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Synthesis and Oxidative Aromatization of 3, 5-disubstituted-2- Pyrazolines by $Ce(SO_4)_2.4H_2O$ as a Convenient Oxidizing Agent.

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ABSTRACT

Ceric sulfate tetra hydrate in aqueous acetic acid acts as an efficient oxidant for the oxidative aromatization of pyrazolines to pyrazoles. Chalcones and hydrazine hydrate are used to prepare pyrazolines in DMSO as solvent. The synthesized pyrazolines are purified by recrystallization and fully characterized by various analytical techniques before oxidation. Ce $(SO_4)_2.4H_2O$ and pyrazolines ratio as 1: 2 was found to be the most favorable condition for oxidative aromatization. The solubility of ceric sulfate tetra hydrate and pyrazolines was enhanced by addition of aqueous acetic acid. The reversible conversion of Ce^{3+} to Ce^{4+} is an electron transfer process achieved by the oxygen present in the air which plays an important role in oxidative aromatization of pyrazolines. For this oxidation a radical cation mechanism is proposed. The oxidation products were isolated in high purity and good to moderate yields. All the oxidized pyrazolines are fine crystalline substances with sharp physical constants.

Keywords: pyrazolines, oxidative aromatization, ceric sulfate tetra hydrate, electron transfer, aqueous acetic acid

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INTRODUCTION

Heterocyclic compounds are well known for their wide range of biological applications [1-5] out of which pyrazolines occupy unique position due to dominant applications. Pyrazolines are known to possess antitubercular [6], anti HIV [7], antiviral [8], antimicrobial [9 -10], cerebroprotective [11], and Molluscicidal [12], antifungal [13], anti-inflammatory [14], properties etc. One of the important applications of pyrazoline is the use of pyrazolines as a fluorescent brightening agent [15]. They can absorb light of 300-400 nm and emit blue fluorescence. Pyrazolines are also acting as hole transporting material in OELD (organic electroluminescent device) because of formation of p-π conjugated system due to one of the nitrogen atom. Furthermore, the oxidative aromatization of 1, 3, 5-trisubstituted 2-pyrazolines to pyrazoles is of great biological importance because of their analgesic, anti-inflammatory, antipyretic, antiarrhythmic, muscle relaxant, psychoanaleptic, antidiabetic and antibacterial activities [16, 17]. Pyrazolines have variety of methods for its synthesis but one of the popular methods is of Fischer and Knoevenagel i.e. the reaction of α, β-unsaturated ketones with phenyl hydrazine in acetic acid under refluxing condition. However depending on the reactivity of molecules and need of the chemist they have synthesized the pyrazolines under different solvent media & acidic or basic conditions [18-20]. Such a glamour history prompted us to synthesize pyrazolines as an urgent need which can possess biological and medicinal importance. Therefore we have synthesized here some pyrazolines from chalcones and hydrazine hydrate in DMSO (scheme 1). In view of the simple preparation of 2-pyrazolines, their aromatization by suitable oxidants should provide a convenient approach to pyrazoles. In this regard, a variety of oxidizing agents such as Zr $(NO_3)_4$, [21] Pd/C, [22]

Co (II) and oxygen, [23] MnO_2, [24] iodobenzene diacetate, [25] and lead tetra acetate [26], I_2-DMSO [27] have been reported. However, most of these reagents present several disadvantages including long reaction times, high temperature, unavailability of the reagents, toxicity because of the presence of certain toxic elements in these reagents, hard work up, and unsatisfactory yields of the products. To overcome these drawbacks, there is a need to search for new high-yielding, environmentally safe, and cheaply available reagents for conversion of 2- pyrazolines to pyrazoles. In continuation of ongoing research on oxidation of 1, 3, 5-trisubstituted 2-pyrazolines [28 - 34], previously we reported that $Ce(SO_4)_2.4H_2O$ works very smoothly for oxidative dehydrogenation of substituted dihydropyridine derivatives in excellent yield [35] and oxidative dehydrogenation of 3, 4-dihydropyrimidin-2-(1*H*)-one by Ce $(SO_4)_2.4H_2O$ [36], so we thought that Ce $(SO_4)_2.4H_2O$ can be used for oxidation of pyrazolines. Here in we report an efficient oxidative aromatization of 3, 5-disubstituted 2-pyrazolines to their corresponding pyrazoles using crystalline Ce $(SO_4)_2.4H_2O$ in aqueous acetic acid (Scheme 2).

