

Article

Synthesis of Novel 1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-aryl-1*H*-pyrazole-4-carbaldehydes

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Abstract: A series of novel 1-[(2,6-dichloro-4-trifluoromethyl)phenyl]-3-aryl-1*H*-pyrazole-4-carbaldehydes **6a-i** were synthesized using the Vilsmeier-Haack reagent. The structures of all the title compounds have been confirmed by elemental analysis, ¹H-NMR and ¹³C-NMR and in addition, the structure of intermediate **5b** was investigated by X-ray crystallography.

Keywords: Vilsmeier-Haack reagent; phenylhydrazine; phenylhydrazone; 1*H*-pyrazole-4-carbaldehyde

1. Introduction

The application of the Vilsmeier-Haack (VH) reagent (POCl₃/DMF) for formylation of a variety of both aromatic and heteroaromatic substrates is well documented [1]. Besides this, the reagent has also been extensively used for effecting various chemical transformations with other classes of compounds. Many of these reactions have led to novel and convenient routes for the synthesis of various heterocyclic compounds [2]. A notable example that finds significant application in heterocyclic

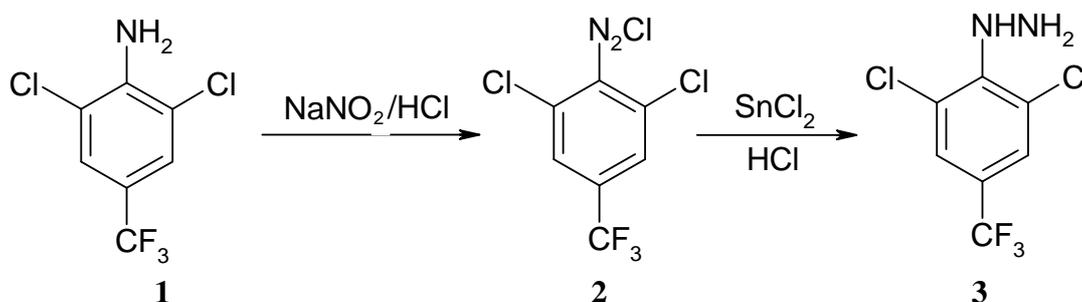
chemistry is the synthesis of 4-formylpyrazoles from the double formylation of hydrazones with the VH reagent [3,4]. These observations, coupled with the recent developments in the simple synthesis of pyrazole derivatives [5], especially 4-functionalized 1,3-diphenylpyrazoles as antibacterial [6], anti-inflammatory [7], antiparasitic [8], and antidiabetic drugs [9], prompted us to undertake the synthesis of pyrazole-4-carbaldehyde derivatives using the VH reagent.

It has been known for some time that fluorine atoms can lead to unexpected biological activity results due to the special properties of the fluorine atom, such as the high electronegativity of fluorine and the high carbon-fluorine bond energy [10]. As a consequence, trifluoromethyl-containing molecules have been found considerable utilization in the agrochemical and pharmaceutical industries [10–12], for example, pyrazole derivatives bearing trifluoromethyl groups, such as fipronil and analogs [13,14] are widely used phenylpyrazole insecticides applied in granular or bait form for residential and commercial control of turf grass pests, and celecoxib [15], widely prescribed to treat acute or chronic inflammation by providing symptomatic pain relief, are examples of such compounds. In this paper, we show a simple and efficient synthetic method using the VH reagent [4,16,17] that affords a series of novel 1-[(2,6-dichloro-4-trifluoromethyl)phenyl]-3-aryl-1*H*-pyrazole-4-carbaldehydes.

