A TYPICAL PROCEDURE FOR SYNTHESIS OF 3-HYDROXY-5(2H)-ISOXAZOLONE DERIVATIVES FROM MESOIONIC HETEROCYCLES AND REACTS WITH NUCLEOPHILES GIVING SOME NEW COMPOUNDS.

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Abstract: In the general class of five-membered mesoionic ring systems one of the most interesting and syntheticaly useful properties and their ability to undergo 1,3- dipolar cycloaddition reaction and development of new method for synthesis of 3-hydroxy- 5(2H)-isoxazolone derivatives is of extreme important in the organic chemistry, therefore our recent investigation shows a developed method for synthesis of 3-hydroxy- 5(2H)-isoxazolone derivatives from five-membered mesoionic ring systems, in excellent yield.

Keywords: 5(2H)-isoxazolone, mesoionic heterocycles, (chlorocarbonyl)phenyl ketene.

INTRODUCTION

The development of new methods for the synthesis of five-membered ring containing nitrogen heterocycles as we know is important in the organic compounds.Hydroxy-5(2H)-isoxazolone derivatives are a class of important compounds besides they are utilized as a synthon to synthesis of imidazoles[1], indols[2], quinolines[3].As well this class of heterocycles also have applied in analytical chemistry for liquid-liquid extraction of lanthanids[4], iron(III)and titanium[5], etc. .That is why much attention has paid to study the scope of these important reactions.

RESULTS AND DISCUSSION

As a part of ongoing interest in the study and synthesis of the isoxazolone promoted us to undertake the synthesis of some new 3-hydroxy-5(2H)-isoxazolone derivatives starting with an approporiate oxime and (chlorocarbonyl)phenyl ketene.
As we know the (chlorocarbonyl)phenyl ketene is a stable ketene and reacts with some oximes such as oxime of benzaldehyde, *p*-chlorobenzaldehyde, 2,4-dichlorobenzaldeyde, *p*-N,N-dimethyl benzaldehyde and *p*-methoxy benzaldehyde.All these reactions are going to produce mesoionic five-membered heterocycles through a zwitter ions as an intermediate[6](scheme 1) .
These zwitter ionic systems are stable because the positive and negative charges are delocalized within the π-electron system.
It seems nucleophiles such as benzylamine attack to iminum carbon and produce N-derivatives of 4-phenyl-3-hydroxy-5(2H)-isoxazolone(a-e)(scheme 2) .The structures of new compounds are confirmed by their IR, ^{1}H-NMR, ^{13}C-NMR and MASS spectrums.

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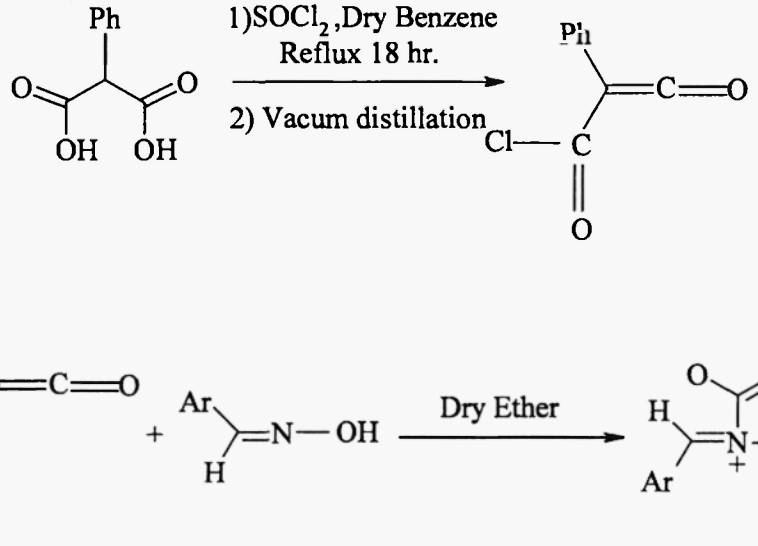
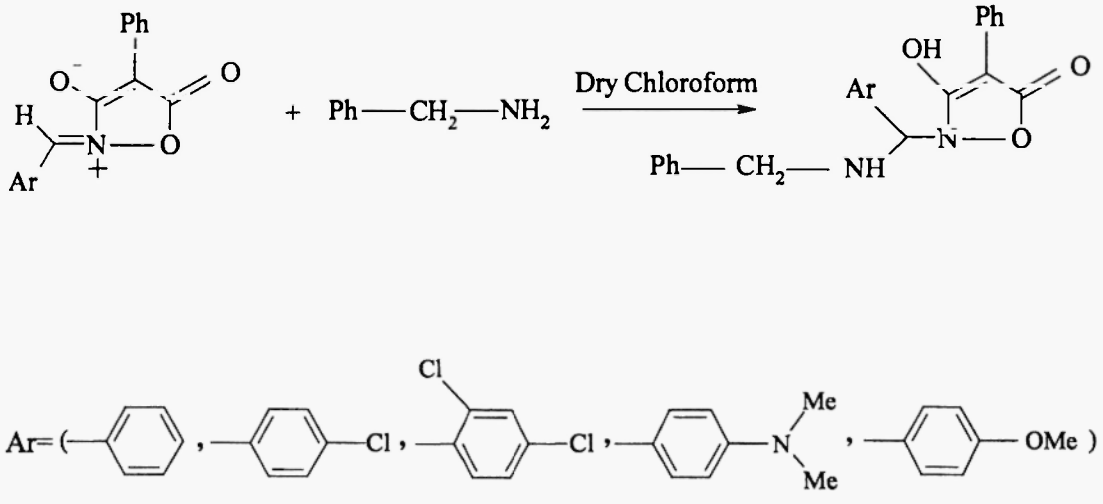
The results of the reactions along with the characterization data are summerised in tables 1-3.



