Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2012, 4(7):3478-3482

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis and antimicrobial activity of substituted 2H-Pyrrole-2-Ones derivatives based on 1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP)

Kokila Parmar*, Shashikant Sutariya, Maharshi Shukla and Kalpeshgiri Goswami

Department of Chemistry, Hemchandracharya North Gujarat University, Patan, Gujarat-India

---

ABSTRACT

Pyrrole are one of the heterocyclic compounds with very important biological activites. In this view, it was proposed to synthesize some novel Pyrrole-2-Ones derivatives from schiff bases. Here the synthesis of some pyrazole and sulphonamides using Maleic anhydride and schiff base under basic condition in presence of chloroform. The structures of synthesized were assigned on the basis of elemental analysis, IR and 1H NMR spectroscopy data. These compounds were screened for their anti-bacterial activity.

Keywords: Synthesis, Pyrazoles, antibacterial activity, schiff base, sulphonamides

---

INTRODUCTION

Heterocycles and medicines are both interrelated because humans are totally dependent on the drugs derived from heterocyclic rings. Nitrogen heterocycles are of special interest as they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities. Pyrroles and their derivatives exhibit different important biological activities like antibacterial, antioxidant, cytotoxic, insecticidal, anti-inflammatory, anticoagulant, antiallergic, antiarhythmic, hypotensive and anticonvulsant [1-7] etc. Pyrazoles and their derivatives exhibit a broad spectrum of biological activities such as antimicrobial [8], anti-inflammatory [9] and antitumor [10] activities, antibacterial [11], antifungal [12], antiviral [13], antitubercular [14], antioxidant [15], antiandrogenic [16] etc. On the other hand, sulfonamides and their different derivatives are extensively used in medicine due to their pharmacological properties such as antibacterial activity [17,18]. The newly synthesized compounds were evaluated as antimicrobial agents against gram positive and gram negative bacteria and fungi.

EXPERIMENTAL SECTION

Synthesis of (1E)-1-(phenyl)-ethanone-(phenyl)-hydrazone (1)
A mixture of phenyl hydrazine (0.01 mol) and acetophenone (0.01 mol) in absolute ethanol was refluxed in water bath for 2 hrs. in presence of 1 ml glacial acetic acid. The crude product was isolated and crystallized from absolute alcohol. Yield was about 94%.

Synthesis of 1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP) (2)
(1E)-1-(phenyl)-ethanone-(phenyl)-hydrazone (0.01 mol) was added in mixture of Vilsmeir-Haack reagent (prepared by drop wise addition of 3 ml of $POCl_3$ in ice cooled 25 ml di-methylformamide [DMF]) and refluxed for 5 hrs. The reaction mixture was poured into ice followed by neutralization using sodium bicarbonate. Crude product was isolated and crystallized from ethanol. Yield was about 82%.

Synthesis of sulfonamide derivatives of Arylidine–[1-N-phenyl-3-phenyl-pyrazole] (3a-h)
1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP) (0.01 mol) and various aromatic amine sulfonamides (0.01 mol) in 50 ml acetic acid was refluxed for about 10-12 hrs.on oil bath with TLC monitoring. The reaction mixture was cooled

and it was poured in to ice water and extracted with ethyl acetate and water. The solvent was evaporated to give the solid product . It was crystallized from ethyl acetate-hexane using decolorizing charcoal to give various anils having good yields.

Synthesis of 5-[1-N-phenyl-3-phenyl- pyrazole]-2-oxo-1-N-(phenyl-sulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4 a-h)

Maleic anhydride (0.1mol) and an imine (0.1mol) were heated at reflux in chloroform (30ml) for about 5 hours with TLC monitoring. After the mixture was allowed to stand for 2 days, the solid was filtered. The product thus formed was recrystallized from ethanol to give pure 5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-aryl-3,5-dihydro-1H-pyrrole-4-carboxylic acid in good yield.

