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Synthesis and characterization of novel 3-substituted-2-butyl-5-chloro-imidazol-4-carbaldehyde derivatives

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Abstract

2-butyl-5-chloro-4-formyl-3H-imidazole 1 was condensed with the potentially bioactive 5-chloromethyl-6-methyl-benzo [1,3] dioxole. Compounds 1 and 2 were subsequently condensed with different aromatic hydrazides to form a novel series of 3-substituted-2-butyl-5-chloro-imidazol-4-carbaldehyde derivatives. Structural elucidation was accomplished by ^{1}H NMR, ^{13}C NMR, IR and elemental analyses of synthesized compounds.

Keywords: Hydrazone, Imidazole.

1. INTRODUCTION

Imidazole is an aromatic heterocycle, a diazole and classified as an alkaloid. Synthesis of imidazoles is synthetically [1] and pharmaceutically important as they possess analgesic [2], cardiovascular [3], antiinflammatory[4], antibacterial [5], antifungal [6], anticonvolusant[7], antituberculosis[8], antiulcer [9], and antileishmanicidal activity [10]. Moreover, synthesis of substituted imidazoles is in great demand for designing metal-chelating agents [11], corrosion inhibitors, and artificial catalysts [12]. Clotrimazole and Miconazole are the two imidazole drugs which have made their appearances in the market as topical antimycotics. Losartan potassium, an orally active antihypertensive agent [13] is a nonpeptide angiotensin II antagonist. 2-butyl-5-chloro-4-formyl-3H-imidazole is one of the key intermediates in the synthesis of Losartan [14]. The great potential for different pharmacological activities of imidazole derivatives and their highlighted chemistry has impelled us to synthesize a novel series of 3-substituted-2-butyl-5-chloro-imidazol-4-carbaldehyde derivatives.

2. MATERIALS AND METHODS

2.1. Chemistry protocols

All the experiments were carried out in an Orbit 6 parallel synthesizer. Melting points were determined on a Thomas Hoover melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 400 MHz spectrometer using $CDCl_3$ as solvent and tetramethylsilane as internal standard. Chemical shifts were expressed in δ and the following abbreviations were used: s = singlet, d = doublet, t = triplet and m = multiplet. IR (KBr) spectra were recorded on Shimadzu 8300 spectrometer. Thin layer chromatography was done with precoated silica gel G plates.

2.1.1. 2-butyl-5-chloro-4-formyl-3H-imidazole 3

A solution of valeronitrile1(5 g, 0.06 mol) in isopropanol (2.166 g, 0.07 mol) and dibutyl ether (5 mL) was cooled to -10 °C. Dry HCl gas was passed over the solution for 2 hour at a temperature below 0 ℃. The mixture was stirred for 48 hour at 0-5 ℃ and the solid formed was filtered off, washed with chilled ether, and dried to give pentaneimidate hydrochloride, a suspension of which was taken into 15 mL diethyl ether and cooled to -10 ℃. Then, slowly added 10 mL of 5 M aqueous NaOH solution and stirred for 15 minutes till the two layers separated. Aqueous layer was extracted with diethyl ether. Ether was evaporated to give crude methyl pentanimidate which was purified by distillation to give pure imidate 2 (2.7 g, 0.02 mol) as oil.

Glycine (1.77 g, 0.02 mol) wascooled to 0-5 ℃ in 7 mL of isopropanol and 1 ml water. The pH was adjusted to 8.0-9.0 using 30% KOH solution. A solution of 2.7 g imidate in 4.86 mL toluene was added and the mixture was stirred at room temperature for 12 hour with the pH adjusted to 7 using Conc. H_2SO_4.The resulting suspension was refluxed at 80 ℃ upon addition of $POCl_3$(10.26 g, 0.06 mol) anddimethyl formamide(4.806 g, 0.06 mol) for 2 h, cooled to room temperature, poured onto ice water. This mixture was extracted into toluene and washed

