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PYRAZOLE BASED GREEN SYNTHESIS OF SCHIFF'S BASE

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Abstract:
A series of pyrazoles containing Schiff's base have been synthesized by grinding free amino pyrazole with aromatic aldehyde in the presence of fresh lemon juice as a catalyst. The comparative studies were done with respect to yield, reaction simplicity, and work-up. The structures of all the synthesized products were confirmed by chemical tests including TLC other physical parameters such as melting, boiling point, and spectral technique such as IR, ^{1}H NMR and ^{13}C NMR.

Keywords: Green Catalyst, Multicomponent, Grinding, Imine

Introduction:

Schiff's base is extensively used as an intermediate in the synthesis of a number of organic derivatives such as azetidinone which are known to have antimicrobial, antifungal, and anticancer activity[i]-[iii]. A number of Pyrazole derivatives are found to have applications as NSAIDs clinically such as antipyrine or phenazone[iv], metamizole or dipyrone, and aminopyrine[v]-[vii]. In view of the diverse application associated with heterocyclic rings, we thought to synthesize some novel Schiff's base with heterocyclic rings [viii]-[xi].

Experimental:

The melting point of all the synthesized compounds was determined in open capillary tubes on an electrothermal apparatus and is uncorrected. The progress of the reaction was monitored by thin layer chromatography on silica gel coated aluminum plates (Merck) as adsorbent and UV light as visualizing agent. I.R spectra were recorded on Bruker FTIR. The purity of the compounds was monitored by TLC and UV light as visualizing agents. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian 500 MHz NMR spectrophotometer using $CDCl_3$/DMSO-d6 as solvent and TMS as an internal standard (chemical shifts in δ ppm).

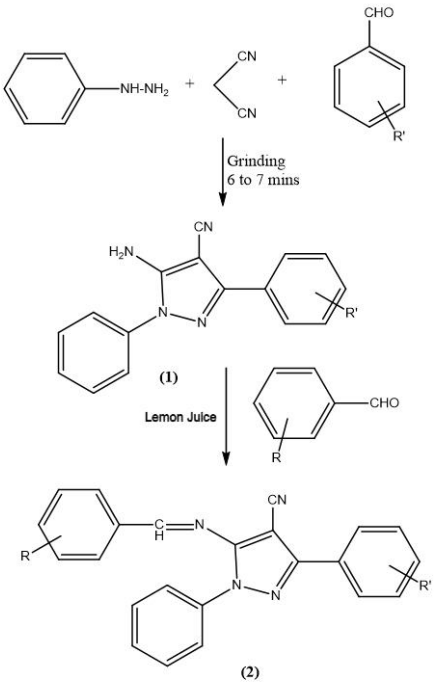
Compound 2a
IR (cm^{-1}): 2350(CN), 3010 (Ar-CH), 1620 (C=N).
^{1}H NMR(δ ppm): 7.2-7.8 (15H, Ar- H), 8.9 (1H,s,CH),
^{13}C NMR(δ ppm): 94.22(CH), 115 (CN) 122.3-153.2 (Ar-C & C=C).
Compound 2b
IR (cm^{-1}): 3015 (Ar-CH), 2345(CN), 1615 (C=N).
^{1}H NMR (δ ppm): 7.2-7.9 (14H, Ar- H), 8.95 (1H,s,CH).
^{13}C NMR (δ ppm): 95.22(CH), 114 (CN) 121.2-154.2 (Ar-C & C=C).
Compound 2c
IR (cm^{-1}): 3010(Ar-CH), 2340(CN), 1630 (C=N), 1100 (C-O).
^{1}H NMR (δ ppm): 3.3(3H,s, OCH_3), 7.2-7.8 (14H, Ar- H), 8.85 (1H,s,CH),
^{13}C NMR (δ ppm): 50.52(OCH_3), 98.22(CH), 117.5 (CN) 121.3-152.4 (Ar-C & C=C).
Compound 2d
IR (cm^{-1}): 3025 (Ar-CH), 2355 (CN), 1610 (C=N).
^{1}H NMR (δ ppm): 7.25-7.8 (14H, Ar- H), 8.9 (1H,s,CH).
^{13}C NMR (δ ppm): 96.55(CH), 114 (CN) 121.2-154.2 (Ar-C & C=C).
Compound 2e
IR (cm^{-1}): 3015 (Ar-CH), 2370(CN), 1625 (C=N).
^{1}H NMR (δ ppm): 7.4-8.1 (13H, Ar- H), 8.9 (1H,s,CH),
^{13}C NMR (δ ppm): 102.65(CH), 114 (CN) 126.5-155.0 (Ar-C & C=C).
Compound 2i
IR (cm^{-1}): 3020 (Ar-CH), 2380(CN), 1630 (C=N), 1100 (C-O).
^{1}H NMR (δ ppm): 3.28 (3H,s, 2xOCH_3), 7.2-7.8 (13H, Ar- H), 8.9 (1H,s,CH),
^{13}C NMR (δ ppm): 50.52(OCH_3), 104.22(CH), 115.5 (CN) 122.3-153.2 (Ar-C & C=C).

Method
Aromatic Aldehyde, Malanonitrile and Phenyl Hydrazine were ground together in equimolar ratio which resulted in an initial brown paste which turned into dry powder indicating completion of the reaction which is monitored by TLC. After completion of the reaction the amino pyrazole is treated with Aromatic aldehyde in presence of few drops of fresh lemon juice. Mixing was done using mortar pestle. Colored solid obtained on completion of the reaction.

Table (1): Physical data of compound 2(a to i)

Compound	R	R'	Molecular Formula*	% Yield Conventional	% Yield Green Method	Melting point (°C)
2a	H	H	$C_{23}H_{16}N_4$	72	79	82-84
2b	H	-Cl	$C_{23}H_{15}N_4Cl$	73	77	38-40
2c	H	4-OCH_3	$C_{24}H_{18}N_4O$	70	75	122-124
2d	4-Cl	H	$C_{23}H_{15}N_4Cl$	60	73	72-74
2e	4-Cl	4-Cl	$C_{23}H_{14}N_4Cl_2$	65	70	44-46
2f	4-Cl	4-OCH_3	$C_{24}H_{17}N_4OCl$	72	76	48-50
2g	4-OCH_3	H	$C_{24}H_{18}N_4O$	76	80	142-144
2h	4-OCH_3	4-Cl	$C_{24}H_{17}N_4OCl$	65	70	52-56
2i	4-OCH_3	4-OCH_3	$C_{25}H_{20}N_4O_2$	73	78	156-158

General Reaction Scheme



Conclusion

The synthesized compounds 2a to 2i can provide great scope for use as drug intermediate. The data reported in this paper may act as a guide for researchers working in this and allied areas. It was seen that the use of green chemistry principles helps to increase the yield above the conventional method.

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