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Regioselective formylation and chemoselective oxidation of 1, 3, 5-triaryl pyrazoline: Synthesis of 4-(3,5-diaryl-1H-pyrazol-1-yl) benzaldehydes

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ABSTRACT

A novel regioselective formylation of 1, 3, 5-triarylpyrazoline by using Vilsmeire- Haack reaction is described. The formylation only observed in N-phenyl ring in the presence of phenolic or methoxy group in 3 & 5-aryl ring. Iodine, a readily available reagent, was found to be effective in carrying out chemoselective oxidation of 1, 3, 5-triaryl pyrazolines to 1, 3, 5-triaryl pyrazoles.

Keywords: Vilsmeire-Haack reaction, Dehydrogenation, 1, 3, 5-triarylpyrazole.

INTRODUCTION

Pyrazole compounds are important in pharmacological properties and biological activities [1-5]. N-aryl pyrazoles with withdrawing electron groups can be effectively utilized as insecticides [6] anti-inflammatory [7] analgesic [8] and cannabinoid type-1 (CB_1) receptor ligands [9].

The literature survey revealed that numerous N-substituted pyrazoles have been synthesized and exhibited wide biological activities.

The Vilsmeir-Haack reaction with electron rich aromatic and heterocyclic substitutes provide one of the widely used methods for formylation [10]. The 2'-hydroxyacetophenones undergo multiple iminoalkylation in the presence of excess of reagent and the resulting intermediate derived into the formation of 3-formylchromones [11]. α-methyl imine groups also under Vilsmeier-Haack condition, due to tautomerism of imine-enamine undergo multiple iminoalkylation reaction. For example the reaction of chloromethyleneiminium salt with 2,3,3-trimethylindolenine [12] and acetophenone phenylhydrazones [13] on alkaline hydrolysis leading to the formation of 2-malonaldehyde-3,3-dimethylindolenine and 4-formylpyrazoles respectively. On the other hand treatment of chloromethyleneiminium salt with α-methylene

imine group such as 6,7-dihydropyrazolo[1,5-a] pyrimidine derivatives [14], leads to mono iminoalkylation.

According to a literature survey, there is no report about reaction of Vilsmeier-Haack reagent on pyrazolines and oxidation which having electron reach aromatic rings, α-methyl and α-methylene imine groups. Herein, we wish to report, reaction of chloromethyleneiminium salt (Vilsmeir-Haack reagent) on, 1-phenyl-3, 5-diarylpyrazolines **2a-f** which possessing phenolic –OH & -OMe groups and N-phenyl moiety and α-methylene imine and oxidation of pyrazolines **3a-f** to pyrazole **4a-f**.

EXPERIMENTAL SECTION

^{1}H NMR spectra were recorded on 300-MHz spectrometer, and chemical shift values were recorded in δ units (ppm) relative to Me_4Si as internal standard. Melting points were determined by using a Buchi melting point apparatus. Infrared spectra (IR) were recorded using KBr pellets on a Perkin-Elmer 240C analyzer. Mass spectra were recorded in an AE-IMS-30 spectrometer. Tine layer chromatography (TLC) was performed on silica gel 60 PF254 plates or aluminum oxide plates from Merck.

General procedure for preparation of 2-(4, 5dihydro-1, 5-diaryl-1H-pyrazol-3-yl) phenol derivatives 2a-f:

To a solution of chalcone **1** (0.02mol) in 30 ml of methanol was added phenyl hydrazine (0.021mol) and refluxed for 6-9 h. After cooling of mixture of reaction, the product was precipitated and filtered. The crud product was crystallized from methanol.

2-(4, 5dihydro-1, 5-diphenyl-1H-pyrazol-3-yl) phenol (2a).

IR (KBr): ν 3236, 3167, 3088, 1596, 1496. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.25(dd, 1H, J_1= 17.4Hz, J_2= 7.5Hz), 3.96(dd, 1H, J_1= 15.9Hz, J_2= 12.6Hz, 5.23(dd, 1H, J_1= 12.3Hz, J_2= 7.2Hz), 6.81-6.91 (m, 2H), 6.94-6.98(m, 2H), 7.06(dd, 1H, J_1= 81Hz, J_2= 1.2Hz), 7.12(dd, 1H, J_1= 8.4Hz, J_2= 1.5Hz), 7.17-7.20(m, 2H), 7.22-7.31(m,2H), 7.33-7.36(m, 4H), 10.81(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 43.2, 55.4, 112.6, 114.2, 118.7, 119.9, 123.4, 127.8, 127.9, 131.6, 131.8, 133.1, 136.0, 146.6, 146.9, 149.3, 163.1. MS *m/z* (%): 314(M^+] (100), 237(86).