with water. The organic phase was concentrated to get a white crystalline solid of 2-Butyl-5-chloro-4-formyl-3H-imidazole **3**(2.26 g, 0.011 mol).Melting point (m.p.) was 98-100 ^{o}C.^{1}H NMR $CDCl_3$: δ 1.11 (t, *J* =1.0 Hz, 3H, CH_3), 1.49 (m, 2H, CH_2), 2.25 (m, 2H, CH_2), 2.85 (t, *J* =1.3 Hz, 2H, CH_2), 9.56 (s, 1H, CHO), 13.28 (bs, 1H, NH). ^{13}C NMR $CDCl_3$: δ 13.2 (q), 23.2 (t), 28.1 (t), 30.1 (t), 128.2 (s), 144.1 (s), 158.8 (s), 179.2 (d). IR (KBr pellets cm^{-1}) *v* 3409, 3070, 2968, 2829, 1671, 1459. Anal.Calcd.for $C_8H_{11}ClN_2O$: C, 51.48; H, 5.94; N, 15.01 %. Found: C, 51.38; H, 5.98; N, 15.10 %.

2.1.2. 2-butyl-5-chloro-4-formyl-3-(6-methyl-benzo[1,3]dioxol-5-ylmethyl)imidazole 4

A parallel synthesis equipment was charged with 2-butyl-5-chloro-4-formyl-3H-imidazole **3** (1 g, 5.37 mmol), anhydrous K_2CO_3 (0.90 g, 6.52 mmol), 5-chloromethyl-6-methyl-benzo [1,3] dioxole (0.98 g, 5.32 mmol) and dimethyl formamide (5 mL). The reaction mixture was stirred overnight at room temperature. After completion of the reaction as marked by TLC (toluene: ethyl acetate = 7: 3), the dark red mass was diluted with 25 mL water and the product was extracted with dichloromethane (25 mL). The extract was washed with water (10 mL) and dried (Na_2SO_4). The solvent was evaporated and the remaining pale yellow oil was crystallized from ethanol as a white crystalline solid 4 with a yield of (1.48g, 83 %), m.p. 110-112 ^{o}C.^{1}H NMR $CDCl_3$: δ 0.79 (t, *J* =1.0 Hz, 3H, CH_3), 1.33 (m, 2H, CH_2), 1.79 (m, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.57 (t, *J* =1.3 Hz, 2H, CH_2), 5.41 (s, 2H, CH_2), 5.90 (s, 2H, CH_2), 6.82 (s, 2H, ArH), 9.62 (s, 1H, CHO). ^{13}C NMR $CDCl_3$: δ 13.8 (q), 23.1 (t), 23.9 (q), 28.2 (t), 30.5 (t), 34.9 (t), 91.5 (t), 113.2 (d), 123.3 (d), 128.1 (s), 130.2 (s), 131.4 (s), 140.1 (s), 141.7 (s), 144.3 (s), 159.1 (s), 189.2 (d). IR (KBr pellets cm^{-1}) *v* 3071, 2961, 2859, 1763, 1667, 1452, 1230. Anal.Calcd.for $C_{17}H_{19}ClN_2O_2$: C, 60.99; H, 5.72; N, 8.37 %. Found: C, 60.95; H, 5.79; N, 8.42 %.

2.1.3. Representative procedure for the synthesis of aroylhydrazones 5 and 6

0.1 g of 3 or 4 was taken in parallel synthesis equipment, equipped with magnetic stirrer. Added an equimolar proportion ofaromatic hydrazides, isopropanol (2 mL) and refluxed for 2h. The progress of the reaction was monitored by TLC (toluene: ethyl acetate: diethylamine = 7.5: 2.5:1). After completion of the reaction, the mass was cooled and the solid formed was filtered to give 5or 6respectively.

The same procedure was used in all cases.

2.1.3.1. [(2-butyl-5-chloro-3H-imidazol-4-yl)methylidene]-4-nitrobenzohydrazone 5a

