Scientific Reviews
&
Chemical Communications

Sci. Revs. Chem. Commun.: 5(1), 2015, 7-12
ISSN 2277-2669

SYNTHESIS AND CHARACTERIZATION OF SOME NOVEL 2-PYRAZOLINE DERIVATIES AND STUDY OF THEIR ANTIBACTERIAL ACTIVITY

MAMTA AHUJA[*] and RAVI SETHI[a]

Department of Chemistry, Govt. Meera Girls College, UDAIPUR – 313001 (Raj.) INDIA
[a]Department of Chemistry, PAHER University, UDAIPUR – 313001 (Raj.) INDIA

(*Received : 25.02.2015; Accepted : 10.03.2015*)

ABSTRACT

A new series of 1-Acetyl-5-(4-nitrophenyl)-3-(2-thienyl/pyridinyl/phenyl)-2-pyrazoline were synthesized by reacting 3-(4-nitrophenyl)-1-(2-thienyl/pyridinyl/phenyl)-2-propene-1-one (chalcones) with hydrazine hydrate in acetic acid. All the prepared compounds were characterized by spectral data (IR, ^{1}H NMR) and microanalysis. All the synthesized compounds were also evaluated for their antibacterial activity against Gram +ve and Gram -ve bacteria.

Key words: 2-Pyrazolines, Chalcones, Hydrazine hydrate, Antibacterial activity.

INTRODUCTION

The prevalence of pyrazoline cores in biologically active molecules has stimulated the need for elegant and efficient ways to make these heterocyclic lead. Pyrazolines have attracted attention and medicinal chemists for both with regard to heterocyclic chemistry and the pharmacological activities associated with them. A classical synthesis of these compounds involve the base-catalyzed aldol condensation reaction of aromatic ketones and aldehydes to give α, β-unsaturated ketones (chalcones), which undergo a subsequent cyclization reaction with hydrazines affording 2-pyrazolines[1]. The pharmaceutical importance of these compounds lies in the fact that they can be effectively utilized as anticonvulsant[2], antidepressant[3], anti-inflammatory[4], antifungal[5-6], antibacterial[7-8], antioxidant[9], anticancer[10], antituberculosis[11], antiviral[12] and antiamoebic[13] activities. Some of these compounds have also COX-2 inhibitor[14] and analgesic[15] activity. Several pyrazolines have shown promising results as chemotherapeutic agent. Keeping the present study aimed to synthesize some new 2-pyrazoline derivatives in order to study the further effect of thienyl, pyridinyl and phenyl moiety on their biological activity.

EXPERIMENTAL

Materials and methods

All the reagents and solvents used were of laboratory grade. The synthesis of new products was

Available online at www.sadgurupublications.com
[*]Author for correspondence; E-mail: ravi.sethi60@yahoo.com; mamdeep@rediffmail.com

monitored by TLC using (Ranbaxy) silica gel-G plates for TLC. IR spectra were recoreded on Shimadzu FTIR 8400 (4000-400 cm^{-1}). ^1H NMR spectra were recoreded on BRUKER AVANCE III NMR 400 MH_Z spectrometer using TMS as internal standard. C, H and N analysis were performed on an automatic elemental analyzer model Vario EL III.

Synthesis of ligands

Synthesis of 2-pyrazoline derivatives

The compounds were synthesized in two steps:

Step I: Synthesis of 3-(4-nitrophenyl)-1-(2-thienyl/pyridinyl/phenyl)-2-propene-1-one (Chalcones)

2-Acetylthiophene/2-Acetylpyridine/Acetophenone (0.02 mol) was dissolved in 5 percent methanolic sodium hydroxide (30 mL) with constant stirring and 4-nitrobenzaldehyde (0.02 mol) was added dropwise into it at 0-5ºC with continuous stirring for 8 hr. The stirrer was removed and the reaction mixture was kept over night. The reaction mixture was poured onto ice cold distilled water, neutralized with dilute sulphuric acid and filtered, washed with cold distilled water, dried and the resulting chalcone was purified by recrystallization from methanol.

