Research Article CODEN: IJPRNK IMPACT FACTOR : 4.278 ISSN: 2277-8713
Piste P, IJPRBS, 2014; Volume 3(4): 284-290 IJPRBS

INTERNATIONAL JOURNAL OF
PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

SYNTHESIS OF SOME N^1-SUBSTITUTED PYRAZOLE DERIVATIVES BY GRINDING TECHNIQUE

PISTE P[1], ZAMBARE D[2]

1. P.G. Department of Chemistry, Yashavantrao Chavan Institute of Science, Satara (Mah.), India. 415001.
2. P. G. Department of Chemistry, Kisan Veer Mahavidyalaya, Wai, Dist.: Satara.

Accepted Date: 09/07/2014; Published Date: 27/08/2014

Abstract: An efficient and operationally simple reaction between N- acetyl pyrazole with different aryl aldehydes gives corresponding chalcones (Ia-d) followed by reaction with phenyl hydrazine in presence of glacial acetic acid afforded N1-(substituted) pyrazole derivatives (IIa-d) by using grindstone with excellent yield and require short time period, solvent free condition, mild reaction condition, environmental safer and notable advantage of this method. The structures of the newly synthesized compounds have been confirmed on the basis of elemental analysis and spectral data. Some of the synthesized compounds exhibit significant antibacterial activity.

Keywords: Pyrazole, Grinding, Solid NaOH, Antibacterial activity

PAPER-QR CODE

Corresponding Author: DR. PRAVINA B. PISTE

Access Online On:

www.ijprbs.com

How to Cite This Article:

Piste P, Zambare D; IJPRBS, 2014; Volume 3(4): 284-290

INTRODUCTION

Grinding finds its usage in industry and manufacturing processes and is a very simple, efficient and effective process. Such reaction are simple to handle, reduce pollution, comparatively cheaper to operate and may be regarded as more economical and ecologically favorable procedure in chemistry. Pyrazole and its derivatives are among the important scaffolds possessing various biological activities and having prestigious position in medicinal and pharmaceutical chemistry. This mainly due to the easy preparation and important biological activity and therefore represents an interesting template for combinatorial as well as medicinal chemistry. Pyrazole framework plays an essential role in biological active compounds .The pyrazole nucleus is a ubiquitous feature of fertile source of medicinal agents such as antimicrobial[1], anticancer[2], antitumor[3], anticonvulsant[4], antihistaminic[5], analgesic[6], anti-inflammatory[7] etc. Many pyrazole have been found to be luminescent and fluorescent agents. In addition, pyrazoles have played a crucial role in the development of theory in heterocyclic chemistry and also used extensively as useful synthon in organic synthesis. In addition, the pyrazole derivatives have many applications on crop protection chemistry such as insecticide and pesticide[8] and used as intermediates for the synthesis of new chemical entities[9]. As a consequence, much attention has been paid to the design and synthesis of pyrazole derivatives by grindstone chemistry prompted us to synthesize some new pyrazole derivatives as per Scheme.

EXPERIMENTAL SECTION

Melting points were taken in open capillary tubes and are uncorrected. Purity of the compound was checked by silica gel G TLC plates using n-hexane and ethyl acetate as solvent system. The visualization of spot was carried out in an iodine chamber. The IR spectra were recorded on Schimadzu spectrophotometer. The ^{1}H NMR spectra were scanned on Perkin Elmer spectrophotometer in $CDCl_3$ using TMS as internal standard and chemical shift are expressed in δ ppm. Elemental analysis was performed on a Heracus CHN analyzer and was within the ±0.5% of the theoretical values.

Experimental Procedure

Synthesis of 1-benzoaceto-3-5-diphenyldihydropyrazole (Ia-d) :

Equimolar quantities of substituted benzaldehyde (0.01mol) and N-acetyl-3-4-diphenylpyrazole were dissolved in minimum amount of alcohol. Sodium- hydroxide solution (0.02mol) was added slowly and the mixture is grinded with agate morter for 2 hrs. until the entire mixture becomes very cloud. Then mixture was poured slowly into 400ml water with constant stirring &

kept in a refrigerator for 24 hrs. The precipitate obtained was filtered, washed and recrystallized from ethanol. The completion of reaction was monitored by TLC.