Obtained from 3 (0.1 g, 0.53 mmol) and 4-nitrobenzohydrazide (0.099 g, 0.53 mmol) as a yellow crystalline solid (0.161 g, 87 %), m.p. 158-160 ^{o}C.^{1}H NMR $CDCl_3$: δ 0.877 (t, *J* =1.0 Hz, 3H, CH_3), 1.28 (m, 2H, CH_2), 1.61 (m, 2H, CH_2), 2.61(t, *J* =1.3 Hz, 2H, CH_2), 7.77 (s, 1H, CH=N-), 8.17 (s, 2H, ArH), 8.34 (s, 2H, ArH), 11.09 (bs, 1H, CONHN), 12.09 (bs, 1H, NH). ^{13}C NMR $CDCl_3$: δ 13.1 (q), 23.2 (t), 28.1 (t), 31.3 (t), 2×122.2 (d), 128.4 (s), 2×130.1 (d), 135.5 (s), 143.9 (s), 147.6 (d), 151.8 (s), 157.2 (s), 168.8 (s). IR (KBr pellets cm^{-1}) *v* 3440, 1666, 1620, 1519, 1342, 709.Anal.Calcd.for $C_{15}H_{16}ClN_5O_3$: C, 51.36; H, 4.88; N, 19.96 %. Found: C, 51.30; H, 4.90; N, 19.92 %.

2.1.3.2. [(2-butyl-5-chloro-3H-imidazol-4-yl)methylidene]-4-bromobenzohydrazone 5b

Obtained from 3 (0.1 g, 0.53 mmol) and 4-bromobenzohydrazide (0.115 g, 0.53 mmol) as a yellow crystalline solid (0.168 g, 83 %), m.p. 106-107 ^{o}C.^{1}H NMR $CDCl_3$: δ 0.876 (t, *J* =1.0 Hz, 3H, CH_3), 1.28 (m, 2H, CH_2), 1.61 (m, 2H, CH_2), 2.63 (t, *J* =1.3 Hz, 2H, CH_2), 7.41 (s, 2H, ArH), 7.62 (s, 2H, ArH), 7.77 (s, 1H, CH=N-), 11.06 (bs, 1H, CONHN), 12.08 (bs, 1H, NH). ^{13}C NMR $CDCl_3$: δ 13.3 (q), 23.2 (t), 28.6 (t), 30.1 (t), 126.9 (s), 127.2 (s), 128.7 (s), 2×129.4 (d), 2×131.7 (d), 144.3 (s), 147.5 (d), 158.2 (s), 168.8 (s). IR (KBr pellets cm^{-1}) *v* 3286, 3085, 1658, 1620, 1550, 524.Anal.Calcd.for $C_{15}H_{16}BrClN_4O$: C, 46.83; H, 4.45; N, 14.56 %. Found: C, 46.87; H, 4.43; N, 14.59 %.

2.1.3.3. [(2-butyl-5-chloro-3H-imidazol-4-yl)methylidene]-4-chlorobenzohydrazone 5c

Obtained from **3** (0.1 g, 0.53 mmol) and 4-chlorobenzohydrazide (0.091 g, 0.53 mmol) as a yellow crystalline solid (0.152 g, 85 %), m.p. 114-116 ^{o}C.^{1}H NMR $CDCl_3$: δ 0.878 (t, *J* =1.0 Hz, 3H, CH_3), 1.25 (m, 2H, CH_2), 1.61 (m, 2H, CH_2), 2.61 (t, *J* =1.3 Hz, 2H, CH_2), 7.38 (s, 2H, ArH), 7.51 (s, 2H, ArH), 7.79 (s, 1H, CH=N-), 11.09 (bs, 1H, CONHN), 12.09 (bs, 1H, NH). ^{13}C NMR $CDCl_3$: δ 13.2 (q), 23.3 (t), 28.9 (t), 30.0 (t), 2× 126.7 (d), 127.6 (s), 128.5 (s), 2×130.4 (d), 137.6 (s), 144.1 (s), 147.5 (d), 157.9 (s), 168.2 (s). IR (KBr pellets cm^{-1}) *v* 3471, 3178, 1635, 1558, 1496, 840, 740.Anal.Calcd.for $C_{15}H_{16}Cl_2N_4O$: C,

2.1.3.4. [(2-butyl-5-chloro-3H-imidazol-4-yl)methylidene]-4-methylbenzohydrazone 5d

Obtained from 3 (0.1 g, 0.53 mmol) and 4-methylbenzohydrazide (0.08 g, 0.53 mmol) as a yellow crystalline solid (0.15 g, 89 %), m.p. 126-128 ^{o}C.^{1}H NMR $CDCl_3$: δ 0.876 (t, *J* =1.0 Hz, 3H, CH_3), 1.28 (m, 2H, CH_2), 2.18 (m, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.61 (t, *J* =1.3 Hz, 2H, CH_2), 7.39 (s, 2H, ArH), 7.58 (s, 2H, ArH), 8.32 (s, 1H, CH=N-), 11.06 (bs, 1H, CONHN), 12.08 (bs, 1H, NH). ^{13}C NMR $CDCl_3$: δ 13.2 (q), 21.1 (q), 23.2 (t), 28.1 (t), 30.1

