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SYNTHESIS AND ANTI OXIDANT ACTIVITY OF N[1]-(4-FORMYL PHENYL)-5-(4-HYDROXY PHENYL)-1H-PYRAZOLE-3-CARBOHYDRAZIDE.

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ABSTRACT

Pyrazoles are important class of heterocyclic compounds possessing interesting biological and Pharmacological properties as anti-inflammatory, anti-cancer, anti-bacterial, anti-viral, antipyretic, antiarrhythmic, tranquilizing, muscle relaxing, anticonvulsant, anti-diabetic and anti-fungal agents. Pyrazolines obtained by cyclization of chalcones with arylhydrazines, can be easily oxidized to pyrazoles. The compounds containing a pyrazole scaffold have been shown to exhibit HIV-1 reverse trancriptase inhibition, as well as anti hyperglycemic, antibacterial, sedative-hypnotics, anti-inflammatory, antipyretic and analgesic activity.

KEYWORDS: Pyrazole, p-hydroxy acetophenone, spectral analysis, anti oxidant.

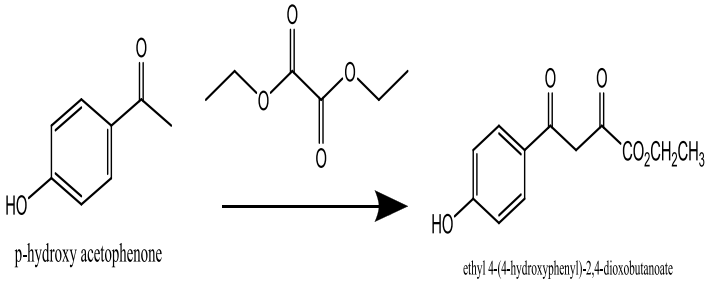
INTRODUCTION

Pyrazole is the chemical species of five-membered heterocyclic ring compound with two nitrogens replacing carbon-hydrogen units in the cyclopentadiene ring structure. The names of the two isomers indicate which of the carbon- hydrogen units in the cyclopentadiene ring position.

MATERIALS AND METHODS

Scheme of the work

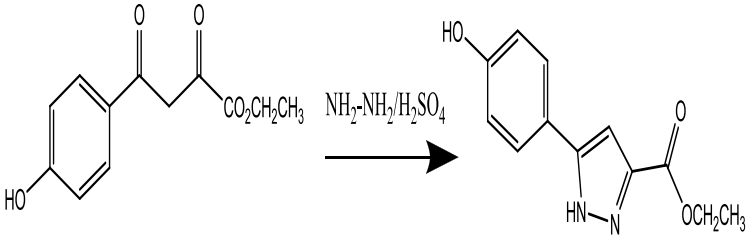
STEP: 1. SYNTHESIS OF P- OH-ETHYL-2, 4-DIOXO-4-PHENYL BUTANOATE.



p-hydroxy acetophenone ethyl 4-(4-hydroxyphenyl)-2,4-dioxobutanoate

Treatment of equimolar amounts of para hydroxy acetophenone with diethyl oxalate in sodium ethoxide and ethanol at room temperature.

STEP: 2. SYNTHESIS OF P-OH-ETHYL-5-PHENYL-1H-PYRAZOLE-3-CARBOXYLATE.

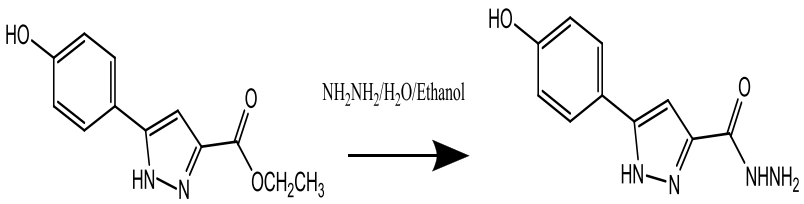


ethyl 4-(4-hydroxyphenyl)-2,4-dioxobutanoate ethyl 5-(4-hydroxyphenyl)-1*H*-pyrazole-3-carboxylate

To a solution of compound1 (0.2mole) in ethanol, hydrazine hydrate (0.2mole) is added. The mixture is refluxed for 8 hours.