2. Results and Discussion

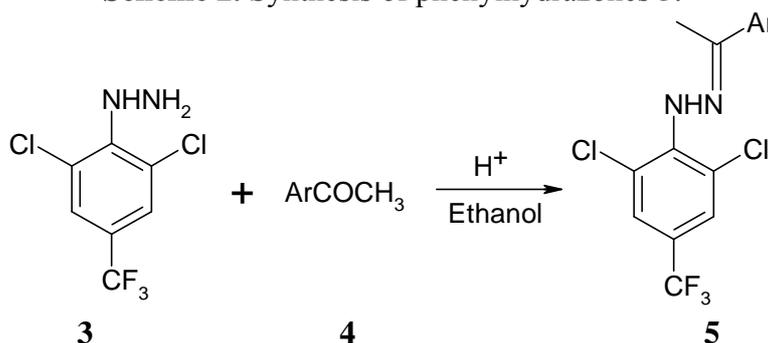
Phenylhydrazine **3** was synthesized from 2,6-dichloro-4-trifluoromethylphenylamine (**1**) through diazotization, reduction and hydration (Scheme 1). The reducing reagent plays an important role in the reaction. When the intermediate **2** was reduced by SnCl₂, an almost quantitative yield of product was obtained. Use of Na₂S₂O₃ or Zn as reducing reagents led to lower yields.

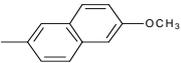
Scheme 1. Synthesis of phenylhydrazine **3**.



Phenylhydrazones **5** were next synthesized in almost quantitative yields by the reaction between the phenylhydrazine **3** and 3 or 4-substituted aryl methyl ketones, regardless of whether the ketones contained electron-withdrawing or electron-donating groups (Scheme 2).

Scheme 2. Synthesis of phenylhydrazones 5.



5a: Ar=C₆H₅; **5b:** Ar =4-ClC₆H₄; **5c:** Ar =3-ClC₆H₄; **5d:** Ar =4-BrC₆H₄;
5e: Ar =3-BrC₆H₄; **5f:** Ar =4-MeOC₆H₄; **5g:** Ar =4-CF₃C₆H₄; **5h:** Ar =4-NO₂C₆H₄;
5i: Ar = 

X-ray diffraction

To verify the structural assignment compound **5b** was selected as an example for an X-ray diffraction study (Figure 1 and Table 1). The purified product **5b** was dissolved in 50 % ethanol/acetone (1:1 v/v) and kept at room temperature for 5 days and single crystals of **5b** were thus formed. CCDC 685556 contains the supplementary crystallographic data for this compound [18].

Figure 1. ORTEP drawing of the compound **5b** showing the atom numbering scheme.

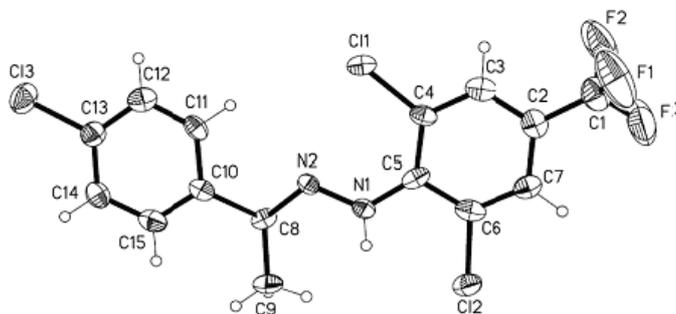


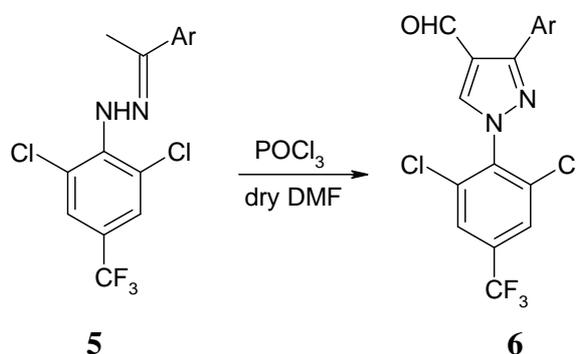
Table 1. Crystal data and summary of data collection and structure refinement.

Compound	C ₁₅ H ₁₀ Cl ₃ F ₃ N ₂
Color	Colorless
Formula weight	381.60
Crystal system	Monoclinic
Temperature, °	25(298K)
Cell constants	
a (Å)	16.8770(7)
b (Å)	8.0054(8)
c (Å)	24.119(2)
α (°)	90
β (°)	99.654(2)
γ (°)	90
Volume (Å ³)	3212.5(4)
Formula units	8
Calculated density (g/cm ³)	1.578

Table 1. Cont.