(t), 2×126.9 (d), 127.7 (s), 128.5 (s), 2×129.4 (d), 140.6 (s), 144.1 (s), 147.2 (s), 158.8 (s), 168.6 (s). IR (KBr pellets cm^{-1}) *v* 3456, 3078-3039, 2947, 1643, 1566, 709.Anal.Calcd.for $C_{16}H_{19}ClN_4O$: C, 60.09; H, 6.30; N, 17.52 %. Found: C, 60.01; H, 6.36; N, 17.58 %.

2.1.3.5. [(2-butyl-5-chloro-3H-imidazol-4-yl)methylidene]pyridine-3-carbohydrazone 5e

Obtained from 3 (0.1 g, 0.53 mmol) and pyridine-3-carbohydrazide (0.073 g, 0.53 mmol) as a yellow crystalline solid (0.128 g, 79 %), m.p. 234-236 ^oC.^1H NMR $CDCl_3$: δ 0.873 (t, *J* =1.0 Hz, 3H, CH_3), 1.21 (m, 2H, CH_2), 1.61 (m, 2H, CH_2), 2.61 (t, *J* =1.3 Hz, 2H, CH_2), 7.54 (s, 1H, CH=N-), 7.5-9.0 (m, 4H, PyH), 11.86 (bs, 1H, CONHN), 12.90 (bs, 1H, NH). ^{13}C NMR $CDCl_3$: δ 13.3 (q), 23.4 (t), 28.4 (t), 30.1 (t), 122.9 (d), 124.1 (s), 128.2 (s), 135.9 (d), 144.1 (s), 147.5 (d), 151.3 (d), 154.9 (s), 158.7 (s), 168.6 (s). IR (KBr pellets cm^{-1}) *v* 3286, 3224, 3062, 1650, 1604, 1542, 1049, 702.Anal.Calcd.for $C_{14}H_{16}ClN_5O$: C, 55.81; H, 5.59; N, 16.47 %. Found: C, 54.85; H, 5.52; N, 16.41 %.

2.1.3.6. [(2-butyl-5-chloro-3H-imidazol-4-yl)methylidene]-2-hydroxybenzohydrazone 5f

Obtained from 3 (0.1 g, 0.53 mmol) and 2-hydroxybenzohydrazide (0.084 g, 0.53 mmol) as a white crystalline solid (0.139 g, 82 %), m.p. 110-112 ^oC.^1H NMR $CDCl_3$: δ 1.32 (t, *J* =1.0 Hz, 3H, CH_3), 1.56 (m, 2H, CH_2), 1.88 (m, 2H, CH_2), 2.56 (t, *J* =1.3 Hz, 2H, CH_2), 6.9-7.7 (m, 4H, ArH), 7.87 (s, 1H, CH=N-), 8.35 (s, 1H, OH), 11.75 (bs, 1H, CONHN), 11.93 (bs, 1H, NH). ^{13}C NMR $CDCl_3$: δ 13.7 (q), 23.2 (t), 28.1 (t), 30.3 (t), 113.8 (d), 115.2 (s), 120.5 (d), 128.3 (s), 129.7 (d), 133.1 (d), 144.2 (s), 147.4 (d), 156.1 (s), 158.4 (s), 169.1 (s). IR (KBr pellets cm^{-1}) *v* 3471, 3263, 3018, 1635, 1542, 848, 748.Anal.Calcd.for $C_{15}H_{17}ClN_4O_2$: C, 55.99; H, 5.64; N, 17.41 %. Found: C, 55.92; H, 5.69; N, 17.45 %.