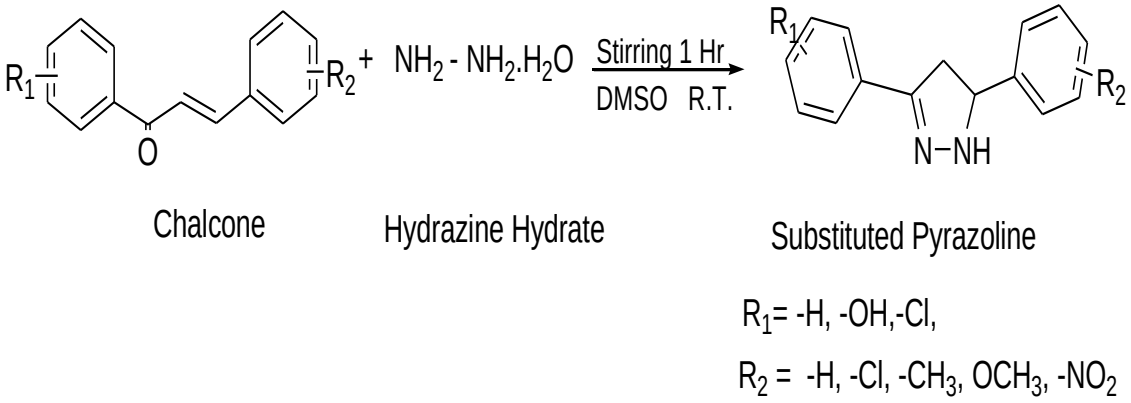
MATERIALS AND METHODS

AR grade chemicals purchased from local companies were used without further purification. IR spectra were recorded on FT-IR 8400 Shimadzu Model.^{1}H NMR spectra were recorded on Varian Mercury, YH- 300 MHz spectrometer in $CDCl_3$ / DMSO and chemical shifts are recorded as delta in ppm units. The reaction products are identified by physical

constant, IR and NMR spectroscopy. The product obtained after work up was purified by recrystallzation from ethanol.

General Procedure for synthesis of 3, 5-disubstituted - 2-Pyrazolines from chalcones

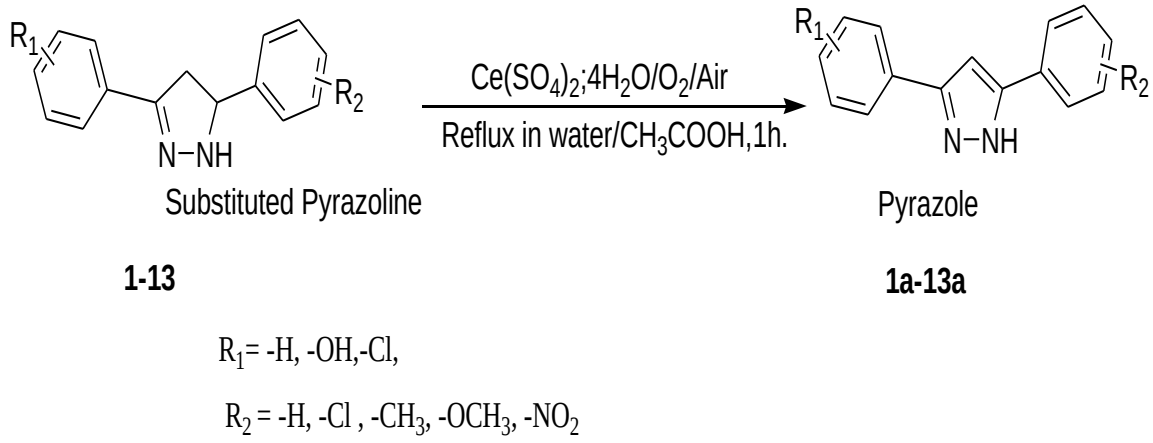
A chalcone, 0.5gm (0.0015 moles) dissolved in DMSO (10 mL) and hydrazine hydrate, 5mL (80% solution) added to it drop wise with constant stirring for 1 hour at room temperature. Yellow colored solution turned colorless with formation of white precipitate, crushed ice (20 gm) added to reaction mixture, white product filtered and washed many times with water, crude product recrystallized from methanol.



Scheme 1. Synthesis of 3, 5-disubstituted 2-Pyrazolines

A typical procedure for the oxidative aromatization of 3, 5-disubstituted 2-Pyrazolines

A mixture of the 3, 5-disubstituted 2-Pyrazolines (1mmol) and ceric sulfate tetra hydrate (0.808 g, 2mmol) in 20mL distilled water and 5 mL of acetic acid heated under reflux for 1h. The solution was cooled to room temperature and neutralized with aqueous $NaHCO_3$. It was then extracted with Et_2O (3x10mL) and dried over anhydrous Na_2SO_4. The solvent was removed by using rotavapour and the resulting crude product obtained was recrystallized from EtOH to give colorless crystals of the product.