The analytical and spectral data of the compounds are described

5-[1-N-phenyl-3-phenyl- pyrazole]-2-oxo-1-N-(phenyl-sulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4a)

IR (cm^{-1}): 3054(Ar-C-H str.), 2855 (C-H str.), 1667 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 1040 (N-N str.), 1095 (C-N str.), 1315-1365 (-SO_2), 3250-3330 (-NH of –SO_2NH); **NMR** (δ,ppm): 6.15-8.13 (m, aromatic H of pyrazole), 4.7 (s, H of C_5H), 5.15(s, H of C_3H), 12.92(s, H of COOH).

5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(4'-chloro-N-phenyl-sulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4b)

IR (cm^{-1}): 3030(Ar-C-H str.), 1670 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 1040 (N-N str.), 1095 (C-N str.), 1315-1365 (-SO_2), 3250-3330 (-NH of –SO_2NH); **NMR** (δ,ppm): 6.13-8.13 (m, aromatic H of pyrazole), 5.15 (s, H of C_5H), 4.8(s, H of C_3H), 12.92(s, H of COOH).

5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(4'-bromo-N-phenyl-sulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4c)

IR (cm^{-1}): 3030(Ar-C-H str.), 1670 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 1040 (N-N str.), 1095 (C-N str.), 1315-1365 (-SO_2), 3250-3330 (-NH of –SO_2NH); **NMR** (δ,ppm): 6.13-8.14 (m, aromatic H of pyrazole), 5.11 (s, H of C_5H), 4.8(s, H of C_3H), 12.92(s, H of COOH.

5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(4'-nitro-N-phenyl-sulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4d)

IR (cm^{-1}): 3032(Ar-C-H str.), 1690 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 1040 (N-N str.), 1095 (C-N str.), 1315-1365 (-SO_2), 3250-3330 (-NH of –SO_2NH); **NMR** (δ,ppm): 6.13-8.14 (m, aromatic H of pyrazole), 4.7 (s, H of C_5H), 5.15(s, H of C_3H), 12.90(s, H of COOH.

5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(4'-methyl-N-phenyl-sulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4e)

IR (cm^{-1}): 3030(Ar-C-H str.), 1670 (C=O str. of COOH),1720 (C=O of pyrrole-2-one), 1040 (N-N str.), 1095 (C-N str.), 1315-1365 (-SO_2), 3250-3330 (-NH of –SO_2NH); **NMR** (δ,ppm): 2.3 (m, aromatic H of pyrazole), 4.7 (s, H of C_5H), 5.15(s, H of C_3H), 2.4(s, 3H of CH_3), 12.90(s, H of COOH.

5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(2',6'-dichloro-4'-nitro-N-phenyl-sulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4f)

IR (cm^{-1}): 3030(Ar-C-H str.), 1672 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 1040 (N-N str.), 1095 (C-N str.), 1315-1365 (-SO_2), 3250-3330 (-NH of –SO_2NH); **NMR** (δ,ppm): 6.1-8.1 (m, aromatic H of pyrazole), 4.7 (s, H of C_5H), 5.15(s, H of C_3H), 12.90(s, H of COOH.