2.1.3.7. [2-butyl-5-chloro-4-formyl-3-(6-methyl-benzo[1,3]dioxol-5-ylmethyl)imidazol-4-yl- methylidine]-4-nitrobenzohydrazone 6a

Obtained from 4 (0.1 g, 0.28 mmol) and 4-nitrobenzohydrazide (0.053 g, 0.28 mmol) as a yellow crystalline solid (0.124 g, 86 %), m.p. 108-109 ^oC.^1H NMR $CDCl_3$: δ 0.92 (t, *J* =1.0 Hz, 3H, CH_3), 1.39 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 2.27 (s, 3H, CH_3), 2.59 (t, *J* =1.3 Hz, 2H, CH_2), 4.91 (s, 2H, CH_2), 5.88 (s, 2H, CH_2), 6.43 (s, 2H, ArH), 7.72 (s, 1H, CH=N-), 8.14 (s, 2H, ArH), 8.51 (s, 2H, ArH), 10.09 (bs, 1H, CONHN). ^{13}C NMR $CDCl_3$: δ 13.8 (q), 23.1 (t), 23.9 (q), 28.4 (t), 30.5 (t), 34.9 (t), 91.6 (t), 113.2 (d), 2×122.1(d), 123.3 (d), 128.1 (s), 2×130.1 (d), 130.3 (s), 131.6 (s), 135.3 (s), 140.1 (s), 141.7 (s), 143.9 (s), 144.3 (s), 147.6 (d), 159.3 (s), 168.5 (s) . IR (KBr pellets cm^{-1}) *v* 3371, 3031, 1612, 1542, 1342, 1033.Anal.Calcd.for $C_{24}H_{24}ClN_5O_5$: C, 57.77; H, 5.05; N, 14.04 %. Found: C, 57.79; H, 5.00; N, 14.08 %.

2.1.3.8. [2-butyl-5-chloro-4-formyl-3-(6-methyl-benzo[1,3]dioxol-5-ylmethyl)imidazol-4-yl- methylidine]-4-bromobenzohydrazone 6b

Obtained from 4 (0.1 g, 0.28 mmol) and 4-bromobenzohydrazide (0.06 g, 0.28 mmol) as a yellow crystalline solid (0.123 g, 80 %), m.p. 178-179 ^oC.^1H NMR $CDCl_3$: δ 0.83 (t, *J* =1.0 Hz, 3H, CH_3), 1.30 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 2.29 (s, 3H, CH_3), 2.55 (t, *J* =1.3 Hz, 2H, CH_2), 5.67 (s, 2H, CH_2), 5.91 (s, 2H, CH_2), 6.40 (s, 2H, ArH), 7.72 (s, 2H, ArH), 7.81 (s, 2H, ArH), 8.32 (s, 1H, CH=N-), 11.77 (bs, 1H, CONHN). ^{13}C NMR $CDCl_3$: δ 14.05 (q), 18.93 (t), 22.12 (q), 26.0 (t), 29.18 (t), 46.45 (t), 91.6 (t), 113.2 (d), 123.4 (d), 126.8 (s), 127.2 (s), 128.4 (s), 2×129.8 (s), 130.2 (s), 131.4 (s), 2×131.7 (d), 140.1 (s), 141.2 (s), 144.3 (s), 147.6 (d), 152.45 (s), 162.01 (s). IR (KBr pellets cm^{-1}) *v* 3193, 3047, 1650, 1558, 1041, 671.Anal.Calcd.for $C_{24}H_{24}$ $BrClN_4O_3$: C, 54.10; H, 4.73; N, 10.51 %. Found: C, 54.15; H, 4.77; N, 10.59 %.

2.1.3.9. [2-butyl-5-chloro-4-formyl-3-(6-methyl-benzo[1,3]dioxol-5-ylmethyl)imidazol-4-yl- methylidine]-4-chlorobenzohydrazone 6c