Step II: Synthesis of 1-acetyl-5-(4-nitrophenyl)-3-(2-thienyl/pyridinyl/phenyl)-2-pyrazolines

A solution of 3-(4-nitrophenyl)-1-(2-thienyl/pyridinyl/phenyl)-2-propene-1-one (0.01 mol) in acetic acid (35 mL) was refluxed with hydrazine hydrate (2.5 mL, excess) for 5-15 hrs. The progress of reaction was monitored by TLC. The reaction mixture was cooled overnight and poured onto ice-water. The separated solids was filtered, washed with distilled water, dried under vacuum and re-crystallized from methanol.

The structure of newly synthesized compounds was characterized by ^1H NMR and IR spectral data.

1-Acetyl-5-(4-nitrophenyl)-3-(2-thienyl)-2-pyrazoline (a)

^1H NMR Spectrum (400 MH_Z, DMSO-d_6) δ: 2.408 (s, 3H, $COCH_3$), 3.111-3.168 (dd, 1H, C_4-H cis), 3.807-3.881 (dd, 1H, C_5-H), 5.632-5.674 (dd, 1H, C_5-H), 7.073-8.256 (m, 7H, Ar-H and thienyl H).

IR spectrum (KBr) υ_{max} cm^{-1}: 1666 (C=O), 1512 (C=N), 1452, 1406 (C=C), 1342 (C-N), 835 (N-N), 707 (C-S).

1-Acetyl-5-(4-nitrophenyl)-3-(2-pyridinyl)-2-pyrazoline (b)

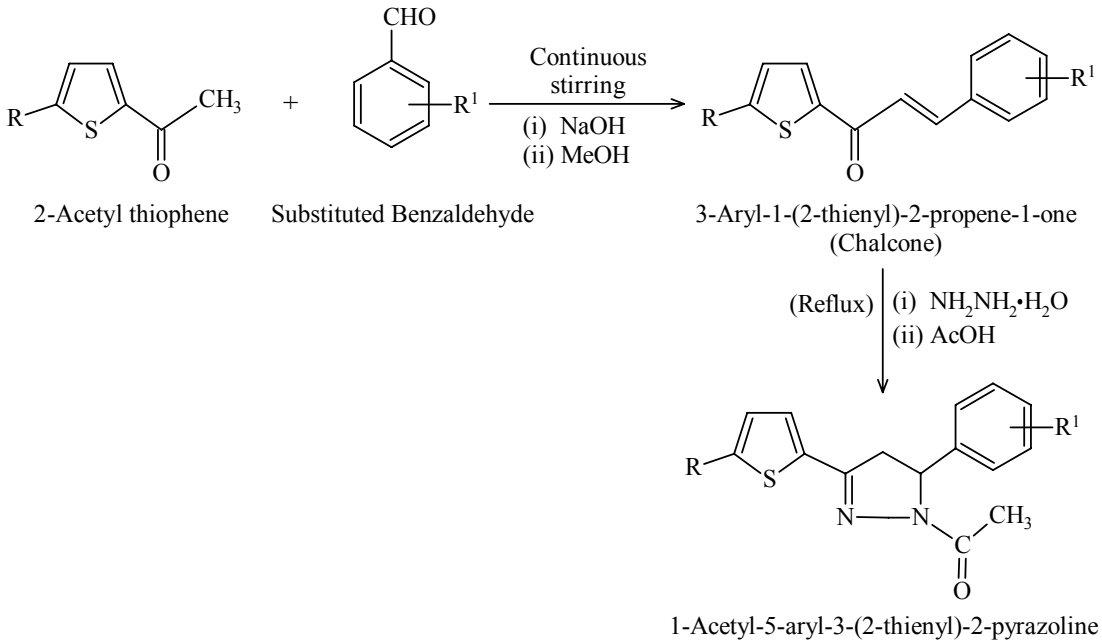
^1H NMR Spectrum (400 MH_Z, DMSO-d_6) δ: 2.370 (s, 3H, $COCH_3$), 3.155-3.211 (dd, 1H, C_4-H trans), 3.267-3.327 (dd, 1H, C_4-H cis), 5.578-5.621 (dd, 1H, C_5-H), 7.196-8.693 (m, 8H, Ar-H and pyridinyl H).

