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Synthesis and Antibacterial Activity of 4,4'-(Arylmethylene)Bis(3-Methyl-1-Phenyl-1H-Pyrazol-5-Ol) Derivatives in Presence $Ce(SO_4)_2.4H_2O$ as a Catalyst Under Solvent free Condition using Ultrasonication Technique

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ABSTRACT

Mixture of aromatic aldehyde(1 mmol) and 1-phenyl-3-methyl-5-pyrazolone (2 mmol) in H2O–EtOH (1:1, 5 mL) at heating condition, was stirred thoroughly in the presence of a catalytic amount of $Ce(SO_4)_2.4H_2O$ (10 mg, 2.5 mol%) to afford 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-pyrazol-5-ols) in excellent yields.

The synthesized derivatives were subjected for anti-bacterial activity using ciprofloxacin as standard drug against *S. aureus* and *Pseudomonas aeruginosa* using agar cup plate method. All the derivatives showed good antibacterial activity. The salient features of this method include simple procedure, mild conditions, easy purification, moderate to good yields of products and high generality.

KEYWORDS: 4,4'-(arylmethylene)bis(3-methyl-1- phenyl-1H-pyrazol-5-ol) derivatives, ultrasonication technique

I. INTRODUCTION

Pyrazoles are azole class aromatic heterocyclic systems that contains five-membered ring with two nitrogen atoms (Nitrogen atom 1 (N1) is ''pyrrole-like" because its unshared electrons are conjugated with the aromatic system. Nitrogen atom 2 (N2) is ''pyridine-like") bound to each other and three carbon atoms. Recent literature explains a broad spectrum of biological activities of Pyrazole derivatives

Pyrazole refers to the class of simple aromatic ring compounds of the heterocyclic series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions. They are known to possess inhibitors of protein glycation,[1] antibacterial,[2–4] antifungal,[5,6] anticancer,[7–9] antidepressant,[10] antiinflammatory,[11] anti-tuberculosis,[12] antioxidant[13] as well as antiviral[14] activities.

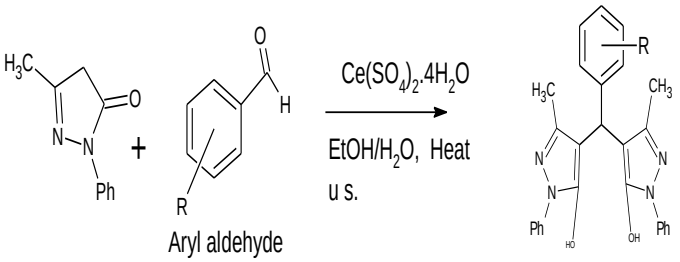
In present research Mixture of aromatic aldehyde(1 mmol) and 1-phenyl-3-methyl-5-pyrazolone (2 mmol) in H2O–EtOH (1:1, 5 mL) at heating condition, was stirred thoroughly in the presence of a catalytic amount of $Ce(SO_4)_2.4H_2O$ (10 mg, 2.5 mol%) to afford 4,4'-(arylmethylene) bis(3-methyl-1-phenyl-pyrazol-5-ols) in excellent yields.

II. EXPERIMENTAL EXPERIMENTAL

All reagents and chemicals were purchased from SD Fine or spectrochem chemical company, Mumbai, India. All reagents and chemicals were of analytical grade and used without further purification. Sonication was performed in ultrasonic cleaner with a frequency of 25 KHz and nominal power 250 W. The reaction temperature was controlled by addition or removal of water from ultrasonic bath.

Mixture of aromatic aldehyde(1 mmol) and 1-phenyl-3-methyl-5-pyrazolone (2 mmol) in H2O–EtOH (1:1, 5 mL) at heating condition, was stirred thoroughly in the presence of a catalytic amount of $Ce(SO_4)_2.4H_2O$ (10 mg, 2.5 mol%) to afford 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-pyrazol-5-ols) in excellent yields.

After completion of the reaction which is confirmed by TLC, the mixture was filtered. The solid product was washed with H_2O and finally was recrystallized from ethanol. The structures of the products were confirmed from physical and spectroscopic data such as melting points, IR and 1H NMR spectra.