F(000)	1536
Absorption coefficient, μm^{-3}	0.599
Limiting indices	$-20 \leq h \leq 16, -7 \leq k \leq 9, -27 \leq l \leq 28$
Reflections collected / unique	8110 / 2841 [R(int) = 0.0402]
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9370 and 0.8314
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2841 / 0 / 208
Goodness-of-fit on F^2	1.015
Final R indices	$R_1 = 0.1641, wR_2 = 0.5152$
Largest diff. peak and hole ($e \text{ \AA}^{-3}$)	0.869 and -0.919

The Vilsmeier cyclization of hydrazones could provide an efficient route for the preparation of 1*H*-pyrazole-4-carbaldehydes. The reaction was carried out at 80–90 °C for 4 h using 3 equiv. of the VH reagent, affording a series of novel 1-[(2,6-dichloro-4-trifluoromethyl)phenyl]-3-aryl-1*H*-pyrazole-4-carbaldehydes in good yields (Scheme 3). The results are shown in Table 2. 1*H*-Pyrazole-4-carbaldehydes **6** cannot be obtained if the DMF used is not anhydrous.

Scheme 3. Synthesis of 1*H*-pyrazole-4-carbaldehydes **6**.**Table 2.** Synthesis of 1*H*-pyrazole-4-carbaldehydes.

Entry	Ar	Products(6)	Yield(%) ^a
1	C ₆ H ₅	6a	89
2	4-ClC ₆ H ₄	6b	88
3	3-ClC ₆ H ₄	6c	83
4	4-BrC ₆ H ₄	6d	86
5	3-BrC ₆ H ₄	6e	82
6	4-MeOC ₆ H ₄	6f	83
7	4-CF ₃ C ₆ H ₄	6g	86
8	4-NO ₂ C ₆ H ₄	6h	85
9		6i	81

^a Isolated yields with regard to the quantity of hydrazones **5**

3. Experimental

3.1. General

All melting points were determined on an XT-4A apparatus and are uncorrected. TLC was performed using precoated silica gel GF₂₅₄ (0.25mm), column chromatography was performed using silica gel (200–300 mesh). The ¹H- and ¹³C-NMR spectra were measured at 25 °C at 300 and 75 MHz, respectively, on a Bruker Advance 300 spectrometer, using TMS as internal standard. *J*-values are given in Hz. The IR spectra were taken on a Bruker Vector 55 spectrometer. Elemental analyses were carried out with an EA 1112 elemental analyzer. All the reagents used were AR grade.

3.2. Synthesis of (2,6-Dichloro-4-trifluoromethyl)phenylhydrazine (**3**)

2,6-Dichloro-4-trifluoromethylphenylamine (**1**, 1.73 g, 7.5 mmol) was dissolved in concentrated HCl (10 mL) and water (10 mL) and cooled to 0 °C, sodium nitrite (0.62 g, 9.0 mmol) was added and the yellow solution was stirred at 0 °C for 2 h to get a solution of diazotized compound **2**. SnCl₂ (2.85 g, 15 mmol) was dissolved in concentrated HCl (10 mL) and cooled to 7 °C, then the diazotized solution of **2** was added slowly dropwise. After 1 h of reaction, the precipitate was filtered, washed with water and air-dried. The precipitate was neutralized by 25% NaOH in water to pH 8, the light yellow sediment was collected and air-dried to afford a brown solid **3** (1.53 g, 83%), m.p. 65–67 °C. ¹H-NMR (CDCl₃) δ: 7.52 (s, 2H, Ar-H), 5.85 (s, 1H, NH), 3.86 (br, 2H, NH₂); ¹³C-NMR (CDCl₃) δ: 137.1, 132.5 (q, *J* = 33.8 Hz), 130.3, 123.8, 122.3 (q, *J* = 271.8 Hz); IR (KBr) v: 3517, 3418, 1622, 1583, 1492, 1329, 1281, 1144, 883 cm⁻¹.

