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Synthesis of Novel Schiff Bases Derived from 4-aminoantipyrine

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ABSTRACT

Schiff bases are important intermediates for the synthesis of some pharmacological compounds and they represent as synthons for synthesis of new deferent organic compounds. Novel Schiff bases were prepared in excellent yields via the condensation of new 4-aminoantypyrine derivative with different aliphatic and aromatic carbonyls. The new 4-aminoantypyrine derivative namely 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)acetohydrazide was synthesized by the substitution reaction of 4-aminantypyrine with methyl bromoacetate followed by condensation reaction with hydrazine. The synthesized compounds were characterized by deferent spectroscopical techniques, Fourier transformer infrared (FT-IR), Nuclear magnetic resonance and mass spectroscopy.

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INTRODUCTION

4-Aminopyrine has potential biological activities (Cechinel Filho, V., 1998; Sondhi, S.M., 1999; Mishra, A.P., 1999; Raman, N., 2002; Raman, N., 2004; Sondhi, S.M., 2001 Sutcliffe, J.A., 2003), such as analgesic, anti-inflammatory, antimicrobial, and anticancer properties. In recent years, a number of research articles have been published on transition metal complexes derived from 4-aminoantipyrine derivatives with aza or aza-oxo donor atoms (Deepa, K., 2005; Radhakrishnan, T., 1976; Ismail, K.Z., 2000**;** Agrawal, R.K., B. Prakash, 2005). Compounds containing the -C=N- (azomethine group) structure are known as Schiff bases, usually synthesized from the condensation of primary amines and active carbonyl groups. Schiff bases are well known for their biological applications as antibacterial, antifungal, anticancer and antiviral agents (Nath, M., 2010; Cheng, L., 2010). Schiff bases are important intermediates for the synthesis of some bioactive compounds such as β-lactams (Venturini, A., J. Gonzalez, 2002; Taggi, A.E., 2002; Delpiccolo, C.M.L., E.G. Mata, 2002). Furthermore, they are reported to show a variety of interesting biological actions, including antibacterial (More, P.G., 2001; Pandeya, S.N., 1999; Baseer, M.A., 2000; El-Masry, A.H., 2000; Karia, F.D., P.H. Parsania, 1999; Kabeer, A.S., 2001), antifungal (Singh, W.M., B.C. Dash, 1988), anti mouse hepatitis virus (MHV) (Wang, P.H., 1990), inhibition of herpes simplex virus type 1 (HSV-1) and adenovirus type 5 (Ad 5) (Das, A., 1999), anticancer (Desai, S.B., 2001; Pathak, P., 2000; Kuz'min, V.E., 2000; Phatak, P., 2000), anti mosquito larvae (Das, B.P., 1994) and herbicidal activities (Samadhiya, S., A. Halve, 2001).

In light of the interesting variety of biological activities seen in compounds containing antipyrine group and azomethine linkages, it was thought of interest to synthesis novel compounds having all of above functionalities present simultaneously in one structure. Based on this notion we thus decided to synthesize of new 4-aminoantipyrine derivative namely 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)acetohydrazide. It was synthesized by the substitution reaction of 4-aminoantipyrine with methyl bromoacetate followed by condensation reaction with hydrazine hydrate. The novel Schiff bases were synthesized by the reaction of 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)acetohydrazide with different aliphatic and aromatic carbonyls. The new compound synthesized with a satisfactory yield was characterized by nuclear magnetic resonance, FT-IR spectroscopy and mass spectrometry, table 1 show the physical data of compounds.

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Table 1: Physical data of compounds.

Compound no.	Colour	Melting point C*	Yeild(%)
2	brown	Oily	75 %
3	light brown	Oily	50 %
4	light brown	Oily	40 %
5	dark brown	Oily	45 %
6	dark brown	Oily	55 %

Experimental Procedure:

General:

All chemicals used in this work were of reagent grade (supplied by either Sigma-Aldrich or Fluka) and used without farther purifications. The FTIR spectra were recorded in the (4000–400) cm−1 range on Potassium bromide disks using a Shimadzu FTIR 8300 Spectrophotometer. Proton NMR spectra were recorded on Bruker-DPX 300 MHz spectrometer with TMS as internal standard. A Gallenkamp M.F.B.600.010 F melting point apparatus was used to measure the melting points of all the prepared compounds.

Synthesis of compound (2) { methyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino) acetate}:

A suspension of (6.17 mmol) 4-aminoantipyrine (1) in acetone (30 mL) was refluxed with methyl bromoacetate (9.15 mmol) and K_2CO_3 (4.69 g, 33.91 mmol) for 12 h. After cooling, the mixture was evaporated to dryness and the residue was partitioned between $CHCl_3$ (50 mL) and water (50 mL). The organic phase was dried (Na_2SO_4), filtered and evaporated to dryness. The residue was recrystallized from acetone.

Synthesis of compound (3) {2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino) acetohydrazide}:

A solution of compound(2) (10 mmol) in ethanol 25 mL was refluxed with hydrazine hydrate (15 mmol) for 4 h. After concentrating the reaction mixture a solid mass separated out and recrystallized using ethanol.