2-(4, 5-dihydro-5-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-3-yl) phenol (2b).

IR (KBr): ν 3132, 3099, 2958, 1601, 1500. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.23(dd, 1H, J_1= 17.25Hz, J_2= 7.5Hz), 3.78(s, 3H), 3.93(dd, 1H, J_1= 17.1Hz, J_2= 12.3Hz), 5.19(dd, 1H, J_1= 12.3Hz, J_2= 7.2Hz), 6.81-6.91(m, 4H), 6.96(d, 2H, J= 8.1Hz), 7.05(d, 1H, J= 8.4Hz), 7.12(d, 1H, J= 7.8Hz), 7.17-7.24(m, 5H), 10.81(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 42.8, 56.8, 57.8, 112.9, 113.5, 119.3, 121.8, 122.8, 122.5, 132.0 133.3, 133.9, 136.2, 138.7, 142.3, 150.9, 154.0, 159.8. MS *m/z* (%): 344(M^+] (100), 237 (90).

2-(5-(4-chlorophenyl)-4, 5-dihydro-1-phenyl-1H-pyrazol-3-yl) phenol (2c).

IR (KBr): ν 3140, 3049, 2924, 1597, 1494. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.22(dd, 1H, J_1= 18.15Hz, J_2= 7.8Hz), 3.96(dd, 1H, J_1= 16.8Hz, J_2= 12Hz), 5.21(dd, 1H, J_1= 11.25Hz, J_2= 7.5Hz), 6.83-6.89 (m, 2H), 6.93(d, 2H, J= 7.5Hz), 7.06(dd, 1H, J_1= 7.8Hz, J_2= 1.2Hz), 7.12(dd, 1H, J_1= 7.8Hz, J_2= 1.5Hz), 7.20(d, 2H, J= 7.5Hz), 7.22-7.35(m, 5H), 10.72(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 42.3, 55.7, 112.5, 115.0, 120.4, 121.4, 124.3, 129.8, 132.3, 132.9, 133.7, 134.0, 134.6, 140.2, 142.6, 149.3, 160.3. MS *m/z* (%): 348 (M^+] (100), 237 (83).

4-chloro-2-(4, 5-dihydro-1, 5-diphenyl-1H-pyrazol-3-yl) phenol (2d).
IR (KBr): ν 3097, 3055, 2935, 1597, 1492. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.23(dd, 1H, J_1= 16.95Hz, J_2= 7.5Hz), 3.93(dd, 1H, J_1= 17.1Hz, J_2= 11.7Hz), 5.27(dd, 1H, J_1= 12.3Hz, J_2= 7.5Hz), 6.85(t, 1H, J=7.5Hz), 6.94-7.00(m, 3H), 7.06(d, 1H, J=2.4Hz), 7.18-7.23(m, 3H), 7.27-7.38(m, 5H), 10.74(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 42.7, 54.8, 111.8, 119.2, 119.8, 122.3, 129.5, 129.7, 130.1, 130.3, 131.2, 135.1, 138.3, 148.0, 148.2, 153.7, 161.2. MS *m/z* (%): 348 (M^+] (100), 271(83).

4-chloro-2-(4, 5-dihydro-5-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-3-yl) phenol (2e).
IR (KBr): ν 3061, 3037, 1602, 1500. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.19(dd, 1H, J_1= 17.01Hz, J_2= 7.5Hz)**,** 3.78(s, 3H), 3.89(dd, 1H, J_1= 17.1Hz, J_2= 12.3Hz)**,** 5.22(dd, 1H, J_1= 12.3Hz, J_2= 7.2Hz)**,** 6.82-6.90(m, 3H), 6.94-7.00(m, 3H), 7.06(d, 1H, J=2.7Hz), 7.17-7.24(m, 5H), 10.75 (s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 42.7, 55.1, 59.3, 111.8, 115.3, 119.0, 119.3, 122.4, 128.0, 128.1, 129.9, 133.5, 133.9, 138.3, 144.9, 153.4, 159.2, 159.6. MS *m/z* (%): 378 (M^+] (100), 271(91).