The solvent is evaporated and the solid obtained is recrystalized from petroleum ether.

STEP: 3. SYNTHESIS OF P- OH-5-PHENYL-1H-PYRAZOLE-3-CARBOHYDRAZIDE.



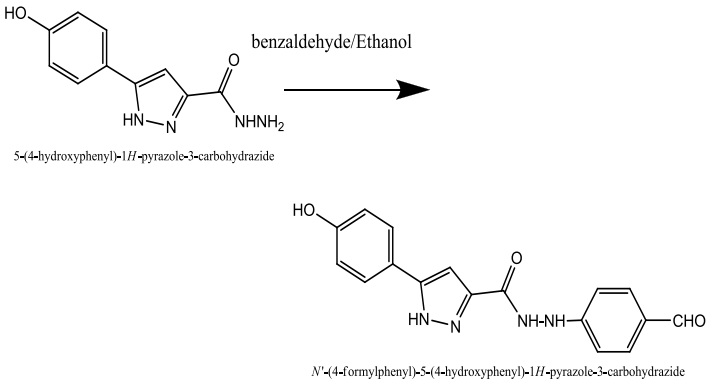
ethyl 5-(4-hydroxyphenyl)-1*H*-pyrazole-3-carboxylate 5-(4-hydroxyphenyl)-1*H*-pyrazole-3-carbohydrazide

Compound 2 (0.1mole) in ethanol (10ml) 2ml of hydrazine hydrate is added.

The mixture is maintained under reflux for 8 hours.

After cooling, the mixture is poured on ice and the solid formed is collected by filtration, washed with cold water and recrystalized from ethanol.

STEP: 4. SYNTHESIS OF N^1-(4-FORMYLPHENYL)-5-(4-HYDROXY PHENYL)-1H-PYRAZOLE-3-CARBOHYDRAZIDE.



Compound 3 (0.1mole) in 20ml of ethanol.

It is added an equimolar amount of benzaldehyde in the presence of acetic acid.

The mixture is maintained under reflux for 3 hours.

Then the reaction mixture is poured in cold water and the precipitate formed was filter, and wash with ethanol and recrystalized from methanol/DMF.

Physical characterization

- ✓ Molecular formula: $C_{17}H_{14}N_4O_3$
- ✓ Molecular weight (gm): 322.32g/mol
- ✓ Soluble in Methanol, Ethanol, DMSO and DMF.
- ✓ Melting point: 155ºC
- ✓ Melting points were determined using Veego Digital melting point apparatus.
- ✓ The purity of synthesis compound was monitored on TLC.
- ✓ Absorbent used: Precoated Silica gel- G plate
- ✓ Mobile Phase: Chloroform: Methnol (4:6)
- ✓ R_f value: 0.80

Biological screening

***IN VITRO* ANTIOXIDANT ACTIVITY**

An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons from a substance to an oxidizing agent. Oxidations reactions can produce free radicals, which start chain reactions that damage cells. Antioxidants terminate these chain reactions by removing free radical intermediates and inhibit other oxidation reaction by being oxidized themselves. Hydrogen peroxide scavenging activity is one of the methods for determining antioxidant *in-vitro* activity.

Nitric oxide radical-Scavenging Activity

Reagents

- Sodium nitroprusside
- Standard phosphate buffer solution
- Griess Reagent (mixing the equal volume of 1% sulphanilamide in 2% phosphoric acid & 0.1% naphthyl ethylene diamine dihydrochloride in water).

Standard: - Ascorbic acid.

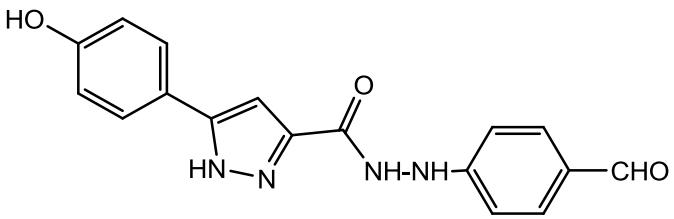
Hydrogen peroxide (H_2O_2) Scavenging Activity

Reagents

- Hydrogen peroxide
- Methanol
- Phosphate buffer saline(PH-7.4)

Standard: - Ascorbic acid.