Scheme 2. Oxidative aromatization of 3, 5-disubstituted 2-Pyrazolines

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SPECTRAL DATA FOR SELECTED COMPOUNDS

Pyrazoline 1:	2-(4,5-dihydro-5-*p*-tolyl-1*H*-pyrazol-3-yl)phenol. M.F. $C_{16}H_{16}N_2O_2$, yield 64 %, mp 131°C, FTIR (KBr) 784,1294,3025, 3374$cm^{-1,}$ ^{1}HNMR (DMSO) 1.22 δ, t, (1H J = 6 Hz), 2.10 δ, s, (3H), 3.06 δ, q, (1H J = 6 Hz, J = 9 Hz), 3.50 δ, q, (1H, J = 6Hz, J = 9Hz), 6.92-7,20 δ, m, (4H J = 8 Hz, J = 2 Hz), 7.22-7.40 δ, m, (4H J = 8 Hz),11.5 δ,s,(1H broad).
Pyrazoline 2:	2-(5-(4-chlorophenyl) - 4, 5-dihydro-1*H*-pyrazol-3-yl) phenol. M.F. $C_{15}H_{13}ClN_2O$, yield 67 %, mp 135°C, FTIR (KBr) 731, 822, 1264, 2919, 3339$cm^{-1,}$ ^{1}HNMR (DMSO1.13 δ, t, (1H J = 6 Hz), 3.22 δ, q, (1H J = 6Hz, J = 9 Hz), 3.65 δ,q, (1H J = 6Hz, J = 9 Hz), 6.84 δ, d,(2H J = 8Hz), 6.96 δ, d,(2H J = 8Hz),7.18-7.46 δ, m,(4H J = 2Hz, J = 8 Hz),11.0 δ, s, (1H broad).
Pyrazoline 3:	4, 5-dihydro-3-phenyl-5-*p*-tolyl-1*H*-pyrazole. M.F. $C_{16}H_{16}N_2$, yield 60 %, mp 108 °C, FTIR (KBr) 784,1294,3025, $cm^{-1,}$ ^{1}HNMR (DMSO) 1.24 δ, t, (1H, J = 6 Hz), 2.08 δ, s, (3H), 3.04 δ, q, (1H J = 6 Hz, J = 9 Hz), 3.44 δ, q, (1H J = 6 Hz, J = 9 Hz), 6.82-7.13 δ, m, (4H J = 2 Hz, J = 8Hz), 7.19-7.36 δ, m, (5H J = 2 Hz, J = 8Hz), 1.98 δ, s, (1Hbroad).
Pyrazoline 4:	5-(4-chlorophenyl) - 4, 5-dihydro-3-phenyl-1*H*-pyrazole. M.F. $C_{15}H_{13}ClN_2$, yield 72 %, mp 120°C, FTIR (KBr) 784,1294,3025 $cm^{-1,}$ ^{1}HNMR (DMSO) 0.9 δ, t, (1H J = 6 Hz), 2.89 δ, q, (1H J = 6 Hz, J = 9Hz),), 3.12 δ, q, (1H J = 6 Hz, J = 9Hz),), 6.91 δ, dd, (2H J = 8Hz),7.14 δ, dd ,(2H J = 8Hz),7.26 δ, m, (5H),1.95 δ, s,(1H broad).
Pyrazoline 5:	4-chloro-2-(4, 5-dihydro-5-phenyl-1H-pyrazol-3-yl) phenol. M.F. $C_{15}H_{13}ClN_2O$, yield 65 %, mp 96 °C, FTIR (KBr) 893, 1273, 2955 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.22 δ, t, (1H, J = 6 Hz), 2.90 δ, dd, (1H J = 6 Hz, J = 9Hz),3.18 δ, dd, (1H, J = 6 Hz, J = 9Hz),3.8 δ, d, (1H J = 9Hz), 6.98 δ, m, (5H), 7.2 δ, s, (1H J = 9Hz), 7.43 δ, dd, (1H J = 2 Hz, J = 8Hz), 7.56 δ, d, (1H J = 8Hz).
Pyrazoline 6:	2-(4, 5-dihydro-5-(3, 5-dimethoxyphenyl)-1*H*-pyrazol-3-yl) phenol.M.F.$C_{17}H_{18}N_2O_3$, yield 68 %, mp 95°C, FTIR (KBr)1203,1514, 1687, 2840,3058 cm^{-1} ^{1}HNMR (DMSO) 1.02 δ, t, (1H J = 6Hz), 2.73 δ, dd, (1H J = 6 Hz, J = 9Hz), 3.09 δ, dd, (1H J = 6 Hz, J = 9Hz), 3.75 δ, s, (3H), 3.80 δ, s, (3H), 6.98,dd, (2H J = 6Hz), 7.12 δ, t, (1H J = 2Hz), 7.24 δ, t, (1H J = 2Hz, J = 8Hz), 7.32-7.44 δ, m, (3H J = 2 Hz, J = 8Hz),
Pyrazoline 7:	2-(4,5-dihydro-5-phenyl-1*H*-pyrazol-3-yl)phenol. M.F. $C_{15}H_{14}N_2O$, yield 66 %, mp 88 °C, FTIR (KBr) 747, 1291, 3031, 3338 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.20 δ, t, (1H J = 6 Hz), 3.04 δ, q, (1H J = 6 Hz, J = 9 Hz), 3.50 δ, q, (1H, J = 6Hz, J = 9Hz), 6.92-7,20 δ, m, (4H J = 8 Hz, J = 2 Hz), 7.22-7.40 δ, m, (4H J = 8 Hz),11.5 δ, s,(1H broad).
Pyrazoline 8:	2-(4,5-dihydro-5-(4-methoxyphenyl)-1*H*-pyrazol-3-yl) phenol. M.F. $C_{16}H_{16}N_2O_2$, yield 74 %, mp 103 °C, FTIR (KBr) 742, 1291, 2916, 3337 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.18 δ, t, (1H J = 6Hz), 3.06 δ, q, (1H, J = 6 Hz, J = 9 Hz), 3.56 δ, q, (1H J = 6 Hz, J = 9 Hz) 6.90 δ, dd, 2H J = 8 Hz), 7.08 δ, dd ,(2H),5.5 δ, s,(1H broad), 6.8 δ, d, (2H),7.2 δ, d, (2H J = 8Hz)), 7.18-7.28 δ, m, (4H J = 2Hz J = 8 Hz).

