Green Synthesis of Pyrazole Derivatives employing 1,3-Dipolar Cycloaddition Reaction using Phenyl hydrazones and Benzoquinone under basic condition

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Abstract

The present study depicts the green synthesis of different Pyrazole derivatives from Phenyl hydrazones. The 1,3-dipolar cycloaddition reaction of Phenyl hydrazones with Benzoquinone is carried out under mild basic condition using bases like Pyridine and Triethyl amine. The reaction is conducted at room temperature so the unwanted by products are not formed. The work-up is also easy and can be accomplished by pouring the reaction mixture on ice and filtration of the solid product formed in the reaction. The crude products are further purified by the Column chromatography or recrystallisation techniques. The purified products are characterized by IR and ^{1}H NMR spectroscopy.

Keywords: *Cycloaddition, Benzoquinone, Phenyl hydrazones, Triethyl amine, Pyridine*

Introduction

Pyrazoles are the important class of organic compounds possessing various biological activities including anti-cancer activity. The synthetic approaches for designing these derivatives have been reported by various researchers. Multicomponent pyrazole synthesis from alkynes, nitriles and Titanium imido complexes have been achieved [1]. Pharmacologically important pyrazoles are synthesized by different approach [2]. A sonication method for pyrazole synthesis is reported recently in the literature [3].

Copper catalysed pyrazole synthesis in continuous flow is clean and rapid one[4]. Synthesis and molecular docking of thiazoyl - pyrazole derivatives and their anti-cancer property has been reported [5]. Silica coated catalyst was employed for the synthesis of pyrazole derivatives [6]. Some pyrazole derivatives also possess the herbicidal properties and were successfully synthesized [7]. Synthesis and anti-cancer activity of some 1,3,5-Trialkyl-1H-Pyrazoles have been successfully accomplished[8]. Pyrazoles are synthesized under solvent free condition[9]. Alkenylchalciones are used as a precursors for the synthesis of pyrazoles involving cyclisation approach with hydrazine. Multisubstituted synthesis of pyrazoles is known to involve (3+2) cycloaddition approach [11]. Amphibilic reactivity of hydrazine has been used for the synthesis of pyrazoles. New 2-(4,5-dihydro-1H-Pyrazlyl) triazole derivatives were synthesized in a one –pot and multistep way has been reported [12]. Synthesis

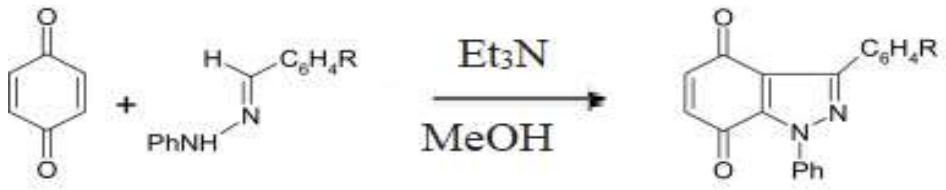
of novel pyrazole derivatives with antimicrobial activity have been reported [13]. In this paper the 1,3-dipolar cycloaddition approach has been used.

Materials and Methods:

All the chemicals were purified prior to use. The reactions are carried out at room temperature under magnetic stirring conditions. The Phenyl hydrazones were prepared as per the existing preparative methods. They were used as it is for cycloaddition reaction. The reactions are carried out under mild basic conditions by either using pyridine of triethyl amine as a base. The reactions are much cleaner when triethyl amine is used as a base. The Products are purified by column chromatography or recrystallisation technique.

General procedure for cycloaddition:

In a round bottom flask Phenyl hydrazone of benzaldehyde 1 g (5.1 mmol) was dissolved in 10 ml of triethyl amine. Benzoquinone 0.5 g (5.1mmol) was added to it as a methanolic solution and the reaction mixture was stirred for two days at room temperature. The course of the reaction was monitored by TLC and the reaction mixture was poured on ice to obtain the crude pyrazole. The crude product was purified by column chromatograph using petroleum ether and ethyl acetate as eluent. The yield of the crude product was 1.39 g (90%). It was obtained as a gray solid with Physical constant of 100 ^{o}C. The procedure was used for other phenyl hydrazones to obtain the pyrazole derivatives. The findings are summarized in the following result table.



Result Table:

S. No.	Phenylhydrazone of weight 1gm	Bezoquinone Weight gm	Base Triethyl amine ml	Time (hrs) & Temperature (^{O}C)	% Yield	Physical Constant (^{O}C)
1	Benzaldehyde	0.5	10	48 hrs , 25	90	100
2	Salicyl Aldehyde	0.5	10	48 hrs, 25	95	230
3	4-Chloro Benzaldehyde	0.5	10	48 hrs, 25	90	110
4	4-Hydroxy Benzaldehyde	0.5	10	48 hrs , 25	96	210

5	3-Nitro Benzaldehyde	0.5	10	48 hrs , 25	87	220

Spectroscopic Data:

IR and ^{1}H NMR Spectral Data :

Pyrazole 1.

IR (cm $^{-1}$) : 3286, 1705, 1661, 1596, 1489, 1243, 749, 689

^{1}H NMR ($CDCl_3$) ppm : 10.8 bs, 1H, 6.65- 8.1 m 11H, 4.15m, 1H , 3.9 m ,1H, 3.5d, 1H

Pyrazole 2.

IR (cm^{-1}) : 3270, 1621, 1596, 1490, 1307, 848

^{1}HNMR (CDCl $_3$) ppm : 11.1bs, 1H, 10.9 bs, 1H,6.7-8.3 m, 11H, 4.0 bs,1H,,3.4 bs,1H, 2.9 bs,1H

Pyrazole 3.

IR (cm^{-1}) : 3313, 1662, 1598, 1488, 1307, 831, 749

^{1}H NMR ($CDCl_3$) ppm : 10.0 bs, 1H, 6.75-8.0 m, 11H, 3.9 bs, 1H, 3.2 t, 1H, 2.8 bs, 1H

Pyrazole 4.

IR (cm^{-1}) : 3500, 3252, 1651, 1592, 1491, 1313, 834, 690

^{1}H NMR ($CDCl_3$) ppm : 9.9 bs, 2H, 6.7-7.9 m, 11H, 4.1 d, 1H, 3.8 d, 1H, 2.8 bs, 1H

Pyrazole 5.

IR (cm^{-1}) : 3305, 1671, 1596, 1523, 1491, 1344, 747, 714

^{1}H NMR ($CDCl_3$) ppm : 6.85-8.3 m, 11H, 4.0 bs, 1H, 3.7 bs, 1H, 2.8 bs, 2H

Result and Discussion:

The present synthetic method is simple and eco-friendly. The reaction is carried out at room temperature hence it is easy to carry out with any basic set up of the laboratory. The work up is very simple and does not involve the use of organic solvents so there will be no effluents as a by products which may cause water pollution. It is green method of pyrazole synthesis hence it may be a tool for organic synthetic chemist.

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