4-chloro-2-(5-(4-chlorophenyl)-4, 5-dihydro-1-phenyl-1H-pyrazol-3-yl) phenol (2f).
IR (KBr): ν 3049, 3027, 1609, 1490. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.29(dd, 1H, J_1= 17.28Hz, J_2= 7.5Hz)**,** 3.93(dd, 1H, J_1= 17.3Hz, J_2= 12.15Hz)**,** 5.33(dd, 1H, J_1= 12.15Hz, J_2= 7.31Hz)**,** 6.92-6.98(m, 3H), 7.02-7.08(m, 3H), 7.18(d, 1H, J=2.7Hz), 7.21-7.24(m, 5H), 10.80 (s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 43.1, 55.7, 112.3, 119.0, 119.4, 122.1, 128.9, 130.6, 130.8, 131.5, 133.6, 136.4, 136.7, 144.3, 146.2, 150.3, 161.7. MS *m/z* (%): 382 (M^+] (100), 271(86).

General procedure of synthesis of 4-(4, 5- dihydro-3,-5-diaryl pyrazol-1-yl) benzal-dehyde 3a-f:
Phosphorus oxychloride (0.02mol) was added drop wise to N, N-dimethyl formamide (20ml) at 0 ^{o}C with stirring. After 20min a solution of 1, 3, 5- triarylpyrazoline **2** (0.01mol) in DMF (10ml) was added at same temperature to the reaction mixture which was, then warmed at room temperature and heated at 70 ^{o}C for 4-7h . After cooling at room temperature the mixture was basified with a cool saturated Na_2CO_3 solution. The precipitate was filtered, washed with water and crystallized from methanol.

4-(4, 5-dihydro-3-(2-hydroxyphenyl)-5-phenylpyrazol-1-yl) benzaldehyde (3a).
IR (KBr): ν 3333, 3163, 3086, 2924, 2829, 2750, 1685, 1595. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.35(dd, 1H, J_1= 17.4Hz, J_2= 5.7Hz)**,** 4.03(dd, 1H, J_1= 17.25Hz, J_2= 12.3Hz)**,** 5.38(dd, 1H, J_1= 12.15Hz, J_2= 5.4Hz)**,** 6.90(t, 1H, J=7.8Hz), 6.99(d, 2H, 8.7Hz), 7.07(d, 1H, J=8.4Hz), 7.14(d, 1H, J=7.8Hz), 7.28-7.38(m, 6H), 7.70(d, 2H, J= 8.7Hz), 9.75(s, 1H), 10.49(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 43.4, 58.6, 112.3, 116.8, 117.1, 120.4, 126.4, 126.6, 126.9, 128.3, 129.8, 130.8, 131.3, 143.9, 149.5, 152.3, 159.2, 190.9. MS *m/z* (%): 342 (M^+] (100), 265 (95).

4-(4,5-dihydro-3-(2-hydroxyphenyl)-5-(4-methoxyphenyl)pyrazol-1-ylbenzaldehyde (3b).
IR (KBr): ν 3338, 3005, 2808, 2727, 1680, 1584, 1514 cm^{-1}. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.33 (dd, 1H, J_1= 17.55Hz, J_2= 5.7Hz)**,** 3.75(s, 3H), 4.00(dd, 1H, J_1= 17.25Hz, J_2= 12.3Hz)**,** 5.35(dd, 1H, J_1= 11.7Hz, J_2=5.7Hz)**,** 6.86-6.94 (m, 3H), 7.01 (d, 2H, J= 8.7Hz), 7.09 (d, 1H, J= 8.4Hz), 7.15-7.21 (m, 3H), 7.32 (t, 1H, J= 7.2Hz), 7.71 (d, 2H, J= 8.7Hz), 9.76 (s, 1H), 10.52(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 43.9, 55.2, 61.5, 112.4, 114.7, 115.6, 116.7, 119.6, 126.7, 127.6, 128.0, 131.3, 131.6, 132.5, 147.4, 152.4, 157.2, 159.3, 190.3. MS *m/z* (%): 372(M^+] (100), 265 (94).

