Research Journal of Chemical Sciences ISSN 2231-606X
Vol. **4(12),** 42-47, December **(2014)** *Res. J. Chem. Sci.*

Microwave Induced Synthesis of New Fused Oxazole

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Available online at: www.isca.in, www.isca.me
Received 15th November 2014, revised 8th December 2014, accepted 15th Decmeber 2014

Abstract

An easy, efficient and novel method for the synthesis of 7-(substituted phenyl)-2-thiophene-2-yl-7H-oxazolo[3,2-a]pyridine-5-ol (4) and 7-(substituted phenyl)-2-pheneyl-7H-oxazolo[3,2-a]pyridine-5-ol ***(5)****. Representative samples were screened for their anti-microbial activity against Gram- positive bacteria, Gram-negative bacteria, fungi and yeast by using disc diffusion method. All the physico- chemical tests as well as spectral technique are used for confirmation of structure of targeted molecule.*

Keywords: α-Bromoacetothiophenone, α-Bromoacetophenone, Fused Oxazoles and Green method.

Introduction

The study of heterocyclic chemistry and compound play very important role in organic field[1]. Substituted oxazole derivatives synthesis is particularly important because of compounds involving the oxazole ring system are known to have diverse range of biological activities in pharmaceutical areas[2]. Oxazoles are continued to be of interest for both their biological activities and synthetic utility[3-6]. The synthesis of aryl-oxazoles is also the subject of on-going improvements[7-8]. It is worth mentioning that a combination of a heterocycles moiety fused with a piperidine ring may increase their biological activities or create new medicinal properties due to the different electronic distribution[9-10]. Oxazole derivatives apply as pesticides, fluorescent whitening agents, lubricants, dyes and pigments[11-13].

Microwave-induced eco-friendly synthesis of organic compound has become a new facilitated area in synthesizing organic molecule. Chemical reactions which are conducted under the microwave irradiation have many advantages as compared to the conventional method involving very high temperature[14].

Material and Methods

Experimental: Physical constant of all synthesized compounds were determined in open capillary tubes on an electro thermal digital apparatus. The conversion of starting material checked by using thin layer chromatography on silica gel coated aluminum plates (Merck) as adsorbent and UV chamber as visualizing agent. ^{1}H and ^{13}CNMR spectra were recorded on Varian 600 MHz NMR spectrophotometer using DMSO-d_6 as solvent and TMS as reference (chemical shifts in δ ppm). C, H, N analysis was recorded on Carlo Erba 1108 (CHN) Elemental Analyzer.

Representative procedure for synthesis of (4a): A mixture of 4-phenyl-pyperidine—4,6-dione(0.01 mol), K_2CO_3 (0.02 mol), α-Bromoacetothiophenone (2) (0.01 mol) and DMF (0.025 mol), was irradiated in micro-wave. The conversion of starting material checked on TLC. Upon completion, the reaction mass was quenched into ice-cold water. The solid thus generated, was filtered, washed and recrystallised from ethanol to get 7-phenyl-2-thiophene-2-yl-7H-oxazolo[3,2-a]pyridine-5-ol (4a).

Representative procedure for synthesis of (5a): A mixture of 4-phenyl-pyperidine—4,6-dione(0.01 mol), K_2CO_3 (0.02 mol), α-Bromoacetophenone (3) (0.01 mol) and DMF (0.025 mol), was irradiated in micro-wave. The conversion of starting material checked on TLC. Upon completion, the reaction mass was quenched into ice-cold water. The solid thus generated, was filtered, washed and recrystallised from ethanol to get 2,7-diphenyl-7H-oxazolo[3,2-a]pyridine-5-ol (5a).