Spectral analysis



IUPAC Name

N'-(4-formylphenyl)-5-(4-hydroxyphenyl)-1H-pyrazole-3-carbohydrazide

^{1}HNMR Interpretation

^{1}HNMR Spectral data Absorption position (in PPM)	
7.02 - 7.49	m, 6H, CH
6.76 – 6.86	d, 6H, CH
5.35	s, 1H, OH
4.0	d, 1H, NH

Mass Spectrum

M/z (M+)	M/B (B+)
310.39	142.21

RESULTS AND DISCUSSION

Synthesis

The present study report the Synthesis of pyrazole derivatives. Electrophilic substitution of diethyl oxalate group in p-hydroxy acetophenone was carried out stepwise at different temperature by hydrazine hydrate. The first step involves the substitution of diethyl oxalate and the next by hydrazine hydrate with sulphuric acid. The final amino group in the synthesized compound-3 was replaced by benzaldehyde. Since the report regarding this compound suggest a good bioactive moiety.

Physical Characterization

Melting point of the synthesize compound was taken in open capillary tubes and was uncorrected and were found to be in the range of 140-160°C.

TLC was performed using precoated silica gel plates of 0.25mm thickness. Eluents used were Chloroform, Methanol (4:6). Spots were visualized in U.V. light.

At room temperature solubility of newly synthesize compound were determined by various organic solvents and it was found that compound were freely soluble in DMSO, DMF, Methanol and Ethanol.

ANTIOXIDANT ACTIVITY

Nitric oxide radical-Scavenging Activity

In the assay, 2ml of sodiumnitroprusside (10mM) in 0.5ml phosphate –buffered saline (PBS) was mixed with 0.5ml of different concentration of sample ranging from (50-250µg/ml) prepared in methanol and incubated at 25ºC for 150min. A control without the test compound, but with an equivalent amount of methanol, was taken. After 30 min, 1.5ml of incubated solution was removed and diluted with 1.5ml of Griess reagent. Absorbance of

chromosphore formed during diazotization of the nitrite with sulphanilamide and subsequent coupling with NEDD was measured at 546nm and the percentage scavenging activity measured with reference to the standard.

$$\% \text{ inhibition} = \frac{\text{Abs.control-Abs.of test}}{\text{Abs. control}} \times 100$$

Hydrogen peroxide (H_2O_2) Scavenging Activity

All the compounds and the standard are dissolved in methanol and the various concentration of sample ranging from 50-250µgm/ml) was prepared using methanol in different 10ml volumetric flasks. To each solution 2ml hydrogen peroxide (2ml) was added and the volume made 10ml with phosphate buffer saline (PH-7.4). A control solution was prepared with methanolic solution in phosphate buffer saline without hydrogen peroxide solution. The absorbance at 230nm was recorded using a UV-visible spectrophotometer against blank samples. The percentage inhibition of Hydrogen peroxide scavenging activity will be calculated using the following formula,

$$\% \text{ inhibition} = \frac{\text{Abs.control-Abs.of test}}{\text{Abs. control}} \times 100$$

Compounds	50µg/ml	100µg/ml	150µg/ml	200µg/ml	250µg/ml
S_1	55	56	66	72	73
STD	64	68	78	84	89

Compounds	50µg/ml	100µg/ml	150µg/ml	200µg/ml	250µg/ml
S_1	59	63	70	81	86
STD	64	69	77	85	92

CONCLUSION

The compound were subjected to *in-vitro* anti-oxidant activity using ascorbic acid as a standard by two methods i.e. by Hydrogen peroxide scavenging method and nitric oxide radical scavenging method. Antioxidant activity revealed that the synthesized compound have shown significant anti-oxidant activity when compared with that of standard drug.

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