4-(5-(4-chlorophenyl)-4, 5-dihydro-3-(2-hydroxyphenyl) pyrazol-1-yl) benzaldehyde (3c). IR (KBr): ν 3155**,** 2922, 1678, 1593. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.32(dd, 1H, J_1= 19.05Hz, J_2= 5.4Hz)**,** 4.04 (dd, 1H, J_1= 17.1 Hz, J_2= 12.3Hz)**,** 5.37(dd, 1H, J_1= 12.15Hz, J_2= 6Hz)**,** 6.92(t, 1H, J= 7.2Hz), 6.98(d, 2H, J= 8.7Hz), 7.09(d, 1H, J= 8.4Hz), 7.15(d, 1H, J= 8.4Hz), 7.22(d, 2H, J= 8.4Hz), 7.31-7.36(m, 3H), 7.72(d, 2H, J= 9.9Hz), 9.78(s, 1H), 10.44(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 43.7, 59.1, 112.9, 113.1, 115.8, 119.5, 124.3, 128.6, 128.9, 130.6, 131.1, 132.0, 132.5, 141.4, 148.3, 150.0, 159.8, 189.9. MS *m/z* (%): 376 (M^+] (100), 265 (94).

4-(3-(5-chloro-2-hydroxyphenyl)-4, 5-dihydro-5-phenylpyrazol-1-yl) benza ldehyde (3d). IR (KBr): ν 3134, 3051, 2941, 2823, 2746, 1639, 1573, 1487. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.32(dd, 1H, J_1= 17.7Hz, J_2= 5.4Hz)**,** 4.00(dd, 1H, J_1= 18.3Hz, J_2= 12.3Hz)**,** 5.42(dd, 1H, J_1= 12.3Hz, J_2= 6.3Hz)**,** 6.98-7.04(m, 3H), 7.11(d, 1H, J= 2.4Hz), 7.23-7.27(m, 3H), 7.31-7.39(m, 3H), 7.71(d, 2H, J= 8.7Hz), 9.77(s, 1H), 10.48(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ43.1, 60.4, 112.4, 117.8, 119.1, 126.3, 127.0, 127.1, 128.6, 129.1, 130.0, 130.2, 132.8, 139.9, 148.7, 149.2, 158.3, 190.4. MS *m/z* (%): 376 (M^+] (100), 299 (94).

4-(3- (5-chloro-2-hydroxyphenyl)- 4, 5- dihydro-5- (4-methoxyphenyl) pyrazol-1-yl) benzaldehyde (3e). IR (KBr): ν 3144, 3063, 2931, 2835, 2742, 1685, 1595. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ3.29 (dd, 1H, J_1= 17.4Hz, J_2= 5.7Hz)**,** 3.78(s, 3H), 3.96(dd, 1H, J_1= 17.4Hz, J_2= 12.3Hz)**,** 5.38(dd, 1H, J_1= 12.3Hz, J_2= 5.7Hz)**,** 6.87(d, 2H, J= 8.7Hz), 6.99-7.03(m, 3H), 7.11(d, 1H, J= 2.7Hz), 7.17(d, 2H, J= 8.4Hz), 7.23-7.35(m, 1H), 7.71(d, 2H, J= 8.7Hz), 9.76(s, 1H), 10.46(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 44.1, 59.4, 61.9, 112.7, 114.2, 117.8, 119.9, 126.1, 127.0, 127.8, 130.2, 130.7, 132.5, 134.3, 147.1, 149.3, 157.6, 159.4, 190.8. MS *m/z* (%): 406 (M^+] (100), 299 (91).

4-(3-(5-chloro-2-hydroxyphenyl)-5-(4-chlorophenyl)-4,5-dihydropyrazol-1-yl)benzalde-hyde (3f). IR (KBr): ν 3099, 3033, 2978, 2815, 2750, 1687, 1585. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.29 (dd, 1H, J_1= 17.4Hz, J_2= 5.4Hz)**,** 4.00(dd, 1H, J_1= 17.55Hz, J_2= 12Hz)**,** 5.40(dd, 1H, J_1= 12.15Hz, J_2= 5.7Hz)**,** 6.98(d, 1H, J= 8.4Hz), 7.03(d, 2H, J= 8.7Hz), 7.10(d, 1H, J= 2.4Hz), 7.19-7.28(m, 3H), 7.35(d, 2H, J= 8.4Hz), 7.73(d, 2H, J= 8.7Hz), 9.79(s, 1H), 10.39(s, 1H). ^{13}C NMR: 43.6, 61.5, 112.6, 116.6, 118.2, 124.3, 126.4 126.8, 128.6, 129.7, 131.0, 131.7, 134.2, 138.7, 146.9, 150.9, 155.7, 190.3. MS *m/z* (%): 410 (M^+] (100), 299 (93).