Pyrazoline 9:	2, 4-dichloro-6-(4, 5- dihydro-5-(4-methoxy phenyl)-1*H*-pyrazol-3-yl) phenol. M.F. $C_{16}H_{14}Cl_2N_2O_2$, yield 72 %, mp 112 °C, FTIR (KBr) 856, 1244, 1258, 3003, 3368 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.25 δ, t, (1H, J = 6 Hz), 2.80 δ, q, (1H J = 6 Hz) 3.15 δ, q,(1H J = 6 Hz, J = 9 Hz), 3.98 δ, s, (1H), 6.86 δ, dd, (2H J = 8 Hz), 7.01 δ, dd, (2H J = 8 Hz), 7.22 δ, d, (1H J = 2 Hz),7.30 δ, d ,(1H J = 2Hz).
Pyrazoline10:	3-(4, 5-dihydro-5-(3-nitrophenyl)-1*H*-pyrazol-3-yl) phenol. M.F. $C_{15}H_{13}N_3O_3$, yield 77 %, mp 114°C, FTIR (KBr) 683, 1477, 2915 cm^{-11}HNMR (DMSO) 1.6 δ, t, (1H J = 6 Hz), 3.05 δ, dd, (1H J = 6 Hz, J = 9 Hz), 3.85 δ, dd, (1H J = 6 Hz, J = 9 Hz),6.8-7.30 δ, m, (4H J = 2Hz, J = 8 Hz), 7.6 δ, dd, (1H J = 2 Hz, J = 8 Hz), 7.8 δ, dd, (1H J = 2 Hz, J = 8 Hz), 8.2 δ, dd, (1H J = 2 Hz, J = 8 Hz), 8.38 δ, d, (1H J = 2 Hz), 6.2 δ, s, (1Hbroad),
Pyrazoline11:	4, 5-dihydro-5-(3-nitrophenyl)-3- phenyl -1*H*-pyrazole. M.F. $C_{15}H_{13}N_3O_2$, yield 75 %, mp 92 °C, FTIR (KBr) 683, 1477, 2915, 3295 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.84 δ, t, (1H J = 6 Hz), 3.15 δ, dd, (1H J = 9Hz), 3.21δ, dd,(1H J = 6 Hz, J = 9Hz), 7.55-7.68 δ, m, (4H J = 2Hz, J = 8 Hz), 7.8-7.96 δ, m, (5H J = 2Hz, J = 8 Hz).
Pyrazoline12:	2, 4-dichloro-6 - (5-(4-chlorophenyl) - 4, 5-dihydro-1*H*-pyrazol-3-yl) phenol. M.F. $C_{15}H_{11}Cl_3N_2O$, yield 73 %, mp 115°C, FTIR (KBr) 1264, 1533, 2986, 3054 cm^{-1}, ^{1}HNMR (DMSO) 0.92 δ, t, (1H J = 6Hz), 3.04 δ q, (1H J = 6Hz, J = 9 Hz), 3.49 δ, q, (1H J = 6Hz, J = 9Hz),4.93δ, t, (1H J = 9 Hz), 6.13 δ, d, (2H J = 2 Hz), 6.8-7.22, m, (4H J = 8Hz), 7.10-7.25 δ, m, (5H J = 2 Hz, J = 8 Hz).
Pyrazoline13:	2, 4-dichloro-6-(4, 5- dihydro-5-(3, 4-dimethoxy phenyl)-1*H*-pyrazol-3-yl) phenol. M.F. $C_{17}H_{16}Cl_2N_2O_3$, yield 69 %, mp 118 °C, FTIR (KBr) 771, 1260, 2954, 3337cm^{-1}, ^{1}HNMR (DMSO) 1.20 δ, t, (1H J = 6Hz), 3.10 δ dd, (1H J = 6Hz, J = 9 Hz), 3.50 δ, dd, (1H J = 6Hz, J = 9 Hz), 6.95 δ, d, (1H J = 8 Hz), 7.08 δ, dd, (1H J = 2Hz, J = 8 Hz), 7.18 δ, d, (1H J = 2Hz), 7.22 δ, d, (1H J = 2Hz), 7.34 δ, d, (1H J = 2Hz).
Pyrazole 1a:	2-(5-*p*-tolyl-1*H*-pyrazol-3-yl) phenol. M.F. $C_{16}H_{14}N_2O$, mp 183 °C, FTIR (KBr) 733, 1264, 1693, 2956 cm^{-1}, ^{1}HNMR (DMSO) 2.10 δ, s, (3H), 3.67 δ, s, (1H), 6.80 δ, dd, (2H, J = 8 Hz),6.94δ, dd, (2H J = 8 Hz), 7.13 δ, dd, (1H J = 8 Hz), 7.22-7.35 δ, m, (3H J = 2 Hz, J = 8 Hz).
Pyrazole 2a:	2-(5-(4-chlorophenyl)-1*H*-pyrazol-3-yl) phenol. M.F. $C_{15}H_{11}ClN_2O$, mp 191 °C, FTIR (KBr) 755, 1091, 1531, 2918,3281 cm^{-1} ^{1}HNMR (DMSO) 3.41 δ, s, (1H), 6.77 δ, dd, (2H J = 2Hz, J = 8 Hz), 7.11 δ, dd, (2H J = 2Hz, J = 8 Hz), 7.26 -7.34 δ, m,(4H).
Pyrazole 3a:	3-phenyl-5-*p*-tolyl-1*H*-pyrazole. M.F. $C_{16}H_{14}N_2$, mp 175 °C, FTIR (KBr) 820, 1351, 1678, 2916 cm^{-1}, ^{1}HNMR (DMSO) 2.15 δ, s, (1H), 3.41 δ, s, (1H), 6.72 δ, dd, (2H, J = 8Hz), 7.08 δ, dd, (2H J = 8 Hz),7.22, δ, m, (5H).
Pyrazole 4a:	5- (4-chlorophenyl)-3-phenyl-1*H*-pyrazole. M.F. $C_{15}H_{11}ClN_2$, mp 215 °C, FTIR (KBr) 756, 1579, 1665, 2921 cm^{-1}, ^{1}HNMR (DMSO) 3.43 δ, s,