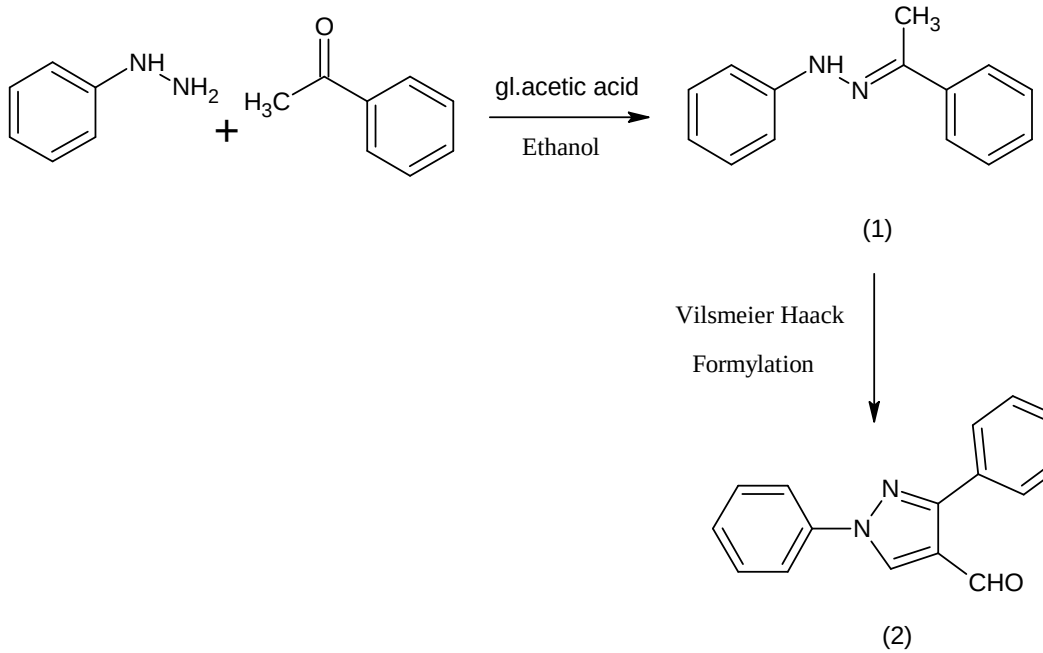
5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(N-(phenylsulfonyl)acetamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4g)

IR (cm^{-1}): 3030(Ar-C-H str.), 1672 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 1040 (N-N str.), 1095 (C-N str.), 1315-1365 (-SO_2), 3250-3330 (-NH of –SO_2NH); **NMR** (δ,ppm): 6.1-8.1 (m, aromatic H of pyrazole), 4.7 (s, H of C_5H), 5.15(s, H of C_3H), 12.90(s, H of COOH.

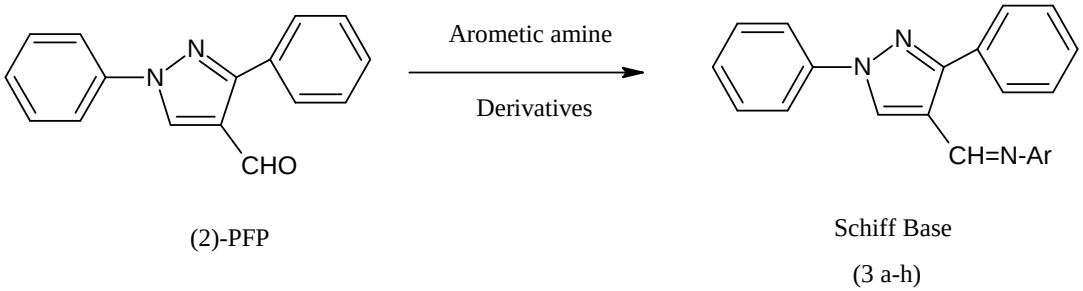
5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(2-pyridinylbenzenesulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4h)

IR (cm^{-1}): 3030(Ar-C-H str.), 1670 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 1040 (N-N str.), 1095 (C-N str.), 1315-1365 (-SO_2), 3250-3330 (-NH of –SO_2NH); **NMR** (δ,ppm): 6.1-8.1 (m, aromatic H of pyrazole), 4.7 (s, H of C_5H), 5.15(s, H of C_3H), 12.92(s, H of COOH