General procedure of synthesis of 4-(3,5-diaryl-1H-pyrazol-1-yl) benzaldehyde 4a-f:
To solution of **3a-f** (10mmol) in DMSO (15ml), iodine (10mol %) was added. Then the reaction mixture was heated at 120 ^{o}C for 25-50min. After cooling, the mixture of reaction was poured onto crushed ice. The separated solid was filtered and washed with cooled dilute sodium thiosulphate solution. Then the crud product crystallized by methanol

4-(3-(2-hydroxyphenyl)-5-phenyl-1H-pyrazol-1-yl) benzaldehyde (4a).
IR (KBr): ν 3419, 3123, 2971, 2848, 1701, 1585, 1510. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 6.92(s, 1H), 6.95(t, 1H, J= 7.8Hz), 7.07(d, 1H, J= 7.8Hz), 7.24-7.31(m, 3H), 7.35-7.42(m, 3H), 7.52(d, 2H, J= 8.7Hz), 7.61(dd, 1H, J_1= 7.8Hz, J_2= 1.8Hz), 7.92(d, 2H, J= 8.7 Hz), 10.11(s, 1H), 10.43(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 105.7, 115.3, 118.5, 118.8, 120.8, 127.3, 127.9, 128.0, 128.7, 129.2, 129.7, 133.3, 133.8, 141.6, 142.1, 152.1, 158.3, 191.1. MS *m/z* (%): 340 (M^+] (100), 208(42).

4- (3- (2-hydroxyphenyl)-5- (4-methoxyphenyl) -1H-pyrazol-1-yl) benzaldehyde 4b.
IR (KBr): 3446, 3103, 3059, 2839, 2744, 1693, 1600, 1581, 1496 cm^{-1}; ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.85 (s, 3H), 6.86(s, 1H), 6.91 (d, 2H, J= 8.7Hz), 6.96 (t, 1H, J= 7.5Hz)

7.07(d,1H, J= 8.4Hz), 7.24(d, 2H, J= 8.4Hz), 7.28-7.31(m, 1H), 7.51(d, 2H, J= 8.7Hz), 7.64(dd, 1H, J_1=7.8Hz, J_2= 1.5Hz), 7.88 (d, 2H, J= 8,7Hz), 10.02 (s, 1H), 10.68(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 55.3, 105.4, 114.3, 115.7, 117.2, 119.4, 121.6, 124.5, 126.6, 129.9, 130.2, 130.4, 134.6, 143.8, 144.2, 152.7, 156.1, 160.2, 190.9. MS *m/z* (%): 370 (M^+] (100), 238(45).

4-(5-(4-chlorophenyl)-3-(2-hydroxyphenyl)-1H-pyrazol-1-yl) benzaldehyde (4c).
IR (KBr): ν 3437, 3134, 2920, 2850, 1693, 1599, 1510. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 6.92(s, 1H), 6.97(t, 1H, J= 8.1Hz), 7.07(d, 1H, J= 7.8Hz), 7.24-7.31(m, 3H), 7.37(d, 2H, J= 8.4Hz), 7.49(d, 2H, J= 8.7Hz), 7.63(dd, 1H, J_1= 7.9Hz, J_2= 1.5Hz), 7.90(d, 2H, J= 8.7 Hz), 10.03(s, 1H), 10.56(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 106.0, 115.5, 117.3, 119.5, 124.6, 126.6, 127.8, 129.2, 130.1, 130.5, 134.9, 135.5, 143.1, 143.4, 152.9, 156.12, 190.7. MS *m/z* (%): 374 (M^+] (100), 242(52).

