Synthesis of Mannich Side Chain of Pyrazolone Derivatives

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Abstract

Pyrazolone is a heterocyclic compound it has five membered hetetrocyclic system (Wade. 1900);, introduced alkyl amino group improve the lipophilicity and hydrophilicity by introducing alkyl amino group to acyl acetoacetate by Mannich reaction, followed by ring closer with reaction the product with phenyl hydrazine. The results were reported in order to identify product by its solubility and TLC and IR spectra.

تم إدخال مجموعة الكيل امينو علي مركب البايرازولون غير المتجانس خماسي الحلقة لزيادة خاصية ذوبان هذا المركب في الدهون والماء. تم أنجاز التفاعل بإدخال مجموعة لكايل امينو علي اسايل استو استيت ثم قفل الحلقة بتفاعل الناتج مع الفينايل هايدرازين. تم تتبع التفاعل بكروموتوغرافيا الطبقة الرقيقة, الذوبان والأشعة تحت الحمراء.

Introduction:-

The Mannich reaction is an important synthetic pathway in the biosynthesis of alkaloid and many such reactions have been duplicated under the laboratory conditions. Many β -amino alcohols showed pharmacological

activity

A carbon atom adjacent to a carbonyl group is called an alpha carbon and a hydrogen atom bonded to it is called an alpha hydrogen, because carbon and hydrogen have comparable electronegativities, a C-H bond normally has little polarity and a hydrogen atom bonded to carbon shows very low acidity.

The unique chemistry of heterocyclic amine derivative mainly from the presence of ring strain or from aromaticity .Heterocyclic compound with rings containing sp^2 hybridized atom of other elements, can also be aromatic nitrogen ,oxygen and sulpher are the most common hetero atoms in heterocyclic aromatic compounds, It is has a six membered or five membered and fused heterocyclic compound (Joule. and Smith. 1978). Nitrogen can be sp^2 or sp^3 hybridized in heterocyclic, some heterocyclic molecules with ring nitrogen atoms have a very low barriers to one pair donation and are able to flip between begin non aromatic and aromatic depending upon the reaction conditions (Stephen, 1982) .

Aim of project

To Increase hydrophilicity and lipophilicity of pyrazolone moiety by introducing alkyl amino side chain.

Experimental and Materials:

Digital Balance, Beaker, Round Bottom Flask, Glass stirring rod, Cylinder, Volumetric flask, Filter paper, Filter funnel, Dropper, Water bath, Test tubes, Paper chromatography , Capillary tubes, Thermometer.

Formalin, Dimethyl amine, Acetoacetic ester, phenyl hydrazine Hydrochloride, Ethanol, Sodium hydroxide, Hydrochloric Acid, Sodium carbonate, Methanol, Sodium bicarbonate, Chloroform, Distilled water.

Procedure:

Formalin (0.033 mol) was added drop wise to a solution of dimethyl amine (0.052 mole) and ethyl actoacetate (0.037 mol) at O ^{o}C. The mixture was stirred at room temperature for 4 hr. The residue was treated with ethanol and Hydrochloric a cid to give product after equal volume by sodium hydroxide.

The above product (0.02 mol) was mixed with phenyl hydrazine chloride (0.02 mol) and sodium carbonate (0.1 g) and then methanol (4ml) was added in around bottom flask, the mixture was heated on a boiling water bath for one hour and stirred from time to time with a glass rod. It has give heavy reddish syrup, after that allowed to cool and evaporated the solvent and gave the final product the Pyrazolone derivative.