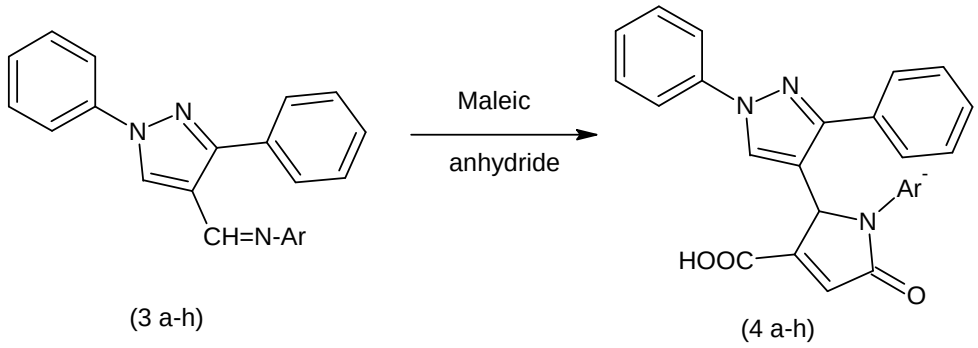
Scheme: 1



Scheme: 2



Scheme:3



Antibacterial susceptibility testing

The study has been conducted according to the method adopted by Cruickshank et al [12]. Nutrient agar broth was melted in a water bath and cooked to $45^{O}C$ with gentle shaking to bring about uniform cooling. It was inoculated with 0.5-0.6 ml of 24 hour old culture especially and mixed well by gentle shaking before pouring on the sterilized Petri dish (25 ml each). The poured material was allowed to set (1.5 hour) and there after the "cups" were made by punching into the agar surface with a sterile cork borer and stooping out the punched part of agar. Into this "cups" 0.1 ml of test solution (prepared by dissolving 10gm of sample in 10ml DMF) was added by sterile micropipette. The plates were noted. Ampicillin, Tetracycline, Gentamycin, and Chloramphenicol were used as standard drugs and a solvent control was also run to know the activity of solvent.

Activity of standards and inhibition due to DMF (solvent) are given in Table-2. The results shown by compounds and standards are corrected for DMF. Typical specimens are shown in figures.

Table: 1 Physical constant of 5-[1-N-phenyl-3-phenyl- pyrazole]-2-oxo-1-N-(aryl-sulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4a-h)

Compd	R	Mol. Formula (Mol. Wt)	m.p. (°C)	Yield %	% of C,H,N Calcd./Found			
					C	H	N	S
4a	$C_{12}H_{12}N_2O_2S$-	$C_{32}H_{24}N_4O_5S$ 576	179°C	64%	66.6	4.2	9.7	5.6
					66.5	4.1	9.5	5.5
4b	$C_{12}H_{11}N_2O_2SCl$-	$C_{32}H_{23}N_4O_5SCl$ 610.5	168°C	69%	62.8	3.7	9.2	5.2
					62.9	3.6	9.0	5.0
4c	$C_{12}H_{11}N_2O_2SBr$-	$C_{32}H_{23}N_4O_5SBr$ 655	172°C	63%	58.6	3.5	8.5	4.9
					58.5	3.4	8.7	5.0
4d	$C_{12}H_{11}N_3O_4S$-	$C_{32}H_{23}N_5O_7S$ 621	170°C	65%	61.8	3.7	11.3	5.2
					61.0	3.5	11.5	5.0
4e	$C_{13}H_{14}N_2O_2S$-	$C_{33}H_{26}N_4O_5S$ 590	174°C	70%	67.1	4.4	9.5	5.4
					67.0	4.2	9.8	5.1
4f	$C_{12}H_9N_3O_4SCl_2$-	$C_{32}H_{21}N_5O_7SCl_2$ 690	168°C	66%	55.6	3.0	10.1	4.6
					53.4	2.9	10.2	4.7
4g	$C_8H_{10}N_2O_3S$-	$C_{28}H_{22}N_4O_6S$ 542	184°C	62%	62.0	4.0	10.3	5.9
					61.5	3.9	10.0	6.0
4h	$C_{10}H_{10}N_4O_2S$-	$C_{30}H_{22}N_6O_5S$ 578	176°C	65%	62.3	3.8	14.5	5.5
					61.2	3.5	14.4	5.6

Table-2 Antimicrobial activity of Standards and Solvent (DMF)

No.	Name of compound	*Zone of inhibition (in mm)*			
		Gram positive		*Gram negative*	
		B.Subtillis	*S.Aureus*	*E.Coli*	*Ps.Aeruginosa*
1	DMF	7	5	5	5
2	Ampicillin	14	12	21	19
3	Tetracyclin	21	22	15	18
4	Gentamycin	20	19	18	22
5	Chloramphenicol	21	23	17	24

