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Synthesis and Characterization of 2-Pyrazoline Derivatives from α,β Unsaturated Ketone

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Abstract:
2-(4, 5-dihydro-5-(4-methoxyphenyl)-1*H*-pyrazole-3-yl) phenol(Compound 1a) and 1-(4, 5-dihydro-3-(2-hyoxyphenyl)-5-(4-methoxyphenyl) pyrazole-3-yl) ethanone(Compound 1b)were synthesised from o-hydroxy acetophenone.Compound 1a, 1bwere prepared from α,β unsaturated carbonyl compound(chalcone)by cyclisation with hydrazine hydrate and hydrazine withacetic acid. Chalcone1-(2-hydroxyphenyl)-3-(4-methoxyphenyl) prop-2-en-1-one(Compound 1) wasprepared by condensing o-hydroxy acetophenone with 4-methoxy benzaldehyde using LiOH as base.

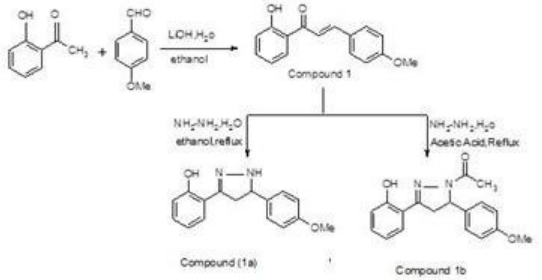
Keywords: LiOH, Pyrazoleand chalcone.

Introduction:

Pyrazoline is 5-membered ring having two adjacent nitrogen atom within ring it has only endocyclic double bond and is basic in nature[1]. Amongst heterocyclic compounds,pyrazoline have most important useful by biological activity.Due to rich biological activity, pyrazol frame work plays an essential role in biological active compound and therefore represents interesting templet for combinatorial as well as medicinal chemistry[2]. A classical synthesis of these compounds involves the base catalysed aldol condensation reaction of ketones and aldehydes to give α, β-unsaturated ketones (chalcone), which undergo a subsequent cyclization reaction with hydrazine`saffording pyrazols[3]. Available data suggest that N containing heterocyclic compounds from chalcone possesses wide variety activites such as

Potential cytotoxic agents, antimicrobial agents, antiviral, anti-inflammatory,anesthetics,mydriatics etc[4]. Pyrazole derivatives have a long history of application in agrochemicals and pharmaceutical industry as herbicides and active pharmaceuticals[5].Compounds containing the fused pyrazole quinololine motifs emerged as potent anti-angiogenic compounds, which also had the ability to inhibit the growth of human breast (MCF-7) and cervical (Hela) carcinoma cells in vitro206many pyrazoles are used for the treatment of thyroid and leukamemia[6]. It has incidental antiviral activity against Herpes and Vaccinia infections[7]. Hetrocyclic chemistry comprises at least half of all organic chemistry research worldwide. It is not surprising that research on the synthesis of poly functionalized heterocyclic compounds has received significant attention.The synthesis of these heterocyclic has been divided according to the number of heteroatoms in the heterocyclic[8].The pyrazole ring is common in a number of biologically active molecules. Considerable interest has been focused on the pyrazole structure, which has been known to possess a broad spectrumof biological activities[9].A number of chalcones having hydroxyl, alkoxy groups in different position have been reported to possess biological activity and inhibition of chemical mediators release, and inhibition of aldose reductase activities[10]

Scheme:



Experimental section:

Preparation of 1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one(Compound1): To a solution of o-hydroxy acetophenone (2gm≈1.76ml,0.01mol)and 4-methoxy benzaldehyde(1.99gm≈1.78ml,0.01mol) in ethanol(2ml), a catalytic amount of LiOH(monohydrated) dissolve in 5 ml water was added. The reaction mixture was stirring for 2hrs. The reaction was monitored by TLC.After completion of reaction,the reaction mixture was poured in ice cold water.After filtration, the product was washed with cold water, dried and crystallized from ethanol to yield a pure compound.