3.3. General procedure for synthesis of *N*-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-(1-phenylethylidene)hydrazines **5a-i**

To a solution of compound **3** (12 mmol) in absolute C₂H₅OH (30 mL) was added substituted acetophenone **4** (10 mmol). Two drops of concentrated HCl were added to a stirred solution, and the mixture was refluxed for 1 h. The solid obtained on cooling was filtered, dried and recrystallized from C₂H₅OH to give compounds **5a-i**.

N-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-(1-phenylethylidene)hydrazine (**5a**): White solid, m.p. 90–91 °C; ¹H-NMR (CDCl₃) δ: 7.82 (d, *J* = 3.6 Hz, 2H, *N'*-Ar-H), 7.67 (s, 1H, NH), 7.58 (s, 2H, N-Ar-H), 7.34–7.42 (m, 3H, *N'*-Ar-H), 2.35 (s, 3H, CH₃); ¹³C-NMR (CDCl₃) δ: 147.2, 140.8, 136.1, 132.5 (q, *J* = 33.8 Hz), 127.3, 126.8, 126.0, 125.8, 123.8, 122.3 (q, *J* = 271.8 Hz), 11.7; IR (KBr) v: 3350, 3072, 2927, 1603, 1538, 1492, 1390, 1351, 1311, 1114, 1009, 887 cm⁻¹.

N-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-[1-(4-chlorophenyl)ethylidene]hydrazine (**5b**): White solid, m.p. 118–120 °C; ¹H-NMR (CDCl₃) δ: 7.68–7.76 (m, 3H, *N'*-Ar-H and NH), 7.58 (s, 2H, N-Ar-H), 7.34–7.37 (m, 2H, *N'*-Ar-H), 2.33 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ: 146.1, 140.7, 136.3, 134.5 (q, *J* = 33.5 Hz), 128.3, 126.7, 126.2, 126.0, 123.9, 121.8 (q, *J* = 271.8 Hz), 11.8; IR (KBr) v: 3360, 3070, 2924, 1605, 1532, 1490, 1392, 1352, 1303, 1114, 1004, 884 cm⁻¹.

N-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-[1-(3-chlorophenyl)ethylidene]hydrazine (**5c**): White solid, m.p. 118–120 °C; ¹H-NMR (CDCl₃) δ: 7.83 (s, 1H, N'-Ar-H), 7.71–7.76 (m, 2H, N'-Ar-H and NH), 7.58 (s, 2H, N-Ar-H), 7.36–7.40 (m, 2H, N'-Ar-H), 2.32 (s, 3H, CH₃); ¹³C-NMR (CDCl₃) δ: 146.1, 140.7, 136.3, 133.5 (q, *J* = 33.3 Hz), 129.2, 128.3, 127.5, 126.7, 126.1, 125.6, 123.9, 122.1 (q, *J* = 271.8 Hz), 12.1; IR (KBr) v: 3358, 3073, 2926, 1603, 1536, 1489, 1390, 1352, 1313, 1108, 1011, 886 cm⁻¹.

N-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-[1-(4-bromophenyl)-ethylidene]hydrazine (**5d**): White solid, m.p. 114–115 °C; ¹H-NMR (CDCl₃) δ: 7.65–7.69 (m, 3H, N'-Ar-H and NH), 7.58 (s, 2H, N-Ar-H), 7.48–7.52 (m, 2H, N'-Ar-H), 2.33 (s, 3H, CH₃); ¹³C-NMR (CDCl₃) δ: 146.5, 141.7, 134.3, 132.5 (q, *J* = 33.5 Hz), 127.6, 127.1, 126.7, 125.6, 123.9, 121.9 (q, *J* = 271.8 Hz), 11.7; IR (KBr) v: 3362, 3074, 2928, 1606, 1540, 1495, 1393, 1354, 1308, 1106, 1012, 887 cm⁻¹.