Obtained from 4 (0.1 g, 0.28 mmol) and 4-chlorobenzohydrazide (0.048 g, 0.28 mmol) as a yellow crystalline solid (0.118 g, 84 %), m.p. 120-121 ^oC.^1H NMR $CDCl_3$: δ 0.91 (t, *J* =1.0 Hz, 3H, CH_3), 1.39 (m, 2H, CH_2), 1.55 (m, 2H, CH_2), 2.27 (s, 3H, CH_3), 2.56 (t, *J* =1.3 Hz, 2H, CH_2), 4.91 (s, 2H, CH_2), 5.93 (s, 2H, CH_2), 6.44 (s, 2H, ArH), 7.39 (s, 2H, ArH), 7.50 (s, 2H, ArH), 7.76 (s, 1H, CH=N-), 10.06 (bs, 1H, CONHN). ^{13}C NMR $CDCl_3$: δ 13.7 (q), 23.1 (t), 23.8 (q), 28.2 (t), 30.5 (t), 34.9 (t), 91.6 (t), 113.8 (d), 123.4 (d), 2×126.5 (d), 127.5 (s), 128.5 (s), 130.1 (s), 2×130.7 (d), 131.6 (s), 137.6 (s), 140.2 (s), 141.6 (s), 144.1 (s), 147.6 (d), 159.2 (s), 168.2 (s). IR (KBr pellets cm^{-1}) *v* 3201, 2954, 1666, 1558, 1157, 1041.Anal.Calcd.for $C_{24}H_{24}Cl_2N_4O_3$: C, 59.02; H, 5.16; N, 11.47 %. Found: C, 59.08; H, 5.11; N, 11.45 %.

2.1.3.10 [2-butyl-5-chloro-4-formyl-3-(6-methyl-benzo[1,3]dioxol-5-ylmethyl)imidazol-4-yl- methylidine]-4-methylbenzohydrazone 6d

Obtained from 4 (0.1 g, 0.28 mmol) and 4-methylbenzohydrazide (0.042 g, 0.28 mmol) as a yellow crystalline solid (0.112 g, 87 %), m.p. 162-163 ^oC.^1H NMR $CDCl_3$: δ 0.94 (t, *J* =1.0 Hz, 3H, CH_3), 1.35 (m, 2H, CH_2), 1.59 (m, 2H, CH_2), 2.29 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.59 (t, *J* =1.3 Hz, 2H, CH_2), 4.97 (s, 2H, CH_2), 5.91 (s, 2H, CH_2), 6.41 (s, 2H, ArH), 7.38 (s, 2H, ArH), 7.56 (s, 2H, ArH), 7.76 (s, 1H, CH=N-), 10.01 (bs, 1H, CONHN). ^{13}C NMR

$CDCl_3$: δ 13.6 (q), 23.1 (q), 23.2 (t), 23.9 (q), 28.1 (t), 30.2 (t), 34.8 (t), 91.1 (t), 113.1 (d), 123.2 (d), 2×126.3 (d), 127.5 (s), 128.2 (s), 2×129.3 (d), 130.2 (s), 131.4 (s), 140.1 (s), 140.9 (s), 141.7 (s), 144.3 (s), 147.2 (d), 159.1 (s), 168.6 (s). IR (KBr pellets cm^{-1}) *v* 3039, 2947, 1650, 1488, 1041.Anal.Calcd.for $C_{25}H_{27}ClN_4O_3$: C, 64.16; H, 6.03; N, 11.97 %. Found: C, 64.12; H, 6.07; N, 11.90 %.

