Short Note

3-(3,5-difluorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde

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Abstract: Vilsmeier–Haack reaction of (*E*)-1-(1-(3,5-difluorophenyl)ethylidene)-2-phenylhydrazine (**1**) using dimethyl formamide in excess of phosphorous oxychloride by conventional method, resulted in the synthesis of title compound 3-(3,5-difluorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (**2**) in good yield and high purity. Structure characterization of the novel title compound was done by IR, ^{1}H NMR, ^{13}C NMR and mass spectral analysis.

Keywords: Vilsmeier–Haack; pyrazole; carbaldehyde

1. Introduction

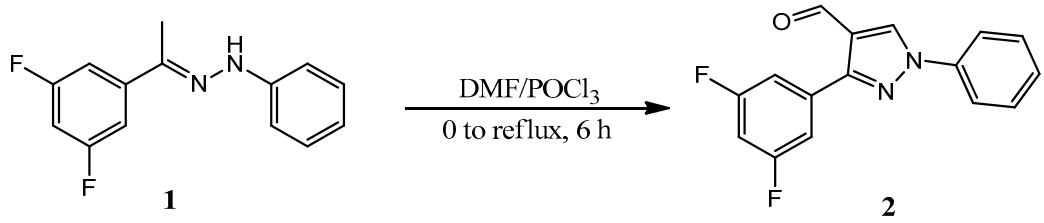
Pyrazoles are very promising motif for medicinal chemists due to their vast pharmacological applications. Several naturally available pyrazole ring containing compounds such as Pyrazomycin, Celecoxib and Derecoxibare found to possess good antitumor activity [1]. Known drugs with pyrazole scaffold such as Antipyrine, Phenylbutazone and Difenamizoleare marketed as analgesic, antipyretic and anti-inflammatory drugs respectively. One of the best methods for the synthesis of pyrazole ring is by cyclization of Schiff's base with suitable reagents [2]. Schiff's bases are known precursor for synthetic modifications and also form a major constituent of the natural products [3]. Pyrazole ring in combination with carbonyl functional group are known to have selective anti-inflammatory, antiviral and antimicrobial activities [4-6]. Presence of double bond in conjugation with carbonyl functionality is reported to be responsible for the biological activities of pyrazole derivatives. Removal of this functionality makes them pharmacologically inactive [7]. A number of synthetic routes have been reported for synthesis of pyrazole derivatives [8-9]. Synthesis of4-formyl pyrazoles using formylation reaction condition (Vilsmeier–Haack reaction) is a most productive and convenient path for the synthesis of heterocycle aldehydes [2].Considering these aspects we have synthesized and characterized 3-(3,5-difluorophenyl)-1-phenyl-1*H*-pyrazole -4-carbaldehyde **(2)** as shown in the **Scheme 1**.

2. Experimental

2.1. Materials and Metods

All the chemicals used were acquired from commercial sources and were of analytical grade. Melting point (m.p) was determined using open capillary tube. IR absorption spectra were obtained in the range 4000–400 cm^{-1} on Shimadzu IR Affinity-1. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance III at 400 and 100 MHz with internal standard tetramethylsilane and chemical shifts were expressed in parts per million (ppm), respectively. Mass was recorded on Water, synapt

G2 high detection mass spectrometry. Reaction completion was monitored by Thin Layer Chromatography using precoated silica 60 F254 aluminum plates and purifications were done by recrystallization.



Scheme 1

2.2. Synthesis of 3-(3,5diflourophenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde **(2)**

The title compund 3-(3,5-difluorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde **(2)** was synthesied according to the reported procedure [2]. One equivalent of (*E*)-1-(1-(3,5-difluorophenyl) ethylidene)-2-phenylhydrazine **(2)** was dissolved in five equivalance of dimethyl formamide (DMF) and the mixture was cooled bellow 0 ^{o}C under stirring. To this cold reaction mixture ten equivalance of phosphorous oxychloride ($POCl_3$) was added drop wise for period of half an hour. Reaction mixture was allowed to attain room temperature and was further refluxed of 6 hours. After completion of the reaction which was confirmed by Thin Layer Chromatograpy, reaction mixture was pourd on to ice pices with vigrous stirring and allowed to stand overnight. Crude compund obtained was filtered, washed with excess of cold water and dried. Pure compound 3-(3,5diflourophenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde **(2)** was obtined after recrystaliztion using aqueous ethanol.

3. Result and Discussion

Molecular Formula $C_{16}H_{10}F_2N_2O$; Yield: 90 %; Melting Point: 142-145 ^{o}C; Mass m/z (%) Obtained (Calculated) 285.08 (M^{+1}) (284.26); FT-IR (KBr) cm^{-1}, 3119.3 (aromatic stretching), 2990.7 (C-H stretching), 1682.0 (C=O stretching), 1626.1 (C=N stretching), 1527.9 (C=C stretching), 1116.3 (C-F stretching); ^{1}H NMR (δ, ppm, 400 MHz, DMSO) 7.41-7.37 (1H, *J* = 9.2, t, ArH), 7.48-7.44 (1H, *J* = 7.2, t, ArH), 7.61-7.57 (2H, *J* = 7.8, t, ArH), 7.80-7.78 (2H, *J* = 7.2, d, ArH), 7.8-8.0 (2H, *J* = 8.0 Hz, d, ArH), 9.43 (1H, s, pyrazole,), 9.99 (1H, s, -CHO); ^{13}C NMR (δ, ppm, 100 MHz, DMSO) 183, 164, 163, 138, 136, 129, 123, 111, 109, 104.

Acknowledgments:

The authors are thankful to SDM College, Ujjire for providing facility to carry out the research work. We also thank Tumkur University for giving me the opportunity to do research work. Also we acknowledge the Manipal University and Mysore University for their support in acquiring spectral data.

Conflicts of Interest: The authors declare no conflict of interest.

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