Spectral Interpretation: 7-(4-Methoxy phenyl)-2-thiophene-2-yl-7H-oxazolo[3,2-a]pyridine-5-ol (4c) Yield: 78%; m.p. =130-132°C: IR (cm-1): 3200 (OH), 1100 (C-O), ^{1}H NMR (DMSO-d6, δ/ ppm): 3.79 (s, 3H, OCH_3), 4.7 (t, 1H, CH), 5.2 (s, 1H,= CH), 5.32 (s, 1H,= CH), 5.5 (s, 1H,= CH), 6.80-8.20 (m, 7H, Ar -H), 10.90 (s, 1H, OH), ^{13}C NMR (DMSO-d6, δ/ ppm): 30 (CH), 56.14 (OCH_3), 74 (=CH), 75.14 (=CH), 115.5-148.0 (Ar-C and C=C), 158.41 (=C-OH). LCMS; m/z: 325; Analytical calculation for $C_{18}H_{15}NO_3$: C, 66.46; H, 4.61; N, 4.53; S, 10.35% Found C, 66.51; H, 4.42; N, 4.23; S, 10.15%.

7- (4-Hydroxy-3-methoxy phenyl) -2-thiophene-2-yl -7H-oxazolo [3,2-a]pyridine-5-ol (4e): Yield: 85%; m.p. =145-148°C: IR (cm-1): 3200 (OH), 1100 (C-O), ^{1}H NMR (DMSO-d6, δ/ ppm): 3.76 (s, 3H, OCH_3), 4.71 (t, 1H, CH), 5.2 (s, 1H,= CH), 5.32 (s, 1H,= CH), 5.6 (s, 1H,= CH), 5.3 (s, 1H, CH), 5.6 (s, 1H, OH), 6.80-8.20 (m, 7H, Ar -H), 8.90 (s, 1H, OH), ^{13}C NMR (DMSO-d6, δ/ ppm): 31 (-CH), 56.14 (OCH_3), 75.0 (=CH), 76.15 (=CH), 115.5- 148.0 (Ar-C and C=C), 157.40 (=C-OH). LCMS; m/z: 341; Analytical calculation for $_{18}H_{15}NO_4S$: C, 63.34; H, 4.39; N, 4.10 % Found C, 63.52; H, 4.42; N, 4.03%.

7-(4-Methoxy phenyl)-2-phenyl-7H-oxazolo[3,2-a]pyridine-5-ol (5c): Yield: 80%; m.p. =166°C: IR (cm-1): 3200 (OH), 1100 (C-O), ^{1}H NMR (DMSO-d6, δ/ ppm): 3.76 (s, 3H, OCH_3), 4.72 (t, 1H, CH), 5.20 (s, 1H,= CH), 5.30 (s, 1H,= CH), 5.4 (s, 1H, CH), 6.80-7.3.20 (m, 9H, Ar -H), 9.95 (s, 1H, OH), ^{13}C NMR (DMSO-d6, δ/ ppm): 34 (-CH), 32 (=CH), 56.14 (OCH_3), 77.0 (=CH), 78.20 (=CH), 115.5- 148.0 (Ar-C and C=C), 157.40 (=C-OH). LCMS; m/z: 319; Analytical calculation
for $C_{20}H_{17}N0_3$: C, 75.23; H, 5.32; N, 4.38 % Found C, 75.33; H, 5.28; N, 4.47 %.

7-(4-Hydroxy phenyl)-2-phenyl-7H-oxazolo[3,2-a]pyridine-5-ol (5d): Yield: 70%; m.p. =126-127°C: IR (cm-1): 3200 (OH), 1100 (C-O), ^{1}H NMR (DMSO-d6, δ/ ppm): 4.7 (t, 1H, CH), 5.0 (s, 1H, OH), 5.15 (s, 1H,= CH), 5.30 (s, 1H,= CH), 5.4 (s, 1H, CH), 6.80-7.3.20 (m, 9H, Ar -H), 9.95 (s, 1H, OH)^{13}C NMR (DMSO-d6, δ/ ppm): 33 (-CH), 75.0 (=CH), 76.15 (=CH), 115.5- 148.0 (Ar-C and C=C), 157.40 (=C-OH). LCMS; m/z: 35; Analytical calculation for $C_{19}H_{17}N0_3$: C, 74.75; H, 5.59; N, 4.59 % Found C, 74.33; H, 5.38; N, 4.45 %.

Antibacterial and antifungal activities: All the newly synthesized fused oxazoles were evaluated for their antibacterial activity against Gram-negative bacteria, Gram-positive bacteria, fungi and yeast using disc diffusion method. The zone of inhibition was measured in mm and the activity was compared with standard drug. The data is given in table-2.