Synthesis of Sciff bases (compounds 4,5,6):

A solution of the compound(3) (0.2 mmol) in ethanol 25 mL was refluxed with aromatic and aliphatic carbonyls (4-aminoantipyrine, 2-methylbenzaldehyde and propan-2-one) (0.2 mmol) for 20 h. After cooling to room temperature, a solid mass separated and recrystallized. Recrystallized from ethanol.

RESULTS AND DISCUSSION

The reaction sequence for the synthesis of compound (4),2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)-N'-(2-methylbenzylidene)acetohydrazide, compound (5), N'-(4-amino-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-ylidene)-2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)acetohydrazide and compound (6) 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)-N'-(propan-2-ylidene)acetohydrazide ,is out lined in Scheme 1.

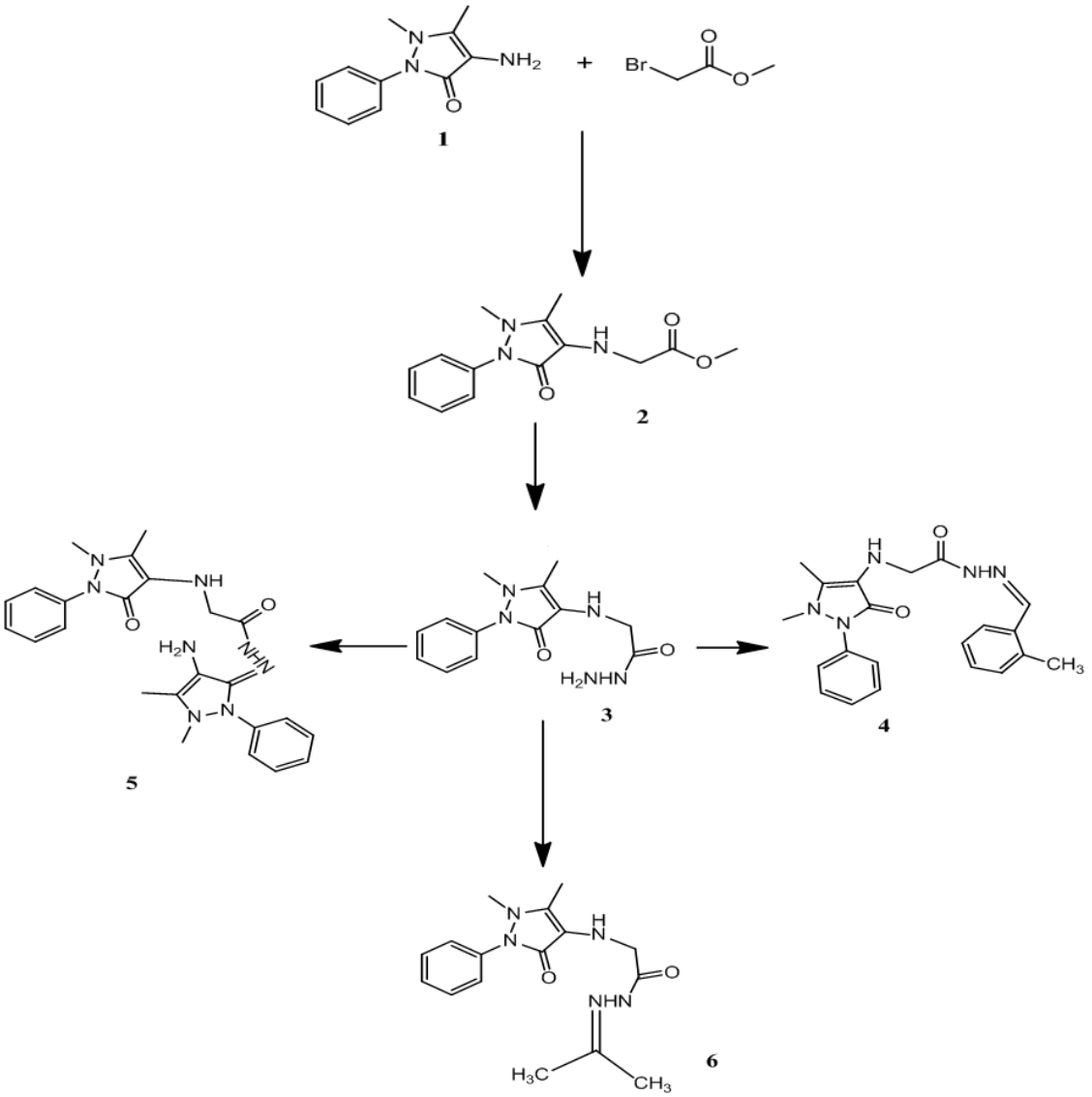
methyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)acetate (2) was conducted via reflux of methyl bromoacetate with 4-aminoantipyrine 1 in the presence of anhydrous potassium carbonate in acetone. The structure of Methyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)acetate was determined by FT-IR ,1HNMR, mass spectrometery as follow : 1H-NMR (CHCl3): d 2.260 (S, 3H, CH3), d 2.240 (S, 1H,NH), d 3.102 (S,3H,CH3) and d3.695(S,3H,CH3-O) ,d 3.904(S, 2H,CH2-N) , d 7.330, d 7.334,d 7.280 (S, 1H) for aromatic ring ;; IR: 2952.6cm-1 (C-H, aliphatic), 3090.6cm-1 (C-H, aromatic), 3436.1 cm-1 (N-H), 1748.1cm-1 (C=O, ester), 1652.3cm-1 (C=C, alkene), 1592.5cm (C=C,aromatic).