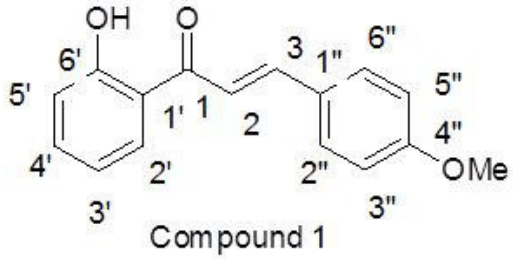
Preparationof 2-(4,5-dihydro-5-(4-methoxyphenyl)-1H-pyrazole-3-yl)phenol(Compound 1a): To the chalcone (1gm,0.003mol) in ethanol(3ml),hydrazine hydrate(0.29gm≈0.28ml,1.5mol),reflux for 3hrs at 80^{0}C.The reaction was monitored by TLC.After completion of reaction, the reaction mixture was poured in ice cold water.The product was filtered and washed with cold water,dried and crystallized from ethanol to yield a pure compound.

Preparation of(2-hyoxyphenyl)-5-(4-methoxyphenyl) pyrazole-3-yl) ethanone(Compound1b):

To thechalcone(1gm, 0.03mol)in ethanol(3ml), hydrazine hydrate(0.294gm≈0.28ml, 1.5mol),glacial acetic acid(0.35gm≈0.33ml, 1.5 mol) and 1 to 2 drop of H_2SO_4 was added,reflux for 3hrs.at80^{o}C. The reaction was monitored by TLC. After completion of reaction,the reaction mixture was poured in ice cold water.The product was washed with cold water, dried and crystallized from ethanol to yield a pure compound.

Results and Discussion:

Compound(1):



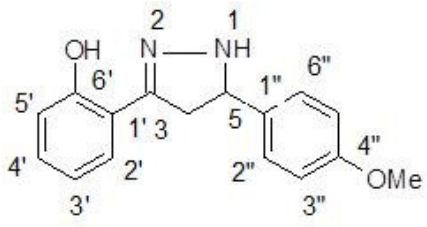
Compound 1

1-(2-hydroxyphenyl)-3-(4-methoxyphenyl) prop-2-en-1-one

1-(2-hydroxyphenyl)-3-(4-methoxyphenyl) prop-2-en-1-one, a yellow crystalline solid, $C_{16}H_{14}O_3$ was purified by crystallization usingethanol;m.p.120^{o}C,^{1}H- NMR spectrum showed characteristic doublets of para disubstituting aromatic protons at δ 7.85 (d, J=8Hz,2H) for H-2′′and H-6′′ and at δ 7.02 (d,J=8Hz,2H) for H-3′′and H-5′′.The singlets at δ 3.85 shows intense peak for methoxy proton H-4′′.The signals at δ 6.91 to 7.60 (m, 4H) for H-3′, H-4′, H-5′and H-6′.The signals shows at δ 7.59 (d,J=16 Hz, 1H) and δ 7.89 (d,J=16Hz, 1H) have been assigned for H-2 olefinic proton attached to aromatic ring and for H-3 olefinic proton attached to carbonyl carbon respectively.This shows Trans nature of olefinic bond.

The ^{13}C NMR spectrum of compound **1** shows total sixteen carbons atoms,multiplicities of carbon signals were determined by the DEPT plus sequence. The signals appeared at δ191.04 for C-1 carbonyl carbon in conjugated with aromatic ring, δ130.16 (s) for C-1′.The signals at 114-129 (d) have been assign for aromatic carbon of C-3′,C-4′& C-5′,C-6′.The signals at δ 132 (d) are assign for aromatic carbon of C-2′′and C-6′′ and δ114 (d) are aromatic carbon of C-3′′& C-5′′. Two singlets observed at δ132(s) & δ144(s) represent the tetrasubstituted aromatic carbon for C-1′′ & C-4′′ position of methoxyphenyl ring.