The sensitivity of micro-organisms to the tested compounds is identified in the following manner*; Highly active =Zone of Inhibition: 15-20 mm, Moderately active = Zone of inhibition: 10-15 mm, Slightly active = Zone of inhibition: 5-10 mm, No activity = Zone of inhibition: 0 mm, * Each result represents the average of triplicate readings.

Result and Discussion

In our present work we have carried out an efficient synthesis of fused oxazole using microwave in excellent yield. Clean reaction profile and good purity of the obtained product in some of the advantages associated with our protocol. The results are summarized in table-1 and table-2. The entire synthesized product were characterized by ^{1}HNMR ^{13}CNMR, IR, MS and elemental analysis and further, the compound were screened for anti-bacterial activities.

Table-1
Characterization data of representative compounds 4 and 5

Compounds	R	Mol. Formula	m.p. °C	%Yields	Time (seconds)	Color
4a	H	$C_{17}H_{13}N0_2S$	95	80	120	Light Brown
4b	4-Cl	$C_{17}H_{12}N0_2SCl$	152	82	110	Brown
4c	4-OCH_3	$C_{18}H_{15}N0_3S$	130-132	78	90	Dark Green
4d	4-OH	$C_{17}H_{12}N0_3S$	176	75	100	Light Brown
4e	3-OCH_3, 4-OH	$C_{18}H_{15}N0_4S$	145-148	85	120	Brown
5a	H	$C_{19}H_{15}N0_3$	109-111	73	120	Light Green
5b	4-Cl	$C_{19}H_{14}N0_2Cl$	176-178	75	100	Light Brown
5c	4-OCH_3	$C_{20}H_{17}N0_4$	166	80	90	Dark Brown
5d	4-OH	$C_{19}H_{15}N0_3$	126-127	70	80	Buff
5e	3-OCH_3, 4-OH	$C_{20}H_{17}N0_4$	196	77	110	Brown

Table-2
Antibacterialal activities of some representative compounds

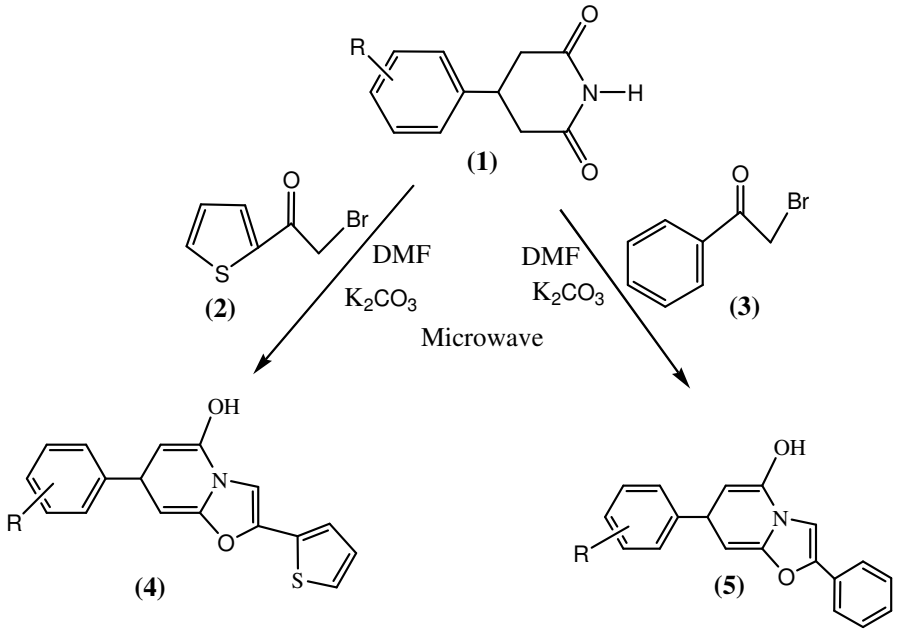
Compounds	Zone of Inhibition (mm)						
	Gram-negative		Gram-positive		Fungi		Yeast
	E.coli	*P.Putide*	*B.Subtilis*	*S.lactis*	*A.niger*	*P.Sp.*	*C.Albicans*
4b	16	15	17	19	16	17	9
4c	17	16	19	20	18	10	10
4d	18	19	18	18	19	10	9
4e	19	18	17	19	20	9	9
5b	17	15	17	21	17	10	10
5c	16	17	17	21	19	10	9
5d	15	14	18	19	18	11	9
5e	19	18	20	20	19	10	9
DMSO	0	0	0	0	0	0	0
Ampicilin®	22	21	20	22	23	15	15