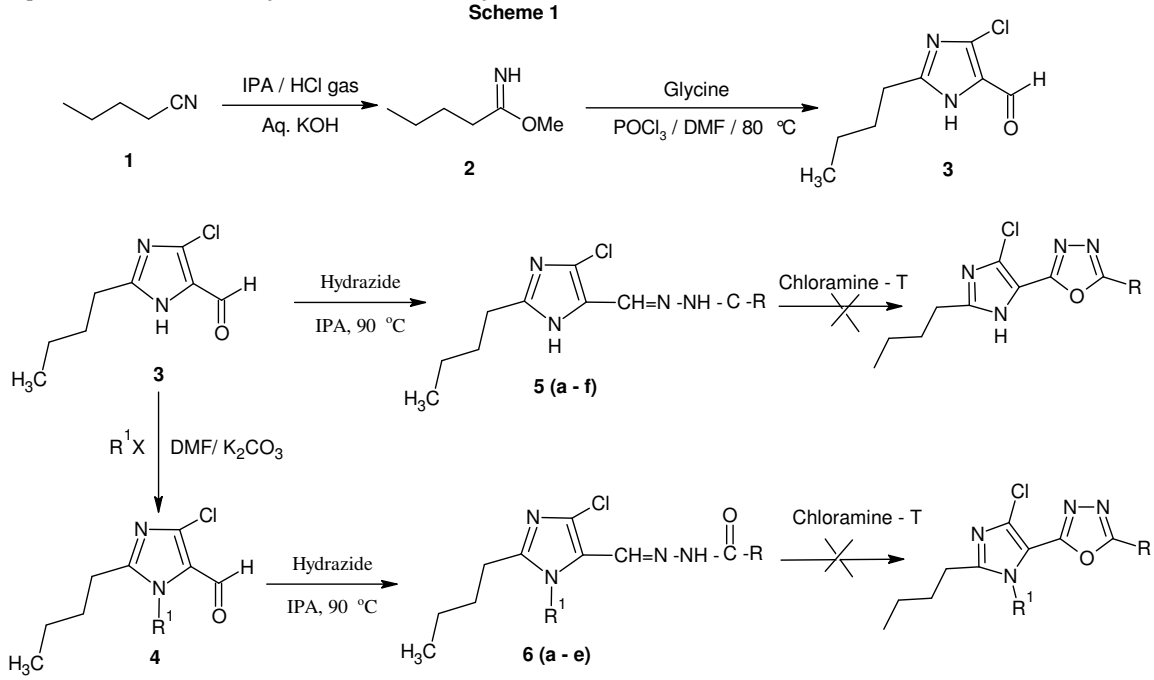
2.1.3.11. [2-butyl-5-chloro-4-formyl-3-(6-methyl-benzo[1,3]dioxol-5-ylmethyl)imidazol-4-yl-methylidine]-pyridine-3-carbohydrazone 6e

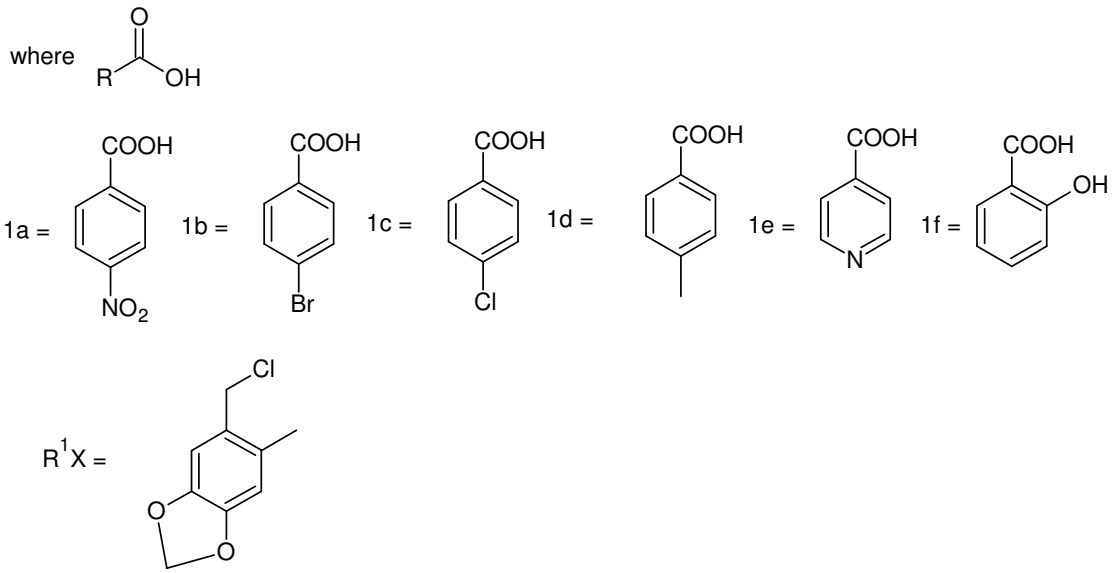
Obtained from 4 (0.1 g, 0.28 mmol) and pyridine-3-carbohydrazide (0.038 g, 0.28 mmol) as a yellow crystalline solid (0.108 g, 81 %), m.p. 117-118 °C.^{1}H NMR $CDCl_3$: δ 0.92 (t, *J* =1.0 Hz, 3H, CH_3), 1.37 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 2.29 (s, 3H, CH_3), 2.56 (t, *J* =1.3 Hz, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.91 (s, 2H, CH_2), 6.42 (s, 2H, ArH), 7.75 (s, 1H, CH=N-), 8.0-8.9 (m, 4H, PyH), 10.06 (bs, 1H, CONHN). ^{13}C NMR $CDCl_3$: δ 13.8 (q), 23.2 (t), 23.9 (q), 28.2 (t), 30.5 (t), 34.9 (t), 91.7 (t), 113.4 (d), 122.8 (d), 123.2 (d), 124.1 (s), 128.6 (s), 130.1 (s), 131.7 (s), 135.8 (d), 140.1 (s), 141.9 (s), 144.2 (s), 147.5 (d), 151.3 (d), 154.8 (d), 159.2 (s), 168.9 (s). IR (KBr pellets cm^{-1}) *v* 3232, 3055, 1612, 1558, 1041, 709.Anal.Calcd.for $C_{23}H_{24}ClN_5O_3$: C, 60.72; H, 5.54; N, 15.39 %. Found: C, 60.75; H, 5.56; N, 15.38 %.