IR spectrum (KBr) υ_{max} cm^{-1}: 1676 (C=O), 1519 (C=N), 1415 (C=C), 1344 (C-N), 854 (N- N).

1-Acetyl-5-(4-nitrophenyl)-3-(2-phenyl)-2-pyrazoline (c)

^1H NMR Spectrum (400 MH_Z, DMSO-d_6) δ: 2.442 (s, 3H, $COCH_3$), 3.125-3.182 (dd, 1H, C_4-H trans), 3.801-3.875 (dd, 1H, C_4-H cis), 5.636-5.678 (dd, 1H, C_5-H), 7.262-8.195 (m, 9H, Ar-H and Phenyl H).

IR spectrum (KBr) υ_{max} cm^{-1}: 1649 (C=O), 1518 (C=N), 1440, 1419 (C=C), 1348 (C-N), 846 (N-N).

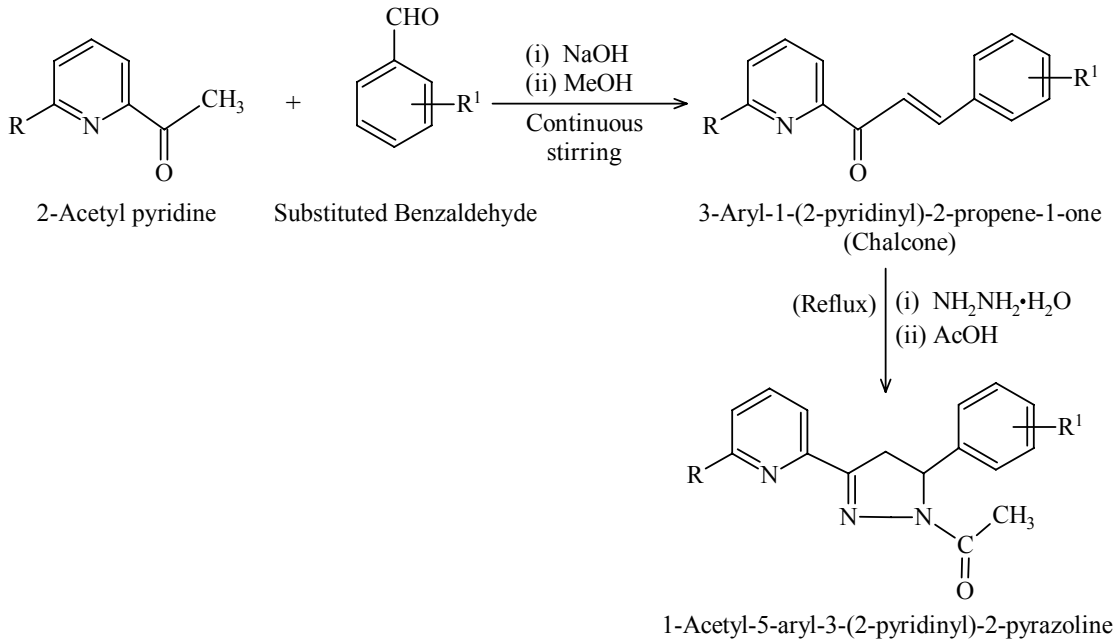


2-Acetyl thiophene Substituted Benzaldehyde 3-Aryl-1-(2-thienyl)-2-propene-1-one (Chalcone)

1-Acetyl-5-aryl-3-(2-thienyl)-2-pyrazoline

Ligand	R	R^1
a	H	4-NO_2

Scheme 1: Synthesis of Pyrazoline (a)