Table-3 Antimicrobial activity of 5-[1-N-phenyl-3-phenyl- pyrazole]-2-oxo-1-N-(aryl-sulfonamide)-3,5-dihydro-1H-pyrrole-4-carboxylic acid (4a-h)

Compound (designation)	*Zone of Inhibition (in mm)*			
	Gram positive		*Gram negative*	
	B. Subtillis	*S. Aureus*	*E. Coli*	*Ps. eruginosa*
4a	11	16	10	22
4b	18	14	17	18
4c	20	18	14	14
4d	24	21	17	17
4e	13	17	16	06
4f	14	14	12	11
4g	14	14	04	19
4h	19	16	15	14

RESULTS AND DISCUSSION

Structures of all synthesized compounds were confirmed by analytical and spectral data. The C, H, N and S contents of the prepared compounds were consistent with their predicted structures as shown in Scheme-I, II and III. The infrared spectra show the band in the region 1680-1710 cm^{-1} for carbonyl (>C=O) group, which is the characteristic band for the cyclic 2H-pyrrole-2-one ring.

The proton magnetic resonance spectra of the prepared compounds show singlet at 5.15 δ for CH proton at position-5 in the 2H-pyrrole-2-one ring. All other signals are at their respective positions in the PMR spectrum. Among all compounds, compound 4b, 4c and 4d show good anti bacterial activity against both gram positive and gram negative bacteria.

REFERENCES

[1] FM Hersheson. *J. Org. Chem.*, **1972**, 20, 3111-3113.
[2] MM Hania. *Asian J. Chem.*, **2002**, 2, 1074-1075.
[3] RH Guy; TK Jeffrey. *Chem. Rev.*, **2006**, 106, 2875-2911.

[4] ND Jaime, AR William. Text book of organic medicinal and pharmaceutical chemistry, 10th Ed, **1997**, 37-38.
[5] G Sharda. *Ind. J. Hetero. Chem.* **2006**, 15, 401-402.
[6] CG Dave; PR Shah; SP Upadhyaya. *Ind. J. Chem.*, **1988**, 27(B), 778-780.
[7] CG Dave; PR Shah; SP Upadhyaya; *Indian J. Chem.*, **1988**, 27(B), 1046-1048.
[8] EM Robin; RG David; S Vijayalekshmi. *J. Phytochem.*, **2008,** 69(3), 2704-2707.
[9] N Gokhan-Kelekci; S Yabanoglu; E Kupeli; U Salgin; O Ozgen; G Ucar; E Yesilada; E Kendi; A Yesilada; AA Bilgin. *J. Bioorg. Med. Chem.*,**2007,** 5(17), 5775-5786.
[10] L Ronghui; C George; Y Yang; JC Peter; L Shengjian; L Yanhua; A Mary; AR Fuentes-Pesquera; LE Stuart; MG Lee. Bioorg. *Med. Chem. Lett.*, **2007,** 17 (16), 4557-4561.
[11] SG Roelfvan; C Arnold; K Wellnga, *J Agric Food Chem*.**, 1979**, 84, 406.
[12] Rajendra; K Wanare. *J. Chem. Pharm. Res*., **2011**, 3(5), 136-144.
[13] Meghasham; N Narule. *J. Chem. Pharm. Res.*, **2011**, 3(3), 38-47.
[14] HZ Katri; SA Vunii. *J. Ind. Chem. Soc.*, **1981,** 58, 168.
[15] Singarave; Mohan; Sarkkarai; Ananthan. *J. Chem. Pharm. Res.*, **2011,** 3(1), 402-413.
[16] G Amr Ael; NA Abdel-Lalif; MM Abdalla. *Bioorg. Med. Chem.*, **2006**, 14(2), 373.
[17] O Zbek; N Katırcıogˇlu; H Karacan; T Baykal. *Bioorg. Med. Chem.*, **2007,** 15, 5105–5109.
[18] BK Mahantesha; VK Manohar; PR Vijaykumar; P Harishchandra; SM Sumit; AM Ashwini. *Euro. J. Med. Chem.*, 45(3), s1151-1157.