Ia: IR (KBr) : λ_{max},3015 (Ar-H str),1705 (>C=O str), 1614(>C=N str) ,1595(>C=< str) cm^{-1}. NMR : ($CDCl_3$):δ,1.83(2H, dd, -CH_2-), 2.03 (1H, t, -CH), 6.2-6.6(2H, d, -CH=), 6.9-7.8 (15H, m, Ar-H), 7.88-7.81 (1H, d,=CH-Ar) ppm.

Ib: IR (KBr) : λ_{max}, 3060 (Ar-H str), 1700 (>C=O str), 1620 (-C=O str), 1620 (>C=N str), 1600(>C=C< str), 1020 (-C-N str), 1430 (-NO_2) cm^{-1}.NMR : ($CDCl_3$):δ ,2.2-2.7(2H, dd,-CH_2-), 3.2 (1H, dd, -CH), 6.6-6.9 (2H, d, -CH=), 6.9-7.8 (14H, m, Ar-H), 7.88-7.81 (1H, d,=CH-Ar) ppm.

Ic: IR (KBr) : λ_{max}, 3430(-OH br), 3099(Ar-H str), 1710(>C=O str), 1615(>C=N str), 1600(>C=C< str) cm^{-1} .NMR : ($CDCl_3$):δ 2.2-2.7(2H, dd, -CH_2-), 3.2 (1H, dd, -CH), 3.5(1H, s, -NH), 6.3-6.7(2H, dd, -CH-), 3.7(1H, s, -OH) 7.1-7.9 (14H, m, Ar-H), 7.88-7.81 (1H, d,=CH-Ar) ppm.

Id: IR (KBr) : λ_{max}, 3055(Ar-H str), 1710(>C=O str), 1620 (>C=N str), 1600 (>C=C< str) cm^{-1}.NMR : ($CDCl_3$):δ ,2.2-2.7(2H, dd, -CH_2-), 3.4(1H, dd, -CH), 6.1-6.5(2H, d, -CH=), 7.1-7.8(14H, m, Ar-H), 7.88-7.81 (1H, d,=CH-Ar) ppm.

Synthesis of N^1-(3,4-diphenyl,5'-dihydro-2,3-pyrazol)-3,5-diphenyl,4- diydro pyrazole (IIa-d):

A mixture of (I) (0.01mol), phenyl hydrazine (0.01mol) and 2-3 drops of glacial acetic acid was grinded in agate morter for 2-3 hrs. The reaction mixture was concentrated in vaccum and the solid so obtained was filtered, washed, dried and recrystallised from ethanol. The completion of reaction was monitored by TLC.

IIa: IR (KBr) : λ_{max}, 3045 (Ar-Hstr), 1617 (-C=N-str) cm^{-1}.NMR : ($CDCl_3$):δ 1.57(4H, dd, -CH_2-), 2.13 (2H, t, -CH), 6.9-7.8(20H, m, Ar-H) ppm.

IIb: IR (KBr) : λ_{max}, 3075(Ar-H str), 1619(-C=O str), 1023(-C=N str) cm^{-1}.NMR : ($CDCl_3$):δ 2.2-2.7(4H, dd, -CH_2-), 3.2 (2H, dd, -CH), 6.9-7.8(19H, m, Ar-H)ppm.

IIc: IR (KBr) : λ_{max}, 3395(-OH br), 3066(Ar-H str), 1618(>C=O str), cm^{-1}. NMR : ($CDCl_3$):δ, 2.2-2.7(4H, dd, -CH_2-), 3.4 (2H, dd, -CH), 3.7(1H, s, -NH), 6.9-7.9 (19H, m, Ar-H)ppm.

IId: IR (KBr) : λ_{max}, 3047(Ar-H str), 1613(-C=N str.) cm^{-1}.NMR : ($CDCl_3$):δ 2.4-2.7(4H, dd, -CH_2-), 3.1(2H, dd, -CH), 3.1 (2H, dd, -CH), 2.2(3H, s, -OCH_3) 7.2-7.9 (19H, m, Ar-H) ppm.