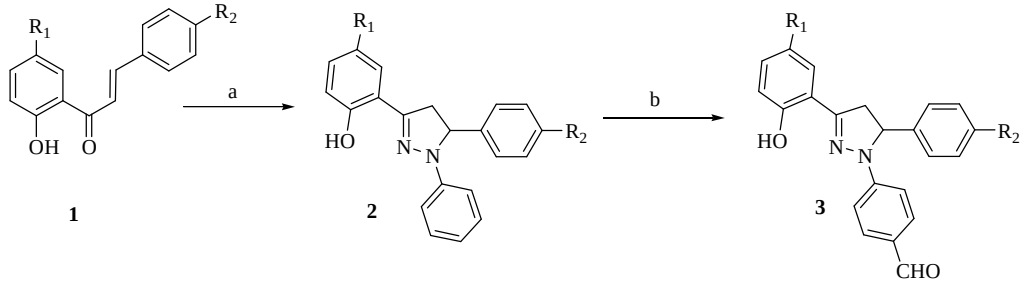
4-(3-(5-chloro-2-hydroxyphenyl)-5-phenyl-1H-pyrazol-1-yl) benzaldehyde (4d).
IR (KBr): ν 3427, 3136, 3078, 2829, 2735, 1701, 1600, 1548, 1508. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 6.90(s, 1H), 7.01(d, 1H, J= 8.4Hz), 7.20-7.31(m, 3H), 7.40-7.42(m, 3H), 7.49(d, 2H, J= 8.7 Hz), 7.60(d, 1H, J= 2.4Hz), 7.88(d, 2H, J= 8.7Hz), 10.02(s, 1H), 10.63(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 105.5, 116.6, 118.7, 121.2, 124.6, 125.9, 127.8, 127.9, 128.1, 128.4, 128.6, 130.0, 136.8, 142.8, 144.8, 156.1, 156.8, 191.1. MS *m/z* (%): 374 (M^+] (100), 208(48).

4-(3-(5-chloro-2-hydroxyphenyl)-5-(4-methoxyphenyl)-1H-pyrazol-1-yl)benzaldehyde (4e).
IR (KBr): ν 3441, 3134, 3007, 2837, 2739, 1701, 1600, 1508. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 3.85(s, 3H), 6.85(s, 1H), 6.92(d, 2H, 8.4Hz), 7.21-7.26(m, 3H), 7.50(d, 2H, J= 8.4Hz), 7.61(d, 1H, J= 7.5Hz), 7.72(d, 1H, J= 2.7Hz), 7.88(d, 2H, J= 8.4Hz), 10.03(s, 1H), 11.76(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 55.3, 105.3, 114.3, 117.0, 118.6, 121.3, 124.1, 124.6, 126.1, 129.5, 130.1, 130.4, 134.8, 143.6, 144.4, 151.6, 154.7, 160.3, 190.8. MS *m/z* (%): 404 (M^+] (100), 238(31).

4-(3-(5-chloro-2-hydroxyphenyl)-5-(4-chlorophenyl)-1H-pyrazol-1-yl) benzaldehyde (4f).
IR (KBr): ν 3423, 3156, 2994, 2881, 1756, 1561, 1497. ^{1}H NMR (300MHz, TMS, $CDCl_3$): δ 6.90(s, 1H), 7.01(d, 1H, J=9Hz) 7.20-7.27(m, 3H) 7.38(d, 2H, J=9Hz) 7.48(d, 2H, J=8.7Hz) 7.59(d, 1H, J=2.4Hz) 7.91(d, 2H, J=8.7Hz) 10.03(s, 1H) 10.55(s, 1H). ^{13}C NMR (75MHz, TMS, $CDCl_3$): δ 106.0, 116.1, 118.6, 124.6, 124.8, 126.3, 127.5, 129.2, 129.7, 130.0, 135.1, 135.6, 138.2, 142.9, 143.6, 150.0, 154.6, 190.6. MS *m/z* (%): 408 (M^+] (100), 242(39).

RESULTS AND DISCUSSION

The starting material, 1-phenyl-3, 5-diarylpyrazolines **2** were prepared by the reaction of phenyl hydrazine with 2'-hydroxy chalcones [15]. The pyrazolines **2** were reacted with two moles of DMF-$POCl_3$ adduct in DMF at 70-80^{o}C and the iminoalkylated intermediate hydrolyzed with saturated aq. sodium carbonate. The information about the structure was obtained by examining chemical shift of pyrazoline –CH_2 and –CH protons. The chemical shifts of these protons are as in the starting pyrazoline; (δCH_2 3.33 and 4.00, δCH = 5.35, for **3b**) however the chemical shift of aromatic protons on N-phenyl were significant. Two doublets (δ=7.71 and 7.01) with same chemical coupling, (J=8.7Hz, for **3b**) indicating formyl group enter at para position of N-phenyl group (Scheme 1).