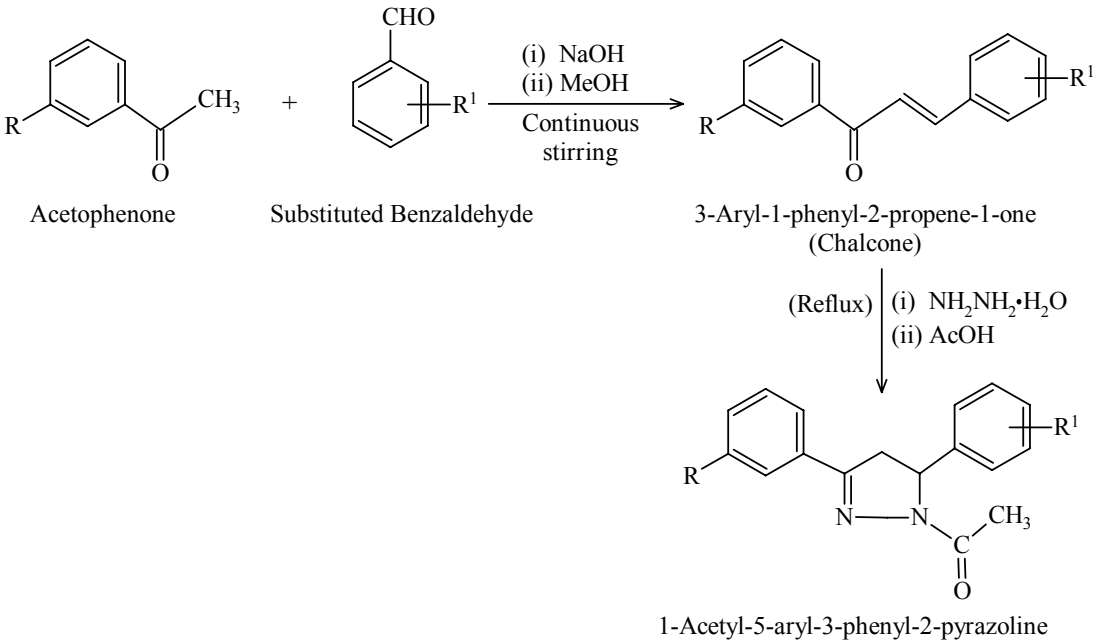


2-Acetyl pyridine Substituted Benzaldehyde 3-Aryl-1-(2-pyridinyl)-2-propene-1-one (Chalcone)

1-Acetyl-5-aryl-3-(2-pyridinyl)-2-pyrazoline

Ligand	R	R^1
b	H	4-NO_2

Scheme 2: Synthesis of Pyrazoline (b)



Ligand	R	R^1
c	H	4-NO_2

Scheme 3: Synthesis of Pyrazoline (c)

Antibacterial activity

Antibacterial activity were evaluated at Department of Microbiology, M. L. Sukhadia University, Udaipur (Raj.) All the synthesized compounds were screened for antibacterial activity by Agar Disc Diffusion method[16] against Gram + ve bacteria *Micrococcus luteus*, *Staphylococcus aureus* and Gram – ve bacteria *Escherichia coli*. Nutrient agar (Microgen, India) was used for bacteria culture. The culture strains of bacteria were maintained on nutrient agar slant at 37 ± 0.5°C for 24 hrs. The known compounds Amoxicillin was used as standard drug for antibacterial comparision study. The compounds was tested at a concentration at 500 μg/mL in DMSO. The diameter of zone of inhibition was measured in mm. DMSO was used as a control. Around 30 mL of sterile nutrient agar media for bacteria was poured into sterile petri dishes and allowed to solidify. The media was seeded with the organism by spread palate method using sterile L-roads and loops. Holes of 6 mm. diameter were punched carefully using a sterile cork borer and these were completely filled with the test solutions. The bacterial petri plates were kept in incubator at 37°C for 24 hrs and then the zones of inhibition were measured.

RESULTS AND DISCUSSION

The synthesized compounds were characterized by elemental analysis and spectral (^{1}H NMR, IR) data.

Antibacterial activity

It has been observed from the activity data that all compounds were found to be mild to moderately active against Gram +ve and Gram –ve bacterial strains. However the maximum activity was observed in compound (a) against *M. luteus*. The significant activity was observed in compound (b) and (c) against *S. aureus* and *E. coli*. The observed increase in antibacterial activities are attributed to the presence of thienyl moiety of synthesized compounds.