Scheme 1



Scheme 2

Table 1. Physical and Yield data for all compounds(a-e)

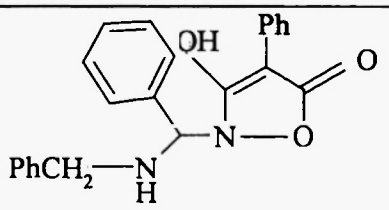
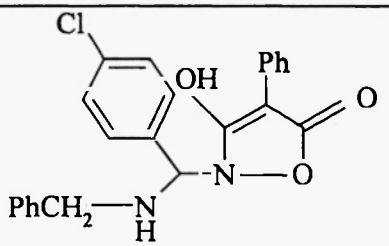
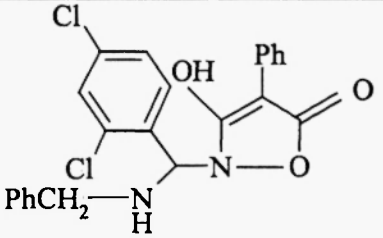
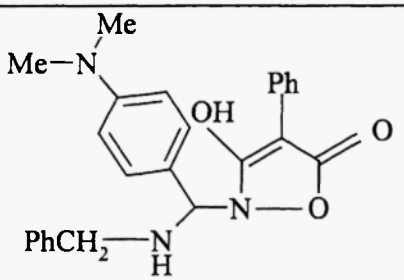
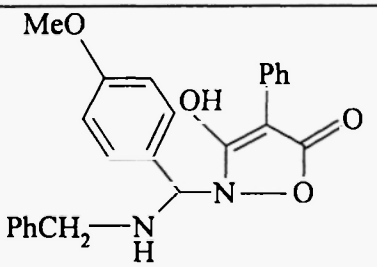
Sr.No.	Products	Compounds	Melting Points°C	Yield(%)
1	a		146-148 °C decomposed	%85
2	b		140-141 °C decomposed	%80
3	c		135-138 °C decomposed	%78
4	d		129-131 °C decomposed	%89
5	e		138-140 °C decomposed	%82

Table-2: Analytical Data of Comounds(a-e)

Sr. No.	Products	Molecular Formula	Analysis(%) Calcd.(found) C H N	Mass Spectrum (m/z)
1	a	$C_{23}H_{20}N_2O_3$	74.19 5.37 7.52 (74.33 5.48 7.64)	372(11%,M^+), 194(90%) , 107(83%) ,91(100%)
2	b	$C_{23}H_{19}ClN_2O_3$	67.89 4.67 6.88 (67.98 4.49 6.71)	408(4%,$(M+2)^+$),406(12%,M^+) 107(80%),91(100%)
3	c	$C_{23}H_{18}Cl_2N_2O_3$	62.58 4.08 6.35 (62.42 4.13 6.51)	444(3%,$(M+4)^+$),442(6%,$(M+2)^+$) 440(12%,M^+),107(62%),91(100%)
4	d	$C_{25}H_{25}N_3O_3$	72.29 6.02 10.12 (72.41 6.12 10.31)	415(8%,M^+),107(90%),91(100%)
5	e	$C_{24}H_{22}N_2O_4$	71.64 5.47 6.97 (71.45 5.63 7.12)	402(5%,M^+),225(70%),135(80%), 91(100%)

EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected.Mass spectra were obtained on a Shimadzu QP 1100 EX mass spectrometer and IR spectra were obtained on a Matson 1000 FT-IR Spectrophotometer. Nuclear magnetic resonance spectra were obtained on a Bruker DRX-500 Avance spectrometer using tetramethylsilane as an internal standard.(chlorocarbonyl)phenyl ketene was prepared by a procedure similar to that of S. Nakanishi[7] method.

General procedure for the mesoionic five-membered systems[8]

A 0.4 mmol of oxime was added to a solution of 0.4 mmol of (chlorocarbonyl) phenyl ketene in 40 ml of dry diethylether at 0 °C under a nitrogen atmosphere. Then a crude mass product was instantly formed. The reaction mixture were filtered and the products were recrystalized from benzene.