	(2H J = 8Hz), 6.80 δ, dd, (2H J = 8Hz), 6.94 δ, dd, (2H J = 8Hz), 7.18, δ, m,(5H).
Pyrazole 5a:	4-chloro-2-(5-phenyl-1*H*-pyrazol-3-yl) phenol. M.F. $C_{15}H_{11}ClN_2O$, mp 170 °C, FTIR (KBr) 733, 1598, 1676, 2914, 3713 cm^{-1}, ^{1}HNMR (DMSO) 3.43 δ, s, (1H), 6.84 -7.14 δ, m,(5H), 7.21, δ, d, (1H, J = 8 Hz). 7.08, δ, d, (1H J = 8 Hz). 7.35, δ, d, (1H, J = 2 Hz).
Pyrazole 6a:	2-(5-(3, 5-dimethoxyphenyl)-1*H*-pyrazol-3-yl) phenol. M.F. $C_{17}H_{16}N_2O_3$, mp 110 °C, FTIR (KBr) 732, 1203, 1514, 1687, 2840,3058 cm^{-1},^{1}H NMR (DMSO) 3.40 δ, s, (1H), 3.83 δ, s, (6H), 6.70, δ, dd, (1H, J = 2 Hz), 7.22, δ, dd, (2H, J = 2Hz), 7.35, δ, dd, (1H J = 2 Hz, J = 8Hz), 7.41-7.88 δ, m, (3H).
Pyrazole 7a:	2- (5-phenyl-1*H*-pyrazol-3-yl) phenol. M.F. $C_{15}H_{12}N_2O_2$, mp 144 °C, FTIR (KBr) 608, 1088, 2923, 3390 cm^{-1},^{1}HNMR (DMSO) 3.34 δ, s, (1H), 6.8 δ, m, (5H), 6.92 δ, dd, (1H J = 2 Hz, J = 8Hz), 7.22, δ, m, (3H).
Pyrazole 8a:	2-(5-(4-methoxyphenyl)-1*H*-pyrazol-3-yl) phenol. M.F. $C_{16}H_{14}N_2O_2$, mp 178 °C, FTIR (KBr) 732, 1264, 1642, 2956,3332 cm^{-1}, ^{1}HNMR (DMSO) 3.31 δ, s, (1H), 3.78 δ, s, (3H), 6.63 δ, dd, (2H J = 8Hz), 6.76, δ, dd, (2H J= 8 Hz). 7.13, δ, dd, (1H J = 2 Hz, J = 8Hz), 7.20, δ, m, (3H).
Pyrazole 9a:	2,4-dichloro-6-(5-(4-methoxyphenyl)-1*H*-pyrazol -3-yl) phenol. M.F. $C_{16}H_{12}Cl_2N_2O_2$, mp 135 °C, FTIR (KBr) 755, 1250, 1642, 2956, 3383cm^{-1}, ^{1}HNMR (DMSO) 3.46 δ, s, (1H), 3.77 δ, s, (3H), 6.70 δ, dd, (2H J = 8 Hz), 6.88, δ, dd, (2H J = 8 Hz). 7.03, δ, d, (1H, J = 2 Hz), 7.11, δ, d, (2H J = 2Hz).
Pyrazole 10a:	3-(5-(3-nitrophenyl)-1*H*-pyrazol-3-yl) phenol. M.F. $C_{15}H_{11}N_3O_3$, mp 114 °C, FTIR (KBr) 735, 1350, 1531, 2849, 3055 cm^{-1} ^{1}HNMR (DMSO) 3.40 δ, s, (1H), 6.93 δ, d, (1H J = 2 Hz), 7.12 δ, m, (3H), 7.21, δ, dd, (1H J = 2 Hz, J = 8 Hz). 7.35, δ, d, (1H, J = 2 Hz), 7.45, δ, m, (2H).
Pyrazole 11a:	5-(3-nitrophenyl)-3-phenyl-1*H*-pyrazole M.F. $C_{15}H_{11}N_3O_2$, mp 98 °C, FTIR (KBr) 732, 1349, 1350, 1709, 2917, 3057 cm^{-1} ^{1}HNMR (DMSO) 3.43 δ, s, (1H), 6.93 δ, m, (5H), 7.32 δ, d, (1H J = 2 Hz), 7.44, δ, m, (2H).
Pyrazole 12a:	2, 4-dichloro-6-(5-(4-chlorophenyl)-1*H*-pyrazol-3-yl) phenol. M.F. $C_{15}H_9Cl_3N_2O$, mp 297°C, FTIR (KBr) 731, 1264, 1533, 2986, 3054 cm^{-1},^{1}HNMR (DMSO) 3.45 δ, s, (1H), 6.80 δ, dd, (2H J = 8Hz), 6.95 δ, dd, (2H J =8 Hz), 7.21 δ, d, (1H J = 2 Hz), 7.30, δ, d, (1H J = 2 Hz).
Pyrazole 13a:	2, 4-dichloro-6-(5-(3, 4-dimethoxyphenyl)-1*H*-pyrazol-3-yl) phenol. M.F.$C_{17}H_{14}Cl_2N_2O_3$, mp 147 °C, FTIR (KBr) 732, 1265, 1511, 2916, 3056 cm^{-1},^{1}HNMR (DMSO) 3.2 δ, s, (1H), 3.94 δ, s, (6H), 6.70 δ, d, (1H J =2Hz), 6.88 δ, dd, (2H J = 2 Hz), 7.07, δ, s, (1H J = 2 Hz), 7.13, δ, s, (1H J = 2 Hz)