Table 1: Physical and analytical data of synthesized compounds (a-c)

Compounds	Molecular formula	M.W. (gm/mole)	Yield (%)	Element % Found (Calculated)		
				C	H	N
a	$C_{15}H_{13}N_3O_3S$	315.2	70	57.0 (57.1)	4.2 (4.1)	13.2 (13.3)
b	$C_{16}H_{14}N_4O$	278.11	85	69.1 (69.0)	50.4 (50.7)	20.0 (20.1)
c	$C_{17}H_{15}N_3O_3$	309.12	65	65.7 (65.9)	4.5 (4.8)	13.4 (13.5)

Table 2: Antibacterial activity data of synthesized compound (a-c) at 500 µg/mL (ppm)

Compounds	Zone of inhibition (in mm)		
	Gram +ve		Gram –ve
	Micrococcus luteus	***Staphylococcus aureus***	***Escherichia coli***
a	17	16	15
b	14	11	12
c	12	10	9
Standard drug (Amoxicillin)	22	20	21

CONCLUSION

The present study leads to a convenient synthetic method for the synthesis of new pyrazoline derivatives, which show significant antibacterial activity. The substitution with thienyl moiety having a nitro group showed better activity. The result revealed that most of the newly synthesized compounds exhibited promising antibacterial activity comparable to amoxicillin against the test organism.

ACKNOWLEDGEMENT

We are thankful to Head, Department of Chemistry and Department of Pharmacy, Pacific University, Udaipur for providing necessary facilities and encouragement for the present research work. We are sincerely thankful to Department of Chemistry (NFDD Center), Saurashtra University, Rajkot for IR and ^{1}H NMR spectral analysis. We are also thankful to Department of Mines and Geology, Udaipur (Raj) for Elemental analysis and Department of Microbiology, MLSU, Udaipur (Raj.) for providing antibacterial activity.

REFERENCES

1. E. Palaska, M. Aytemir, D. Erol and I. T. Uzbay, Eur. J. Med. Chem., **36(6)**, 539-543 (2001).
2. Z. Ozdemir, U. Calis, A. A. Bilgin, H. B. Kandilci and B. Gumusel, Eur. J. Med. Chem., **42(3)**, 373-379 (2007).
3. M. Abdel-Aziz, A. El-Din, G. Abuo-Rahma and A. A. Hassan, Eur. J. Med. Chem., **44**, 3480-3487 (2009).
4. A. Kumar, V. K. Srivastava and P. Rani, Eur. J. Med. Chem., **39**, 449-452 (2004).

5. S. Radi, S. Salhi and A. Radi, Lett. in Drug Des. & Discov. Bentham Science Publishers Ltd., **7**, 27-30 (2010).

6. R. Gupta, A. Jain and N. Gupta, Indian J. Chem., **49B**, 351-355 (2010).

7. A. Solankee and J. Patel, Ind. J. Chem., **43B**, 1580-1584 (2004).

8. Y. S. Chovatia, S. B. Bagade, S. P. Gandhi and P. L. Gorde, Orient J. Chem., **26 (1)**, 275-278 (2010).

9. K. Dasary, A. Lavania, M. Yadav and A. V. K. Anand, Int. J. Res. Engin. Sci., **1(7)**, 08-13 (2013).

10. G. M. Nitulescu, A. V. Missir and C. Draghici, Eur. J. Med. Chem., **45(11)**, 4914-4919 (2010).

11. M. A. Ali, M. Shaharyar and A. A. Siddiqui, Eur. J. Med. Chem., **42(2)**, 268-275 (2007).

12. O. I. El-Sabbagh, M. M. Baraka, S. M. Ibrahim, P. Pannecouque, G. Anderi, R. Snoeck. J. Balzarini and A. A. Rashad, Eur. J. Med. Chem., **44**, 3746-3753 (2009).

13. N. Adhikari, M. K. Maiti and T. Jha, Bioorg. Med. Chem. Lett., **20(14)**, 4021-4026 (2010).

14. M. V. R. Reddy, V. K. Billa, V. R. Pallela, M. R. Mallireddigari, R. Boomi-nathan, J. L. Gabriel and E. P. Reddy, Bioorg. Med. Chem., **16**, 3907-3916 (2008).

15. S. Sridhar and Y. Rajendra Prasad, E.-J. Chem., **9(4)**, 1810-1815 (2012).

16. M. S. Al-Rawi, J. H. Tomma and R. M. Abdullah, Ibn Al-Haitham J. Pure Appl. Sci., **26(1)**, 208-217 (2013).