N-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-[1-(3-bromophenyl)ethylidene]hydrazine (**5e**): White solid, m.p. 114–115 °C; ¹H-NMR (CDCl₃) δ: 7.94 (s, 1H, N'-Ar-H), 7.70–7.75 (m, 2H, N'-Ar-H and NH), 7.58 (s, 2H, N-Ar-H), 7.46–7.49 (m, 2H, N'-Ar-H), 2.32 (s, 3H, CH₃); ¹³C-NMR (CDCl₃) δ: 147.1, 141.9, 139.3, 132.3 (q, *J* = 33.5 Hz), 128.3, 127.6, 127.1, 126.7, 126.0, 124.6, 123.9, 121.9 (q, *J* = 271.8 Hz), 11.9; IR (KBr) v: 3360, 3072, 2924, 1600, 1538, 1492, 1390, 1356, 1307, 1115, 1019, 889 cm⁻¹.

N-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-[1-(4-methoxyphenyl)ethylidene]-hydrazine (**5f**): White solid, m.p. 89–90 °C; ¹H-NMR (CDCl₃) δ: 7.81 (s, 1H, N'-Ar-H), 7.79 (s, 1H, N'-Ar-H), 7.67 (s, 1H, NH), 7.58 (m, 2H, N-Ar-H), 6.73–6.89 (m, 2H, N'-Ar-H), 3.83 (s, 3H, OCH₃), 2.32 (s, 3H, CH₃). ¹³C-NMR (CDCl₃) δ: 158.1, 147.5, 136.2, 133.6 (q, *J* = 33.6 Hz), 127.8, 126.2, 125.6, 124.7, 121.9 (q, *J* = 270.2 Hz), 114.2, 55.1, 11.7; IR (KBr) v: 3355, 3072, 2925, 1603, 1530, 1489, 1391, 1351, 1307, 1112, 1016, 887 cm⁻¹.

N-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-[1-(4-trifluoromethylphenyl)-ethylidene]hydrazine (**5g**): White solid, m.p. 165–166 °C; ¹H-NMR (CDCl₃) δ: 7.91 (d, *J* = 8.4 Hz, 2H, N'-Ar-H), 7.78 (s, 1H, NH), 7.59–7.65 (s, 4H, N' and N-Ar-H), 2.36 (s, 3H, CH₃); ¹³C-NMR (CDCl₃) δ: 145.5, 144.7, 133.5 (q, *J* = 32.6 Hz), 130.4 (q, *J* = 32.1 Hz), 126.3, 125.8, 125.2, 124.6, 124.4, 123.2 (q, *J* = 270.2 Hz), 121.8 (q, *J* = 272.6 Hz), 11.9; IR (KBr) v: 3351, 3070, 2926, 1601, 1535, 1490, 1389, 1350, 1313, 1116, 1021, 889 cm⁻¹.

N-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-[1-(4-nitrophenyl)ethylidene]hydrazine (**5h**): Yellowish solid, m.p. 146–147 °C; ¹H-NMR (CDCl₃) δ: 8.24 (d, *J* = 6.0 Hz, 2H, N'-Ar-H), 7.88–7.97 (m, 3H, N'-Ar-H and NH), 7.60 (s, 2H, N-Ar-H), 2.38 (s, 3H, CH₃); ¹³C-NMR (CDCl₃) δ: 147.5, 144.3, 143.9, 140.4, 132.8 (q, *J* = 33.6 Hz), 126.5, 125.1, 124.7, 123.6, 120.9 (q, *J* = 272.6 Hz), 11.8; IR (KBr) v: 3320, 3073, 2926, 1583, 1513, 1393, 1339, 1307, 1117, 890 cm⁻¹.