SCHEME

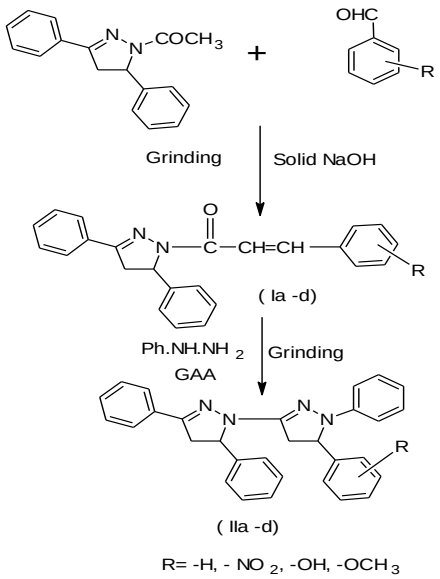


Table- 1: Physical and Analytical data of substituted pyrazole derivatives (Ia – IId):

Compound No.	- R	M.P. ^{0}C	Yield %	Mol. Formula	Elemental Analysis Calc./ (Found) %		
					C	H	N
I_a	-H	98	87	$C_{24}H_{20}ON_2$	81.82 (81.80)	5.68 (5.60)	7.95 (7.91)
II_a	-H	78	76	$C_{30}H_{26}N_4$	81.45 (81.46)	5.88 (5.88)	12.67 (12.65)
Ib	$-NO_2$	94	73	$C_{24}H_{19}O_3N_3$	72.54 (72.53)	4.79 (4.75)	10.58 (10.59)
IIb	$-NO_2$	80	68	$C_{30}H_{25}O_2N_5$	73.92 (73.90)	5.13 (5.11)	14.37 (14.37)
Ic	-OH	116	78	$C_{24}H_{20}O_2N_2$	78.26 (78.25)	5.43 (5.42)	7.61 (7.62)
IIc	-OH	102	65	$C_{30}H_{26}ON_4$	78.60 (78.58)	4.37 (4.38)	12.23 (12.19)
Id	$-OCH_3$	85	69	$C_{25}H_{22}O_2N_2$	78.53 (78.51)	5.76 (5.75)	7.33 (7.34)
IId	$-OCH_3$	104	63	$C_{31}H_{28}ON_4$	78.81 (78.80)	5.93 (5.90)	11.86 (11.85)

Table II: Antibacterial activity of Synthesized compounds (IIa-IVc):

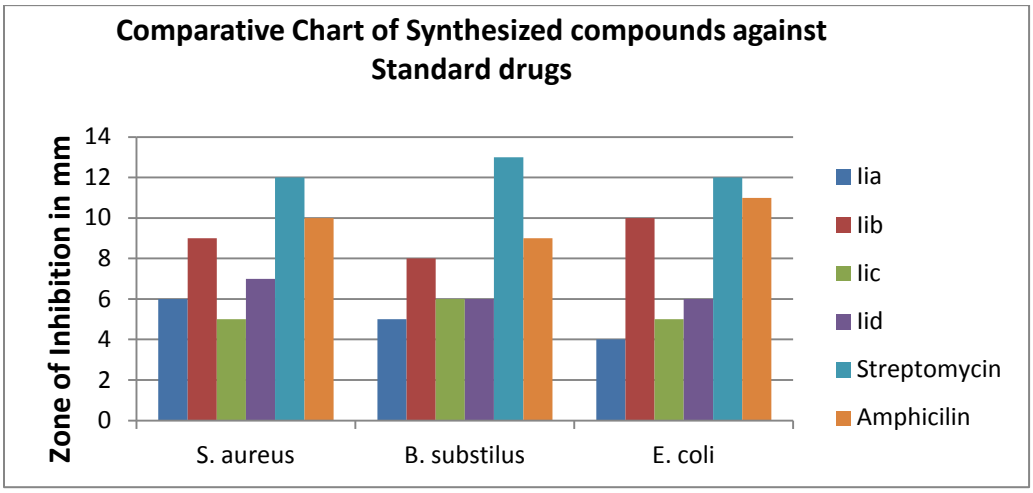
Compound No.	Zone of inhibition in mm		
	Gram Positive		Gram Negative
	S. aureus	B. substilus	E. Coli
IIa	06	05	04
IIb	09	08	10
IIc	05	06	05
IId	07	06	06
Standard Drug			
1. Streptomycin	12	13	12
2. Amphicilin	10	09	11
Duration 24 hours			

RESULTS AND DISCUSSION

The synthesis of 1-(sub.) benzoaceto-3,5-diphenyldihydropyrazole Ia-d Were carried out by the reaction of substituted benzaldehyde and N-acetyl-3-4-diphenylpyrazole by grinding technique as a key intermediate which further mixed by using agate morter with phenyl hydrazine in glacial acetic acid targeted corresponding N^1-(3,4-diphenyl,5′-dihydro-2,3-pyrazol)-3,5-diphenyl,4- diydropyrazole (IIa-d). The structures of the newly synthesized compounds were confirmed on the basis of elemental analysis (Table-I) and spectral data. The completion of reaction was monitored by TLC by using n-hexane and ethyl acetate as solvent system (2:8).The reagents utilized in the proposed method are readily available and does not involve any critical reaction conditions or tedious sample preparation.