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RESULTS AND DISCUSSION

In our previous work we had reported oxidative dehydrogenation of substituted dihydropyridine dicarboxylates [34] and 3, 4-dihydro pyrimidin-2-(1*H*)-one by Ce $(SO_4)_2.4H_2O$ [35]. In present work we studied the optimization of reaction conditions for oxidative aromatization of 3, 5-disubstituted 2-Pyrazolines using ceric sulfate tetra hydrate as convenient reagent in aqueous acetic acid for 1 hour. There is no any report in which the effect of medium has been studied for pyrazolines leaving considerable scope for the development of an environmental friendly aqueous medium for this transformation.

Optimization of reaction condition

Effect of solvent

Initially this oxidation was carried out in presence of ceric sulfate tetra hydrate and water only, the reaction mixture contained the oxidized and unoxidized pyrazolines; this may be due to less solubility of ceric sulfate in water at room temperature. Generally the ceric sulfate is soluble in acidic medium and warm condition. To enhance the solubility of ceric sulfate tetra hydrate. To start with 1mL acetic acid was added in reaction mixture and reaction was monitored by TLC. It was found that unoxidized pyrazolines still remained in reaction mixture due to less solubility of ceric sulfate tetra hydrate. So we increased volume of acetic acid from 1mL to 5mL and it was found that reaction goes to complete oxidation smoothly by using 5 mL acetic acid.

