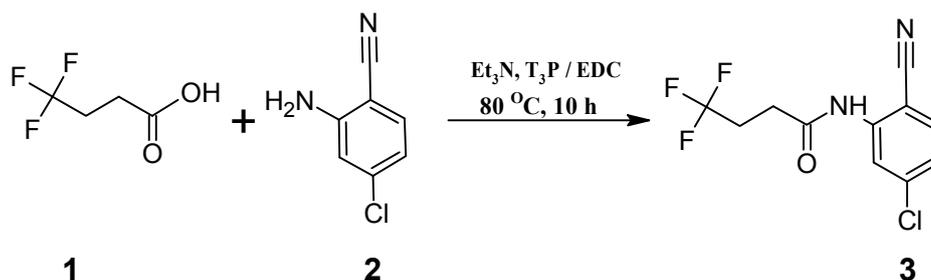
In the past decades, because of their wide variety of pharmacological applications, amides have been considered as important pharmacophores. Amides bearing a trifluoromethyl substituent show a broad spectrum of pharmacological properties, including antitumour [1], anti-inflammatory [2], antioxidant [3], analgesic [4] and antiviral activity [5]. It was also reported that substituted amides show higher anticonvulsive [6], hypoglycemic [7], antiarrhythmic [8] and fungicidal activity [9]. Encouraged by these reports, we have synthesised a new compound, *N*-(2-chloro-5-cyanophenyl)-4,4,4-trifluorobutanamide (**3**) by coupling 2-amino-4-chlorobenzonitrile with trifluorobutanoic acid, and it was fully characterized.

### **Experimental**

All reagents were purchased from commercial sources and used without further purification. The melting point was determined in a one-end open capillary tube on a liquid paraffin bath and it is not corrected. The reaction was carried out under an inert nitrogen atmosphere. Mass spectra, <sup>1</sup>H-NMR

and  $^{13}\text{C}$ -NMR spectra were recorded for the compound on an Agilent Mass spectrometer and on a Bruker Avance II (399.65 MHz for  $^1\text{H}$ -NMR, 100.50 MHz for  $^{13}\text{C}$ -NMR) instrument, respectively. Chemical shifts are reported in parts per million (ppm) using tetramethylsilane (TMS) as an internal standard. Elemental (C, H and N) analysis was performed on an Elementar vario MICRO cube. The purity of the compound was confirmed using TLC on precoated silica gel plates and further purification was done using column chromatography.

**Scheme 1.** Synthetic route for the title compound, *N*-(2-chloro-5-cyanophenyl)-4,4,4-trifluorobutanamide (**3**).



#### Synthesis of *N*-(2-Chloro-5-cyanophenyl)-4,4,4-trifluorobutanamide (**3**)

2-Amino-4-chlorobenzonitrile (**2**) (1.00 g, 6.5 mmol) was dissolved in dry ethylene dichloride (10 mL) and cooled to  $0\text{ }^\circ\text{C}$ . To this solution, triethylamine (1.99 g, 19.0 mmol), 4,4,4-trifluorobutanoic acid (**1**) (1.12 g, 7.8 mmol) and propylphosphonic anhydride (T3P®) (6.04 g, 19.0 mmol) were added and the solution was stirred for 10 h at  $80\text{ }^\circ\text{C}$  with TLC monitoring. Then, the reaction mixture was quenched by addition of ice-cold water. The organic layer was separated, washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The crude compound was purified by column chromatography, using petroleum ether/ethyl acetate (7:3) as eluent to give the title compound (**3**) as a colorless solid with  $R_f = 0.79$ .

Yield: 1.63 g (90%).

Melting point:  $151\text{--}153\text{ }^\circ\text{C}$ .

MS:  $m/z = 277.64$  ( $\text{M}^+ + 1$ ).

IR:  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3340 (N-H), 2228 (CN), 1698 (CO), 1342–1140 ( $\text{CF}_3$  stretching).

$^1\text{H}$ -NMR (DMSO- $d_6$ )  $\delta$ : 10.47 (s, 1H, NH), 7.88 (d,  $J = 8.7$  Hz, 1H, Ar-H), 7.80 (d,  $J = 1.9$  Hz, 1H, Ar-H), 7.45 (dd,  $J = 8.3$  Hz and  $J = 1.5$  Hz, 1H, Ar-H), 2.74 (t,  $J = 7.5$  Hz, 2H,  $\text{COCH}_2$ ), 2.67–2.55 (m, 2H,  $\text{CF}_3\text{CH}_2$ ).

$^{13}\text{C}$ -NMR (DMSO- $d_6$ )  $\delta$ : 169.3, 141.2, 138.3, 134.8, 128.7  $\text{CF}_3$ , 125.9, 124.6, 115.9, 104.9, 28.7, 27.8.

Elemental analysis: Calculated for  $\text{C}_{11}\text{H}_8\text{ClF}_3\text{N}_2\text{O}$ : C, 47.76%; H, 2.91%; N, 10.13%. Found: C, 47.79%; H, 2.96%; N, 10.19%.

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