Compound (1a):



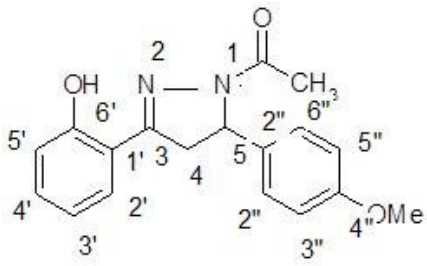
Compound (1a)

2-(4, 5-dihydro-5-(4-methoxyphenyl)-1H-pyrazole-3-yl) phenol

2-(4,5-dihydro-5-(4-methoxyphenyl)-1H-pyrazole-3-yl)phenol a faint yellow crystalline solid, $C_{16}H_{16}O_2N_2$ was purified by crystallization using ethanol, m .p.126° C,^{1}H-NMR spectrum showed characteristic doublets of para disubsitituted aromatic proton at δ2.68(d, 2H) for H-4.The signal appered at δ6.9(d, 2H) for H-5. The singlets at δ 3.85 shows intense peak for methoxy proton H-4′′.The signal observed at δ6.95 (d, 2H) for H-5′′ & H-3′′ and the signal shows at δ7.79 (d, 2H) for H-2′′ & H-6′′ respectively. The signal appered at δ8.61(s, 1H) for H-1 and signal observed at δ13.24 (s, 1H) for H-6′′.

The ^{13}C NMR spectrum of compound 1 shows sixteen carbons atoms,multiplicities of carbon signals were determined by the DEPT plus sequence. The signals appeared at δ169(s) for C-3 tetrasubstituted carbon of pyrazol ring which is conjugation with aromatic ring. δ130.13, δ161.09(s) for C-1′ & C-4′ carbon aromatic ring, δ127.03 (d) & δ114.26 (d) are assigns for aromatic carbon of C-2′ & C-6′ and C-3′ & C-5′ respectively. A methylene signals noticed at δ55.40 (t) for C-4 position of pyrazol ring. Signals at δ127.03 (d) & δ130.14 (d) are assigns for aromatic carbons of C-2′′ & C-6′′andC-3′′ &C-5′′ respectively. Two singlets are observed at δ 133.40 (s) and δ 136.40 (s) represents the tetrasubstituted aromatic carbon for C-1′′ & C-4′′ position of methoxyphenyl ring.

Compound (1b):



Compound 1b

2-hyoxyphenyl)-5-(4-methoxyphenyl) pyrazole-3-yl) ehanone

(2-hyoxyphenyl)-5-(4-methoxyphenyl) pyrazole-3-yl)ethanone a greyish powder,$C_{18}H_{18}O_3N_2$ was purified by crystallization in ethanol, m.p.115°C, ^{1}H NMR spectrum shows characteristic doublets of para substituted aromatic proton at δ 7.78(d,J=8Hz,2H) andδ 6.94(d,J=8Hz,2H) for H-2′′ & H-6′′ andH-3′′ & H-5′′ respectively.The singlets at δ 3.85 shows intense peak for methoxy proton H-4′′.The Signals observed at δ 2.57 (s,3H) shows for acetoxy methyl proton. Multiplates δ 6.88 toδ 7.02 assign for aromatic protons ofH-3′,H-4′, H-5′,and H-6′.Signals δ 2.67(dd, 2H) assign for H-4 and at δ6.95 (dd, J=4H, 6Hz, 1H)assign for H-5 proton of pyrazol ring.

The ^{13}C NMR spectrum of compound shows 18 carbons atoms,multiplicities of carbon signals were determined by ^{13}C-NMR and DEPT plus sequence. The signals appeared at δ161.55 (s) for C-3 tetrasubstitud carbon of pyrazol ring which is conjugation with aromatic ring. The signals at δ 130. (s)For C -1′, & δ 115 to 129 (d) assign for aromatic carbon C-3′, C-4′, C-5′, C-6′.The dept spectrum indicates presence of three methylene carbon. A methylene signals notice at δ14.21 (t) for methyl carbon at C-4 position of pyrozoline

ring. Signals at δ 130.1 (d) & δ114 (d) are assign for aromatic carbon C-2˝ & C-6 ˝ and C-3˝ & C-5˝ respectatively .Two singlets are observed at δ132 (s) and δ1118.99(s) represents the tetrasubstituted aromatic carbon for C-1˝&C-4˝ position of methoxyphenyl ring.

Conclusion: The Pyrazole were synthesized from chalcone using LiOH as a base instead of NaOHgives good yield.The result of the present investigation will help researchers in several area like Pharmacognosy, synthetic chemistry, drug chemistry, Pharmacology etc.

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