Scheme 1: 4,4'-(arylmethylene)bis(3-methyl-1- phenyl-1H-pyrazol-5-ol) derivatives

Antibacterial activities of synthesized compounds that screened against two bacteria species, namely *Pseudomonas aeruginosa and Staphylococcus aureus.* The Antibacterial activity was biologically assayed using the agar cup plate technique were performed. The investigation of antibacterial data revealed that all the tested compounds showed comparatively good activity against all the bacterial strains. The organisms were tested against the activity of solutions with concentration of 1.0 mg/mL of each compound and after 24 h of incubation at 37°C, the zones of inhibitions were measured (IZD) in centimeter as the criterion for Antibacterial activity.

III. RESULTS

Good yields were obtained for synthesis 4,4'-(arylmethylene)bis(3-methyl-1- phenyl-1H-pyrazol-5-ol) derivatives in presence Ce(SO4)2.4H2O as a catalyst under solvent free condition using ultrasonication technique.

Table 1: 4,4'-(arylmethylene)bis(3-methyl-1- phenyl-1H-pyrazol-5-ol) derivatives

Sr no	Product no	Product name	Melting point ^{0}c	Reaction time in min	% yield
1.	1a	4,4'-[(2,4-Dichlorophenyl)methylene] bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)	229-231	18	79
2.	1b	4,4'-[(Phenyl methylene)bis (3-methyl-1-Phenyl-1Hpyrazol-5-ol)	170-173	20	90
3.	1c	4,4'-[(4-Chlorophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)	213-215	19	92
4.	1d	4,4'-[(4-Methylphenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)	203-205	18	93
5.	1e	4,4'-[(4-Methoxyphenyl)methylene] bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)	142-145	20	88

Representative Spectra of compound 1d

IR (KBr) υmax/cm$^-$1:3432 (OH), 2923, 1602, 1503, 1410, 1296, 1028; ^{1}H NMR (500 MHz; DMSO; Me_4Si); d 2.21 (s, 3H, CH_3), 2.28 (s, 6H, CH_3), 4.87 (s, 1H), 7.03–7.65 (m, 14H, $H_{aromatic}$); ^{13}C NMR (125.13 MHz; DMSO; Me4Si); d 12.2, 21.1, 33.3, 121.0, 122.8, 124.7, 125.1, 126.1, 127.6, 129.2, 129.5, 135.3, 139.7, 146.8.

Table2: Elemental analysis of 4,4'-[(4-Methylphenyl) methylene]bis(3-methyl-1-phenyl- 1H-pyrazol-5-ol)

Serial no	Element	Calculated %	Found %
1.	Carbon	74.65	74.62
2.	Hydrogen	5.82	5.85
3.	Nitrogen	12.44	12.40
4.	Oxygen	7.10	7.14

Antibacterial activity of 4,4'-(arylmethylene)bis(3-methyl-1- phenyl-1H-pyrazol-5-ol):

The *in vitro* Antibacterial activity of compounds **1a-1e** were determined by agar cup plate method, the results of which are summarized in table belwo. The Antibacterial data clearly indicated that the halogen, nitro and hydroxyphenyl substituents of pyrazoles ring were by far the most active substitutents. The methoxy group generally confered week Antibacterial activity. The compounds **1c**, **1d** showed significant activity against *S. aureus* and *Pseudomonas aeruginosa*; however, the entire tested compounds were found to be less active as antibacterial in comparison to ciprofloxacin.

Table 3: antibacterial activity of 4,4'-(arylmethylene) bis(3-methyl-1- phenyl-1H-pyrazol-5-ol) derivatives

Sr. no	Compound no	Zone of Inhibition *Pseudomonas aeruginosa*	Zone of Inhibition *Staphylococcus aureus*
1.	1a	17	19
2.	1b	17	18
3.	1c	18	19
4.	1d	20	23
5.	1e	14	16
6.	Ciprofloxacin	20	24

IV. CONCLUSION

In conclusion, we have achieved 4,4'-(arylmethylene)bis(3-methyl-1- phenyl-1H-pyrazol-5-ol) derivatives synthesis using green synthetic protocol under ultrasound irradiation technique. Further the compounds showed good antibacterial activity. Striking features of this method are short reaction time, easy work up procedure, water solvent, use of ultrasound waves, atom economy.

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