Anti-microbial screening

In the present study, all the newly synthesized compounds were screened for their antibacterial activity using cup plate method against various gram positive i.e. *Staphylococcus aureus* and *Bacillus Substilus* while gram negative i.e. *E. Coli* using Streptomycin and Amphicilin as standard drugs**.** All the compounds were tested at the concentration of 100mg/mL .The zone of inhibition was measured in mm and DMF was used as a solvent**.** Most of the compounds were found to be more active against gram positive than gram negative bacterial species**.** Among the screened compounds, IIb was exhibited more activity against *E.coli*, *B. substilus* and *S.aureus* due to presence of electron withdrawing group $–NO_2$ which enhances the activity against standard drug. The compound IId was found to be moderately active against S. aureus, B. substilus and E. coli . The remaining pyrazole derivatives were found to be less activity against gram positive and gram negative bacterial species as per Table-II.



CONCLUSION

We have demonstrated eco-friendly, operationally simple and time efficient protocol for the synthesis of pyrozolidine derivatives of pyrrozole . Reaction procedures are very simple and yield of products are also excellent. The reagents utilized in the proposed method are readily available without the need for expensive instrumentation. All synthesized compounds were screened for antimicrobial activities and found to be moderate to excellent activity as compare to standard drug. A few exhibited activities comparable to those of a standard drug while one of them showed antibacterial activity more pronounced than that of the standard drug.

ACKNOWLEDGEMENT

We are very much thankful to Department of Chemistry, Shivaji University Kolhapur and Dahiwadi College, Dahiwadi (Dist.:- Satara) for spectral interpretation and to Department of Chemistry and Biotechnology, Y. C. Institute of Science, Satara for providing Laboratory and Antibacterial screening facilities.

REFERENCES

1. Chauhana A, Sharma PK, Kaushik N, Kumar N: Synthesis of Novel Pyrazole Analogues as Efficacious Antimicrobial Agents. Int J Pharm Pharm Sci, 2011; 5: 166-76.

2. Riyadh SM, Farghaly TA, Abdallah MA, Abdalla MM, Abd El-Aziz MR. Eur J Med Chem, 2010; 45: 1042. (b) El-borai MA, Rizk HF, Abd-Aal MF, El-Deeb IY. Eur J Med Chem, 2012; 48: 92.

3. Park HJ, Lee K, Park SJ, Ahn B, Lee JC, Cho HY, and Lee KI: Identification of antitumor activity of pyrazole oxime ethers. Bioorg Med Chem Lett, 2005;15: 3307-3312.

4. Bouabdallah I, Barret LA, Zyad A, Ramadan A, Zidane I and Melhaoui A: Anticancer effect of three pyrazole derivatives. Nat Prod Res, 2006; 20:1024-1030.

5. Yildirim I, Özdemir N, Akçamur Y, Dinçer M, Andaç O: 4-Benzoyl-1,5-diphenyl-1*H*-pyrazole-3-carboxylic acid methanol solvate . Acta Crystallogr, 2005; 61: 256.

6. El-Gazzar ABA, Hafez HN, Nawwar GAM: New acyclic nucleosides analogues as potential analgesic, anti-inflammatory, anti-oxidant and anti-microbial derived from pyrimido[4,5-*b*]quinolines . Eur J Med Chem, 2009; 44: 1427.

7. Malhotra P, Pattan S, Nikalje AP: Microwave assisted synthesis and anti-inflammatory Activity of 3, 5diaryl Substituted –2pyrazolines. Int J Pharm Pharm sci, 2010; 2(2): 21-26.

8. Chu CK, Cutler J: Chemistry and antiviral activities of acyclonucleosides. J Heterocycl Chem, 1986; 23: 289-319.

9. Yashumati R and Kishore D: Novel Pyrazole and Isoxazole derivatives from deoxybenzoin as intermediates for the synthesis of new chemical entities. Int J Adv Res Pharm and Bio Sci, 2013; 3(2): 95-101.