Effect of amount of ceric sulfate tetra hydrate

The oxidation of pyrazolines were also tried by using various molar ratio of pyrazolines : ceric sulfate tetra hydrate (1:1, 1:1.5, 1:2 and 1: 2.5) in presence of water (20 ml) and acetic acid (5 ml) under reflux condition. It was found that when 1:1and 1:1.5 molar ratios were taken a mixture of oxidized and unoxidized derivatives were obtained. When 2 equivalent of ceric sulfate and 5 ml of acetic acid were taken and the product obtained was studied by TLC, IR, ^{1}HNMR, to check for any unoxidized pyrazolines there was no trace amount of starting material in the product. Negligible change was observed by taking 2.5 equivalent of ceric sulfate. Finally under the condition of 2 equivalent ceric sulfate and 5 ml of acetic acid were taken and thirteen pyrazolines were successfully oxidized.

Role of water

Cost, safety, synthetic efficiency, simple operation, environmental benefits, potential for new synthetic methodologies, solvation, and hydrophobic effect are the benefits of water. It is important to note here that until now in the literature, the oxidation of pyrazolines was carried out in a variety of reagent or catalyst in different organic solvent. However, to the best of our knowledge nobody has reported the oxidation of pyrazolines using water as solvent which probably may be due to low solubility of both pyrazolines and ceric sulfate which was overcome by using 5 ml acetic acid. This process also reports the efficiency of this reagent towards the oxidation of pyrazolines. By using ceric sulfate tetra

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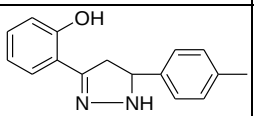
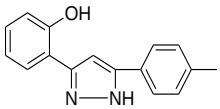
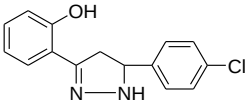
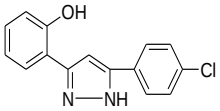
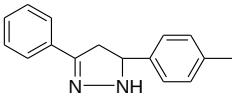
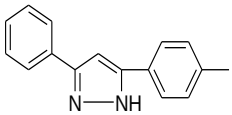
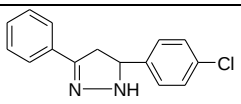
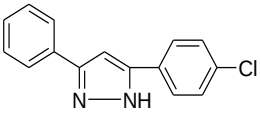
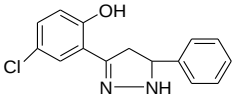
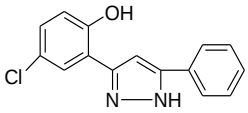
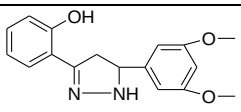
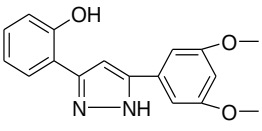
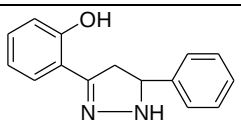
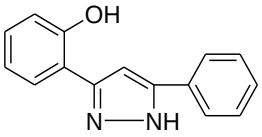
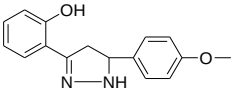
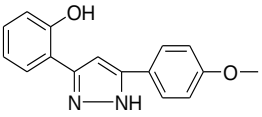
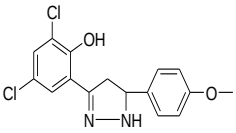
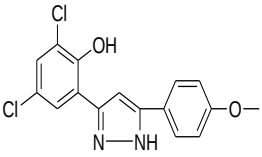
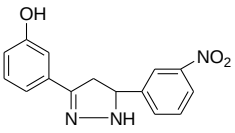
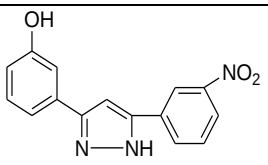
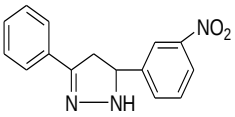
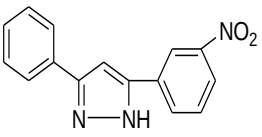
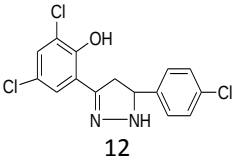
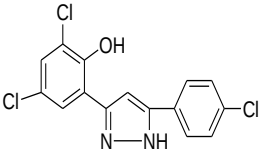
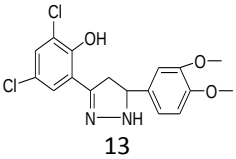
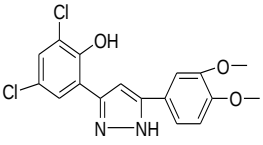
hydrate in water along with 5ml acetic acid, fine solids with sharp melting points for these compounds were obtained by oxidation.