N-(2,6-Dichloro-4-trifluoromethyl)phenyl-*N'*-[1-(6-methoxy-naphthalen-2-yl)-ethylidene]hydrazine (**5i**): White solid, m.p. 191–193 °C; ¹H-NMR (CDCl₃) δ: 8.11 (d, *J* = 6.2 Hz, 1H, N'-Ar-H), 8.00 (s, 1H, N'-Ar-H), 7.71–7.78 (m, 3H, N'-Ar-H and NH), 7.58 (s, 2H, N-Ar-H), 7.14–7.17 (m, 2H, N'-Ar-

H), 3.84 (s, 3H, OCH₃), 2.43 (s, 3H, CH₃); ¹³C-NMR (CDCl₃) δ: 157.9, 147.5, 134.6, 133.2 (q, *J* = 32.5 Hz), 129.6, 128.2, 126.7, 126.2, 126.1, 125.3, 124.8, 123.8, 123.7, 121.7 (q, *J* = 271.6 Hz), 118.7, 105.5, 55.0, 11.7; IR (KBr) ν: 3353, 3069, 2938, 1602, 1528, 1487, 1390, 1346, 1305, 1127, 1026, 889 cm⁻¹.

3.4. General procedure for synthesis of 1-[(2,6-dichloro-4-trifluoromethyl)phenyl]-3-aryl-1H-pyrazole-4-carbaldehydes **6a-i**

POCl₃ (0.5 g, 3.0 mmol) was added dropwise to an ice-cold stirred solution of hydrazone **5** (1.0 mmol) in dry DMF (4 mL), the reaction mixture was allowed to attain room temperature and then heated at 80 °C for 4 h. The resulting mixture was poured onto crushed ice, neutralized with dilute sodium hydroxide and left standing overnight. The pale yellow precipitate obtained was purified by flash column chromatography with ethyl acetate–petroleum ether mixture to yield the products **6a-i**.

1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-phenyl-1H-pyrazole-4-carbaldehyde (6a): White solid, m.p. 147–149 °C; ¹H-NMR (CDCl₃) δ: 10.11 (s, 1H, CHO), 8.22 (s, 1H, pyrazole H), 7.79–7.83 (m, 4H, 1 and 3-Ar-H), 7.27–7.54 (m, 3H, 3-Ar-H); ¹³C-NMR (CDCl₃) δ: 182.4, 153.8, 137.8, 135.0, 133.9 (q, *J* = 33.8 Hz), 129.0, 126.1, 125.8, 125.3, 124.6, 123.7, 122.6, 121.9 (q, *J* = 271.8 Hz); IR (KBr) ν: 3107, 3062, 2843, 1695, 1602, 1531, 1403, 1310, 1131, 850, 719 cm⁻¹; Anal. Calcd. for C₁₇H₉Cl₂F₃N₂O: C, 53.01; H, 2.36; N, 7.27. Found: C, 53.30; H, 2.45; N, 7.33%.

1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-(4-chlorophenyl)-1H-pyrazole-4-carbaldehyde (6b): White solid, m.p. 108–110 °C; ¹H-NMR (CDCl₃) δ: 10.08 (s, 1H, CHO), 8.22 (s, 1H, pyrazole H), 7.79–7.83 (m, 4H, 1 and 3-Ar-H), 7.45–7.48 (m, 2H, 3-Ar-H); ¹³C-NMR (CDCl₃) δ: 183.6, 152.8, 138.8, 136.0, 133.8 (q, *J* = 33.8 Hz), 129.1, 128.5, 126.1, 125.8, 125.3, 123.7, 122.6, 121.9 (q, *J* = 271.8 Hz); IR (KBr) ν: 3107, 3060, 2845, 1695, 1600, 1529, 1401, 1314, 1130, 858, 719 cm⁻¹; Anal. Calcd. for C₁₇H₈Cl₃F₃N₂O: C, 48.66; H, 1.92; N, 6.68. Found: C, 48.77; H, 2.03; N, 6.60%.

1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-(3-chlorophenyl)-1H-pyrazole-4-carbaldehyde (6c): White solid, m.p. 105–106 °C; ¹H-NMR (CDCl₃) δ: 10.09 (s, 1H, CHO), 8.21 (s, 1H, pyrazole H), 7.83–7.91 (m, 3H, 1 and 3-Ar-H), 7.31–7.62 (m, 3H, 3-Ar-H); ¹³C-NMR (CDCl₃) δ: 183.6, 152.8, 137.8, 136.0, 159.6, 133.8 (q, *J* = 33.8 Hz), 129.1, 128.5, 128.1, 126.1, 125.8, 125.2, 123.6, 122.7, 121.8 (q, *J* = 271.8 Hz); IR (KBr) ν: 3106, 3062, 2840, 1696, 1602, 1530, 1403, 1310, 1134, 856, 719 cm⁻¹; Anal. Calcd. for C₁₇H₈Cl₃F₃N₂O: C, 48.66; H, 1.92; N, 6.68. Found: C, 48.81; H, 1.90; N, 6.80%.