Conclusion

In conclusion, we have developed a rapid and efficient method for the synthesis of fused oxazoles with excellent yields. The main advantage of this method is that reactions were found to clean and has operational simplicity. Since, column chromatography was not required to get the pure products, hence makes more attractive for chemist.

Acknowledgement

We are thankful to the Management of Guru Nanak College, G.T.B. Nagar, Mumbai for continuous support and respective facilities. We are also thankful to, The Director, TIFR Mumbai for providing spectral data.



Scheme-1

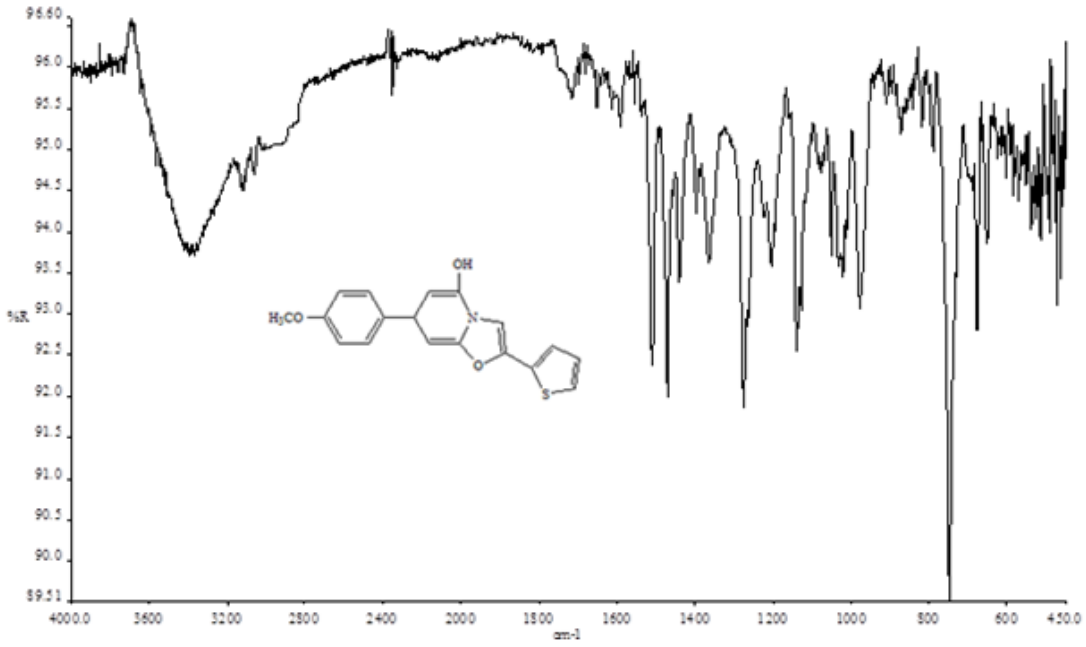


Figure-1
IR

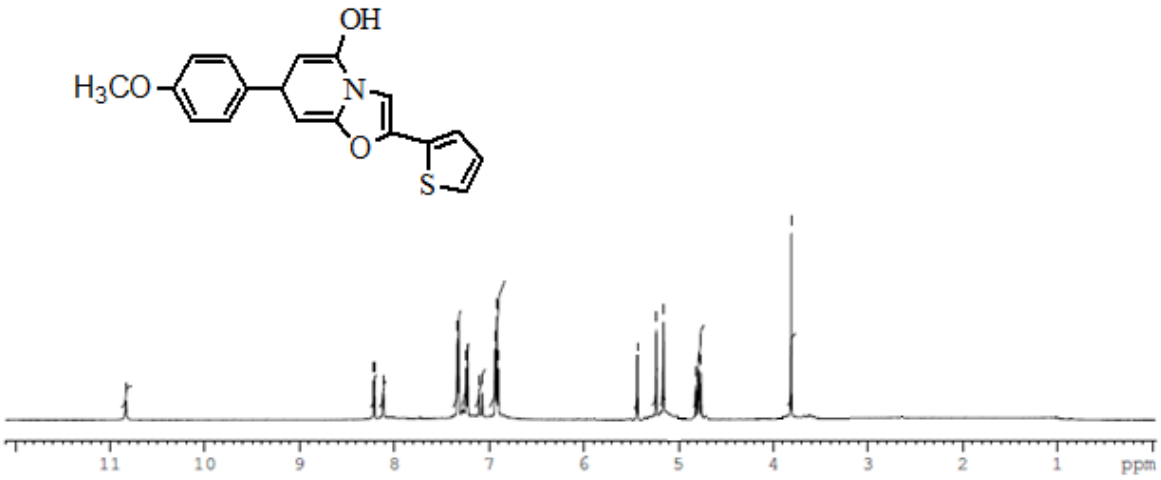


Figure-2
H1 NMR

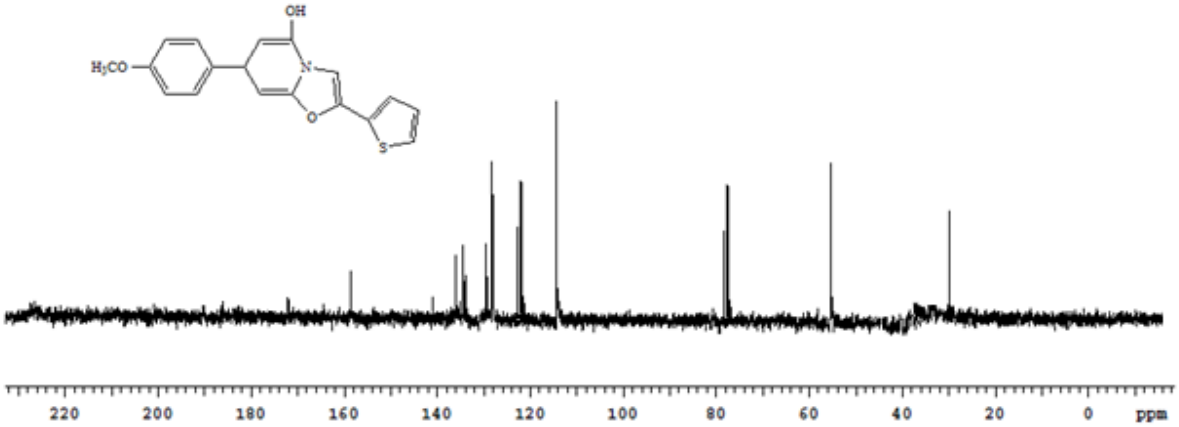


Figure-3
C13 NMR

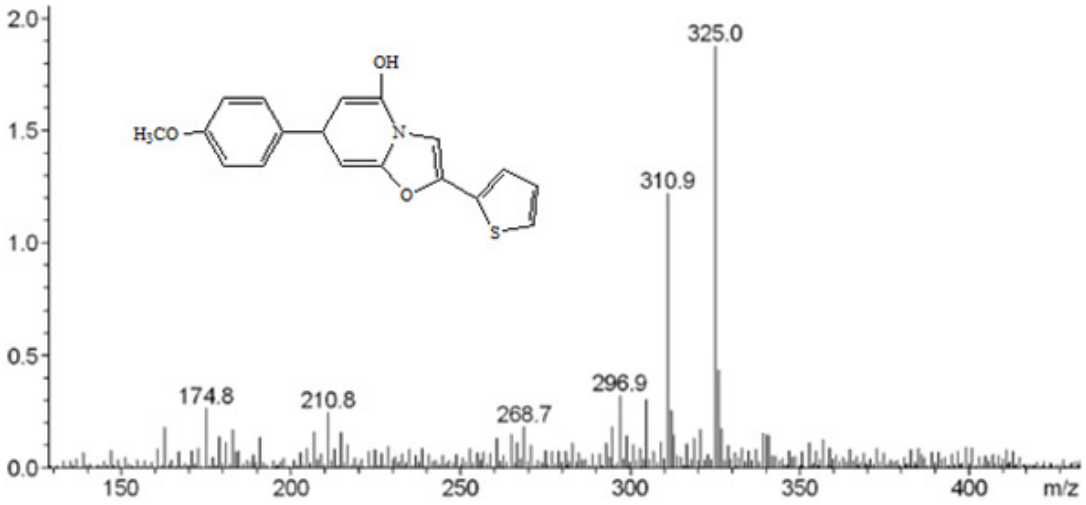


Figure-4
Mass