Results

no	Structure	Chemical name	Formula	Molecular weight
1	CH_2O	Formalin	CH_2O	30
2	$(CH_3)_2NH$	Dimethyl amine	C_2H_7N	45

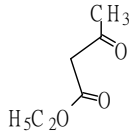
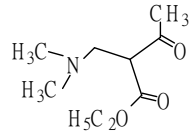
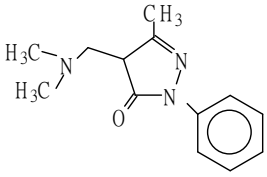
3		Ethylacetoacetate	$C_6H_{10}O_3$	130
4		α -Dimethlaminoethylacetoacetate	$C_6H_{17}NO_3$	187
5		Phenylhydrazine hydrochloride	$C_6H_8N_2HCl$	192.5
6		3- Dimethylamino,4- methyl,1- phenyl-2-pyrazolne	$C_{13}H_{17}NO$	231

Table2 − Solubility of intermediates and final product

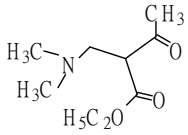
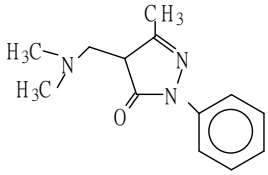
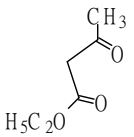
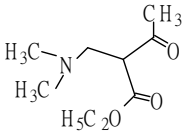
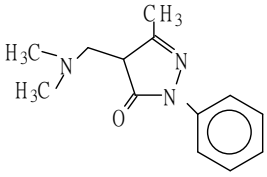
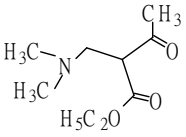
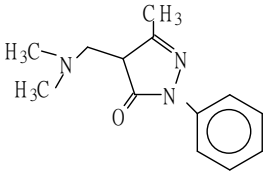
no	**Structure**	**Chemical name**	H_2O	$NaHCO_3$	HCl	NaOH
4		α-Dimethlaminoethylacetoacetate	-	-	+	−
6		3-Dimethylamino,4-methyl,1-phenyl-2-pyrazolne	+	+	-	+

Table2 - R_f value of intermediates and final product

no	**Structure**	**Chemical name**	**R_f value (Chloroform)**

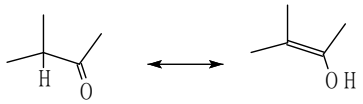
3		Ethylacetoacetate	0.33
4		α -Dimethlaminoethylacetoacetate	0.47
5		Phenyl hydrazine hydrochloride	0.37
6		3- Dimethylamino,4- methyl,1-phenyl-2 -pyrazolne	0.83

	Structure	C = N Str . vib	C – H Ar. Str . vib	C – C	C = O Ester	C –H Str. Vib
4		-	-	-	1622 cm^{-1}	2926 cm^{-1}
6		1590 cm^{-1}	3003 cm^{-1}	1497 cm^{-1}	-	3208 cm^{-1}

Discussion

The intermediate product (**4**) was not dissolved in sodium hydroxide and sodium bicarbonate but soluble in hydrochloric acid due to basicity of product

which contain lone pair of electron on nitrogen. The pyrazolone derivative (**6**) soluble in sodium hydroxide, insoluble in sodium bicarbonate this may be due to enol form of the keto group which illustrated in figure below



Also the pyrazolone derivative (**6**) dissolve in hydrochloric acid due to basicity. This observation of solubility indicate that the reaction go forwarded to the final product (**6**).

Thin layer chromatography it's one of chromatography methods to know the new product which gives a new R_f values different from reactants this indicate that the reaction achieved to the final product (**6**).

Infrared is very important spectroscopic tools in structure elucidation there for the pyrazolone derivative (**6**) gave different groups in their structure. The absorption band caused by the presence of C=N group which can be clearly identified in region 1590 cm^{-1}. Also the pyrazalone pyrazolone derivative (**6**) gave absorption band in region 3003 cm^{-1} due to C –H aromatic str. vib.

References:

1- Stephen. A. I, (1982); Amines "Synthesis" Preparation and Application; five edition; p 92-19.

2- Joule. J, A. and Smith. G. F., 1978., Heterocyclic Chemistry, Second edition, p 24-31, 184-219.

3- Volk. R., (1700)., Essentials of Medical Microbiology; four edition ; p 41-

77.

4- Briet. A., (1800) ;. Holum. J. R., Organic chemistry course. Five edition.

6- Wade. L.G (1900); Organic chemistry.; sixth edition; page: 723-726