Oxidative aromatization of 3, 5-disubstituted-2-pyrazolines under optimized condition

All 13 pyrazolines are oxidized under the same reaction condition. In an optimized reaction condition various pyrazolines (1–13) were subjected to the oxidation reaction in the presence of ceric sulfate tetra hydrate in water along with 5mL acetic acid for 1 hour. TLC monitoring was followed until total disappearance of pyrazolines. The results are summarized in **Table 1**.

Table 1. Oxidative aromatization of 3, 5-disubstituted 2 – Pyrazolines

Entry	Pyrazolines (Substrate)	Oxidized products		
		Pyrazoles	Yield (%)	M.P. ^{o}C
1	 1	 1a	62	183
2	 2	 2a	59	191
3	 3	 3a	61	175
4	 4	 4a	71	215
5	 5	 5a	66	170
6	 6	 6a	57	110

7	 7	 7a	52	144
8	 8	 8a	62	178
9	 9	 9a	59	135
10	 10	 10a	63	114
11	 11	 11a	61	98
12	 12	 12a	58	297
13	 13	 13a	55	147

Mechanism for oxidative aromatization of 3, 5-disubstituted - 2 – pyrazolines

A probable mechanism towards oxidative aromatization of 3, 5-disubstituted - 2 - pyrazolines is illustrated in **Figure 1**. In the context of oxidative aromatization, the 3, 5-disubstituted - 2 – pyrazolines (I) undergoes formation of N1 radical cation (II) by providing single electron which reduces Ce^{4+} to Ce^{3+}, whereas Ce^{4+} is regenerated by air oxidation of Ce^{3+} to Ce^{4+} . The N1 radical cation (II) is converted into N1 cation (III) by loss of a proton

from C5 position during second cerium redox cycle. Consequently, III loses a proton to give more stable, aromatic product i.e. 3, 5 - disubstituted pyrazole (IV).

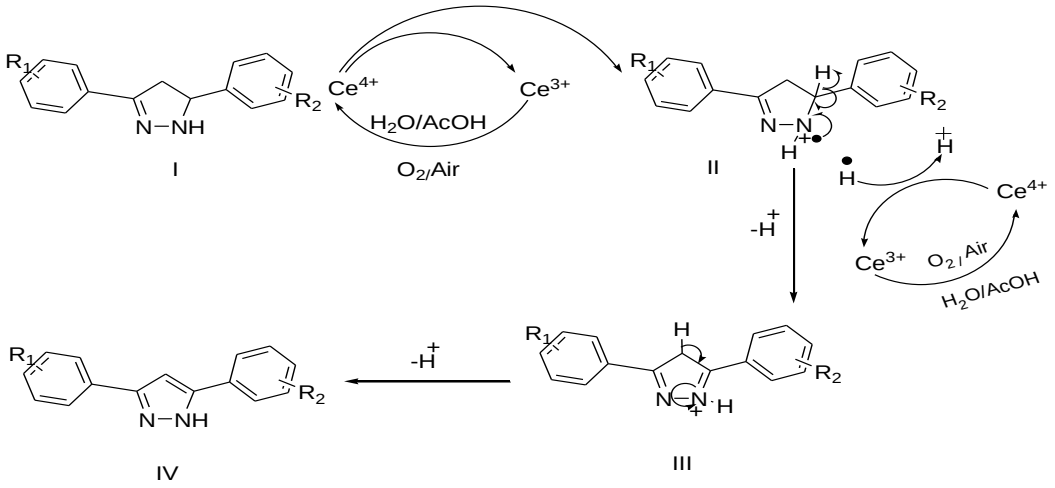


Figure 1: probable mechanism for oxidative aromatization of 3, 5-disubstituted - 2 - pyrazolines

CONCLUSIONS

3, 5-disubstituted - 2 - pyrazolines of different groups were synthesized by a simple catalyst free procedure. A clean oxidative aromatization of 3, 5-disubstituted - 2 - pyrazolines have been achieved in good yields within one hour .The solubility of both pyrazolines and ceric sulfate tetra hydrate was enhanced by using 5mL acetic acid. Substituted pyrazolines: $Ce(SO_4)_2.4H_2O$ ratio as 1:2 in acetic acid and water was found to be the best combination with 100 % conversion into pyrazoles. The reversible conversion of Ce^{3+} to Ce^{4+} is an electron transfer process achieved by the oxygen present in the air, due to which no external oxidant is required in oxidative aromatization. The aromatization proceeds via N radical cation.

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