Scheme 1: Reagent and conditions a: $PhNHNH_2$, MeOH, ref, 6-9hr. b: DMF/ $POCl_3$, 70°C, 4-7hr

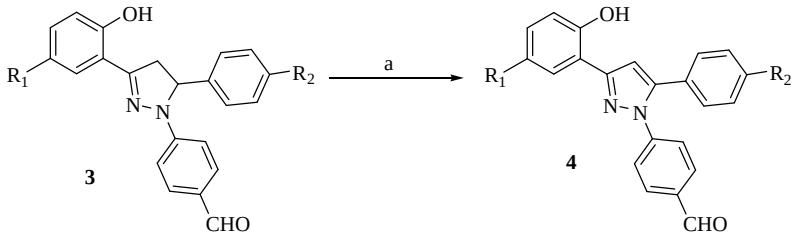
Table 1: Physico-chemical data of 2-(4, 5-dihydro-1,5-diaryl-1H-pyrazol-3-yl) phenol (2a-f) and 4-(4, 5-dihydro-3,5-diarylpyrazol-1-yl) benzaldehyde (3a-f)

Entry	R_1	R_2	m.p °C	Yield%
2a	H	H	162-163	67
2b	H	OMe	167-168	67
2c	H	Cl	152-153	68
2d	Cl	H	164-165	65
2e	Cl	OMe	156-157	69
2f	Cl	Cl	180-181	66
3a	H	H	164-165	85
3b	H	OMe	178-179	87
3c	H	Cl	186-188	89
3d	Cl	H	195-197	91
3e	Cl	OMe	174-175	86
3f	Cl	Cl	190-192	85

Other substitutes 2'-hydroxychalcones **1** similarly converted to pyrazolines **2** and they are reacted similarly to afford respective 4-(4, 5-dihydro-3,5-diarylpyrazol-1-yl) benzaldehyde **3a-f** in 85-91% yield (Table 1). All the pyrazolines use as substrates were having phenolic –OH & -OMe groups along with tautomery (imine-enamine) of α-methylene imine group. The electron donating ability of nitrogen in *N*-phenyl of pyrazoline is predominant the electron donating phenolic -OH & -OMe groups in other aryl ring and tautomery of α-methylene imine in five member ring. The formylation to 4-position of five member ring and in other aryl ring did not affected on increasing the molar ratio of reagent up to six molar for 48hrs.

The formyl group of N-arylpyrazoles could be utilized in the synthesis of derivative that could have potentially application as drugs. Hence we synthesized 4-(3,5-diaryl-1H-pyrazol-1-yl) benzaldehydes **4a-f** by oxidation of earlier prepared pyrazolines using extremely facile and environmental friendly method (Scheme 2). Actually, pyrazolines have been oxidized to the corresponding pyrazoles by several reagents such as lead tetra acetate [16], manganese dioxide [17], potassium permanganate [18], iodobenzene diacetate [19], $Zr(NO_3)_4$ [20] and Pd/C [21]. A careful examination reveals that most of these methods suffer from some serious drawback, the use of excess reagent, longer reaction time and toxicity associated with reagents such as lead tetra acetate make their use undesirable.

As we reported earlier, iodine mediated dehydrogenation of pyrazolines [22] to be general and most significantly, controllable for different substrate. Thus as shown in Scheme 2, pyrazoline **3** could be directly converted to pyrazole (**4e**, 92%yield) simply, by using 10% of iodine in dimethyl sulphoxide at 120°C in 40-60min (Table 2). We investigated dehydrogenation of 4-(4, 5-dihydro-3,5-diarylpyrazol-1-yl) benzaldehyde **3a-f** to 4-(3,5-diaryl-1H-pyrazol-1-yl) benzaldehydes **4a-f** without effecting the formyl group. The formyl & phenolic groups in aryl ring remain intact. On the basis of this favorable result several other pyrazolines containing formyl & phenolic group were oxidized to corresponding pyrazoles (86-92%), (Table 2).