1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-(4-bromophenyl)-1H-pyrazole-4-carbaldehyde (6d): White solid, m.p. 116–118 °C; ¹H-NMR (CDCl₃) δ: 10.08 (s, 1H, CHO), 8.22 (s, 1H, pyrazole H), 7.74–7.79 (m, 4H, 1 and 3-Ar-H), 7.61–7.64 (m, 2H, 3-Ar-H); ¹³C-NMR (CDCl₃) δ: 183.6, 152.8, 138.8, 136.0, 134.6, 133.8 (q, *J* = 33.8 Hz), 129.1, 128.5, 125.8, 125.3, 123.5, 122.6, 121.9 (q, *J* = 271.8 Hz); IR (KBr) ν: 3108, 3063, 2841, 1697, 1604, 1532, 1407, 1315, 1131, 858, 719 cm⁻¹; Anal. Calcd. for C₁₇H₈BrCl₂F₃N₂O: C, 44.00; H, 1.74; N, 6.04. Found: C, 43.87; H, 1.79; N, 5.96%.

1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-(3-bromophenyl)-1H-pyrazole-4-carbaldehyde (**6e**): White solid, m.p. 110–112 °C; ¹H-NMR (CDCl₃) δ: 10.09 (s, 1H, CHO), 8.22 (s, 1H, pyrazole H), 7.79–7.83 (m, 4H, 1 and 3-Ar-H), 7.59–7.62 (m, 1H, 3-Ar-H), 7.35–7.38 (m, 1H, 3-Ar-H); ¹³C-NMR (CDCl₃) δ: 182.9, 153.8, 139.0, 136.7, 134.2, 133.8 (q, *J* = 33.8 Hz), 129.1, 128.5, 126.1, 125.9, 125.3, 123.7, 123.3, 122.6, 121.8 (q, *J* = 271.8 Hz); IR (KBr) v: 3106, 3062, 2840, 1695, 1602, 1530, 1401, 1313, 1132, 856, 719 cm⁻¹; Anal. Calcd. for C₁₇H₈BrCl₂F₃N₂O: C, 44.00; H, 1.74; N, 6.04. Found: C, 43.70; H, 1.83; N, 6.36%.

1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-(4-methoxyphenyl)-1H-pyrazole-4-carbaldehyde (**6f**): White solid, m.p. 75–77 °C; ¹H-NMR (CDCl₃) δ: 10.08 (s, 1H, CHO), 8.20 (s, 1H, pyrazole H), 7.76–7.79 (m, 4H, 1 and 3-Ar-H), 7.00–7.03 (m, 2H, 3-Ar-H), 3.87 (s, 3H, OCH₃); ¹³C-NMR (CDCl₃) δ: 183.2, 160.4, 154.5, 136.1, 134.9, 133.8 (q, *J* = 33.8 Hz), 130.0, 128.2, 125.8, 125.7, 122.8, 121.9 (q, *J* = 271.6 Hz), 113.9, 55.0; IR (KBr) v: 3110, 3060, 2963, 2850, 1695, 1600, 1530, 1403, 1312, 1130, 858, 719 cm⁻¹; Anal. Calcd. for C₁₈H₁₁Cl₂F₃N₂O₂: C, 52.07; H, 2.67; N, 6.75. Found: C, 52.10; H, 2.65; N, 6.78%.