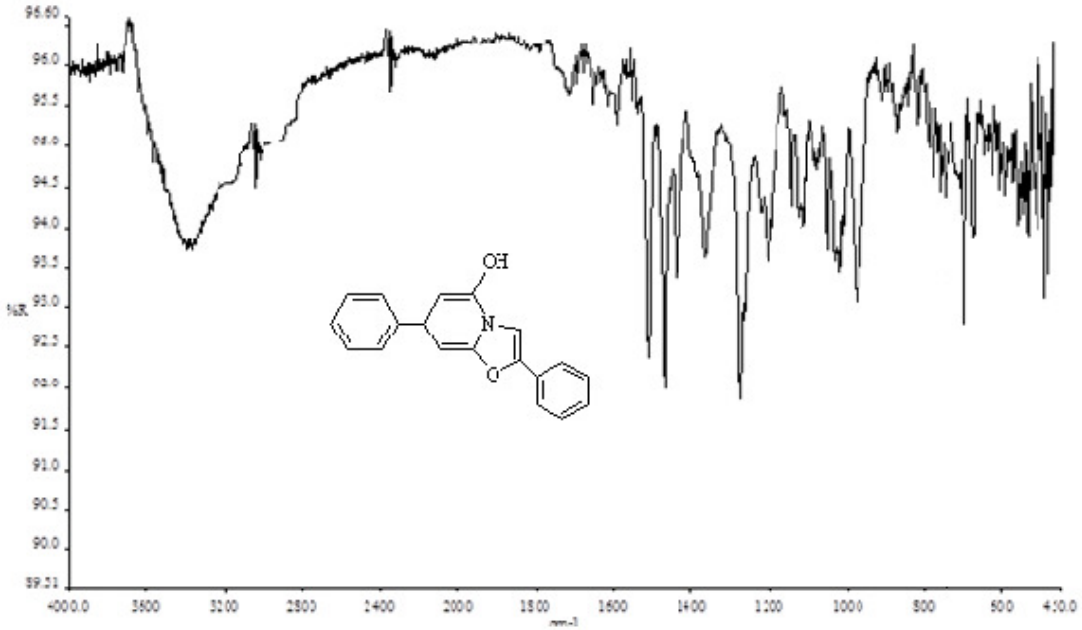


Figure-5
IR

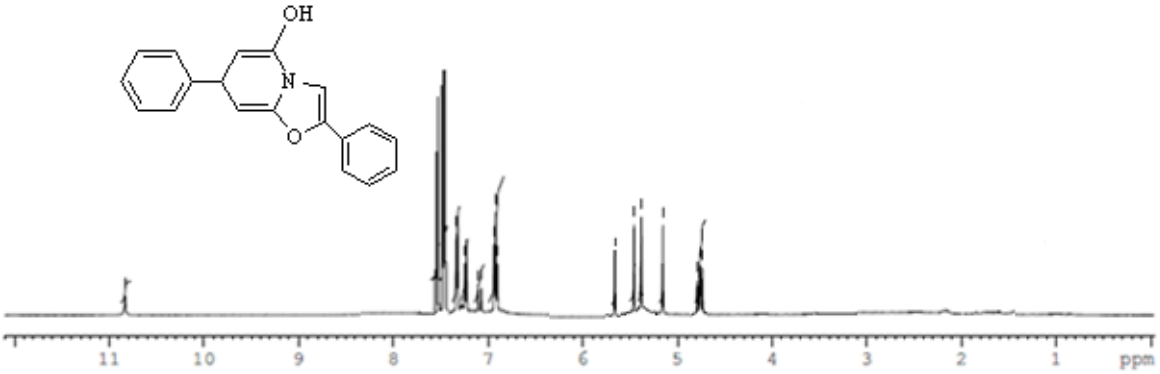


Figure-6
PMR

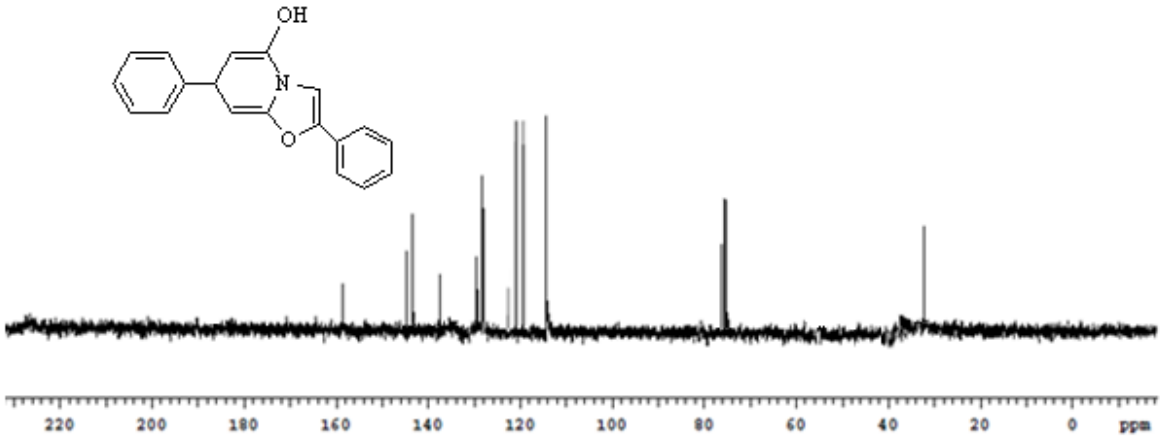


Figure-7
C13 NMR

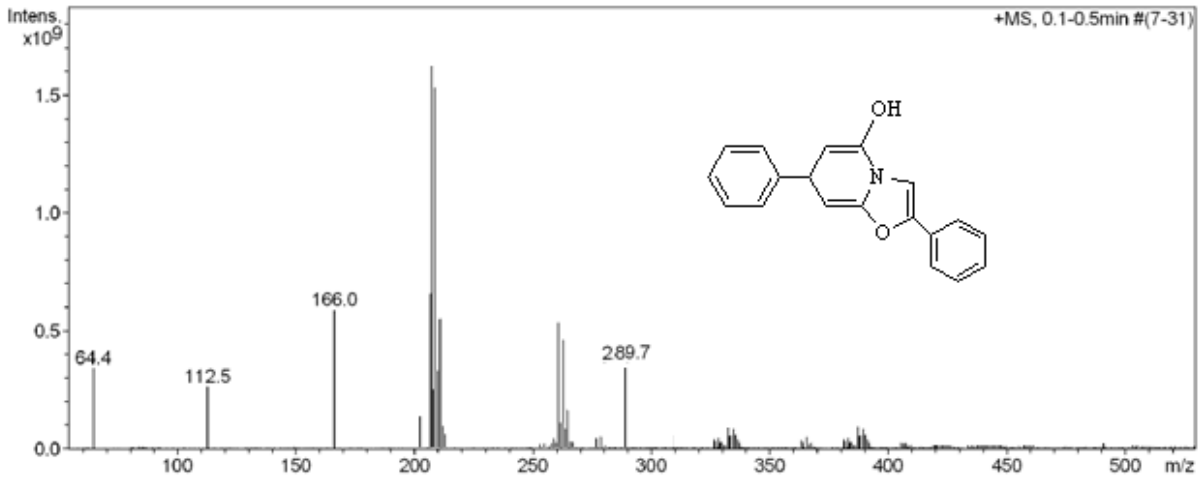


Figure-8
Mass

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