Scheme 2: Reagent and condition: a) Iodine (10mol %.)/ DMSO, 120^{o}C, 25-50min

Table 2: Physico-chemical data of 4-(3,5-diaryl-1H-pyrazol-1-yl) benzaldehydes (4a-f)

Entry	R_1	R_2	m.p ^{o}C	Yield% [a]
4a	H	H	189-191	89
4b	H	OMe	196-198	86
4c	H	Cl	209-211	88
4d	Cl	H	202-204	87
4e	Cl	OMe	218-220	92
4f	Cl	Cl	224-226	91

[a] Yield refers to the yield of pure isolated products

CONCLUSION

The formylation on 1-phenyl-3, 5-diarylpyrazolines **2** regioselectively occurred at para position of N-phenyl group in presence of phenolic in 3-aryl, methoxy group in 5-aryl and methylene group in five member ring. The resulting formyl pyrazolines aromatized to corresponding pyrazoles by extremely facile and environmentally benign oxidation by using catalytic iodine in dimethylsulfoxide. The reaction is chemoselective for generation of double bond in presence of formyl group. The advantages of the present oxidation method are the operational simplicity and elimination of the toxic metal oxidant.

REFERENCES

[1] G Menozzi; L Mosti; P Fossa; F Mattioli; Ghia *J. Heterocycl. Chem***. 1997**, 34, 963.
[2] J Haufel; E Breitmaier. *Angew. Chem*. **1974**, 13, 604.
[3] DJ Wustrow; T Capiris; R Rubin; JA Knobelsdorf; H Akunne; MD Davis; R MacKenzie; TA Pugsley; KT Zoski; TG Heffner; LD Wise *Bioorg. Med. Chem. Lett*. **1998**, 8, 2067.
[4] AI Eid; MA Kira; HH Fahmy *J. Pharm. Belg*. **1978**, 33, 303.
[5] F Bondavalli; O Bruno; A Ranise; P Schenone; D Donnoli; ML Cenicola; C Matera; S Russo; E Marmo *Farmaco*, **1989**, 44, 655.
[6] RE Sammelson; P Caboni; KA Durkin; JE Casida *Bioorg. Med. Chem*. **2004**, 12, 3345.
[7] R Sridhar; PT Perumal.; S Etti; G Shanmugam; MN Ponnuswamy; VR Prabayathy; N Mathivanan *Bioorg. Med. Chem. Lett*. **2004**, 14, 6035.
[8] E Banoglu; M Sukuroglu; B Caliskan; S Nacak; E Aypar; M Ark *Turk J. Chem*. **2007**, 31, 677.
[9] SR Donohue; C Halldin; VW Pike *Bioorg. Med. Chem*. **2006**, 14, 3712.
[10] a) CM Massa *Tetrahedron* **1992**, 48, 3659. b) C Jutz; In Advances in Organic Chemistry 9: Taylor EC,Wiley; New York: **1976**. p.225-342.
[11] a) S Shrestha; SY Hwang; KH Lee; H Cho *Bull.Korean Chem. Soc*. **2005**, 26, 1138. b) M Lacova; D Loos; M Furdik; M Matulova; HM El-Shaaer *Molecules*, **1998**, 3, 149.
[12] MM Baradarani; A Afghan; F Zebarjadi; K Hasanzadeh; JA Joule *J. Heterocyclic Chem*. **2006**, 43, 1591.

[13] a) MA Kira; MO Abdel-Rahman; KZ Gadalla *Tetrahedron Lett*. **1969**, 10, 109. b) O Prakash; R Kumar; V Bhardwaj; PK Sharma *Heterocycle. Commun*. **2003**, 9, 515. c) O Prakash; K Pannu; A Kumar *Molecules* **2006**, 11, 43.
[14] J Quiroga; J Trilleras; B Insuast; R Abonia; M Nogueras; J Cobo *Tetrahedron Lett*. **2008**, 49, 2689.
[15] a) OM Hafez; KM Ahmed; EE Haggag *Molecules*, **2001**, 6, 396. b) D Azarifar; M Shaebanzadeh *Molecules*, **2002**, 7, 885.
[16] WA Gladston; OC Norman *J. Chem. Soc., Chem. Commun*.**1966**, 1536.
[17] I Bhatnagar; MV George *Tetrahedron* **1968**, 24, 1293.
[18] LI Smith; KL Haward *J. Am. Chem. Soc*. **1943**, 65, 159.
[19] SP Singh; D Kumar; O Prakash; RP Kapoor *Synth. Commun*.**1997**, 27, 2683.
[20] G Sabitha; GSK Kumar Reddy.; CS Reddy; N Fatima; JS Yadav *Synthesis* **2003**, 1267.
[21] N Nakamichi; Y Kawashita; M Hayashi *Org. Lett.* **2002**, 4, 3955.
[22] PD Lokhande; BY Waghmare; SS Sakate *Indian J. Chem. Sect. B*, **2006**, 44, 2338.