1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-(4-trifluoromethylphenyl)-1H-pyrazole-4-carbaldehyde (**6g**): White solid, m.p. 88–90 °C; ¹H-NMR (CDCl₃) δ: 10.11 (s, 1H, CHO), 8.25 (s, 1H, pyrazole H), 8.01–8.03 (m, 2H, 3-Ar-H), 7.74–7.83 (m, 4H, 1 and 3-Ar-H); ¹³C-NMR (CDCl₃) δ: 183.2, 151.8, 148.3, 139.1, 137.8, 136.9, 135.0, 133.9 (q, *J* = 33.8 Hz), 129.8 (q, *J* = 32.6 Hz), 129.0, 126.1, 123.7 (q, *J* = 270.1 Hz), 122.6, 121.9 (q, *J* = 271.8 Hz); IR (KBr) v: 3110, 3060, 2842, 1695, 1600, 1528, 1400, 1313, 1130, 858, 719 cm⁻¹; Anal. Calcd. for C₁₈H₈Cl₂F₆N₂O: C, 47.71; H, 1.78; N, 6.18. Found: C, 47.84; H, 1.85; N, 6.23%.

1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-(4-nitrophenyl)-1H-pyrazole-4-carbaldehyde (**6h**): Yellowish solid, m.p. 206–208 °C; ¹H-NMR (CDCl₃) δ: 10.12 (s, 1H, CHO), 8.33–8.36 (m, 2H, 3-Ar-H), 8.27 (s, 1H, pyrazole H), 8.13–8.15 (m, 2H, 3-Ar-H), 7.82 (s, 2H, 1-Ar-H); ¹³C-NMR (CDCl₃) δ: 183.2, 151.8, 148.3, 139.1, 137.8, 136.9, 135.0, 133.8 (q, *J* = 33.8 Hz), 129.6, 126.1, 123.7, 122.6, 121.9 (q, *J* = 271.6 Hz); IR (KBr) v: 3106, 3062, 2843, 1695, 1602, 1530, 1403, 1310, 1132, 858, 719 cm⁻¹; Anal. Calcd. for C₁₇H₈Cl₂F₃N₃O₃: C, 47.47; H, 1.87; N, 9.77. Found: C, 47.56; H, 1.93; N, 9.62%.

1-[(2,6-Dichloro-4-trifluoromethyl)phenyl]-3-(6-methoxy-naphthalen-2-yl)-1H-pyrazole-4-carbaldehyde (**6i**): White solid, m.p. 144–146 °C; ¹H-NMR (CDCl₃) δ: 10.19 (s, 1H, CHO), 8.25 (s, 1H, pyrazole H), 7.80–7.92 (m, 5H, 1 and 3-Ar-H), 7.19–7.23 (m, 3H, 3-Ar-H), 3.94 (s, 3H, OCH₃); ¹³C-NMR (CDCl₃) δ: 183.2, 158.2, 155.0, 136.4, 134.9, 134.7, 133.8 (q, *J* = 33.8 Hz), 129.7, 128.3, 128.2, 127.0, 126.4, 125.8, 125.4, 123.5, 122.1, 121.9 (q, *J* = 271.6 Hz), 119.2, 105.4, 55.0; IR (KBr) v: 3108, 3062, 2963, 2840, 1695, 1600, 1528, 1400, 1313, 1130, 858, 719 cm⁻¹; Anal. Calcd. for C₂₂H₁₃Cl₂F₃N₂O₂: C, 56.79; H, 2.82; N, 6.02. Found: C, 56.65; H, 2.93; N, 6.15%.

4. Conclusions

In conclusion, The Vilsmeier cyclization of hydrazones provided an efficient route for the preparation of 1H-pyrazole-4-carbaldehydes, and we have successfully developed a general method

for the synthesis in good yields of a series of 1-[(2,6-dichloro-4-trifluoromethyl)phenyl]-3-aryl-1*H*-pyrazole-4-carbaldehydes **6a-i** using the Vilsmeier-Haack reagent. The structures of all the title compounds have been confirmed by elemental analysis, ¹H-NMR and ¹³C-NMR and in addition, the structure of intermediate **5b** was confirmed by X-ray crystallography.

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18. CCDC 685556 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; E-Mail: deposit@ccdc.cam.ac.uk.

Sample Availability: Samples of the compounds **6a-i** are available from the authors.

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