3. RESULTS AND DISCUSSION

Compounds were synthesized as per scheme 1. ^{1}H NMR, ^{13}C NMR, IR and elemental analyses characterized all the synthesized compounds. 2-butyl-5-chloro-4-formyl-3H-imidazole 3 was prepared by the reaction between imidate and glycine. ^{1}H NMR spectrum of this aldehyde showed a broad singlet at δ 13.28 due to NH group of imidazole ring and an aldehydic proton at δ 9.56. The aldehydic carbon was observed at δ 179.2. 2-butyl-5-chloro-4-formyl-3-(6-methyl-benzo[1,3] dioxol-5-ylmethyl) imidazole 4was synthesized by condensing compound 3with 5 -chloromethyl-6-methyl-benzo [1,3] dioxoleR^1X. 2-butyl-5-chloro-4-formyl-3-(6-methyl-benzo[1,3] dioxol-5-ylmethyl) imidazole has proven to show antiinflammatory activity [4]. Compound4showed the aldehydic proton at δ 9.62 and aldehydic carbon at δ189.2. Disappearance of peak at δ 13.28 due to NH group of imidazole ringand appearance of a new peak at δ 5.41 due to NCH_2 group indicated the formation of compound4. All other substituents were observed in the expected region.[(2-butyl-5-chloro-3H-imidazol-4-yl)methylidene]-carbohydrazones5(a-f) and [2-butyl-5-chloro-4-formyl-3-(6-methyl-benzo[1,3]dioxol-5-ylmethyl)imidazol-4-yl-methylidine]carbohydrazones6(a-e) were synthesized by the condensation of 3 and 4with hydrazidesrespectively. ^{1}H NMR spectra of synthesized aryl hydrazones showed the disappearance of the aldehydic proton at δ 9.5-9.6 and appearance of a singlet at δ 7.75-9.06 due to CH=N- group and a broad singlet at δ 10.02-12.09 due to CONHN group. Furthermore, ^{13}C NMR spectra showed the disappearance of the aldehydic carbon at δ 179-189 and appearance of a doublet at δ 147.1-147.8 due to CH=N- group and a singlet at δ 168-169 due to CONHN group. All the other substituents were observed in the expected regions.

Scheme 1





We have also attempted to synthesize 2-(2-butyl-5-chloro-3-substituted-imidazol-4-yl)-5-substituted-1,3,4-oxadiazoles from aryl hydrazones5(a-f) and 6(a-e) using mild oxidant Chloramine-T. Chloramine – T is preferred over the classical oxidants like acetic anhydride and $KMnO_4$ to avoid side reactions.But, the reaction failed to afford the desired products. This may be due to the presence of bulky -Cl group attached to C-5 of 3and4 which sterically hinders the oxidative cyclization pathway.

4. CONCLUSION

A novel series of[(2-butyl-5-chloro-3-substituted-imidazol-4-yl)methylidene]carbohydrazones were synthesized and characterized based on their physical and spectral data. This work rules out the formation of 2-(2-butyl-5-chloro-3-substituted-imidazol-4-yl)-5-substituted-1,3,4-oxadiazoles form the synthesized hydrazones owing to the steric hindrance in *N*-substituted 2-butyl-5-chloro-4-formyl-3H-imidazole.

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