Hydrazinolysis of compound 2 with hydrazine hydrate produced hydrazide2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino) acetohydrazide (3) in good yield. The FT-IR spectrum of compound 3 showed absorption bands in the 3245.9, 3330 cm−1 (hydrazide NH-NH2), 1660 cm−1 (lactonic -C=O carbonyl stretching), and 1592. cm−1 (amide -C=O carbonyl stretching).

Compound (3) ,was then condensed with 2-methylbenzaldehyde to make compound (4) .The IR spectrum of compound (4) showed characteristic bands at 3233.4 cm−1 (NH), 2966.6for methyl group, 1661.3 (C=O, lactone) cm−1.

Compound (3), was then condensed with 4-aminoantipyrine to make compound (5). The IR spectrum of compound (5) showed characteristic bands at 3396.6 cm−1 (NH), 1663.8 (C=O, lactone) cm−1,

Compound (3), was then condensed propan-2-one to make compound (6). The IR spectrum of compound (6) showed characteristic bands at 3221.8 cm−1 (NH), 2912.3 for methyl group, 1667.0(C=O, lactone) cm−1,



Scheme 1: Synthesis of new Shiff bases.

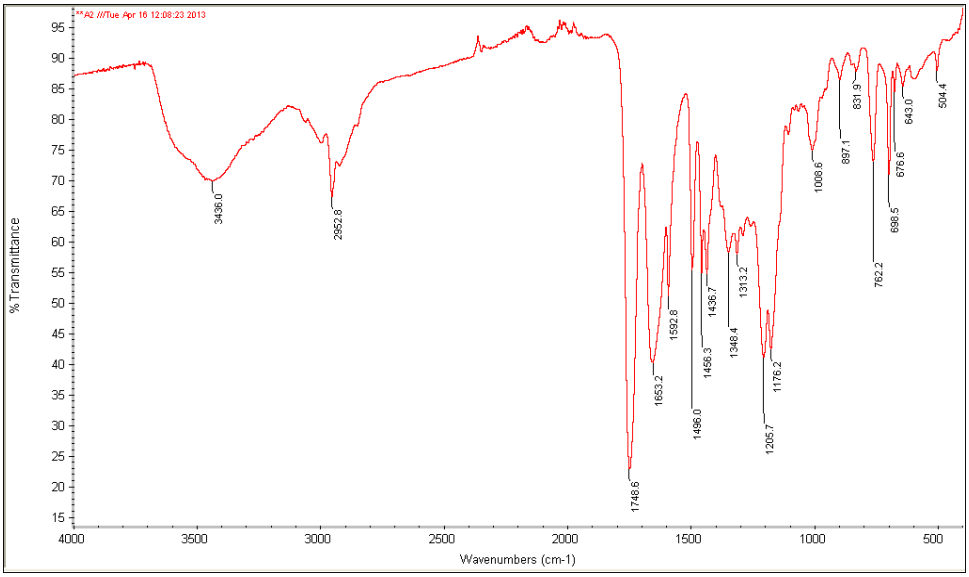


Fig. 1: The FT-IR spectroscopy of Compound (2) Methyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro1H-pyrazol-4-yl)amino)acetate.

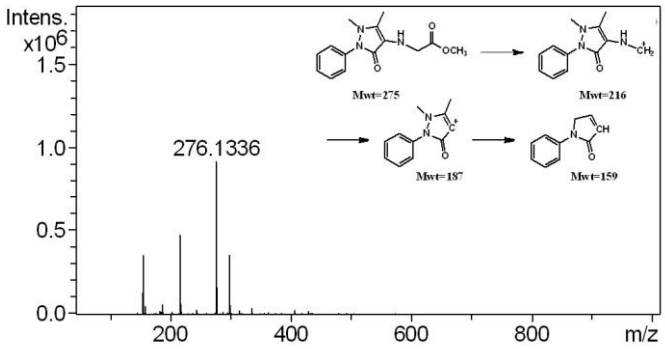


Fig. 2: The mass spectrometery of Compound (2) Methyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3 dihydro-1H-pyrazol-4-yl)amino)acetate.

Conclusion:

In this study, new compound, namely Methyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)acetate has been successively synthesized, and characterized by using various spectroscopic techniques (FT-IR, NMR and Mass spectrum). Postulated mechanism has been proposed for the fragmentation of new synthesized compound according to mass spectrum.

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