Table-3: NMR Spectral Data of Compounds (a-e)

Sr.No.	Products	IR(KBr)cm^{-1}	^{1}H-NMR(δ.ppm)(DMSO)	^{13}C-NMR(δ,ppm)(DMSO)
1	a	1691(C=O), 2741-3031(OH), 3331(NH),	4.05(s,2H), 6.83(s,1H),7.12-8.19(m,15H),9.12(m,2H)	42.8,70.7,76.7,121.5-136.9,171.6,174.7
2	b	1706(C=O), 2692-3156 (OH), 3347(NH)	4.05(s,2H), 6.83(s,1H),7.13-8.21(m,14H),9.09(m,2H)	42.8,70.6,75.7,122.7-135.5,173.5,174.8
3	c	1706(C=O), 2712-3055 (OH), 3347(NH)	4.06(s,2H), 6.81(s,1H),7.09-8.31(m,13H),9.37(m,2H)	42.8,76.2,79.6,121.5-136.8,171.3,173.9
4	d	1716(C=O), 2710-3112 (OH), 3355(NH)	3.39(s,6H),4.02(s,2H), 6.82(s,1H), 7.13-8.47(m,14H),9.19(m,2H)	42.5,70.9,75.8,121.4-137.1,173.6,178.1
5	e	1691(C=O), 2706-3120(OH), 3379(NH)	3.71(s,3H),4.06(s,2H), 6.83(s,1H),7.07-8.24(m,14H), 9.12(m,2H)	42.8,55.3,75.8, 76.9,121.6-136.8,173.6,174.9

2-[(Benzylamino)(phenyl)methyl]-3-hydroxy-4-phenyl-5(2H)-isoxazolone : (a)

To a solution of 0.1 mmol (0.26gr) 5-oxo-4-phenyl-2-[1-phenylmethylidene]-isoxazol-2-ium-3(5H)-olate in 40 ml of dry chloroform was added dropwise 0.1 mmol (0.11gr) benzylamine at room temprature.The mixture was stirred for 20 min., then 50 ml of cooled n-hexan was added to the reaction mixture.A white precipitate was formed ,then filtered and washed with dry chloroform. The residue was recrystalized from chloroform-n –hexan (1:1) giving a white crystals.

2-[(Benzylamino)(4-chlorophenyl)methyl]-3-hydroxy-4-phenyl-5(2H)-isoxazolone: (b)

To a solution of 0.1 mmol (0.30gr) 2-[1-(4-chlorophenyl)methylidene]-5-oxo-4-phenylisoxazol-2-ium-3(5H)-olate in 40 ml of dry chloroform was added dropwise 0.1 mmol (0.11gr) benzylamine at room temprature. . The mixture was stirred for 15 min.,

then 40 ml of cooled n-hexan was added to the reaction mixture, till a white precipitate was formed, the product was filtered and washed with dry chloroform.The residue was recrystalized from n-hexan –chloroform (2:1) giving a white crystals.

2-[(Benzylamino)(2,4-di chlorophenyl)methyl]-3- hydroxy-4-phenyl-5(2H)-isoxazolone: (c)

To a solution of 0.1 mmol (0.34gr) 2-[1-(2,4-dichlorophenyl)methylidene]-5-oxo-4-phenylisoxazol-2-ium-3(5H)-olate in 40 ml of dry chloroform was added dropwise 0.1 mmol (0.11gr) benzylamine at room temprature . The mixture was stirred for 25 min., then 30 ml of cooled n-hexan was added to the reaction mixture. A white precipitate was formed, then filtered and washed with dry chloroform.The residue was recrystalized from n-hexan-chloroform (2:1) giving a white crystals.

2-{(Benzylamino)[4-dimethylamino)phenyl]methyl}-3-hydroxy-4-phenyl -5(2H)-isoxazolone: (d)

To a solution of 0.1 mmol (0.31gr) 2-{1-[4-(dimethylamino)phenyl]methylidene}-5- oxo-4-phenylisoxazol-2-ium-3(5H)-olate in 40 ml of dry chloroform was added dropwise 0.1 mmol (0.11gr) benzylamine at room temprature. The mixture was stirred for 10 min., then 30 ml of cooled n-hexan was added to the reaction mixture. When a white precipitate was formed, the product was filtered and washed with dry chloroform.The resulting solid was recrystalized from n-hexan-chloroform (3:1) giving a white crystals.

2-[(Benzylamino)(4-methoxyphenyl)methyl]-3-hydroxy-4-phenyl-5(2H)-isoxazolone: (e)

To a solution of 0.1 mmol (0.30gr) 2-[1-(4-methoxyphenyl)methylidene]-5-oxo-4-phenylisoxazol-2-ium-3(5H)-olate in 40 ml of dry chloroform was added dropwise 0.1 mmol (0.11gr) benzylamine at room tempature. The mixture was stirred for 10 min.,then 40 ml of cooled n-hexan was added to reaction mixture. A white precipitate was formed, ,then filtered and washed with dry chloroform.The residue was recrystalized from n-hexan-chloroform (3:1) giving white crystals.

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